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Standards of Care in Diabetes—2026



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Standards of Care in Diabetes—2026



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Diabetes Care

THE JOURNAL OF CLINICAL AND APPLIED RESEARCH AND EDUCATION

January 2026 Volume 49, Supplement 1

[T]he simple word *Care* may suffice to express [the journal's] philosophical mission. The new journal is designed to promote better patient care by serving the expanded needs of all health professionals committed to the care of patients with diabetes. As such, the American Diabetes Association views *Diabetes Care* as a reaffirmation of Francis Weld Peabody's contention that "the secret of the care of the patient is in caring for the patient."

—Norbert Freinkel, *Diabetes Care*, January-February 1978

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This issue is freely accessible online at https://diabetesjournals.org/care/issue/49/Supplement_1.

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Introduction and Methodology: Standards of Care in Diabetes—2026

American Diabetes Association Professional Practice Committee for Diabetes*

Diabetes Care 2026;49(Suppl. 1):S1–S5 | <https://doi.org/10.2337/dc26-SINT>

Diabetes is a complex, chronic condition requiring continuous care with comprehensive risk-reduction strategies beyond glycemic management. Ongoing diabetes self-management education and support are critical to empowering people, preventing acute complications, and reducing the risk of long-term complications. Significant evidence exists that supports a range of interventions to improve diabetes outcomes.

The American Diabetes Association (ADA) “Standards of Care in Diabetes,” referred to here as the Standards of Care, serves as a comprehensive resource to clinicians, researchers, policymakers, and other stakeholders. It outlines key elements of diabetes care, sets treatment goals, and provides tools to assess care quality, all directed at improving diabetes care and outcomes across diverse populations.

The ADA Professional Practice Committee for Diabetes (PPC) updates the Standards of Care annually. Discussion of emerging clinical considerations is included in the text, and, as evidence evolves, clinical guidance is updated within the recommendations. The Standards of Care is a “living” document where important updates are published online should the PPC determine that new evidence or regulatory changes (e.g., medication or technology approvals, label changes) merit immediate inclusion. More information on the living standards can be found on the

ADA professional website Diabetes Pro at professional.diabetes.org/standards-of-care/living-standards-update. The Standards of Care supersedes all previously published ADA scientific documents—and the guidance therein—on clinical topics within the purview of the Standards of Care.

The Standards of Care is internally reviewed by the ADA Medical Affairs scientific team for methodological rigor, accuracy, clarity, and implementation; the Standards of Care then undergoes external peer review, ADA leadership review, and ADA Board of Directors review and approval.

SCOPE OF THE GUIDELINES

The recommendations in the Standards of Care include screening, diagnostic, and therapeutic actions that are scientifically proved or known based on expert clinical practice or believed to favorably affect health outcomes of people with diabetes. They also cover the prevention, screening, diagnosis, and management of diabetes-associated complications and comorbidities. The recommendations encompass care throughout the life span for children (aged birth to 11 years), adolescents (aged 12–17 years), adults (aged 18–64 years), and older adults (aged ≥65 years). The recommendations cover the management of type 1 diabetes, type 2 diabetes, gestational diabetes mellitus,

and other types of diabetes and/or hyperglycemic conditions.

The Standards of Care does not provide comprehensive treatment plans for complications associated with diabetes, such as diabetic retinopathy or diabetic foot ulcers, but offers guidance on how and when to screen for diabetes complications, management of complications in the primary care and diabetes care settings, and referral to specialists as appropriate. Similarly, regarding the psychosocial and behavioral health factors often associated with diabetes and that can affect diabetes care, the Standards of Care provides guidance on how and when to screen, management in the primary care and diabetes care settings, and referral but does not provide comprehensive management plans for conditions that require specialized care, such as mental illness.

INTENDED AUDIENCE

The intended audience for the Standards of Care includes primary care physicians, endocrinologists, nurse practitioners, physician associates/assistants, pharmacists, registered dietitian nutritionists, diabetes care and education specialists, and all members of the diabetes care team. The Standards of Care also provides guidance to specialists caring for people with diabetes and its multitude of complications, such as cardiologists, gastroenterologists,

The “Standards of Care in Diabetes,” formerly called “Standards of Medical Care in Diabetes,” was originally approved in 1988 and published in 1989. The most recent full review and revision was in December 2025.

*A complete list of members of the American Diabetes Association Professional Practice Committee for Diabetes is provided in this section.

Duality of interest information for each contributor is available at <https://doi.org/10.2337/dc26-SDIS>.

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nephrologists, emergency physicians, internists, pediatricians, psychologists, neurologists, ophthalmologists, and podiatrists. Additionally, these recommendations help payors, policymakers, researchers, research funding organizations, and advocacy groups align their policies and resources and deliver optimal care for people living with diabetes. A consumer-facing plain language summary of the Standards of Care for people with diabetes can be found at diabetesjournals.org/clinical/article/43/3/335/160650/Your-Rights-and-Care-Standards-A-Guide-for-People.

The ADA strives to improve and update the Standards of Care to ensure that clinicians, health plans, and policymakers can continue to rely on it as the most authoritative source for current guidelines for diabetes care. The Standards of Care recommendations are not intended to preclude clinical judgment. They must be applied in the setting and context of excellent clinical care, with adjustments for individual preferences, comorbidities, and other person-specific factors. For more detailed information about the management of diabetes, please refer to *Medical Management of Type 1 Diabetes* (1) and *Medical Management of Type 2 Diabetes* (2).

METHODOLOGY AND PROCEDURE

The Standards of Care includes discussion of evidence and clinical practice recommendations intended to optimize care for people with diabetes by assisting health care professionals and individuals in making shared decisions about diabetes care. These recommendations are based on a comprehensive evaluation of the available evidence, along with a careful assessment of the benefits and risks associated with different care strategies.

Professional Practice Committee for Diabetes

The diabetes PPC of the ADA is responsible for the Standards of Care content. The PPC is an interprofessional expert committee comprising physicians, nurse practitioners, pharmacists, diabetes care and education specialists, registered dietitian nutritionists, behavioral health scientists, and others who have expertise in a range of areas including but not limited to adult and pediatric endocrinology, epidemiology, public health, behavioral health, cardiovascular risk management, microvascular complications, nephrology, neurology, ophthalmology, podiatry, clinical pharmacology,

preconception and pregnancy care, weight management and obesity treatment, diabetes prevention, and use of technology in diabetes management. Each year, ADA conducts a national call for applications to recruit members of the PPC. Appointment to the PPC is based on excellence in clinical practice and research, with attention to appropriate representation of members based on considerations including but not limited to demographic, geographic, work setting, or identity characteristics (e.g., gender, race and ethnicity, ability level). A PPC chair or co-chairs are appointed by the ADA (M.B. and R.G.M. are co-chairs for the 2026 Standards of Care) and oversee the committee. In addition to the PPC members, several professionals serve as designated subject matter experts to support the PPC in the development of specific content areas of the Standards of Care. While designated subject matter experts assist with content development, only PPC members formally vote on Standards of Care recommendations for final approval.

Additionally, several organizations have endorsed specific sections of the 2026 Standards of Care. The American Society for Bone and Mineral Research (ASBMR) reviewed and approved the “Bone Health” subsection in section 4, “Comprehensive Medical Evaluation and Assessment of Comorbidities.” The Obesity Society (TOS) reviewed and approved section 8, “Obesity and Weight Management for the Prevention and Treatment of Diabetes.” The American College of Cardiology (ACC) reviewed and approved section 10, “Cardiovascular Disease and Risk Management.” The American Geriatrics Society (AGS) reviewed and approved section 13, “Older Adults.” New to the 2026 Standards of Care, the National Kidney Foundation (NKF) reviewed and approved section 11, “Chronic Kidney Disease and Risk Management,” and the International Society for Pediatric and Adolescent Diabetes (ISPAD) reviewed and approved section 14, “Children and Adolescents.”

Each section of the Standards of Care is reviewed annually and updated with the latest evidence-based recommendations by a subcommittee. The subcommittees perform systematic literature reviews to identify and summarize the latest scientific evidence. An information specialist with knowledge and experience in literature searching (a librarian) is consulted as necessary. A guideline methodologist (R.R.B. for the 2026 Standards of Care)

with expertise and training in evidence-based medicine and guideline development methodology oversees all methodological aspects of the development of the Standards of Care and serves as a statistical analyst.

Disclosure and Duality of Interest Management

All members of the PPC, subject matter experts, and the ADA scientific team are required to comply with the ADA policy on duality of interest, which requires disclosure of any financial, intellectual, or other interests that might be construed as constituting an actual, potential, or apparent conflict, regardless of relevancy to the guideline topic. For transparency, ADA requires full disclosure of all relationships. Full disclosure statements from all committee members are solicited and reviewed during the appointment process. Disclosures are then updated throughout the guideline development process (specifically before the start of every meeting), and disclosure statements are submitted by every Standards of Care contributor upon submission of the updated Standards of Care section. Members are required to disclose conflicts for a time frame that includes 1 year prior to initiation of the committee appointment process until publication of that year's Standards of Care. Potential dualities of interest are evaluated by a panel of experts and, if necessary, the Legal Affairs Division of the ADA. The duality of interest assessment is based on the relative weight of the financial relationship (i.e., the monetary amount) and the relevance of the relationship (i.e., the degree to which an independent observer might reasonably interpret an association as related to the topic or recommendation of consideration). In addition, the ADA adheres to section 7 of the Council of Medical Specialty Societies “Code for Interactions with Companies” (3). The ADA also ensures the majority of the PPC and the PPC chair or co-chairs are without potential conflict relevant to the subject area. Furthermore, the PPC chair or co-chairs are required to remain unconflicted for 1 year after the publication of the Standards of Care. Members of the committee who disclose a potential duality of interest pertinent to any specific recommendation are prohibited from voting or their votes are excluded. No PPC members or subject matter experts were employees of any pharmaceutical or medical

device company during the development of the 2026 Standards of Care. Members of the PPC and subject matter experts, their employers, and their disclosed potential dualities of interest are listed in the section “Disclosures: Standards of Care in Diabetes—2026.”

Funding Source

The Standards of Care guideline is funded by ADA general revenue. No other entity, including industry, provides financial support for the guideline. Committee members received no remuneration for their participation in the development of this guideline.

Evidence Review

The Standards of Care subcommittee for each section creates an initial list of relevant clinical questions that is reviewed and discussed by the PPC. In consultation with a systematic review expert and librarian, each subcommittee devises and executes systematic literature searches. For the 2026 Standards of Care, PubMed, Medline, and EMBASE were searched for the time periods of 1 June 2024 to 18 July 2025. Searches are limited to studies published in English. Subcommittee members also manually search journals, reference

lists of conference proceedings, and regulatory agency websites. All potentially relevant citations are then subjected to a full-text review. In consultation with the methodologist, the subcommittees prepare the evidence summaries and grading for each section of the Standards of Care. All PPC members discuss and review the evidence summaries and make revisions as appropriate. The final evidence summaries are then deliberated on by the PPC, and the recommendations that will appear in the Standards of Care are drafted.

Grading of Evidence and Recommendation Development

A grading system (Table 1) developed by the ADA and modeled after existing methods is used to clarify and codify the evidence that forms the basis for the recommendations in the Standards of Care. All recommendations in the Standards of Care are critical to comprehensive care regardless of rating. ADA recommendations are assigned ratings of **A**, **B**, or **C**, depending on the quality of the evidence in support of the recommendation. Expert opinion **E** is a separate category for recommendations for which there is no evidence from clinical trials,

clinical trials may be impractical, or there is conflicting evidence. Recommendations assigned an **E** level of evidence are informed by key opinion leaders in diabetes (members of the PPC and subject matter experts) and cover important elements of clinical care. All Standards of Care recommendations receive a rating for the strength of the evidence and not for the strength of the recommendation. Recommendations with **A**-level evidence are based on large, well-designed randomized controlled trials or well-done meta-analyses of randomized controlled trials. Generally, these recommendations have the best chance of improving outcomes when applied to the population for which they are appropriate. Recommendations with lower levels of evidence may be equally important but are not as well supported by the evidence.

Of course, published evidence is only one component of clinical decision-making. Clinicians care for people, not populations; guidelines must always be interpreted with the individual person in mind. Individual circumstances, such as comorbid and coexisting diseases, age, education, disability, and, above all, the values and preferences of the person with diabetes, must be considered and may lead to different treatment goals and strategies. Furthermore, conventional evidence hierarchies, such as the one adapted by the ADA, may miss nuances important in diabetes care. For example, although there is excellent evidence from clinical trials supporting the importance of achieving multiple risk factor control, the optimal way to achieve this result is less clear. It is difficult to assess each component of such a complex intervention.

Evidence to Recommendations

All accumulated evidence was reviewed and discussed by all PPC members and subject matter experts during multiple virtual meetings and a 2-day in-person meeting in Arlington, Virginia, in July 2025. Standards of Care recommendations were updated based on the newly acquired evidence, and each recommendation was voted on by the PPC, with 80% consensus required for any recommendation to be approved.

Revision Process

Public comment is particularly important in the development of clinical practice recommendations; it promotes transparency and provides key stakeholders,

Table 1—ADA evidence-grading system for “Standards of Care in Diabetes”

Level of evidence	Description
A	Clear evidence from well-conducted, generalizable randomized controlled trials that are adequately powered, including: • Evidence from a well-conducted multicenter trial • Evidence from a meta-analysis that incorporated quality ratings in the analysis Supportive evidence from well-conducted randomized controlled trials that are adequately powered, including: • Evidence from a well-conducted multicenter trial • Evidence from a meta-analysis that incorporated quality ratings in the analysis
B	Evidence from randomized controlled trials with an identified flaw that may limit validity of the results Supportive evidence from well-conducted cohort studies, including: • Evidence from a well-conducted prospective cohort study or registry • Evidence from a well-conducted meta-analysis of cohort studies Supportive evidence from a well-conducted case-control study
C	Supportive evidence from poorly controlled or uncontrolled studies, including: • Evidence from randomized clinical trials with one or more major or three or more minor methodological flaws that could invalidate the results • Evidence from observational studies with high potential for bias (such as case series with comparison with historical controls) • Evidence from case series or case reports Conflicting evidence with the weight of evidence supporting the recommendation
E	Expert consensus or clinical experience

including people with diabetes and their caregivers, the opportunity to identify and address gaps in care. The ADA holds a year-long public comment period requesting feedback on the Standards of Care. The PPC reviews all compiled feedback from the public in preparation for the annual update but considers more pressing updates throughout the year, which may be published as living standards updates. Feedback from the larger clinical community and general public was invaluable for the revision of the 2025 Standards of Care. Readers who wish to comment on the 2026 Standards of Care are invited to do so at professional.diabetes.org/SOC.

Feedback for the Standards of Care is also obtained from external peer reviewers and from the aforementioned endorsing societies (ACC, AGS, ASBMR, ISPAD, NKF, and TOS). The Standards of Care is reviewed by the ADA Medical Affairs scientific team for methodological rigor, accuracy, clarity, and implementation; the Standards of Care then undergoes external peer review, ADA leadership review, and ADA Board of Directors review and approval (this includes review by health care professionals, scientists, and other stakeholders). Feedback received from every stakeholder is adequately addressed by the committee, and the final version is approved by all parties prior to publication. The ADA adheres to the Council of Medical Specialty Societies revised “CMSS Principles for the Development of Specialty Society Clinical Guidelines” (4).

ADA GUIDANCE CATEGORIES

The ADA has been actively involved in developing and disseminating diabetes care clinical practice recommendations and related documents for more than 35 years. The ADA Standards of Care is an essential resource for health care professionals caring for people with diabetes. ADA Statements, Consensus Reports, and Scientific Reviews support the recommendations included in the Standards of Care.

Standards of Care

The annual Standards of Care supplement to the *Diabetes Care* journal contains the official ADA position, is authored by the ADA under the guidance of the PPC, and

provides all the ADA’s current clinical practice recommendations.

Consensus Report

An ADA consensus report is a document on a particular topic that is authored by a technical expert panel under the auspices of ADA. The document does not reflect the official ADA position but rather represents the panel’s collective analysis, evaluation, and expert opinion. The primary objective of a consensus report is to provide clarity and insight on a medical or scientific matter related to diabetes for which the evidence is contradictory, emerging, or incomplete. The report also aims to highlight evidence gaps and to propose avenues for future research. Consensus reports undergo a formal review process, including external peer review and review by the ADA PPC and ADA scientific team, for publication.

When participating in a joint consensus report, ADA, in collaboration with the partner organization, designates representatives who will be involved in all phases of consensus report development (i.e., from initiation through publication). Similar to an ADA consensus report, the joint consensus report is intended to highlight an emerging area in diabetes care, follows the same rigorous review procedures, and does not reflect the official ADA position.

Scientific Review

A scientific review is a balanced systematic review and analysis of literature on a scientific or medical topic related to diabetes. A scientific review is not an ADA position and does not contain clinical practice recommendations but is produced under the auspices of the ADA by invited experts. The scientific review may provide a scientific rationale for clinical practice recommendations in the Standards of Care. The category may also include task force and expert committee reports.

ADA Statement

An ADA statement is an ADA point of view or position that does not contain clinical practice recommendations and may be issued on advocacy, policy, economic, or medical issues related to diabetes. ADA statements undergo a formal review process, including external peer review and review by the ADA Professional

Practice Committee for Diabetes, ADA clinical leadership, ADA scientific team, and, as warranted, the ADA Board of Directors.

ADA ENDORSEMENT PROCESS

Endorsement by ADA signifies formal support for a scientific document, such as a clinical guideline or consensus report. The endorsement process involves a thorough review by the PPC for alignment with ADA’s mission, the Standards of Care, and evidence-based principles. The endorsement indicates that the content is scientifically accurate, relevant, and valuable to health care professionals caring for people with diabetes. While endorsement conveys support for the scientific concepts, it may not extend to every specific statement or phrasing. Although ADA representatives are generally involved throughout the development of these documents, ADA endorsement does not reflect the official ADA position. The type and level of ADA endorsement may vary based on the type of document and the extent of ADA involvement in the development process.

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Summary of Revisions: Standards of Care in Diabetes—2026

American Diabetes Association
Professional Practice Committee for
Diabetes*

Diabetes Care 2026;49(Suppl. 1):S6–S12 | <https://doi.org/10.2337/dc26-SREV>

GENERAL CHANGES

The field of diabetes care is rapidly changing as new research, technology, and treatments that can improve the health and well-being of people with diabetes continue to emerge. With annual updates since 1989, the American Diabetes Association has long been a leader in producing guidelines that capture the most current state of the field.

The 2026 “Standards of Care in Diabetes” has continued to incorporate person-first and inclusive language. Efforts were made to consistently apply terminology that empowers people with diabetes and recognizes the individual at the center of diabetes care. Minor updates were made to figures and tables to align with current accessibility standards.

Although levels of evidence for several recommendations have been updated, these changes are not outlined below where the clinical recommendation has remained the same. That is, changes in evidence level from, for example, **E** to **C**, are not noted below. The 2026 Standards of Care contains, in addition to many minor changes that clarify recommendations or reflect new evidence, more substantive revisions detailed below.

SECTION CHANGES

Endorsements

For the third consecutive year, the “Bone Health” subsection in section 4, “Comprehensive Medical Evaluation and Assessment of Comorbidities,” received endorsement from the American Society for Bone and Mineral Research and section 8, “Obesity and Weight Management for the Prevention of Diabetes,” received endorsement from The Obesity Society. For the eighth consecutive year, section 10, “Cardiovascular Disease and Risk Management,” received endorsement from the American College of Cardiology. For the second consecutive year, section 13, “Older Adults,” received endorsement from the American Geriatrics Society. For the first time, section 11, “Chronic Kidney Disease and Risk Management,” and section 14, “Children and Adolescent,” received endorsement from the National Kidney Foundation and the International Society for Pediatric and Adolescent Diabetes, respectively.

1. Improving Care and Promoting Health in Populations

(<https://doi.org/10.2337/dc26-S001>)

Recommendation 1.1 was revised to highlight the importance of shared decision-making based on individual values,

preferences, prognoses, comorbidities, and informed financial considerations.

Recommendation 1.5 was updated to emphasize the importance of continuous quality improvement by health systems to improve quality of care and health outcomes.

Recommendation 1.8 was revised to include consideration of digital self-management tools or coaches as appropriate to provide support for people with diabetes.

Recommendation 1.9 was modified to highlight the important role of community health workers in supporting the management of kidney disease risk factors, in addition to diabetes and cardiovascular disease risk factors, in underserved communities and health care systems.

Table 1.1 was enhanced to specify additional care team members whose expertise may be beneficial for older adults with diabetes.

2. Diagnosis and Classification of Diabetes

(<https://doi.org/10.2337/dc26-S002>)

Recommendation 2.8 was divided into two components to emphasize the importance of prompt evaluation for stage 3, overt type 1 diabetes in people with one or more islet autoantibodies

*A complete list of members of the American Diabetes Association Professional Practice Committee for Diabetes can be found at <https://doi.org/10.2337/dc26-SINT>.

Duality of interest information for each contributor is available at <https://doi.org/10.2337/dc26-SDIS>.

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(Recommendation 2.8a); Recommendation 2.8b maintains the original guidance that people with multiple islet autoantibodies should be referred to a specialized center for education and possibly preventative interventions.

Recommendation 2.9 was added to highlight that people with a confirmed single IA-2 autoantibody should be monitored similarly to people with stage 2 type 1 diabetes but negative for IA-2 autoantibodies, as they have a comparable risk of progression to stage 3.

Recommendation 2.18 was added to reinforce monitoring of postprandial or random plasma glucose in the setting of recurrent or long-term treatment with glucocorticoids.

Recommendation 2.19 was added to underscore the role of counseling and education regarding the risk of hyperglycemia in people initiating treatment with immune checkpoint inhibitors, phosphoinositidylinositol 3-kinase α (PI3K α) inhibitors, and other anticancer therapy medications.

Recommendation 2.20 was added to provide guidance regarding plasma glucose monitoring at each visit in people treated with immune checkpoint inhibitors.

Recommendation 2.21 was added to emphasize close monitoring of plasma glucose in people initiating treatment with PI3K α inhibitors, which are associated with a particularly high risk of hyperglycemia during the first weeks of treatment.

Recommendation 2.22 was added to prompt fasting or random plasma glucose monitoring at each visit in people treated with mammalian target of rapamycin (mTOR) inhibitors.

Recommendation 2.24a was updated to reiterate that, when feasible, an annual oral glucose tolerance test (OGTT) starting at the age of 10 years is the preferred screening test for cystic fibrosis-related diabetes.

Recommendation 2.24b was modified to highlight that A1C can be used as a part of an alternative two-step screening strategy for cystic fibrosis-related diabetes when OGTT is not feasible.

Previous Recommendations 2.26b and 2.26c on gestational diabetes mellitus screening were consolidated and updated and are now Recommendation 2.31b; the associated narrative text was moved to section 15, "Diabetes Management in Pregnancy," and updated to reflect recent evidence and controversies in the management of

early abnormal glucose metabolism in pregnancy. The text in the "Gestational Diabetes Mellitus" subsection was updated and more closely integrated with the information in section 15, "Diabetes Management in Pregnancy."

3. Prevention or Delay of Diabetes and Associated Comorbidities

(<https://doi.org/10.2337/dc26-S003>)

Recommendation 3.1 was broadened to include monitoring of progression from prediabetes to all types of diabetes, not only type 2 diabetes.

Recommendation 3.2 was enhanced to include consideration of continuous glucose monitoring (CGM) data when monitoring for disease progression among individuals with presymptomatic type 1 diabetes.

Recommendation 3.3 was clarified to recommend referral of individuals with overweight or obesity at high risk for type 2 diabetes to a diabetes prevention program with the goal of achieving and maintaining weight reduction of at least 5–7% of initial body weight.

Recommendation 3.4 was revised to focus on eating patterns with the strongest evidence base for preventing type 2 diabetes, including Mediterranean and low carbohydrate eating patterns.

Recommendation 3.6 was clarified to indicate that certified technology-assisted diabetes prevention programs can be delivered through smartphones, web-based applications, and telehealth modalities.

Recommendation 3.8 was added to recommend considering using metformin to prevent hyperglycemia in high-risk individuals treated with a PI3K α inhibitor (e.g., alpelisib and inavolisib).

Recommendation 3.9 was added to recommend considering using metformin to prevent hyperglycemia in high-risk individuals treated with high-dose glucocorticoids.

4. Comprehensive Medical Evaluation and Assessment of Comorbidities

(<https://doi.org/10.2337/dc26-S004>)

Recommendation 4.3 was changed to include assessment for glycemic status and previous and current treatment at the initial visit and follow-up visits as appropriate. Support systems and available resources were added in addition to identifying care partners at the initial visit and follow-up visits as appropriate.

Recommendation 4.5, regarding vaccinations, was revised to include adolescents.

Recommendation 4.13a was revised to recommend considering osteoporosis drug therapy in older adults with increased risk of fracture with a T-score ≤ -2.5 , and Recommendation 4.13b was added to state that treatment may be considered in adults with diabetes with a T-score between -2.0 and -2.5 in the presence of additional fracture risk.

Recommendation 4.26 was updated to specify that a glucagon-like peptide 1 receptor agonist (GLP-1 RA) with demonstrated benefits in metabolic dysfunction–associated steatohepatitis (MASH) can be considered for treatment in adults with type 2 diabetes, metabolic dysfunction–associated steatotic liver disease (MASLD), and overweight or obesity.

Recommendation 4.27a was updated to specify that a GLP-1 RA with demonstrated benefit is preferred for glycemic management due to beneficial effects on MASH in adults with type 2 diabetes and biopsy-proven MASH or those at high risk for liver fibrosis.

In **Fig. 4.1**, MASLD was added to be considered as a specific factor that impacts choice of treatment.

Figure 4.2 was modified to clarify that the algorithm for individuals with fibrosis-4 (FIB-4) index >2.67 should be managed by a liver specialist.

Figure 4.3 was modified to include a GLP-1 RA with demonstrated benefit for MASH pharmacotherapy in individuals with MASLD and high risk for MASH.

5. Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes

(<https://doi.org/10.2337/dc26-S005>)

Recommendation 5.4 was revised to recommend using behavioral strategies to support diabetes self-management education and support (DSMES) and engagement in positive health behaviors.

Recommendation 5.5 was modified to state that DSMES should be culturally and socially appropriate based on personal preferences and needs and that DSMES participation should be communicated with the diabetes care team.

Recommendation 5.12 was revised to advise that an overweight or obesity treatment plan including nutrition, physical activity, and behavioral health support should be provided to aim for at least 5–7% weight loss from baseline body weight.

Recommendation 5.23 was amended to recommend counseling and regular

monitoring for individuals pursuing intentional weight loss on adequate nutrition intake.

Recommendation 5.32 was modified to state that the updated comprehensive prefasting risk assessment should be used to generate a risk score for the safety of religious fasting.

Recommendation 5.34 was modified to encourage increases in physical activity levels with the goal of meeting activity guidelines, and the narrative discussion on the role of physical activity during obesity treatment was updated.

Recommendation 5.40 was revised to recommend routine assessment and avoidance of tobacco and e-cigarette/vaping use. It also suggests providing or referring individuals for combination treatment, which includes tobacco and e-cigarette/vaping cessation counseling and pharmacologic therapy.

Recommendation 5.45 was updated to recommend referral to a qualified behavioral health professional if diabetes distress is not adequately addressed during the medical appointment.

Recommendation 5.46 was updated to recommend screening for anxiety symptoms at least annually in people with diabetes and encourage health care professionals to address anxiety symptoms within their scope of practice.

Recommendation 5.47 was updated to recommend screening individuals at high risk for hypoglycemia or with severe or frequent hypoglycemia for fear of hypoglycemia at least annually or when clinically appropriate and to refer to a trained health care professional for evidence-based intervention.

Recommendation 5.56 was amended to recommend screening for sleep health in people with diabetes and in those at risk for diabetes.

Table 5.3 now contains updated criteria for the comprehensive prefasting risk assessment for people with diabetes who seek to fast during Ramadan.

6. Glycemic Goals, Hypoglycemia, and Hyperglycemic Crises

(<https://doi.org/10.2337/dc26-S006>)

Recommendation 6.17 was added to promote inclusion of oral glucose in first aid kits for use in treating hypoglycemia in workplaces, schools, and other institutions and public settings.

The section “Intercurrent Illness” was expanded to include criteria for holding

specific diabetes medication classes during acute illness.

The section “Hyperglycemic Crises: Diagnosis, Management, and Prevention” was revised to include more content on the outpatient prevention and management of diabetic ketoacidosis. Reflecting this expanded content, “Hyperglycemic Crises” was added to the section title.

Figure 6.1, which shows an individualized approach to setting glycemic goals, was expanded to include individualized goals for CGM metrics based on health status and other person- and treatment-specific factors.

7. Diabetes Technology

(<https://doi.org/10.2337/dc26-S007>)

Recommendations were added regarding education and training of people with diabetes and health care professionals based on the type of device. In the narrative text, more details were added about education and training based on the type of device. Major updates include content about the support health care professionals may need and information about device initiation for different types of diabetes.

Recommendation 7.3 was divided into two recommendations and includes guidance regarding prescribing and initiating device use. Recommendation 7.3a discusses prescribing, initiating, and following a CGM device, and Recommendation 7.3b describes the same aspects for automated insulin delivery (AID) systems.

Recommendation 7.6 was changed to specify children and adolescents in a school setting and states that children and adolescents should be supported at school in the use of diabetes technology, such as CGM systems, continuous subcutaneous insulin infusion (CSII), connected insulin pens, and AID systems. Older students (aged ≥ 18 years) are discussed in the new Recommendation 7.7, which also discusses workplace accommodation. Recommendation 7.7, for those aged ≥ 18 years, states that for adults with diabetes using diabetes technology, reasonable accommodations in educational and work settings should include having sufficient time to manage their devices and respond to high and low glucose levels.

Recommendation 7.8 discusses early initiation of all devices, as indicated based on a person's circumstances. New Recommendation 7.8a states that there should be no requirement of C-peptide

level, the presence of islet autoantibodies, or duration of insulin treatment before initiation of CSII or AID.

The “Blood Glucose Monitoring” section includes updated literature highlighting the benefits of glucose monitoring for people with type 2 diabetes. Additionally, it reinforces the importance of ensuring that individuals using CGM also have access to blood glucose monitoring.

Recommendation 7.15 states that use of CGM is now recommended at diabetes onset and anytime thereafter for children, adolescents, and adults with diabetes who are on insulin therapy, on noninsulin therapies that can cause hypoglycemia, and on any diabetes treatment where CGM helps in management.

Recommendation 7.17 briefly discusses use of diabetes devices in pregnancy, which is discussed in detail in section 15, “Diabetes Management in Pregnancy.”

Recommendation 7.25a states that AID systems are the preferred insulin delivery system for people with type 1 diabetes and adults and children with type 2 diabetes on multiple daily injections, CSII, or sensor-augmented pump therapy and for other forms of insulin-deficient diabetes.

Recommendation 7.25b states that AID systems can be considered in people with type 2 diabetes on basal insulin who are not meeting their individualized glycemic goals.

The narrative text further discusses that the benefits of CGM have been shown regardless of age, sex, education or income levels, or baseline diabetes characteristics.

Table 7.3 provides updated definitions of types of CGM devices. Intermittently scanned CGM (isCGM) is no longer discussed, although it is referenced as an older option. The three types of devices are now real-time CGM (rtCGM), over-the-counter CGM (OTC-CGM), and professional CGM.

8. Obesity and Weight Management for the Prevention and Treatment of Diabetes

(<https://doi.org/10.2337/dc26-S008>)

Recommendation 8.2a was updated to state that screening for overweight and obesity should occur annually using BMI and that an additional measurement of body fat (e.g., anthropometric assessment or direct measurement) should be

incorporated to confirm excess adiposity where available and feasible.

Recommendation 8.5 was revised to clarify that weight loss of 5–7% of baseline body weight improves glycemia and other intermediate cardiovascular risk factors.

Recommendation 8.8b was updated to clarify components of alternative structured lifestyle programs and examples of modes of delivery.

Recommendation 8.14 was amended to recommend counseling and regular monitoring for individuals pursuing intentional weight loss on adequate nutrition intake.

Recommendation 8.15 was modified to recommend engaging other care team members to minimize use of weight-promoting medications whenever clinically appropriate.

Recommendation 8.20 was added to state that the individualized dose and dose titration for obesity pharmacotherapy should balance efficacy, benefits, and tolerability.

Recommendation 8.21 on treatment modification and intensification approaches now includes considering alternative pharmacologic agents.

Recommendation 8.29 was added to include GLP-1 RA–based therapy and/or metabolic surgery as treatment options for obesity in people with type 1 diabetes.

Table 8.2 was updated with obesity pharmacotherapy costs as of 15 July 2025.

9. Pharmacologic Approaches to Glycemic Treatment

(<https://doi.org/10.2337/dc25-S009>)

For the glycemic treatment plan for people with type 2 diabetes and symptomatic heart failure with preserved ejection fraction (HFpEF), Recommendation 9.9a was added to recommend use of a dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 RA with demonstrated benefits for heart failure–related symptoms and reduction in heart failure events, and Recommendation 9.9b was revised to include a GLP-1 RA with demonstrated benefits in heart failure–related symptoms and/or reduction in heart failure events.

Recommendation 9.11 was updated to include information about initiation and continuation of a GLP-1–based therapy for people with type 2 diabetes and advanced chronic kidney disease (CKD).

Recommendation 9.12 was revised to recommend a GLP-1 RA with demonstrated

benefits in MASH or a dual GIP and GLP-1 RA with potential benefits in MASH in people with type 2 diabetes, MASLD, and overweight or obesity for glycemic management.

Recommendation 9.13a was changed to state that a GLP-1 RA with beneficial effects on MASH is preferred for glycemic management and a pioglitazone or a dual GIP and GLP-1 RA with potential beneficial effects on MASH can be considered for glycemic management in adults with type 2 diabetes, biopsy-proven MASH, or those at high risk for liver fibrosis.

Recommendation 9.24 was revised to include healthy behaviors, DSMES, avoidance of therapeutic inertia, and social determinants of health as essential components of the glycemic treatment plan in all people with diabetes.

Recommendation 9.25 was updated to recommend use of CGM at diabetes onset and anytime thereafter for adults with diabetes on insulin therapy, on noninsulin therapies that can cause hypoglycemia, and on any diabetes treatment where CGM aids in management.

Recommendation 9.27 was modified to recommend that AID systems should be offered to all adults with type 1 or type 2 diabetes on insulin.

New recommendations for glycemic management in the context of cancer treatment were added. For individuals on immunotherapy who develop hyperglycemia, Recommendation 9.33 was added to recommend the assessment of these individuals for the need of insulin therapy to prevent potential diabetic ketoacidosis and to use additional testing to determine if hyperglycemia is related to immunotherapy-associated diabetes. For individuals with hyperglycemia due to mTOR inhibitors or PI3K inhibitors, Recommendations 9.34 and 9.35a state that metformin should be considered as first-line treatment, and Recommendation 9.35b states that insulin should be reserved for severe hyperglycemia and hyperglycemic crises due to its potential impact on PI3K inhibitor efficacy. For individuals undergoing glucocorticoid treatment, Recommendation 9.36 was added to recommend adjustment or initiation of additional glucose-lowering therapies to maintain individualized glycemic goals based on the glucocorticoid treatment plan and ongoing assessment of glucose levels.

New recommendations on glycemic treatment in the context of organ transplant were added for adults with post-transplantation diabetes mellitus or preexisting type 2 diabetes and undergoing organ transplantation. For glycemic management in the postoperative setting, Recommendation 9.37 was added to recommend that insulin is preferred and that a dipeptidyl peptidase 4 inhibitor can be considered for mild hyperglycemia. For long-term glycemic management, Recommendation 9.38a states that noninsulin pharmacotherapy can be used and that the selection of medication may be contingent upon the transplanted organ(s), and Recommendation 9.38b states that a GLP-1 RA can be considered due to additional cardiometabolic benefits. Recommendation 9.38c was added to recommend the addition of insulin to noninsulin pharmacotherapy if individualized long-term glycemic goals cannot be achieved or maintained.

A new insulin algorithm for type 1 diabetes (**Fig. 9.2**) was added.

Figure 9.4 was revised to include a dual GIP and GLP-1 RA or GLP-1 RA for glycemic management for those with type 2 diabetes, symptomatic HFpEF, MASLD or MASH, and obesity.

Figure 9.5 was revised to suggest considering CGM for individuals with type 2 diabetes on basal insulin.

Tables 9.3 and **9.4** were updated with glucose-lowering medication and insulin costs as of 15 July 2025.

10. Cardiovascular Disease and Risk Management

(<https://doi.org/10.2337/dc26-S010>)

Recommendation 10.4 was updated to state that a systolic blood pressure goal <120 mmHg should be encouraged for individuals with high cardiovascular or kidney risk.

Recommendation 10.6 was modified to indicate that blood pressure–lowering pharmacologic therapy should be titrated to achieve individualized blood pressure goals.

Recommendation 10.10 was revised to include that an ACE inhibitor or angiotensin receptor blocker (ARB) is strongly recommended to treat hypertension for those with severely increased albuminuria and/or estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m² to the maximally tolerated dose to prevent progression of kidney disease and to reduce cardiovascular events.

Recommendation 10.11 was modified to specify monitoring frequency for a drop in eGFR and increase in serum potassium levels when ACE inhibitors, ARBs, or mineralocorticoid receptor antagonists (MRAs) are used and monitoring frequency for hypokalemia when diuretics are used.

For individuals receiving statin therapy, Recommendation 10.32 was revised to advise against the addition of fibrates, niacin, or dietary supplements containing n-3 fatty acids, as they do not confer additional cardiovascular risk reduction.

Recommendation 10.40c was modified to include people with type 2 diabetes and CKD and to recommend a GLP-1 RA with demonstrated cardiovascular benefit to reduce the risk of cardiovascular events.

Recommendation 10.44c was updated to recommend a GLP-1 RA with heart failure prevention benefit for people with type 2 diabetes and asymptomatic (stage B) heart failure with high risk of or established cardiovascular disease.

Recommendations 10.44d and 10.44e were revised and added to recommend a dual GIP and GLP-1 RA or a GLP-1 RA with demonstrated benefit for reduction in heart failure events and heart failure symptoms, respectively, in adults with type 2 diabetes, obesity, and symptomatic heart failure with preserved ejection fraction.

Recommendation 10.44h was added to recommend a nonsteroidal MRA (nsMRA) with proven benefit in reducing worsening heart failure events for people with diabetes and symptomatic stage C heart failure with ejection fraction >40%.

Figure 10.5 was added to include an overview of prevention and treatment of symptomatic heart failure in people with diabetes, and **Fig. 10.6** was added to illustrate the approach to prevent atherosclerotic cardiovascular disease (ASCVD) in people with type 2 diabetes.

11. Chronic Kidney Disease and Risk Management

(<https://doi.org/10.2337/dc26-S011>)

Recommendation 11.1a was amended to clarify the frequency of assessment for kidney function.

Recommendation 11.5 was amended to clarify goals for blood pressure management with specific emphasis on systolic blood pressure goals.

Recommendation 11.6a was updated to clarify guidance on intolerance to medication in nonpregnant individuals with diabetes and hypertension.

Recommendation 11.6b was revised to specify monitoring frequency for a drop in eGFR and increase in serum potassium levels and for hypokalemia when ACE inhibitors, ARBs, or MRAs are used.

Recommendation 11.8 was changed to enhance clarity on potassium level monitoring after initiation of an nsMRA to reduce CKD progression and cardiovascular risk.

New Recommendation 11.9 was added to state that simultaneous initiation of a sodium-glucose cotransporter 2 (SGLT2) inhibitor and an nsMRA can be considered in individuals with type 2 diabetes and urine albumin-to-creatinine ratio ≥ 100 mg/g with eGFR 30–90 mL/1.73 m² on a renin-angiotensin-aldosterone system (RAS) inhibitor.

Recommendation 11.10 was revised to clarify guidance on kidney-protective medications that are potentially harmful in pregnant and sexually active individuals of childbearing potential.

Recommendation 11.11a was added to address SGLT2 inhibitor use in individuals who are not on dialysis to reduce the risk of CKD progression and for cardiovascular benefits.

Recommendation 11.11b was added to provide guidance on initiation or continuation of GLP-1-based therapy in individuals on dialysis to reduce cardiovascular risk.

Figure 11.2 was modified to reorder the placement of the RAS inhibitor dose to reflect that the majority of the participants in kidney outcome trials investigating SGLT2 inhibitors, GLP-1 RAs, and nsMRAs were receiving background optimized RAS inhibitor therapy.

12. Retinopathy, Neuropathy, and Foot Care

(<https://doi.org/10.2337/dc26-S012>)

A new introduction has been added to provide appropriate pathophysiological context for the subsections, including discussion of the 40-year Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) study results.

The narrative was expanded to discuss the effect of GLP-1 RA treatment on eye health, including nonarteritic anterior ischemic optic neuropathy, glaucoma, neovascular age-related macular

degeneration, and diabetic retinopathy progression.

The role of adjunctive therapies was broadened to emphasize a holistic, multifactorial approach to eye health in diabetes.

Neuropathy diagnosis discussion was updated to align more closely with the “Foot Care” subsection, incorporating the Ipswich touch test.

Recommendation 12.22 was updated to emphasize the importance of combination therapy for additional relief of neuropathic pain.

The narrative was strengthened regarding prevention and management of diabetic foot complications. In this regard, the importance of infection and its prompt management was added throughout the text.

Emerging technologies in foot care are now discussed, including self-monitoring of foot temperatures using smart mats, insoles, or socks for early identification of impending ulceration.

The importance of adjunctive advanced therapies was emphasized, particularly for diabetic foot ulcers unresponsive to standard care or surgical care. Discussion of the Wound Ischemia foot Infection (WIFI) staging system for diabetic foot lesions was expanded; it is now described as increasingly used to stage peripheral artery disease severity, predict diabetic foot ulcer healing, and assess amputation risk.

The narrative was updated to highlight the need for holistic and interventional approaches in managing diabetes with peripheral artery disease. Emerging evidence was added for GLP-1 RA therapies, which may reduce lower-extremity amputations.

13. Older Adults

(<https://doi.org/10.2337/dc26-S013>)

In the “Hypoglycemia” section, Recommendation 13.5 now recommends use of CGM for older adults with type 1 diabetes or type 2 diabetes on insulin to improve glycemic outcomes, reduce hypoglycemia, and reduce treatment burden.

In “Treatment Goals,” Recommendation 13.9 now provides a more specific on-treatment blood pressure goal for most older adults of <130/80 mmHg when it can be achieved safely and a more relaxed blood pressure goal (e.g., <140/90 mmHg) for people with poor health, limited life expectancy, or high risk for adverse effects of hypertensive therapy.

In the “Lifestyle Management” section, Recommendation 13.11a now includes more specific guidance on protein intake (at least 0.8 g/kg body weight/day).

In the “Lifestyle Management” section, Recommendation 13.11b is now a separate recommendation for types of exercise and physical activity to maintain lean body mass, especially in those pursuing intentional weight loss.

Terminology for care in nursing home and assisted living settings was standardized by using the term post-acute and long-term care (PALTC).

Table 13.1 has been introduced to provide specific guidance for assessing older adults with diabetes for geriatric syndromes and other functional impairments using sample screening questions and validated languages.

Figure 13.2 has been introduced to illustrate a stepwise approach for assessing difficulties in the diabetes treatment plan; reevaluating glycemic goals through shared decision-making; deintensifying, simplifying, or modifying the treatment plan; and reassessing the safety and burdens of any interventions.

14. Children and Adolescents

(<https://doi.org/10.2337/dc26-S014>)

Section 14 was reorganized to clearly differentiate guidance for type 1 versus type 2 diabetes in children and adolescents while merging sections that applied to both types of diabetes in children and adolescents.

Narrative discussions of developmental considerations and the impact of obesity and psychosocial factors were expanded.

Language in Recommendation 14.1 was strengthened to emphasize child and family-centered care, ongoing reassessment of self-care transfer, and training of daycare and school personnel.

Recommendation 14.2 was modified to reinforce comprehensive nutrition education at diagnosis and annually, tailored to growth, eating patterns, and risk factors.

Recommendation 14.3 was expanded to include evidence on macronutrient composition (carbohydrate, fat, and protein) and its impact on insulin dosing, glycemic excursions, and long-term outcomes.

The “Physical Activity and Exercise” section recommendations now emphasize ≥ 60 min/day of moderate-to-vigorous activity, with bone- and muscle-strengthening activities ≥ 3 times/week. New guidance on strategies to prevent exercise-related

hypoglycemia and hyperglycemia and importance of treatment availability during activity was added.

The “Psychosocial Care” section was updated to include behavioral health professionals as integral team members; routine screening for food insecurity, housing stability, literacy, and social support; confidential time for adolescents with providers at developmentally appropriate ages; screening for diabetes distress, depression, anxiety, fear of hypoglycemia, and disordered eating behaviors starting as early as age 7–8 years; and collaboration with behavioral health providers for individualized interventions (e.g., cognitive behavioral therapy and mindfulness-based approaches).

Table 14.1 was added to provide easier comparison of type 1 and type 2 diabetes recommendations. **Table 14.1** and text were updated to reflect the current evidence on lipid screening, microalbuminuria, retinopathy, and neuropathy in children and adolescents. New evidence from SEARCH for Diabetes in Youth (SEARCH), Treatment Options for Type 2 Diabetes in Adolescents and Youth (TODAY), and T1D Exchange studies was incorporated to refine timing and frequency of screening.

Recommendation language around use of CGM, artificial intelligence–based retinal screening tools, and pharmacotherapies (i.e., GLP-1 RAs, SGLT2 inhibitors, and a dual GIP and GLP-1 RA) was added.

In the “Type 2 Diabetes in Children and Adolescents” section, new pharmacotherapy data for GLP-1 RAs, SGLT2 inhibitors, and the dual GIP and GLP-1 RA and their U.S. Food and Drug Administration approval status in the pediatric population were added with up-to-date randomized controlled trial discussion, and discussion of metabolic and bariatric surgery outcomes was expanded with ≥ 10 -year follow-up data.

Recommendations and references in the section “Transition From Pediatric to Adult Care for All Children and Adolescents With Diabetes” were updated to emphasize structured transition programs, improved clinic attendance, and digital tools to support continuity of care.

15. Management of Diabetes in Pregnancy

(<https://doi.org/10.2337/dc26-S015>)

Recommendation 15.3 was modified to emphasize that preconception counseling

should include the importance of avoiding excessive hypoglycemia in achieving preconception glycemic goals.

The narrative sections “Preconception Counseling” and “Preconception Care” were reorganized, including consolidation of the counseling pertinent to weight management.

The narrative text was updated to include preconception glucose goals (in addition to the preconception A1C goal) to guide therapeutic adjustments.

The narrative text was updated to provide guidance regarding preconception discontinuation of GLP-1 RA and dual GIP and GLP-1 RA therapy and to emphasize that preconception glycemic goals should be achieved following discontinuation of GLP-1 RA or dual GIP and GLP-1 RA therapy before attempting conception.

The narrative text regarding early abnormal glucose metabolism was moved from section 2, “Diagnosis and Classification of Diabetes,” to the present section and updated to include recent evidence and controversies regarding optimal management strategies.

The narrative text was updated to include recent randomized controlled trials evaluating CGM use in gestational diabetes mellitus.

The narrative text was updated to provide additional information regarding use of currently available insulin preparations during pregnancy.

The narrative text subsections regarding CGM use in pregnancy and A1D use in pregnancy that were previously included in both section 7, “Diabetes Technology,” and section 15, “Management of Diabetes in Pregnancy,” were consolidated and are now found in the present section only.

Recommendation 15.24 was modified to use the blood pressure threshold of 140/90 mmHg for initiation or titration of antihypertensive therapy, for both clarity and alignment with recent randomized controlled trial data.

Recommendation 15.25b was updated to include severe hypertriglyceridemia as an additional factor that may in some circumstances warrant continued use of lipid-lowering therapy during pregnancy.

The narrative text was updated to state that, in a small subset of individuals who are unable to tolerate or decline the postpartum OGTT, an A1C performed at 6–12 months postpartum may be considered as supplementary diagnostic information, noting that it should

not replace the gold standard postpartum OGTT.

16. Diabetes Care in the Hospital
(<https://doi.org/10.2337/dc26-S016>)

Two new recommendations were added for glycemic goals in the perioperative period. To improve postoperative outcomes, Recommendation 16.14 suggests an A1C goal <8% (<64 mmol/mol) within 3 months of elective surgery. Alternatively, a 14-day glucose management indicator goal <8% or time in

range >50% can also be used. Recommendation 16.15 was added to advise a blood glucose range 100–180 mg/dL (5.6–10.0 mmol/L) during the perioperative period.

For individuals with diabetes not being discharged to their home, Recommendation 16.18 was updated to suggest considering the capabilities of the facility for diabetes management.

Tables 16.1 and **16.2** were included to provide information on diagnostic

criteria and clinical presentation for diabetic ketoacidosis and hyperglycemic hyperosmolar state.

The narrative text was updated to expand upon technology use in the hospital setting and noninsulin therapies in the perioperative period.

17. Diabetes Advocacy
(<https://doi.org/10.2337/dc26-S017>)

No revisions have been made for the 2026 Standards of Care.



1. Improving Care and Promoting Health in Populations: Standards of Care in Diabetes—2026

American Diabetes Association
Professional Practice Committee for
Diabetes*

Diabetes Care 2026;49(Suppl. 1):S13–S26 | <https://doi.org/10.2337/dc26-S001>

The American Diabetes Association (ADA) “Standards of Care in Diabetes” includes the ADA’s current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. Members of the ADA Professional Practice Committee for Diabetes, an interprofessional expert committee, are responsible for updating the Standards of Care annually, or more frequently as warranted. For a detailed description of ADA standards, statements, and reports, as well as the evidence-grading system for ADA’s clinical practice recommendations and a full list of Professional Practice Committee members, please refer to Introduction and Methodology. Readers who wish to comment on the Standards of Care are invited to do so at professional.diabetes.org/SOC.

SYSTEMS TO SUPPORT DIABETES POPULATION HEALTH

Recommendations

1.1 Ensure treatment decisions are timely, rely on evidence-based guidelines, address social determinants of health, and incorporate shared decision-making based on individual values, preferences, prognoses, comorbidities, and informed financial considerations. **B**

1.2 Align approaches to diabetes management with evidence-based care models. These models emphasize person-centered team care, integrated long-term treatment approaches to diabetes and comorbidities, and ongoing collaborative communication and goal setting among all team members and with people with diabetes. **A**

1.3 Care systems should facilitate in-person and virtual team-based care, include those knowledgeable and experienced in diabetes management as part of the team, and utilize patient registries, decision support tools, proactive care planning, and community involvement to meet needs of individuals with diabetes. **B**

1.4 Assess diabetes management, risk factors, and complications using reliable and relevant data metrics to improve processes of care and health outcomes, with attention to individual values, preferences, goals for care, and treatment burden, including costs of care. **B**

1.5 Health systems should adopt a culture of continuous quality improvement, implement benchmarking programs, and engage interprofessional teams to support sustainable and scalable process changes to improve quality of care and health outcomes. **A**

*A complete list of members of the American Diabetes Association Professional Practice Committee for Diabetes can be found at <https://doi.org/10.2337/dc26-SINT>.

Duality of interest information for each contributor is available at <https://doi.org/10.2337/dc26-SDIS>.

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Diabetes and Population Health

Population health is a multidimensional concept that refers to the health outcomes of a group of individuals and the potentially varied distribution of those outcomes within the group (1). These outcomes can be measured in terms of health indicators (mortality, morbidity, quality of life, and functional status), disease epidemiology (incidence and prevalence), and behavioral and metabolic factors (physical activity, nutrition, A1C, time in range, etc.) (1). In clinical practice, population health commonly refers to the measurement and improvement of health outcomes for a defined group of individuals, often those receiving care within a particular health system or practice, and is central to operational “population health management,” or the proactive, team-based, and data-driven approaches to improving health care experiences and team well-being while minimizing costs and addressing inequities, in alignment with the Quadruple Aim (2). More broadly, population health refers to the health of all people living in a geographic area or community, and it centers on upstream drivers of health that must be addressed, often through cross-sector collaboration and policy, to improve the broader conditions that influence health.

Clinical practice recommendations are tools for health care professionals who seek to improve health across populations; however, for optimal outcomes, diabetes care must also be individualized for each person with diabetes and for each person’s context, as well as across the life span. Thus, efforts to improve population health will require a combination of policy-level, system-level, and person-level approaches. With such an integrated approach in mind, the American Diabetes Association (ADA) highlights the importance of person-centered care, defined as care that considers an individual’s comorbidities and prognoses; is respectful of and responsive to individual preferences, needs, and values; and ensures that the individual’s values guide all clinical decisions (3). Social determinants of health (SDOH)—factors often beyond an individual’s direct control and potentially representing lifelong risks—play a significant role in both clinical and psychosocial outcomes. SDOH are defined as the economic, environmental, political, and social conditions in which people live, and their uneven distribution is responsible for a major part of health inequality worldwide

(4). To improve health, support overall well-being, and eliminate disparities, it is crucial to address these determinants, particularly for individuals from racial and ethnic minoritized communities, underserved geographic areas (rural or urban), and those facing socioeconomic barriers to care and health (5). This section discusses the current state of diabetes and diabetes care in the U.S. and provides guidance for health care professionals as well as health systems, community partners, payors, and policymakers on improving the delivery of diabetes care to improve the health of all people at risk for or living with diabetes.

To provide actionable guidance for improving the health outcomes of people with or at risk for diabetes, this section examines care delivery and payment models demonstrated to support high-quality, evidence-based care; offers guidance on practical strategies for system-level improvement, including identifying and addressing gaps in diabetes care and outcomes experienced by population subgroups; and discusses opportunities to expand access to health care and diabetes self-management education and support (DSMES) through telehealth, mobile platforms, interprofessional team care, and engagement of community-based care partners and resources.

State of Diabetes and Diabetes Care

In 2021, an estimated 38.4 million people were living with diabetes, representing 11.6% of the U.S. population. This includes 38.1 million adults aged 18 years and older (14.7% of U.S. adults), of whom 8.7 million were unaware of their diagnosis. An additional 97.6 million adults aged 18 years and older (38.0% of the U.S. population) were living with prediabetes (6), and over 100 million adults 20 years and older (41.9% of U.S. adults) were living with obesity (7), placing them at high risk for developing type 2 diabetes. The prevalence of diabetes is increasing among children and adolescents as well. In 2017, the year for which the most recent data are available, the prevalence of type 1 diabetes was 2.15 per 10,000 individuals aged 19 years and under, and the prevalence of type 2 diabetes was 0.67 per 1,000 individuals 10–19 years of age (prevalence among those under 10 years old was too low to be reported) (8). Obesity prevalence has also increased significantly among children and adolescents in recent

years, affecting approximately 14.7 million individuals between 2 and 19 years (19.7% of all U.S. children and adolescents) (9).

Most concerning is the recent rise in the rates of diabetes complications among adults with diabetes across the U.S. observed since the early 2010s, particularly for kidney failure, nontraumatic lower-extremity amputations, stroke, heart failure, and hyperglycemic crises, while rates of myocardial infarction have plateaued, reversing decades of earlier improvements (10). The proportion of people with diabetes who achieve recommended A1C, blood pressure, and cholesterol levels has fluctuated over the years, with some improvement over time (11,12). However, in 2015–2018 (the time frame for which the most recent population-level data are available), just 50.5% of U.S. community-dwelling adults with diabetes achieved A1C <7%, and 75.4% achieved A1C <8% (12). The goal blood pressure of <130/80 mmHg was achieved by just 47.7%, non-HDL cholesterol <130 mg/dL was achieved by 55.7%, and all three risk factors were treated to goal in just 22.2% (12). Importantly, many people who did not attain A1C, blood pressure, and lipid goals were not receiving any or adequate pharmacotherapy for glycemia, hypertension, and dyslipidemia management, respectively (i.e., were undertreated), which underscores the urgent need for care delivery systems and structural facilitators (i.e., health and public health policies and payment models) that enable timely and equitable delivery of evidence-based care and address diabetes prevention and treatment in communities (12).

Many segments of the population face additional and unique challenges to diabetes management, resulting in higher rates of diabetes complications, morbidity, and mortality. These include children, adolescents, and young adults; individuals with complex health needs, financial or other social hardships, and/or limited English proficiency; and individuals in groups and communities that have been historically marginalized (6,10,12,13). The prevalence of diabetes among adults is higher among non-Hispanic Black individuals (17.4%), non-Hispanic Asian individuals (16.7%), and Hispanic individuals (15.5%) than among White individuals (13.6%). Diabetes prevalence is also higher among adults with less than a high school education (13.1%) than among those with more than a high school education (6.9%), higher

among those from families living below the federal poverty level (13.1%) than among those at 500% of federal poverty level of higher (5.1%), and higher among those living in nonmetropolitan areas (9.5%) than among those living in metropolitan areas (8.1%) (6). There is also substantial county-level variation in diabetes complications, mortality, and disparities in complications and mortality experienced by minoritized racial and ethnic groups across the U.S. (13), underscoring the impacts of broader structural factors on health among historically marginalized populations.

Gaps and disparities in diabetes management and outcomes are also prevalent among children, adolescents, and young adults with diabetes in the U.S. Improving diabetes management early in life is essential for preventing adverse health outcomes and disability and improving quality of life both in the short- and long-term. There are important and nuanced considerations in treating diabetes and supporting children, adolescents, and young adults with diabetes that are distinct from those of older adults (14). Data from SEARCH for Diabetes in Youth (SEARCH), a population-based registry network of five centers across five U.S. states, showed that in 2014–2019, mean A1C was 9.1% (76 mmol/mol) among youth and young adults with type 1 diabetes and 8.9% (74 mmol/mol) in youth and young adults with type 2 diabetes; these values increased from 8.5% (70 mmol/mol) and 8.4% (68 mmol/mol), respectively, in 2002–2007 (15). Youth and young adults with type 1 diabetes who are non-Hispanic Black or Native American (compared with those who are non-Hispanic White), younger, not treated with insulin pump therapy, and from households with low annual income have significantly higher A1C levels (15). Data from a network of academic pediatric and adult centers across the U.S. revealed that between 2016 and 2018, mean A1C was 8.1% (65 mmol/mol) among children with type 1 diabetes at 5 years of age and 9.3% (78 mmol/mol) among children 15–18 years of age. Only 17% of youth under 18 years of age with type 1 diabetes achieved the recommended A1C goal of <7.5% (<58 mmol/mol), and A1C levels for non-Hispanic Black youth were higher than those for non-Hispanic or Hispanic White youth, a disparity that persisted after adjustment for socioeconomic status (16).

Diabetes and its associated health complications pose a significant financial

hardship to individuals and society. It is estimated that the annual cost of diagnosed diabetes in the U.S. in 2022 was ≥\$413 billion, including ≥\$307 billion in direct health care costs and ≥\$106 billion in reduced productivity (17). After adjusting for inflation, the economic costs of diabetes increased by 7% between 2017 and 2022 and by 35% between 2012 and 2022 (17). This is attributed to both the increased prevalence of diabetes and the higher cost per person with diabetes. People living with diabetes also face individual financial hardship, resulting in rationing or not taking prescribed medications, delaying care, and foregoing or rationing other expenditures, among other behaviors, and ultimately correlating with higher A1C, greater diabetes distress, and depressive symptoms (18).

The growing gaps in diabetes care quality and outcomes, the high and rising costs of diabetes care across the U.S., and the disparities experienced by individuals from racial and ethnic minoritized backgrounds and those facing socioeconomic barriers to care call for urgent, substantial, and multisectoral system-level improvements to care delivery (19).

Evidence-Based Care Delivery and Payment Models to Improve Population Health

A major barrier to comprehensive high-quality diabetes care is a delivery system that is often fragmented, lacks clinical information capabilities, is not appropriately incentivized and funded, does not adequately engage people with diabetes and the communities where they live, and is poorly designed for the coordinated and longitudinal delivery of chronic care (20). Several models have been demonstrated to improve aspects of diabetes care delivery and health outcomes.

The Chronic Care Model (CCM) is a commonly used framework for describing diabetes care programs (21). It includes six core elements to optimize the care of people with chronic disease:

1. Delivery system design (moving from a reactive to a proactive care delivery system where planned visits are coordinated through a team-based approach)
2. Self-management support
3. Decision support, particularly at the point of care during a clinical encounter (basing care on evidence-based, effective care guidelines)

4. Clinical information systems (using registries that can provide person-specific and population-based support to the care team)
5. Community resources and policies (identifying or developing resources to support healthy lifestyles)
6. Health systems (to create a quality-oriented culture)

Randomized controlled trials of CCM interventions have shown that while interventions vary, programs that include core components of the CCM decrease A1C (mean difference [MD] −0.21% [95% CI −0.30 to −0.13], $P < 0.001$ compared with usual care), with greater improvements seen among adults with higher baseline A1C and with interventions that include four or more CCM elements (22). CCM-aligned programs also improved blood pressure levels and processes of diabetes care (e.g., screening for complications of diabetes), though there was no impact on cholesterol levels, tobacco use, or weight (23). Multiple studies have examined individual components of the CCM with respect to diabetes management and have found inconsistent levels of benefit with case management, team-based care, use of electronic patient registries, clinician education, clinician and patient reminders, and patient education and promotion of individual self-management (24). The inconsistencies in findings may be driven by heterogeneity of interventions, settings, and evaluation strategies as well as structural barriers to program utilization and needs of communities served.

Collaborative, interprofessional teams, which can bring together multiple disciplines within the health care system, payors, and community partners, are best suited to provide care for people with chronic conditions such as diabetes and to facilitate individuals' self-management (Table 1.1) (25–27). The care team, which centers around the person with diabetes, should avoid therapeutic inertia and prioritize timely and appropriate modification of behavior change interventions (nutrition and physical activity), pharmacologic therapy, technology use, and/or social and financial support systems for individuals who have not achieved recommended individualized metabolic goals or are experiencing high burden of treatment. Engagement of an endocrinology team with expertise in diabetes management is important in situations when the complexity of diabetes

Table 1.1—Considerations for engaging interprofessional members of a comprehensive, person-centered diabetes care team to identify and meet the needs of people with diabetes across the life span

Subpopulation of a person with diabetes	Team members to engage in care	Unique care considerations
All adults with diabetes	Primary care clinician, CDCES, RDN, and other specialists as available and appropriate to treat comorbidities (Table 4.1)	Assess for and address social determinants of health.
Adults treated with intensive insulin therapy, including multiple daily injections of insulin and insulin pump therapy	Clinicians and other health care team members experienced in advanced diabetes management, including technology use	
All children and adolescents with diabetes	Primary care clinician, pediatric endocrinologist, CDCES, RDN, other specialists as available and appropriate to treat comorbidities (Table 14.1), daycare or school nurse or other professional, behavioral health professional (as needed), and parent(s) or caregiver(s)	Assess for and address social determinants of health and barriers to safety, well-being, and academic performance in school. Engage professionals within the school and extracurricular/after-school activities to ensure safe diabetes management. An individualized diabetes medical management plan should be developed in collaboration with school professionals and parent(s) or caregiver(s). Support gradual developmentally appropriate transfer of self-management from caregivers to the children and adolescents with diabetes.
Individuals with diabetes and diabetes-related complications or comorbidities	Specialist referrals as appropriate and available (e.g., behavioral health professional, cardiologist, endocrinologist, eye specialist, gastroenterologist or hepatologist, neurologist, nephrologist, obesity medicine specialist, or podiatrist), care coordinator/navigator or case manager, and clinical pharmacist (for those with polypharmacy or complex medication plans)	Screen for functional, cognitive, financial, and logistical barriers to self-management and evidence that self-care demands exceed capacity and available resources and support systems.
Individuals with social and/or structural barriers to care	Care coordinator/navigator, social services professional, insurance specialist/navigator, peer-to-peer support (as available), community health worker and/or community paramedic (as available), public health professional, and interpreter (as applicable)	Consider each person's psychosocial needs, available resources, and support systems.
Older adults	Geriatric medicine specialist, clinical pharmacist (for those with polypharmacy or complex medication plans), CDCES and/or RDN with expertise in the care for older adults, social services professional, case manager, community services provider, and physical and/or occupational therapist as available and appropriate based on functional status and independence	Consider the older adult's nutritional status, including ability to afford (financial barriers), acquire (accessibility), prepare (cooking), and consume (oral health) nutritious food. Assess for and address needs related to vision, hearing, dexterity, cognition, mobility, and other challenges.
Individuals in long-term care settings	Long-term care facility clinicians, nurses, other health care professionals, physical and occupational therapists, and RDN	Engage professionals within the long-term care facility to ensure safe and appropriate diabetes management.
Pregnant individuals with diabetes	Maternal-fetal medicine specialist or obstetrician experienced in the care of pregnant individuals with diabetes (particularly for individuals with type 1 diabetes or requiring intensive insulin therapy), CDCES, RDN, eye specialist (particularly for individuals with preexisting type 1 or type 2 diabetes), other specialists as appropriate, and lactation consultant as appropriate	Ensure appropriate postpartum follow-up and care, including transition from obstetric care to established primary care.
Individuals with behavioral health conditions	Behavioral health professional, care coordinator/navigator, and social services professional as age and situation appropriate	Use age- and situation-appropriate screening protocols for general and diabetes-related psychosocial concerns.

CDCES, certified diabetes care and education specialist; RDN, registered dietitian nutritionist.

treatment exceeds the capacity of the primary care team to effectively manage, including in the setting of high clinical complexity and multimorbidity and difficult-to-manage hyperglycemia and/or hypoglycemia (28–32).

Initiatives such as the Patient-Centered Medical Home (PCMH) model can improve health outcomes by fostering comprehensive primary care and offering new opportunities for team-based chronic disease management (33–35). Accountable Care Organizations (ACOs), primary care-centered delivery and payment models, can support the implementation of the CCM and ultimately improve diabetes-related metrics in participating organizations (36). The Accountable Health Communities Model was introduced to support identifying and addressing health-related social needs to improve disease management and health outcomes (37); early evidence showed reduction in emergency department use among Medicare and Medicaid beneficiaries, but diabetes-specific metrics were not examined, and program effectiveness has been limited by scarcity of resources to meet identified health-related social needs (38). Alternative Payment Models (APMs) have had mixed effects on diabetes care delivery and outcomes, with higher-risk APMs (i.e., models with greater financial risk assumed by the provider, such as capitated payment models) generally associated with greater improvements in diabetes care processes than lower-risk APMs (39). Value-based payment models are hypothesized to better support the implementation and sustainability of innovative care delivery models seeking to improve population health (33,40), though evidence for currently available value-based insurance designs is limited (39).

Flexible Modalities of Care Delivery: Telehealth and Support for Behavioral Change and Well-being

Telehealth uses digital tools like video conferencing, mobile apps, and remote monitoring to deliver a range of health services remotely, including clinical care, education, and administrative support. Telemedicine, a subset of telehealth, focuses specifically on remote clinical care, supporting diagnosis, treatment, and consultations through real-time communication. Increased access to and effective use of telehealth services, alongside in-person care, can enhance timely access to diabetes care

and DSMES services for individuals with diabetes (41–45).

Telehealth should be used to complement and not replace in-person visits for optimal glycemic management (46,47). A growing body of evidence supports the effectiveness of telehealth for glycemic management in people with diabetes. In a 2025 systematic umbrella review of 30 systematic reviews and meta-analyses, 28 reviews analyzed A1C and reported a significant reduction in A1C for people with diabetes (48). In the meta-analytic estimate, 16 of the 30 systematic reviews covering 681 unique trials showed mean reduction in A1C of 0.37% (95% CI –0.41% to –0.32%). Another 2025 systematic review and meta-analysis of 54 randomized controlled trials with people with type 2 diabetes and hypertension found a reduction in A1C of 0.45% (95% CI –0.90% to 0.00%) at 6 months and 0.18% (95% CI –0.41% to –0.05%) at 12 months compared with standard care, and systolic blood pressure was reduced by 5.63 mmHg (95% CI –9.13 to –2.13) at 6 months and 5.59 mmHg (95% CI –10.03 to –1.14) at 12 months compared with standard care (49). For people with type 1 diabetes, a 2023 systematic review and meta-analysis of 22 randomized controlled trials showed a reduction in A1C of 0.26% (95% CI –0.37% to –0.15%) (50). Furthermore, telehealth has been increasingly shown to help rural populations or those with limited physical access to health care in glycemic management as measured by A1C (51–54). In addition, evidence supports the effectiveness of telehealth in hypertension and dyslipidemia interventions (55). Interactive strategies that facilitate communication between health care professionals and people with diabetes, including the use of web-based portals or text messaging and those that incorporate medication adjustment, appear to be effective in improving outcomes (52,56).

Telehealth and other virtual environments can be used to offer diabetes self-management education (DSME), carbohydrate counting instruction, and clinical support while reducing geographic and transportation barriers for individuals living in underresourced areas or with disabilities (57). Telehealth resources can also have a role in improving diabetes management in children and adolescents with type 1 diabetes (58) and addressing SDOH in young adults with diabetes (59). Beyond pediatric populations,

telehealth has demonstrated effectiveness in reducing disparities and improving glycemic outcomes in racially and ethnically diverse adults with type 2 diabetes. A systematic review and meta-analysis of nine telehealth randomized controlled trials aimed at improving A1C among Black and Hispanic adults with type 2 diabetes (>50% sample) found a –0.47% (95% CI –0.65% to –0.28%) change in A1C (60). While this systematic review and meta-analysis reported improved glycemic outcomes in marginalized populations, these successes typically depend on substantial investments in infrastructure (laptops, mobile phone access, internet access) and targeted support (digital literacy education, community health workers [CHWs]) that are rarely part of routine care (61). Without this infrastructure and support, attrition is high. Research on technology and inequities highlights that the digital divide is driven by financial (cost of data plans, high-speed internet), informational (numeracy, literacy, digital skills), and technical (interoperability gap, complex user interfaces) barriers (62). Therefore, effective telehealth design must consider accessibility, affordability, connectivity, trust, and contextual tailoring (62). Failure to do so risks exacerbating existing inequities.

Successful diabetes care also requires a systematic approach to supporting the behavior change efforts of people with diabetes. High-quality DSMES has been shown to improve a person's self-management, satisfaction, and glycemic outcomes (see section 5, "Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes," for a detailed review of the evidence supporting DSMES). National DSMES standards call for an integrated approach that includes clinical content and skills, behavioral strategies (goal setting, problem-solving, etc.), and engagement with psychosocial concerns (63). Increasingly, such support is available through online or mobile platforms that can support user access and effectiveness. Findings from a 2025 systematic review and meta-analysis of 43 randomized controlled trials comparing DSME, diabetes self-management support, or DSMES delivered via mHealth interventions versus usual care or attention placebo control showed modest A1C benefits: DSME MD –0.3% (95% CI –0.6% to –0.1%; $P = 0.002$), diabetes self-management support MD –0.4% (95% CI –0.6% to –0.2%;

$P < 0.001$), and DSMES MD -0.2% (95% CI -0.3% to -0.0% ; $P < 0.001$) (64). These curricula should be tailored to the needs of their intended populations, including demographic characteristics, diabetes knowledge, emotional support, and cultural beliefs, and address the digital divide, i.e., access to the technology required for implementation (54,65,66).

Strategies for System-Level Improvement

Optimal diabetes management requires a systematic approach and coordinated team of health care professionals working in an environment where person-centered, high-quality care is a priority (23,67–69). While many diabetes care processes and access to technologies have improved nationally in the past decade, the overall quality of care for people with diabetes remains suboptimal (13). Efforts to increase the quality of diabetes care include providing care that is concordant with evidence-based guidelines (70), expanding the role of teams to implement more intensive disease management strategies (71), tracking medication-taking behavior (70), redesigning care processes (71), implementing electronic health record (EHR) population health tools (72), empowering and educating people with diabetes (73), reducing financial barriers (74), leveraging telehealth to improve access to care (51), assessing and addressing psychosocial issues (63,75), and engaging community resources and public policies that support healthy lifestyles (76). The National Diabetes Education Program maintains an online resource (cdc.gov/diabetes/php/toolkits/index.html) to help health care professionals design and implement more effective health care delivery systems for people with diabetes. Given the pluralistic needs of people with diabetes and the challenges they experience (complex insulin treatment plans, new technologies, changes in capacity for self-management, etc.) vary over the course of disease management and life span, engagement of an interprofessional team with complementary expertise is essential (25). Findings from a systematic review and meta-analysis of 35 team-based care interventions with adults with type 1 or type 2 diabetes showed a -0.5% (95% CI -0.7 to -0.3) change in A1C, -5.5 mmHg (95% CI -8.1 to -3.0) change in systolic blood pressure, -3.2 mmHg (95% CI -4.8 to -1.5) change in

diastolic blood pressure, -8.0 mg/dL (95% CI -11.8 to -4.3) change in LDL cholesterol, and -7.4 mg/dL (95% CI -13.9 to -0.9) change in total cholesterol (25). Team-based care has also been shown to reduce atherosclerotic cardiovascular disease (ASCVD) risks. Results from the Center for Integrated and Novel Approaches in Vascular-Metabolic Disease (CINEMA) Program demonstrated improvements in ASCVD risk factors and evidence-based therapies with team-based care for adults with type 2 diabetes or prediabetes via reductions in body weight (-5.5 lb [-2.5 kg]), BMI (-0.9 kg/m²), systolic (-3.6 mmHg) and diastolic (-1.2 mmHg) blood pressure, A1C (-0.5%), LDL (-9.0 mg/dL) and total cholesterol (-10.7 mg/dL), triglycerides (-13.5 mg/dL), and absolute 10-year ASCVD risk (-2.4%) (77).

A systematic review concluded that quality improvement (QI) initiatives can significantly improve outcomes for people with diabetes (24). As mandated by the Affordable Care Act, the Agency for Healthcare Research and Quality developed a National Quality Strategy based on three aims: improving the health of populations, improving overall quality and the personal experience of care, and reducing per capita cost (78). QI methods have been documented to improve diabetes device uptake, increase screening for psychosocial needs, and reduce inequities in access to diabetes technologies (79–82). Information and guidance specific to quality improvement and practice transformation for diabetes care are available from the National Institute of Diabetes and Digestive and Kidney Diseases guidance on diabetes care and quality (83).

A successful QI team should include a clinical champion, administrative leader, QI/data specialist, and an individual living with or affected by diabetes. Using patient registries and EHRs, health systems can evaluate the quality of diabetes care being delivered, benchmark metrics, and perform intervention cycles as part of QI strategies (19,72,83). QI can also be used as an effective strategy to support application of clinical practice recommendations by health care professionals.

The ADA recommends that health systems use proven QI methods to translate the Standards of Care recommendations into routine standards of practice.

In addition to QI approaches, other strategies that simultaneously improve the quality of care and potentially reduce

costs are gaining momentum and include reimbursement structures that, in contrast to visit-based billing, reward the provision of appropriate and high-quality care to achieve metabolic goals (84), value-based payments, and incentives that accommodate personalized care goals (67,85). Alignment of payment models, health system care delivery models and resource availability, community-based organizations and supports, and regulatory policies is needed to fully support whole-person, comprehensive care for people with diabetes. See EVIDENCE-BASED CARE DELIVERY AND PAYMENT MODELS TO IMPROVE POPULATION HEALTH, above, for more information.

Access to Care

The Affordable Care Act and Medicaid expansion have increased access to care for many individuals with diabetes, emphasizing the protection of people with preexisting conditions, health promotion, and disease prevention (86). In 2024, population-level data for the U.S. civilian noninstitutionalized population included in the National Health Interview Survey (NHIS) showed that just 4.9% of children and adolescents (aged 17 years and younger), 11.1% of adults aged 18–64 years, and 0.6% of adults aged 65 years and older were uninsured (87). People with diabetes who have consistent private or public insurance coverage (i.e., are not uninsured) are more likely to meet quality indicators for diabetes care (86). However, even individuals with insurance coverage can experience financial barriers to care, particularly if enrolled in high-deductible health plans. In 2021, 28% of individuals with employer-sponsored health plans were enrolled in high-deductible health plans (88). Such plans are increasing in popularity; by 2023, 51% of private industry employees had the option to enroll in a high-deductible health plan, although only 36% had access to health savings accounts, which can offset some of the out-of-pocket costs incurred with high-deductible plans (89). Switching to a high-deductible health plan has been shown to increase financial hardship among people with diabetes (90), decrease and delay screening for retinopathy (91), decrease monitoring of blood pressure and A1C (91), and increase the risks of experiencing both acute (severe hypoglycemia, hyperglycemic crises) (92) and chronic (myocardial infarction, stroke, hospitalization for heart

failure, kidney failure, lower-extremity complications, proliferative retinopathy, and blindness) (93) diabetes complications. However, health plan adoption of preventive drug lists that reduce or eliminate out-of-pocket cost sharing for a wide range of medications used to treat chronic conditions like diabetes reduces out-of-pocket expenditures for people with diabetes and narrows gaps in diabetes care (94). Insurance coverage and formulary design influence treatment decisions; it is essential that payors cover evidence-based diabetes care with minimal cost sharing by people with diabetes. Health care teams should also discuss insurance coverage and financial barriers to care with all individuals with diabetes and pursue therapeutic strategies that minimize financial hardship (74).

Access to primary and specialty care is essential for people with diabetes. While most adults with diabetes have access to a primary care clinician—a 2016 nationally representative population-based study found that 88% of adults with diabetes saw a primary care clinician in the prior year (95)—fewer have access to specialty endocrinology/diabetes care (96). A study of Medicare beneficiaries found that just 33% of older adults with type 1 diabetes, 14% of adults with type 2 diabetes and history of severe hypoglycemia, and 9% of other adults with type 2 diabetes saw an endocrinologist in 2019 (96). Racial and ethnic minoritized individuals, those with low income, those living in rural areas, and those residing in a long-term care facility were less likely to receive endocrinology care. Improving health outcomes for people with diabetes will therefore require improving availability of and access to primary and specialty services, and interdisciplinary care from the full diabetes care team, to meet the full range of their health care needs (Table 1.1).

Cost Considerations

The cost of diabetes medications and devices is an ongoing barrier to achieving glycemic goals and preventing diabetes complications. Medication underuse due to cost has been termed “cost-related medication nonadherence” (here referred to as cost-related barriers to medication use). Based on a national survey conducted in 2021, 18.6% of U.S. adults with type 1 diabetes and 15.8% of adults with insulin-treated type 2 diabetes reported

rationing (i.e., skipping, taking less, and/or delaying) their insulin to save money (97). The ADA Insulin Access and Affordability Working Group has recommended system-level approaches to address this issue, including concepts such as cost-sharing for insured people with diabetes based on the lowest price available, a list price for insulins that closely reflects the net price, and health plans that ensure people with diabetes can access insulin without undue administrative burden or excessive cost (98). In 2021, the Centers for Medicare & Medicaid Services (CMS) launched the Part D Senior Savings Model (99), which required capped monthly out-of-pocket payments for covered insulins at \$35 per insulin per month. In 2022, 43% of stand-alone Part D plan enrollees and 60% of Medicare Advantage Part D plan enrollees participated in the Senior Savings Model (99). Most recently, the Inflation Reduction Act of 2022 capped out-of-pocket payments for insulin at \$35 per insulin per month for all Medicare beneficiaries. A patchwork of solutions has also been introduced for individuals with commercial insurance and those without health insurance. Over the past 5 years, 25 states and the District of Columbia have capped out-of-pocket expenditures for insulin in select state-regulated commercial health plans (100), which has resulted in modest decreases in insulin out-of-pocket spending for eligible enrollees (101). Between 2023 and 2024, three major insulin manufacturers similarly lowered the price of insulin to \$35 per month in select circumstances (102). These programs may help reduce the financial hardship of diabetes management, though many are challenging to navigate, not all people with diabetes can benefit, and costs for insulin delivery and glucose monitoring remain high. Thus, all people with diabetes should be screened for financial hardship of treatment, cost-related barriers to medication use, and rationing of other essential services due to medical costs (103).

The cost of medications (not only insulin) influences prescribing patterns and medication use because of the financial strain on the person with diabetes and the lack of secondary payor support (public and private insurance) for effective approved glucose-lowering, cardiovascular and kidney disease risk-reducing, and obesity management therapies. There is robust evidence of gaps in the use of evidence-

based therapies among individuals from racial and ethnic minoritized backgrounds, those with lower income levels, those living in rural areas, and those with limited insurance coverage (11,104–112). Identifying and addressing financial barriers should be a focus of treatment goals and clinical decisions (104). (See TAILORING TREATMENT FOR SOCIAL CONTEXT.)

TAILORING TREATMENT FOR SOCIAL CONTEXT

Recommendations

1.6 Health systems should assess and address gaps in diabetes care and health outcomes (e.g., by stratifying clinical quality data by factors such as insurance status, race, ethnicity, preferred language for health care discussions, disability, and social determinants of health). **B**

1.7 During clinical encounters, assess for social determinants of health, including food insecurity, **A** housing insecurity, financial barriers, health insurance and health care access, environmental and neighborhood factors, and social capital/social community support, **B** to inform treatment decisions, with referral to appropriate local community resources.

1.8 Provide people with diabetes additional self-management support from lay health coaches, navigators, or community health workers when available. **A** Digital self-management tools or coaches may be considered as appropriate. **B**

1.9 Consider the involvement of community health workers to support management of diabetes and cardiovascular and kidney risk factors, especially in underserved communities and health care systems. **B**

Health inequities related to diabetes and its complications are well documented, are heavily influenced by SDOH, and have been associated with greater risk for developing diabetes, higher disease prevalence, and worse diabetes-related outcomes (4). Greater exposure to adverse SDOH over the life course results in poor health (113). Interventions to address SDOH can improve diabetes-related outcomes (114,115). Using clinical quality data to identify inequities

and opportunities for improvement is valuable for health care professionals, health systems, payors, policymakers, and people with diabetes (116). The Joint Commission requires that all accredited organizations in its ambulatory health care, behavioral health care and human services, critical access hospital, and hospital accreditation programs collect race and ethnicity information and implement specific steps to reduce health care disparities. The Joint Commission specifically requires that organizations designate an individual or individuals to lead efforts to reduce health care disparities, assess health-related social needs and provide information on community resources to meet these needs, identify health care disparities by stratifying quality and safety data using sociodemographic characteristics, develop an action plan to address health care disparities, work to actively reduce health care disparities, and inform key stakeholders about progress to reduce health care disparities (117). The CMS Framework for Health Equity similarly prioritizes collection, reporting, and analysis of standardized individual-level demographic (including race, ethnicity, language, gender identity, sex, sexual orientation, and disability status) and SDOH data as well as assessing for and addressing disparities through improved access to culturally tailored services, team-based care, and community resources (118). Quality measures assessing SDOH screening and intervention have been introduced by the National Committee for Quality Assurance (focused on food, housing, and transportation insecurity) (113) and CMS (focused on food, housing, and transportation insecurity, utility difficulties, and interpersonal safety) (119).

Other than the SDOH, there are many contributors to inequities, including implicit and explicit bias, discriminatory policies and procedures, institutional practices, and both current and historical structural factors that affect health and well-being for individuals and communities (120–122). The ADA recognizes the association between interpersonal, social, economic, and environmental factors and the prevention and treatment of diabetes and has issued a call for research that seeks to better understand how social determinants influence behaviors and how the relationships between these variables can be modified for enhancing the prevention and management of diabetes (114). While a comprehensive strategy to reduce diabetes-related health

disparities in populations is yet to be formally studied, general recommendations from other chronic disease management and prevention models can be drawn upon to inform system-level strategies in diabetes (62). For example, the National Academy of Medicine has published a framework for educating health care professionals on the importance of SDOH (123). Furthermore, there are resources available for the inclusion of standardized sociodemographic variables in EHRs to facilitate the assessment of health disparities and the impact of interventions designed to reduce those disparities (78,124,125).

SDOH are not consistently recognized and often go undiscussed—and are ultimately not addressed—during clinical encounters (126). Even financial barriers to care and health, which directly affect the ability to implement prescribed care plans, are rarely discussed. Among people with chronic illnesses, two-thirds of those who reported not taking medications as prescribed due to cost-related barriers never shared this information with their physician (123). A study using data from the NHIS found that half of adults with diabetes reported financial stress and about 20% reported food insecurity (126). Studies of both type 1 diabetes and type 2 diabetes have noted an association of one or more adverse SDOH with health care utilization and poor diabetes outcomes among individuals with diabetes (123,127). It is therefore important for people with diabetes to be screened for SDOH during clinical encounters and be referred to appropriate clinical and community resources to address these needs (**Table 1.1**). Furthermore, health systems may benefit from compiling an inventory of local resources to facilitate referrals at the point of care, augmenting as necessary existing tools such as find-help.org, Unite Us, 211 (United Way), and others. Policies and payment models that support addressing SDOH, both within and outside the health care setting, are needed to ensure that these efforts are both feasible and sustainable. One example of a statewide payment model that incentivizes value-based care, addressing SDOH and funding community-based health care professionals, is the Maryland Total Cost of Care Model, although it is currently limited by a narrow focus on preventing diabetes and does not consider diabetes care

quality or health outcomes in people with diabetes (116,128).

A population in which such issues must be particularly considered is older adults, for whom social difficulties may further impair quality of life and increase the risk of functional dependency (129) (see section 13, “Older Adults,” for a detailed discussion of social considerations in older adults).

Creating system-level mechanisms to screen for SDOH may help overcome structural barriers and communication gaps between people with diabetes and health care professionals (126,130). A number of studies have proven the effectiveness of identifying SDOH by using validated screening tools (131). In addition, brief, validated screening tools for some SDOH exist and could facilitate discussion around factors that significantly impact treatment during clinical encounters.

Food Insecurity

Food insecurity is a household-level economic and social condition of limited or uncertain access to adequate food (132). In 2022, almost 13% of Americans were food insecure (132), and food insecurity is associated with increased risk of type 2 diabetes and higher-than-recommended glycemia (133–135). The rate is disproportionately higher among some groups that have been historically marginalized, low-income households, and households headed by single mothers. Additionally, those facing food insecurity have lower engagement in self-care behaviors and medication use, have higher rates of depression and diabetes distress, and have worse glycemic management compared with individuals who are food secure (133,134). Older adults with food insecurity are more likely to have emergency department visits and hospitalizations compared with older adults who do not report food insecurity (136). The risk for food insecurity can be assessed with a validated two-item screening tool that includes the following statements: 1) “Within the past 12 months, we worried whether our food would run out before we got money to buy more” and 2) “Within the past 12 months the food we bought just didn’t last, and we didn’t have money to get more” (137). Interventions such as food prescription programs are considered promising to address food insecurity by integrating community resources into primary care settings and directly dealing

with food deserts in underserved communities (135).

In those with diabetes and food insecurity, the priority is mitigating the increased risk for severe hyperglycemia and hypoglycemia (138,139). The reasons for the increased risk of hyperglycemia can include the consumption of inexpensive carbohydrate-rich processed foods, binge eating, financial constraints to filling diabetes medication prescriptions, anxiety and depression, and poor sleep, all contributing to hyperglycemia and poor diabetes self-care behaviors. Hypoglycemia can occur as a result of inadequate or inconsistent carbohydrate consumption following the administration of a sulfonylurea or insulin. Health care professionals should consider these factors when making treatment decisions for people with food insecurity and seek local resources to help people with diabetes and their family members obtain appropriate food more regularly (140).

Housing Insecurity

Housing insecurity has been shown to be directly associated with a person's ability to maintain appropriate diabetes self-management (141). Housing insecurity often coexists with other barriers that challenge diabetes self-management. Food insecurity, lack of health insurance, cognitive impairment, behavioral health concerns, and low literacy and numeracy skills are also factors (140). The prevalence of diabetes among people experiencing housing insecurity is estimated to be around 8% in the U.S. (142). Additionally, people with diabetes and housing insecurity need secure places to keep their diabetes medications and supplies as well as refrigerator access to safely store insulin. The risk for housing insecurity can be ascertained using a brief risk assessment tool developed and validated for use among veterans (143). Given the potential challenges, health care professionals who care for housing-insecure individuals should be familiar with resources to support these individuals or have access to social workers who can facilitate stable housing as a way to improve diabetes care (144).

Refugee Populations and Migrant and Seasonal Agricultural Workers

Refugee status, like having a diabetes diagnosis, is an independent risk factor for cardiovascular disease (145). In areas experiencing humanitarian crises, refugees are at greater risk for obstacles to

optimal chronic disease management, but unfortunately there are few quality investigations into diabetes care and its outcomes among refugees. There have been efforts to develop models of care specifically aimed at improving the health of refugee populations, but more work is needed to demonstrate effectiveness of those care models and approaches (146).

Migrant and seasonal agricultural workers likely have a higher risk of type 2 diabetes than the general population. While migrant farmworker-specific data are lacking, most agricultural workers in the U.S. are Latino, a population with a high rate of type 2 diabetes. In addition, living in severe poverty brings with it food insecurity, high chronic stress, and an increased risk of diabetes; there is also an association between the exposure to certain pesticides and the incidence of diabetes (147).

Data from the Department of Labor indicate that there are approximately 2.18 million agricultural workers in the U.S. (148). These agricultural workers often travel throughout the country seasonally (149). In 2022, 175 health centers across the U.S. reported providing care to 843,071 adult migrant farmworkers, and 91,839 had encounters for diabetes (147). In a 2023 report on the National Agricultural Workers Survey, age-adjusted self-reported diabetes prevalence was 13.51% (95% CI 10.0–17.1) among migrant farmworkers and 10.8% (95% CI 9.0–12.6) among nonmigrant farmworkers (147).

Migrant farmworkers and other agricultural workers encounter numerous and overlapping barriers to receiving care. Migration, which might occur as frequently as every few weeks for some, disrupts care. Common barriers to adequate diabetes care include those related to cost, culture, language, literacy, transportation, geographic distance, food access, long work hours, unfamiliarity with new communities, the complexity of the U.S. health care system, and limited access to various other resources like medications and DSMES (149). Without regular care, farmworkers with diabetes can experience severe and often expensive complications that incur morbidity and mortality and affect quality of life. Nontraditional care delivery models, including mobile integrated health and telehealth, should be leveraged to improve access to care.

Health care professionals need to be attuned to the working and living conditions of people with diabetes. For example,

if a farmworker with diabetes presents for care, appropriate referrals should be initiated to social workers and community resources, as available, to assist with removing barriers to care.

Language Barriers

Health systems and health care professionals caring for those with limited English proficiency should develop or offer educational programs and materials in culturally appropriate languages. Professional language assistance (i.e., interpreters) should be provided to individuals with limited English proficiency and/or other communication needs at no cost to them (150). Use of untrained interpreters, including family members, should be avoided when possible, as this can result in confusing or inaccurate conveyance of information. Accompanying written materials should be in the language appropriate for the individual being supported and at a reading level that is not overly complicated—typically this is defined as a sixth-grade reading level. Numerous medical translation tools are available and show promise in addressing language barriers, although further research is needed to establish their efficacy in diabetes care (151).

The National Standards for Culturally and Linguistically Appropriate Services in Health and Health Care (National CLAS Standards) provide guidance on how health care professionals can reduce language barriers by improving their cultural competency, addressing health literacy, and ensuring communication with professional language assistance (150). In addition, the National CLAS Standards website offers several resources and materials that can be used to improve the quality of care delivery to individuals with limited English proficiency.

Health Literacy and Numeracy

Health literacy is the degree to which individuals can obtain, process, and understand basic health information and services needed to make appropriate decisions (152,153). Health literacy is strongly associated with individuals engaging in complex disease management and self-care (154). Approximately 9 out of 10 American adults are estimated to have limited or low health literacy (152,155). Health care professionals and diabetes care and education specialists should provide easy-to-understand

information and reduce unnecessary complexity when developing care plans. Interventions addressing low health literacy in populations with diabetes demonstrate improvements in A1C, diabetes knowledge, and self-management behaviors (156). However, more research is needed to establish the most effective strategies for enhancing retention and application of diabetes knowledge among various populations of people with diabetes (154,157).

Health numeracy is also essential in diabetes prevention and management. Health numeracy requires primary numeric skills, applied health numeracy, and interpretive health numeracy, which is especially important for people using diabetes technologies like insulin pumps (158). People with prediabetes or diabetes often need to perform numeric tasks, such as interpreting glucose readings, decoding food labels, and understanding medication doses, timings, and refills, to make treatment decisions. Thus, both health literacy and numeracy are necessary for enabling effective communication between people with diabetes and health care professionals, arriving at a treatment plan, and making diabetes self-management task decisions. If people with diabetes appear not to understand concepts associated with treatment decisions, both can be assessed using standardized screening measures (159). Adjunctive education and support may be indicated if limited health literacy and numeracy are barriers to optimal care decisions (75).

Social and Community Support

Social support, which comprises community and personal network instrumental support, promotes better health, whereas lack of social support is associated with poorer health outcomes in individuals with diabetes (114). Of particular concern are the SDOH, including, among others, racism and discrimination (160). These factors are rarely addressed in routine clinical practice but may be drivers of adverse health outcomes and lower engagement in beneficial self-care behaviors and medication use. Identifying and leveraging community resources are core components of chronic care management (21,161).

Various organizations, including the American Medical Association and the Agency for Healthcare Research and Quality, among others, promote the translation of clinical recommendations for nutrition

and physical activity into practice through health care community linkages and community-based care delivery (162). CHWs (160), community paramedics (163,164), peer supporters (162,165), and lay leaders (166) may assist in the delivery of DSMES services (124,167), particularly in underserved communities. The American Public Health Association defines a CHW as a “frontline public health worker who is a trusted member of and/or has an unusually close understanding of the community served” (168). CHWs can be part of an evidence-based strategy to improve the management of diabetes and cardiovascular risk factors in underserved communities and health care systems (169). The CHW scope of practice in areas such as outreach and communication, advocacy, social support, basic health education, referrals to community clinics, and other services has successfully provided social and primary preventive services to underserved populations in rural and hard-to-reach communities. Even though CHWs’ core competencies are not clinical in nature, in some circumstances, clinicians may delegate limited clinical tasks to CHWs. If such is the case, these tasks must always be performed under the direct supervision of the delegating health professional and following state health care laws and statutes (170,171). Community paramedics are advanced paramedics with training in chronic disease monitoring and education, medication management, care coordination, and SDOH in addition to their emergency medical services expertise. While their scope of practice varies across states, community paramedics can engage and support people living with diabetes under the direction of a medical director by delivering diabetes education, assisting with medication management, performing health assessments and wound care, and connecting people with diabetes and care partners with clinical and community resources (163,164).

SUMMARY

Improving individual and population health for people with and at risk for diabetes requires engagement of and collaboration between people with diabetes and their caregivers, interprofessional health care teams, health systems, community partners, payors, policymakers, and public health agencies. This section provides guidance to facilitate implementation of evidence-based diabetes care recommendations

that are discussed in the Standards of Care with the goal of improving health, eliminating health disparities, and reducing the impact of diabetes and its complications on individuals and society.

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2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes—2026

American Diabetes Association
Professional Practice Committee for
Diabetes*

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The American Diabetes Association (ADA) “Standards of Care in Diabetes” includes the ADA’s current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. Members of the ADA Professional Practice Committee for Diabetes, an interprofessional expert committee, are responsible for updating the Standards of Care annually, or more frequently as warranted. For a detailed description of ADA standards, statements, and reports, as well as the evidence-grading system for ADA’s clinical practice recommendations and a full list of Professional Practice Committee members, please refer to Introduction and Methodology. Readers who wish to comment on the Standards of Care are invited to do so at professional.diabetes.org/SOC.

Diabetes mellitus is a group of metabolic disorders of carbohydrate metabolism in which glucose is both underutilized as an energy source and overproduced due to inappropriate gluconeogenesis and glycogenolysis, resulting in hyperglycemia (1). Diabetes can be diagnosed by demonstrating increased concentrations of glucose in venous plasma or increased A1C in the blood. Diabetes is classified conventionally into several clinical categories (e.g., type 1 or type 2 diabetes, gestational diabetes mellitus, and other specific types derived from other causes, such as monogenic diabetes, exocrine pancreatic disorders, and high-risk medications) (2).

DIAGNOSTIC TESTS FOR DIABETES

Diabetes may be diagnosed based on A1C or plasma glucose criteria. Plasma glucose criteria include either the fasting plasma glucose (FPG), 2-h plasma glucose (2-h PG) during a 75-g oral glucose tolerance test (OGTT), or random glucose accompanied by classic symptoms of hyperglycemia (e.g., polyuria, polydipsia, and unexplained weight loss) or hyperglycemic crises (i.e., diabetic ketoacidosis [DKA] and/or hyperglycemic hyperosmolar state [HHS]) (Table 2.1).

Recommendations

2.1a Diagnose diabetes based on A1C or plasma glucose criteria. Plasma glucose criteria include either fasting plasma glucose (FPG), 2-h plasma glucose (2-h PG) during a 75-g oral glucose tolerance test (OGTT), or random glucose accompanied by classic hyperglycemic symptoms or crises (Table 2.1). **B**

2.1b In the absence of unequivocal hyperglycemia (e.g., hyperglycemic crises), diagnosis requires confirmatory testing (Table 2.1). **B**

*A complete list of members of the American Diabetes Association Professional Practice Committee for Diabetes can be found at <https://doi.org/10.2337/dc26-SINT>.

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Table 2.1—Criteria for the diagnosis of diabetes in nonpregnant individuals

A1C $\geq 6.5\%$ (≥ 48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*

OR

FPG ≥ 126 mg/dL (≥ 7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*

OR

2-h PG ≥ 200 mg/dL (≥ 11.1 mmol/L) during OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*

OR

In an individual with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥ 200 mg/dL (≥ 11.1 mmol/L). Random is any time of the day without regard to time since previous meal.

DCCT, Diabetes Control and Complications Trial; FPG, fasting plasma glucose; OGTT, oral glucose tolerance test; NGSP, National Glycohemoglobin Standardization Program; WHO, World Health Organization; 2-h PG, 2-h plasma glucose. *In the absence of unequivocal hyperglycemia, diagnosis requires two abnormal results from different tests, which may be obtained at the same time (e.g., A1C and FPG), or the same test at two different time points.

Screening and Diagnosis of Diabetes

FPG, 2-h PG during 75-g OGTT, and A1C are appropriate for screening and diagnosis. It should be noted that detection rates of different screening tests vary in both populations and individuals. FPG, 2-h PG, and A1C reflect different aspects of glucose metabolism, and diagnostic cut points for the different tests will identify groups with incomplete concordance (3). Compared with FPG and A1C cut points, the 2-h PG value diagnoses more people with prediabetes and diabetes (4). Moreover, the efficacy of interventions for primary prevention of type 2 diabetes (i.e., preventing conversion of prediabetes to type 2 diabetes) has been demonstrated mainly among individuals with prediabetes who have impaired glucose tolerance (IGT) with or without elevated fasting glucose, not for individuals with isolated impaired fasting glucose (IFG) or for those with

prediabetes defined by A1C criteria (5–8).

The same tests may be used to screen for and diagnose diabetes and to detect individuals with prediabetes (9) (Table 2.1 and Table 2.2). Diabetes may be identified anywhere along the spectrum of clinical scenarios—in seemingly low-risk individuals who coincidentally undergo glucose monitoring, in individuals screened based on diabetes risk assessment, and in individuals with symptoms and signs of hyperglycemia. There is presently insufficient evidence to support the use of continuous glucose monitoring (CGM) for screening or diagnosis of prediabetes or diabetes. For additional details on the evidence used to establish the criteria for the diagnosis of diabetes or prediabetes, see the American Diabetes Association (ADA) position statement “Diagnosis and Classification of Diabetes Mellitus” (2) and other reports (1,3,10,11).

Table 2.2—Criteria defining prediabetes in nonpregnant individuals

A1C 5.7–6.4% (39–47 mmol/mol)

OR

FPG 100 mg/dL (5.6 mmol/L) to 125 mg/dL (6.9 mmol/L) (IFG)

OR

2-h PG during 75-g OGTT 140 mg/dL (7.8 mmol/L) to 199 mg/dL (11.0 mmol/L) (IGT)

For all three tests, risk is continuous, extending below the lower limit of the range and becoming disproportionately greater at the higher end of the range. FPG, fasting plasma glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test; 2-h PG, 2-h plasma glucose.

Use of Fasting Plasma Glucose or 2-Hour Plasma Glucose for Screening and Diagnosis of Diabetes

In the clinical scenario where a person has classic symptoms of hyperglycemia (e.g., polyuria, polydipsia, unexplained weight loss) or presents with hyperglycemic crisis, measurement of random plasma glucose is sufficient to diagnose diabetes (symptoms of hyperglycemia or hyperglycemic crisis plus random plasma glucose ≥ 200 mg/dL [≥ 11.1 mmol/L]). In these cases, knowledge of the plasma glucose level is critical because, in addition to confirming that symptoms are due to diabetes, it will inform management decisions. In this context, testing A1C helps determine the chronicity of hyperglycemia. However, in an individual without symptoms, FPG or 2-h PG can be used for screening and diagnosis of diabetes. In nonpregnant individuals, FPG (or A1C) is typically preferred for routine screening due to the ease of administration (Table 2.3); however, the 2-h PG (OGTT) testing protocol is significantly more sensitive than the other two tests and is preferentially recommended for screening for some conditions (e.g., cystic fibrosis-related diabetes or post-transplantation diabetes mellitus). In the absence of classic symptoms of hyperglycemia, repeat testing is required to confirm the diagnosis regardless of the test used (see CONFIRMING THE DIAGNOSIS, below).

Major advantages of glucose monitoring are its low cost and availability. Disadvantages include the high diurnal variation in glucose and the 8-h fasting requirements (Table 2.3). Recent physical activity, illness, or acute stress can affect glucose concentrations. Glycolysis is also an important and underrecognized concern with glucose testing. Glucose concentrations will be falsely low if samples are not processed and analyzed promptly (1).

People should follow a mixed eating pattern with at least 150 g of carbohydrates on the 3 days prior to OGTT (12–14). Antecedent carbohydrate restriction in the days prior to OGTT can falsely elevate postchallenge glucose levels, potentially resulting in a false-positive OGTT (12).

Use of A1C for Screening and Diagnosis of Diabetes

Recommendations

2.2a The A1C test should be performed using a method that is certified by the National Glycohemoglobin

Table 2.3—Considerations related to the use and interpretation of laboratory measurements of glucose and A1C

	Glucose	A1C
Cost	Inexpensive and available in most laboratories across the world	More expensive than glucose and not as widely available globally
Time frame of hyperglycemia	Acute measure	Chronic measure of glucose exposure over the past ~2–3 months
Preanalytic stability	Poor; plasma must be separated immediately or samples must be kept on ice to prevent glycolysis	Good
Sample	Measurement can vary depending on sample type (plasma, serum, whole blood) and source (capillary, venous, arterial)	Requires whole-blood sample
Assay standardization	Not standardized	Well standardized
Fasting	Fasting or timed samples required	Nonfasting test; no participant preparation is needed
Within-person variability	High	Low
Acute factors that can affect levels	Food intake, stress, recent illness, activity	Unaffected by recent food intake, stress, illness, activity
Other individual factors that can affect test results	Diurnal variation, medications, alcohol, smoking, bilirubin	Altered erythrocyte turnover (e.g., anemia, iron status, splenectomy, blood loss, transfusion, hemolysis, glucose-6-phosphate dehydrogenase deficiency, erythropoietin), HIV, cirrhosis, kidney failure, dialysis, pregnancy
Test interferences	Depends on specific assay: sample handling/processing time, hemolysis, severe hypertriglyceridemia, severe hyperbilirubinemia	Depends on specific assay: hemoglobin variants, severe hypertriglyceridemia, severe hyperbilirubinemia

Data are from Selvin (236).

Standardization Program (NGSP) as traceable to the Diabetes Control and Complications Trial (DCCT) reference assay. **B**

2.2b Point-of-care A1C testing for diabetes screening and diagnosis should be restricted to devices approved for diagnosis by the U.S. Food and Drug Administration at Clinical Laboratory Improvement Amendments–certified laboratories that perform testing of moderate complexity or higher by trained personnel. **B**

2.3 Evaluate for the possibility of a problem or interference with either test when there is consistent and substantial discordance between blood glucose values and A1C test results. **B**

2.4 In conditions associated with an altered relationship between A1C and glycemia, such as some hemoglobin variants, pregnancy, glucose-6-phosphate dehydrogenase deficiency, HIV, and conditions that may alter red blood cell turnover, plasma glucose criteria should be used to diagnose diabetes. **B**

The A1C test should be performed using a method that is certified by the National Glycohemoglobin Standardization Program (NGSP) (ngsp.org) and standardized or traceable to the Diabetes Control and Complications Trial (DCCT) reference assay. Outside the U.S., some assays are NGSP certified but many more are International Federation of Clinical Chemistry (IFCC) certified (a similarly stringent process) (1).

Point-of-care A1C assays may be NGSP certified and cleared by the U.S. Food and Drug Administration (FDA) for use in monitoring glycemic management in people with diabetes in both Clinical Laboratory Improvement Amendments (CLIA)–regulated and CLIA-waived settings. FDA-approved point-of-care A1C testing can be used in laboratories or sites that are CLIA certified and inspected and meet the CLIA quality standards. These standards include specified personnel requirements (including documented annual competency assessments) and participation three times per year in an approved proficiency testing program (1,15,16).

A1C has several advantages compared with FPG and OGTT, including greater

convenience (fasting is not required), greater preanalytical stability, and fewer day-to-day perturbations during stress, changes in nutrition, or illness. However, it should be noted that there is lower sensitivity of A1C at the designated cut point compared with that of 2-h PG as well as limited access in some parts of the world (**Table 2.3**).

A1C reflects glucose bound to hemoglobin over the life span of the erythrocyte (~120 days) and is thus a “weighted” average that is more heavily affected by recent blood glucose exposure. Thus, clinically meaningful changes in A1C can be seen in <120 days. A1C is an indirect measure of glucose exposure, and factors that affect hemoglobin concentrations or erythrocyte turnover can affect A1C (e.g., thalassemia or folate deficiency) (**Table 2.3**). A1C may not be a suitable diagnostic test in people with anemia, people treated with erythropoietin, or people undergoing hemodialysis or HIV treatment (1,17). Some A1C assays can be affected by hemoglobin variants. For instance, an A1C assay without interference from

hemoglobin variants should be used in individuals with sickle cell trait. An updated list of A1C assays with interferences is available at ngsp.org/interf.asp. Another genetic variant, X-linked glucose-6-phosphate dehydrogenase G202A, carried by 11% of Black individuals in the U.S., is associated with a decrease in A1C of about 0.8% in homozygous men and 0.7% in homozygous women compared with levels in individuals without the variant (18).

There is controversy regarding racial differences in A1C. Studies have found that Black individuals have slightly higher A1C levels (approximately 0.3%) than non-Hispanic White or Hispanic people (19–22). A more precise understanding of the genetic determinants of A1C in diverse populations (18) is the focus of ongoing investigations (23,24). While some genetic variants might be more common in certain race or ancestry groups, it is important that we do not use race or ancestry as proxies for poorly understood genetic differences. Reassuringly, studies have shown that the association of A1C with risk for complications appears to be similar in Black and non-Hispanic White populations (25).

Confirming the Diagnosis

In the absence of a clear clinical diagnosis (e.g., individual with classic symptoms of hyperglycemia or hyperglycemic crisis and random plasma glucose ≥ 200 mg/dL [≥ 11.1 mmol/L]), confirmatory tests are necessary to establish the diagnosis. This can be accomplished by two abnormal screening test results, measured either at the same time (26) or at two different time points. If using samples at two different time points, it is recommended that the second test, which may be either a repeat of the initial test or a different test, be performed in a timely manner. For example, if the A1C is 7.0% (53 mmol/mol) and a repeat result is 6.8% (51 mmol/mol), the diagnosis of diabetes is confirmed. Two different tests (such as A1C and FPG) both having results above the diagnostic threshold when collected at the same time or at two different time points would also confirm the diagnosis. On the other hand, if an individual has discordant results from two different tests, then the test result that is above the diagnostic cut point should be repeated, with careful consideration of

factors that may affect measured A1C or glucose levels. The diagnosis is made based on the confirmatory screening test. For example, if an individual meets the diagnostic criterion for A1C (two results $\geq 6.5\%$ [≥ 48 mmol/mol]) but not FPG (< 126 mg/dL [< 7.0 mmol/L]), that person should nevertheless be considered to have diabetes.

Test results close to the diagnostic threshold should prompt the health care professional to educate the individual about the onset of possible symptoms of hyperglycemia and to repeat the test in 3–6 months.

Consistent and substantial discordance between glucose values and A1C test results should elicit additional follow-up to determine the underlying reason for the discrepancy (including evaluation for the possibility of an analytical problem or interference with either test) and its clinical implications, if any, for the individual (Table 2.3). In this context, alternative validated biomarkers of chronic hyperglycemia such as fructosamine and glycated albumin should be considered for monitoring glycemic management in people with diabetes.

CLASSIFICATION

Recommendation

2.5 Classify people with hyperglycemia into appropriate diagnostic categories to aid in personalized management. **E**

Diabetes is classified conventionally into several clinical categories, although these are being reconsidered based on genetic, metabolomic, and other characteristics and pathophysiology (1):

1. Type 1 diabetes (due to autoimmune β -cell destruction, usually leading to absolute insulin deficiency, including latent autoimmune diabetes in adults)
2. Type 2 diabetes (due to a nonautoimmune progressive loss of adequate β -cell insulin secretion, frequently on the background of insulin resistance)
3. Specific types of diabetes due to other causes, e.g., monogenic diabetes syndromes, diseases of the exocrine pancreas, and drug- or chemical-induced diabetes
4. Gestational diabetes mellitus (diabetes diagnosed in the second or third trimester of pregnancy that was not

clearly overt diabetes prior to gestation or other types of diabetes occurring throughout pregnancy, such as type 1 diabetes)

Type 1 diabetes and type 2 diabetes are heterogeneous diseases in which clinical presentation and disease progression may vary considerably. Classification is important for determining personalized therapy, but some individuals cannot be clearly classified as having type 1 or type 2 diabetes at the time of diagnosis. The traditional paradigms of type 2 diabetes having onset only in adults and type 1 diabetes having onset only in children are not accurate, as both diseases occur in all age groups. Children with type 1 diabetes are often diagnosed in the setting of hallmark symptoms of polyuria/polydipsia, and approximately half present with DKA (27–29). The onset of type 1 diabetes may be more variable in adults, who may not present with the classic symptoms seen in children and may progress to insulin replacement more slowly (30,31). The features most useful in determination of type 1 diabetes include younger age at diagnosis (< 35 years), lower BMI (< 25 kg/m²), unintentional weight loss, ketoacidosis, and plasma glucose > 360 mg/dL (> 20 mmol/L) at presentation (32) (Fig. 2.1). Occasionally, people with type 2 diabetes may present with DKA (33) in the context of ketosis-prone diabetes, particularly members of certain racial, ethnic, and ancestral groups (e.g., Black and Hispanic/Latino adults) (27). The initial requirement for insulin replacement therapy in individuals presenting with ketosis-prone diabetes is generally transient. It is important for health care professionals to realize that classification of diabetes type is not always straightforward at presentation and that misdiagnosis can occur in up to 40% of adults with new type 1 diabetes (e.g., adults with type 1 diabetes misdiagnosed as having type 2 diabetes). In comparison, individuals with maturity-onset diabetes of the young (MODY) may be misdiagnosed as having type 1 diabetes (32). Although difficulties in distinguishing diabetes type may occur in all age groups at onset, the diagnosis generally becomes more obvious in people with marked loss of β -cell function as they rapidly require insulin therapy (Fig. 2.1). Although not prospectively validated, the AABCC approach is a useful tool to help distinguish

Flowchart for investigation of suspected type 1 diabetes in newly diagnosed adults, based on data from White European populations

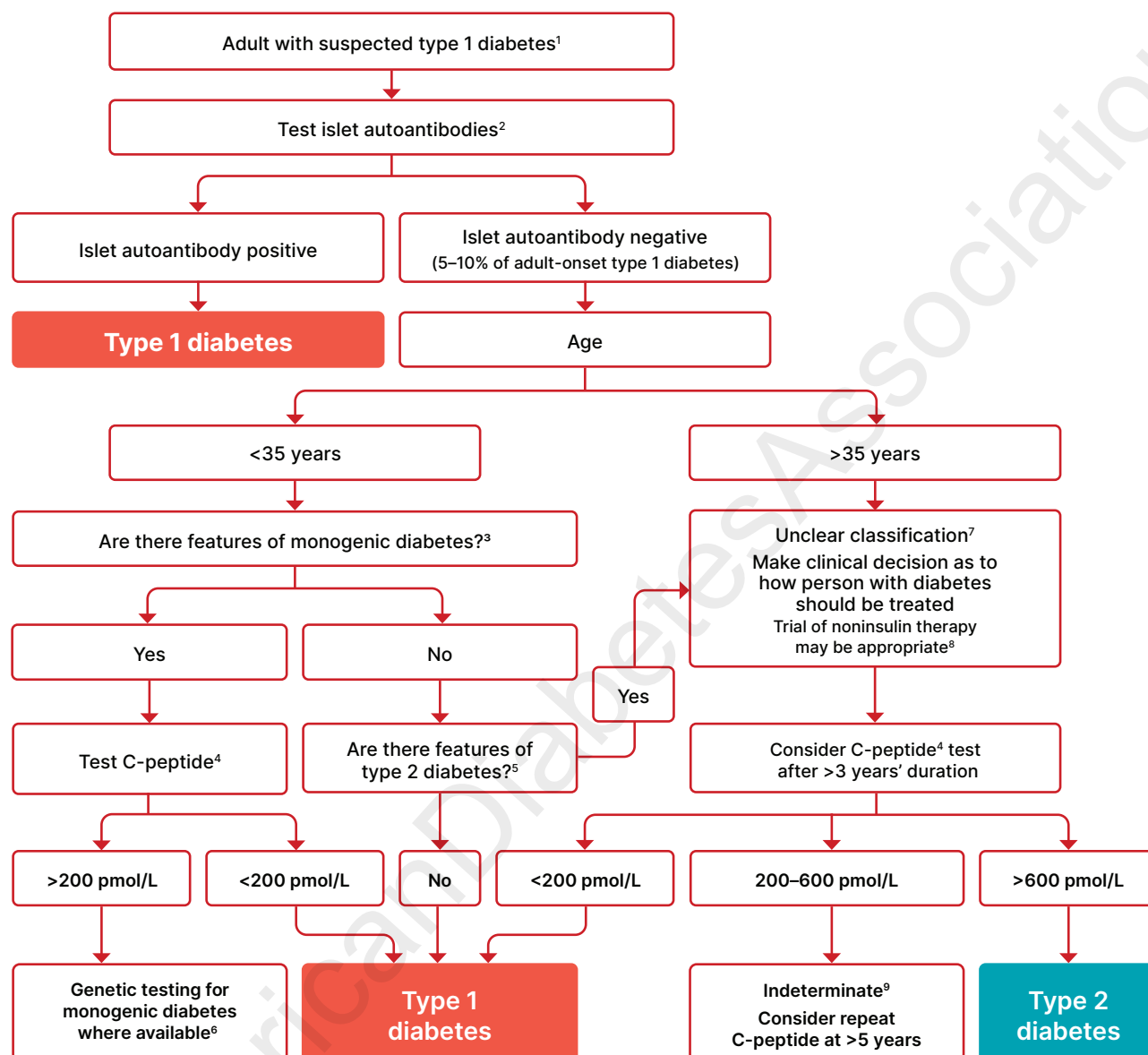


Figure 2.1—Flowchart for investigation of suspected type 1 diabetes in newly diagnosed adults, based on data from White European populations. ¹No single clinical feature confirms type 1 diabetes in isolation. ²Glutamic acid decarboxylase (GAD) should be the primary antibody measured and, if negative, should be followed by islet tyrosine phosphatase 2 (IA-2) and/or zinc transporter 8 (ZnT8) where these tests are available. In individuals who have not been treated with insulin, antibodies against insulin may also be useful. In those diagnosed at <35 years of age who have no clinical features of type 2 diabetes or monogenic diabetes, a negative result does not change the diagnosis of type 1 diabetes, since 5–10% of people with type 1 diabetes do not have antibodies. ³Monogenic diabetes is suggested by the presence of one or more of the following features: A1C <58 mmol/mol (<7.5%) at diagnosis, one parent with diabetes, features of a specific monogenic cause (e.g., renal cysts, partial lipodystrophy, maternally inherited deafness, and severe insulin resistance in the absence of obesity), and monogenic diabetes prediction model probability >5% (diabetesgenes.org/exeter-diabetes-app/Modycalculator). ⁴A C-peptide test is only indicated in people receiving insulin treatment. A random sample (with concurrent glucose) within 5 h of eating can replace a formal C-peptide stimulation test in the context of classification. If the result is ≥600 pmol/L (≥1.8 ng/mL), the circumstances of testing do not matter. If the result is <600 pmol/L (<1.8 ng/mL) and the concurrent glucose is <4 mmol/L (<70 mg/dL) or the person may have been fasting, consider repeating the test. Results showing very low levels (e.g., <80 pmol/L [<0.24 ng/mL]) do not need to be repeated. Where a person is insulin treated, C-peptide must be measured prior to insulin discontinuation to exclude severe insulin deficiency. Do not test C-peptide within 2 weeks of a hyperglycemic emergency. ⁵Features of type 2 diabetes include increased BMI (≥25 kg/m²), absence of weight loss, absence of ketoacidosis, and less marked hyperglycemia. Less discriminatory features include non-White ethnicity, family history, longer duration and milder severity of symptoms prior to presentation, features of metabolic syndrome, and absence of a family history of autoimmunity. ⁶If genetic testing does not confirm monogenic diabetes, the classification is unclear and a clinical decision should be made about treatment. ⁷Type 2 diabetes should be strongly considered in older individuals. In some cases, investigation for pancreatic or other types of diabetes may be appropriate. ⁸A person with possible type 1 diabetes who is not treated with insulin will require careful monitoring and education so that insulin can be rapidly initiated in the event of glycemic deterioration. ⁹C-peptide values 200–600 pmol/L (0.6–1.8 ng/mL) are usually consistent with type 1 diabetes or maturity-onset diabetes of the young but may occur in insulin-treated type 2 diabetes, particularly in people with normal or low BMI or after long duration. Reprinted and adapted from Holt et al. (32).

type 1 from type 2 diabetes: **Age** (e.g., for individuals <35 years old, consider type 1 diabetes); **Autoimmunity** (e.g., personal or family history of autoimmune disease or polyglandular autoimmune syndromes); **Body habitus** (e.g., BMI <25 kg/m²); **Background** (e.g., family history of type 1 diabetes); **Control** (preferred term is “goal,” i.e., the inability to achieve glycemic goals on noninsulin therapies); and **Comorbidities** (e.g., treatment with immune checkpoint inhibitors for cancer can cause acute autoimmune diabetes) (34).

In both type 1 and type 2 diabetes, genetic and environmental factors can result in the progressive loss of β -cell mass and/or function that manifests clinically as hyperglycemia. Once hyperglycemia occurs, people with all forms of diabetes are at risk for developing the same chronic complications, although rates of progression may differ. The identification of individualized therapies for diabetes in the future will be informed by better characterization of the many paths to β -cell demise or dysfunction (35). Ongoing research efforts aim to combine clinical, pathophysiological, and genetic characteristics to more precisely define the subsets of diabetes that are clustered into the current nomenclature with the goal of devising personalized treatment approaches (24). A diagnosis of type 1 diabetes does not preclude also having features classically associated with type 2 diabetes (e.g., insulin resistance, obesity, and other metabolic abnormalities), and until more precise subsets are used in clinical

practice, it may be appropriate to categorize such an individual as having features of both type 1 and type 2 diabetes to facilitate access to glucose monitoring systems and appropriate treatment (e.g., glucagon-like peptide 1 receptor agonist [GLP-1 RA] or sodium–glucose cotransporter 2 [SGLT2] inhibitor therapies for potential weight and other cardiometabolic benefits).

Regarding the pathophysiology of type 1 diabetes, prospective studies showed that the persistent presence of two or more islet autoantibodies is a near-certain predictor of clinical diabetes (36). In at-risk cohorts followed from birth or a very young age, seroconversion rarely occurs before 6 months of age and there is a peak in seroconversion between 9 and 24 months of age (37–39). The rate of progression from preclinical to symptomatic stages of type 1 diabetes is dependent on the age at first detection of an autoantibody, number of autoantibodies, autoantibody specificity, and autoantibody titer. Glucose and A1C levels may rise well before the clinical onset of diabetes (e.g., changes in FPG and 2-h PG can occur about 6 months before diagnosis) (40), making diagnosis feasible under ideal situations of serial monitoring of individuals at high risk of type 1 diabetes before the onset of DKA. The current paradigm of the progression of type 1 diabetes across three distinct stages (**Table 2.4**) also serves as a framework for research and regulatory decision-making (35,41).

There is debate as to whether slowly progressive autoimmune diabetes with an adult onset should be termed latent autoimmune diabetes in adults (LADA) or type 1 diabetes. For this classification, all forms of diabetes mediated by autoimmune β -cell destruction independent of age of onset are included under the rubric of type 1 diabetes. Use of the term LADA is common and acceptable in clinical practice and has the practical impact of heightening awareness that slow autoimmune β -cell destruction can occur in adults (42), thus accelerating insulin initiation prior to deterioration of glucose management or development of DKA (31,43). There is evidence that relying on nonvalidated autoantibody tests for the diagnosis of LADA may lead to misclassification of some individuals with type 2 diabetes. Diagnostic accuracy of LADA may be improved by using higher-specificity tests and confirmatory testing for other autoantibodies and by restricting testing to those with clinical features suggestive of autoimmune diabetes (44).

The paths to β -cell demise and dysfunction are more heterogeneous in type 2 diabetes, but deficient β -cell insulin secretion and β -cell dysfunction, frequently in the setting of insulin resistance, appear to be common denominators. Type 2 diabetes is associated with insulin secretory defects related to genetic predisposition, epigenetic changes, inflammation, and metabolic stress. Future classification schemes for diabetes will likely focus on the pathophysiology of the underlying β -cell dysfunction (24,35,45).

Table 2.4—Staging of type 1 diabetes

	Stage 1	Stage 2	Stage 3
Characteristics	- Autoimmunity - Normoglycemia - Presymptomatic	- Autoimmunity - Dysglycemia - Presymptomatic	- Autoimmunity - Overt hyperglycemia - Symptomatic
Diagnostic criteria	- Multiple islet autoantibodies - No IGT or IFG, normal A1C	- Islet autoantibodies (usually multiple) - Dysglycemia: - IFG: FPG 100–125 mg/dL (5.6–6.9 mmol/L) or - IGT: 2-h PG 140–199 mg/dL (7.8–11.0 mmol/L) or - A1C 5.7–6.4% (39–47 mmol/mol) or $\geq 10\%$ increase in A1C	- Autoantibodies may become absent - Diabetes by standard criteria

Adapted from Skyler et al. (35). FPG, fasting plasma glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; 2-h PG, 2-h plasma glucose. Alternative additional stage 2 diagnostic criteria of 30-, 60-, or 90-min plasma glucose on oral glucose tolerance test ≥ 200 mg/dL (≥ 11.1 mmol/L) and confirmatory testing in those aged ≥ 18 years have been used in clinical trials (82). Dysglycemia can be defined by one or more criteria as outlined in the table.

TYPE 1 DIABETES

Recommendations

2.6 Screen for presymptomatic type 1 diabetes by testing autoantibodies against insulin (IA), glutamic acid decarboxylase (GAD), islet antigen 2 (IA-2), or zinc transporter 8 (ZnT8). **B**

2.7 Autoantibody-based screening for presymptomatic type 1 diabetes should be offered to those with a family history of type 1 diabetes or otherwise known elevated genetic risk. **B**

2.8a Individuals with screening results positive for one or more islet autoantibodies should be evaluated for stage 3 (overt) type 1 diabetes (using A1C, urinalysis, and/or plasma glucose), which would require prompt clinical management and education. **B**

2.8b Individuals with multiple confirmed islet autoantibodies and without overt type 1 diabetes have a high risk for progression to stage 3 type 1 diabetes and should be referred to a specialized center for metabolic staging (Table 2.4), education, and consideration of prevention trials or approved treatments (e.g., teplizumab). **B**

2.9 Individuals with a single confirmed IA-2 autoantibody should be monitored similarly to individuals with multiple islet autoantibodies, as IA-2 autoantibody positivity is an independent risk factor for progression. **B** Individuals with a single confirmed islet autoantibody should undergo repeat antibody testing every 6 months to 3 years (depending on age) to assess for persistence or seroconversion. **E**

2.10 Standardized islet autoantibody tests are recommended for classification of diabetes in adults who have phenotypic risk factors that overlap with those for type 1 diabetes (e.g., younger age at diagnosis, unintentional weight loss, ketoacidosis, or short time to insulin treatment). **E**

Immune-Mediated Diabetes

Autoimmune type 1 diabetes accounts for 5–10% of diabetes and is caused by autoimmune destruction of the pancreatic β -cells. Autoimmune markers include islet cell autoantibodies and autoantibodies to glutamic acid decarboxylase (GAD) (e.g., GAD65), insulin, the tyrosine phosphatases islet antigen 2 (IA-2) and IA-2b, and zinc transporter 8 (ZnT8). Clinical studies are

being conducted to test various methods of preventing or delaying type 1 diabetes in those with evidence of islet autoimmunity (trialnet.org/our-research/prevention-studies) (36–38,43,46,47). The disease has strong HLA associations, with linkage to the *DQB1* and *DRB1* haplotypes, and genetic screening has been used in some research studies to identify high-risk populations. Specific alleles in these genes can be either predisposing (e.g., *DRB1**0301-*DQB1**0201 [DR3-DQ2] and *DRB1**0401-*DQB1**0302 [DR4-DQ8]) or protective (e.g., *DRB1**1501 and *DQA1**0102-*DQB1**0602).

Stage 1 of type 1 diabetes is defined by the presence of two or more of these autoantibodies and normoglycemia (Table 2.4). At stage 1, the 5-year risk of developing symptomatic type 1 diabetes is ~44% overall but varies considerably based on number, titer, and specificity of autoantibodies as well as age of seroconversion and genetic risk (41). Stage 2 includes individuals with islet autoantibodies (usually multiple) and dysglycemia not yet diagnostic of diabetes (dysglycemia can be defined by one or more criteria as outlined in Table 2.4). At time of progression to stage 2, the risk of developing stage 3 type 1 diabetes is ~60% within 2 years and ~75% within 5 years (48,49).

Early diagnostic testing (Table 2.4) for stage 3 type 1 diabetes should be performed promptly in any individual with one or more islet autoantibodies to avoid delays in treatment, which can occur with long wait times for specialty referrals. Identifying overt hyperglycemia early can help prevent DKA at stage 3 diagnosis and guide urgency of referral. In the Diabetes Prevention Trial-Type 1, semiannual OGTT in high-risk family members was associated with a relatively low risk of DKA (4%) at disease presentation compared with individuals who had not been enrolled in a monitoring program (50). A consensus report provides guidance on when to perform repeat antibody testing, how metabolic status should be monitored, and how often these factors should be monitored in individuals with positive autoantibodies (51). A single autoantibody result requires metabolic evaluation, as some individuals may lose detectable antibodies as they approach stage 3. Specifically, individuals who have a single IA-2 autoantibody should be monitored at the same frequency as

multiple-autoantibody-positive individuals, as they have a comparable risk of progressing through type 1 diabetes stages (52). For single non-IA-2 antibody positivity, progression risk is more heterogeneous and depends on age, antibody type, and other risk factors. Evidence from pediatric cohorts shows that among children with a persistent single islet autoantibody, the 10-year cumulative risk of progression to clinical type 1 diabetes is ~14–15%, with much of the risk accruing in the first 2 years after seroconversion and the highest risk being associated with younger age and single IA-2 autoantibody positivity (36). In adults, progression risk is lower and decreases with age, and prospective data to define an optimal cadence are limited; therefore, intervals are extrapolated from pediatric patterns and clinical diabetes expertise. The practical implication of this information is that the four islet autoantibodies (GAD autoantibody, IA-2 autoantibody, insulin autoantibody, ZnT8 autoantibody), a random venous or capillary blood glucose, and an A1C test should be repeated at intervals of 6 months to 3 years based on age. In children ≤ 3 years, test every 6 months for 3 years and then annually for 3 more years. In children and adolescents 3–18 years old, test annually and consider discontinuing after 3 years if no progression to multiple antibodies or onset of dysglycemia. In adults, test every 3 years or annually if additional risk factors are present, such as another autoimmune disease, elevated genetic risk score, or first-degree relative with type 1 diabetes (51).

In adults with stage 3 type 1 diabetes, isolated GAD autoantibody positivity is common and has been associated with slower loss of endogenous insulin production after diagnosis (32). In early stages of type 1 diabetes, single GAD65 autoantibody positivity is also associated with slower progression to stage 3 compared with IA-2 or ZnT8A autoantibody positivity (1,53).

The rate of β -cell destruction is quite variable, being rapid in some individuals (particularly but not exclusively in infants and children) and slow in others (mainly but not exclusively adults) (40,54). Children and adolescents often present with DKA as the first manifestation of the disease, and rates in the U.S. have increased over the past 20 years (27–29). Others have modest fasting hyperglycemia

that can rapidly change to severe hyperglycemia and/or DKA with infection or other stress. Adults may retain sufficient β -cell function to prevent DKA for many years; such individuals may have remission characterized by decreased insulin needs for months or years, but they eventually become insulin dependent and are at risk for DKA (30,31,55–57). At this later stage of the disease, there is little or no insulin secretion, as manifested by low or undetectable levels of plasma C-peptide. Autoimmune destruction of β -cells has multiple genetic factors and is also related to environmental factors that are still poorly defined. Although individuals do not classically have obesity when they present with type 1 diabetes, obesity is increasingly common in the general population; as such, obesity should not preclude testing for type 1 diabetes. People with type 1 diabetes are also prone to other autoimmune disorders, such as Hashimoto thyroiditis, Graves disease, celiac disease, Addison disease, vitiligo, autoimmune hepatitis, myasthenia gravis, and pernicious anemia (see section 4, “Comprehensive Medical Evaluation and Assessment of Comorbidities”). Type 1 diabetes can be associated with monogenic polyglandular autoimmune syndromes, including immune dysregulation, polyendocrinopathy, enteropathy, and X-linked (IPEX) syndrome, which is an early-onset systemic autoimmune, genetic disorder caused by mutation of the forkhead box protein 3 (*FOXP3*) gene, and another disorder caused by the autoimmune regulator (*AIRE*) gene mutation (58,59).

Certain viruses have been associated with type 1 diabetes, including enteroviruses (e.g., Coxsackievirus B). During the early coronavirus disease 2019 (COVID-19) pandemic, several reports noted an increased incidence of hyperglycemia, DKA, and new-onset type 1 diabetes, raising the possibility that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a trigger or accelerator of disease in susceptible individuals (60). More recent large cohort and registry studies from multiple countries report mixed findings, with some showing a modest increased risk of type 1 diabetes following COVID-19 infection and others reporting that the association is largely due to challenges with health care access and diagnostic delays (61,62). These data suggest that both viral effects and indirect pandemic-related factors may have contributed to the initial observed spike of

type 1 diabetes. Research is ongoing to clarify the long-term relationship between SARS-CoV-2 infection and type 1 diabetes risk, including the development of a global registry, the CovidIAB Registry (63).

Immune Checkpoint Inhibitor–Induced Autoimmune Diabetes

The introduction of immunotherapy, specifically immune checkpoint inhibitors (ICIs), for cancer treatment has led to unexpected adverse events, including immune system activation precipitating autoimmune disease. Fulminant onset of autoimmune diabetes can occur with DKA and low or undetectable levels of C-peptide as a marker of endogenous β -cell function (64,65). Fewer than half of these individuals have islet autoantibodies, and most do not experience a phase of partial remission, which is commonly seen in type 1 diabetes, supporting the emerging view of a partially distinct pathophysiology. ICI-induced diabetes occurs in 0.6–1.4% of treated individuals and is more frequent with agents that block the programmed cell death protein 1 (PD-1)/programmed cell death ligand 1 (PDL-1) pathway, alone or in combination with other checkpoint inhibitors (e.g., anticytotoxic T-cell 4-antigen [CTLA-4] antibody) (66). Also, the majority of ICI-related cases of autoimmune diabetes occur in people with high-risk HLA susceptibility haplotype for type 1 diabetes; however, people with either a neutral or typically protective HLA haplotype for type 1 diabetes can also develop ICI-associated diabetes (67). To date, risk cannot be predicted by family history or autoantibodies, so all health care professionals administering these medications or caring for people who have a history of current or past exposure to these agents should be mindful of this adverse effect and educate and monitor individuals appropriately.

Idiopathic Type 1 Diabetes

Some forms of type 1 diabetes have no known etiologies. Individuals have permanent insulinopenia and are prone to DKA but have no evidence of β -cell autoimmunity. However, only a minority of people with type 1 diabetes fall into this category.

Screening for Type 1 Diabetes Risk

The incidence and prevalence of type 1 diabetes are increasing (68). People with type 1 diabetes often present with acute

symptoms of diabetes and markedly elevated blood glucose levels, and 25–50% are diagnosed with life-threatening DKA (27–29). Family history of type 1 diabetes increases the risk of developing type 1 diabetes compared with the general population, but the majority, ~90%, of individuals who develop type 1 diabetes do not have a known relative with the disease. Multiple studies indicate that measuring islet autoantibodies in relatives of those with type 1 diabetes (41), in children from the general population (69,70), or in children from the general population with high genetic risk (71) can identify many individuals who will develop type 1 diabetes. A study reported the risk of progression to type 1 diabetes from the time of seroconversion to autoantibody positivity in three pediatric cohorts from Finland, Germany, and the U.S. Of the 585 children who developed more than two autoantibodies, nearly 70% developed type 1 diabetes within 10 years and 84% within 15 years (36). These findings are highly significant, because while the German group was recruited from offspring of parents with type 1 diabetes, the Finnish and American groups were recruited from the general population. Remarkably, the findings in all three groups were the same, suggesting that the same sequence of events led to clinical disease in both “sporadic” and familial cases of type 1 diabetes. Indeed, the risk of type 1 diabetes increases as the number of relevant autoantibodies detected increases (46,72,73). In The Environmental Determinants of Diabetes in the Young (TEDDY) study, type 1 diabetes developed in 21% of 363 subjects with at least one autoantibody at 3 years of age (74). Such testing, coupled with education about diabetes symptoms and close follow-up, has been shown to enable earlier diagnosis and to prevent DKA (75,76). In several cohort studies, up to 50% of children with only a single autoantibody revert to being islet autoantibody negative during follow-up (77,78). Therefore, it is recommended that the first autoantibody-positive test be confirmed with a second test within 3 months, preferably in a laboratory that meets the performance standards set by the Islet Autoantibody Standardization Program (IASP) (51).

Type 1 diabetes genetic risk scores have been used in newborn screening to identify those at risk for future presentation of the disease. In a simulation

using one such genetic risk score, the majority of those who would go on to develop type 1 diabetes, >77%, could be identified within just 10% of the general population, identifying a subset who may most benefit from autoantibody testing (79). As many genetic risk studies have been performed in populations of European ancestry and discriminatory ability may differ in those of different ancestry, more large case-control cohorts from non-European populations are still needed (80).

Screening programs are available in Europe (e.g., Fr1da and gppad.org), Australia (e.g., type1screen.org), and the U.S. (e.g., trialnet.org, askhealth.org, and cascadekids.org). General population-based screening programs may offer broader testing where high-quality, validated assays and resources for appropriate follow-up of results are available, with several countries considering making such testing part of standard care. In 2023, Italy introduced nationwide screening for type 1 diabetes and celiac disease in the general population aged 1–17 years (81). Individuals who test autoantibody positive should be provided with or referred for counseling about the risk of developing diabetes, diabetes symptoms, and DKA prevention and should be

given consideration for referral to a specialized center for further evaluation and/or consideration of a clinical trial or approved therapy to potentially delay development of clinical diabetes (82).

PREDIABETES AND TYPE 2 DIABETES

Recommendations

2.11 Screening for risk of prediabetes and type 2 diabetes with an assessment of risk factors or validated risk calculator should be done in asymptomatic adults. **B**

2.12a Testing for prediabetes or type 2 diabetes in asymptomatic people should be considered in adults of any age with overweight or obesity who have one or more risk factors (Table 2.5). **B**

2.12b For all other people, screening should begin at age 35 years. **B**

2.12c In people without prediabetes or diabetes after screening, repeat screening recommended at a minimum of 3-year intervals is reasonable, sooner with symptoms or change in risk (e.g., weight gain). **C**

2.13 To screen for prediabetes and type 2 diabetes, FPG, 2-h PG during

75-g OGTT, and A1C are each appropriate (Table 2.1 and Table 2.2). **B**

2.14 When using OGTT as a screening tool for prediabetes or diabetes, adequate carbohydrate intake (at least 150 g/day) should be assured for 3 days prior to testing. **C**

2.15 Risk-based screening for prediabetes or type 2 diabetes should be considered after the onset of puberty or after 10 years of age, whichever occurs earlier, in children and adolescents with overweight (BMI $\geq$ 85th percentile) or obesity (BMI $\geq$ 95th percentile) and who have one or more risk factors for diabetes. (See Table 2.6 for evidence grading of risk factors.) **B**

2.16a Consider screening people for prediabetes or diabetes if they are on certain medications, such as statins, thiazide diuretics, and some HIV medications, as these agents are known to increase the risk of these conditions. **C**

2.16b In people who are prescribed second-generation antipsychotic medications, screen for prediabetes and diabetes at baseline and repeat 12–16 weeks after medication initiation or sooner, if clinically indicated, and annually thereafter. **B**

2.17 People with HIV should be screened for diabetes and prediabetes with an FPG test before starting antiretroviral therapy, at the time of switching antiretroviral therapy, and 3–6 months after starting or switching antiretroviral therapy. If initial screening results are normal, FPG should be checked annually. **E**

2.18 Monitor postprandial or random glucose levels with recurrent or long-term use of glucocorticoids. **B**

Table 2.5—Criteria for screening for diabetes or prediabetes in asymptomatic adults

- Testing should be considered in adults with overweight or obesity (BMI $\geq$ 25 kg/m² or $\geq$ 23 kg/m² in individuals of Asian ancestry) who have one or more of the following risk factors:
 - First-degree relative with diabetes
 - High-risk race, ethnicity, and ancestry (e.g., African American, Latino, Native American, Asian American)
 - History of cardiovascular disease
 - Hypertension ($\geq$ 130/80 mmHg or on therapy for hypertension)
 - HDL cholesterol level $<$ 35 mg/dL ($<$ 0.9 mmol/L) and/or triglyceride level $>$ 250 mg/dL ($>$ 2.8 mmol/L)
 - Individuals with polycystic ovary syndrome
 - Physical inactivity
 - Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans, metabolic dysfunction-associated steatotic liver disease)
- People with prediabetes (A1C $\geq$ 5.7% [$\geq$ 39 mmol/mol], IGT, or IFG) should be tested yearly.
- People who were diagnosed with GDM should have testing at least every 1–3 years.
- For all other people, testing should begin at age 35 years.
- If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results and risk status.
- Individuals in other high-risk groups (e.g., people with HIV, exposure to high-risk medicines, evidence of periodontal disease, history of pancreatitis) should also be closely monitored.

GDM, gestational diabetes mellitus; IFG, impaired fasting glucose; IGT, impaired glucose tolerance.

Prediabetes

Prediabetes is the term used to identify glucose or A1C levels that do not meet the criteria for diabetes yet fall in an intermediate range between normoglycemia and diabetes (25,83). People with prediabetes are defined by the presence of IFG and/or IGT and/or A1C 5.7–6.4% (39–47 mmol/mol) (Table 2.2). Prediabetes is a significant risk factor for progression to diabetes as well as cardiovascular disease and several other cardiometabolic outcomes. Criteria for screening

Table 2.6—Risk-based screening for type 2 diabetes or prediabetes in asymptomatic children and adolescents in a clinical setting

Screening should be considered in youth* who have overweight (≥ 85 th percentile) or obesity (≥ 95 th percentile) **A** and who have one or more additional risk factors:

- Maternal history of diabetes or GDM during the child's gestation **A**
- Family history of type 2 diabetes in first- or second-degree relative **A**
- High-risk race, ethnicity, and ancestry **A** (see **Table 2.5**)
- Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, large- or small-for-gestational-age birth weight) **B**

GDM, gestational diabetes mellitus. *After the onset of puberty or after 10 years of age, whichever occurs earlier. If tests are normal, repeat testing at a minimum of 3-year intervals (or more frequently if BMI is increasing or risk factor profile is deteriorating) is recommended. Reports of type 2 diabetes before age 10 years exist, and this can be considered with numerous risk factors.

for diabetes or prediabetes in asymptomatic adults are outlined in **Table 2.5**. Prediabetes is associated with obesity (especially abdominal or visceral obesity), dyslipidemia with high triglycerides and/or low HDL cholesterol, and hypertension. The presence of prediabetes should prompt a comprehensive screening for cardiovascular risk factors.

Diagnosis of Prediabetes

IFG is defined as FPG levels from 100 to 125 mg/dL (from 5.6 to 6.9 mmol/L) (76,82) and IGT as 2-h PG levels during 75-g OGTT from 140 to 199 mg/dL (from 7.8 to 11.0 mmol/L) (10). It should be noted that the World Health Organization and several diabetes organizations define the IFG lower limit at 110 mg/dL (6.1 mmol/L). The ADA also initially endorsed this IFG lower limit in 1997 (10). However, in 2003 the ADA adopted the new range of 100–125 mg/dL (5.6–6.9 mmol/L) to better define IFG so that the population at risk for developing diabetes with IFG would be comparable to that with IGT (11).

As with the glucose measures, several prospective studies that used A1C to predict the progression to diabetes demonstrated a strong, continuous curvilinear association between A1C and risk of diabetes. In a systematic review of 44,203 individuals from 16 cohort studies with a follow-up interval averaging 5.6 years (range 2.8–12 years), those with A1C between 5.5% and 6.0% (between 37 and 42 mmol/mol) had a substantially increased risk of diabetes (5-year incidence from 9 to 25%). Those with an A1C range of 6.0–6.5% (42–48 mmol/mol) had a 5-year risk of

developing diabetes between 25% and 50% and a relative risk 20 times higher than that with A1C of 5.0% (31 mmol/mol) (84). In a community-based study of Black and non-Hispanic White adults without diabetes, baseline A1C was a stronger predictor of subsequent diabetes and cardiovascular events than fasting glucose (85). Another analysis also indicates that A1C at baseline was a strong predictor of the development of glucose-defined diabetes during the Diabetes Prevention Program (DPP) and its follow-up (7).

An A1C range of 5.7–6.4% (39–47 mmol/mol) identifies a group of individuals at high risk for diabetes and cardiovascular outcomes. These individuals should be informed of their increased risk for diabetes and cardiovascular disease and counseled about effective strategies to lower their risks (see section 3, “Prevention or Delay of Diabetes and Associated Comorbidities”). Similar to glucose measurements, the continuum of risk is continuous and curvilinear: as A1C rises, the diabetes risk rises disproportionately (84). Aggressive interventions and vigilant follow-up should be pursued for those considered at very high risk (e.g., those with A1C $>6.0\%$ [>42 mmol/mol]) and individuals with both IFG and IGT).

Table 2.5 outlines the criteria for screening for prediabetes. The ADA risk test is an additional option (i.e., an awareness tool for the layperson and the health care professional) to determine the appropriateness of screening for diabetes or prediabetes in asymptomatic adults (diabetes.org/diabetes-risk-test). For additional background regarding risk factors and screening

for prediabetes, see screening and testing for prediabetes and type 2 diabetes in asymptomatic adults and screening and testing for prediabetes and type 2 diabetes in children and adolescents, below. For details regarding individuals with prediabetes most likely to benefit from a formal behavioral or lifestyle intervention, see section 3, “Prevention or Delay of Diabetes and Associated Comorbidities.”

Type 2 Diabetes

Type 2 diabetes accounts for 90–95% of all diabetes cases and encompasses individuals who generally have relative (rather than absolute) insulin deficiency in association with insulin resistance (i.e., decreased biological responses to insulin).

The heterogeneity of type 2 diabetes is increasingly recognized and is the subject of intense investigation (86). Although most people with type 2 diabetes have overweight or obesity, which alone causes some degree of insulin resistance, individuals who do not meet BMI criteria for overweight or obesity may have an increased distribution of body fat in the abdominal region, including sites involved in metabolic dysfunction–associated steatotic liver disease (MASLD) and/or ectopic sites (e.g., skeletal muscle).

DKA seldom occurs spontaneously in type 2 diabetes (27) but can arise in individuals with relative insulinopenia in the context of precipitating factors such as the stress of another illness (e.g., COVID-19 infection or myocardial infarction), use of illicit drugs (e.g., cocaine), or with the use of certain medications including glucocorticoids and SGLT2 inhibitors (87,88). HHS is more typically associated with type 2 diabetes (existing or new diagnosis) and is characterized by severe hyperglycemia, hyperosmolality, and dehydration in the absence of significant ketoacidosis. People with diabetes can also have mixed clinical features of both DKA and HHS (27).

Type 2 diabetes frequently goes undiagnosed for many years, because hyperglycemia develops gradually and, at earlier stages, may not be accompanied by classic symptoms and signs of hyperglycemia, such as blurry vision, dehydration, or unintentional weight loss. People with undiagnosed diabetes are exposed to variable degrees of untreated hyperglycemia and are at increased risk of

developing macrovascular and microvascular complications (89).

People with type 2 diabetes initially may have insulin levels that appear normal or elevated, yet the failure to normalize blood glucose reflects a relative defect in glucose-stimulated insulin secretion that is insufficient to compensate for insulin resistance. Insulin resistance may improve with weight reduction, physical activity, and/or pharmacologic treatment of hyperglycemia but is seldom restored to normal. Intensive lifestyle interventions and/or metabolic surgery can lead to diabetes remission (90–93) (see section 8, “Obesity and Weight Management from the Prevention and Treatment of Diabetes”).

The risk of developing type 2 diabetes increases with age, obesity, and lack of physical activity (94,95). It occurs more frequently in individuals with prediabetes, prior gestational diabetes mellitus, or polycystic ovary syndrome. It is also more common in people with hypertension or dyslipidemia and in certain racial, ethnic, and ancestral subgroups (Table 2.5). Finally, treatment with certain medications (e.g., glucocorticoids) can represent a significant risk factor for developing type 2 diabetes. In adults without traditional risk factors for type 2 diabetes and/or of younger age, consider islet autoantibody testing to exclude the diagnosis of type 1 diabetes (32) (Fig. 2.1).

Screening and Testing for Prediabetes and Type 2 Diabetes in Asymptomatic Adults

Screening for prediabetes and type 2 diabetes risk through a targeted assessment of risk factors (Table 2.5) or with an assessment tool, such as the ADA risk test (diabetes.org/diabetes-risk-test), is recommended to guide health care professionals on whether performing a diagnostic test (Table 2.1) is appropriate. Prediabetes and type 2 diabetes meet criteria for conditions in which early detection via screening is appropriate. Both conditions are common and impose significant clinical and public health burdens. There is often a long presymptomatic phase before the diagnosis, and simple tests to detect preclinical disease are readily available (96). The duration of glycemic burden is a strong predictor of adverse outcomes. When considering strategies to prevent the progression to diabetes in people with prediabetes, it is important

to individualize the risk-to-benefit ratio of formal interventions and assess person-centered goals. Risk models have often found higher benefit of intervention in those at highest risk (97) (see section 3, “Prevention or Delay of Diabetes and Associated Comorbidities”) and reduced the risk of diabetes complications (98) (see section 10, “Cardiovascular Disease and Risk Management,” section 11, “Chronic Kidney Disease and Risk Management,” and section 12, “Retinopathy, Neuropathy, and Foot Care”). In the National Institutes of Health (NIH) Diabetes Prevention Program Outcomes Study (DPPOS) report, prevention of progression from prediabetes to diabetes (99) resulted in lower rates of developing retinopathy and nephropathy (100).

Despite the numerous benefits of screening and early diagnosis for prediabetes or diabetes, unfortunately many people in the U.S. and globally either remain undiagnosed or are diagnosed when complications have already arisen.

Additional considerations regarding testing for type 2 diabetes and prediabetes in asymptomatic individuals are described below.

Age

Age is a major risk factor for diabetes. Testing should begin at no later than age 35 years for all people (101). Screening should be considered in adults of any age with overweight or obesity and one or more risk factors for diabetes.

Medications

Screening for prediabetes or diabetes should be performed in people treated with certain medications, such as glucocorticoids, statins (102), thiazide diuretics, some HIV medications (103), and second-generation antipsychotic medications (104), as these drug classes increase the risk of glucose abnormalities, often by promoting insulin resistance.

Alone or in combination with other drugs, glucocorticoids are frequently used for the treatment of a diverse set of conditions including, but not limited to, autoimmune disease (e.g., rheumatoid arthritis), as part of the immunosuppression plan after transplant, or in conjunction with systemic anticancer therapy. The prevalence of glucocorticoid-induced diabetes (hyperglycemia in the absence of preexisting diabetes) depends on the drug’s half-life, dose, and frequency of administration as

well as the duration of treatment. In addition, the presence of common risk factors for diabetes (e.g., obesity) or concomitant use of other offending drugs (e.g., tacrolimus) may also play a role (105). Screening protocols for glucocorticoid-induced diabetes (and worsening hyperglycemia, in people with preexisting diabetes) are not implemented consistently, despite an incidence of up to 18–32% in people treated with supraphysiologic doses (≥ 5 mg of prednisolone or equivalent alternative synthetic glucocorticoid) (106). Thus, educating individuals treated with recurrent or long-term courses of glucocorticoids regarding symptoms of hyperglycemia is essential (107). Of note, it is recommended that screening be performed by checking postprandial plasma glucose (possibly 1–2 h after meals) or random glucose rather than in the fasting state, as glucocorticoid-induced hyperglycemia generally results from insulin resistance. In fact, relying on fasting glucose as a screening test can lead to underdiagnosis and delayed treatment (105,108) (see also section 9, “Pharmacologic Approaches to Glycemic Treatment”).

The ideal frequency of glucose monitoring for screening is not established, as a direct comparison of different monitoring schedules and their diagnostic performance is not available. In the outpatient setting, a proposed pragmatic approach is to check glucose twice weekly and to intensify frequency to daily monitoring if glucose is ≥ 200 mg/dL (109). In the context of cancer treatment, other organizations advocate for daily capillary glucose monitoring and prompt institution of treatment for glucose ≥ 220 mg/dL on two occasions (108,110,111). People treated with second-generation antipsychotic medications require close monitoring because of an increased risk of type 2 diabetes associated with this class of medications, often clustering with dyslipidemia and weight gain. People treated with these agents should be screened for prediabetes or diabetes at baseline, re-screened 12–16 weeks after medication initiation, and annually thereafter (112). Repeat testing can occur sooner if clinically warranted.

People With HIV

People living with HIV are at higher risk for developing prediabetes and diabetes. In addition, some antiretroviral (ARV) therapies may further increase the risk

(113). Therefore, a screening protocol for prediabetes and type 2 diabetes is recommended (114). As the A1C test may underestimate glycemia in people with HIV, plasma glucose criteria are preferred to diagnose prediabetes and diabetes (17).

Diabetes risk is increased with certain protease inhibitors (PIs) and nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs). New-onset diabetes is estimated to occur in more than 5% of individuals infected with HIV on PIs, whereas more than 15% may have prediabetes (115). PIs are associated with insulin resistance and may also lead to apoptosis of pancreatic β -cells. NRTIs also affect fat distribution (both lipohypertrophy and lipoatrophy), which is associated with insulin resistance. For people with HIV and ARV-associated hyperglycemia, it may be appropriate to consider discontinuing the offending ARV agents if safe and effective alternatives are available (116). Before making ARV substitutions, carefully consider the possible effect on HIV virological control and the potential adverse effects of new ARV agents. In some cases, glucose-lowering agents may still be necessary.

Testing Interval

The appropriate interval between screening tests is not known (117). The rationale for the 3-year interval is that with this interval, the number of false-positive tests that require confirmatory testing will be reduced, and individuals with false-negative tests will be retested before substantial time elapses and complications develop (117). In especially high-risk individuals such as those with previous values nearer to the diabetes diagnostic cut point or ongoing treatment with medications listed above, shorter intervals between screenings may be useful.

Community Screening

Ideally, screening should be carried out within a health care setting (including appropriately resourced pharmacies) because of the need for follow-up and treatment (118). Community screening outside a health care setting is generally not recommended because people with positive tests may not seek, or have access to, appropriate follow-up testing and care. However, in specific situations where an adequate referral system is established beforehand for positive tests,

community screening may be considered. Community screening may also be poorly targeted; i.e., it may fail to reach the groups most at risk and inappropriately test those at very low risk or even those who have already been diagnosed (119).

Screening in Dental Practices

Because of the bidirectional relationship between periodontal disease and diabetes, the utility of screening in a dental setting and referral to primary care as a means to improve the diagnosis of prediabetes and diabetes has been explored (120,121). For example, one study estimated that 30% of individuals ≥ 30 years of age seen in general dental practices (including both people with and without periodontal disease) had newly diagnosed dysglycemia (121). Further research is needed to demonstrate the feasibility, effectiveness, and cost-effectiveness of screening in this setting. For additional background on oral health in relation to prediabetes and type 2 diabetes, see section 4, "Comprehensive Medical Evaluation and Assessment of Comorbidities."

Screening and Testing for Prediabetes and Type 2 Diabetes in Children and Adolescents

The epidemiologic studies that formed the basis for the recommendations to use A1C and plasma glucose criteria to diagnose prediabetes and diabetes included only adult populations (122). However, ADA clinical guidance concluded that A1C, FPG, or 2-h PG also could be used to test for prediabetes or type 2 diabetes in children and adolescents (123).

In the last decade, the incidence and prevalence of type 2 diabetes in children and adolescents has increased dramatically, especially in certain high-risk racial, ethnic, and ancestral subgroups (124). See **Table 2.6** for recommendations on risk-based screening for type 2 diabetes or prediabetes in asymptomatic children and adolescents in a clinical setting (123). See **Table 2.1** and **Table 2.2** for the criteria for the diagnosis of diabetes and prediabetes, respectively, that apply to children, adolescents, and adults. See section 14, "Children and Adolescents," for additional information

on type 2 diabetes in children and adolescents.

DIABETES INDUCED BY SYSTEMIC ANTI-CANCER THERAPY

Recommendations

2.19 People starting cancer treatment with immune checkpoint inhibitors (ICIs), including anti-PD-1 or anti-PDL-1 therapy (e.g., nivolumab, pembrolizumab, atezolizumab), phosphoinositidylinositol 3-kinase α (PI3K α) inhibitors (e.g., alpelisib, inavolisib), or mammalian target of rapamycin (mTOR) inhibitors (e.g., everolimus), should be educated regarding risks, symptoms, and signs of hyperglycemia and hyperglycemic crises. **E**

2.20 In people treated with ICIs, fasting or random plasma glucose should be tested before initiating treatment, during each visit, or if symptoms and signs of hyperglycemia develop during or after treatment cessation. **E**

2.21 In people treated with PI3K α inhibitors, fasting or random plasma glucose and A1C should be tested before initiating treatment, and random plasma glucose should be tested weekly for the first 2 weeks of treatment and then every 4 weeks during treatment. **C** Consider testing A1C every 3 months during treatment. **E**

2.22 In people treated with mTOR inhibitors, fasting or random plasma glucose should be tested before starting and at each visit throughout the duration of treatment. Consider testing A1C every 3 months during treatment. **C**

Both acute and chronic endocrine disorders account for a large portion of adverse events reported with cancer treatment (125). Hyperglycemia occurs in 15–50% of people receiving systemic anticancer treatment, as a direct effect of chemotherapeutic agents (e.g., busulfan) or the frequently associated glucocorticoid treatment (126), and represents a risk factor for poor cancer- and treatment-related outcomes (127,128). In this context, people treated with chemotherapy, glucocorticoids, immunotherapy or inhibitors of the phosphatidylinositol 3-kinase (PI3K)/Akt/mammalian target of rapamycin (mTOR) pathway should be provided with education and counseling regarding symptoms of hyperglycemia and glucose testing tools. Specifically,

regarding ICIs, PD-1 (e.g., nivolumab) and PDL-1 inhibitors (e.g., durvalumab) and, to a lesser extent, anti-CTLA-4 antibodies (e.g., ipilimumab), are associated with new-onset autoimmune diabetes in addition to other immune-related adverse events. ICI-induced autoimmune diabetes occurs in 0.6–1.4% of treated people, often presents as DKA, and almost invariably requires lifelong insulin therapy (129). Despite a peak of incidence within 2–3 months from the initiation of treatment (67,130), new onset of ICI-induced diabetes can occur anytime during treatment and has been reported even after discontinuation of ICIs (65,130). Similar to people with newly diagnosed type 1 diabetes, people who develop ICI-induced diabetes should be promptly referred to an endocrinologist and receive appropriate diabetes self-management education. Thus, testing either fasting or random plasma glucose before initiating treatment and at each visit (or for intervening symptoms of hyperglycemia) is a reasonable approach to increase health care professionals' awareness of the metabolic risk of ICIs and reduce the risk of presentation with DKA. Further epidemiological insight and validation of HLA-based risk prediction scores may guide future targeted screening strategies.

Inhibitors targeting the α isoform of PI3K have been approved (e.g., alpelisib, inavolisib) for the treatment of advanced or metastatic breast cancer. Pivotal trials demonstrated that PI3K α inhibitors, when added to standard of care treatment, provided survival benefits but were also associated with the emergence of grade 3 or 4 hyperglycemia in up to 36% of participants, which was the most common reason for drug discontinuation (131,132). A retrospective analysis of adverse events accrued in a phase 3 randomized controlled trial (RCT) showed that the median time to onset for alpelisib-induced hyperglycemia was 13 days, with a range extending to approximately 1 year (133). The current data inform the recommendation to check fasting and random plasma glucose before initiating treatment and to monitor random plasma glucose weekly for the first 2 weeks of therapy and then every 4 weeks or sooner if symptoms of hyperglycemia develop in the interim. Testing A1C every 3 months can also be considered, while recognizing that alone

A1C may not capture the early peak of hyperglycemia noted with PI3K α inhibitors. Inhibitors of mTOR (e.g., everolimus) are associated with hyperglycemia of variable severity but without a definitive peak of onset. In a large meta-analysis that included 3,900 participants treated with everolimus across nine RCTs, the incidence of all-grade hyperglycemia was as high as 27%, whereas grades 3 and 4 were reported in 2.5% of participants (134). In a single-center retrospective cohort study in people with cancer treated with everolimus, the estimated median time to onset of hyperglycemia was 5–6 months, but the incidence distribution extended from a few weeks to several years after the initiation of treatment (135). In the absence of a clear-cut temporal pattern for the onset of hyperglycemia, fasting or random plasma glucose should be checked before treatment initiation and at each visit during treatment with mTOR inhibitors, or sooner if symptoms of hyperglycemia develop in the interim, while monitoring A1C every 3 months can also be considered.

Finally, hyperglycemia is also a relatively frequent complication of Akt inhibitors (e.g., capivasertib) and antibody drug conjugates (e.g., enfortumab vedotin), which will not be reviewed.

PANCREATIC DIABETES OR DIABETES IN THE CONTEXT OF DISEASE OF THE EXOCRINE PANCREAS

Recommendation

2.23 Screen people for diabetes within 3–6 months following an episode of acute pancreatitis and annually thereafter. Screening for diabetes is recommended annually for people with chronic pancreatitis. **E**

Pancreatic diabetes (also termed pancreatogenic diabetes or type 3c diabetes) includes both structural (e.g., destruction or removal of normal pancreatic tissue) and functional loss of insulin secretion in the context of exocrine pancreatic insufficiency and is commonly misdiagnosed as type 2 diabetes. The diverse set of etiologies includes pancreatitis (acute and chronic pancreatic inflammation and associated fibrosis leading to loss of functional exocrine and endocrine pancreatic function),

trauma or pancreatectomy, neoplasia, cystic fibrosis (addressed later in this section), hemochromatosis, fibrocalculous pancreatopathy, rare genetic disorders, and idiopathic forms (2); as such, pancreatic diabetes is the preferred umbrella term (136).

Acute (even a single bout) and chronic pancreatitis can lead to postpancreatitis diabetes mellitus (137). A distinguishing feature is concurrent pancreatic exocrine insufficiency (consider screening individuals with acute and chronic pancreatitis for exocrine pancreatic insufficiency by measuring fecal elastase), pathological pancreatic imaging (endoscopic ultrasound, MRI, and computed tomography), and absence of type 1 diabetes-associated autoimmunity (138–141). Risk for microvascular complications appears to be similar to that of other forms of diabetes.

For people with pancreatitis and diabetes, glucose-lowering therapies potentially associated with increased risk of pancreatitis (i.e., incretin-based therapies) should be avoided. Early initiation of insulin therapy should be considered. In the context of pancreatectomy, islet autotransplantation can be considered for selected individuals with medically refractory chronic pancreatitis in specialized centers to preserve, fully or partially, endogenous islet function and insulin secretion (142,143).

Cystic Fibrosis–Related Diabetes

Recommendations

2.24a Annual screening for cystic fibrosis–related diabetes (CFRD) should begin by age 10 years in all people with cystic fibrosis, preferably using OGTT. **B**

2.24b If an OGTT is not feasible, A1C can be used as an alternative method as part of a two-step screening strategy. Individuals with A1C values between 5.5% and 6.4% (37 and 47 mmol/mol, respectively) should undergo an OGTT within 3 months. **C** An A1C value of $\geq 6.5\%$ (≥ 48 mmol/mol) is consistent with a diagnosis of CFRD. **B**

2.25 Beginning 5 years after the diagnosis of CFRD, annual monitoring for complications of diabetes is recommended. **E**

Cystic fibrosis is an autosomal recessive multisystem condition arising from

recessive mutations in the gene encoding the cystic fibrosis transmembrane conductance regulator (CFTR) protein. Cystic fibrosis-related diabetes (CFRD) is a common comorbidity in people living with cystic fibrosis that is distinct from type 1 or type 2 diabetes and is often accompanied by pancreatic exocrine insufficiency (144). CFRD occurs in about 20% of adolescents and 50% of adults (145) and is associated with worse nutritional status and increased morbidity and mortality (146). Although insufficient insulin secretion is the primary defect in CFRD, insulin resistance can also occur in the setting of intervening illnesses and treatment with glucocorticoids. Current guidelines recommend screening for CFRD in people living with cystic fibrosis starting at age 10 years. Although screening for diabetes before the age of 10 years can identify risk for progression to CFRD in those with IGT, no benefit has been established with respect to weight, height, BMI, or lung function (145). Based on its elevated predictive value (147), OGTT is the recommended screening test for CFRD in all people living with cystic fibrosis, if feasible, and should be repeated annually. However, engagement in current CFRD screening guidelines is poor, with only 30–40% of adults with cystic fibrosis having annual OGTTs (148,149).

In this context, other professional organizations have advocated for the use of A1C as part of a two-step screening strategy as an alternative to OGTT and to maximize the diagnostic yield of OGTT (150). Specifically, a retrospective study investigating the diagnostic performance of OGTT vis-à-vis A1C in 256 community-dwelling people living with cystic fibrosis, age 10–18 years, showed that A1C of 5.5% and 5.8% provided a sensitivity of 91% and 95%, respectively, to detect CFRD by OGTT (151). A1C 5.5% also afforded a negative predictive value for CFRD of approximately 98%, thus making A1C an effective first-line screening tool to identify people living with cystic fibrosis who should not undergo further testing with OGTT. In this framework alternative to the annual OGTT, only people living with cystic fibrosis with A1C 5.5–6.4% would proceed with OGTT. A1C $\geq 6.5\%$ (≥ 48 mmol/mol) is consistent with a diagnosis of CFRD (152–154) and should be followed by a confirmatory test (preferably a repeat A1C or an

OGTT, as the sensitivity of FPG is lower in people living with cystic fibrosis). Regardless of age, weight loss or failure of expected weight gain is a risk for CFRD and should prompt screening (152,153). In the Cystic Fibrosis Foundation Patient Registry (155) that evaluated 3,553 people living with cystic fibrosis, of whom 13% had CFRD, early diagnosis and treatment of CFRD was associated with preservation of lung function. While CGM (156) may be more sensitive than OGTT for capturing early phases of dysglycemia, the lack of validated CGM thresholds or metrics to diagnose CFRD precludes, for now, recommending the use of CGM as a screening tool outside the research setting (145). There is inadequate evidence presently to alter CFRD screening based on use of highly effective CFTR modulator therapy, which uses small-molecule compounds that directly correct the basic defect of the CFTR channel and restore channel function (145).

Limited clinical trial data exist to inform optimal therapy for CFRD. People with CFRD should be treated with insulin to attain individualized glycemic goals. See section 9, “Pharmacologic Approaches to Glycemic Treatment,” for further information.

POSTTRANSPLANTATION DIABETES MELLITUS

Recommendations

2.26 After organ transplantation, screening for hyperglycemia should be done. A formal diagnosis of posttransplantation diabetes mellitus (PTDM) is best made once the individual is stable on an immunosuppressive plan and in the absence of an acute infection. **B**

2.27 The OGTT is the preferred test to make a diagnosis of PTDM. **B**

2.28 Immunosuppressive plans shown to provide the best outcomes for individuals and graft survival should be used, irrespective of PTDM risk. **E**

Several terms are used in the literature to describe the presence of diabetes following organ transplantation (157). New-onset diabetes after transplantation (NODAT) is one such designation that describes individuals who develop new-onset diabetes following transplant. NODAT

excludes people with pretransplant diabetes who were undiagnosed as well as posttransplant hyperglycemia that resolves by the time of discharge (158). Another term, posttransplantation diabetes mellitus (PTDM) (158,159), describes the presence of diabetes in the posttransplant setting irrespective of the timing of diabetes onset. The clinical importance of PTDM lies in its impact as a significant risk factor for cardiovascular disease and chronic kidney disease in solid-organ transplantation (157).

Hyperglycemia is very common during the early posttransplant period, with ~90% of kidney allograft recipients exhibiting hyperglycemia in the first few weeks following transplant (158–161). In most cases, such stress- or glucocorticoid-induced hyperglycemia resolves by the time of discharge (161,162). Although the use of immunosuppressive therapies is a major contributor to the development of PTDM, the risks of transplant rejection outweigh the risks of PTDM, and the role of the diabetes health care professional is to treat hyperglycemia appropriately regardless of the type of immunosuppression (158). Risk factors for PTDM include both general diabetes risks (such as age, family history of diabetes, and obesity) and transplant-specific factors, such as use of immunosuppressant agents (163–165). Whereas hyperglycemia in the early period after transplantation is an important risk factor for subsequent PTDM, a formal diagnosis of PTDM is optimally made once the individual is stable on maintenance immunosuppression (usually 3 months) and in the absence of acute infection (158,161–163,166).

OGTT is the recommended test for the diagnosis of PTDM as early as 3 months posttransplant (158). However, screening people with FPG and/or A1C can identify high-risk individuals who require further assessment and may reduce the number of overall OGTTs required.

Few RCTs have reported on the short- and long-term use of glucose-lowering medications in the setting of PTDM (163,167,168). Most studies have reported that transplant individuals with hyperglycemia and PTDM after transplantation have higher rates of rejection, infection, and rehospitalization (161,163,169). Insulin therapy is the agent of choice for the management of hyperglycemia and diabetes in the hospital setting and can be continued

postdischarge. Noninsulin glucose-lowering therapies can also be used for long-term management. The choice of agent is usually made based on the side effect profile of the medication, possible interactions with the individual's immunosuppression plan, and potential cardiovascular and kidney benefits in individuals with PTDM (163). See section 9, "Pharmacologic Approaches to Glycemic Treatment," for further information.

MONOGENIC DIABETES SYNDROMES

Recommendations

- 2.29a** Regardless of current age, all people diagnosed with diabetes in the first 6 months of life should have genetic testing for neonatal diabetes. **A**
- 2.29b** Children and young adults who do not have typical characteristics of type 1 or type 2 diabetes and have a family history of diabetes in successive generations (suggestive of an autosomal-dominant pattern of inheritance) should have genetic testing for maturity-onset diabetes of the young (MODY). **A**
- 2.29c** In both instances, consultation with a center specializing in diabetes genetics is recommended to understand the significance of genetic mutations and how best to approach further evaluation, treatment, and genetic counseling. **E**

Monogenic defects that cause β -cell dysfunction (e.g., neonatal diabetes and MODY) or insulin resistance syndromes (e.g., monogenic lipodystrophies) are present in a small fraction of people with diabetes (<5%) (170). **Table 2.7** describes the most common causes of monogenic diabetes. For a comprehensive list of causes, see *Genetic Diagnosis of Endocrine Disorders* (171) and ISPAD 2022 clinical practice consensus guidelines (170).

Diagnosis of Monogenic Diabetes

The diagnosis of monogenic diabetes should be considered in children and adults diagnosed with diabetes in early adulthood with the following findings:

- Diabetes diagnosed within the first 6 months of life (170,172)
- Diabetes without typical features of type 1 or type 2 diabetes (negative

diabetes-associated autoantibodies, no obesity, and lacking other metabolic features, especially strong family history of diabetes)

- Stable, mild fasting hyperglycemia (100–150 mg/dL [5.6–8.5 mmol/L]), stable A1C between 5.6 and 7.6% (between 38 and 60 mmol/mol), especially if no obesity

Neonatal Diabetes

Diabetes occurring under 6 months of age is termed neonatal diabetes, and about 80–85% of cases can be found to have an underlying monogenic cause (32,172–175). Neonatal diabetes occurs much less often after 6 months of age, whereas autoimmune type 1 diabetes rarely occurs before 6 months of age. Neonatal diabetes can either be transient or permanent. Transient diabetes is most often due to overexpression of genes on chromosome 6q24, is recurrent in about half of cases, and may be treatable with medications other than insulin. Permanent neonatal diabetes is most commonly due to autosomal dominant mutations in the genes encoding the Kir6.2 subunit (*KCNJ11*) and SUR1 subunit (*ABCC8*) of the β -cell K_{ATP} channel.

The ADA-European Association for the Study of Diabetes type 1 diabetes consensus report recommends that regardless of current age, individuals diagnosed under 6 months of age should have genetic testing (32). Correct diagnosis has critical implications, because 30–50% of people with K_{ATP} -related neonatal diabetes will exhibit improved blood glucose levels when treated with high-dose oral sulfonylureas instead of insulin. Insulin gene (*INS*) mutations are the second most common cause of permanent neonatal diabetes, with insulin therapy being the preferred treatment strategy.

Maturity-Onset Diabetes of the Young

MODY is frequently characterized by onset of hyperglycemia at an early age (classically before age 25 years, although diagnosis may occur at older ages). MODY is characterized by impaired insulin secretion with minimal or no defects in insulin action (in the absence of coexistent obesity). It is inherited in an autosomal dominant pattern with abnormalities in at least 14 genes on different chromosomes identified to date (170). The most common forms

are GCK-MODY (MODY2), HNF1A-MODY (MODY3), and HNF4A-MODY (MODY1).

Correct diagnosis of monogenic forms of diabetes is critical because people who have them may be incorrectly diagnosed with type 1 or type 2 diabetes, leading to suboptimal, even potentially harmful, treatment plans and delays in diagnosing other family members (170). A diagnosis of MODY should be considered in individuals who have atypical diabetes and multiple family members with diabetes not characteristic of type 1 or type 2 diabetes (173–180) (**Fig. 2.1**). In most cases, the presence of autoantibodies for type 1 diabetes precludes further testing for monogenic diabetes, but the presence of autoantibodies in people with monogenic diabetes has been reported. Individuals in whom monogenic diabetes is suspected should have genetic testing. Genetic screening (i.e., next-generation sequencing) is increasingly available and cost-effective (170). Consultation with a center specializing in diabetes genetics is recommended to understand the significance of genetic mutations and how best to approach further evaluation, treatment, and genetic counseling. Genetic counseling is recommended to ensure that affected individuals understand the patterns of inheritance and the importance of a correct diagnosis and to address comprehensive cardiovascular risk.

A diagnosis of one of the three most common forms of MODY, HNF1A-MODY, GCK-MODY, and HNF4A-MODY, allows for more cost-effective personalized therapy (i.e., no therapy for GCK-MODY and sulfonylureas as first-line therapy for HNF1A-MODY and HNF4A-MODY). See section 9, "Pharmacologic Approaches to Glycemic Treatment," for further information. Additionally, diagnosis can lead to identification of other affected family members and can indicate potential extrapancreatic complications in affected individuals.

GESTATIONAL DIABETES MELLITUS

Recommendations

- 2.30** In individuals who are planning pregnancy, screen those with risk factors (**Table 2.5**) **B** and consider testing all individuals of childbearing potential for undiagnosed prediabetes or diabetes. **E**

Table 2.7—Most common causes of monogenic diabetes

	Gene	Inheritance	Clinical features
MODY	<i>HNF1A</i>	AD	HNF1A-MODY: progressive insulin secretory defect with presentation in adolescence or early adulthood; lowered renal threshold for glucosuria; large rise in 2-h PG level on OGTT (>90 mg/dL [>5 mmol/L]); low hs-CRP; sensitive to sulfonylureas
	<i>GCK</i>	AD	GCK-MODY: higher glucose threshold (set point) for glucose-stimulated insulin secretion, causing stable, nonprogressive elevated fasting blood glucose; typically does not require treatment in nonpregnant individuals; microvascular complications are rare; small rise in 2-h PG level on OGTT (<54 mg/dL [<3 mmol/L])
	<i>HNF4A</i>	AD	HNF4A-MODY: progressive insulin secretory defect with presentation in adolescence or early adulthood; may have large birth weight (macrosomia) and transient neonatal hypoglycemia; sensitive to sulfonylureas
	<i>HNF1B</i>	AD	HNF1B-MODY: developmental renal disease (typically cystic); genitourinary abnormalities; atrophy of the pancreas; hyperuricemia; gout
Neonatal diabetes			
Permanent	<i>KCNJ11</i>	AD	IUGR; possible developmental delay and seizures; responsive to sulfonylureas
	<i>ABCC8</i>	AD	IUGR; rarely developmental delay; responsive to sulfonylureas
	<i>INS</i>	AD	IUGR; insulin requiring
	<i>FOXP3</i>	X-linked	Immunodysregulation, polyendocrinopathy, enteropathy X-linked (IPEX) syndrome: autoimmune diabetes, autoimmune thyroid disease, exfoliative dermatitis; insulin requiring
Transient	6q24 (<i>PLAGL1</i> , <i>HYMA1</i>)	AD for paternal duplications	IUGR; macroglossia; umbilical hernia; may be treatable with medications other than insulin

Adapted from Carmody et al. (171). AD, autosomal dominant; AR, autosomal recessive; IUGR, intrauterine growth restriction; OGTT, oral glucose tolerance test; UPD6, uniparental disomy of chromosome 6; 2-h PG, 2-h plasma glucose.

2.31a Before 15 weeks of gestation, test individuals with risk factors (Table 2.5) **B** and consider testing all individuals **E** for undiagnosed diabetes at the first prenatal visit using standard diagnostic criteria if not screened preconception.

2.31b Before 15 weeks of gestation, screen for abnormal glucose metabolism (defined as A1C 5.9–6.4% [41–47 mmol/mol] or FPG 110–125 mg/dL [6.1–6.9 mmol/L]) to identify individuals who are at higher risk of adverse pregnancy and neonatal outcomes and are at high risk of a later gestational diabetes mellitus (GDM) diagnosis. **B**

2.32 Screen for GDM at 24–28 weeks of gestation in pregnant individuals not previously found to have diabetes or high-risk abnormal glucose metabolism detected earlier in the current pregnancy. **A**

2.33 Screen individuals with GDM for prediabetes or diabetes at 4–12 weeks postpartum, using the 75-g

OGTT and clinically appropriate non-pregnancy diagnostic criteria. **B**

2.34 Individuals with a history of GDM should have lifelong screening for the development of prediabetes or diabetes every 1–3 years. **B**

Definition

For many years, gestational diabetes mellitus (GDM) was defined as any degree of glucose intolerance that was first recognized during pregnancy (11) regardless of the degree of hyperglycemia. This definition facilitated a uniform strategy for detection and classification of GDM, but it also has limitations. First, the best evidence reveals that many cases of GDM represent preexisting hyperglycemia that is detected by routine screening in pregnancy, as routine screening is not widely performed in nonpregnant individuals of reproductive age. The ongoing epidemic of obesity and diabetes has led to more type 2 diabetes in people of reproductive age, with an increase in

the number of pregnant individuals with undiagnosed type 2 diabetes in early pregnancy (181–183). Ideally, undiagnosed diabetes should be identified preconception in individuals with risk factors or in high-risk populations (184–189), as they are likely to benefit from preconception care. The preconception care of people with known preexisting diabetes results in lower A1C and reduced risk of birth defects, preterm delivery, perinatal mortality, small-for-gestational-age birth weight, and neonatal intensive care unit admission (190). If individuals are not screened prior to pregnancy, universal early screening at <15 weeks of gestation for undiagnosed diabetes may be considered over selective screening (Table 2.5), particularly in populations with high prevalence of risk factors and undiagnosed diabetes in people of childbearing age. Strong racial and ethnic disparities exist in the prevalence of undiagnosed diabetes. Therefore, early screening provides an initial step to identify and address these health disparities (186–189). Diagnostic criteria

for identifying undiagnosed diabetes in early pregnancy are the same as those used in nonpregnant individuals (**Table 2.1**). Individuals found to have diabetes should be classified as having diabetes complicating pregnancy (most often type 2 diabetes, rarely type 1 diabetes or monogenic diabetes) and managed accordingly.

Early abnormal glucose metabolism, defined as a fasting glucose threshold of 110 mg/dL (6.1 mmol/L) or an A1C of 5.9% (41 mmol/mol), may identify individuals who are at higher risk of adverse pregnancy and neonatal outcomes (pre-eclampsia, macrosomia, shoulder dystocia, and perinatal death) and are at high risk of a later GDM diagnosis (191–194). Some, but not all, studies showed that an A1C threshold of 5.7% (39 mmol/L) was associated with adverse perinatal outcomes (193,195–197). Professional society guidance regarding early-pregnancy diagnosis and treatment of hyperglycemia less than overt diabetes differs (see section 15, “Management of Diabetes in Pregnancy”).

If early screening for undiagnosed diabetes was negative, individuals should be rescreened for GDM between 24 and 28 weeks of gestation, and individuals not previously screened should be screened

for GDM at the same time point (see section 15, “Management of Diabetes in Pregnancy”). The GDM diagnostic criteria for the 75-g OGTT from the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) and the GDM screening and diagnostic criteria with the two-step approach were not derived from data in the first half of pregnancy and should not be used for early screening (198).

Both the FPG and A1C are low-cost tests. An advantage of the A1C test is its convenience, as it can be added to the prenatal laboratory tests and does not require an early-morning fasting appointment. Disadvantages include inaccuracies in the presence of conditions such as increased or decreased red blood cell turnover (usually decreases and increases A1C, respectively), hemoglobinopathies, and iron deficiency anemia (increases A1C) (199,200).

GDM is often indicative of underlying β -cell dysfunction (201), which confers markedly increased risk for later development of glucose intolerance and diabetes in the mother after delivery (202–204). Individuals diagnosed with GDM should receive lifelong screening for prediabetes and type 2 diabetes to allow prompt implementation of effective diabetes

prevention interventions (205,206) and early treatment of diabetes (207).

Diagnosis

GDM carries risks for the mother, fetus, and neonate. The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study (208), a large-scale multinational cohort study completed by more than 23,000 pregnant individuals, demonstrated that risk of adverse maternal, fetal, and neonatal outcomes continuously increased as a function of maternal glycemia at 24–28 weeks of gestation, even within ranges previously considered normal for pregnancy. For most complications, there was no threshold for risk. These results have led to careful reconsideration of the diagnostic criteria for GDM.

GDM diagnosis (**Table 2.8**) can be accomplished with either of two strategies:

1. The “one-step” 75-g OGTT derived from the IADPSG criteria, or
2. The older “two-step” approach with a 50-g (nonfasting) screen followed by a 100-g OGTT for those who screen positive based on the work of Carpenter-Coustan’s interpretation of the older O’Sullivan and Mahan criteria (209).

Different diagnostic criteria will identify different degrees of maternal hyperglycemia and maternal/fetal risk, leading experts to debate optimal strategies for the diagnosis of GDM.

One-Step Strategy

The IADPSG examined data from the HAPO study and defined diagnostic cut points for GDM as the average fasting, 1-h, and 2-h PG values during a 75-g OGTT in individuals at 24–28 weeks of gestation, wherein the cut points were those at which odds for adverse outcomes reached 1.75 times the estimated odds. This one-step strategy was anticipated to significantly increase the incidence of GDM (from 5 to 6% to 15–20%), primarily because only one abnormal value, not two, became sufficient to make the diagnosis (210). Many regional studies have seen a roughly one- to threefold increase in GDM cases using the IADPSG criteria (211). A study of pregnancy OGTTs with glucose levels blinded to caregivers found that 11 years after their pregnancies, individuals who would have been diagnosed with GDM by the one-step approach, as

Table 2.8—Screening for and diagnosis of GDM

One-step strategy

Perform a 75-g OGTT, with plasma glucose measurement when an individual is fasting and at 1 and 2 h, at 24–28 weeks of gestation in individuals not previously diagnosed with diabetes.

The OGTT should be performed in the morning after an overnight fast of at least 8 h.

The diagnosis of GDM is made when any of the following plasma glucose values are met or exceeded:

- Fasting: 92 mg/dL (5.1 mmol/L)
- 1 h: 180 mg/dL (10.0 mmol/L)
- 2 h: 153 mg/dL (8.5 mmol/L)

Two-step strategy

Step 1:

Perform a 50-g GLT (nonfasting), with plasma glucose measurement at 1 h, at 24–28 weeks of gestation in individuals not previously diagnosed with diabetes.

If the plasma glucose level measured 1 h after the load is ≥ 130 , 135, or 140 mg/dL (7.2, 7.5, or 7.8 mmol/L, respectively),* proceed to a 100-g OGTT.

Step 2:

The 100-g OGTT should be performed when the individual is fasting.

The diagnosis of GDM is made when at least two† of the following four plasma glucose levels (measured fasting and at 1, 2, and 3 h during OGTT) are met or exceeded (Carpenter-Coustan criteria [208]):

- Fasting: 95 mg/dL (5.3 mmol/L)
- 1 h: 180 mg/dL (10.0 mmol/L)
- 2 h: 155 mg/dL (8.6 mmol/L)
- 3 h: 140 mg/dL (7.8 mmol/L)

GDM, gestational diabetes mellitus; GLT, glucose load test; OGTT, oral glucose tolerance test. *American College of Obstetricians and Gynecologists (ACOG) recommends any of the commonly used thresholds of 130, 135, or 140 mg/dL for the 1-h 50-g GLT (223). †ACOG notes that one elevated value can be used for diagnosis (223).

compared with those without GDM, were at 3.4-fold higher risk of developing prediabetes and type 2 diabetes and had children with a higher risk of obesity and increased body fat, suggesting that the group identified as having GDM by the one-step approach would benefit from the increased screening for diabetes and prediabetes after pregnancy (212). The ADA recommends the IADPSG diagnostic criteria to optimize gestational outcomes, because these criteria are the only ones based on pregnancy outcomes rather than end points such as prediction of subsequent maternal diabetes.

Expected benefits of using IADPSG criteria for offspring are inferred from intervention trials focusing on individuals with lower levels of hyperglycemia than those identified using older GDM diagnostic criteria. Those trials found modest benefits, including reduced rates of large-for-gestational-age births and preeclampsia (213, 214). Of note, 80–90% of participants being treated for mild GDM in these two RCTs could be managed with lifestyle therapy alone. The OGTT glucose cutoffs in these two trials overlapped the thresholds recommended by the IADPSG, and in one trial (214), the 2-h PG threshold (140 mg/dL [7.8 mmol/L]) was lower than the cutoff recommended by the IADPSG (153 mg/dL [8.5 mmol/L]).

No RCTs of treating versus not treating GDM diagnosed by different criteria have been published to date. However, a randomized trial of testing for GDM at 24–28 weeks of gestation by the one-step method using IADPSG criteria versus the two-step method by Carpenter-Coustan criteria identified twice as many individuals with GDM using the one-step method. Despite treating more individuals for GDM using the one-step method, there was no difference in pregnancy and perinatal complications (215), though concerns were raised about sample size estimates and unanticipated suboptimal engagement with the screening and treatment protocol. For example, in the two-step group, 165 participants not counted as having GDM were treated for isolated elevated FPG >95 mg/dL (>5.3 mmol/L) (216).

The one-step method identifies long-term risks of maternal prediabetes and diabetes as well as offspring glucose intolerance and adiposity. Post hoc GDM in individuals diagnosed with this method in the HAPO cohort was associated with

higher prevalence of IGT; higher 30-min, 1-h, and 2-h glucose levels during the OGTT; and reduced insulin sensitivity and oral disposition index in their offspring at 10–14 years of age compared with offspring of mothers without GDM. Associations of mother's fasting, 1-h, and 2-h values on the 75-g OGTT were continuous with a comprehensive panel of offspring metabolic outcomes (217,218). HAPO Follow-up Study (HAPO FUS) data demonstrate that neonatal adiposity and fetal hyperinsulinemia (cord C-peptide), both higher across the continuum of maternal hyperglycemia, are mediators of childhood body fat (219).

Data are lacking on how the treatment of mother's hyperglycemia in pregnancy affects her offspring's risk for obesity, diabetes, and other metabolic disorders (220,221). Additional well-designed clinical studies are needed to determine the optimal intensity of monitoring and treatment of individuals with GDM diagnosed by the one-step strategy.

Two-Step Strategy

In 2013, the NIH convened a consensus development conference to consider diagnostic criteria for diagnosing GDM (222). The panel recommended continuing a two-step approach to screening that used a 1-h 50-g glucose loading test (GLT) followed by a 3-h 100-g OGTT for those who screened positive. The American College of Obstetricians and Gynecologists (ACOG) recommends any of the commonly used thresholds of 130, 135, or 140 mg/dL for the 1-h 50-g GLT (223). A 2021 U.S. Preventive Services Task Force systematic review concluded that one-step versus two-step screening is associated with increased likelihood of GDM (11.5% vs. 4.9%) but without improved health outcomes (224). The use of A1C at 24–28 weeks of gestation as a screening test for GDM does not function as well as the GLT (225).

Importantly, the NIH panel noted the lack of clinical trial data demonstrating the benefits of the one-step strategy and the potential negative consequences of identifying a large group of individuals with GDM, including medicalization of pregnancy with increased health care utilization and costs. Moreover, screening with a 50-g GLT does not require fasting and therefore is easier to accomplish for many individuals. Treatment of higher-threshold maternal hyperglycemia, as identified by the two-step approach,

reduces rates of neonatal macrosomia, large-for-gestational-age births (226), and shoulder dystocia without increasing small-for-gestational-age births. ACOG currently supports the two-step approach but notes that one elevated value, as opposed to two, may be used for the diagnosis of GDM (223). If this approach is implemented, the incidence of GDM will likely increase markedly. ACOG recommends either of two sets of diagnostic thresholds for the 3-h 100-g OGTT Carpenter-Coustan or National Diabetes Data Group (227,228). Each is based on different mathematical conversions of the original recommended thresholds by O'Sullivan and Mahan (209), which used whole blood and nonenzymatic methods for glucose determination. A secondary analysis of data from a randomized clinical trial of identification and treatment of mild GDM (229) demonstrated that treatment was similarly beneficial in people meeting only the lower thresholds per Carpenter-Coustan (227) and in those meeting only the higher thresholds per National Diabetes Data Group (228). If the two-step approach is used, it would appear advantageous to use the Carpenter-Coustan lower diagnostic thresholds, as shown in step 2 in **Table 2.8**.

Future Considerations

Data exist to support each strategy, as demonstrated by differing recommendations by expert groups. A systematic review of economic evaluations of GDM screening found that the one-step method identified more cases of GDM and was more likely to be cost-effective than the two-step method (230). The decision of which strategy to implement must therefore be made based on the relative values placed on factors that have yet to be measured (e.g., willingness to change practice based on correlation studies rather than intervention trial results, available infrastructure, and importance of cost considerations).

The IADPSG criteria (one-step strategy) have been adopted internationally as the preferred approach. Data that compare population-wide outcomes with one-step versus two-step approaches have been inconsistent to date (215,231–233). Pregnancies complicated by GDM per the IADPSG criteria, but not recognized as such, have outcomes comparable to pregnancies with diagnosed GDM by the more stringent two-step criteria (234,235). There remains strong consensus that establishing

a uniform approach to diagnosing GDM will benefit people with GDM, caregivers, and policymakers. Longer-term outcome studies are currently underway.

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3. Prevention or Delay of Diabetes and Associated Comorbidities: Standards of Care in Diabetes—2026

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American Diabetes Association
Professional Practice Committee for
Diabetes*

The American Diabetes Association (ADA) “Standards of Care in Diabetes” includes the ADA’s current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. Members of the ADA Professional Practice Committee for Diabetes, an interprofessional expert committee, are responsible for updating the Standards of Care annually, or more frequently as warranted. For a detailed description of ADA standards, statements, and reports, as well as the evidence-grading system for ADA’s clinical practice recommendations and a full list of Professional Practice Committee members, please refer to Introduction and Methodology. Readers who wish to comment on the Standards of Care are invited to do so at professional.diabetes.org/SOC.

For guidelines related to screening for increased risk for type 1 diabetes, prediabetes and type 2 diabetes, and other forms of diabetes, please refer to section 2, “Diagnosis and Classification of Diabetes.” For guidelines related to screening, diagnosis, and management of diabetes in children and adolescents, please refer to section 14, “Children and Adolescents.”

Recommendations

3.1 In people with prediabetes, monitor for the development of diabetes at least annually; modify frequency of testing based on individual risk assessment. **E**

3.2 In people with presymptomatic type 1 diabetes, monitor for disease progression using A1C approximately every 6 months and 75-g oral glucose tolerance test (i.e., fasting and 2-h plasma glucose) annually; modify frequency of monitoring and consider augmenting with other glycemic assessment tools such as continuous glucose monitoring metrics based on individual risk assessment incorporating age, number and type of autoantibodies, and glycemic metrics. **E**

Screening for prediabetes (which refers to hyperglycemia preceding the diagnosis of type 2 diabetes only) and type 2 diabetes risk through an assessment of risk factors (Table 2.5) or with an assessment tool, such as the American Diabetes Association risk test, which can be used by either a layperson or a health care professional (diabetes.org/diabetes-risk-test), is recommended to guide whether to perform a diagnostic test for prediabetes (Table 2.2) and type 2 diabetes (Table 2.1) (see section 2, “Diagnosis and Classification of Diabetes”). Testing high-risk individuals for prediabetes is warranted because the laboratory assessment is safe and reasonable

*A complete list of members of the American Diabetes Association Professional Practice Committee for Diabetes can be found at <https://doi.org/10.2337/dc26-SINT>.

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in cost, and early detection of hyperglycemia affords substantial time to intervene and delay or prevent the onset of type 2 diabetes and/or its long-term complications. Indeed, once identified, several effective therapeutic approaches exist that can delay type 2 diabetes in those with prediabetes with an A1C 5.7–6.4% (39–47 mmol/mol), impaired glucose tolerance (IGT) on 75-g oral glucose tolerance test (OGTT), or impaired fasting glucose (IFG). The utility of screening with A1C for prediabetes and diabetes may be limited in the presence of certain hemoglobinopathies and conditions that affect red blood cell turnover (Table 2.3). See section 2, “Diagnosis and Classification of Diabetes,” and section 6, “Glycemic Goals, Hypoglycemia, and Hyperglycemic Crises,” for additional details on the appropriate use and limitations of A1C testing.

Three stages of type 1 diabetes have been defined, with symptomatic type 1 diabetes classified as stage 3 (Table 2.4). In individuals at risk for developing clinical type 1 diabetes, younger age of seroconversion (particularly under age 3 years), the total number of diabetes-related autoantibodies (1), and the development of autoantibodies against islet antigen 2 (IA-2) have all been associated with a more rapid progression to stage 3 type 1 diabetes. While continuous glucose monitoring can predict progression to stage 3 type 1 diabetes in children and adolescents with autoantibodies (2), OGTT-based metrics are more predictive of progression compared with continuous glucose monitoring (3). The decision to perform an OGTT may depend on such factors as eligibility and interest for stage-specific treatments, interest in participation in clinical research, OGTT availability, and the burden of testing. Consensus guidance provides expert recommendations on what should be monitored and how often in people with presymptomatic type 1 diabetes (4). Cost-effectiveness of population-based screening programs for type 1 diabetes has not been established (5,6), but such screening is being implemented outside the U.S. (7).

LIFESTYLE BEHAVIOR CHANGE FOR TYPE 2 DIABETES PREVENTION

Recommendations

3.3 Refer adults with overweight or obesity at high risk of type 2 diabetes to a diabetes prevention

program to achieve and maintain a weight reduction of at least 5–7% of initial body weight through a healthy reduced-calorie eating pattern and ≥ 150 min/week of moderate-intensity physical activity. **A**

3.4 Prescribe an evidence-based eating pattern (e.g., Mediterranean, low carbohydrate) to individuals with prediabetes to prevent type 2 diabetes. **B**

3.5 Offer diabetes prevention programs to adults at high risk for type 2 diabetes. **A** Diabetes prevention programs should be covered by third-party payors, and inconsistencies in access should be addressed. **E**

3.6 Based on individual preference, certified technology-assisted diabetes prevention programs through smartphones, web-based applications, and telehealth can be effective in preventing type 2 diabetes and should be considered. **B**

The Diabetes Prevention Program

Several major randomized controlled trials, including the Diabetes Prevention Program (DPP) (8), the Finnish Diabetes Prevention Study (DPS) (9), and the Da Qing Diabetes Prevention Study (Da Qing study) (10), demonstrated that lifestyle/behavioral intervention with an individualized reduced-calorie meal plan is highly effective in preventing or delaying type 2 diabetes and improving other cardiometabolic risk factors such as blood pressure, lipids, and markers of inflammation (11). The strongest evidence for diabetes prevention in the U.S. comes from the DPP trial (8). The DPP demonstrated that intensive lifestyle intervention could reduce the risk of incident type 2 diabetes by 58% over 3 years. Follow-up of three large trials of lifestyle intervention for diabetes prevention showed sustained reduction in the risk of progression to type 2 diabetes: 39% reduction at 30 years in the Da Qing study (12), 43% reduction at 7 years in the Finnish DPS (9), and 34% reduction at 10 years (13), 27% reduction at 15 years (14), and 24% reduction at 21 years in the U.S. Diabetes Prevention Program Outcomes Study (DPPOS) (15,16).

The DPP lifestyle intervention was a goal-based intervention. A complete description of the DPP and how to access it is available online at coveragetoolkit.org/about-national-dpp/ndpp-overview/. Briefly,

the DPP administered a 16-session structured core curriculum, completed within the first 6 months of the program, followed by an additional 6 months of a flexible maintenance program. The core curriculum included sessions on reducing calories, increasing physical activity, self-monitoring, maintaining healthy lifestyle behaviors (such as how to make healthy choices when eating out), and guidance on managing psychological, social, and motivational challenges (17).

Two major goals of the DPP were to achieve and maintain at least 7% weight loss and to obtain 150 min of moderate-intensity physical activity per week, such as brisk walking. Weight loss was the most important factor in reducing incident diabetes. Obtaining at least 150 min of physical activity per week, even without achieving the weight loss goal, reduced incidence of type 2 diabetes by 44% (18). Participants were encouraged to distribute physical activity throughout the week with a minimum frequency of three times per week and at least 10 min per session. A maximum of 75 min of strength training could be applied toward the total 150 min/week physical activity goal. The initial focus of the nutrition intervention was on reducing total fat intake rather than caloric restriction. However, the concepts of calorie balance and the need to restrict total calories and fat were also introduced. Overall, the DPP's lifestyle intervention was designed to produce a 700 kcal/week energy deficit (17).

The 7% weight loss goal was selected because it was feasible to achieve and maintain, hypothesized to reduce incident diabetes risk, and improved other cardiometabolic risk factors. Further analysis suggested greater benefit for diabetes prevention with at least 7–10% weight loss with lifestyle interventions (18). The recommended pace of weight loss was 1–2 lb/week.

While the DPP interventions were successful in preventing or delaying the onset of type 2 diabetes, major cardiovascular events were not significantly different 21 years after the DPP concluded, which may be due to the widespread use of statin, antihypertensive, and metformin therapy among all participants well after the conclusion of the study (19). However, the incidence of diabetes continued to be significantly

lower at 21 years of follow-up in both intensive lifestyle therapy and metformin groups, when compared with placebo, corresponding to increases in median diabetes-free survival of 3.5 years and 2.5 years, respectively (15). Importantly, the overall treatment effect was driven almost entirely by benefit seen during the initial DPP phase (15), underscoring the importance of early intervention and continued implementation of diabetes prevention efforts. Still, individuals can derive benefit from lifestyle interventions to prevent progression of prediabetes to diabetes irrespective of the duration of prediabetes prior to initiation of lifestyle intervention (20). Thus, there is clear potential benefit in diabetes prevention and minimal to no risk of harm with these interventions.

Nutrition

Nutrition counseling for weight loss in the DPP lifestyle intervention arm focused on reduction of total fat and calories (8,17,18). However, current evidence suggests there is no ideal percentage of calories from carbohydrate, protein, and fat to prevent diabetes; therefore, macronutrient distribution should be based on an individualized assessment of current eating patterns, preferences, and metabolic goals. A variety of eating patterns (21) can be appropriate for individuals with prediabetes or diabetes, including Mediterranean-style, plant-based (which may or may not be omnivorous), Dietary Approaches to Stop Hypertension (DASH), and low-carbohydrate (22–25). The overall quality of food consumed (as measured by the Healthy Eating Index, Alternative Healthy Eating Index, and DASH score), with an emphasis on whole grains, legumes, nuts, fruits, and vegetables and minimal refined and processed foods, is also associated with a lower risk of type 2 diabetes (26–28). For people at risk for or living with diabetes, individualized medical nutrition therapy (see section 5, “Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes,” for more detailed information) is effective in lowering A1C (29,30).

Physical Activity

Moderate-intensity physical activity, such as brisk walking for 150 min/week, has shown beneficial effects in those with prediabetes (8). Similarly, moderate-

intensity physical activity has been shown to improve insulin sensitivity and reduce abdominal fat in children, adolescents, and young adults (31,32). Health care professionals are encouraged to promote a DPP-style program to all individuals who have been identified to be at an increased risk of type 2 diabetes. In addition to aerobic activity, a physical activity plan designed to prevent diabetes can include resistance training (17,33). Breaking up prolonged sedentary time may also be encouraged, as it lowers postprandial glucose levels (34). The effects of regular physical activity participation appear to extend to the prevention of gestational diabetes mellitus (GDM) as well (35,36).

Delivery and Dissemination of Lifestyle Behavior Change for Diabetes Prevention

Because the intensive lifestyle intervention in the DPP was effective in preventing type 2 diabetes among those at high risk, and both DPP and adapted lifestyle behavior change programs for diabetes prevention were shown to be cost-effective across multiple applications, broader efforts to disseminate scalable DPP-like lifestyle behavior change programs for diabetes prevention with coverage by third-party payors ensued (37–42). Group delivery of DPP content in community or primary care settings has demonstrated the potential to reduce overall program costs while still producing weight loss and diabetes risk reduction (43,44). Interventions to prevent type 2 diabetes can also be delivered through workplace programming, with interventions that most closely adhere to DPP content shown to be most effective (45).

The Centers for Disease Control and Prevention (CDC) developed the National Diabetes Prevention Program (National DPP), a resource designed to bring such evidence-based lifestyle change programs for preventing type 2 diabetes to communities (cdc.gov/diabetes-prevention). To be eligible for this program, individuals must have a BMI in the overweight range and be at risk for diabetes based on laboratory testing, a previous diagnosis of GDM, or a positive risk test (cdc.gov/prediabetes/risktest/). The CDC has also developed the Diabetes Prevention Impact Tool Kit (nccd.cdc.gov/toolkit/diabetesimpact) to help organizations assess the economics of providing or

covering the National DPP (46). To expand preventive services using a cost-effective model, the Centers for Medicare & Medicaid Services expanded Medicare reimbursement coverage for the National DPP to organizations recognized by the CDC that become Medicare suppliers for this service (innovation.cms.gov/innovation-models/medicare-diabetes-prevention-program). The locations of Medicare DPPs are available online at innovation.cms.gov/innovation-models/medicare-diabetes-prevention-program/mdpp-map. To qualify for Medicare coverage, individuals must have BMI >25 kg/m² (or BMI >23 kg/m² if self-identified as Asian) and glycemic testing consistent with prediabetes in the last year. Medicaid DPP coverage is also expanding on a state-by-state basis.

While CDC-recognized behavioral counseling programs, including Medicare DPP services, have met minimum quality standards and are reimbursed by many payors, lower retention rates have been reported for younger adults and racial and ethnic minoritized populations (47). Therefore, other programs and modalities of behavioral counseling for diabetes prevention may also be appropriate and efficacious based on individual preferences and availability. Use of community health workers to support DPP-like interventions can be appropriate and cost-effective (48,49) (see section 1, “Improving Care and Promoting Health in Populations,” for more information). The use of community health workers may facilitate the adoption of behavior changes for diabetes prevention while bridging barriers related to social determinants of health. However, coverage by third-party payors remains limited. Counseling by a registered dietitian nutritionist has been shown to help individuals with prediabetes improve eating habits, increase physical activity, and achieve 7–10% weight loss (50–53). Individualized medical nutrition therapy (see section 5, “Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes,” for more detailed information) is also effective in improving glycemia in individuals diagnosed with prediabetes (51,54). Furthermore, trials involving medical nutrition therapy for adults with prediabetes found significant reductions in weight, waist circumference, and glycemia (54,55). Individuals with prediabetes can benefit

from referral to a registered dietitian nutritionist for individualized medical nutrition therapy upon diagnosis and at regular intervals throughout their treatment plan (52,56). Other health care professionals, such as pharmacists and diabetes care and education specialists, can also be considered for diabetes prevention efforts (56,57).

Technology-assisted programs may effectively deliver a DPP-like intervention (58–61). Such technology-assisted programs may deliver content through smartphones, web-based applications, and telehealth and may be an acceptable and efficacious option to bridge barriers, particularly for individuals with low income and/or in rural locations; however, not all technology-assisted programs are effective (58,62–64). The CDC Diabetes Prevention Recognition Program (DPRP) (<https://www.cdc.gov/diabetes-prevention/php/program-provider/program-requirements.html>) certifies technology-assisted modalities as effective vehicles for DPP-based interventions; such programs must use an approved curriculum, include interaction with a coach, and attain the DPP outcomes of participation, physical activity reporting, and weight loss. Health care professionals should consider referring adults with prediabetes to certified technology-assisted programs.

The CDC's Division of Diabetes Translation National DPP toolkit ([coveragetoolkit.org/recruitment-referral-for-the-national-dpp-lifestyle-change-program](https://www.cdc.gov/diabetes-prevention/php/program-provider/program-requirements.html)) provides diabetes care team members resources for how to increase referral and uptake of the DPP. Some ways to increase DPP utilization include direct mailings, phone scripts, and text-based outreach. Using multiple methods of outreach to increase awareness among those at risk, and among health care professionals, in addition offering the DPP virtually can improve participation and uptake (65,66). However, more work is needed to improve uptake among high-risk populations (67,68).

Sleep Characteristics Associated With Increased Risk of Type 2 Diabetes

Sleep occupies approximately one-third of the day for most people and modulates important metabolic, endocrine, and cardiovascular processes (69). Sleep can be characterized using three key

constructs: quantity, quality, and timing (i.e., chronotype). There is now established evidence for a U-shaped association between sleep duration and type 2 diabetes incidence, with the nadir typically occurring at 7 h per day, with short (typically defined as <6 h) and long (typically defined as >9 h) sleep duration having up to a 50% increase in the risk of type 2 diabetes, including progression from prediabetes (70). Sleep quality is defined as “an individual's self-satisfaction with all aspects of the sleep experience” (71,72). A meta-analysis reported that poor overall sleep quality was associated with a 40% increased risk of developing type 2 diabetes (73). Chronotype preference has been linked with many chronic diseases, including type 2 diabetes. For example, for those with a preference for evenings (i.e., going to bed late and getting up late), there was a 2.5-fold higher odds ratio for type 2 diabetes than for those with a preference for mornings (i.e., going to bed early and getting up early), independent of sleep duration and sleep sufficiency (74). More detailed information concerning sleep and the impact of sleep on prediabetes and diabetes risk and management can be found in section 5, “Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes.”

PHARMACOLOGIC INTERVENTIONS TO DELAY TYPE 2 DIABETES

Recommendations

3.7 Metformin for the prevention of type 2 diabetes should be considered in adults at high risk of type 2 diabetes, as typified by the Diabetes Prevention Program, especially those aged 25–59 years with BMI ≥ 35 kg/m², higher fasting plasma glucose (e.g., ≥ 110 mg/dL [≥ 6 mmol/L]), and higher A1C (e.g., $\geq 6.0\%$ [≥ 42 mmol/mol]), and in individuals with prior gestational diabetes mellitus. **A**

3.8 Consider using metformin to prevent hyperglycemia in high-risk individuals treated with a phosphatidylinositol 3-kinase α (PI3K α) inhibitor (e.g., alpelisib and inavolisib). **B**

3.9 Consider using metformin to prevent hyperglycemia in high-risk individuals treated with high-dose glucocorticoids. **B**

3.10 Consider periodic assessment of vitamin B12 levels in individuals receiving long-term metformin therapy, especially in those with anemia or peripheral neuropathy. **B**

Because weight loss and maintenance through lifestyle (e.g., nutrition and physical activity) behavior changes might not be sufficient on their own (13), some people at high risk for type 2 diabetes may benefit from additional pharmacotherapy support. Various pharmacologic agents used to treat diabetes have also been evaluated for diabetes prevention. Metformin, α -glucosidase inhibitors, incretin receptor agonists (e.g., liraglutide, semaglutide, and tirzepatide), thiazolidinediones, and insulin have all been shown to lower the incidence of diabetes in specific populations (75–83). However, whether initiating glucose-lowering treatment early—before hyperglycemia reaches the diagnostic threshold of diabetes—improves long-term health outcomes is unknown. Indeed, the benefits of glucose lowering to the normoglycemic range need to be balanced against the potential adverse effects of these therapies and the burden and cost of treatment. There are currently no long-term data to support the use of pharmacologic treatments other than metformin for the sole purpose of preventing type 2 diabetes. However, use of glucagon-like peptide 1–based therapies for weight management in individuals with overweight or obesity—an essential component of type 2 diabetes prevention—is highly beneficial and should be considered, as discussed in detail in section 8, “Obesity and Weight Management for the Prevention and Treatment of Diabetes.” Importantly, in the DPP, weight loss was key to reducing the risk of progression to diabetes, with every kilogram of weight loss conferring a 16% reduction in risk of progression over 3.2 years (18). In individuals with previous history of GDM, the risk of type 2 diabetes increased by 18% for every 1-unit increase in BMI above the preconception baseline (84). Several medications evaluated for obesity treatment (e.g., orlistat, phentermine and topiramate, liraglutide, semaglutide, and tirzepatide) have been shown to decrease the incidence of type 2 diabetes in those with prediabetes (80,85–87).

Other medications have also been assessed for their efficacy in preventing type 2 diabetes. The antihypertensive valsartan was found to modestly reduce the incidence of diabetes among individuals with prediabetes and cardiovascular disease or risk factors, but with no difference in cardiovascular outcomes (88). Thus, we do not recommend using valsartan for the prevention of diabetes. Testosterone therapy also reduced the risk of incident type 2 diabetes by 41% in men aged 50–74 years with central obesity and prediabetes (89). However, the benefit of testosterone was observed only when added to a structured lifestyle program. Indeed, the TRAVERSE Diabetes Study (a prespecified efficacy trial nested within the large multicenter TRAVERSE trial whose primary objective was to assess the cardiovascular outcomes of testosterone therapy in men aged 45–80 years with hypogonadism) found no benefit of testosterone as compared with placebo with respect to progression from prediabetes to diabetes or remission of diabetes among those who had prediabetes or diabetes at baseline, respectively (90). Testosterone therapy also did not alter glucose or A1C levels among participants with prediabetes or diabetes, nor were there any differences in outcomes by baseline testosterone level, preexisting cardiovascular disease, age, or race. Thus, we do not recommend testosterone therapy for the prevention of type 2 diabetes in men with hypogonadism; the decision to initiate testosterone replacement needs to be informed by individualized treatment considerations that weigh the expected benefits and harms of treatment.

There has been significant interest in understanding the potential of vitamin D therapy to prevent progression of high-risk prediabetes to type 2 diabetes in adults (91). Three randomized controlled trials tested whether vitamin D therapy in combination with lifestyle modification reduces the risk of developing diabetes in adults with high-risk prediabetes (i.e., IGT or meeting two or three criteria for the diagnosis of prediabetes [fasting glucose, A1C, 2-h glucose after a 75-g OGTT]): the Tromsø study in Norway, with 511 participants; the Vitamin D and Type 2 Diabetes (D2d) study in the U.S., with 2,423 participants; and the Diabetes Prevention with Active Vitamin D (DPVD) study

in Japan, with 1,256 participants (92–94). Although vitamin D therapy consistently appeared to modestly reduce the risk of developing diabetes in all three trials, none of the results were statistically significant, which was attributed to insufficient statistical power. Subsequently, several meta-analyses pooling the three randomized clinical trials along with other smaller studies suggested a modest (i.e., 10–15% risk reduction) potential benefit in specific populations, such as older adults, individuals with lower baseline vitamin D levels, and individuals without obesity (95,96). However, there are several concerns and uncertainties regarding recommending widespread vitamin D therapy for adults with high-risk prediabetes. First, these trials used varying dosages of vitamin D that were higher than the recommended daily allowance (i.e., 600 IU/day for those aged 18–70 years and 800 IU/day for those older than 70 years). Second, the benefit-to-risk ratio of vitamin D therapy for people with high-risk prediabetes remains uncertain. Although there were no safety concerns identified in these trials, the anticipated treatment of many millions of adults with prediabetes in the U.S. and globally could increase the risk of adverse events (such as hypercalcemia, hypercalciuria, nephrolithiasis, and kidney failure), especially treatment with unspecified doses of vitamin D without monitoring blood 25-hydroxy vitamin D levels.

Thus, the expected benefit, harm, treatment burden, and cost of using any medication to prevent type 2 diabetes must be considered for each individual as part of informed shared decision-making. This is particularly important because any pharmacologic intervention is likely to be needed to be used long-term because of waning effects after stopping the medication. At the present time, there are no pharmacologic agents approved by the U.S. Food and Drug Administration specifically for the prevention of type 2 diabetes.

Metformin

Metformin has the most robust efficacy and safety data as a pharmacologic therapy for diabetes prevention among people with prediabetes (82). Importantly, metformin was overall less effective than lifestyle modification in the DPP, although

group differences attenuated over time in the DPPOS (14) and metformin was as effective as lifestyle modification in participants with BMI ≥ 35 kg/m² and in younger participants aged 25–44 years (8). In individuals with a history of GDM, metformin and intensive lifestyle modification led to an equivalent 50% reduction in diabetes risk (97). Both interventions remained effective during a 10-year follow-up period (98), with lifestyle therapy being highly cost-effective (\$12,878 per quality-adjusted life-year [QALY]) and metformin marginally cost-saving compared with placebo (37). By the time of the 15-year follow-up (DPPOS), exploratory analyses demonstrated that participants with a higher baseline fasting glucose (≥ 110 mg/dL [≥ 6 mmol/L] vs. 95–109 mg/dL [5.3–5.9 mmol/L]), those with a higher A1C (6.0–6.4% [42–46 mmol/mol] vs. $<6.0\%$ [<42 mmol/mol]), and individuals with a history of GDM (vs. individuals without a history of GDM) experienced higher risk reductions with metformin, identifying subgroups of participants that may benefit the most from metformin (83). In the Indian Diabetes Prevention Program (IDPP-1), metformin and lifestyle intervention reduced diabetes risk similarly at 30 months; however, the lifestyle intervention in IDPP-1 was less intensive than that in the DPP (99). Based on findings from the DPP, metformin should be recommended as an option for high-risk individuals (e.g., younger individuals, those with history of GDM, or those with BMI ≥ 35 kg/m²).

Individuals receiving high-dose and/or long-duration glucocorticoid therapy are at risk for developing glucocorticoid-induced diabetes (see section 2, “Diagnosis and Classification of Diabetes”). Metformin can be considered to prevent the development of glucocorticoid-induced hyperglycemia in high-risk individuals, notably those receiving higher doses of glucocorticoids, with longer treatment duration, and in the presence of other risk factors for diabetes. The efficacy of metformin to prevent hyperglycemia—particularly insulin resistance and postprandial hyperglycemia—has been demonstrated in small randomized clinical trials both in healthy individuals (100) and in individuals receiving high-dose glucocorticoids for the treatment of cancer (101) and rheumatologic/autoimmune disorders (102,103). In one trial with 40 participants receiving high-

dose prednisolone for the treatment of inflammatory conditions, metformin also reduced rates of infection and all-cause hospital readmissions (103).

Proactive use of metformin may also be beneficial in preventing hyperglycemia in individuals receiving phosphatidylinositol 3-kinase α (PI3K α) inhibitors (e.g., alpelisib and inavolisib) for the treatment of cancer (see section 2, “Diagnosis and Classification of Diabetes,” for additional details on diabetes induced by systemic anticancer therapy). This is particularly important because hyperglycemia is the most frequent adverse event of PI3K α inhibitor therapy that leads to treatment discontinuation (104). In a phase 2 trial of metformin to prevent hyperglycemia in individuals receiving alpelisib for advanced breast cancer (metformin was started 1 week prior to starting alpelisib and continued for the duration of treatment), metformin prevented the development of grade 3–4 hyperglycemia in all but four participants, and none had to discontinue alpelisib therapy (105). Similar benefits were seen with implementation of a metformin hyperglycemia-prevention protocol in routine practice (106). Individuals at highest risk for developing hyperglycemia with PI3K α inhibitor therapy include those who are older (≥ 70 years old), with obesity (BMI ≥ 30 kg/m²), concurrently treated with glucocorticoids, and with hyperglycemia at baseline (e.g., A1C $\geq 5.7\%$ [39 mmol/mol] or fasting plasma glucose ≥ 100 mg/dL [5.6 mmol/L]) (107, 108). However, it is important to weigh the benefits of preventing hyperglycemia with the potential adverse effects of metformin therapy, particularly diarrhea, which is also a frequent adverse effect of PI3K α therapy (though there is no evidence that concurrent use of these two medications further exacerbates diarrhea risk) (108).

Decreased vitamin B12 levels are a known consequence of long-term treatment with metformin (109). Periodic assessment of vitamin B12 level in those taking metformin chronically should be considered to check for possible deficiency, especially in those receiving a higher dose (e.g., $\geq 1,500$ mg/day) (110), with longer treatment duration (4–5 years) (111), with other risk factors for vitamin B12 deficiency, and if a deficiency is suspected, such as in people with anemia,

peripheral neuropathy, or chronic kidney disease (109,112,113) (see section 9, “Pharmacologic Approaches to Glycemic Treatment,” for more details). A person who has been taking metformin for more than 4 years or is at risk for vitamin B12 deficiency for other reasons (e.g., vegan dietary pattern, previous gastric/small bowel surgery) should be monitored for vitamin B12 deficiency annually (114,115).

PREVENTION OF VASCULAR DISEASE AND MORTALITY

Recommendations

3.11 Prediabetes is associated with heightened cardiovascular risk; therefore, screening for and treatment of modifiable risk factors for cardiovascular disease are suggested. **B**

3.12 Statin therapy may increase the risk of type 2 diabetes in people at high risk of developing type 2 diabetes. In such individuals, glucose status should be monitored regularly and diabetes prevention approaches reinforced. It is not recommended that statins be avoided or discontinued for this adverse effect. **B**

3.13 In people with a history of stroke and evidence of insulin resistance and prediabetes, pioglitazone may be considered to lower the risk of stroke or myocardial infarction. However, this benefit needs to be balanced with the increased risk of weight gain, edema, and fractures. **A** Lower doses may mitigate the risk of adverse effects but may be less effective. **C**

People with prediabetes often have other cardiovascular risk factors, including hypertension and dyslipidemia (116), and are at increased risk for cardiovascular disease (117,118). Evaluation for tobacco use and referral for tobacco cessation should be part of routine care for those at risk for diabetes. Of note, the years immediately following smoking cessation may represent a time of increased risk for diabetes (119,120), and individuals should be monitored for diabetes development and receive evidence-based lifestyle behavior change for diabetes prevention as described in this section. See section 5, “Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes,” for more detailed information. The lifestyle interventions for weight loss in study populations at risk for

type 2 diabetes have shown a reduction in cardiovascular risk factors and the need for medications used to treat these cardiovascular risk factors (121,122). The lifestyle intervention in the Da Qing study was associated with lowering cardiovascular disease and mortality at 23 and 30 years of observational follow-up (10,12). Treatment goals and therapies for hypertension and dyslipidemia in the primary and secondary prevention of cardiovascular disease for people with prediabetes should be based on their level of cardiovascular risk. Increased vigilance is warranted to identify and treat these and other cardiovascular disease risk factors (123).

Statin use increases risk of diabetes (124,125). In the DPP, statin use was associated with greater diabetes risk irrespective of the treatment group (pooled hazard ratio [HR] [95% CI] for incident diabetes 1.36 [1.17–1.58]) (124). In trials of primary and secondary prevention of cardiovascular disease, cardiovascular and mortality benefits of statin therapy exceed the risk of diabetes (126,127), suggesting a highly favorable benefit-to-harm balance with statin therapy. Hence, discontinuation of statins due to concerns of diabetes risk is not recommended in this population.

Results of cardiovascular outcome trials in people without diabetes also provide important evidence for cardiovascular risk reduction in people with increased cardiometabolic risk, though not specifically prediabetes (see section 10, “Cardiovascular Disease and Risk Management,” for more details). The IRIS (Insulin Resistance Intervention after Stroke) trial of people with a recent (< 6 months) stroke or transient ischemic attack, without diabetes but with insulin resistance (as defined by a HOMA of insulin resistance index of ≥ 3.0), evaluated pioglitazone (goal dose of 45 mg daily) compared with placebo. At 4.8 years, the risk of stroke or myocardial infarction, as well as the risk of diabetes, was lower in the pioglitazone group than in the placebo group; weight gain, edema, and fractures were higher in the pioglitazone treatment group (128–130). Lower doses may mitigate the adverse effects but may also be less effective (131).

PERSON-CENTERED CARE GOALS

Recommendations

3.14 In adults with overweight or obesity at high risk of type 2 diabetes, care goals should include weight

loss and maintenance, minimizing the progression of hyperglycemia, and attention to cardiovascular risk. **B**

3.15 Pharmacotherapy (e.g., for weight management, minimizing the progression of hyperglycemia, and cardiovascular risk reduction) should be considered to support person-centered care goals. **A**

3.16 More intensive preventive approaches should be considered in individuals who are at particularly high risk of progression to diabetes, including individuals with BMI ≥ 35 kg/m², those with higher glucose levels (e.g., fasting plasma glucose 110–125 mg/dL [6.1–6.9 mmol/L], 2-h postchallenge glucose 173–199 mg/dL [9.6–11.0 mmol/L], and A1C $\geq 6.0\%$ [≥ 42 mmol/mol]), and individuals with a history of gestational diabetes mellitus. **A**

Individualized risk-to-benefit ratio should be considered in screening, intervention, and monitoring to lower the risk of type 2 diabetes and associated comorbidities. Multiple factors, including age, BMI, and other comorbidities, may influence the risk of progression to diabetes and lifetime risk of complications (132,133). Prediabetes is associated with increased cardiovascular disease and mortality (118), which emphasizes the importance of attending to cardiovascular risk in this population. However, the new diagnosis of prediabetes in older adults (aged >70 years) is less relevant for progression to diabetes; indeed, regression to normoglycemia or death was more frequent than progression to diabetes in the Atherosclerosis Risk in Communities (ARIC) study (132). Moreover, diabetes-related morbidity and mortality is lower and the benefits of treatment are not established in those who develop type 2 diabetes after age 70 years (134).

In the DPP, which enrolled high-risk individuals with IGT, elevated fasting glucose, and elevated BMI, the crude incidence of diabetes within the placebo group was 11 cases per 100 person-years, with a cumulative 3-year incidence of diabetes of 29% (8). Characteristics of individuals in the DPP and DPPOS who were at particularly high risk of progression to diabetes (crude incidence of diabetes 14–22 cases per 100 person-years)

included BMI ≥ 35 kg/m², higher glucose levels (e.g., fasting plasma glucose 110–125 mg/dL [6.0–6.9 mmol/L], 2-h postchallenge glucose 173–199 mg/dL [9.6–11.0 mmol/L], A1C $\geq 6.0\%$ [≥ 42 mmol/mol]), or a history of GDM (8,97,98). In contrast, in the community-based ARIC study, observational follow-up of adults with mean age 75 years with laboratory evidence of prediabetes (based on A1C 5.7–6.4% [39–47 mmol/mol] and/or fasting glucose 100–125 mg/dL [5.6–6.9 mmol/L]), but not meeting specific BMI criteria, found lower progression to diabetes over 6 years: 9% of those with A1C-defined prediabetes and 8% of those with IFG (133).

Thus, it is important to individualize the risk-to-benefit ratio of intervention and consider person-centered goals. Risk models have generally found a higher benefit of the intervention in those at highest risk (18). Diabetes prevention trials and observational studies highlight key principles that may guide person-centered goals. In the DPP, which enrolled a high-risk population meeting criteria for overweight or obesity, weight loss was an important mediator of diabetes prevention or delay, with greater metabolic benefit seen with greater weight loss (18,135). In the DPP and DPPOS, progression to diabetes, duration of diabetes, and mean level of glycemia were important determinants of the development of microvascular complications (14). Achieving normal glucose regulation, even once, during the DPP was associated with a lower risk of diabetes and lower risk of microvascular complications irrespective of the treatment arm (136). Observational follow-up of the Da Qing study also showed that regression from IGT to normal glucose tolerance or remaining with IGT rather than progressing to type 2 diabetes at the end of the 6-year intervention trial resulted in significantly lower risk of cardiovascular disease and microvascular disease over 30 years (137).

Pharmacotherapy for weight management and cardiovascular risk reduction (see section 8, “Obesity and Weight Management for the Prevention and Treatment of Diabetes,” and section 10, “Cardiovascular Disease and Risk Management,” for more details) can be considered to support individualized person-centered goals, with more intensive preventive approaches

considered in individuals at high risk of progression.

PREVENTION OR DELAY OF SYMPTOMATIC TYPE 1 DIABETES

Lifestyle and Type 1 Diabetes Progression

Observational studies have identified several factors that increase β -cell demand and risk of progression to clinical type 1 diabetes among individuals with islet autoantibodies, including lower levels of physical activity (138), higher glycemic index eating patterns (139), and total sugar intake (140). Similar associations have not been observed for the development of autoantibodies. In The Environmental Determinants of Diabetes in the Young (TEDDY) longitudinal study, daily minutes spent in moderate to vigorous physical activity were associated with a reduced risk of progression to type 1 diabetes in children 5–15 years of age with multiple islet autoantibodies (HR 0.92 [95% CI 0.86–0.99] per 10-min increase; $P = 0.02$) (138). In the Diabetes Autoimmunity Study in the Young (DAISY), also in children with islet autoantibodies, consumption of higher glycemic index foods (HR 2.20 [95% CI 1.17–4.15]) and total sugar intake (HR 1.75 [95% CI 1.07–2.85]) (139,140) were both associated with progression to type 1 diabetes. In nonobese diabetic mice, an animal model for the development of type 1 diabetes, sustained high-glucose drinking significantly aggravated islet inflammation and accelerated the onset of type 1 diabetes (141). However, efficacy of lifestyle interventions that modify these factors in individuals with stage 1 or stage 2 type 1 diabetes has not yet been reported.

Pharmacologic Interventions to Delay Symptomatic Type 1 Diabetes

Recommendation

3.17 Teplizumab-mzwv infusion to delay the onset of symptomatic type 1 diabetes (stage 3) should be discussed with selected individuals aged ≥ 8 years with stage 2 type 1 diabetes. Treatment should be in a setting with appropriately trained personnel. **B**

Teplizumab, a CD3-directed humanized monoclonal antibody engineered to have decreased Fc receptor binding, has been

approved to delay the onset of stage 3 type 1 diabetes in people 8 years and older with stage 2 type 1 diabetes based in part on the results of a single trial in relatives of people with type 1 diabetes (142). In this study, 44 individuals were randomized to a 14-day course of teplizumab and 32 to placebo. The median time to stage 3 type 1 diabetes diagnosis was 48.4 months in the teplizumab group and 24.4 months in the placebo group. Type 1 diabetes was diagnosed in 19 (43%) participants who received teplizumab and 23 (72%) participants who received placebo (HR 0.41 [95% CI 0.22–0.78]). In prespecified analyses, the presence of HLA-DR4, absence of HLA-DR3, and absence of antizinc transporter 8 antibody predicted response to teplizumab (HR 0.20 [95% CI 0.09–0.45], 0.18 [0.07–0.45], and 0.07 [0.02–0.26], respectively). The most common adverse reactions were transient lymphopenia (73%) followed by rash (36%).

Numerous clinical studies are being conducted to test methods for preventing or delaying the onset of stage 3 type 1 diabetes in those with evidence of autoimmunity without symptoms or for delaying loss of insulin secretory capacity after onset of stage 3, some with promising results (see ClinicalTrials.gov and TrialNet.org).

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4. Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Care in Diabetes—2026

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American Diabetes Association
Professional Practice Committee for
Diabetes*

The American Diabetes Association (ADA) “Standards of Care in Diabetes” includes the ADA’s current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. Members of the ADA Professional Practice Committee for Diabetes, an interprofessional expert committee, are responsible for updating the Standards of Care annually, or more frequently as warranted. For a detailed description of ADA standards, statements, and reports, as well as the evidence-grading system for ADA’s clinical practice recommendations and a full list of Professional Practice Committee members, please refer to Introduction and Methodology. Readers who wish to comment on the Standards of Care are invited to do so at professional.diabetes.org/SOC.

PERSON-CENTERED COLLABORATIVE CARE

Recommendations

4.1 A communication style that uses person-centered, culturally sensitive, and strength-based language and active listening; elicits individual preferences and beliefs; and assesses literacy, numeracy, and potential barriers to care should be used to optimize health outcomes and health-related quality of life. **B**

4.2 People with diabetes can benefit from a coordinated interprofessional team that may include but is not limited to diabetes care and education specialists, primary care and subspecialty clinicians, nurses, registered dietitian nutritionists, exercise specialists, pharmacists, dentists, podiatrists, and behavioral health professionals. **C**

A successful medical evaluation and care plan depends on the beneficial interactions and care coordination between the person with diabetes and the care team. The Chronic Care Model (1) and other evidence-based care delivery models (see section 1, “Improving Care and Promoting Health in Populations”) can support a person-centered approach to care that requires a close working relationship between the person with diabetes, their clinicians, and the broader health care team involved in treatment planning and implementation. People with diabetes should receive health care from a coordinated interprofessional team that may include but is not limited to diabetes care and education specialists, primary care and subspecialty clinicians, nurses, registered dietitian nutritionists, exercise specialists, pharmacists, dentists, podiatrists, behavioral health professionals, and community

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The BONE HEALTH subsection has received endorsement from the American Society for Bone and Mineral Research.

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partners such as community health workers and community paramedics. Individuals with diabetes and their care partners or caregivers must assume an active role in their care. Based on the preferences and values of the person with diabetes, elicited by the care team, the person with diabetes, their family or support group, and the health care team together formulate the management plan, which includes lifestyle management (see section 5, “Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes”) and pharmacotherapy, as appropriate.

The goals of treatment for diabetes are to prevent or delay complications and optimize quality of life (Fig. 4.1). Treatment goals and plans should be cocreated by the care team and people with diabetes based on their individual

preferences, values, and goals. This individualized management plan should take into account the person's age, cognitive abilities, school/work schedule and conditions, health beliefs, support systems, eating patterns, physical activity, social situation, financial concerns, cultural factors, literacy and numeracy (mathematical literacy), diabetes history (duration, complications, and current use of medications), comorbidities, disabilities, health priorities, other medical conditions, preferences for care, access to health care services, and life expectancy. People living with diabetes should be engaged in conversation about these aspects of their lives and diabetes management, with routine reassessment as necessary given their changing circumstances across the life span. Various strategies and techniques

should be used to support the person's self-management efforts, including providing education on problem-solving and coping skills for all aspects of diabetes management.

Communication between health care professionals and people with diabetes and their families should acknowledge that multiple factors impact diabetes management but also emphasize that collaboratively developed treatment plans and a healthy lifestyle can significantly improve disease outcomes and well-being (2). Thus, the goal of communication between health care professionals and people with diabetes is to establish a collaborative relationship and to assess and address self-management barriers without blaming people with diabetes for “noncompliance” or “nonadherence”

Decision cycle for person-centered glycemic management in type 2 diabetes

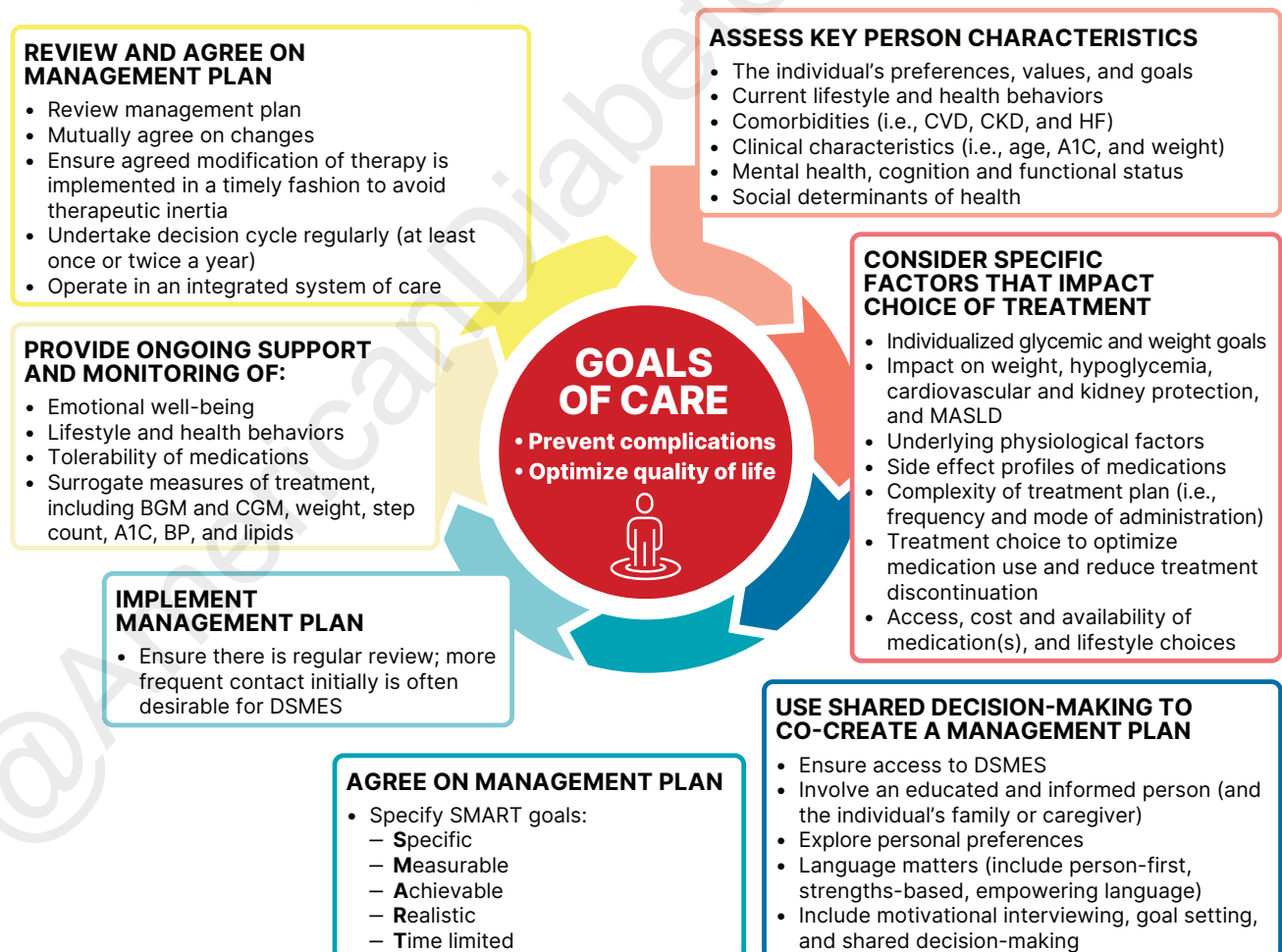


Figure 4.1—Decision cycle for person-centered glycemic management in type 2 diabetes. BGM, blood glucose monitoring; BP, blood pressure; CGM, continuous glucose monitoring; CKD, chronic kidney disease; CVD, cardiovascular disease; DSMES, diabetes self-management education and support; HF, heart failure. MASLD, metabolic dysfunction-associated steatotic liver disease. Adapted from Davies et al. (307).

when the outcomes of self-management are not optimal (3). The familiar terms noncompliance and nonadherence denote a passive, obedient role for a person with diabetes in “following doctor’s orders,” which is at odds with the active role people with diabetes take in the day-to-day decision-making, planning, monitoring, evaluation, and problem-solving involved in diabetes self-management. Using a nonjudgmental approach that normalizes periodic lapses in management may help minimize the person’s resistance to reporting problems with self-management. Empathizing and using active listening techniques, such as open-ended questions, reflective statements, and summarizing what the person said, can help facilitate communication. Perceptions of people with diabetes about their own ability, or self-efficacy, to self-manage diabetes constitute one important psychosocial factor related to improved diabetes self-management and treatment outcomes in diabetes (4) and should be a goal of ongoing assessment, education, and treatment planning.

Language has a strong impact on perceptions and behavior. Empowering language can help to inform and motivate, while shame and judgement can be discouraging. The American Diabetes Association (ADA) and the Association of Diabetes Care & Education Specialists (ADCES) (formerly called the American Association of Diabetes Educators) joint consensus report, “The Use of Language in Diabetes Care and Education,” provides the authors’ expert opinion regarding the use of language by health care professionals when speaking or writing about diabetes for people with diabetes or for professional audiences (3,5). Although further research is needed to address the impact of language on diabetes outcomes, the report includes five key consensus recommendations for language use:

- Use language that is neutral, nonjudgmental, and based on facts, actions, physiology, or biology.
- Use language free from stigma.
- Use language that is strength based, respectful, and inclusive and that imparts hope.
- Use language that fosters collaboration between people with diabetes and health care professionals.

- Use language that is person centered (e.g., “person with diabetes” is preferred over “diabetic”).

COMPREHENSIVE MEDICAL EVALUATION

Recommendations

4.3 A complete medical evaluation should be performed at the initial visit and follow-up, as appropriate, to:

- Confirm the diagnosis and classify diabetes. **A**
- Assess glycemic status and previous and current treatment. **A**
- Evaluate for diabetes complications, potential comorbid conditions, and overall health status. **A**
- Identify care partners, support systems, and available resources. **E**
- Assess social determinants of health and structural barriers to optimal health and health care. **A**
- Review risk factor management in the person with diabetes. **A**
- Begin engagement with the person with diabetes in the formulation of a care management plan including goals of care. **A**
- Develop a plan for continuing care. **A**

4.4 Ongoing management should be guided by the assessment of overall health and functional status, diabetes complications, cardiovascular risk, hypoglycemia risk, and shared decision making to set therapeutic goals. **B**

The comprehensive medical evaluation includes the initial and follow-up evaluations, which comprise assessment of complications, psychosocial assessment, management of comorbid conditions, overall health, functional and cognitive status, and engagement of the person with diabetes throughout the process. While a comprehensive list is provided in **Table 4.1**, in clinical practice the health care professional may need to prioritize select components of the medical evaluation given the available resources and time. Engaging other members of the health care team can also support comprehensive diabetes care. The goal of these recommendations is to provide the health care team with guidance and information so it can optimally support people with diabetes and their care partners. In addition to the medical history, physical examination, and

laboratory tests, health care professionals should assess diabetes self-management behaviors, nutrition, social determinants of health, and psychosocial health (see section 5, “Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes”) and give guidance on routine immunizations. The assessment of sleep pattern and duration, bone health, and sexual health should also be considered as an important part of the comprehensive evaluation of a person with diabetes. Follow-up visits should occur at least every 3–6 months individualized to the person and then at least annually.

Lifestyle management and behavioral health care are cornerstones of diabetes management. People with diabetes should be referred for diabetes self-management education and support, medical nutrition therapy, and assessment of behavioral health concerns as appropriate. People with diabetes should receive recommended preventive care services (e.g., immunizations and age- and sex-appropriate cancer screening); tobacco use cessation counseling; and ophthalmological, dental, podiatric, and other referrals, as needed.

The assessment of risk of acute and chronic diabetes complications and treatment planning are key components of initial and follow-up visits (**Table 4.2**). The risk of atherosclerotic cardiovascular disease (CVD) and heart failure (see section 10, “Cardiovascular Disease and Risk Management”), chronic kidney disease (CKD) staging (see section 11, “Chronic Kidney Disease and Risk Management”), presence of retinopathy and neuropathy (see section 12, “Retinopathy, Neuropathy, and Foot Care”), and risk of treatment-associated hypoglycemia should be used to individualize goals for glycemia (see section 6, “Glycemic Goals, Hypoglycemia, and Hyperglycemic Crises”), blood pressure, and lipids and to select specific glucose-lowering medication(s) (see section 9, “Pharmacologic Approaches to Glycemic Treatment”), antihypertension medications, and lipid lowering treatment intensity.

Additional referrals should be arranged as necessary (**Table 4.2**). Clinicians should ensure that people with diabetes are appropriately screened for complications, comorbidities, and treatment burden. Glycemic management is a part, not the sole goal, of the clinical encounter.

Table 4.1—Components of the comprehensive diabetes medical evaluation at initial, follow-up, and annual visits

	Visit		
	Initial	Every follow-up	Annual
Past medical and family history			
Diabetes history			
• Characteristics at onset (e.g., age and symptoms and/or signs)	✓		
• Review of previous treatment plans and response	✓		
• Assess frequency, cause, and severity of past hospitalizations	✓		
Family history			
• Family history of diabetes in a first-degree relative	✓		
• Family history of autoimmune disorders	✓		
Personal history of complications and common comorbidities			
• Common comorbidities (e.g., obesity, OSA, and MASLD)	✓		✓
• High blood pressure or abnormal lipids	✓		✓
• Macrovascular and microvascular complications	✓		✓
• Hypoglycemia: awareness, frequency, causes, and timing of episodes	✓	✓	✓
• Presence of hemoglobinopathies or anemias	✓		✓
• Last dental visit	✓		✓
• Last foot exam	✓		✓
• Last dilated eye exam	✓		✓
• Visits to specialists	✓		✓
• Disability assessment and use of assistive devices (e.g., physical, cognitive, vision and auditory, history of fractures, and podiatry)	✓	✓	✓
• Personal history of autoimmune disease	✓		
Surgical and procedure history			
• Surgeries (e.g., metabolic surgery and transplantation)	✓	✓	✓
Interval history			
• Changes in medical or family history since last visit		✓	✓
Behavioral factors			
• Physical activity, sleep behaviors, eating patterns and weight history	✓	✓	✓
• Assess familiarity with carbohydrate counting (e.g., type 1 diabetes or type 2 diabetes treated with MDI)	✓		✓
• Screen for OSA	✓	✓	✓
• Tobacco, alcohol, and substance use	✓		✓
Medications and vaccinations			
• Current medication plan	✓	✓	✓
• Medication-taking behavior, including rationing of medications and/or medical equipment	✓	✓	✓
• Medication intolerance or side effects	✓	✓	✓
• Complementary and alternative medicine use	✓	✓	✓
• Vaccination history and needs	✓		✓
Technology use			
• Assess use of health apps, online education, patient portals, etc.	✓	✓	✓
• Glucose monitoring (meter/CGM): results and data use	✓	✓	✓
• Review insulin pump settings and use and connected pen and glucose data	✓	✓	✓
Social life assessment			
Social network			
• Identify existing social supports	✓		✓
• Identify surrogate decision maker and advanced care plan	✓		✓
• Identify social determinants of health (e.g., food security, housing stability, transportation access, financial security, and community safety)	✓		✓

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IMMUNIZATIONS**Recommendation**

4.5 Provide routinely recommended vaccinations for children, adolescents, and adults with diabetes as indicated by age (see **Table 4.3**). **A**

Children, adolescents, and adults with diabetes should receive vaccinations according to age-appropriate recommendations (6,7). The Centers for Disease Control and Prevention (CDC) provides vaccination schedules specifically for children, adolescents, and adults with diabetes (cdc.gov/vaccines/). The CDC Advisory Committee on Immunization Practices (ACIP) makes recommendations based on its own review and rating of the evidence, provided in **Table 4.3** for selected vaccinations. The ACIP evidence review has evolved over time with the adoption of Grading of Recommendations Assessment, Development, and Evaluation (GRADE) in 2010 and then the Evidence to Decision or Evidence to Recommendation frameworks in 2020 (8). Here, we discuss the particular importance of specific vaccines.

COVID-19

People with underlying medical conditions, including diabetes, are more likely to become severely ill with coronavirus disease 2019 (COVID-19). COVID-19 vaccination using an appropriate number of doses of updated vaccines is recommended for everyone aged 6 months and older in the U.S. (6,7).

Hepatitis B

Compared with the general population, people with type 1 or type 2 diabetes have higher rates of hepatitis. Because of the higher likelihood of transmission of the disease, hepatitis B vaccine is recommended for adults with diabetes aged <60 years. For adults aged ≥60 years, hepatitis B vaccine may be administered at the discretion of the treating clinician based on the person's likelihood of acquiring hepatitis B infection (6,7).

Influenza

Influenza is a common, preventable infectious disease associated with high mortality and morbidity in vulnerable populations, including youth, older adults, and people with chronic diseases. Influenza vaccination

Table 4.1—Continued

	Visit		
	Initial	Every follow-up	Annual
Assess daily routine and environment, including school or work schedules and ability to engage in diabetes self-management	✓	✓	✓
Physical examination			
Height, weight, and BMI; growth and pubertal development in children and adolescents	✓	✓	✓
Blood pressure determination	✓	✓	✓
Orthostatic blood pressure measures (when indicated)	✓		✓
Fundoscopy examination (refer to eye specialist)	✓		✓
Thyroid palpation	✓		✓
Skin examination (e.g., acanthosis nigricans, insulin injection or insertion sites, and lipodystrophy)	✓	✓	✓
Comprehensive foot examination, determination of temperature, vibration or pinprick sensation, and 10-g monofilament exam	✓		✓
Visual inspection (e.g., skin integrity, callous formation, foot deformity or ulcer, and toenails)*	✓	✓	✓
Check pedal pulses and screen for PAD with ABI testing if a PAD diagnosis would change management	✓		✓
Screen for depression, anxiety, diabetes distress, fear of hypoglycemia, and disordered eating	✓		✓
Assessment for cognitive performance if indicated	✓		✓
Assessment for functional performance if indicated	✓		✓
Assessment for bone health (e.g., loss of height and kyphosis)	✓		✓
Laboratory evaluation			
A1C, if the results are not available within the past 3 months or if earlier assessment is necessary	✓	✓	✓
Lipid profile, including total, LDL, and HDL cholesterol and triglycerides‡	✓		
Liver function tests (i.e., FIB-4)‡	✓		✓
Spot urinary albumin-to-creatinine ratio	✓		✓
Serum creatinine and estimated glomerular filtration rate§	✓		✓
Thyroid-stimulating hormone in people with type 1 diabetes‡	✓		✓
Celiac disease screening in people with type 1 diabetes	✓		
Vitamin B12 if taking metformin for >5 years	✓		✓
CBC with platelets	✓		✓
Serum potassium levels in people treated with ACE inhibitors, ARBs, or diuretics§	✓		✓
Calcium, vitamin D, and phosphorous as appropriate	✓		✓

ABI, ankle brachial index; ARBs, angiotensin receptor blockers; CBC, complete blood count; CGM, continuous glucose monitor; FIB-4, fibrosis-4 index; MASLD, metabolic-associated steatotic liver disease; MDI, multiple daily injections; OSA, obstructive sleep apnea; PAD, peripheral arterial disease. *Should be performed at every visit in people with diabetes with sensory loss, previous foot ulcers, or amputations. †At 65 years of age or older. ‡May also need to be checked after initiation or dose changes of medications that affect these laboratory values (i.e., diabetes medications, blood pressure medications, cholesterol medications, or thyroid medications). §May be needed more frequently in people with diabetes with known chronic kidney disease or with changes in medications that affect kidney function and serum potassium (see Table 11.2). ||In people with presence of gastrointestinal symptoms, signs, laboratory manifestations, or clinical suspicion suggestive of celiac disease.

cardiovascular events (10). Given the benefits of the annual influenza vaccination, it is recommended for all individuals ≥ 6 months of age who do not have a contraindication. The live attenuated influenza vaccine, which is delivered by nasal spray, is an option for people who are 2–49 years of age and are not pregnant, but people with chronic conditions such as diabetes are cautioned against taking the live attenuated influenza vaccine and are instead recommended to receive the inactive or recombinant influenza vaccination. For the 2025–2026 season, all influenza vaccines offered in the U.S. are trivalent (6,7).

Pneumococcal Pneumonia

Like influenza, pneumococcal pneumonia is a common, preventable disease. People with diabetes are at increased risk for pneumococcal infection and have been reported to have a high risk of hospitalization and death, with a mortality rate as high as 50% (11). All people with diabetes should receive one of the CDC-recommended pneumococcal vaccines (12).

Respiratory Syncytial Virus

Respiratory syncytial virus (RSV) is a cause of respiratory illness in some individuals, including older adults. People with chronic conditions such as diabetes have a higher risk of severe illness. The U.S. Food and Drug Administration (FDA) approved the first vaccines for prevention of RSV-associated lower respiratory tract disease in adults aged ≥ 60 years. The ACIP recommends that all adults aged ≥ 75 years and adults aged 60–74 years who are at increased risk for severe RSV should receive a single dose of RSV vaccine (13).

ASSESSMENT OF COMORBIDITIES

Besides assessing diabetes-related complications, clinicians and people with diabetes need to be aware of common comorbidities that affect people with diabetes and that may complicate its management (14–16). Diabetes comorbidities are conditions that affect people with diabetes more often than age-matched people without diabetes. This section discusses the common comorbidities observed in people with diabetes but is not necessarily inclusive of all the conditions that have been reported.

in people with diabetes has been found to significantly reduce influenza and diabetes-related hospital admissions (9). In people

with diabetes, the influenza vaccine has been associated with lower risk of all-cause mortality, cardiovascular mortality, and

Table 4.2—Essential components for assessment, planning, and referral**Assessing risk of diabetes complications**

- ASCVD and heart failure history
- ASCVD risk factors and 10-year ASCVD risk assessment
- Staging of chronic kidney disease (see **Table 11.2**)
- Hypoglycemia risk (see section 6, “Glycemic Goals, Hypoglycemia, and Hyperglycemic Crises”)
- Assessment for retinopathy
- Assessment for neuropathy
- Assessment for MASLD and MASH

Goal setting

- Set A1C, blood glucose, and time-in-range goals
- Set lipid goal
- If hypertension is present, establish blood pressure goal
- Weight management and physical activity goals
- Diabetes self-management goals

Therapeutic treatment plans

- Lifestyle management (e.g., registered dietitian nutritionist)
- Pharmacologic therapy: glucose lowering
- Pharmacologic therapy: cardiovascular and kidney disease risk factors
- Weight management with pharmacotherapy or metabolic surgery, as appropriate
- Use of glucose monitoring and insulin delivery devices
- Referral to diabetes education and medical specialists (as needed)

Referrals for initial care management

- Eye care professional for annual dilated eye exam
- Family planning for individuals of childbearing potential
- Registered dietitian nutritionist for medical nutrition therapy
- Diabetes self-management education and support
- Dentist for comprehensive dental and periodontal examination
- Behavioral health professional, if indicated
- Audiology, if indicated
- Social worker and community resources, if indicated
- Rehabilitation medicine or another relevant health care professional for physical and cognitive disability evaluation, if indicated
- Other appropriate health care professionals

Assessment and treatment planning are essential components of initial and all follow-up visits. ASCVD, atherosclerotic cardiovascular disease; MASH, metabolic dysfunction-associated steatohepatitis; MASLD, metabolic dysfunction-associated steatotic liver disease.

Autoimmune Diseases**Recommendations**

4.6 Screen people with type 1 diabetes for autoimmune thyroid disease soon after diagnosis and thereafter at repeated intervals if clinically indicated. **B**

4.7 Adults with type 1 diabetes should be screened for celiac disease in the presence of gastrointestinal symptoms, signs, laboratory manifestations, or clinical suspicion suggestive of celiac disease. **B**

People with type 1 diabetes are at increased risk for other autoimmune diseases, with thyroid disease, celiac disease, and pernicious anemia (vitamin B12 deficiency) being among the most common (17). Other autoimmune conditions associated with type 1 diabetes include autoimmune liver disease, primary

adrenal insufficiency (Addison disease), vitiligo, collagen vascular diseases, and myasthenia gravis (18,19). Type 1 diabetes may also occur with other autoimmune diseases in the context of specific genetic disorders such as polyglandular autoimmune syndromes (20). Given the high prevalence, nonspecific symptoms, and insidious onset of primary hypothyroidism, routine screening for thyroid dysfunction is recommended for all people with type 1 diabetes. Screening for celiac disease should be considered in adults with diabetes with suggestive symptoms (e.g., diarrhea, malabsorption, and abdominal pain) or signs (e.g., osteoporosis, vitamin deficiencies, and iron deficiency anemia) (21). Measurement of vitamin B12 levels (and reflex methylmalonic acid) should be considered for people with type 1 diabetes and peripheral neuropathy or unexplained anemia.

Bone Health**Recommendations**

4.8 Assess fracture risk in older adults with diabetes as a part of routine care in diabetes clinical practice, according to risk factors and comorbidities. **A**

4.9 Monitor bone mineral density using dual-energy X-ray absorptiometry in older adults with diabetes (aged ≥ 65 years) and younger individuals with diabetes and multiple risk factors every 2–3 years (**Table 4.4**). **A**

4.10 Consider the potential adverse impact on skeletal health when selecting pharmacological options to lower glucose levels in people with diabetes. Avoiding medications with a known association with higher fracture risk (e.g., thiazolidinediones and sulfonylureas) is recommended, particularly for those at elevated risk for fractures. **B**

4.11 To reduce the risk of falls and fractures, glycemic management goals should be individualized for people with diabetes at a higher risk of fracture. **C** Prioritize use of glucose-lowering medications that are associated with low risk for hypoglycemia to avoid falls. **B**

4.12 Advise people with diabetes on their intake of calcium (1,000–1,200 mg/day) and vitamin D to ensure it meets the recommended daily allowance for those at risk for fracture, either through their food choices or supplemental means. **B**

4.13a Consider osteoporosis drug therapy in older adults with diabetes who are at increased risk of fracture, including those with low bone mineral density (T-score ≤ -2.5), history of fragility fracture, or elevated Fracture Risk Assessment Tool score ($\geq 3\%$ for hip fracture or $\geq 20\%$ for major osteoporotic fracture). **B**

4.13b Treatment may be considered for adults with diabetes with a T-score between -2.0 and -2.5 in the presence of additional risk factors for fracture. **C**

Determination of fracture risk traditionally has relied on measurements of bone mineral density (BMD) and the World Health Organization–defined T-score of ≤ -2.5 SD. However, it is now established that the consideration of other risk factors improves the categorization of fracture risk

Table 4.3—Highly recommended immunizations for people with diabetes (from the Advisory Committee on Immunization Practices and Centers for Disease Control and Prevention)

Vaccine	Recommended ages	Schedule	GRADE evidence type*	References
COVID-19	All people 6 months of age and older	Current initial vaccination and boosters	3	Centers for Disease Control and Prevention, Interim Clinical Considerations for Use of COVID-19 Vaccines in the United States (305)
Hepatitis B	Adults with diabetes aged <60 years; for adults aged ≥60 years, hepatitis B vaccine may be administered at the discretion of the treating clinician based on the person's likelihood of acquiring hepatitis B infection		1	Sandul et al., Updated Recommendation for Universal Hepatitis B Vaccination in Adults Aged 19–59 Years - United States, 2024 (306)
Influenza	All people with diabetes advised to receive a trivalent influenza vaccine and not to receive live attenuated influenza vaccine	Annual	3	Advisory Committee on Immunization Practices Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger - United States, 2025, and Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older - United States, 2025 (6,7)
Pneumonia (PPSV23 [Pneumovax])	19–64 years of age, vaccinate with Pneumovax	One dose is recommended for those who previously received PCV13; if PCV15 was used, follow with PPSV23 ≥1 year later; PPSV23 is not indicated after PCV20; adults who received only PPSV23 may receive PCV15 or PCV20 ≥1 year after their last dose	2	Advisory Committee on Immunization Practices Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger - United States, 2025, and Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older - United States, 2025 (6,7)
	≥65 years of age	One dose is recommended for those who previously received PCV13; if PCV15 was used, follow with PPSV23 ≥1 year later; PPSV23 is not indicated after PCV20; adults who received only PPSV23 may receive PCV15 or PCV20 ≥1 year after their last dose	2	Advisory Committee on Immunization Practices Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger - United States, 2025, and Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older - United States, 2025 (6,7)
PCV20 or PCV15	Adults 19–64 years of age with an immunocompromising condition (e.g., chronic renal failure), cochlear implant, or cerebrospinal fluid leak Adults 19–64 years of age, immunocompetent ≥65 years of age, immunocompetent, have shared decision-making	One dose of PCV15 or PCV20 is recommended by the Centers for Disease Control and Prevention For those who have never received any pneumococcal vaccine, the Centers for Disease Control and Prevention	2	Advisory Committee on Immunization Practices Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger - United States, 2025, and Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19

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Table 4.3—Continued

Vaccine	Recommended ages	Schedule	GRADE evidence type*	References
	discussion with health care professionals	recommends one dose of PCV15 or PCV20 One dose of PCV15 or PCV20; PPSV23 may be given ≥ 8 weeks after PCV15; PPSV23 is not indicated after PCV20		Years or Older - United States, 2025 (6,7)
RSV	Older adults ≥ 60 years of age with diabetes appear to be a risk group	Adults aged ≥ 75 years and those aged ≥ 60 years and at high risk may receive a single dose of an RSV vaccine	1	Advisory Committee on Immunization Practices Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger - United States, 2025, and Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older - United States, 2025 (6,7)
Tetanus, diphtheria, pertussis (Tdap)	All adults; pregnant individuals should have an extra dose	Booster every 10 years	2	Advisory Committee on Immunization Practices Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger - United States, 2025, and Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older - United States, 2025 (6,7)
Zoster	≥ 50 years of age	Two-dose Shingrix, even if previously vaccinated	1	Advisory Committee on Immunization Practices Recommended Immunization Schedule for Children and Adolescents Aged 18 Years or Younger - United States, 2025, and Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older - United States, 2025 (6,7)

For a comprehensive list of vaccines, refer to the Centers for Disease Control and Prevention web site at cdc.gov/vaccines/. Advisory Committee on Immunization Practices recommendations can be found at cdc.gov/acip/?CDC_AAref_Val=https://cdc.gov/vaccines/acip/recommendations. COVID-19, coronavirus disease 2019; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; PCV13, 13-valent pneumococcal conjugate vaccine; PCV15, 15-valent pneumococcal conjugate vaccine; PCV 20, 20-valent pneumococcal conjugate vaccine; PPSV23, 23-valent pneumococcal polysaccharide vaccine; RSV, respiratory syncytial virus. *Evidence type: 1, randomized controlled trials (RCTs) or overwhelming evidence from observational studies; 2, RCTs with important limitations or exceptionally strong evidence from observational studies; 3, observational studies or RCTs with notable limitations; 4, clinical experience and observations, observational studies with important limitations, or RCTs with several major limitations.

(Table 4.4). There are factors beyond BMD that contribute to bone strength in people with diabetes.

A low-trauma fracture (defined as a fracture occurring from minimal trauma, such as falling from standing height or

less) of the hip, pelvis, vertebra, or forearm in adults aged ≥ 65 years is diagnostic of osteoporosis, regardless of BMD. Such fractures are among the strongest predictors of future fracture risk, especially in the first 1–2 years after a

fracture (22,23). Osteoporotic fractures, especially those of the hip, are associated with significant morbidity, mortality, and societal costs (24). It is estimated that 20% of individuals do not survive to 1 year after hip fracture, while 60% do

Table 4.4—Diagnostic assessment

Individuals who should receive BMD testing

People aged ≥ 65 yearsPostmenopausal women and men aged ≥ 50 years with history of adult-age fracture or with diabetes-specific risk factors:

- Frequent hypoglycemic events
- Diabetes duration >10 years
- Diabetes medications: insulin, thiazolidinediones, sulfonylureas
- A1C $>8\%$
- Peripheral or autonomic neuropathy, retinopathy, nephropathy
- Frequent falls
- Glucocorticoid use: prednisone at doses >2.5 mg per day for ≥ 3 months

not regain their prior functionality, living with permanent disability (25).

Hip fractures in people with diabetes are associated with higher risk of mortality (28% in women and 57% in men), longer recovery, and delayed healing (26) compared with individuals without diabetes.

Epidemiology and Risk Factors

Age-specific fracture risk is significantly increased in people with type 1 or type 2 diabetes in both sexes, with a 34% increase in fracture risk compared with those without diabetes (27).

Type 1 Diabetes. Fracture risk in people with type 1 diabetes is increased by 4.35 times for hip fractures, 1.83 times for upper-limb fractures, and 1.97 times for ankle fractures (28). Fractures occur at young ages, 10–15 years earlier than they do in people without diabetes. Type 1 diabetes is often associated with low bone mass, although BMD underestimates the high risk of fracture observed in young individuals (28). Risk of fracture is increased in people with type 1 diabetes with microvascular complications or neuropathy compared with those without these complications. (26). Moreover, average A1C $>7.9\%$ (risk ratio [RR] 3.57 [CI 1.08–11.78]), duration of diabetes >26 years (RR 7.6 [CI 1.67–34.6]), and family history of fractures (RR 2.64 [CI 1.15–6.09]) have been independently associated with high risk of nonvertebral fractures (29).

Type 2 Diabetes. In people with type 2 diabetes, even with normal or higher BMD, hip fracture risk is increased by 1.79 times, and risk throughout life is 40–70% higher than in it is in individuals without diabetes (27,30,31). According to a meta-analysis that included 15 studies, people with type 2 diabetes had a

35% higher incidence of vertebral fractures, causing increased risk of mortality (hazard ratio [HR] 2.11 [95% CI 1.72–2.59]) (32). Fracture risk is also increased in the upper limbs and ankle. Despite normal to high BMD compared with individuals without type 2 diabetes, the velocity of bone loss with age is greater in individuals with type 2 diabetes, and low BMD remains a risk factor for fractures (33,34).

Glycemic management significantly impacts fracture risk in people with diabetes. A meta-analysis revealed an 8% increased fracture risk per 1% rise in A1C level (RR 1.08 [95% CI 1.03–1.14]) (35). Poor glycemic management (A1C $>9\%$) over 2 years in individuals with type 2 diabetes correlated with a 29% heightened fracture risk (36). Notably, this risk was higher among White individuals than in other racial groups. Hypoglycemia also escalates the risk of fractures at the hip and other skeletal sites (RR 1.52 [95% CI 1.23–1.88]) (35). A Japanese study echoed these findings, showing a fracture risk increase (HR 2.24 [95% CI 1.56–3.21]) with severe hypoglycemia episodes (37).

Longer diabetes duration further elevates fracture risk (38,39). Data indicate individuals who have had type 2 diabetes for >10 years face significantly higher fracture risks. Longer duration of disease may be associated with deposition of advanced glycation end products into the bone matrix, microvascular damage, and a proinflammatory state, which all impair bone cell activity and bone microdamage repair (40). Additionally, high fracture risk is seen in people with CVD, nephropathy, retinopathy, neuropathy, poor physical function, and frequent falls (41–43).

Screening

Most evidence on screening in individuals at risk for fracture is available from

people with type 2 diabetes; fracture risk prediction using BMD in type 1 diabetes has not been extensively studied. Health care professionals should assess fracture history and risk factors in people with diabetes and recommend measurement of BMD if appropriate according to the individual's age and sex.

Type 2 Diabetes. People with type 2 diabetes have 5–10% higher BMD than people without diabetes, although they present with lower bone strength, impaired bone microarchitecture, and accelerated bone loss (33,44–46). Fracture risk was higher in large observational studies in participants with diabetes compared with those without diabetes for a given T-score and age (34). Therefore, a T-score adjustment of -0.5 has been proposed to improve fracture prediction by dual-energy X-ray absorptiometry (DXA). For example, a T-score ≤ -2.0 should be interpreted as equivalent to -2.5 in a person without diabetes. Notably, the Fracture Risk Assessment Tool (FRAX), a medical calculator that predicts 10-year risk of fractures, does not incorporate type 2 diabetes as a risk factor and thus has also been shown to underestimate fracture risk for this population (34). Building on the recognized limitations of FRAX in type 2 diabetes, multiple large cohort studies and meta-analyses consistently demonstrate that type 2 diabetes is an independent risk factor for fracture and that FRAX systematically underestimates fracture risk in this population. This underestimation is observed across diverse ethnic groups, increases with longer diabetes duration, and is particularly pronounced for hip fractures and in older adults with diabetes. Several strategies have been proposed to improve FRAX performance in type 2 diabetes, including 1) using the rheumatoid arthritis input as a surrogate for diabetes, 2) lowering the femoral neck T-score input by 0.5 SD, 3) increasing the age by 10 years, or 4) incorporating trabecular bone score adjustments (47–49). However, recent findings indicate that fracture risk may be similar for a given femoral neck T-score in people with and without diabetes (39).

Fracture risk prediction may be enhanced by use of trabecular bone score (50,51), although such studies are not available for individuals with type 1

diabetes and are based on data from the U.S. or Canada.

In people with type 2 diabetes, BMD should be monitored by DXA scan in older adults (aged ≥ 65 years) in the absence of other comorbidities and in younger individuals (≥ 50 years of age) with bone or diabetes-related risk factors, such as insulin use or diabetes duration >10 years (Table 4.4). Reassessment is recommended every 2–3 years (48), depending on the screening evaluation, antihypertension medication initiation/monitoring, and the presence of additional risk factors, although the evidence on how frequently DXA should be repeated is less robust. According to the European Association for the Study of Obesity (EASO), DXA should be performed every 2 years in individuals undergoing metabolic surgery.

DXA-assisted vertebral fracture assessment is a convenient and low-cost method to assess vertebral fractures, although traditional lateral thoracic/lumbar spine X-ray is still considered the gold standard (52). MRI or computed tomography imaging studies performed for other purposes should be analyzed for presence of vertebral fractures as well as chest X-rays in hospitalized individuals.

Type 1 Diabetes. Because hip fracture risk in type 1 diabetes starts to increase after the age of 50 years, clinicians may consider assessing BMD after the 5th decade of life or earlier in the presence of low-trauma fracture or additional risk factors for bone loss (28). In people with type 1 diabetes, BMD underestimates fracture risk, but studies do not address the extent of underestimation of fracture risk.

According to the International Society for Pediatric and Adolescent Diabetes (ISPAD), regular assessment of bone health using bone densitometry in children and adolescents with type 1 diabetes is still controversial and not recommended, but it may be considered in association with celiac disease (51).

Management

Appropriate glycemic management and minimizing hypoglycemic episodes are crucial for bone health in people with diabetes. Individuals with prolonged disease, microvascular and macrovascular complications, or frequent hypoglycemic episodes face higher fracture risks and fall risks due to factors like

poor vision, neuropathy, sarcopenia, and impaired gait. Health care professionals should advocate for moderate physical activity to enhance muscle health, gait coordination, and balance as part of fracture preventive strategies (42,43,53). For specific recommendations on physical activity for older adults, please refer to section 13, "Older Adults."

Osteoporosis and fracture prevention are first based on measures applied to the general population. All people with diabetes should receive an adequate daily intake of protein, calcium, and vitamin D and stop smoking (54–56). All individuals should engage in regular physical activity, including aerobic activities and weight-bearing, flexibility, and balance exercise.

Intake of calcium (1,000–1,200 mg) should reflect the age-specific recommendations for the general population and should be obtained through nutrition plan and/or oral supplements (57).

The optimal level of 25-hydroxyvitamin D is a matter of controversy (58), although serum levels 20–30 ng/mL are generally thought to be sufficient (59). For individuals receiving antiresorptive therapy (including bisphosphonate therapy), a 25-hydroxyvitamin D level of >30 ng/mL has been recommended (60,61).

The safe upper limit is also a matter of debate, and there is substantial disagreement over whether to treat to a specified serum level. In the U.S., the recommended daily allowance of vitamin D is 600 IU for people aged 51–70 years and 800 IU for people aged >70 years (59). In clinical practice, this dose of supplement may not be sufficient to reach recommended serum levels of vitamin D, particularly in those at risk for vitamin D deficiency, and therefore supplementation should be individualized. Of note, recent draft recommendations made by the U.S. Preventive Services Task Force caution against supplementation with vitamin D (with or without calcium) for the primary prevention of fractures in community-dwelling postmenopausal women and men aged 60 years or older (62).

Fractures are important outcomes of frailty, a predisability condition that should be mitigated with individualized interventions to prevent falls, maintain mobility, and delay disability (63). In many circumstances, conservative management (calcium, vitamin D, and lifestyle measures) are not enough to reduce fracture risk.

When pharmacological treatment is needed, treatment initiation strategies are the same as those used for the general population. Antihypertension medications reduce bone resorption (bisphosphonates, selective estrogen receptor modulators, and denosumab), stimulate bone formation (teriparatide and abaloparatide), or have dual actions by stimulating bone formation and reducing bone resorption (romosozumab). These agents improve bone density and reduce the risk of vertebral and nonvertebral fractures. Although there are no studies specifically designed for people with diabetes, data on antiresorptive and osteoanabolic agents suggest efficacy in type 2 diabetes is similar to that for individuals without diabetes (64–66). Using individual participant data from randomized trials, antiresorptive therapies reduce fracture risk in people with and without type 2 diabetes for vertebral, hip, and nonvertebral fractures (64). No similar studies of efficacy of antihypertension treatment in people with type 1 diabetes have been published.

Primary Prevention of Fragility Fractures in People With Diabetes

In the general population, it is recommended that people with diabetes with a T-score ≤ -2.5 or an elevated FRAX score ($\geq 3\%$ for hip fracture or $\geq 20\%$ for major osteoporotic fracture) should be considered for pharmacological treatment with first-line drug therapy (alendronate, risedronate, ibandronate, and zoledronate or denosumab). In type 2 diabetes, since T-score underestimates fracture risk (as discussed above), pharmacological treatment should be strongly considered for adults with diabetes with a T-score between -2.0 and -2.5 in the presence of additional risk factors for fracture such as falls and elevated FRAX score.

The risk of hypocalcemia associated with denosumab use in individuals with CKD is markedly increased in advanced CKD (estimated glomerular filtration rate <30 mL/min/1.73 m²) and is highest in dialysis-dependent individuals. This risk must be proactively managed with pretreatment assessment, supplementation, close monitoring, and specialist consultation. Data from a phase 3 trial, Future Revascularization Evaluation in Patients With Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM), and its 10-year extension have shown that people with diabetes treated with denosumab

experienced positive effects on fasting glucose (67) and significant improvements in BMD and lower vertebral fracture risk (49). However, according to a post hoc subgroup analysis, a higher risk of nonvertebral fractures was observed in people with diabetes treated with denosumab (49). Self-management abilities of the person with diabetes should be considered in medication selection because inability to maintain the every 6-month denosumab injection schedule can lead to rebound bone loss and spontaneous vertebral fractures, careful individual selection and counseling are important prior to drug initiation. Bisphosphonate therapy (oral or intravenous) may be more appropriate in individuals with poor medication-taking behavior or gaps in access to medical care. As diabetes is a low-bone-turnover condition, very-high-risk individuals should be considered for osteoanabolic therapy (teriparatide, abaloparatide, romosozumab). Teriparatide showed positive effects on BMD and fracture risk in people with diabetes (65,66).

Romosozumab received FDA approval only for postmenopausal women with a box warning because it may increase risk of myocardial infarction, stroke, or cardiovascular death. Although real-world data suggests that romosozumab may not lead to an increase in cardiac events (68), it should not be prescribed in individuals who experienced a myocardial infarction or a stroke within the past year (69,70). Osteoanabolic treatments must be followed by antiresorptives to preserve BMD gains. Without consolidation, BMD declines within a year as increased bone turnover leads to rapid loss of newly formed bone.

Secondary Prevention of Fragility Fractures.

The risk of subsequent low-trauma fracture (hip, spine, nonvertebral site) is high, especially in the first 1–2 years after a fracture. Antiosteoporosis treatment reduces the risk of fracture in older individuals with prior hip or vertebral fracture.

As in the general population, people with diabetes who experience fragility fracture should 1) be given the diagnosis of osteoporosis regardless of bone density data and 2) receive the appropriate work-up and therapy to prevent future fractures (71). Individuals on long-term treatment with antiosteoporosis medications, with multiple fragility fractures, or with multiple comorbidities should be referred to a bone metabolic specialist. In these more complicated cases, a bone specialist may

choose to initiate an osteoanabolic agent to optimize bone formation and reduce immediate fracture risk (72). It is strongly recommended that all individuals with a fragility fracture be started on antiosteoporosis therapy and adequate calcium and vitamin D supplementation (if required) as soon as possible. In the appropriate individual, therapy may even be initiated during an inpatient stay to reduce care delays (71).

Glucose-Lowering Medications and Bone Health

Care plans for type 2 diabetes treatment should consider individual fracture risk and the potential effect of medications on bone metabolism. Metformin has a safe bone health profile (73,74). Studies have reported increased fracture incidences in women using thiazolidinediones (TZD), with the risk doubling with 1–2 years of TZD use compared with placebo or other glucose-lowering medications (HR 2.23 [95% CI 1.65–3.01]) (75,76). According to the Action to Control Cardiovascular Risk in Diabetes (ACCORD) study, reduced risk is noted in women who had discontinued TZD use for 1–2 years (HR 0.57 [95% CI 0.35–0.92]) or >2 years (HR 0.42 [95% CI 0.24–0.74]) compared with current users (77). Furthermore, individuals with type 2 diabetes on sulfonylureas exhibit a heightened fracture risk (RR 1.30 [95% CI 1.18–1.43]) (78) because of accelerated bone loss (46) and a higher rate of hypoglycemic events, which can trigger falls and fractures (79). Dipeptidyl peptidase 4 inhibitors have been used in clinical practice for more than 15 years, and both clinical trials and postmarketing data suggest a neutral impact on bone health (80,81). Glucagon-like peptide 1 receptor agonists (GLP-1 RAs) at low doses are likely neutral to beneficial with respect to BMD and fracture risk (82), though data are lacking for higher doses in which weight loss may be higher and more rapid with potential counteractive skeletal risk. Use of sodium–glucose cotransporter 2 (SGLT2) inhibitors has raised some concerns. The Canagliflozin Cardiovascular Assessment Study (CANVAS) showed that the proportion of subjects with fracture was higher in the canagliflozin groups than the non-canagliflozin groups (2.7% vs. 1.9%, respectively). Further analyses from the same trial and from the Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation (CREDENCE) study found a neutral effect on fracture risk

(83–86). Although few data are available, use of empagliflozin, ertugliflozin, or dapagliflozin has not been associated with negative effects on bone health (85–87). Use of insulin has been shown to be associated with a doubling of the risk of hip fractures (79), likely because of higher risk of hypoglycemia, longer duration of the disease, and comorbidities that may contribute to diminished bone strength.

In conclusion, glucose-lowering medications with a good bone safety profile are preferred. This is especially true in older adults, in people with longer duration of diabetes, or in people with complications. Aggressive therapeutic approaches should be avoided in those who are frail and in older adults to prevent hypoglycemic events and falls.

Cancer

Diabetes is associated with increased risk of cancers of the liver, pancreas, endometrium, colon and rectum, breast, and bladder (88). The association may result from shared risk factors between type 2 diabetes and cancer (older age, obesity, and physical inactivity) but may also be due to diabetes-related factors (89), such as underlying disease physiology or diabetes treatments, although evidence for these links is scarce. People with diabetes should be encouraged to undergo recommended age- and sex-appropriate cancer screenings, coordinated with their primary health care professional, and to reduce their modifiable cancer risk factors (obesity, physical inactivity, alcohol use, and smoking). New onset of atypical diabetes (lean body habitus and negative family history) in a middle-aged or older person may precede the diagnosis of pancreatic adenocarcinoma (90). Additionally, in a nationwide cancer registry in New Zealand, postpancreatitis diabetes mellitus was associated with significantly higher risk (2.4-fold) of pancreatic cancer compared with pancreatitis after type 2 diabetes (91). However, in the absence of other symptoms (e.g., weight loss and abdominal pain), routine screening for pancreatic cancer is not currently recommended. Metformin and sulfonylureas may have anticancer properties. Data for pioglitazone are mixed, with a previous concern for bladder cancer association. Recommendations cannot be made at this time (92–94). Thus far, the use of GLP-1 RAs has not been shown to be

associated with the incidence of thyroid cancer, pancreatic cancer, or any other type of cancer in humans (95,96). For information on glycemic management in the context of cancer treatment, see section 9, "Pharmacologic Approaches to Glycemic Treatment."

Cognitive Impairment/Dementia

Recommendation

4.14 In the presence of cognitive impairment, diabetes treatment plans should be simplified as much as possible and tailored to minimize the risk of hypoglycemia. **B**

Diabetes is associated with a significantly increased risk and rate of cognitive decline and an increased risk of dementia (97). A meta-analysis of 122 prospective observational studies found that individuals with diabetes had a 43% higher risk of all types of dementia, a 43% higher risk of Alzheimer dementia, and a 91% higher risk of vascular dementia compared with individuals without diabetes (97). In a 15-year prospective study of community-dwelling people >60 years of age, the presence of diabetes at baseline significantly increased the age- and sex-adjusted incidence of all-cause dementia, Alzheimer dementia, and vascular dementia compared with rates in those with normal glucose tolerance (98). The reverse is also true: people with Alzheimer dementia are more likely to develop diabetes than people without Alzheimer dementia, possibly linking critical metabolic processes that contribute to neurodegeneration (99). A new clinical entity of diabetes-related dementia is being recognized as distinct from Alzheimer dementia or vascular dementia. It is characterized by slow progression of dementia, absence of typical neuroimaging findings seen in Alzheimer or vascular dementia, old age, high A1C levels, long duration of diabetes, high frequency of insulin use, frailty, and sarcopenia or dynapenia (100). See section 13, "Older Adults," for a more detailed discussion regarding assessment of cognitive impairment.

Glycemic Status and Cognition

In individuals with diabetes, higher A1C level is associated with lower cognitive function (101). A meta-analysis of randomized trials found that intensive

glycemic management, compared with higher A1C goals, was associated with a slightly lower rate of cognitive decline. However, these findings were driven by an older study with an A1C goal of <7.0% in the intensive treatment arm. Analyses within the ACCORD, Action in Diabetes and Vascular Disease: Preterax and Diamicon MR Controlled Evaluation (ADVANCE), and Veterans Affairs Diabetes Trial (VADT) studies found that intensive glycemic management (A1C goal of <6.0–6.5%) resulted in no differences in cognitive outcomes compared with standard control (102,103).

Results from the China Health and Retirement Study (CHARLS) report that in adults aged >45 years with type 2 diabetes, excessively low and high A1C levels (>9%) were associated with increased risk of cognitive impairment (104). Therefore, intensive glycemic management should not be advised for the improvement of cognitive function in individuals with type 2 diabetes. Additionally, people with type 2 diabetes and dementia are at heightened risk for experiencing hyperglycemic crises (diabetic ketoacidosis and hyperglycemic hyperosmolar state) compared with people without dementia (105), underscoring the importance of supporting and simplifying diabetes management for individuals experiencing cognitive decline and diminished capacity for self-care. In addition, these individuals have increased difficulty with complex treatment and monitoring plans and are at risk for frailty, hypoglycemia, and disability (106).

In type 2 diabetes, severe hypoglycemia is associated with reduced cognitive function, and those with poor cognitive function have more severe or repeated episodes of hypoglycemia. Multiple observational studies of adults with diabetes have found an association between severe hypoglycemic episodes and cognitive decline or incident dementia (107–110). Decreased cognitive function also increases the risk for severe hypoglycemia, likely through impaired ability to recognize and respond appropriately to hypoglycemic symptoms (107,111,112). Additionally, long-term follow up of Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) showed recurrent severe hypoglycemia was associated with the highest risk of long-term psychomotor and mental function decline (113). Simplifying

or deintensifying glycemic therapy and/or liberalizing A1C goals may prevent hypoglycemia in individuals with cognitive dysfunction. See section 13, "Older Adults," for more detailed discussion of hypoglycemia in older people with type 1 and type 2 diabetes.

Dental Care

Recommendations

4.15 People with diabetes should be referred for a dental exam at least once per year. **E**

4.16 Coordinate efforts between the medical and dental teams to appropriately adjust glucose-lowering medication and treatment plans prior to and in the postdental procedure period as needed. **B**

Periodontal disease is more severe, and may be more prevalent, in people with diabetes than in those without and has been associated with higher A1C levels (114,115). Longitudinal studies suggest that people with periodontal disease have higher rates of incident diabetes, suggesting a bidirectional relationship between diabetes and periodontal disease. Current evidence suggests that periodontal disease adversely affects diabetes outcomes, and periodontal treatment using subgingival instrumentation may improve glycemic outcomes (116,117).

The proportion of U.S. adults with diabetes seeing a dentist in the past year was significantly lower than that of individuals without diabetes (56.7% vs. 65.4%). The majority of clinicians do not discuss oral health with individuals (118). Increased engagement in toothbrushing has been shown to be associated with improved oral health and better glycemic management in people with type 2 diabetes (119). Dental health professionals should be included in the diabetes care team when possible, using a collaborative interprofessional care approach (120). Early detection of oral health problems by clinicians may be helpful to promote prompt referral to dental care and mitigate the expensive and extensive procedures needed to treat advanced oral disease (121,122). Clinical assessment of people with diabetes should include a dental history and an oral examination, and dental professionals should be informed about key aspects of the person's

health and diabetes treatment plan, including glycemic goals, medications, and comorbid conditions (121,122). It is important for dental professionals to know when people with diabetes have high A1C levels, as this population may have lower oral healing capacity (123,124). Hepatic, cardiovascular, kidney, and pulmonary conditions should also be known by dental professionals to assist in appropriate dosing of antibiotics and other medications. Coordination between dental professionals and the diabetes care team will be especially important for people treated with insulin, sulfonylureas, or meglitinides who are at risk for hypoglycemia during dental procedures, especially if fasting. Hypoglycemia can be mitigated by medication adjustment, blood glucose monitoring before and during the procedure, and treatment of hypoglycemia if appropriate. Therefore, dental professionals caring for people with diabetes should have access to blood glucose monitors during procedures as well as carbohydrates and glucagon to treat any hypoglycemia that occurs.

Disability

Recommendation

4.17 Assess for disability at the initial visit and for decline in function at each subsequent visit in people with diabetes. If a disability is impacting functional ability or capacity to manage their diabetes, a referral should be made to an appropriate health care professional specializing in disability (e.g., physical medicine and rehabilitation specialist, physical therapist, occupational therapist, or speech-language pathologist). **C**

A disability is defined as a physical or mental impairment that substantially limits one or more major life activities of an individual (125,126). Activities of daily living (ADLs) and instrumental activities of daily living (IADLs) comprise basic and complex life care tasks, respectively. The capacity to accomplish such tasks serves as an important measure of function. Diabetes is associated with an increase in the risk of work and physical disability, with estimates of 50–80% increased risk of disability for people with diabetes compared with people without diabetes (127). Reviews have shown that lower-body functional

limitation was the most prevalent disability (47–84%) among people with diabetes (128,129). In a systematic review and meta-analysis, the presence of diabetes increased the risk of mobility disability (15 studies; odds ratio [OR] 1.71 [95% CI 1.53–1.91]; RR 1.51 [95% CI 1.38–1.64]), of IADL disability (10 studies; OR 1.65 [95% CI 1.55–1.74]), and of ADL disability (16 studies; OR 1.82 [95% CI 1.63–2.04]; RR 1.82 [95% CI 1.40–2.36]) (127). In a meta-analysis, diabetes was shown to be associated with an increased risk of falls in older adults; falls occurred in 25% of individuals with diabetes compared with 18.2% of those without diabetes (130). The mechanisms underlying disability are multifactorial and include obesity, coronary artery disease, stroke, lower extremity complications, and physiological factors such as hyperglycemia, sarcopenia, inflammation, and insulin resistance (131).

Diabetic peripheral neuropathy (DPN) is a common complication of both type 1 and 2 diabetes and may cause impaired postural balance and gait kinematics (132), leading to functional disability. DPN can be found in up to half of people with type 1 or type 2 diabetes, resulting in physical disability, and neuropathic pain, resulting in a diminished quality of life (133). Glycemic management prevents DPN development in type 1 diabetes; in contrast, glycemic management has modest or no benefit in individuals with type 2 diabetes, possibly due to the combined effect of coexisting comorbidities (133). People with lower-extremity involvement due to DPN have 3 times more risk of restricted mobility, resulting in them experiencing more physical dysfunctions and impairments than people who have diabetes but not neuropathy (134). Furthermore, DPN may progress to nontraumatic lower-limb amputation, which significantly impacts quality of life (135).

In addition to complications of diabetes from microvascular conditions such as CKD, retinopathy, autonomic neuropathy, and peripheral neuropathy, it is important to recognize the disabilities caused by macrovascular complications of diabetes. These macrovascular complications, which include coronary heart disease, stroke, and peripheral arterial disease, can lead to further impairments (128).

An assessment of disability should be performed to evaluate individuals' ability to perform ADLs and IADLs, ensuring they can manage basic self-care and more complex tasks necessary for specific living situations. Referrals may be made as necessary to appropriate health care professionals specializing in disability (e.g., physical medicine and rehabilitation physician, physical therapist, occupational therapist, or speech-language pathologist) (127,136,137). Customized rehabilitation interventions for individuals with a disability from diabetes can recover function, allowing for safe physical activity (138), and improve quality of life (139). Additionally, frailty is commonly associated with diabetes, with progression to disability, morbidity, and mortality in older adults. People with diabetes as well as frailty or disability may be sedentary and contend with comorbid conditions such as hypoglycemia, sarcopenia, falls, nutritional deficiencies, obesity, polypharmacy, and cognitive dysfunction. A thorough medical evaluation is imperative to identify the best approaches to preventative and therapeutic interventions for frailty and diabetes management (140).

A psychosocial assessment should be conducted to screen for behavioral health conditions like depression and anxiety and to understand the individual's social support and coping mechanisms. Functional capacity evaluations, involving tests for physical endurance and strength, are used to gauge the ability of the person with diabetes to work and carry out daily activities. Additionally, standardized disability questionnaires and scales, such as the Diabetes Distress Scale (DDS) and the World Health Organization Disability Assessment Schedule (WHODAS 2.0), are employed to measure the emotional burden of diabetes and overall disability (141,142). These suggested structured assessments are particularly relevant if individuals have fallen, had emergency department visits, missed appointments, made significant errors in the treatment plan, or exhibit apathy and depressed mood.

Moreover, when treating people with an acquired disability from diabetes, it is vital to consider social determinants of health, race and ethnicity, and socioeconomic status (143). Rates of diabetes-related major amputations are higher in individuals who are from racial and ethnic minoritized groups (144), live in rural areas, and are from regions with the

lowest socioeconomic levels (145). Addressing the complex challenges faced by individuals with acquired disabilities from diabetes requires a multifaceted approach involving solutions from both within and outside the health care system. By focusing on social determinants of health, health care professionals can develop appropriate interventions, provide advocacy, and establish support systems that cater to the specific needs of this population. See section 1, "Improving Care and Promoting Health in Populations."

Hepatitis C

Infection with hepatitis C virus (HCV) is associated with a higher prevalence of type 2 diabetes, which is present in up to one-third of individuals with chronic HCV infection. HCV may impair glucose metabolism by several mechanisms, including directly via viral proteins and indirectly by altering proinflammatory cytokine levels (146). The use of newer direct-acting antiviral drugs produces a sustained virological response (cure) in nearly all cases and has been reported to improve glucose metabolism in individuals with diabetes (147). A meta-analysis of mostly observational studies found a mean reduction in A1C levels of 0.45% (95% CI −0.60 to −0.30) and reduced requirement for glucose-lowering medication use following successful eradication of HCV infection (148).

Sexual Health in Men

Recommendations

4.18 In men with diabetes or prediabetes, screen for erectile dysfunction (ED), particularly in those with high cardiovascular risk, retinopathy, cardiovascular disease, chronic kidney disease, peripheral or autonomic neuropathy, longer duration of diabetes, depression, and hypogonadism and in those who are not meeting glycemic goals. **B**

4.19 In men with diabetes or prediabetes, inquire about sexual health (e.g., low libido and ED). If symptoms and/or signs of hypogonadism are detected, screen with a morning serum total testosterone level. **B**

The most common sexual dysfunction in men is erectile dysfunction (ED), with an estimated prevalence of 52.5% in men

with diabetes (149). The best predictors of ED are age (>40 years), CVD, diabetes, hypertension, obesity, dyslipidemia, metabolic syndrome, hypogonadism, smoking, depression, and use of medications such as antidepressants and opioids (150). Because diabetes, poor nutrition, obesity, lack of exercise, and CVD are often interrelated, it may be challenging to identify the primary risk factor (151), although the most likely primary underlying risk factor is vascular disease (151).

Men with diabetes are at increased risk for both CVD and ED, and ED is a predictor of cardiovascular events in men with diabetes (152,153) as well as in men without diabetes. The significant factors associated with ED in men with diabetes are age, peripheral or autonomic neuropathy, presence of microvascular disease including retinopathy, CVD, duration of diabetes, poor glycemic management, hypogonadism, and diuretic therapy (154). Physical activity may be protective. Men with diabetes and ED report a significant decline in quality-of-life measures and an increase in depressive symptoms (155), and depression is a well-recognized risk factor for ED. Given the bidirectional relationship between ED and depression, treatment of either one can result in improvement in the other condition. CKD is also a risk factor for CVD and ED, with prevalence rates of ED >75% in men on hemodialysis (156).

Awareness and identification of these characteristics, factors, and behaviors can guide clinicians in early screening, treatment, prevention, and counseling in all men with diabetes and particularly those at higher risk for ED (154). Given the evidence that ED is strongly associated with diabetes and CVD, men with ED should be evaluated and managed for cardiovascular and endocrine risk factors. Glycemic assessment in men not previously diagnosed with diabetes, lipid profile, and morning total and free testosterone should be considered mandatory in all men newly presenting with ED (157).

In a recent meta-analysis, testosterone was superior to placebo in improving erectile function in men with testosterone deficiency; however, the magnitude of the effect was lower in the presence of diabetes and obesity (158).

Meta-analyses show that all phosphodiesterase type 5 inhibitors (PDE5Is) are superior to placebo in treating ED, lower dosages had effects comparable with

those of higher dosages, and various PDE5Is show comparable efficacy (151). PDE5Is are associated with an increased risk of headaches, flushing, and dyspepsia (151). First-line therapy for ED in men with diabetes is PDE5Is, but men with diabetes may be less responsive than men without diabetes (149). Strategies to improve response to PDE5Is include daily therapy and optimization of comorbidities. In men with diabetes not responding to PDEIs, other potentially effective treatments may include intracavernosal injections, intraurethral prostaglandin, vacuum erection devices, and penile prosthetic surgery (149).

Mean levels of testosterone are lower in men with diabetes than in age-matched men without diabetes, but obesity is a major confounder (159,160). Testosterone replacement in men with symptomatic hypogonadism may have benefits, including improved sexual function, well-being, muscle mass and strength, and bone density (161). In men with diabetes who have symptoms or signs of low testosterone (hypogonadism), a morning total testosterone level should be measured using an accurate and reliable assay (162). In men who have total testosterone levels close to the lower limit, it is reasonable to determine free testosterone concentrations either directly from equilibrium dialysis assays or by calculations that use total testosterone, sex hormone binding globulin, and albumin concentrations (162). Further tests (such as prolactin, luteinizing hormone and follicle-stimulating hormone levels) may be needed to further evaluate the individual. Testosterone replacement in older men with hypogonadism has been associated with increased coronary artery plaque volume, with no conclusive evidence that testosterone supplementation is associated with increased cardiovascular risk in all men with hypogonadism (162,163). Furthermore, ED is also common in people with diabetes (164), and it is reasonable to measure and correct testosterone levels close to the lower limit to address the libido component that contributes to erectile difficulties (151).

Sexual Health in Women

Recommendations

4.20 In women with diabetes or prediabetes, inquire about sexual health by

screening for desire (libido), arousal, and orgasm difficulties, particularly in those who experience depression and/or anxiety and those with recurrent urinary tract infections. **B**

4.21 In postmenopausal women with diabetes or prediabetes, screen for symptoms and/or signs of genitourinary syndrome of menopause, including vaginal dryness and dyspareunia. **B**

Female sexual dysfunction (FSD) is common in women with diabetes. In an epidemiologic cross-sectional study of community-residing middle-aged and older adults (57–85 years), women with diagnosed diabetes were less likely than men with diagnosed diabetes (adjusted OR 0.28 [95% CI 0.16–0.49]) and women without diabetes (0.63 [0.45–0.87]) to be sexually active (165). Older women with diabetes are as likely as men to have sexual problems but are significantly less likely to have discussed sex with a physician (165).

While studies showing the association between diabetes and FSD are less conclusive than those in men, most have reported a higher prevalence of FSD in women with diabetes compared with women without diabetes (166), and a meta-analysis found that FSD is more common in women with type 1 and type 2 diabetes (OR 2.27 and 2.49, respectively) than in women without diabetes (167).

A wide range of prevalence rates of sexual dysfunctions has been reported in women with diabetes. In women with type 1 diabetes, 16–85% (vs. 0–66% in women without diabetes) report problems with desire, 11–76% (vs. 0–41%) report problems with arousal, and 9–66% (vs. 0–39%) report problems with orgasm; 9–57% (vs. 0–28%) report problems with lubrication, and 7–61% (vs. 5–39%) report problems with pain. In women with type 2 diabetes, 70–82% (vs. 10–66% in women without diabetes) report problems with desire, 54–68% (vs. 3–41%) report problems with arousal, and 33–84% (vs. 2–39%) report problems with orgasm; 33–66% (vs. 4–28%) report problems with lubrication, and 33–46% (vs. 8–39%) report problems with pain (168).

Medical comorbidities that are risk factors for FSD include hypertension, obesity,

metabolic syndrome, smoking, and hyperlipidemia. Clinical factors for consideration include longer duration of diabetic retinopathy and neuropathy and individuals not meeting glycemic goals. The prevalence of FSD in women with kidney disease is 74% (169).

In women with diabetes, social and psychological components play a major role in FSD. Depression, anxiety, and emotional adjustments to diabetes have been found to be associated with sexual dysfunction in women with diabetes. A study from Norway reported that women with type 1 diabetes with scores on the Female Sexual Function Index (FSFI) (a validated instrument) indicating sexual dysfunction were more likely than women without sexual dysfunction to have diabetes distress, depression, and menopausal symptoms. They were also older and more likely to be single and postmenopausal (170). Another study also showed that women with sexual dysfunction were significantly more likely to report impaired well-being, elevated diabetes distress, poor adjustment to diabetes, and moderate to severe anxiety than women without sexual dysfunction (168).

In a qualitative study exploring the experiences of sexual health and sexual challenges, women with type 1 diabetes reported that diabetes affected their relationship, including sex life, and had an impact on their partner. Challenges included reduced sexual desire, decline in frequency, less spontaneous desire resulting in lack of initiation, and physical challenges such as pain, vaginal dryness, and impaired sensitivity. Several women explained that vaginal dryness was an obstacle during sexual intercourse, leading to pain or even refraining from sexual activity. Sexual challenges were perceived to become a source of disappointment to the partners and consequential guilt for the women. Women also reported fear of hypoglycemia during sex, and some reported trying to maintain mild hyperglycemia. Technology devices, such as glucose monitors and insulin pumps, could be perceived as both a physical and mental obstacle during sexual activity (171).

Many women with diabetes would like their health care professional to initiate a discussion on how diabetes is affecting their sex life (172). Women with type 1 diabetes almost unanimously

endorsed that sexual health should be addressed, that they would find it a relief that they were not alone, that they should be provided with information when they are young, and that it would be difficult to address the topic themselves (171). Unfortunately, many health care professionals do not actively discuss sexual functioning in consultations, meaning that when the topic is discussed it is mostly the person with diabetes who initiates the conversation (165). This leads to a marked underdiagnosis and undertreatment of sexual dysfunctions in people with diabetes.

While no specific guidelines are available for the treatment of FSD in this population, women with type 1 or type 2 diabetes should be encouraged to engage in lifestyle interventions and, in the absence of contraindications, may benefit from already-approved treatments for FSD (173). The Look AHEAD (Action for Health in Diabetes) study on intervention demonstrated statistical improvements in the FSFI total score and all domains of sexual dysfunction (174). Lifestyle factors that enhance desire and sexual function include nutrition (such as the Mediterranean eating pattern), exercise (such as walking), and smoking cessation. Other interventions include improving glycemic management and prevention of diabetes complications; diagnosis and treatment of menopausal symptoms with hormonal therapies; addressing vaginal dryness and dyspareunia as well as urinary tract and mycotic genital infections; screening and addressing depression, anxiety, diabetes distress, and related psychosocial issues; and considering FDA-approved centrally acting medications for hypoactive sexual desire disorder, including flibanserin and bremelanotide.

Metabolic Dysfunction–Associated Steatotic Liver Disease and Metabolic Dysfunction–Associated Steatohepatitis

Screening

Recommendations

4.22a Screen adults with type 2 diabetes or with prediabetes, particularly those with obesity or other cardiometabolic risk factors or established cardiovascular disease, for their risk of having or developing cirrhosis related to metabolic dysfunction–

associated steatohepatitis (MASH) using a calculated fibrosis-4 index (FIB-4) (derived from age, ALT, AST, and platelets [mdcalc.com/calc/2200/fibrosis4-fib-4-index-liver-fibrosis]), even if they have normal liver enzymes. **B**

4.22b Adults with diabetes or prediabetes with persistently elevated plasma aminotransferase levels for >6 months and low FIB-4 should be evaluated for other causes of liver disease. **B**

4.23 Adults with type 2 diabetes or prediabetes with a FIB-4 ≥ 1.3 should have additional risk stratification by liver stiffness measurement with transient elastography, or, if unavailable, the enhanced liver fibrosis (ELF) test. **B**

4.24 Refer adults with type 2 diabetes or prediabetes at higher risk for significant liver fibrosis (i.e., as indicated by FIB-4, liver stiffness measurement, or ELF) to a gastroenterologist or hepatologist for further evaluation and management. **B**

Metabolic dysfunction-associated steatotic liver disease (MASLD) has replaced the term nonalcoholic fatty liver disease (NAFLD) to identify steatotic liver disease. The definition includes the presence of steatotic liver disease and at least one cardiometabolic risk factor associated with insulin resistance (e.g., prediabetes, diabetes, atherogenic dyslipidemia, or hypertension) without other identifiable causes of steatosis (175). This is in the absence of ongoing or recent consumption of significant amounts of alcohol (defined as ingestion of >21 standard drinks per week in men and >14 standard drinks per week in women over a 2-year period preceding evaluation) or other secondary causes of hepatic steatosis (176). It is estimated that in adults in the U.S., the prevalence of MASLD is >70% of people with type 2 diabetes (177–179). This is consistent with studies from other countries (180,181). The new definition of MASLD aims to remove potential stigma from the term “fatty” when referring to steatosis, highlights the role of prediabetes and type 2 diabetes in MASLD, and provides a positive diagnosis by using cardiometabolic risk factors as surrogates for insulin resistance, the main driver for the development of steatosis. The new definition correlates well with the past definition

of MASLD for people with prediabetes or type 2 diabetes (who already have, by definition, one cardiometabolic risk factor). A separate category outside of MASLD, named metabolic dysfunction and alcoholic liver disease, was created for circumstances in which alcohol intake is greater than that allowed for MASLD but less than that attributed to alcoholic liver disease. More research is needed to better characterize the predictive value for metabolic dysfunction-associated steatohepatitis (MASH) of different cardiometabolic risk factors and the natural history of metabolic dysfunction and alcoholic liver disease or steatosis in young adults without cardiometabolic risk factors.

Diabetes is a major risk factor for developing MASH (formerly nonalcoholic steatohepatitis, or NASH) and worse liver outcomes (180,181). MASH is defined histologically as having $\geq 5\%$ hepatic steatosis with inflammation and hepatocyte injury (hepatocyte ballooning), with or without evidence of liver fibrosis (176). Steatohepatitis is estimated to affect more than half of people with type 2 diabetes with MASLD (182,183). Fibrosis stages are classified histologically as the following: F0, no fibrosis; F1, mild; F2, moderate (significant); F3, severe (advanced); and F4, cirrhosis. In the U.S., between 12 and 20% of people with type 2 diabetes have “at-risk” MASH (i.e., steatohepatitis with clinically significant fibrosis [$\geq F2$] and at risk for cirrhosis) (177,178,182). A similar or higher prevalence has been observed worldwide (180,181,183). People with type 2 diabetes and at-risk MASH are at an increased risk of future cirrhosis, hepatocellular carcinoma (HCC) (184,185), and liver transplantation (186). The prevalence of MASLD in people with type 1 diabetes is $\sim 20\%$ and is driven by obesity, which is becoming more common in this population (187), with a large variability across studies using different steatosis measurement methods (188). The prevalence of liver steatosis in a population with type 1 diabetes by MRI (i.e., the gold standard) with low prevalence of obesity was only 8.8% compared with 68% in people with type 2 diabetes (189). The prevalence of clinically significant fibrosis ($\geq F2$) is estimated to be $\sim 5\%$ (190), which is much lower than the prevalence in type 2 diabetes (177,178,182). Therefore, screening for fibrosis in people

with type 1 diabetes should only be considered in the presence of additional risk factors for MASLD, such as obesity, incidental hepatic steatosis on imaging, or elevated plasma aminotransferases.

Clinicians underestimate the prevalence of at-risk MASH and do not consistently implement appropriate screening strategies in people with prediabetes or type 2 diabetes, thus missing a chance to establish an early diagnosis. This pattern of underdiagnosis is compounded by sparse referral to specialists and inadequate prescription of medications with potential efficacy in MASH (191,192). The goal of screening for MASLD is to identify people with at-risk MASH to prevent future cirrhosis, HCC, liver transplantation, and all-cause mortality (193–196). This risk is higher in people who have central obesity and cardiometabolic risk factors or insulin resistance, are >50 years of age, and/or have persistently elevated plasma aminotransferases (AST and/or ALT >30 units/L for >6 months) (178,197). Some genetic variants that alter hepatocyte triglyceride metabolism may also increase the risk of MASH progression and cirrhosis (198,199), amplifying the impact of obesity, but the role of genetic testing in clinical practice remains to be established. Individuals with MASLD also are at a greater risk of developing extrahepatic cancer (185), type 2 diabetes (194), and CVD (200,201). Emerging evidence suggests that MASLD increases the risk of CKD in people with type 2 diabetes, particularly when liver fibrosis is present (202,203), although the association of MASLD with diabetic retinopathy is less clear (204).

The fibrosis-4 index (FIB-4) is the most cost-effective strategy for the initial screening of people with prediabetes and cardiometabolic risk factors or with type 2 diabetes for at-risk MASH in primary care and diabetes clinical settings (181,192,197,205–208). The diagnostic algorithm for the screening and liver fibrosis risk stratification of people with prediabetes or type 2 diabetes is shown in **Fig. 4.2**. A screening strategy relying on elevated plasma aminotransferases >40 units/L would miss most individuals with MASH in these settings, as at-risk MASH with clinically significant fibrosis ($\geq F2$) is frequently observed with plasma aminotransferases below the commonly used cutoff of 40 units/L (177–179,182,209,210). The American College of Gastroenterology considers

the upper limit of normal ALT levels to be 29–33 units/L for male individuals and 19–25 units/L for female individuals (211), as higher levels are associated with increased liver-related mortality. The FIB-4 estimates the risk of hepatic cirrhosis and is calculated from the computation of age, plasma aminotransferases (AST and ALT), and platelet count (mdcalc.com/calc/2200/fibrosis-4-fib-4-index-liver-fibrosis). A value of <1.3 is considered low risk of having advanced fibrosis (F3–F4) and for developing adverse liver outcomes, while ≥ 1.3 is considered as having a higher probability of at-risk MASH clinically significant fibrosis ($\geq F2$) and increased risk of adverse liver outcomes. A value of >2.67 confers a high risk of having advanced fibrosis (F3–F4), and referral to the liver specialist is warranted without additional testing. FIB-4 predicts changes over time in hepatic fibrosis (212,213) and allows risk stratification of individuals in terms of future liver-related morbidity and mortality (214). FIB-4 has reasonable sensitivity but low specificity; hence, a negative result may rule out fibrosis while a positive result requires confirmatory

testing (213,215,216). Therefore, a FIB-4 score <1.3 should be taken as a general guidance of having a lower risk of MASH with advanced fibrosis but does not replace clinical judgment. Its low cost, simplicity, and good specificity make it the initial test of choice (Fig. 4.2). FIB-4 has not been validated in pediatric populations or in adults aged <35 years. In individuals with diabetes ≥ 65 years of age, higher cutoffs for FIB-4 have been recommended (1.9–2.0 rather than ≥ 1.3) (217). In some individuals with at-risk MASH, FIB-4 score may be <1.3 , especially in those with obesity and type 2 diabetes. Additional testing may be required if the FIB-4 score is between 1.0 and 1.3 in individuals with type 2 diabetes with multiple cardiometabolic risk factors.

In individuals with a FIB-4 ≥ 1.3 , there is need for additional risk stratification with a liver stiffness measurement (LSM) by transient elastography (Fig. 4.2). Use of a second nonproprietary diagnostic panel is not recommended (e.g., MASLD fibrosis score and others), as they generally do not perform better than FIB-4 (176,179,215). Transient elastography (LSM) is the best-validated imaging technique for

fibrosis risk stratification, and it predicts future cirrhosis and all-cause mortality in MASLD (176,197,205,206,218). An LSM value of <8.0 kPa has a good negative predictive value to exclude advanced fibrosis ($\geq F3$ –F4) (219–221) and indicates lower risk for clinically significant fibrosis. Such individuals with prediabetes or type 2 diabetes can be followed in nonspecialty clinics with repeat surveillance testing every ≥ 2 years, although the precise time interval remains to be established. If the LSM is ≥ 8.0 kPa, the risk for advanced fibrosis ($\geq F3$ –F4) is higher and such individuals should be referred to the hepatologist (176,182,197,205) within the framework of an interprofessional team (222–224). FIB-4 followed by LSM helps stratify individuals with diabetes by risk level and minimize specialty referrals (218,225–228) (Fig. 4.2). Given the lack of widespread availability of LSM, the ELF test is a good alternative (229). Individuals with ELF <9.8 are considered at low risk for adverse liver outcomes. Individuals with ELF ≥ 9.8 are considered at high risk of having MASH with advanced liver fibrosis ($\geq F3$ –F4) and therefore are at risk for adverse liver outcomes (176,206,208).

Diagnostic algorithm for the prevention of cirrhosis in people with metabolic dysfunction–associated steatotic liver disease (MASLD)

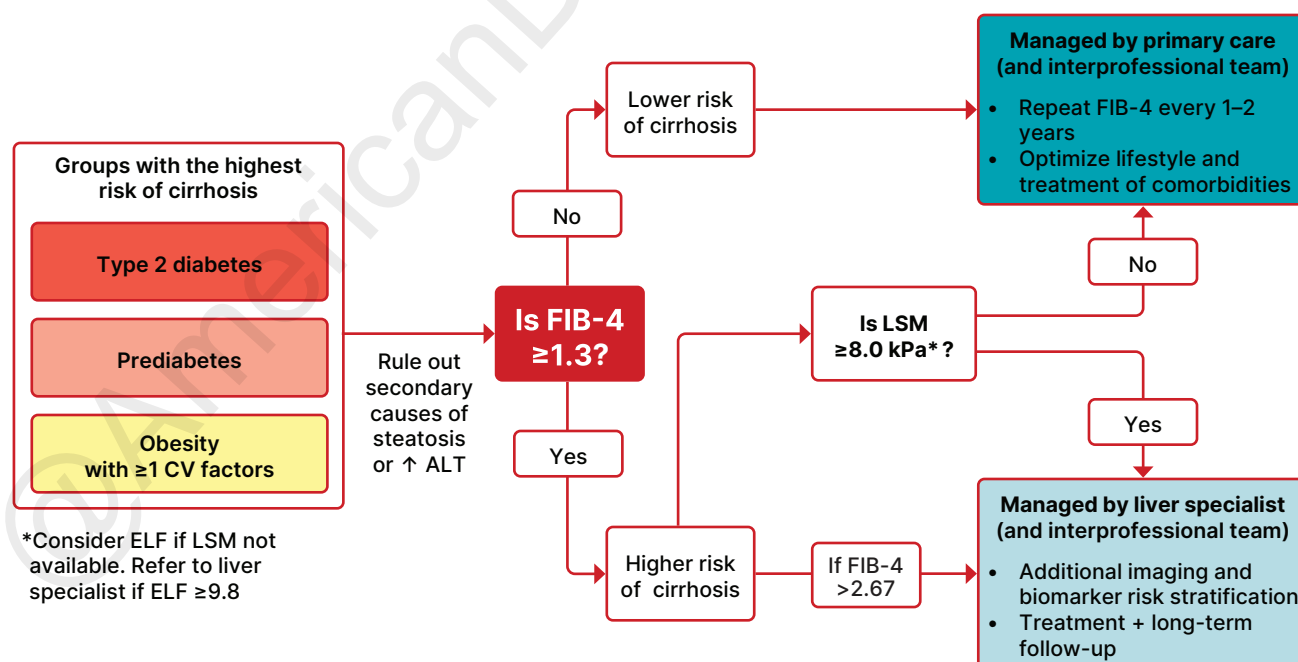


Figure 4.2—Diagnostic algorithm for risk stratification and the prevention of cirrhosis in individuals with metabolic dysfunction-associated steatotic liver disease (MASLD). CV, cardiovascular; ELF, enhanced liver fibrosis test; FIB-4, fibrosis-4 index; LSM, liver stiffness measurement, as measured by vibration-controlled transient elastography. *In the absence of LSM, consider ELF a diagnostic alternative. If ELF ≥ 9.8 , an individual is at high risk of metabolic dysfunction-associated steatohepatitis with advanced liver fibrosis ($\geq F3$ –F4) and should be referred to a liver specialist.

They should be referred to a gastroenterologist or hepatologist. The optimal cutoff for clinical use of ELF in primary care and endocrinology settings is evolving (230–233). An ELF <9.8 suggests an individual is at low risk of advanced liver fibrosis and may be followed in the nonspecialty clinic with repeat testing in ≥ 2 years but may need repeat testing more often if ELF is between 9.2 and 9.7.

Specialists may order additional tests for fibrosis risk stratification in MASH (175,197,205,208), including magnetic resonance elastography (MRE) (best overall performance, particularly for early fibrosis stages) or multiparametric iron-corrected T1 MRI (cT1) (234) and patented blood-based fibrosis biomarkers. While liver biopsy remains the gold standard for the diagnosis of MASH, its indication is reserved to the discretion of the specialist within an interprofessional team approach due to high costs and potential for morbidity associated with this procedure.

Management

Recommendations

4.25 Adults with type 2 diabetes or prediabetes, particularly with overweight or obesity, who have metabolic dysfunction–associated steatotic liver disease (MASLD) should be recommended lifestyle changes using an interprofessional approach that promotes weight loss, ideally within a structured nutrition plan and physical activity program for cardiometabolic benefits **B** and histological improvement. **C**

4.26 In adults with type 2 diabetes, MASLD, and overweight or obesity, consider using a glucagon-like peptide 1 receptor agonist (GLP-1 RA) with demonstrated benefits in MASH **A** or a dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 RA with potential benefits in MASH **B** for the treatment of obesity as an adjunctive therapy to lifestyle interventions for weight loss.

4.27a In adults with type 2 diabetes and biopsy-proven MASH or those at high risk for liver fibrosis (based on noninvasive tests), a GLP-1 RA is preferred for glycemic management due to beneficial effects on MASH. **A** Pioglitazone **B** or a dual GIP and GLP-1 RA **B** can be considered for

glycemic management due to potential beneficial effects on MASH.

4.27b Combination therapy with pioglitazone plus GLP-1 RA can be considered for the treatment of hyperglycemia in adults with type 2 diabetes with biopsy-proven MASH or those at high risk of liver fibrosis (identified with noninvasive tests) because of potential beneficial effects on MASH. **B**

4.28 For consideration of treatment with a thyroid hormone receptor- β agonist in adults with type 2 diabetes or prediabetes with MASLD with moderate (F2) or advanced (F3) liver fibrosis on liver histology, or by a validated imaging-based or blood-based test, refer to a gastroenterologist or hepatologist with expertise in MASLD management. **A**

4.29 Treatment initiation and monitoring should be individualized and within the context of an interprofessional team that includes a gastroenterologist or hepatologist, consideration of individual preferences, and a careful shared-decision cost-benefit discussion. **B**

4.30a In adults with type 2 diabetes and MASLD, use of glucose-lowering therapies other than pioglitazone or GLP-1 RAs may be continued as clinically indicated, but these therapies lack evidence of benefit in MASH. **B**

4.30b Insulin therapy is the preferred agent for the treatment of hyperglycemia in adults with type 2 diabetes with decompensated cirrhosis. **C**

4.31a Adults with type 2 diabetes and MASLD are at increased cardiovascular risk; therefore, comprehensive management of cardiovascular risk factors is recommended. **B**

4.31b Statin therapy is safe in adults with type 2 diabetes and compensated cirrhosis from MASLD and should be initiated or continued for cardiovascular risk reduction as clinically indicated.

B In people with decompensated cirrhosis, statin therapy should be used with caution, and close monitoring is needed, given limited safety and efficacy data. **B**

4.32a Consider metabolic surgery in appropriate candidates as an option to treat MASH in adults with type 2

diabetes and obesity **B** and to improve cardiovascular outcomes. **B**

4.32b Metabolic surgery should be used with caution in adults with type 2 diabetes with compensated cirrhosis from MASLD **B** and is not recommended in decompensated cirrhosis. **B**

While steatohepatitis and cirrhosis occur in lean people with diabetes and are believed to be linked to genetic predisposition, insulin resistance, and environmental factors (235,236), ample evidence implicates excess visceral fat and overall adiposity in individuals with overweight and obesity in the pathogenesis of the disease (236,237). Obesity in the setting of type 2 diabetes worsens insulin resistance and steatohepatitis, promoting the development of cirrhosis (238). Therefore, clinicians should enact evidence-based interventions (as discussed in section 5, “Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes”) to promote healthy lifestyle change and weight loss for individuals with overweight or obesity and MASLD. There is consensus that a minimum weight loss goal of 5%, preferably $\geq 10\%$, is needed to improve liver histology (176,197,205,208), with fibrosis requiring the larger weight reduction to promote change (239,240). However, there is significant individual variability in histological outcomes with weight loss. Individualized, structured weight loss and exercise programs offer greater benefit than standard counseling in people with MASLD (241).

Nutrition plan recommendations to induce an energy deficit are not different from those for individuals with diabetes with obesity without MASLD and should include a reduction of macronutrient content, limiting saturated fat, refined carbohydrates, and added sugar, with adoption of healthier eating patterns. The Mediterranean eating pattern has the best evidence for improving liver and cardiometabolic health (205–208,241,242). Both aerobic and resistance training improve MASLD in proportion to treatment engagement and intensity of the program (243). Obesity pharmacotherapy may assist with weight loss in the context of lifestyle modification if not achieved by lifestyle modification alone (see section 8,

“Obesity and Weight Management for the Prevention and Treatment of Diabetes”).

Given the high prevalence of at-risk MASH (~12–20%) (178,179,181,182), higher risk of disease progression and liver-related mortality (180,196,244), and the lack of pharmacological treatments once cirrhosis is established (245,246), optimizing the pharmacological management of hyperglycemia and obesity in individuals with type 2 diabetes and MASH could serve the dual purpose of addressing these comorbidities while treating the liver disease (Fig. 4.3). Therefore, early diagnosis and treatment of MASLD offers the best opportunity for cirrhosis prevention. In phase 2 clinical trials, pioglitazone and some GLP-1 RAs have been shown to be potentially effective to treat steatohepatitis (205,247–250) and to slow fibrosis progression (251,252). They may also decrease CVD (248), which is the number one cause of death in individuals with type 2 diabetes and MASLD (200).

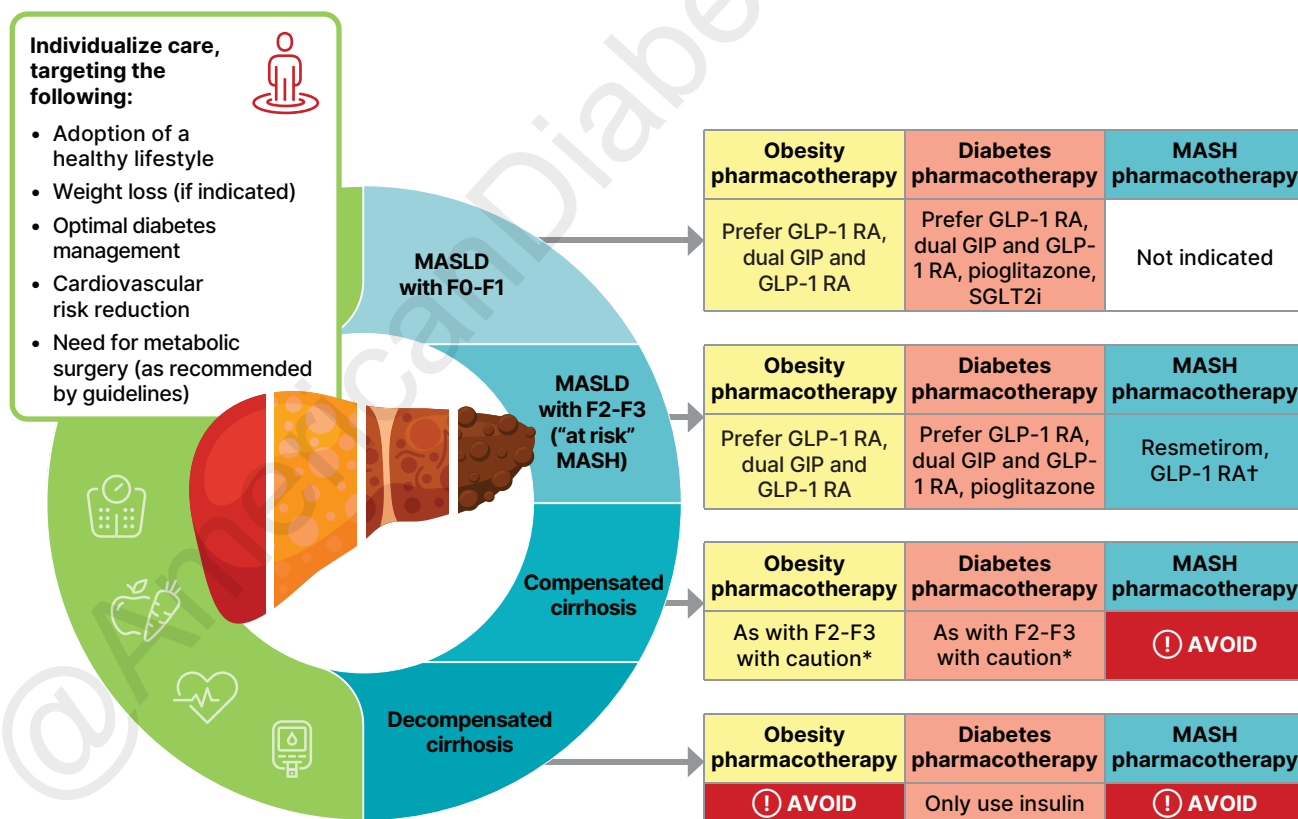
Recently, a phase 3 clinical trial examined the effect of semaglutide in subjects with MASH without cirrhosis (ESSENCE) (253). The trial reported that in 36.8% of individuals treated for 72 weeks with semaglutide 2.4 mg subcutaneously once weekly, improvement in liver fibrosis was achieved with no worsening of steatohepatitis, compared with 22.4% on placebo ($P < 0.001$), while 62.9% achieved resolution of steatohepatitis with no worsening of liver fibrosis, compared with 34.3% on placebo ($P < 0.001$). Based on the phase 3 trial results, the FDA recently approved semaglutide for the treatment of MASH with moderate to advanced liver fibrosis (254).

Semaglutide is currently the only glucose-lowering or obesity medication that is FDA approved for the treatment of MASH. The recommendation to treat hyperglycemia with other GLP-1 RA–based therapies and/or pioglitazone in individuals with type 2 diabetes and MASLD is

based on consistent histological benefit for steatohepatitis in several phase 2 randomized controlled trials (RCTs) with GLP-1 RAs (254–259) and with pioglitazone (255,256) compared with no benefit with metformin or other glucose-lowering medications in MASH (176,197,205).

Pioglitazone improves glucose and lipid metabolism and reverses steatohepatitis in individuals with prediabetes or type 2 diabetes (252,255,257) and even in individuals without diabetes (256,258,259) (Fig. 4.3). Fibrosis also improved in some trials (247,259). A meta-analysis (251) concluded that pioglitazone treatment results in resolution of MASH and may improve fibrosis. Furthermore, combination therapy with pioglitazone plus a GLP-1 RA has been reported safe and effective for the treatment of hyperglycemia in adults with type 2 diabetes (260–263) as well as in reducing hepatic steatosis (260,262), suggesting additive benefit in individuals with MASLD. It is important

Metabolic dysfunction–associated steatotic liver disease (MASLD) treatment algorithm



† Only semaglutide among GLP-1 RAs has been approved by the FDA for treatment of MASH.

* Individualized care and close monitoring needed in compensated cirrhosis given limited safety data available.

Figure 4.3—Metabolic dysfunction-associated steatotic liver disease (MASLD) treatment algorithm. F0-F1, no to minimal fibrosis; F2-F3, moderate fibrosis; F4, cirrhosis; GIP, glucose-dependent insulintropic polypeptide; GLP-1 RA, glucagon-like peptide 1 receptor agonist; MASH, metabolic dysfunction-associated steatohepatitis; SGLT2i, sodium–glucose cotransporter 2 inhibitor.

to note that these studies are based on phase 2 clinical trials and await further phase 3 evidence. However, these plans are attractive because they offer potential benefit compared with lack of histological benefit (or clinical trial data) from other oral glucose-lowering therapies in MASLD. In the context of treating hyperglycemia in individuals with type 2 diabetes with MASLD, where the low cost of pioglitazone and any liver improvement would be an added benefit to glycemic management, these plans would be potentially cost-effective for the treatment of MASLD (264,265). Vitamin E may be beneficial for the treatment of MASH in individuals without diabetes (258). However, in individuals with type 2 diabetes, vitamin E monotherapy was found to be ineffective in a small RCT (252), and it did not seem to enhance pioglitazone's efficacy when used in combination, as reported in an earlier trial in this population (257). Pioglitazone causes dose-dependent weight gain (15 mg/day, mean weight gain of 1–2%; 45 mg/day, mean weight gain of 3–5%), which can be blunted or reversed if combined with SGLT2 inhibitors or GLP-1 RAs (248,262,263,266). Pioglitazone increases fracture risk, may promote heart failure if used in individuals with preexisting congestive heart failure, and may increase the risk of bladder cancer, although this remains controversial (176,197,205,248,249).

GLP-1 RAs are effective at inducing weight loss and ameliorating elevated plasma aminotransferases and steatosis (247) (**Fig. 4.3**). As discussed above, semaglutide was effective as a treatment for MASH with moderate to advanced liver fibrosis in a phase 3 RCT (253). However, there are few phase 2 RCTs of other GLP-1 RAs in individuals with MASH proven by biopsy. A small RCT reported that liraglutide improved some features of MASH and may delay fibrosis progression (267). Tirzepatide is a dual GIP and GLP-1 RA known to reduce liver steatosis in MASLD (268), and a phase 2 paired-biopsy study of 190 adults with overweight or obesity with MASH (50–60% of whom had type 2 diabetes) recently reported that doses of 5, 10, and 15 mg/day resulted in resolution of steatohepatitis without worsening of fibrosis in 44%, 56%, and 62% of participants, respectively, compared with 10% of participants receiving placebo ($P < 0.001$ for all three comparisons) (269). Improvement of at least one fibrosis stage

without worsening of MASH occurred in 55%, 51%, and 51% of participants, respectively, compared with 30% of participants receiving placebo. Survodutide is a dual GLP-1 and glucagon receptor agonist that is in development, and a phase 2 paired-biopsy trial recently reported benefit in MASH (270). In summary, other GLP-1-based therapies (besides semaglutide) and/or pioglitazone are recommended to treat type 2 diabetes in adults with MASH based on histological benefit for steatohepatitis in several phase 2 RCTs (269,270) compared with no benefit with metformin or other glucose-lowering or obesity medications. Within the context of their approved indication (e.g., obesity or type 2 diabetes), these medications are cost-effective to treat the comorbidity, while potentially improving MASH, which becomes an added benefit.

SGLT2 inhibitors (271–273) and insulin (249) reduce hepatic steatosis, but their effects on steatohepatitis remain unknown. The use of glucose-lowering agents other than pioglitazone or GLP-1 RAs may be continued in individuals with type 2 diabetes and MASLD for glycemic management, as clinically indicated. However, these agents have either failed to improve steatohepatitis in paired-biopsy studies (metformin) or have no RCTs with liver histological end points (i.e., sulfonylureas, glitinides, dipeptidyl peptidase 4 inhibitors, or acarbose).

Resmetirom is a thyroid hormone receptor- β agonist approved by the FDA for the treatment of adults with MASLD with moderate (F2) or advanced (F3) liver fibrosis on liver histology or a validated imaging- or blood-based test. In a phase 3 RCT, resmetirom for 52 weeks in 966 adults at the highest dose of 100 mg (or placebo) met the primary end point of MASH resolution without worsening of fibrosis in 29.9% of individuals compared with 9.7% on placebo ($P < 0.001$) (274). Fibrosis improved in up to 25.9% and 14.2%, respectively ($P < 0.001$). Nausea, vomiting, and diarrhea occurred more often with resmetirom. The gastrointestinal side effects are dose dependent and improve with continued treatment. Resmetirom decreased free thyroxine (T4) levels by ~20% and increased sex hormone-binding protein levels two- to threefold. Although a recent review of the data concluded that there is little concern about these changes, long-term postmarketing data must be collected (275). Guidance by the

American Association for the Study of Liver Diseases (AASLD) about optimal individual identification for treatment, safety, and long-term monitoring has recently been published (276). This is especially relevant because hypothyroidism and hypogonadism are more prevalent in people with MASLD than in the general population (176,205), and clinicians should monitor all individuals with MASLD for symptoms of endocrine deficiency and manage according to clinical practice guidelines. Per its label, candidates for resmetirom treatment are those with MASLD and moderate (F2) to advanced (F3) liver fibrosis but not with cirrhosis or other active liver disease (i.e., alcohol-related liver disease, autoimmune hepatitis, or primary biliary cholangitis) or inadequately managed hypothyroidism or hyperthyroidism. Given complexities associated with selection of an individual for therapy, drug cost, and treatment monitoring, therapy should be individualized and initiated by a hepatologist or gastroenterologist with expertise in MASH within an interprofessional team.

Insulin is the preferred glucose-lowering agent for the treatment of hyperglycemia in adults with type 2 diabetes with decompensated cirrhosis given the lack of robust evidence about the safety and efficacy of oral agents and noninsulin injectables (i.e., GLP-1 RAs and dual GIP and GLP-1 RAs) (246), although a recent 48-week study suggested that GLP-1 RAs are safe in individuals with MASH and compensated cirrhosis (277).

Metabolic surgery leading to sustained weight loss and improvement of type 2 diabetes can improve MASH and cardiometabolic health, altering the natural history of the disease (278). Meta-analyses report that 70–80% of people have improvement in hepatic steatosis, 50–75% of people have improvement in inflammation and hepatocyte ballooning (necrosis), and 30–40% of people have improvement in fibrosis (279,280). It may also reduce the risk of HCC (280). It is important to note that currently metabolic surgery is not indicated solely for treatment of MASH. Given that many individuals with MASH have metabolic risks (type 2 diabetes and obesity) that are indications for metabolic surgery, the improvement in liver health is expected, but surgical indication should follow current practice guidelines. Metabolic surgery should be used with caution in individuals with compensated cirrhosis (i.e., asymptomatic stage of

cirrhosis without associated liver complications), but with experienced surgeons the risk of hepatic decompensation is similar to that for individuals with less advanced liver disease. Because of the paucity of safety and outcome data, metabolic surgery is not recommended in individuals with decompensated cirrhosis (i.e., cirrhosis stage with complications such as variceal hemorrhage, ascites, hepatic encephalopathy, or jaundice) who also have a much higher risk of postoperative development of these liver-related complications (176,197,205).

Adults with type 2 diabetes and MASLD are at an increased risk of CVD and require comprehensive management of cardiovascular risk factors (176,197,205). Within an interprofessional approach, statin therapy should be initiated or continued for cardiovascular risk reduction as clinically indicated. Overall, its use appears to be safe in adults with type 2 diabetes and MASH, including in the presence of compensated cirrhosis (Child-Pugh class A or B cirrhosis) from MASLD. Some studies even suggest that statin use in individuals with chronic liver disease may reduce episodes of hepatic decompensation and/or overall mortality (281,282). Statin therapy is not recommended in decompensated cirrhosis given limited safety and efficacy data (176,197,206).

Obstructive Sleep Apnea

Age-adjusted rates of obstructive sleep apnea, a risk factor for CVD, are significantly higher (4- to 10-fold) with obesity, especially with central obesity (283) (see section 5, "Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes"). The prevalence of obstructive sleep apnea in the population with type 2 diabetes may be as high as 23%, and the prevalence of any sleep-disordered breathing may be as high as 58% (284,285). In participants with obesity and type 2 diabetes enrolled in the Look AHEAD trial, the prevalence exceeded 80% (286). Obstructive sleep apnea should be evaluated in individuals with suggestive symptoms (e.g., excessive daytime sleepiness, snoring, and witnessed apnea) (287). Sleep apnea treatment (lifestyle modification, continuous positive airway pressure, oral appliances, and surgery) significantly improves quality of life and blood pressure management. Recently, two phase 3 randomized trials found that among adults

with obesity and moderate-to-severe obstructive sleep apnea but without diabetes, treatment with the dual GIP and GLP-1 RA tirzepatide substantially reduced sleep apnea severity (288). More research is needed to determine the effects of GLP-1 and dual GIP and GLP-1 RAs on sleep apnea in individuals with diabetes.

Pancreatitis

Diabetes is linked to diseases of the exocrine pancreas, such as pancreatitis, which may disrupt the global architecture or physiology of the pancreas, often resulting in both exocrine and endocrine dysfunction. Up to half of individuals with diabetes may have some degree of impaired exocrine pancreas function (289). People with diabetes are at an approximately twofold higher risk of developing acute pancreatitis (290).

Conversely, prediabetes and/or diabetes has been found to develop in approximately one-third of individuals after an episode of acute pancreatitis (291); thus, the relationship is likely bidirectional. Post-pancreatitis diabetes may include either new-onset disease or previously unrecognized diabetes (292). Studies of individuals treated with incretin-based therapies for diabetes have also reported that pancreatitis may occur more frequently with these medications, but results have been mixed and causality has not been established (293,294).

Islet autotransplantation should be considered for individuals requiring total pancreatectomy for medically refractory chronic pancreatitis to prevent postsurgical diabetes. Approximately one-third of individuals undergoing total pancreatectomy with islet autotransplantation are insulin free 1 year postoperatively, and observational studies from different centers have demonstrated islet graft function up to a decade after the surgery in some individuals (294–298). Both personal factors for the individual with diabetes and disease factors should be carefully considered when deciding the indications and timing of this surgery. Surgeries should be performed in skilled facilities that have demonstrated expertise in islet autotransplantation.

Sensory Impairment

Hearing impairment, both in high-frequency and low- to midfrequency ranges, is more common in people with diabetes than in

those without, with stronger associations found in studies of younger people (299). Proposed pathophysiologic mechanisms include the combined contributions of hyperglycemia and oxidative stress with cochlear microangiopathy and auditory neuropathy (300). In a National Health and Nutrition Examination Survey (NHANES) analysis, hearing impairment was about twice as prevalent in individuals with diabetes as in those without, after adjusting for age and other risk factors for hearing impairment (301). Low HDL cholesterol, coronary heart disease, peripheral neuropathy, and general poor health have been reported as risk factors for hearing impairment for individuals with diabetes, but an association of hearing loss with glycemia has not been consistently observed (302). In the DCCT/EDIC cohort, increases in the time-weighted mean A1C was associated with increased risk of hearing impairment when tested after long-term (>20 years) follow-up, with every 10% increase in A1C leading to 19% high-frequency impairment (303). Impairment in smell, but not taste, has also been reported in individuals with diabetes (304).

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5. Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes: Standards of Care in Diabetes—2026

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American Diabetes Association
Professional Practice Committee for
Diabetes*

The American Diabetes Association (ADA) “Standards of Care in Diabetes” includes the ADA’s current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. Members of the ADA Professional Practice Committee for Diabetes, an interprofessional expert committee, are responsible for updating the Standards of Care annually, or more frequently as warranted. For a detailed description of ADA standards, statements, and reports, as well as the evidence-grading system for ADA’s clinical practice recommendations and a full list of Professional Practice Committee members, please refer to Introduction and Methodology. Readers who wish to comment on the Standards of Care are invited to do so at professional.diabetes.org/SOC.

Building positive health behaviors and maintaining psychological well-being are foundational for achieving diabetes management goals and maximizing quality of life (1,2). Essential to achieving these goals are diabetes self-management education and support (DSMES), medical nutrition therapy (MNT), routine physical activity, adequate quality sleep, support for cessation of tobacco products and vaping, health behavior counseling, and psychosocial care. Following an initial comprehensive health evaluation (see section 4, “Comprehensive Medical Evaluation and Assessment of Comorbidities”), health care professionals should engage in person-centered collaborative care with people with diabetes (3–7). Person-centered collaborative care is guided by shared decision-making in treatment plan selection; facilitating access to medical, behavioral, psychosocial, educational, and technological resources and support; and shared monitoring of agreed-upon diabetes care plans and behavioral goals (8,9). Routine care evaluations should include assessments of medical and behavioral health outcomes, particularly during periods of changes in health and well-being.

DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT

Recommendations

- 5.1** Advise all people with diabetes to participate in developmentally and culturally appropriate diabetes self-management education and support (DSMES) to facilitate informed decision-making, self-care behaviors, problem-solving, and active collaboration with the health care team. **A**
- 5.2** Provide DSMES at diagnosis, annually and/or when not meeting treatment goals, when complicating factors develop (e.g., medical, functional, and psychosocial), and when transitions in life and care occur. **E**

*A complete list of members of the American Diabetes Association Professional Practice Committee for Diabetes can be found at <https://doi.org/10.2337/dc26-SINT>.

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5.3 Assess clinical outcomes, health status, and well-being as key goals of DSMES on an individualized timeframe. **C**

5.4 Use behavioral strategies (e.g., motivational interviewing, goal setting, problem-solving) to support DSMES and engagement in behaviors known to optimize health-related quality of life and outcomes. **A**

5.5 Provide culturally and socially appropriate DSMES responsive to personal preferences and needs in group or individual settings. **A** Communicate DSMES participation with the diabetes care team. **E**

5.6 Offer DSMES via telehealth and/or digital interventions to meet individual preferences, reduce access barriers, and improve satisfaction. **B**

5.7 DSMES can improve outcomes and reduce costs, so reimbursement by third-party payors is recommended. **B**

5.8 Identify and address barriers to DSMES that exist at the payor, health system, clinic, health care professional, and individual levels. **E**

5.9 Assess the social determinants of health to guide and design delivery of DSMES to maximize health equity across populations. **C**

The overall objectives of DSMES are to support informed decision-making, self-care behaviors, problem-solving, and active collaboration with the health care team to improve clinical outcomes, health status, and well-being in a cost-effective manner (2). DSMES facilitates the knowledge, decision-making, and skills mastery necessary for optimal diabetes self-care and incorporates the needs, goals, and life experiences of the person with diabetes (10). When providing DSMES, health care professionals should consider a person's burden of treatment, level of self-efficacy for self-care behaviors, and degree of social and family support. Engagement in self-management behaviors and subsequent clinical outcomes, health status, and quality of life, in addition to psychosocial factors affecting the person's ability to self-manage, should be monitored on an individualized timeframe (e.g., the four critical times listed in Recommendation 5.2). A randomized controlled trial (RCT) that evaluated a decision-making education and skill-building program (11) improved health outcomes and quality of care (12).

Using judgmental words is associated with increased feelings of shame and guilt; therefore, health care professionals should consider the impact language has on building therapeutic and productive relationships. Health care professionals should use positive, strengths-based words and phrases that put people first (13). See section 4, "Comprehensive Medical Evaluation and Assessment of Comorbidities," for more on use of language.

In accordance with the "2022 National Standards for Diabetes Self-Management Education and Support" (here referred to as the National Standards for DSMES) (10), all people with diabetes should participate in developmentally appropriate and culturally sensitive DSMES, as it helps people with diabetes identify and implement effective self-management strategies and coping skills (2). DSMES includes collaborative goal setting that improves empowerment, self-management, and quality of life as the person with diabetes encounters new challenges and as advances in treatment become available (14–16). Moreover, DSMES should be thought of as an ongoing process—not a one-time occurrence. The National Standards for DSMES (10) include delivery of content addressing:

- Pathophysiology of diabetes and treatment options
- Healthy coping
- Healthy eating
- Being active
- Taking medication
- Monitoring
- Reducing risk (treating acute and chronic complications)
- Problem-solving and behavior change strategies

In addition to providing DSMES upon diagnosis, there are additional critical time points when the need for DSMES should be evaluated by the health care professional and/or interprofessional team, with referrals made as needed (2):

- Annually and/or when not meeting treatment goals, whichever is more frequent
- When complicating factors (e.g., health conditions, physical or functional limitations, emotional factors, and basic living needs) that influence self-management develop
- When transitions in life and care occur

DSMES empowers individuals with diabetes and their families by providing tools to make informed self-management decisions (10,13). DSMES should be person-centered—placing the person with diabetes and their family and/or support system at the center of the care model as they work in collaboration with health care professionals. Person-centered care is respectful of and responsive to individual and cultural preferences, needs, and values and ensures the personal values of those living with diabetes guide decision-making (17).

Evidence for the Benefits

DSMES is associated with improved diabetes knowledge and self-care behaviors (18,19), lower A1C (19–22), lower self-reported weight (23), improved quality of life (24,25), reduced all-cause mortality risk (26), positive coping behaviors (6,27), and lower health care costs (28–30). DSMES is also associated with an increased use of primary care and preventive services (28,31) and less frequent use of acute care and inpatient hospital services (23). People with diabetes who participate in DSMES are more likely to follow best practice treatment recommendations, particularly those with Medicare, and have lower Medicare and insurance claim costs (31,32). DSMES interventions have better outcomes when they are >10 h over the course of 6–12 months (20) and provide ongoing culturally (31,33,34) and age-appropriate (35,36) support (14,15,37). Additionally, DSMES is also more effective when it is tailored to individual needs and preferences, addresses psychosocial issues, and incorporates behavioral strategies (13,27,38,39). Individual and group approaches are effective (23,40), with a slight benefit realized by those who engage in both (20).

Strong evidence now exists for the benefits of telehealth, telemedicine, and telephone-based or internet-based (i.e., virtual) DSMES for diabetes prevention and management in a wide variety of populations and age-groups (10,41–43). When feasible, the best choice for delivery of DSMES is whatever approach aligns best with individual preferences. A 2023 systematic review and meta-analysis of RCTs reported moderate evidence indicating digital health technologies (e.g., mobile apps, websites, digital coaching, and SMS [i.e., texting]) can be effective modes of intervention delivery for DSMES. In fact, telehealth-based interventions have been

found to produce a greater reduction in A1C (−0.30 percentage points; 95% CI −0.42 to −0.19) compared with control (42). Importantly, these digital methods provide outcomes that are comparable with or even better than those seen with traditional in-person care (42). Greater A1C reductions are demonstrated with increased virtual engagement, although data from trials are heterogeneous.

Diabetes care and education specialists (DCES) are effective providers of DSMES. Members of the DSMES team can include a variety of health care professionals such as nurses (registered nurses and nurse practitioners), registered dietitian nutritionists (RDNs), pharmacists, social workers, certified health education specialists, exercise physiologists, psychologists and behavioral health professionals, community health workers, care coordinators or navigators, and others who can tailor curricula to individual needs (44–46). Team members acting in a DCES capacity should have specialized clinical knowledge of diabetes and behavior change principles. In addition, a DCES needs to be knowledgeable about technology-enabled services and can serve as a technology champion within their practice (47). Credentials such as certified DCES (cbdce.org/) and/or board certification in advanced diabetes management (BC-ADM) (diabeteseducator.org/education/certification/bc_adm) demonstrates an individual's specialized training and expertise in diabetes management, education, and support (10), and engagement with qualified professionals has been shown to improve diabetes-related outcomes (48). There is also continued and growing evidence for the role of community health workers, peer educators, peer support, and lay leaders in providing ongoing diabetes self-management support (49,50). In locations where there are no DCES services available, other members of the diabetes care team can provide some aspects of DSMES; however, billing restrictions need to be considered (51).

Social determinants of health (SDOH) are an important aspect of diabetes care and should be assessed and weighed in guiding the design and delivery of DSMES. The DSMES team needs to consider characteristics such as racial identity, ethnic and cultural background, biological sex and gender identity, age, geographic location, technology access, education, literacy, and numeracy (13). Barriers to equitable DSMES access can be mitigated by

assessing the impact of the individual's SDOH and leveraging creative delivery options (e.g., telehealth and online) that will work best for the population in need of DSMES (10). For example, a systematic review and meta-analysis of telehealth DSMES interventions with Black and Hispanic adults with diabetes showed a 0.465% decrease in A1C, demonstrating the importance of considering demographic factors in relation to DSMES interventions (43).

Despite the recognized benefits of DSMES, fewer than 10% of individuals referred for DSMES through their health insurance or Medicare receive it, while about half the participants in an analysis of Behavioral Risk Factors Surveillance System (BRFSS) data report getting diabetes education (22,52). Barriers to DSMES exist at multiple levels, including the health system, payor, clinic, health care professional, and individual, for a myriad of reasons from lack of administrative leadership support to ineffective DSMES referral processes and transportation challenges. Low participation can be due to lack of referrals, logistical issues (e.g., accessibility, timing), cost, and lack of a perceived benefit (53). Thus, in addition to educating referring health care professionals about the benefits of DSMES and the critical times to refer, efforts to identify and address potential barriers at all levels need to be made (2). This was illustrated in a multilevel diabetes care intervention that combined clinical outreach, standardized protocols, and DSMES, with SDOH screening and referrals to social needs support. A 15% increase in receipt of DSMES, including among people on Medicaid, was documented (54). Support from institutional leadership is foundational for DSMES success. Expert stakeholders, including those external to an organization, should also support DSMES by advocating for it and for people with diabetes (10).

Diabetes Technologies

Technology-enabled diabetes self-management solutions (e.g., continuous glucose monitors [CGM], automated insulin delivery [AID] systems, and connected glucose meters) improve A1C most effectively when there is two-way communication between the person with diabetes and the health care team, individualized (e.g., tailored to suit a particular person for their needs) feedback, use of person-generated health data, and education (55). Technology

can facilitate self-management decisions and improve access to DSMES (55). Use of diabetes technologies warrants broader adoption because they can reduce therapeutic inertia and should be explored as part of continuous improvement (55,56). One potential model is virtual environments, which allow people with diabetes to self-represent as avatars and interact in a world with embedded informational resources accessed using principles of gamification. An example of this is from an RCT that tested DSMES in a virtual environment that demonstrated greater weight loss and similar decreases in A1C, blood pressure, cholesterol, and triglycerides compared with DSMES via a standard website (57). These nontraditional versions of DSMES may not always be reimbursed; however, adopting reimbursement policies that increase DSMES access and use will positively affect beneficiaries' clinical outcomes, quality of life, health care use, and costs (10,58).

Of all the newer diabetes technologies, CGM might be the most widely adopted. When combined with individualized DSMES or behavioral interventions, CGM demonstrated greater improvement of glycemic and psychosocial outcomes than CGM alone (59,60). Similarly, DSMES plus intermittently scanned CGM (isCGM) demonstrated increased time in range (70–180 mg/dL [3.9–10.0 mmol/L]), less time above range, and greater reduction in A1C compared with DSMES alone (61). Incorporating a systematic approach for technology assessment, adoption, and integration into the diabetes care plan could help ensure equity in access and standardized application of technology-enabled solutions (9,47,62–64).

Reimbursement

Medicare reimburses DSMES (known as diabetes self-management training [DSMT] by Medicare) when the services are provided in accordance with the National Standards for DSMES (2,10) and is recognized by the American Diabetes Association (ADA) through the Education Recognition Program (professional.diabetes.org/diabetes-education) or by the Association of Diabetes Care & Education Specialists (ADCES) (<https://www.adces.org/diabetes-education-dsmes/diabetes-education-accreditation-program>).

DSMES is also covered by most insurance plans. Ongoing support has been shown to be instrumental for improving outcomes when it is implemented after the completion of formal DSMES. For comprehensive

information about Medicare reimbursement, readers may find the following website useful: www.cdc.gov/diabetes-toolkit/php/reimbursement/medicare-reimbursement-guidelines.html. In brief, the Medicare Part B initial DSMT is a “once-in-a-lifetime” benefit. Individual encounters are reimbursable for the first 10 h (1 h of individual training and 9 h of group training). Two hours of follow-up DSMT are allowed each year after the initial DSMT. If a person has special needs that could interfere with effective group participation, these should be identified on the referral order to allow for individual sessions. For Medicaid, DSMES coverage varies by state, but further guidance can be found at <https://coveragetoolkit.org/evidence-based-programs/diabetes-self-management-education-and-support/>. Additional information addressing implementation of a successful DSMES program can be found in the Centers for Disease Control and Prevention DSMES toolkit at www.cdc.gov/diabetes-toolkit/php/index.html.

Programs recognized by the ADA and accredited by the ADCES were included on the list of telehealth professionals approved by Centers for Medicare & Medicaid Services (CMS) via the Consolidated Appropriations Act of 2023 (65). However, as of 1 October 2025, Medicare recipients must be in a U.S.-based rural office or medical facility for most telehealth services (66,67).

DSMES uses an evidence-based curriculum designed to educate people with diabetes about all elements from the National Standards for DSMES, as described above, that can be delivered and billed by a variety of health care professionals on the diabetes care team. While the overarching healthy eating concepts used in DSMES can be taught by all members of the team, MNT, which is more in-depth and individualized (e.g., tailored to suit a particular person for their sociocultural preferences and needs) and derived from the evidence-based Nutrition Care Process, can only be delivered and billed by RDNs. For Medicare Part B, the MNT benefit includes individual encounters billed 3 h in the first year of the benefit. Each subsequent year can be billed up to 2 h. However, additional hours are available if a subsequent referral identifies a change in treatment. For further information on Medicare coverage of MNT, readers are encouraged to review www.cdc.gov/diabetes-toolkit/php/reimbursement/medical-nutrition-therapy.html.

MEDICAL NUTRITION THERAPY

When the first ADA Standards of Care guidelines were published in 1989, nutrition was mentioned in only two sentences of the entire 4-page document (68). Even today, the science of nutrition for diabetes continues to evolve. There has also been a change in how we talk about nutrition. We continue to encourage health care professionals to shift away from emphasizing macronutrients (i.e., carbohydrates, proteins, and fats) and micronutrients (i.e., vitamins and minerals) and to instead focus on foods. More broadly, we encourage people to think in terms of eating patterns, also known as dietary patterns or food patterns, or the totality of the foods and beverages a person consumes. Additionally, encourage nutrient-dense food choices. Nutrient dense is defined as foods high in micronutrients while being relatively low in calories (e.g., vegetables, fruits, and legumes). This integrative food-based approach aligns with numerous guidelines from multiple professional health societies (69–71) and the *Dietary Guidelines for Americans, 2020–2025* (72). Simply put, people eat food, not nutrients, and nutrition recommendations need to be applicable to what people actually eat. Additionally, macronutrients are not interchangeable entities and vary by nutrient type and quality. For example, carbohydrates include legumes, whole grains, and fruits, which are in the same category as refined grains, but their health effects are quite different (73).

MNT is effective and beneficial to people with diabetes. When delivered by an RDN, MNT is associated with A1C absolute decreases of 1.0–1.9% for people with type 1 diabetes and 0.3–2.0% for people with type 2 diabetes (74). Because diabetes is progressive, behavior modification alone may not be adequate to maintain euglycemia over time. However, even after pharmacotherapy is initiated, MNT continues to be an important component of ongoing diabetes self-management, and RDNs providing diabetes-specific MNT should assess and monitor medication changes in relation to nutrition care plans (46,75). All health care team members should be empowered to reiterate the general and evidence-based nutrition advice promoted herein—limit processed foods and foods high in added salt, sugars, and fats and, when possible, choose whole foods.

For more detailed information on nutrition therapy for people with diabetes,

please refer to the ADA consensus report on nutrition therapy (46). Contained in the report is an important and often repeated tenet, i.e., there is no one-size-fits-all eating pattern for individuals with diabetes, and meal planning should be individualized. Nutrition therapy plays an integral role in overall diabetes management, and each person with diabetes should actively engage in education, self-management, and treatment planning with the health care team and participate in collaborative development of an individualized eating plan (46,75).

All people with diabetes should be referred for individualized MNT provided by an RDN who is experienced and skilled in providing diabetes-specific MNT (76–78), at diagnosis and as needed throughout the life span, like DSMES. Referrals to RDNs are particularly warranted when a person with diabetes is dealing with additional health conditions such as hypertension, dyslipidemia, heart failure, gastrointestinal disorders, chronic kidney disease (CKD), pregnancy-related nutrition concerns, pediatric growth issues, or obesity (79). See **Table 5.1** for nutrition recommendations and **Table 5.2** for nutrition behaviors that should be encouraged.

Eating Patterns and Meal Planning

To better understand the role of nutrition in diabetes, it is important to clarify terminology. Food patterns, eating plans, and approaches are terms that are often used interchangeably, but they are different and relevant in individualizing nutrition care plans (80).

- **Eating pattern, dietary pattern, or food pattern.** The totality of all foods and beverages consumed over a given period of time. An eating pattern can be ascribed to an individual, but it is also the term used in prospective cohort and observational nutrition studies to classify nutrition patterns. Examples include Mediterranean style, Dietary Approaches to Stop Hypertension (DASH), low carbohydrate, vegetarian, and plant based (80).
- **Eating/meal plan (historically referred to as a diet).** An individualized guide to plan when, what, and how much to eat on a daily basis, completed by the person with diabetes and the RDN. The eating plan could incorporate an eating pattern combined with a strategy to direct some of the choices. Eating plans are based on an individual's usual

Table 5.1—Nutrition recommendations

	Recommendations
5.10	Provide individualized medical nutrition therapy by referring people with prediabetes or diabetes to a registered dietitian nutritionist, preferably one who has comprehensive experience in diabetes care. A
5.11	Diabetes medical nutrition therapy can result in cost savings B and improved cardiometabolic outcomes A and should be reimbursed by insurance. E
5.12	Provide an overweight or obesity treatment plan based on their nutrition, physical activity, and behavioral health status for all people with overweight or obesity, aiming for at least 5–7% weight loss. A
5.13	For diabetes prevention and management of people with prediabetes or diabetes, recommend individualized meal plans that keep nutrient quality, total calories, and metabolic goals in mind. B
5.14	Eating patterns should emphasize key nutrition principles (inclusion of nonstarchy vegetables, whole fruits, legumes, lean proteins, whole grains, nuts and seeds, and low-fat dairy or nondairy alternatives) and minimize consumption of red meat, sugar-sweetened beverages, sweets, refined grains, processed and ultraprocessed foods in people with prediabetes and diabetes. B
5.15	Consider reducing carbohydrate intake for some adults with diabetes to improve glycemia. An effective way to achieve this is by limiting consumption of processed foods. B
5.16	Assess intake of supplements, as supplementation with micronutrients (e.g., vitamins and minerals, such as magnesium or chromium) or herbs or spices (e.g., cinnamon and aloe vera) is not recommended for glycemic benefits. C
5.17	Counsel against β -carotene supplementation, as there is evidence of harm for certain individuals and it confers no benefit. B
5.18	Advise adults with diabetes and those at risk for diabetes who consume alcohol to not exceed the recommended daily limits. B Advise abstainers to not start drinking alcohol, even in moderation. B
5.19	Counsel people with diabetes about the signs, symptoms, and self-management of delayed hypoglycemia and the importance of monitoring glucose after drinking alcohol to reduce hypoglycemia risk, especially when using insulin or insulin secretagogues. B
5.20	Counsel people with diabetes to limit sodium consumption to <2,300 mg/day, as clinically appropriate, and the best way to achieve this is through limiting consumption of processed foods. B
5.21	Encourage people with diabetes and those at risk for diabetes to consume water over other beverages. A
5.22	Counsel people with diabetes and those at risk for diabetes that nonnutritive sweeteners can be used in place of sugar-sweetened products if consumed in moderation and for the short term to reduce overall calorie and carbohydrate intake. B
5.23	Counsel and regularly monitor individuals pursuing intentional weight loss to ensure adequate nutritional intake, with particular attention to preventing protein insufficiency and micronutrient deficiencies. E
5.24	Emphasize minimally processed, nutrient-dense, high-fiber sources of carbohydrate (at least 14 g fiber per 1,000 kcal). B
5.25	Advise people with diabetes and those at risk for diabetes to replace sugar-sweetened beverages (including any juices) with water or low-calorie or no-calorie beverages and minimize foods with added sugar to manage glycemia and reduce risk for cardiometabolic disease. B
5.26	Educate individuals with diabetes who are at risk for developing diabetic ketoacidosis and who are treated with sodium–glucose cotransporter inhibition on the risks and signs of ketoacidosis and methods of risk mitigation management, provide them with appropriate tools for ketone measurement (i.e., serum β -hydroxybutyrate), and discourage a ketogenic eating pattern. E
5.27	Provide education on the glycemic impact of carbohydrate, A fat, and protein B tailored to an individual's needs, insulin plan, and preferences for care to optimize mealtime insulin dosing.
5.28	Counsel people using fixed insulin doses about consistent patterns of carbohydrate intake with respect to time and amount while considering the insulin action time, as it can result in improved glycemia and reduce the risk for hypoglycemia. B
5.29	Counsel people with diabetes and those at risk for diabetes to incorporate more plant-based protein sources (e.g., nuts, seeds, and legumes) as part of an overall diverse eating pattern to reduce cardiovascular disease risk. B
5.30	Counsel people with diabetes and those at risk for diabetes to consider an eating plan emphasizing elements of a Mediterranean eating pattern, which is rich in fatty fish, nuts, and seeds, to reduce cardiovascular disease risk A and improve glucose metabolism. B
5.31	Counsel people with diabetes and those at risk for diabetes to limit intake of foods high in saturated fat to help reduce cardiovascular disease risk. B

eating style, cultural background, SDOH, and food preferences.

- **Eating/meal plan approach.** Method to individualize a desired eating pattern and provide practical tools for developing healthy eating patterns. Examples include the plate method, carbohydrate choice,

carbohydrate counting, and highly individualized behavioral approaches (81).

Meal Planning

There is no ideal percentage of calories from carbohydrate, protein, or fat for

people with diabetes. Therefore, macronutrient distribution should be based on an individualized assessment of current eating patterns, preferences, and metabolic goals. Members of the health care team should complement and reinforce MNT by providing evidence-based guidance to help

Table 5.2—Nutrition behaviors to encourage

- Vegetables—especially nonstarchy vegetables that are dark green, red, and orange in color; fresh, frozen, or low-sodium canned are all acceptable vegetable options.
- Legumes—dried beans, peas, and lentils.
- Fruits—especially whole fruit—fresh, frozen, or canned in own juice (or no added sugar) are all acceptable fruit options.
- Foods with at least 3 g of fiber per serving are generally considered higher fiber choices. Whole-grain foods—where culturally appropriate, whole-grain versions of commonly consumed foods, such as 100% whole-wheat breads or pastas and brown rice. When not culturally appropriate, focus more on portion control.
- Water should be the primary beverage of choice.
- For individuals who do not prefer plain water, no-calorie alternatives are the next best choice. Options include adding lemon, lime, berries, or cucumber slices to water; sparkling no-calorie water or flavored no-calorie waters; no-calorie carbonated beverages.
- Plant-based proteins can include legumes (e.g., soybeans, pinto beans, black beans, garbanzo beans, dried peas, and lentils), nuts, and seeds.
- Meats and poultry should be from fresh, frozen, or low-sodium canned and in lean forms (e.g., chicken breast and ground turkey).
- Heart-healthy wild-caught fatty fish such as salmon, tuna, sardines, and mackerel. Fresh, frozen, or low-sodium canned are all acceptable options.
- Use herbs (e.g., basil, fennel, mint, parsley, rosemary, and thyme) and spices (e.g., cinnamon, garam masala, ginger, pepper, and turmeric) to season foods instead of salt or salt-containing preparations.
- Incorporate onions, garlic, celery, carrots, and other vegetables as a base for preparing various homemade foods.
- Cook with vegetable oil (e.g., avocado, canola, and olive) in place of fats high in saturated fat (e.g., butter, coconut oil, lard, and shortening).
- Plan out meals for the week. Grocery shop using a list. Cook on a day off so there are ready-to-eat and ready-to-reheat homemade meals waiting in the fridge or freezer.
- Include family or roommates in meal preparation; share the responsibilities of grocery shopping and cooking and use time off for meal preparation in advance when possible.

people with diabetes make healthy food choices that meet their individualized needs and improve overall health. Ultimately, ongoing diabetes and nutrition education paired with appropriate support to implement and sustain health behaviors are recommended (78).

Research confirms a variety of eating patterns are acceptable for diabetes management (46,74,82,83). Evidence-based eating patterns most frequently recommended include Mediterranean, DASH, low-fat, carbohydrate-restricted, vegetarian, and vegan eating patterns. Until evidence around benefits of specific eating patterns is strengthened, health care professionals should focus on the common core characteristics among healthful patterns: inclusion of nonstarchy vegetables, whole fruits, legumes, whole grains, nuts, seeds, and low-fat dairy products or nondairy replacements and minimizing consumption of red meat, sugar-sweetened beverages, sweets, refined grains, and processed and ultraprocessed foods (84,85). The recent Dietary Approaches to Stop Hypertension for Diabetes (DASH4D) RCT further supports this guidance (86). In their randomized crossover feeding study conducted from 2021 to 2024, adults with type 2 diabetes and

hypertension improved time in range (mean difference 5.2%; $P < 0.001$) and blood pressure. The intervention eating pattern was moderate in carbohydrates (45% of total calories), rich in fruits, vegetables, whole grains, lean proteins, and low-fat dairy, and low in saturated fat, sugar-sweetened beverages, and sodium.

Referral to and ongoing support from an RDN is essential to assess the overall nutrition status of the person with diabetes. RDNs work collaboratively with people to create a personalized meal plan aligned with the overall lifestyle treatment plan, including physical activity, work and life schedules, and medication use. Using shared decision-making to execute the plan is also often part of the nutrition care process.

Eating/Meal Plan Approaches and Methods

Few head-to-head studies have compared different eating approaches. The diabetes plate method (87) is a commonly used visual approach for providing basic meal planning guidance for individuals with type 1 and type 2 diabetes. One RCT found that both the diabetes plate method and carbohydrate counting were effective in helping achieve improved A1C (88). The

diabetes plate method uses a simple graphic (featuring a 9-in plate) to portion foods (one-half of the plate for nonstarchy vegetables, one-quarter of the plate for protein, and one-quarter of the plate for carbohydrates).

Carbohydrate counting is a more advanced skill that helps plan for and track how much carbohydrate is consumed at meals and snacks. In a systematic review and meta-analysis of carbohydrate counting versus other forms of meal planning advice (e.g., standard education, low glycemic index [GI], and fixed carbohydrate quantities), no significant differences were seen in A1C levels compared with standard education (89). In another RCT, a simplified carbohydrate counting tool based on individual glycemic response was noninferior to conventional carbohydrate counting in 85 adults with type 1 diabetes (90). In a randomized crossover trial, carbohydrate counting and qualitative meal size (i.e., low, medium, and high carbohydrate) were compared. Time in range was 74% for carbohydrate counting and 70.5% for the quantitative meal size estimates. Noninferiority was not confirmed for the qualitative method (91). Newer technologies (e.g., smart phone apps and CGM) and

AID systems may reduce the need for precise carbohydrate counting and allow for personalized nutrition approaches (92,93).

Meal planning approaches should be customized to the individual, including their numeracy and food literacy level (88). Health numeracy refers to understanding and using numbers and numerical concepts in relation to health and self-management. Food literacy generally describes proficiency in food-related knowledge and skills that ultimately affect health, although specific definitions vary across initiatives (94,95).

Nutrition Therapy Goals for All People With Diabetes

1. To promote and support healthful eating patterns, emphasizing a variety of nutrient-dense foods in appropriate portion sizes, contributing to improved overall health, and to:
 - achieve and maintain body weight goals
 - attain individualized glycemic, blood pressure, and lipid goals
 - delay or prevent the complications of diabetes
2. To address individual nutrition needs based on personal and cultural preferences, health literacy and numeracy, access to healthful foods, willingness and ability to make behavioral changes, and existing barriers to change
3. To maintain the pleasure of eating by providing nonjudgmental messages about food choices while also reducing or limiting certain foods only when indicated by scientific evidence
4. To provide an individual with diabetes the practical tools for developing healthy eating patterns rather than focusing on individual macronutrients, micronutrients, or single foods

Carbohydrates

Studies examining the optimal amount of carbohydrate intake for people with diabetes are inconclusive, although monitoring carbohydrate intake is a key strategy in reaching glucose goals in people with type 1 and type 2 diabetes (96,97).

The amount of carbohydrate intake for people with type 2 diabetes has been a focus of research for many years. Systematic reviews and meta-analyses of RCTs report carbohydrate-restricted eating patterns, particularly those considered very

low carbohydrate (<26% total energy), were effective in reducing A1C in the short term (<6 months), with less difference in eating patterns beyond 1 year (80,98,99). However, in a 12-week RCT among adults with prediabetes and type 2 diabetes, a well-formulated ketogenic eating pattern (20–50 g total carbohydrate/day and keeping protein to ~1.5 g/kg ideal body weight/day, with the remainder of energy from fat) did not significantly improve A1C and increased LDL cholesterol compared with a low-carbohydrate Mediterranean eating pattern (99). Additionally, a systematic review and meta-analysis of six RCTs at least 12 months in duration and including a total of 524 participants with type 2 diabetes reported that a low-carbohydrate eating pattern was beneficial for lipids but not glycemic management (standardized mean difference -0.11 , 95% CI -0.33 to 0.11 , $P = 0.32$) (100).

Reduction in body weight and the wide range of definitions for low-carbohydrate eating plans are important challenges in interpreting carbohydrate-restricted research studies (101–103). As studies on low-carbohydrate eating plans generally indicate challenges with long-term sustainability (104), it is important to reassess and individualize meal plan guidance regularly for those interested in this approach.

Health care professionals should maintain consistent medical oversight of individuals following very-low-carbohydrate eating plans and recognize that insulin and other diabetes medications may need to be adjusted to prevent hypoglycemia, and blood pressure will need to be monitored. In addition, very-low-carbohydrate eating plans are not currently recommended for individuals who are pregnant or lactating, children, people who have kidney disease, or people with or at risk for disordered eating (46).

Very-low-carbohydrate eating plans should be avoided in those taking sodium–glucose cotransporter 2 (SGLT2) inhibitors because of the potential risk of ketoacidosis (105,106). Numerous case reports have now been published illustrating that diabetic ketoacidosis (DKA) can occur in people with type 1 and type 2 diabetes using SGLT2 inhibitors in combination with very-low-carbohydrate or ketogenic eating patterns. Additionally, excessive alcohol intake should be avoided when taking SGLT2 inhibitors (105). Maintaining adequate hydration is also very important.

Regardless of carbohydrate quantity in the meal plan, the focus should be on high-quality, minimally processed, nutrient-dense, high-fiber carbohydrate sources. Fiber modulates gut microbiota composition and increases gut microbial diversity. Although there is still much to be elucidated about the gut microbiome and chronic disease, higher-fiber eating patterns are advantageous (107). Both children and adults with diabetes are encouraged to minimize intake of refined carbohydrates with added sugars, fat, and sodium and instead focus on carbohydrates from vegetables, legumes, fruits, dairy (milk and yogurt) or fortified nondairy alternatives, and whole grains. People with diabetes and those at risk for diabetes are encouraged to consume a minimum of 14 g of fiber/1,000 kcal, with at least half of grain consumption being whole, intact grains, according to the *Dietary Guidelines for Americans, 2020–2025* (72). Regular intake of sufficient fiber is associated with lower all-cause mortality in people with diabetes, and prospective cohort studies have found fiber intake is inversely associated with risk for type 2 diabetes (108, 109). Consumption of sugar-sweetened beverages and processed food products with large amounts of refined grains and added sugars is strongly discouraged (72), as these can displace healthier, more nutrient-dense foods and increase inflammation (110).

The literature on GI and glycemic load (GL) in individuals with diabetes is complex, often with varying definitions of low- and high-GI foods (111–113). The GI ranks carbohydrate foods on their postprandial glycemic response, and GL considers both the GI of foods and the amount of carbohydrate eaten. Studies report mixed effects of GI and GL on fasting glucose levels and A1C, with one systematic review finding no significant effect on A1C (112) while others demonstrated A1C reductions of 0.15% (111) to 0.5% (114,115). More recently, however, a meta-analysis of large cohorts ($\geq 100,000$ participants) reported that when people had larger intakes of high-GI foods, there was increased incidence of type 2 diabetes (risk ratio 1.27 [95% CI 1.21–1.34]; $P < 0.0001$), total cardiovascular disease (CVD) (1.15 [1.11–1.19]; $P < 0.0001$), diabetes-related cancer (1.05 [1.02–1.08]; $P = 0.0010$), and all-cause mortality (1.08 [1.05–1.12]; $P < 0.0001$) (113). It is important to note that low GI or low GL is synonymous with higher-fiber eating patterns.

Individuals with type 1 or type 2 diabetes taking insulin at mealtime should be offered comprehensive and ongoing education about nutrition content and the need to couple insulin administration with carbohydrate intake. For people whose meal schedule or carbohydrate consumption is variable, education on the relationship between carbohydrate intake and insulin needs is important. In addition, assessing food literacy, numeracy, interest, and capability should be evaluated, especially if teaching more advanced methods of MNT diabetes management such as insulin-to-carbohydrate ratios. Teaching insulin-to-carbohydrate ratios for meal planning can assist individuals with effectively modifying insulin dosing from meal to meal to improve glycemic management (74,96). Consumption of fat and protein can affect early and delayed postprandial glycemia (116), and it appears to have a dose-dependent response (117,118). However, more research is needed to determine the optimal insulin dose and delivery strategy. A cautious approach to increasing insulin doses for high-fat and/or high-protein mixed meals is recommended to address delayed hyperglycemia that may occur after eating (46,119). For individuals using an insulin pump, a split bolus feature (part of the bolus delivered immediately and the remainder over a programmed duration of time) may provide better insulin coverage for high-fat and/or high-protein mixed meals (120,121).

Insulin dosing decisions should be confirmed with a structured approach to blood glucose monitoring or CGM to evaluate individual responses and guide insulin dose adjustments. Checking glucose 3 h after eating may help determine if additional insulin adjustments are required (i.e., increasing or stopping bolus) (120,121). For individuals on a fixed daily insulin schedule, meal planning should emphasize a relatively fixed carbohydrate consumption pattern with respect to both time and amount while considering insulin action. Attention to hunger and satiety cues also helps (46).

Most commercially available AID systems still require basic diabetes management skills, including carbohydrate counting and understanding of the effect of protein and fat on postprandial glucose response, but the algorithms included in the systems work with less accurate carbohydrate entry (122,123). The most advanced AID system provides

adaptive closed-loop algorithms enabling fully autonomous insulin delivery automatically titrating all therapeutic insulins, including basal, correction, and prandial insulins. For more on AID and carbohydrates, see section 7, "Diabetes Technology."

Protein

There is no evidence that adjusting the daily protein intake above or below the recommended amount for the general public (typically 0.8–1.5 g/kg body weight/day or 15–20% of total calories) will improve health, and research is inconclusive regarding the ideal amount of dietary protein to optimize either glycemic management or CVD risk (72,124). Therefore, protein intake goals should be individualized based on current eating patterns. Some research has found successful management of type 2 diabetes with meal plans including slightly higher levels of protein (20–30%), which may contribute to increased satiety (125).

Historically, low-protein eating plans were advised for individuals with diabetes-related CKD (with albuminuria and/or reduced estimated glomerular filtration rate [eGFR]); however, current evidence does not suggest that people with CKD need to restrict protein to less than the generally recommended protein intake (126). Reducing the amount of protein below the recommended daily allowance of 0.8 g/kg is not recommended because it does not alter glycemic measures, cardiovascular risk measures, or the rate at which eGFR declines and may increase risk for malnutrition (126).

Growing evidence suggests higher plant protein intake and replacement of animal protein with plant protein is associated with lower risk of all-cause and cardiovascular mortality. A meta-analysis of 13 RCTs showed that replacing animal proteins with plant proteins leads to small improvements in A1C and fasting glucose in adults with type 2 diabetes (127). A 2023 systematic review and meta-analysis of 13 RCTs and 7 cohort studies concluded that there is limited suggestive evidence to support replacing animal protein with plant-based protein based on a moderate degree of bias in cohort studies (128). However, a prospective observational study of more than 11,000 community-dwelling adults over 22 years of follow-up reported that those with higher intakes of plant foods and lower intakes of animal foods had

lower diabetes risk (129). Plant proteins are lower in saturated fat, higher in fiber, and also support planetary health (130).

Fats

There is no optimal percentage of calories from fat for people with or at risk for diabetes, and macronutrient distribution should be individualized according to the individual's eating patterns, cultural and personal preferences, and metabolic goals (46). The type of fat consumed is more important than total amount of fat when looking at metabolic goals and CVD risk, and the percentage of total calories from saturated fats should be limited (72,131–133). Multiple RCTs including people with type 2 diabetes have reported that a Mediterranean eating pattern can improve both glycemic management and blood lipids (134–136). The Mediterranean eating pattern is based on traditional eating patterns in the countries bordering the Mediterranean Sea. Although eating styles vary by country and culture (i.e., customs and behaviors of a particular group of people or other social group), they share a number of common features, including consumption of fresh fruits and vegetables, whole grains, beans, and nuts/seeds; olive oil as the primary fat source; low to moderate amounts of fish, eggs, and poultry; and limited added sugars, sugary beverages, sodium, highly processed foods, refined carbohydrates, saturated fats, and fatty or processed meats.

People with diabetes should be advised to follow the same guidelines as the general population for the recommended intakes of saturated fat, cholesterol, and *trans* fat (72). In a 12-week double-blinded randomized controlled feeding study among 61 adults with overweight and obesity, without diabetes, higher intakes of saturated fat, compared with polyunsaturated fat, were found to increase liver fat deposition (137). A 2021 systematic review and meta-analysis including over 22,500 prospective study participants followed for 9.8 years reported that replacing saturated fats with other macronutrients, such as polyunsaturated fats, was associated with reduced CVD occurrence (138). *Trans* fats should be avoided. Importantly, it should be noted that as foods high in saturated fats are progressively decreased, they should be replaced with foods high in unsaturated fats and not with refined carbohydrate foods (139).

Evidence does not conclusively support recommending n-3 (eicosapentaenoic acid and docosahexaenoic acid) supplements for people with diabetes for the prevention or treatment of cardiovascular events (46,140). In individuals with type 2 diabetes, two systematic reviews with n-3 and n-6 fatty acids concluded that the dietary supplements did not improve glycemic management (141,142). In the ASCEND (A Study of Cardiovascular Events in Diabetes) trial, when compared with placebo, supplementation with n-3 fatty acids at a dose of 1 g/day did not lead to cardiovascular benefit in people with diabetes without evidence of CVD (143). However, results from the Reduction of Cardiovascular Events with Icosapent Ethyl-Intervention Trial (REDUCE-IT) found that supplementation with 4 g/day pure eicosapentaenoic acid significantly lowered the risk of adverse cardiovascular events. REDUCE-IT included 8,179 participants, of whom over 50% had diabetes, and found a 5% absolute reduction in cardiovascular events for individuals with established atherosclerotic CVD already treated with a statin with residual hypertriglyceridemia (135–499 mg/dL [1.52–5.63 mmol/L]) (144). See section 10, “Cardiovascular Disease and Risk Management,” for more information.

Sodium

As for the general population, people with diabetes are advised to limit their sodium consumption to <2,300 mg/day (46,145). Sodium intake has been shown to mediate glucose metabolism in a number of studies and affect eGFR, so limiting sodium intake is a valuable strategy for people with diabetes with or without kidney disease (145,146). In their post hoc analysis of the DASH-sodium RCT, Morales-Alvarez et al. (147) reported that participants randomized to the low-sodium DASH eating pattern (containing ~1,150 mg sodium/day [50 mmol sodium/day]) had change in eGFR of $-3.10 \text{ mL/min/1.73 m}^2$ (95% CI -5.46 to -0.73) after 4 weeks compared with 3,450 mg sodium/day (150 mmol sodium/day).

The DASH4D trial, which was a randomized 4-period crossover community-based feeding study, reported that in comparison with the eating pattern formulated with higher levels of sodium, the DASH4D eating pattern with lower sodium (1,500 mg/day at 2,000 kcal) resulted in improved systolic blood pressure

by 4.6 mmHg (95% CI, 7.2–2.0; $P < 0.001$) and diastolic blood pressure by 2.3 mmHg (95% CI, 3.7–0.9) (86). It was noted that the largest blood pressure reduction occurred during the first 3 weeks of each treatment period, and the effect of sodium reduction appeared stronger than the effect of the DASH4D eating pattern.

Limiting sodium intake is most easily achieved through focusing on whole, fresh foods. Additionally, it is important to reduce consumption of processed and ultraprocessed foods, which are major contributors of sodium intake. Encouraging people to avoid adding salt to foods and during cooking can also help. People providing nutrition advice should consider palatability, availability, affordability, clinical appropriateness, and the difficulty of achieving low-sodium recommendations in a nutritionally adequate eating plan.

Micronutrients and Other Supplements

Despite lack of evidence of benefit from dietary supplements, consumers continue to take them. Estimates show that up to 59% of people with diabetes in the U.S. use supplements (148). Without underlying deficiency, there is no benefit from herbal or other (i.e., vitamin or mineral) supplementation for people with diabetes (46,149).

U.S. federal law broadly defines dietary supplements as products having one or more dietary ingredients, including vitamins, minerals, herbs or other botanicals, amino acids, enzymes, tissues from organs or glands, or extracts of these (150). Dietary supplements are not regulated like other over-the-counter medications or prescription drugs in the U.S. (151). In combination with the strong views on dietary supplements (both positive and negative), this can contribute to consumer confusion (152). Readers can consult the U.S. Food and Drug Administration (FDA) Dietary Supplement Ingredient Directory to locate information about ingredients used in dietary supplements and any action taken by the agency with regard to that ingredient (153).

Specific nutrient supplementation for people with diabetes is generally not recommended outside the presence of deficiencies or overt malnutrition. Routine antioxidant supplementation (such as vitamins E and C) is not recommended due to lack of evidence of efficacy and concern related to long-term safety. Based

on the 2022 U.S. Preventative Services Task Force statement, the harms of β -carotene outweigh the benefits for the prevention of CVD or cancer. β -Carotene was associated with increased lung cancer and cardiovascular mortality risk (154).

Vitamin D in the context of diabetes has generated much research, but universal vitamin D supplementation for people with type 1 or type 2 diabetes without deficiency is not recommended at this time. Although post hoc analyses of the Vitamin D and Type 2 Diabetes Study (D2d) prospective RCT and Diabetes Prevention and Active Vitamin D (DPVD) and some meta-analyses suggest a potential benefit in specific populations (155–157), other studies have found no benefit or mixed results (158–160). Furthermore, adopting healthy lifestyle habits, including the eating patterns recommended herein, are strongly advised. Additional research is needed to define individual characteristics, clinical indicators, and appropriate dosages if and when vitamin D supplementation might benefit people with type 1 or type 2 diabetes.

There is also insufficient evidence to support routine use of herbal supplements and micronutrients, such as cinnamon (161), curcumin (e.g., turmeric), aloe vera, or chromium, to improve glycemia in people with type 1 or type 2 diabetes (46).

While not a dietary supplement, metformin is associated with vitamin B12 deficiency based on findings from the Diabetes Prevention Program Outcomes Study (DPPOS). Therefore, periodic testing of vitamin B12 levels should be considered in people taking metformin, particularly in those with anemia or peripheral neuropathy (162) (see section 9, “Pharmacologic Approaches to Glycemic Treatment”).

For special populations, including pregnant or lactating individuals, older adults, vegetarians, vegans, and people following very-low-calorie or low-carbohydrate eating patterns, a multivitamin may be necessary (163).

Alcohol

Long-term effects of alcohol consumption for people with diabetes are unknown. The World Health Organization declared there is no safe amount of alcohol intake (164,165). Associated risks of alcohol consumption include hypoglycemia and/or delayed hypoglycemia (particularly for those

using insulin or insulin secretagogue therapies), weight gain, and hyperglycemia (for those consuming excessive amounts) (46,166). People with diabetes should be educated about these risks and encouraged to monitor glucose frequently before and after drinking alcohol to minimize such risks. People with diabetes who consume alcohol can follow the same guidelines as people without diabetes consistent with the *Dietary Guidelines for Americans, 2020–2025* (72), which does not promote alcohol consumption in people who do not already drink. To reduce risk of alcohol-related harms, adults can choose not to drink or to drink in moderation by limiting intake to ≤ 2 drinks a day for men or ≤ 1 drink a day for women (one drink is equal to a 12-oz beer, a 5-oz glass of wine, or 1.5 oz of distilled spirits) (72). Recent meta-analyses have reported the previously recognized J-shaped relationship between alcohol intake and health risks likely varies by sex, obesity status, genetics, and alcohol intake behaviors (167,168).

Nonnutritive Sweeteners and Water

The FDA has approved many nonnutritive sweeteners (NNS) (containing few or no calories; commonly referred to as artificial sweeteners) for consumption by the general public, including people with diabetes (46,169). However, the safety and role of NNS continue to be sources of concern and confusion for the public.

For some people with diabetes who are accustomed to regularly consuming sugar-sweetened foods or beverages (e.g., regular soda pop, juice drinks, and other items sweetened with cane sugar or high-fructose corn syrup), NNS may be an acceptable substitute for nutritive sweeteners (those containing calories, such as sugar, honey, and agave syrup) when consumed in moderation (i.e., consuming no more than the acceptable daily intake) (170). NNS do not appear to have a significant effect on glycemic management (171,172), and they can reduce overall calorie and carbohydrate intake as long as individuals are not compensating with additional calories from other food sources (46,173). A meta-analysis and systematic review of RCTs found no evidence that NNS raise liver enzymes (174).

There is mixed evidence from systematic reviews and meta-analyses for NNS use with regard to weight management, with some finding benefit for weight loss

(175–177) while other research suggests an association with weight gain (178,179). This may be explained by reverse causality and residual confounding variables (179). The addition of NNS to eating plans poses no benefit for weight loss or reduced weight gain without energy restriction (180). In a systematic review and meta-analysis using low-calorie and no-calorie sweetened beverages as an intended substitute for sugar-sweetened beverages, a small improvement in body weight and cardiometabolic risk factors was seen without evidence of harm and had a direction of benefit similar to that seen with water (181). While health care professionals should promote water as the healthiest beverage option, people with overweight or obesity and diabetes may also use a variety of no-calorie or low-calorie sweetened products so that they do not feel deprived (181).

Health care professionals should encourage reductions in foods and beverages with added sugars and promote reducing overall sugar intake and calories with or without the use of NNS. Assuring people with diabetes that NNS have undergone extensive safety evaluation by regulatory agencies and are continually monitored can allay unnecessary concern for harm. Health care professionals can regularly assess individual use of NNS based on the acceptable daily intake (amount of a substance considered safe to consume each day over a person's life) and recommend moderation. Readers are directed to the FDA for additional information on NNS including safety, graphics, and the acceptable daily intake levels for the six major ones used in the U.S. ([fda.gov/food/food-additives-petitions/aspartame-and-other-sweeteners-food](https://www.fda.gov/food/food-additives-petitions/aspartame-and-other-sweeteners-food)).

Weight Management

Management and reduction of weight is important for people with type 1 diabetes, type 2 diabetes, or prediabetes with overweight or obesity. To support weight loss and improve A1C, CVD risk factors, and well-being in adults with overweight or obesity and prediabetes or diabetes, MNT and DSMES services should include an individualized eating plan resulting in an energy deficit in combination with enhanced physical activity (46). Lifestyle intervention programs should be intensive and have frequent follow-up to achieve significant reductions in excess body weight and

improve clinical indicators. Behavior modification goals should address physical activity, calorie restriction, healthy weight management strategies, and motivation. There is strong and consistent evidence that modest, sustained weight loss can delay the progression from prediabetes to type 2 diabetes (78,182,183) (see section 3, “Prevention or Delay of Diabetes and Associated Comorbidities”) and is beneficial for type 2 diabetes management (see section 8, “Obesity and Weight Management for the Prevention and Treatment Diabetes”).

In prediabetes, the weight loss goal is at least 5–7% from baseline body weight, and it is higher for reducing risk of progression to type 2 diabetes. Some RCTs report less than 5% weight loss in adults with diabetes and overweight or obesity following a lifestyle behavioral intervention, but this limited amount of weight loss has not been shown to improve glycemia, lipids, or blood pressure; rather, a minimum weight loss of 5% or more seems necessary to achieve metabolic improvements (184). In conjunction with support for healthy lifestyle behaviors, medication-assisted weight loss can be considered for people at risk for type 2 diabetes when needed to achieve and sustain 7–10% weight loss (185,186) (see section 8, “Obesity and Weight Management for the Prevention and Treatment of Diabetes”). People with prediabetes and healthy weight range should also be considered for behavioral interventions to help establish routine aerobic and resistance exercise (182,187,188) and healthy eating patterns. Services delivered by health care professionals familiar with diabetes and its management, such as an RDN, have been found to be effective (77).

For many individuals with overweight or obesity alongside type 2 diabetes, at least 5% weight loss is needed to achieve beneficial outcomes in glycemic management, lipids, and blood pressure (189). However, any magnitude of weight loss is recommended. It also should be noted that the clinical benefits of weight loss are progressive, and more intensive weight loss goals (i.e., 15%) may be appropriate to maximize benefit depending on need, feasibility, and safety (190,191). Long-term sustainability of weight loss remains a challenge (192). For example, in some South Asian adult populations, traditional interventions have not been as effective in prevention or remission of type 2 diabetes, so

those groups will benefit from more culturally tailored interventional approaches (193).

Medications can augment MNT to support weight loss, weight loss maintenance, and improve cardiovascular outcomes. Newer medications (e.g., glucagon-like peptide 1 receptor agonists [GLP-1 RAs]) may be more viable, positively affect cardiovascular outcomes, and produce weight reduction beyond 10–15% (194–198). For more information on the nutritional considerations important for people undergoing significant weight loss, see **MONITORING NUTRITION INTAKE**, below.

Overweight and obesity are increasingly prevalent in people with type 1 diabetes and present clinical challenges regarding diabetes treatment and CVD risk factors (199,200). There is some evidence that GLP-1 RAs are useful in achieving weight loss among adults with type 1 diabetes, although with a higher risk of nausea and ketosis (201).

Regardless of diabetes type, weight loss maintenance is challenging (184,202) but has well-recognized long-term benefits. Weight loss maintenance physiology is complex and involves many hormonal, psychosocial, behavioral, and environmental factors. Following a weight loss of at least 8%, a subsequent “weight loss maintenance” intervention was reported to be only moderately beneficial, as it helped sustain physical health improvements but not glucose metabolism improvements (203). However, in another RCT with long-term, real-world, clinic-based follow-up of 10 years, Tomah et al. (204) reported lasting glycemic benefits in their cohort with an average weight loss of 7.7 ± 0.9 kg ($-6.9 \pm 0.8\%$) maintained for 10 years.

Starting a conversation about weight management should be based on motivational interviewing techniques (205), beginning with first asking the individual if they want to discuss their weight. Health care professionals should never assume a person with overweight or obesity wants to discuss weight at a medical appointment, especially if the appointment is for a seemingly unrelated issue (e.g., back pain, which many people do not realize is often secondary to excess body weight). Using person-centered approaches to weight management conversations involves meeting the individual where they are in their life and working with what they and their health care professional agree is the most beneficial approach. Guidance from an RDN

with expertise in motivational interviewing and diabetes and weight management MNT during any comprehensive structured weight loss program is strongly recommended.

Along with routine medical management visits, people with diabetes and pre-diabetes should be screened during DSMES and MNT encounters for a history of dieting and past or current disordered eating behaviors. Characterizing an individual's past efforts with weight loss and their body weight history can also be very useful. Nutrition therapy should be individualized to help address maladaptive eating behavior (e.g., purging) or compensatory changes in medical treatment plan (e.g., overtreatment of hypoglycemic episodes and reduction in medication dosing to reduce hunger) (46) (see **DISORDERED EATING BEHAVIOR**, below). Caloric restriction may be necessary for glycemic and weight management, but rigid meal plans and strict tracking of food intake and/or body weight can be contraindicated for individuals at increased risk of significant maladaptive eating behaviors (206). If eating disorders are identified during screening with diabetes-specific questionnaires, individuals should be referred to a qualified behavioral health professional (1).

Meal Replacements

Use of partial or total meal replacements is an additional strategy for energy restriction. Meal replacements are prepackaged foods (bars, shakes, and soups) that contain fixed amounts of macronutrients and micronutrients. They can improve nutrient quality and glycemic management and, consequently, reduce portion size and energy intake. In a meta-analysis involving 17 studies incorporating both partial and total meal replacements, greater weight loss and improvements in A1C and fasting blood glucose were demonstrated compared with conventional meal plans (207). Furthermore, meal replacements have been used in several landmark clinical trials, including Look AHEAD (Action for Health in Diabetes) (208), DiRECT (Diabetes Remission Clinical Trial) (209), and PREVIEW (Prevention of Diabetes Through Lifestyle Intervention and Population Studies in Europe and Around the World) (210). Results of these trials showed that partial or total meal replacements can be a potential short-term (i.e., <6 months) strategy for weight loss.

Regardless of the specific eating pattern or meal plan selected, long-term follow-up and support from members of the diabetes care team are needed to optimize self-efficacy and maintain behavioral changes (211).

Fasting and Timing of Food Intake

Chrononutrition is an emerging nutrition and biology subspecialty aimed toward increasing the understanding of how the timing of food ingestion affects metabolic health (212). Glucose metabolism follows a circadian rhythm through diurnal variation of glucose tolerance and peaks during daylight hours when food is consumed. Some preliminary studies show cardiometabolic benefits when food is consumed earlier (213). Similarly, circadian disruptions found in shift workers increase risk of type 2 diabetes (214). This evolving area of research currently lacks conclusive evidence, but future studies are anticipated.

Nonreligious Fasting

The primary forms of nonreligious fasting are intermittent fasting or time-restricted eating. These are popular strategies for weight and glucose management. One of the key distinctions between nonreligious and religious fasting is water intake. See **Fig. 5.1** for further details on how religious and nonreligious fasting practices compare.

Intermittent fasting is an umbrella term that includes three main forms of restricted eating: alternate-day fasting (energy restriction of 500–600 calories on alternate days), the 5:2 eating pattern (energy restriction of 500–600 calories on consecutive or nonconsecutive days with usual intake the other five), and time-restricted eating (daily calorie restriction based on window of time of 8–15 h). Each produces mild to moderate weight loss (3–8% loss from baseline) over short durations (8–12 weeks) with no significant differences in weight loss when compared with continuous calorie restriction (215,216). A 2024 systematic review and meta-analysis of RCTs examined the most common types of fasting in studies lasting 2–52 weeks. The authors concluded that intermittent energy restriction produces small but significant reductions in waist circumference and fat-free mass but were otherwise not superior to continuous energy restriction eating patterns (217). Generally, time-restricted eating or shortening the eating window can be adapted to any

Religious and intermittent fasting: differences and similarities

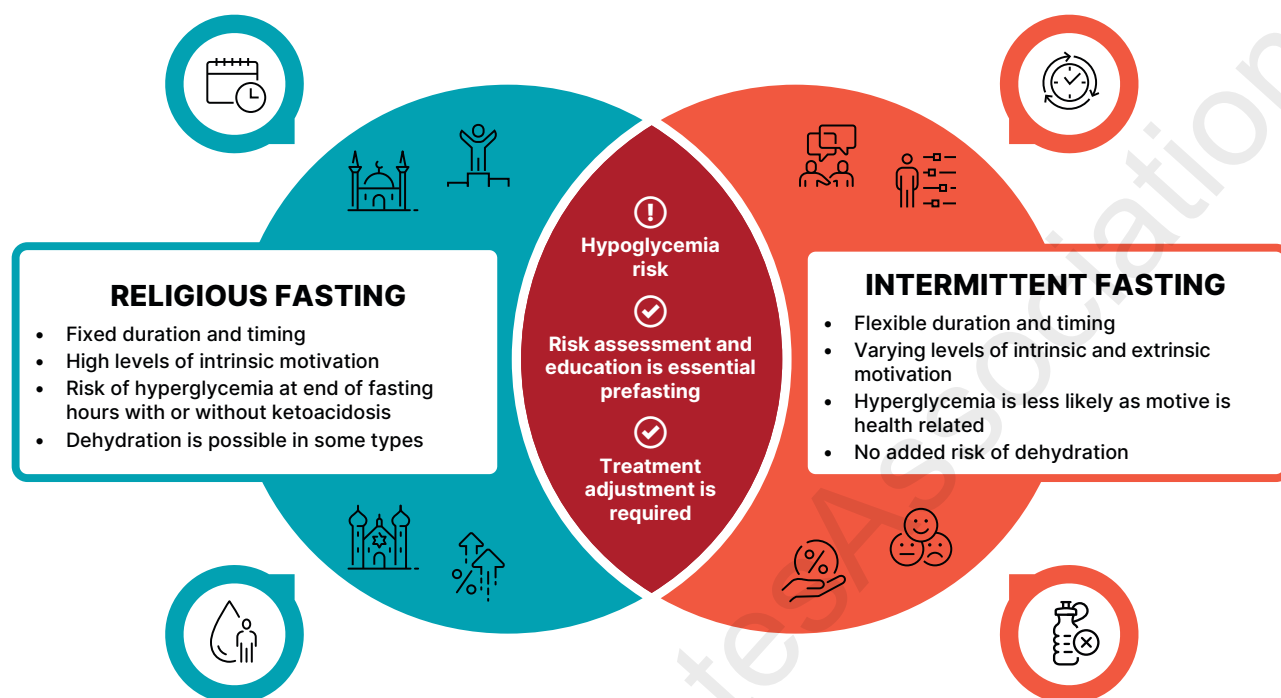


Figure 5.1—Differences and similarities between religious and intermittent fasting for people with diabetes.

eating pattern and has been shown to be safe for adults with type 1 or type 2 diabetes (218). People with diabetes who are taking insulin and/or secretagogues should be medically monitored during the fasting period (219). Because of the simplicity of intermittent fasting and time-restricted eating, these may be useful strategies for people with diabetes who are looking for practical eating management tools. It should also be noted that the principles of healthy eating still apply during non-fasting times.

Religious Fasting

Recommendations

5.32 Use the updated International Diabetes Federation along with Diabetes and Ramadan International Alliance comprehensive prefasting risk assessment to generate a risk score for the safety of religious fasting. Provide fasting-focused education to minimize risks. **B**

5.33 Assess and optimize treatment plan, dose, and timing for people with diabetes well in advance of religious fasting to reduce risk of hypoglycemia, dehydration, hyperglycemia, and/or ketoacidosis. **B**

Although intermittent fasting and time-restricted eating are specific dietary strategies for energy restriction, religious fasting has been practiced for thousands of years and is part of many faith-based traditions. Duration, frequency, and type of fast vary among different religions (220). For example, Jewish people abstain from any intake for ~25 h during Yom Kippur (221,222). For Muslims, Ramadan fasting lasts for a full month, when abstinence from any food or drink is required from dawn to dusk (223). Individuals with diabetes who fast have an increased risk for hypoglycemia, dehydration, hyperglycemia, and ketoacidosis (224,225).

Prefasting risk assessment is essential to increase level of safety (224,225). Various risk factors need to be considered for every individual wishing to fast. Some of these factors are related to the type of fast, type of diabetes, and/or the individual. Indeed, health care professionals should inquire about any religious fasting for people with diabetes and provide education and support to accommodate their choice. The number of fasting days is an important factor to consider. In Ramadan fasting, a person fasts from dawn to dusk for a lunar

month (29–30 days). It is important for the health care professional to comprehensively assess these risk factors well in advance of the planned fasting date, as some of them are modifiable. Some of these factors are related to the nature of the fasting practice, others are related to diabetes, and others might be due to individual factors such as the physical intensity of their work and/or the nutrition choices when they break their fast. The International Diabetes Federation along with Diabetes and Ramadan International Alliance adopted a risk calculator for the various risk factors (224,226). Several clinical studies from different countries have been published that assess the validity of the fasting risk score and the ease of use of it (226–229). The accumulation of these risk factors provides a risk score as low, moderate, or high (**Table 5.3**) (224). While the risks of different religious fasting practices may vary, this risk calculator provides some useful guidance for other types of religious fasting.

Prefasting education regarding the importance of increasing the frequency of glucose monitoring for people wishing to fast is very important. Timing of glucose monitoring is also especially important,

Table 5.3—Elements for risk calculation and suggested risk score for people with diabetes who seek to fast during Ramadan

Fasting risk element	Risk score
1. Pregnancy with any type of diabetes	
• Yes	6.5
2. Diabetes type	
• Type 1 diabetes or LADA	1
• Type 2 diabetes or any other type of diabetes	0
3. Duration of diabetes (years)	
• >20 years	1
• 10–20 years	0.5
• <10 years	0
4. Type of diabetes treatment (select all that are relevant)	
• Multiple daily premixed insulin injections	2
• Once-daily premixed insulin	1.5
• Open-loop insulin pump	1.5
• Automated insulin delivery system	1
• Standard basal insulin (NPH, detemir, or glargine 100)	1
• Ultra-long-acting basal insulin (glargine 300 or degludec)	0.75
• Short-acting insulin	0.75
• Glibenclamide or glipizide	0.75
• Modern sulfonylurea (gliclazide, gliclazide MR, glimepride) or repaglinide	0.5
• ≥2 glucose-lowering medications excluding insulin or sulfonylurea	0.25
• Nutrition modification only or monotherapy (excluding insulin or sulfonylurea)	0
5. Presence of hypoglycemia	
• Impaired hypoglycemia awareness	6.5
• Severe* hypoglycemia during last 4 weeks	5
• Hypoglycemia more than once daily	4
• 6–7 episodes of hypoglycemia/week	3
• 3–5 episodes of hypoglycemia/week	2
• 1–2 episodes of hypoglycemia/week	1
• Hypoglycemia <1 time per week	0.5
• No hypoglycemia in last 4 weeks	0
6. Level of A1C	
• >9% (>75 mmol/mol)	1
• 7.5–9% (58–75 mmol/mol)	0.5
• <7.5% (<58 mmol/mol)	0
7. Glucose monitoring	
• Not done	2
• Done suboptimally	1
• Done as indicated	0
• Any type of CGM	–0.5
8. Hyperglycemic emergencies	
• DKA or HHS in the last month	3.5
• DKA or HHS in last 2–3 months	2
• DKA or HHS in last 4–6 months	1
• No DKA or HHS in last 6 months	0
9. Macrovascular** complications	
• Unstable macrovascular disease	6.5
• Stable macrovascular disease	2
• No macrovascular disease	0
10. Microvascular complications	
a. Nephropathy	
• eGFR <30 mL/min	6.5
• eGFR 30–45 mL/min	4
• eGFR 45–60 mL/min	2
• eGFR >60 mL/min	0
b. Neuropathy, foot complications, or diabetic retinopathy	
• 3 microvascular complications	3
• 2 microvascular complications	2
• 1 microvascular complication	1
• 0 microvascular complications	0

Continued on p. S102

as the last few hours of fasting are frequently associated with approximately 50% of hypoglycemic events (230). Consequently, avoiding intense physical activity during the last few hours of fasting seems to be a sensible approach.

During religious fasting, some people change their nutrition habits and overindulge after fasting concludes. In many communities, the meal consumed to break the fast is rich in carbohydrates and includes foods and beverages high in added sugars and fat (224). Indeed, in one recent study 16.5% of people with type 2 diabetes who fasted for Ramadan reported high blood glucose of >300 mg/dL (>16.6 mmol/L) during fasting days (230). Individualized fluid adjustment and meal advice should be provided with emphasis on higher intake of fiber and replacing added sugars with complex carbohydrates to minimize hypoglycemia and hyperglycemia and emphasis on sustaining adequate daily fluid intake (231).

Treatment before and after fasting should be culturally sensitive and individualized. Specific recommendations for diabetes management during religious fasting in different faiths are available (224,225). In general, for people planning to fast for long hours and multiple consecutive days, choice of treatment should prioritize drugs with low hypoglycemia risk. Hypoglycemia risk while fasting in people using insulin, sulfonylureas, and other insulin secretagogues is higher than that for individuals treated with other types of diabetes medications (224). The safety of SGLT2 inhibitors was assessed in several studies during Ramadan fasting. These studies did not show significant change in kidney function, dehydration rates, or ketosis (232). Guidelines do not advise any change in SGLT2 inhibitor dose during fasting; however, they advise against initiating SGLT2 inhibitors close to the start of fasting days to avoid excessive thirst (224). **Table 5.4** summarizes the effect of fasting on different treatment options and the possible change in doses or timing for people with diabetes.

Technology could be an important tool to enhance safety during fasting. Several studies have investigated the use of monitoring technology during Ramadan fasting (e.g., flash glucose monitoring and CGM) and confirmed that these tools are able to support high-risk groups wishing to fast, especially if combined with Ramadan-focused education (232–234). Meanwhile, the use of insulin pumps

Table 5.3—Continued

Fasting risk element	Risk score
11. Cognitive function, frailty, and age	
• Impaired cognitive function	6.5
• Advanced frailty	6.5
• Mild to moderate frailty	4
• Age >70 years with no home support	1
• Normal cognitive function and no frailty	0
12. Physical labor	
• High intensity	4
• Moderate intensity	2
• Low intensity	0
13. Fasting-focused education	
• Yes	0
• No	1
14. Fasting hours	
• ≥16 h	1
• <16 h	0

Based on risk scoring, people with diabetes can be categorized as having:

- Score 0–3.0: low risk, fasting is probably safe
- Score 3.5–6.0: moderate risk, fasting safety is uncertain
- Score >6.0: high risk, fasting is probably unsafe

AID, automated insulin delivery; CGM, continuous glucose monitoring; DKA, diabetic ketoacidosis; eGFR, estimated glomerular filtration rate; HHS, hyperglycemic hyperosmolar state; LADA, latent autoimmune diabetes in adults (type 1 diabetes). *Hypoglycemia requiring assistance for treatment. **Macrovascular disease includes cardiac, cerebral, or peripheral. Adapted from Hassanein et al. (224).

has been associated with low rates of hypoglycemia during fasting in people with type 1 diabetes. Diabetes technologies should be considered as a useful adjunct to risk calculation and/or nutrition planning and education during religious fasting for people with diabetes (224).

Monitoring Nutrition Intake

It is important to monitor for adequate nutritional intake to prevent nutrient deficiencies, especially in people with diabetes who are seeking intentional weight loss. Health care professionals should advise a healthy, whole foods–based eating pattern with sufficient micro- and macronutrients, protein, fiber, and fluid intake alongside regular resistance training to maintain lean body mass and prevent nutritional deficiencies (235,236). Referral to an RDN is also important to optimize nutrition status, especially if they have experience conducting a nutrition-focused physical exam (235,237) (see section 8, “Obesity and Weight Management for the Prevention and Treatment of Diabetes”).

Food Insecurity and Access

Food insecurity is a household-level economic and social condition of limited or

uncertain access to adequate food (238). In 2023, 13.5% of Americans were food insecure (238), and food insecurity affects 16% of adults with diabetes compared with 9% of adults without diabetes (239). There is a complex bidirectional association between food insecurity and co-occurring diabetes. Food security screening should happen at all levels of the health care system. Any member of the health care team can screen for food insecurity using the Hunger Vital Sign. Households are considered at risk if they answer either or both of the following statements as “often true” or “sometimes true” (compared with “never true”) (240):

- “Within the past 12 months, we worried whether our food would run out before we got money to buy more.”
- “Within the past 12 months, the food we bought just didn’t last, and we didn’t have money to get more.”

If screening is positive for food insecurity, efforts should be made to refer to appropriate programs and resources. See section 1, “Improving Care and Promoting Health in Populations,” for more information concerning the social determinants of health and related issues like food insecurity and access.

PHYSICAL ACTIVITY

Recommendations

5.34 Evaluate baseline physical activity and sedentary time for all people with diabetes and those at risk for diabetes. For people who do not meet activity guidelines, encourage an increase in physical activities above baseline with the goal of meeting activity guidelines. **B** Counsel that prolonged sitting should be interrupted at least every 30 min for blood glucose and other benefits. **C**

5.35 Counsel children and adolescents with type 1 diabetes **C** or type 2 diabetes **B** to engage in 60 min/day or more of moderate- or vigorous-intensity aerobic activity, with muscle-strengthening and bone-strengthening activities at least 3 days/week, and to limit the amount of time being spent sedentary, including recreational screen time. **C**

5.36 Counsel most adults with type 1 diabetes **C** and type 2 diabetes **B** to engage in 150 min or more of moderate- to vigorous-intensity aerobic activity per week, spread over at least 3 days/week, with no more than 2 consecutive days without activity. Shorter durations (minimum 75 min/week) of vigorous-intensity or interval training may be sufficient for more physically fit individuals.

5.37 Counsel adults with type 1 diabetes **C** and type 2 diabetes **B** to engage in 2–3 sessions/week of resistance exercise on nonconsecutive days.

5.38 Counsel most older adults with diabetes to engage in flexibility training and balance training 2–3 times/week. **C**

5.39 Counsel all people with diabetes who are treated with obesity pharmacotherapy or metabolic surgery that meeting physical activity recommendations, in particular muscle-strengthening exercises, may be beneficial for maintaining lean body mass. **C**

Physical activity includes all movement that increases energy use, and exercise is a more specific form of physical activity that is structured and designed to improve physical fitness. Both physical activity and exercise demonstrate numerous benefits for people with and at

Table 5.4—Changes in medications during fasting

Medication name	Risk of hypoglycemia	Timing	Total daily dose
Metformin, SGLT2 inhibitor, DPP-4 inhibitor, GLP-1 receptor agonist, acarbose, or pioglitazone	Low	• If once daily, then take at main mealtime. • If twice daily, then split dose between the two meals. • If once weekly, no change of time.	• No change
New generation of sulfonylurea (glimepiride and gliclazide)	Low to moderate	• If once daily, then take at main mealtime. • If twice daily, then split dose between the two meals.	• Reduce dose if glucose levels are within individualized goal range and if no hypoglycemia or hyperglycemia is present at baseline.
Older generation of sulfonylurea (glyburide)	Moderate to high	• Take at time of main meal	• Replace with newer-generation sulfonylurea or reduce dose by 50%.
Basal insulin	Moderate to high	• For longer-acting basal analogs (glargine 300 or degludec), no need to change timing. • For other basal insulins, take at beginning of breaking fast meal.	• Choose the insulin with lower risk of hypoglycemia among the class. • Reduce dose by 25–35% if not well managed.
Prandial insulin	High	• At mealtime	• Reduce dose of insulin for the meal followed by fasting (35–50%). • For other meals, insulin dose should match carbohydrate intake.
Mixed insulin and insulin coformulations	High	• If once daily, then take at main mealtime. • If twice daily, then split dose between the two meals	• Reduce dose of insulin for the meal followed by fasting (35–50%). • For other meals, no change of dose.

DPP-4, dipeptidyl peptidase 4; GLP-1, glucagon-like peptide 1; SGLT2, sodium–glucose cotransporter 2.

risk for diabetes and are important for the diabetes management plan. Higher levels of total and leisure-time physical activity are associated with a lower risk of cardiovascular and overall mortality in people with diabetes (241,242). Leisure-time activity may also help prevent type 2 diabetes (243) and reduce A1C in those with diabetes (244). Moreover, data from the DPPOS noted that self-reported habitual physical activity is positively associated with 6-min walking distance, which suggests long-term benefits of regular physical activity engagement (245). Exercise and physical activity have favorable effects on glycemia, cardiovascular risk factors, weight loss, body composition, mobility, mortality, psychosocial well-being, and physical function in people with diabetes (242,246–254).

Given the benefits of physical activity and exercise for people with diabetes, they should be recommended and prescribed to all individuals who are at risk for or have diabetes as part of the diabetes care plan, unless otherwise contraindicated. Specific recommendations and precautions on the type of activity will vary by diabetes type, age, and presence of complications. Health care professionals should support people with diabetes to set

stepwise goals toward meeting the recommended exercise volume. As individuals intensify their exercise program, medical monitoring may be indicated to ensure safety and evaluate the effects on glycemic management. Exercise and activity plans should be tailored to meet the specific needs of each individual (255), and different strategies can be used to increase engagement (256,257). Individuals with diabetes may experience obstacles to exercise, such as not having enough time or inadequate access to equipment or education for safe participation. The care team should help identify these obstacles and individualize approaches to improve long-term adoption of physical activity and exercise as a key part of the diabetes care plan.

Furthermore, activity plans can be modified to best suit the fitness level of the individual, which may vary due to ability level or complications. The plan might also need to be modified over time due to changes in health status, goals, or preferences or if the therapeutic response reaches a plateau. For this reason, individuals with diabetes benefit from a team-based approach, including working with an exercise physiologist, physical therapist,

or personal trainer, among others, where available and affordable (258). The ADA position statement “Physical Activity/Exercise and Diabetes” reviews the evidence for the benefits of exercise in people with type 1 and type 2 diabetes and offers more specific guidance (255).

Physical Activity and Glycemic Management

In people with type 2 diabetes, exercise training has demonstrated multiple cardio-metabolic improvements, including but not limited to improved glycemia, cardiovascular function, and lipid profiles (259,260). A meta-analysis primarily consisting of aerobic training studies revealed that structured exercise interventions of at least 8 weeks have been shown to lower A1C by 0.66% in people with type 2 diabetes, even without a significant change in BMI (247). Data also suggest that combining aerobic and resistance exercise may provide greater glycemic benefits compared with performing either mode of exercise alone (260).

In people with type 1 diabetes, the data for improving A1C are somewhat unclear (261,262). Interestingly, adding resistance training to an exercise plan for adults with type 1 diabetes who were

already aerobically active did not impact glycemia, even with improvements in waist circumference and strength (263). Real-world data from the Type 1 Diabetes and Exercise Initiative (T1DEXI) show that aerobic exercise reduces glycemia after an acute exercise session compared with high-intensity interval exercise and resistance exercise; however, all three modes of exercise improve time in range over a 24-h period (264). Furthermore, meeting daily step count of ~7,000–10,000 steps/day may support marginal improvements in time in range and reduced insulin requirements (265). Though there may be some benefits in glycemic response to exercise, this variability should be taken into consideration when recommending the type, intensity, and duration of exercise and insulin adjustments for a given individual with type 1 diabetes to prevent hypoglycemia and hyperglycemia (266,267).

Individuals of childbearing potential with preexisting diabetes, particularly type 2 diabetes, and those at risk for or presenting with gestational diabetes mellitus should be encouraged to engage in regular moderate-intensity physical activity prior to and during their pregnancies, as tolerated (255). Regular exercise can reduce the odds of developing gestational diabetes mellitus by nearly 40% (268), and acute and long-term prenatal exercise can positively impact glycemia, with a larger effect noted in people with diabetes (269). For more information, see section 15, “Management of Diabetes in Pregnancy.”

Evaluating Pre-exercise Risk and Baseline Physical Activity

As discussed more fully in section 10, “Cardiovascular Disease and Risk Management,” the best protocol for assessing asymptomatic people with diabetes for coronary artery disease remains unclear. The ADA consensus report “Screening for Coronary Artery Disease in Patients With Diabetes” (270) concluded that routine testing is not recommended. However, health care professionals should perform a careful history prior to exercise engagement, assess cardiovascular risk factors, be aware of the atypical presentation of coronary artery disease, such as a recently reported or measured decrease in exercise tolerance, and determine if testing for cardiac abnormality (e.g., arrhythmia) is warranted. Certainly, those with high risk should be encouraged to start with short periods of low-intensity exercise and

slowly increase the duration and intensity as tolerated. Additionally, individuals with complications may warrant a more thorough evaluation prior to engaging in a physical activity or exercise plan to ensure the plan is safe and appropriate. Health care professionals should assess for conditions that might contraindicate certain types of exercise or predispose to injury, such as inadequately managed hypertension, untreated proliferative retinopathy, autonomic neuropathy, orthostatic hypotension, peripheral neuropathy, balance impairment, and a history of foot ulcers or Charcot foot.

An evaluation of baseline physical activity and time spent in sedentary behavior is recommended to help guide initial increases in physical activity levels. When discussing physical activity, health care professionals should consider inquiring about motivators (e.g., health benefits, enjoyable activities with family) and potential barriers (e.g., lack of time, fear of hypoglycemia, no safe place to perform activity) to exercise and activity participation (271,272). Understanding these barriers may help with devising practical solutions for sustainable exercise participation, as complete uptake of the recommended total exercise volume may be initially challenging for some people with diabetes (273,274). People who do not meet activity guidelines should be encouraged to increase physical activity levels above baseline by performing activities such as walking, yoga, housework, gardening, swimming, and dancing (275). Sedentary behaviors (e.g., time seated at work, on a computer, tablet, smartphone, or watching television) should be discussed regularly. People with diabetes should be counseled to reduce sedentary time and break up sedentary activities at least every 30 min by briefly standing, walking, or performing other light physical activities to support glycemic and other cardiometabolic benefits, such as vascular function (276–279).

Exercise for Children and Adolescents

Similar to children and adolescents in general, children and adolescents with diabetes or who are at risk for diabetes should be encouraged to engage in regular physical activity, including at least 60 min of moderate-to-vigorous aerobic activity every day and muscle- and bone-strengthening activities at least 3 days per week to support development and health

benefits (254,280). Exercise programs promoting nutrition modification, increasing physical activity levels, and reducing sedentary time in children and adolescents at risk for type 2 diabetes have been shown to reduce risk of type 2 diabetes development (281–283), and vigorous-intensity physical activity participation is associated with lower CVD risk in youth with type 2 diabetes (284). In general, children and adolescents with type 1 diabetes benefit from being physically active, with meta-analyses reporting significant associations between physical activity and lower A1C (285) and an absolute A1C reduction of nearly 0.8% (286). Thus, an active lifestyle should be recommended to all children and adolescents with diabetes to support health outcomes and health-related quality of life (287,288). Children and adolescents are recommended to limit sedentary time, including recreational screen time, to less than 2 h per day (289–291). See section 14, “Children and Adolescents,” for details.

Frequency and Type of Physical Activity

A comprehensive physical activity and exercise plan should encompass multiple modes of activities, including aerobic, resistance, flexibility, balance, and leisure-time activities. Each activity type offers unique benefits for diabetes management, overall health, and quality of life. Age, previous physical activity experiences, fitness level, and goals should be considered when discussing physical activity and exercise plans. For more specific guidance, see the ADA position statement “Physical Activity/Exercise and Diabetes” (255).

Aerobic Activity

Aerobic activities encompass prolonged rhythmic activities using large muscle groups, such as walking, running, and cycling (255), and provide multiple cardiometabolic benefits for people with diabetes (241,247,259,260,292). Adults with diabetes are encouraged to engage in 150 min or more of moderate- to vigorous-intensity aerobic activity weekly (254,255). Aerobic activity bouts should last at least 10 min, with the goal of ~30 min/day or more most days of the week to accumulate at least 150 min per week (e.g., 30 min/day, 5 days per week). Daily exercise, or at least not allowing more than 2 days to elapse between exercise sessions, is recommended to decrease insulin resistance,

regardless of diabetes type (293,294). Over time, aerobic activities should progress in intensity, frequency, and/or duration to meet the recommended exercise volume. Though exercise at higher intensities can facilitate greater reductions in A1C (295), many adults may be unable or unwilling to participate in high-intensity exercise. In those cases, diabetes care professionals should encourage engagement in moderate exercise for the recommended duration for A1C reduction and other cardiometabolic benefits (241,259,292).

Resistance Activity

Resistance activity refers to movements working against an external force for the purpose of improving skeletal muscle strength and size, which typically includes free weight, weight machine, body weight, or resistance band movements to target the major muscle groups. Resistance training can improve glycemia, strength, hypertrophy, bone mineral density, and cardiometabolic health (296–298), and higher relative muscle mass is associated with better insulin sensitivity and lower diabetes risk (298). Adults with diabetes are encouraged to participate in 2–3 sessions/week of resistance exercise on non-consecutive days (254,255). Although it has been suggested that high-intensity resistance exercise training provides a greater benefit for glycemic management when compared with lower intensities (299), resistance training of any intensity is recommended to improve strength, balance, and the ability to engage in activities of daily living throughout the lifespan.

Flexibility and Balance Activities

Flexibility and balance activities serve to improve the range of motion around joints and reduce the risk of falls, respectively (254,255). Older adults with diabetes are encouraged to participate in flexibility and balance training 2–3 times/week. A variety of activities, including yoga, tai chi, and resistance training, can significantly improve A1C, flexibility, muscle strength, balance, and gait (254,300–304). Older adults in particular can benefit from flexibility and resistance training for maintenance of range of motion, strength, and balance (255,305,306) (Fig. 5.2).

High-Intensity Interval Training

High-intensity interval training (HIIT) involves short bursts of aerobic training performed

between 65% and 90% $\text{VO}_{2\text{peak}}$ (a measure of maximal aerobic capacity) or 75% and 95% heart rate peak for 10 s to 4 min with 12 s to 5 min of active or passive recovery. HIIT is a potentially time-efficient modality that can elicit significant physiologic and metabolic adaptations for individuals with type 1 and type 2 diabetes, including improvements in glycemia, β -cell function, central adiposity, and cardiac function (307–310).

When matched for energy expenditure, a 4-month HIIT-style walking program provided greater improvement in glycemia, physical fitness, and body composition compared with a continuous-walking program in people with type 2 diabetes (311). In contrast, a 12-week study in people with type 2 diabetes noted that HIIT cycling and continuous cycling programs, matched for energy expenditure, were not different in efficacy compared with each other or with a nonexercise control group (312). Both cycling protocols demonstrated improvements in aerobic capacity and A1C compared with baseline, but only continuous cycling showed improvements in cardiovascular response and visceral adiposity compared with baseline (312).

Because an acute bout of HIIT can lead to transient increases in postexercise hyperglycemia, individuals with type 1 diabetes may need to use bolus correction (313) and individuals with type 2 diabetes are encouraged to monitor blood glucose when starting HIIT (314). In type 1 diabetes, weeks of HIIT reduce A1C and insulin requirements and improve cardiometabolic risk profiles (310). Variability in glucose may occur with an increased risk in delayed hypoglycemia, so careful monitoring of glucose during and after HIIT is advised (310). Though HIIT may be an attractive mode of activity due to lowered required time commitment, individuals may be unable or unwilling to participate in activity at a high intensity. It may be of interest to intersperse HIIT within the broader activity plan with considerations for adequate recovery to prevent potential exercise-related injury (293).

Other Considerations

Exercise During Obesity Treatment

As many people with diabetes and obesity are often treated with obesity pharmacotherapy or metabolic surgery, additional emphasis on meeting physical activity guidelines, particularly muscle-strengthening activities, is warranted. Both obesity pharmacotherapy and metabolic surgery lead

to reductions in body weight, which often induces loss of both fat mass (adipose tissue) and fat-free mass (nonadipose tissues). This has raised concern about the loss of fat-free mass (particularly skeletal muscle and bone) and its potential long-term consequences on strength, physical function, resting energy expenditure, and the potential development or worsening of frailty, sarcopenia, and sarcopenic obesity. Engagement in exercise programs prior to and after metabolic surgery may support muscle mass and strength (315,316), reduce weight recurrence and promote better weight maintenance (317,318), and improve insulin sensitivity (319). Even modest increases in physical activity after metabolic surgery may contribute to greater fat mass loss and better retention of skeletal muscle mass (320). Though aerobic exercise may be beneficial, combined aerobic and resistance training may produce greater weight loss and better improvements in functional capacity, muscle mass, and strength compared with aerobic exercise alone (316). In addition to metabolic surgery, combining obesity pharmacotherapy with exercise programs may lead to some synergistic benefits. Combination of structured exercise training plus a GLP-1 RA has demonstrated improvements in β -cell function, glucose tolerance, and insulin sensitivity (321,322), reductions in abdominal adiposity and inflammation (323), and more favorable effects on body composition such as fat mass loss, fat-free mass maintenance, and reduced waist circumference (321–324). Conversely, a 16-week RCT reported that combined exercise training and GLP-1 RA therapy did not show synergistic benefits on cardiac function but rather showed potential inhibitory effects on left ventricular diastolic function in people with type 2 diabetes (325). However, this was a predefined sub-study that was not designed to detect changes in myocardial function. As data in this area for people with diabetes are emerging, more studies of longer duration and with newer-generation medications are needed.

Hypoglycemia

For individuals taking insulin and/or insulin secretagogues, physical activity may cause hypoglycemia if the medication dose or carbohydrate consumption is not adjusted for the exercise session and postbout effect on glucose. Individuals on these therapies may need to ingest carbohydrates if

Importance of 24-hour physical behaviors for type 2 diabetes

SITTING/BREAKING UP PROLONGED SITTING

- Limit sitting. Breaking up prolonged sitting (at least every 30 min) with short regular bouts of slow walking or simple resistance exercises can improve glucose metabolism.



STEPPING

- An increase of only 500 steps/day is associated with 2-9% decreased risk of cardiovascular morbidity and all-cause mortality.
- A 5- to 6-min brisk-intensity walk per day equates to ~4 years' greater life expectancy.



SLEEP

Aim for consistent, uninterrupted sleep, even on weekends.



Quantity - Long (>8 h) and short (<6 h) sleep durations negatively impact A1C.



Quality - Irregular sleep results in poorer glycemic levels, likely influenced by the increased prevalence of insomnia, obstructive sleep apnea, and restless leg syndrome in people with type 2 diabetes.



Chronotype - Evening chronotypes (i.e., night owl: go to bed late and get up late) may be more susceptible to inactivity and poorer glycemic levels than morning chronotypes (i.e., early bird: go to bed early and get up early).

SWEATING (MODERATE-TO-VIGOROUS ACTIVITY)

- Encourage ≥150 min/week of moderate-intensity physical activity (i.e., uses large muscle groups, rhythmic in nature) OR ≥75 min/week vigorous-intensity activity spread over ≥3 days/week, with no more than 2 consecutive days of inactivity. Supplement with two to three resistance, flexibility, and/or balance sessions.
- As little as 30 min/week of moderate-intensity physical activity improves metabolic profiles.



PHYSICAL FUNCTION

Physical function/ frailty/sarcopenia

- The frailty phenotype in type 2 diabetes is unique, often encompassing obesity alongside physical frailty, at an earlier age. The ability of people with type 2 diabetes to undertake simple functional exercises in middle-age is similar to that in those over a decade older.



STRENGTHENING

Resistance exercise (i.e., any activity that uses the person's own body weight or works against a resistance) also improves insulin sensitivity and glucose levels; activities like tai chi and yoga also encompass elements of flexibility and balance.



	Glucose/ insulin	Blood pressure	A1C	Lipids	Physical function	Depression	Quality of life
SITTING/BREAKING UP PROLONGED SITTING	↓	↓	↓	↓	↑	↓	↑
STEPPING	↓	↓	↓	↓	↑	↓	↑
SWEATING (MODERATE-TO-VIGOROUS ACTIVITY)	↓	↓	↓	↓	↑	↓	↑
STRENGTHENING	↓	↓	↓	↓	↑	↓	↑
ADEQUATE SLEEP DURATION	↓	↓	↓	↓	?	↓	↑
GOOD SLEEP QUALITY	↓	↓	↓	↓	?	↓	↑
CHRONOTYPE/CONSISTENT TIMING	↓	?	↓	?	?	↓	?

IMPACT OF PHYSICAL BEHAVIORS ON CARDIOMETABOLIC HEALTH IN PEOPLE WITH TYPE 2 DIABETES

- ↑ Higher levels of improvement (physical function, quality of life) ↓ Lower levels of improvement (glucose/insulin, blood pressure, A1C, lipids, depression)
 ? No data available
 ↑ Green arrows = strong evidence ↑ Yellow arrows = medium-strength evidence ↑ Red arrows = limited evidence

Figure 5.2—Importance of 24-h physical behaviors for type 2 diabetes. Adapted from Davies et al. (633).

pre-exercise glucose levels are <90 mg/dL (<5.0 mmol/L), depending on whether they are able to lower insulin doses during the workout (such as with an insulin pump

or reduced pre-exercise insulin dosage), the time of day exercise is done, and the intensity and duration of the activity (267). Due to heterogeneity of glycemic responses

to physical activity, the approach to carbohydrate intake and medication adjustments around the activity or exercise session should be individualized. More

guidance on carbohydrate intake and medication considerations can be found in the ADA position statement “Physical Activity/Exercise and Diabetes” (255). In some people with diabetes, hypoglycemia after exercise may occur and last for several hours due to increased insulin sensitivity. Hypoglycemia is not common in those who are not treated with insulin or insulin secretagogues, and no routine preventive measures for hypoglycemia are usually advised in these cases. Intense activities, such as HIIT, may actually raise glucose levels instead of lowering them, especially if pre-exercise glucose is elevated (267). Because of variation in glycemic response to exercise, people with diabetes should be taught to check blood glucose levels and/or monitor CGM values during and after exercise, how to understand the effect of exercise on glucose, about the potential prolonged effects (depending on intensity and duration), and how to manage and use AID technology around and during the time of exercise (266,326). See section 6, “Glycemic Goals, Hypoglycemia, and Hyperglycemic Crises,” for more information on hypoglycemia prevention and management.

Exercise in the Presence of Complications

See section 11, “Chronic Kidney Disease and Risk Management,” and section 12, “Retinopathy, Neuropathy, and Foot Care,” for more information on these long-term complications. A meta-analysis demonstrated that high versus low levels of physical activity were associated with lower CVD incidence and mortality (summary risk ratio 0.84 [95% CI 0.77–0.92], $n = 7$, and 0.62 [0.55–0.69], $n = 11$) and fewer microvascular complications (0.76 [0.67–0.86], $n = 8$). Dose-response meta-analyses showed that physical activity was associated with lower risk of diabetes-related complications even at lower activity levels (327).

Retinopathy

If proliferative diabetic retinopathy or severe nonproliferative diabetic retinopathy is present, then vigorous-intensity aerobic or resistance exercise may be contraindicated because of the risk of triggering vitreous hemorrhage or retinal detachment (328). Consultation with an ophthalmologist prior to engaging in an intense exercise plan may be appropriate.

Peripheral Neuropathy

Decreased pain sensation and a higher pain threshold in the extremities can result

in an increased risk of skin breakdown, infection, and Charcot joint destruction with some forms of exercise. Therefore, a thorough assessment should be done to ensure that neuropathy does not alter kinesthetic or proprioceptive sensation during physical activity, particularly in those with more severe neuropathy. Moderate-intensity walking may not lead to an increased risk of foot ulcers or reulceration in those with peripheral neuropathy who use proper footwear (329,330). In addition, 150 min/week of moderate exercise improved outcomes in people with prediabetic neuropathy (331). All individuals with peripheral neuropathy should wear proper footwear and examine their feet daily to detect lesions early. Anyone with a foot injury or open sore should be restricted to non-weight-bearing activities.

Autonomic Neuropathy

Autonomic neuropathy can increase the risk of exercise-induced injury or adverse events through decreased cardiac responsiveness to exercise, postural hypotension, impaired thermoregulation, impaired night vision due to impaired papillary reaction, and greater susceptibility to hypoglycemia (332). Cardiovascular autonomic neuropathy is also an independent risk factor for cardiovascular death and silent myocardial ischemia (333). Therefore, individuals with diabetic autonomic neuropathy should undergo cardiac investigation before beginning physical activity more intense than that to which they are accustomed.

Chronic Kidney Disease

Physical activity can acutely increase urinary albumin excretion. However, there is no evidence that vigorous-intensity exercise accelerates the rate of progression of CKD, and there appears to be no need for specific exercise restrictions for people with CKD in general (328).

SMOKING CESSATION: TOBACCO, E-CIGARETTES, AND CANNABIS

Recommendations

5.40 Ask people with diabetes routinely about the use of tobacco or vape products. **A** Advise complete avoidance of tobacco and vaping. **A** For individuals who use these products, provide or refer for combination treatment consisting of tobacco and/or vape product(s) cessation counseling and pharmacologic therapy. **A**

5.41 Advise people with type 1 diabetes **C** and those with other forms of diabetes at risk for diabetic ketoacidosis not to use recreational cannabis in any form. **E**

A causal link between cigarette smoking and diabetes has been well established for over a decade (334). Results from epidemiologic, case-control, and cohort studies support the causal link between cigarette smoking and multiple health risks that profoundly affect the morbidity and mortality of people with diabetes (334). People with diabetes who smoke and are exposed to second-hand smoke have a heightened risk of macrovascular complications (e.g., cardiovascular and peripheral vascular disease), microvascular complications (e.g., kidney disease and visual impairment), elevated A1C, and premature death compared with those who do not smoke and are not exposed to second-hand smoke (335,336). Findings from a systematic review and meta-analysis show a dose-response relation for current smoking and the risk for type 2 diabetes; this risk decreases as the time since quitting increases (337).

Routine (every visit with every person), thorough assessment of all types of tobacco use is essential to prevent tobacco product initiation and promote cessation. Evidence demonstrates quitting smoking reduces or reverses adverse health effects in addition to increasing life expectancy by up to 10 years (338). However, tobacco use among adults with chronic conditions remains higher than the general population, despite recent declines in smoking among middle-aged and older adults with diabetes (339). Numerous RCTs demonstrate the efficacy and cost-effectiveness of both intensive and brief counseling on smoking cessation, including the use of telephone quit lines and web-based interventions, in reducing tobacco use and maintaining abstinence from smoking (338,340). The World Health Organization recommends both counseling and pharmacologic therapy to assist with smoking cessation in nonpregnant adults (341). A secondary data analysis of the Evaluating Adverse Events in a Global Smoking Cessation Study (EAGLES), a randomized, double-blind, triple-dummy, placebo-controlled and active-controlled trial, found varenicline to be the most efficacious pharmacotherapy for people with diabetes compared

with placebo (342). These findings support the American Thoracic Society 2020 guideline recommending varenicline as a first-line pharmacotherapy for tobacco dependence (343). However, despite the effectiveness of pharmacologic therapy and counseling, more than two-thirds of people trying to quit do not receive treatment following evidence-based guidelines (338).

Weight gain after smoking cessation is a concern for diabetes management and risk for new onset of disease (344). While postcessation weight gain is an identified issue, studies have found that an average weight gain of 3–5 kg does not necessarily persist long term or diminish the substantial cardiovascular benefit realized from smoking cessation (337). A systematic review and meta-analysis comparing those who quit smoking to those who smoke stratified by postcessation weight gain found smoking cessation lowered the risk of CVD and all-cause mortality regardless of postcessation weight gain (345). Another systematic review and meta-analysis of interventions to prevent weight gain following smoking cessation identified several approaches that may modestly reduce weight gain, including personalized weight management programs, exercise programs, nicotine replacement therapy, and fluoxetine (346). Emerging research suggests GLP-1 RAs may improve smoking cessation, reduce cravings and withdrawal symptoms, and decrease weight gain in adults with overweight and/or prediabetes (347). More clinical trials are needed to examine the efficacy of GLP-1 RAs and other incretin pharmacotherapies as a possible treatment for tobacco use disorders and preventing weight gain postcessation.

In recent years, there has been an increase in the use and availability of multiple noncigarette nicotine products. The impact of these products on diabetes is less well established than that of combustible cigarettes. Smokeless tobacco products, such as dip and chew, pose an increased risk for CVD and oral cancer (348,349). Vaping with e-cigarettes and related devices has become more popular due to perceptions that e-cigarette use is less harmful than combustible cigarettes (350). While combustible tobacco products are the most harmful, e-cigarettes pose significant health risks to the cardiovascular and respiratory systems (351,352). Findings from the Population Assessment of Tobacco and Health (PATH) Study suggest e-cigarettes contribute to nicotine

dependence, confirming that there is no safe tobacco product (353,354). Individuals with diabetes should be advised to avoid vaping and using e-cigarettes, either as an approach to stop smoking combustible cigarettes or as a recreational drug. If people are using e-cigarettes for cessation, they should be advised to avoid using both combustible and electronic cigarettes, and if only using only e-cigarettes, they should be advised to discontinue those too (340). Diabetes education programs provide an opportunity to systematically reach and engage individuals with diabetes in smoking cessation efforts. A cluster randomized trial demonstrated statistically significant increases in quit rates and long-term abstinence rates (>6 months) when cessation interventions were delivered through diabetes education clinics, regardless of motivation to quit at baseline (355).

Increased legalization and multiple formulations of cannabis products have resulted in increased prevalence in the use of these products in all age-groups (356,357). Cannabidiol (CBD), which in its pure form has no psychoactive effect, has received attention for its potential therapeutic benefits in diabetes management. However, research shows no noticeable effect on glucose or insulin levels in adults with type 2 diabetes who use CBD (358). Significant increases in tetrahydrocannabinol (THC) concentrations in CBD products and use of additional psychoactive cannabinoid products, such as delta-8 THC, are of specific concern (359). Most of these products are currently unregulated by the FDA, and public health warnings regarding use have been issued (360). The FDA reports adverse effects related to delta-8 THC, some of which may have health implications for people with diabetes (e.g., vomiting) (360). Evidence of specific increased risk of hyperglycemic ketosis associated with cannabis use has been reported in adults with type 1 diabetes (361–363). Hyperglycemic ketosis in individuals with type 1 diabetes using cannabis is associated with cannabis hyperemesis syndrome, which is marked by severe nausea, abdominal pain, and vomiting (361–363). Recommended diagnostic criteria for hyperglycemic ketosis cannabis hyperemesis syndrome include a blood glucose of ≥ 250 mg/dL, an anion gap of > 10 , a serum β -hydroxybutyrate level of > 0.6 mmol/L, a pH level of ≥ 7.4 , and a bicarbonate level of ≥ 15 mmol/L (363). Health care professionals should consider

hyperglycemic ketosis cannabis hyperemesis syndrome in people with type 1 diabetes with pH ≥ 7.4 and bicarbonate > 15 mmol/L in the presence of ketosis (363).

The increased availability and use of tobacco and cannabis products highlights the importance of assessing use, educating individuals about the associated risks, and providing support for cessation.

SUPPORTING POSITIVE HEALTH BEHAVIORS

Given the impact on glycemic outcomes and risk for future complications (364,365), diabetes care professionals should support health-promoting behaviors (preventive, treatment, and maintenance), including glucose monitoring, taking medications, using diabetes technologies, engaging in physical activity, and healthy eating. Evidence-based behavioral strategies and multicomponent interventions, including motivational interviewing (366,367), activation (368), goal setting and action planning (367,369,370), problem-solving (8,369), tracking or self-monitoring health behaviors with or without feedback from a health care professional (367,369,370), and facilitating opportunities for social support (367,369,370), help people with diabetes and their caregivers develop health behavior routines and overcome barriers to self-management. While behavioral economics approaches (e.g., financial incentives, social norms messaging) show mixed results, they tend to enhance motivation and demonstrate short-term (i.e., < 6 months) benefits for behavior change (371). Multicomponent interventions are the most effective for improving behavior and glycemic outcomes (370,372), particularly in children and adolescents with diabetes, when delivered as family-based or multisystem behavioral interventions (373). Adapting and tailoring behavior change strategies to the characteristics and needs of individuals and populations is essential (374,375). These health behavior change strategies can be delivered by behavioral health professionals, certified DCES, qualified community health workers (369), or other trained health care professionals (376,377). They can also be implemented via digital health tools (370,377,378). To deliver these strategies effectively, diabetes care professionals should receive training in evidence-based methods such as motivational interviewing (379).

PSYCHOSOCIAL CARE

Recommendations

5.42 Provide psychosocial care to all people with diabetes as part of routine medical care delivered by trained health care professionals using a collaborative, person-centered, culturally informed approach. **A**

5.43 Implement screening protocols for psychosocial concerns, preferably using age-appropriate standardized and validated tools. Screen at least annually or when there is a change in health status, treatment, or life circumstances. **C**

5.44 Refer to behavioral health professionals or other trained health care professionals, ideally those with experience in diabetes, for further assessment and treatment of psychosocial concerns as indicated. **B**

Please refer to the ADA position statement “Psychosocial Care for People With Diabetes” for a list of assessment tools and additional details (1) and the ADA Behavioral Health Toolkit for assessment questionnaires and surveys (professional .diabetes.org/meetings/behavioral-health-toolkit). Throughout the Standards of Care, the broad term “behavioral health” is used to encompass both 1) health behavior engagement and relevant factors and 2) behavioral health concerns and care related to living with diabetes.

Psychosocial well-being is a critical component of diabetes care and self-management. Psychosocial factors, including environmental, social, family, behavioral, emotional, religious, and SDOH factors, influence living with diabetes and the ability to achieve optimal health outcomes. People with diabetes and their families or caregivers face complex, multifaceted challenges integrating diabetes care into daily life (380). Clinically significant behavioral health diagnoses are considerably more prevalent in people with diabetes than in those without diabetes (381,382). Psychological and social problems can interfere with a person's (383–385) or family's (385) ability to perform diabetes care tasks and negatively affect health status. Furthermore, these conditions are associated with reduced short-term (i.e., <6 months) glycemic stability and increased mortality risk (382,386). Therefore, addressing both clinical and subclinical

psychological symptoms is essential to comprehensive care.

Diabetes health care professionals should routinely monitor and screen for psychosocial concerns in a timely and efficient manner and refer to appropriate services (387,388). Psychosocial care can be provided by various health care professionals based on training, experience, need, and availability (377,389,390). Health care professionals can integrate brief, person-centered psychosocial interventions into routine diabetes care by creating a supportive environment for emotional disclosure. Validating an individual's experiences, asking open-ended questions, and employing empathetic listening can foster trust and increase engagement in treatment decisions (391). Furthermore, health care professionals can implement brief counseling strategies to address psychosocial concerns and promote adaptive coping, including motivational interviewing, collaborative goal setting, cognitive behavioral techniques to reframe negative thoughts, structured problem-solving, and emotion regulation strategies (8,366,367, 369,370,392,393). Practical examples include using “importance” and “confidence” rulers, conducting week-long behavioral experiments within a cognitive behavioral therapy (CBT) framework, demonstrating breathing exercises to promote mindfulness, setting SMART goals to facilitate problem-solving, and teaching grounding techniques to support emotion regulation.

When psychosocial concerns cannot be addressed adequately in routine diabetes care, referral to a behavioral health professional is necessary. Ideally, qualified behavioral health professionals with specialized training and experience in diabetes should be integrated with or provide collaborative care as part of diabetes care teams (394,395). A behavioral health professional should conduct a comprehensive assessment and deliver evidence-based treatment (396,397).

Screening

Health care teams and clinical practices should develop and implement psychosocial screening protocols to ensure routine monitoring of psychosocial well-being and to identify potential concerns among people with diabetes, following published guidance and recommendations (398,399). Topics to screen for may include, but are not limited to, attitudes about diabetes, expectations for treatment and outcomes

(especially related to starting a new treatment or technology), general and diabetes-related mood, stress, and/or quality of life (e.g., diabetes distress, depressive symptoms, anxiety symptoms, and fear of hypoglycemia), available resources (financial, social, family, and emotional), and/or psychiatric history. Given elevated rates of suicidality among people with diabetes (400,401), screening for suicidality may also be appropriate (402–404). A list of age-appropriate screening and evaluation measures is provided in the ADA position statement “Psychosocial Care for People with Diabetes” (1), and guidance has been published about selection of screening tools, clinical thresholds, and frequency of screening (405,406).

Key opportunities for psychosocial screening include diagnosis, routine visits, hospitalizations, new onset of complications, transitions in care (e.g., pediatric to adult care teams [407]), changes in medical treatment, and when problems with achieving A1C goals, quality of life, or self-management arise. Additionally, changes in life circumstances and SDOH affect a person's ability to self-manage their diabetes. Thus, screening for SDOH should also be incorporated into routine care (408). When caregivers or family members play a significant role in diabetes care, their psychosocial concerns should be assessed and addressed by appropriate professionals (407,409).

Standardized, validated, age-appropriate tools for psychosocial monitoring and screening can also be used (1). The ADA provides access to tools for screening specific psychosocial topics, such as diabetes distress, fear of hypoglycemia, and other relevant psychological symptoms, at professional.diabetes.org/sites/default/files/media/ada_mental_health_toolkit_questionnaires.pdf. Additional information about developmentally specific psychosocial screening topics is available in section 14, “Children and Adolescents,” and section 13, “Older Adults.” Health care professionals may also use informal verbal inquiries, for example, by asking whether there have been persistent changes in mood during the past 2 weeks or since the individual's last appointment and whether the person can identify a triggering event or change in circumstances. Diabetes care professionals should also ask whether there are new or different barriers to treatment and self-management, such as feeling overwhelmed or stressed

by having diabetes (see *DIABETES DISTRESS*, below), changes in finances, or competing medical demands (e.g., the diagnosis of a co-occurring condition).

Psychological Assessment and Treatment

When psychosocial concerns are identified and cannot be addressed adequately in routine diabetes care, referral to a qualified behavioral health professional, preferably one specializing in diabetes, should be made for comprehensive evaluation, diagnosis, and treatment (377,396,397). Indications for referrals may include positive screening for diabetes distress, depression, anxiety, disordered eating, or cognitive dysfunction (see **Table 5.5** for a complete list). Incorporating psychosocial assessment and treatment into routine care is preferable to waiting for a specific problem or deterioration in glycemic or psychological status to occur (38,385). Health care professionals should identify and refer to behavioral health professionals knowledgeable about diabetes and psychosocial care. The ADA provides a list of behavioral health professionals who have specialized expertise or who have received education about psychosocial and behavioral issues related to diabetes in the ADA Mental Health Professional Directory (professional.diabetes.org/ada-mental-health-provider-directory). Ideally, behavioral health professionals should be embedded in diabetes care settings. Given limited behavioral health resources, other trained health care professionals may also provide this specialized psychosocial care (389,394,410). Although some health care professionals may not feel qualified to treat psychosocial concerns (411), strengthening the relationship between a person with diabetes and the health care professional may increase referral acceptance. Collaborative care interventions and a team approach have demonstrated efficacy in diabetes self-management, depression outcomes, and psychosocial functioning (6,7). The ADA provides resources for a range of health professionals to support behavioral health in people with diabetes at professional.diabetes.org/meetings/behavioral-health-toolkit.

Successful evidence-based approaches include cognitive behavioral (392,396,412) and mindfulness-based therapies (413). See the sections below for details about interventions for specific psychosocial concerns. Behavioral interventions may also

be indicated in a preventive manner even in the absence of positive psychosocial screeners, such as resilience-promoting interventions to prevent diabetes distress in adolescence (414,415) and behavioral family interventions to promote collaborative family diabetes management in early adolescence (416,417) or to support adjustment to a new treatment plan or technology (60). Psychosocial interventions can be delivered via digital health platforms (418,419) or integrated into group-based or shared diabetes appointments that address both medical and psychosocial concerns relevant to living with diabetes (390,420).

Although psychosocial interventions have demonstrated short-term (i.e., <6 months) efficacy, their success in sustained engagement in health behaviors and improved glycemic outcomes has varied. Thus, health care professionals should systematically monitor these outcomes to assess ongoing needs following implementation of current evidence-based psychosocial treatments.

Diabetes Distress

Recommendation

5.45 Screen for diabetes distress at least annually in people with diabetes, caregivers, and family members, and repeat screening when treatment goals are not met, at transitional times, and/or in the presence of diabetes complications. Health care professionals should consider referral to a qualified behavioral health professional, ideally one with experience in diabetes, for further assessment and treatment if not adequately addressed during medical appointments. **B**

Diabetes distress is common and refers to the emotional burdens and worries associated with living with and managing a demanding chronic condition (421,422). Diabetes distress is distinct from depression and anxiety and has unique relationships with glycemia and other outcomes (423,424) (**Tables 5.6** and **5.7**). The constant behavioral demands of diabetes self-management (taking medications, monitoring glucose levels, moderating food intake, and participating in physical activity) and the potential or actual disease progression are associated with increased diabetes distress (425,426). In individuals with type 2 diabetes, prevalence rates of diabetes distress exceed 60%

(425,427), whereas in those with type 1 diabetes, rates surpass 70% (426). Parents of children and adolescents with type 1 diabetes also experience diabetes distress, which is associated with greater family conflict and reduced self-management behaviors (428). Among adults, diabetes distress negatively affects medication-taking behaviors and is linked to elevated A1C, lower self-efficacy, and less optimal eating and exercise behaviors (429). In addition, diabetes distress frequently co-occurs with symptoms of anxiety, depression, and reduced health-related quality of life (430). Importantly, the experience of stigma related to living with diabetes may further exacerbate diabetes distress (431,432).

Diabetes distress should be routinely monitored (433) using diabetes-specific validated measures appropriate for each person or population (e.g., age and diabetes type) (1). Once diabetes distress is identified, it should be acknowledged and addressed (434). Addressing diabetes distress in routine diabetes care involves initiating a conversation about feelings and beliefs in a respectful, sensitive, and direct manner (421). In practice, this involves creating a space for emotional disclosure, validating the emotional aspects of diabetes, and linking emotions to self-management behaviors. Health care professionals can introduce brief coping strategies (e.g., values affirmation, mindful breathing, cognitive reframing) and highlight past successes to reinforce resilience. When diabetes distress cannot be addressed in routine diabetes care, referral for follow-up care is recommended (397), such as DSMES, to address distressing areas of diabetes management that may also be affecting self-care; a behavioral intervention from a qualified behavioral health professional, ideally one with expertise in diabetes; and/or an intervention from another trained health care professional (421).

Several intervention strategies have been shown to reduce diabetes distress and, to a lesser degree, improve glycemic outcomes. These include educational, psychological, and health behavior change approaches such as DSMES, CBT, mindfulness-based therapies, motivational interviewing, and others (392,412,435–439). In addition, interventions delivered via telephone, smartphone applications, video visits, and/or self-help modalities can be effective in reducing diabetes distress (416,440–442). DSMES has been shown to reduce diabetes distress (6,443) and may benefit A1C

Table 5.5—Situations that warrant referral of a person with diabetes to a qualified behavioral health professional for evaluation and treatment

- A positive screen on a validated screening tool for depressive symptoms, diabetes distress, anxiety, fear of hypoglycemia, suicidality, or cognitive impairment
- The presence of symptoms or suspicions of disordered eating behavior, an eating disorder, or disrupted patterns of eating
- Intentional omission or underdosing of insulin or noninsulin medication to cause weight loss
- A serious mental illness is suspected
- In children and adolescents and families with behavioral self-care difficulties, repeated hospitalizations for diabetic ketoacidosis, failure to achieve expected developmental milestones, or significant distress
- Low engagement in diabetes self-management behaviors, including declining or impaired ability to perform diabetes self-management behaviors
- Before undergoing metabolic surgery and after surgery, if assessment reveals an ongoing need for adjustment support

when combined with peer support (444). Counseling about expected diabetes distress may be helpful in several contexts, including new diagnosis, changes in treatment, life context, presence of complications, and other stressors (421). A multisite RCT with adults with type 1 diabetes, elevated diabetes distress, and elevated A1C demonstrated clinically meaningful improvements in both outcomes using a combination of group-based diabetes self-management education and emotion-focused skills (441). In adults with type 2 diabetes in the Veterans Affairs system, an RCT found that integrating a single session of mindfulness into DSMES, followed by a booster session and mobile app practice over 24 weeks, significantly reduced diabetes distress compared with DSMES alone (445). An RCT of CBT in adults with type 2 diabetes and elevated symptoms of distress or depression demonstrated improvements in diabetes distress, A1C, and depressive symptoms for up to 1 year (446). Another RCT among individuals with type 1 and type 2 diabetes found mindful self-compassion training increased self-compassion, reduced depression and diabetes distress, and improved A1C (447). In teens with type 1 diabetes, an RCT of a resilience-focused cognitive behavioral and social problem-solving intervention reduced diabetes distress and depressive symptoms for up to 3 years compared with diabetes education, although neither A1C nor self-management behaviors improved over time (415). Lastly, the use of AID systems can also contribute to decreases in diabetes distress among adults with type 1 diabetes and caregivers of children and adolescents; however, evidence of benefit

among children and adolescents remains mixed (448,449).

A combination of educational, behavioral, and psychological approaches is needed to address distress, depression, and A1C. There are few outcome data on long-term systematic treatment of diabetes distress integrated into routine care. As the burden of diabetes management can vary over time, diabetes distress may fluctuate and may need varying treatment approaches at different life stages and at different levels of diabetes progression.

Anxiety

Recommendations

5.46 Screen for anxiety symptoms at least annually in people with diabetes. Health care professionals can address anxiety symptoms within the scope of their practice. Consider referral to a qualified behavioral health professional for further assessment and treatment if anxiety symptoms interfere with diabetes self-management behaviors or quality of life, if not adequately addressed during medical appointments. **B**

5.47 Screen individuals at high risk for hypoglycemia or with severe and/or frequent hypoglycemia for fear of hypoglycemia at least annually and when clinically appropriate. **E** Refer to a trained health care professional for evidence-based intervention. **A**

Anxiety symptoms are common in people with diabetes and significantly affect clinical outcomes and self-management (450) (Tables 5.6 and 5.7). Rates of generalized anxiety disorder, agoraphobia, panic disorder, social phobia, and posttraumatic

stress disorder are higher in people with diabetes than in those without diabetes (450). A systematic review and meta-analysis found that the pooled prevalence of anxiety disorders among individuals with diabetes was 28% (451). This systematic review and meta-analysis also reported that individuals with anxiety disorders had a 19% higher risk for type 2 diabetes, while those with type 2 diabetes had a 41% greater risk of developing anxiety disorders (451). It is important to note that anxiety symptoms may overlap with diabetes distress and/or hyperglycemia symptoms, which can complicate screening practices (434). This highlights the importance of conducting screening for both diabetes distress and anxiety at least annually in people with diabetes, followed by further clinical assessment to ensure accurate identification.

Fear of hypoglycemia is a common diabetes-specific concern (452–454) that can lead to avoidance of glucose-lowering behaviors, such as increasing insulin doses or monitoring frequency. Factors contributing to fear of hypoglycemia in people with diabetes and family members include history of nocturnal hypoglycemia, co-occurring psychological concerns, and sleep disturbances (455). See section 6, “Glycemic Goals, Hypoglycemia, and Hyperglycemic Crises,” for more information about impaired awareness of hypoglycemia and related fear of hypoglycemia. Other common sources of diabetes-related anxiety include not meeting glycemic goals (456), insulin injections or infusion (457), and onset of complications (1). People with diabetes who exhibit excessive diabetes self-management behaviors well beyond what is prescribed or needed to achieve glycemic goals may be experiencing

Table 5.6—Psychosocial concerns and their association with diabetes-related outcomes in adults with type 1 diabetes

	Increased A1C	Increased blood pressure	Increased cholesterol	Increased macrovascular complications	Increased microvascular complications	Decreased self-care behaviors	Comorbid psychosocial concerns	Decreased quality of life	Increased mortality
Diabetes distress (576–579)	+++	?	+	+++	+++	+++	+++	+++	?
Depression and depressive symptoms (577,578,580,581)	+++	?	+++	+++	+++	+++	+++	+++	+++
Anxiety (383,582,583)	+++	?	?	?	?	+++	+++	+++	?
Disordered eating behaviors (insulin omission) (495,584)	+++	?	?	?	+++	+++	+++	+++	+++
Serious mental illness (schizophrenia, personality disorders) (585–587)	+++	?	+	+++	+++	?	+++	?	+++
Cognitive impairment (588–592)	+++	++	+++	+++	+++	++	+++	?	+++

+++, strong evidence (consistent findings in multiple studies of good methodological quality or one study of excellent methodological quality); ++, moderate evidence (consistent findings in multiple studies of fair methodological quality or one study of good methodological quality); +, limited evidence (evidence from one study of fair methodological quality); ?, no data available.

symptoms of obsessive-compulsive disorder (458). General anxiety is also associated with injection-related anxiety and fear of hypoglycemia (459).

Evidence-based psychosocial interventions for anxiety include collaborative care and CBT. An RCT in adults with type 2 diabetes, depression, and anxiety showed that those randomized to collaborative care were more likely to achieve a clinically significant reduction in anxiety symptoms at 6 and 12 months compared with those receiving usual care (460). Another RCT of CBT with adults with type 2 diabetes showed a reduction in health anxiety, with CBT accounting for 77% of the reduction in health anxiety at 16 weeks of follow-up; this trial also found decreased depressive symptoms and diabetes distress (461). For individuals with type 1 diabetes, a systematic review and meta-analysis found that using diabetes technologies, specifically real-time CGM, sensor-augmented pumps, and AID, reduced fear of hypoglycemia independent of the reduction of hypoglycemia frequency (462). Another RCT for young adults with type 1 diabetes found that a CBT-based intervention reduced fear of hypoglycemia by 8.5% compared with control participants and led to increased time in range and improved self-management behaviors over an 8-week period (463). These findings highlight the need for specialized behavioral interventions with a positive adjunct of diabetes technology delivered by qualified professionals to effectively address hypoglycemia-related anxiety.

Depression

Recommendations

5.48 Screen for depressive symptoms in all people with diabetes at least annually and more frequently among those with a history of depression. **B** Refer to qualified behavioral health professionals or other health care professionals with experience using evidence-based treatment approaches for depression in collaboration with the diabetes care team. **A**

5.49 Rescreen for depression at diagnosis of complications or when there are significant changes in medical status. **B**

Elevated depressive symptoms and depressive disorders are common among people with diabetes (381,454) (Tables 5.6

Table 5.7—Psychosocial concerns and their association with diabetes-related outcomes in adults with type 2 diabetes

	Increased A1C	Increased blood pressure	Increased dyslipidemia	Increased macrovascular complications	Increased microvascular complications	Decreased self-care behaviors	Comorbid psychosocial concerns	Decreased quality of life	Increased mortality
Diabetes distress (593–599)	+++	+	+	+++	+++	+++	+++	+++	+++
Depression and depressive symptoms (600–607)	+++	++	+++	+++	+++	+++	+++	+++	+++
Anxiety (382,430,601,608–611)	+++	++	+	+++	+	+++	+++	+++	+++
Disordered eating behaviors (binge eating disorder, night eating syndrome) (492,496,612–615)	+/-	+	?	?	+	+	+++	+++	?
Serious mental illness (schizophrenia, bipolar disorder) (616–624)	+/-	++	++	+++	+++	+++	+++	+++	+++
Cognitive impairment (625–632)	+++	+++	+++	+++	+++	+++	+++	+++	+++

++++, strong evidence (consistent findings in multiple studies of good methodological quality or one study of excellent methodological quality); ++, moderate evidence (consistent findings in multiple studies of fair methodological quality or one study of good methodological quality); +, limited evidence (evidence from one study of fair methodological quality); +/-, inconclusive evidence; ?, no data available.

and 5.7), affecting approximately one in four people with type 1 or type 2 diabetes (384,464), and parents of children and adolescents with diabetes (465). Co-occurring depressive symptoms and diabetes are associated with reduced self-management, elevated A1C (466), and increased CVD and mortality risk (423,467). History of depression, current depression, and antidepressant medication use are also risk factors for the development of type 2 diabetes, particularly in individuals with other risk factors, such as overweight, obesity, and family history of type 2 diabetes (468–470). At least annual depression screening, and more frequent screening for those with a history of depression, is indicated for people with type 1 or type 2 diabetes and gestational diabetes mellitus. Screening is particularly important given that women report higher rates of depression than men (471). For individuals with type 2 diabetes, the experience of diabetes-related stigma is associated with increased depressive symptoms (432). Importantly, depressive symptoms often overlap with diabetes distress, anxiety symptoms, and hyperglycemia, complicating screening and increasing the risk for false positives (434). Conducting annual screening for depression, anxiety, and diabetes distress will help distinguish overlapping symptoms. Positive findings should be followed by a comprehensive clinical assessment to ensure an accurate diagnosis. In practice, routine monitoring with age-appropriate validated measures (1) can help to identify if referral is warranted (397). Multisite studies have demonstrated the feasibility of implementing depressive symptom screening protocols in diabetes clinics and have published practical guides for implementation (405,472).

Person-centered integrated care approaches have been shown to improve both depression and glycemic outcomes (5). The behavioral health professional providing treatment for depression should be incorporated into, or collaborate closely with, the diabetes treatment team (473). Because depressive symptoms may also indicate reduced quality of life due to diabetes burden (also see DIABETES DISTRESS, above), it is important to query origins and exacerbating factors for those symptoms to distinguish between diabetes distress and depression. RCTs examining pharmacologic treatment, group therapy, psychotherapy, parenting interventions, mindfulness-based approaches, or collaborative care have

consistently shown improvements in depressive symptoms, with mixed effects on A1C when depression is treated simultaneously with diabetes (5,7,392,474–478). Additionally, psychological interventions, such as CBT, delivered via internet, phone, and self-guided interventions have improved depressive symptoms (475,479,480). Lifestyle interventions targeting nutrition and/or physical activity also demonstrate benefits for depressive symptoms and A1C (251) on their own and when combined with CBT (481–483). Finally, one meta-analysis found that use of GLP-1 RAs led to improvement in depressive symptoms among adults with type 2 diabetes (484), while another meta-analysis did not find significant change in depressive symptoms (485). It is important to note that the medical treatment plan should also be monitored and potentially adjusted in response to reduction in depressive symptoms.

Disordered Eating Behavior

Recommendations

5.50 Screen for disordered or disrupted eating using validated screening measures. Review the medical treatment plan to identify potential treatment-related effects on hunger/caloric intake. **B**

5.51 Reevaluate the treatment plan of people with diabetes who present with symptoms of disordered eating behaviors, an eating disorder, or disrupted patterns of eating, ideally in consultation with a qualified professional. **B**

The estimated prevalence of disordered eating behaviors and diagnosable eating disorders in people with diabetes varies (486–488) (see **Tables 5.6** and **5.7**). People with type 1 diabetes are at increased risk for eating disorders compared with people without diabetes (489). The median prevalence of insulin restriction for weight control is 15%, with mixed findings on whether the behavior is more prevalent among women than men (489–491). In people with type 2 diabetes, binge eating (excessive food intake with an accompanying sense of loss of control) and night eating syndrome are commonly reported (492). Among those with type 2 diabetes treated with insulin, intentional omission is also frequently reported (493). People with diabetes and diagnosable eating disorders have high rates of co-occurring psychosocial concerns, including diabetes distress, depression, fear of hypoglycemia,

and anxiety (494). Eating disorders and disordered eating behaviors are also associated with elevated A1C (495–497). Among individuals with type 1 diabetes, body image concerns and emotional distress are common and associated with disordered eating behavior (491,494,498). A systematic review with limited available studies found a higher prevalence of disordered eating behaviors among children and adolescents with type 2 diabetes compared with children and adolescents with type 1 diabetes (499). Data from the SEARCH for Diabetes in Youth study showed that children and adolescents with type 1 and type 2 diabetes and household food insecurity reported more disordered eating behaviors than those with high food security (500).

Diabetes care professionals should monitor for disordered eating behaviors using validated measures. Diabetes-specific measures are recommended to assess for intentional insulin omission and, according to a meta-analysis, show strong associations with A1C (498). For individuals with type 1 diabetes, the Diabetes Eating Problem Survey–Revised (DEPS-R) (501) is recommended to screen for disordered eating behaviors, while the mSCOFF (502), a five-item screening questionnaire, is for eating disorders and includes a question on insulin omission. Any “yes” response should prompt a comprehensive evaluation. For type 2 diabetes, recommended screening measures include the Questionnaire on Eating and Weight Patterns-5 (QEWP-5) (503), the Binge Eating Scale (504), and the Night Eating Questionnaire (505).

Given the complexities of treating disordered eating behaviors and disrupted eating patterns in people with diabetes, interprofessional care teams should include, or closely collaborate with, a health professional trained to identify and treat eating behaviors in individuals with diabetes (506). Key qualifications for such professionals include familiarity with diabetes physiology, weight-related and psychological risk factors for disordered eating behaviors, and treatments for diabetes and disordered eating behaviors. Caution should be taken in labeling individuals with diabetes as having a diagnosable eating disorder, as disordered or disrupted eating patterns are frequently found to be associated with diabetes and its treatment. Maladaptive food intake patterns that appear to have a psychological origin may be driven by

physiologic disruption in hunger and satiety cues, metabolic perturbations, and/or secondary distress because of the individual’s inability to control their hunger and satiety (507). More rigorous methods to identify underlying mechanisms of action that drive change in eating and treatment behaviors, as well as associated emotional distress, are needed (508).

Reevaluating the treatment plan for people with diabetes in consultation with trained professionals is essential to ensure safety (avoid stigmatizing language, do not focus solely on A1C), to minimize harm (risk of DKA, severe hypoglycemia, complications), and to avoid reinforcing maladaptive patterns (avoid rigid carbohydrate counting and intensive weight monitoring). Inconsistent intervention findings highlight the importance of addressing eating disorders and disordered eating behaviors in the context of the condition and its treatment. Additionally, health care teams may consider the appropriateness of technology use among people with diabetes and disordered eating behaviors, although more research on the risks and benefits is needed (509). Some efforts have focused on preventing disordered eating behaviors among individuals with type 1 diabetes and on supporting parents of children and adolescents with type 1 diabetes who are at risk for disordered eating; however, more RCTs with longer-term follow-up are needed (510,511). A feasibility study of a 12-session CBT and diabetes education program for individuals with type 1 diabetes and disordered eating found that participants reported improvements in disordered eating, diabetes distress, anxiety, and depressive symptoms (512). A 12-week pilot self-guided online program for individuals with type 2 diabetes and binge eating disorder showed promise in benefiting eating behaviors, depression, and anxiety (513).

The use of incretin therapies, specifically GLP-1 RAs and potentially dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 RAs, may have relevance to the treatment of disrupted or disordered eating (see section 8, “Obesity and Weight Management for the Prevention and Treatment of Diabetes”). These therapies work in the appetite and reward circuitries to modulate food intake, reducing uncontrollable hunger and overeating (514). A systematic review found early evidence for GLP-1 RAs being effective in reducing binge-eating behaviors, and a meta-analysis

found GLP-1 RAs are associated with decreases in emotional eating (485,515).

Serious Mental Illness

Recommendations

5.52 Provide an increased level of support for people with diabetes and serious mental illness through enhanced monitoring of and assistance with diabetes self-management behaviors. **B**

5.53 Monitor changes in body weight, glycemia, and lipids in adolescents and adults with diabetes who are prescribed second-generation antipsychotic medications; adjust the treatment plan accordingly, if needed. **C**

Type 2 diabetes incidence is 1.5- to 2.5-fold higher in individuals with serious mental illness, particularly schizophrenia and other thought disorders, compared with those without a major mental disorder (516,517) (see **Tables 5.6** and **5.7**). People with serious mental illness who are treated with antipsychotics and other psychotropic medications should be monitored routinely for prediabetes and type 2 diabetes, as these medications are associated with metabolic dysregulation, including elevated glucose levels, increased weight, BMI, total cholesterol, and LDL cholesterol, as well as decreased HDL cholesterol (518,519). Changes in glycemia, body weight, and lipids should be monitored every 12–16 weeks, unless clinically indicated to be monitored sooner (520). Disordered thinking and judgment can make it difficult to engage in behaviors that reduce risk factors for type 2 diabetes, such as restrained eating for weight management. Further, people with serious mental illness and diabetes frequently experience moderate psychological distress, indicating pervasive intrusion of behavioral health issues into daily functioning (521). Serious mental illness is often associated with the inability to evaluate and apply information to make judgments about treatment options. For a person with an established diagnosis of a serious mental illness affecting judgment, activities of daily living, and the ability to collaborate with care professionals, the inclusion of a nonmedical caretaker in treatment decision-making is beneficial. This caretaker can assist with care coordination, engagement with self-management behaviors, and participation in social activities to

improve the well-being of people with diabetes and serious mental illness (522).

Coordinated management of prediabetes or diabetes and serious mental illness is recommended to achieve diabetes treatment goals. The diabetes care team, in collaboration with other care professionals, should work to provide an enhanced level of care and self-management support for people with diabetes and serious mental illness based on individual capacity and needs. Such care may include remote monitoring, health care aides, and diabetes training for family members, community support personnel, and other caregivers. A systematic review and meta-analysis of nonpharmacologic interventions for people with type 2 diabetes and serious mental illness showed significant reductions in psychiatric symptoms, total cholesterol, and LDL cholesterol but not improvements in A1C, triglycerides, or BMI (523). Qualitative research suggests that educational and behavioral interventions provide benefit via group support, accountability, and assistance with applying diabetes knowledge (524).

Cognitive Capacity and Impairment

Recommendations

5.54 Monitor cognitive capacity throughout the life span for all individuals with diabetes, particularly in those who have documented cognitive disabilities, those who experience severe hypoglycemia, very young children, and older adults. **B**

5.55 Consider referral for a formal assessment if cognitive capacity changes or appears to be suboptimal for decision-making and/or behavioral self-management. **E**

Cognitive capacity refers to attention, memory, logic and reasoning, and auditory and visual processing, all of which are involved in diabetes self-management (525) (see **Tables 5.6** and **5.7**). Long-term diabetes (type 1 or type 2) is associated with cognitive decline (526,527). In people with type 1 diabetes, cognitive impairment is associated with diabetes-specific factors (e.g., younger age at diagnosis, longer disease duration, more time in glycemic extremes, recurrent DKA, elevated A1C, and presence of microvascular complications), other medical factors (e.g., dyslipidemia, intestinal flora, and poorer sleep quality), and sociodemographic factors

(e.g., female sex, lower educational level) (528). Similarly, in people with type 2 diabetes, cognitive decline is associated with diabetes-specific factors (e.g., longer duration, elevated A1C, higher fasting blood glucose, microvascular complications, macrovascular complications), other medical factors (e.g., hypertension, depression, physical inactivity), and sociodemographic factors (e.g., older age, male sex, lower education) (529–531). Diagnosis of dementia is more prevalent among people with diabetes, both type 1 and type 2 (532).

Executive functioning is an aspect of cognitive capacity that has relevance to diabetes management. Executive functions refer to a set of cognitive processes that enable a person to plan, organize, and execute tasks; regulate emotions; and control impulses. Declines in cognitive capacity affect executive functioning and information processing speed; they are not consistent between people, and evidence is lacking regarding a known course of decline (533). Attention deficit hyperactivity disorder, which involves deficits in executive functions, is associated with a twofold increased risk of type 2 diabetes (534). Among children, adolescents, and young adults with type 1 diabetes, lower executive functioning is linked with more self-management difficulties and elevated A1C (535). Conversely, higher self-regulation is associated with improved emotional and diabetes-related functioning (536). Thus, monitoring cognitive capacity among individuals with or at risk for diabetes is recommended, particularly their self-monitoring, symptom recognition, and decision-making, all of which are mediated by executive function (532).

As with other conditions affecting mental capacity (e.g., major psychiatric disorders), the key concern is whether the person can collaborate with the care team to achieve metabolic goals and prevent both short-term and long-term complications (521). When cognitive ability is altered, declining, or absent, a lay care professional should be introduced into the care team to serve as a daily monitor and liaison to the care team (1). Individuals with cognitive impairment may require tailored approaches to DSMES that simplify self-management behaviors and introduce remote monitoring. Children and adolescents will need second-party monitoring (e.g., parents and adult caregivers) until they are developmentally able to evaluate information

and make appropriate self-management decisions.

Episodes of severe hypoglycemia are independently associated with cognitive decline and are a risk factor for accelerated decline (537). Early-onset type 1 diabetes is associated with long-term deficits in intellectual abilities, especially when accompanied by repeated episodes of severe hypoglycemia (538), and is correlated with elevated A1C and sensor glucose values (539) (see section 14, “Children and Adolescents,” for information on early-onset diabetes and cognitive abilities and the effects of severe hypoglycemia on children’s cognitive and academic performance). For this reason, cognitive capacity should be routinely assessed to determine a person’s ability to maintain and adjust self-management behaviors (e.g., dosing of medications, corrections) and to evaluate the need for caregiver support. If concerns arise, an age-appropriate test of cognitive capacity is recommended (1), with consideration given to the developmental stage; for example, young children who are not expected to self-manage independently or older adults who may require ongoing monitoring.

Importantly, the risk of cognitive decline can be reduced through improved A1C (540). A systematic review and meta-analysis comparing cardioprotective glucose-lowering therapy with control therapy found GLP-1 RAs were associated with a statistically significant reduction in dementia but not SGLT2 inhibitors or pioglitazone (541). Additionally, exercise may be a potential nonpharmacologic treatment pathway for cognitive impairment in older adults with type 2 diabetes (542).

Sleep Health

Recommendations

5.56 Screen for sleep health in people with prediabetes or diabetes and in those at risk for diabetes, including screening for sleep disorders and diabetes-related sleep disruptions. Refer to sleep medicine specialists and/or qualified behavioral health professionals or diabetes care team as indicated. **B**

5.57 Counsel people with diabetes to practice sleep-promoting routines and habits. **A**

The associations between sleep problems and diabetes are complex: sleep

disorders are a risk factor for developing type 2 diabetes (543,544) and possibly gestational diabetes mellitus (545). Across the life span, people with diabetes experience sleep disruptions and reduced sleep quality (546,547). Sleep problems are also common in parents of children and adolescents with diabetes, especially after diagnosis (548,549). Disrupted sleep and sleep disorders, including obstructive sleep apnea (OSA) (550), insomnia, and restless leg syndrome (551), are common among people with diabetes. In people with type 1 diabetes, estimates of poor sleep range from 30% to 50% (552), and estimates of moderate to severe OSA are >50% (550). In type 2 diabetes, 55% of people are estimated to have OSA (553), 39% to have insomnia, and 8–45% to have restless leg syndrome (i.e., an uncontrollable urge to move legs) (554). Furthermore, people with type 2 diabetes and restless leg syndrome are more likely to experience microvascular and macrovascular complications (555) as well as depression (556). Additionally, people with diabetes who perform shift work increase their risk for circadian rhythm disorders, which are associated with elevated A1C (557), neuropathy (558), and decreased psychological well-being (558). Health care professionals should consider a comprehensive evaluation of the daily lifestyles of people with diabetes, including sleep duration, shift work schedules, and actual days taken off work, given their associations with hyperglycemia, hypertension, dyslipidemia, and weight gain (559).

The high prevalence of OSA in people with diabetes poses significant clinical implications for diabetes management. Sleep fragmentation and hypoxemia activate the sympathetic nervous system, contributing to hyperglycemia, insulin resistance, increased circulating free fatty acids, impaired microcirculation, oxidative stress, and psychological stress (560). A systematic review and meta-analysis found that continuous positive airway pressure (CPAP) significantly reduced A1C by 0.24% (561). Another systematic review and meta-analysis compared GLP-1 RAs alone or combined with the same interventions in the control group in adults with obesity, prediabetes, and/or type 2 diabetes. Findings showed that the GLP-1 RAs were more effective in reducing apnea-hypopnea index compared with the control group in the population with type 2

diabetes (562). Two phase 3, double-blind RCTs in adults with OSA and obesity showed that a dual GIP and GLP-1 RA significantly reduced sleep apnea severity and body weight compared with placebo after 52 weeks (563). More RCTs with people with diabetes are needed to determine the effectiveness of GLP-1 RAs and dual GIP and GLP-1 RAs as potential treatments for OSA.

Sleep disturbances are associated with less engagement in diabetes self-management and can interfere with achieving and maintaining glucose levels within the goal range (547,550). In type 1 diabetes, risk of hypoglycemia poses specific sleep challenges and may require detailed assessment and treatment approaches (564). People with type 1 diabetes and their family members report worries about poor sleep and diabetes self-management needs interfering with sleep (565). Diabetes technology has been described as both helpful and challenging for sleep (565), with the greatest perceived benefits attributed to AID systems (566–568). Given these challenges, screening and treatment of sleep disorders should be considered a part of standardized care for people with type 1 and type 2 diabetes.

Importantly, nonpharmacological evidence-based strategies are available to improve sleep in people with diabetes. CBT, including CBT for insomnia (392), has been shown to improve sleep outcomes, A1C (569), fasting glucose (569), and depressive symptoms (570). Evidence also suggests sleep extension and pharmacologic treatments can improve sleep outcomes and possibly insulin resistance (564,569). Three RCTs have evaluated insomnia in people with diabetes. Suvorexant improved total sleep time and sleep efficiency, ramelteon improved sleep quality and sleep latency, and lemborexant improved sleep onset and sleep maintenance (571–573). Finally, sleep education, or sleep hygiene, has been shown to improve sleep quality, reduce A1C, and decrease insulin resistance in adults with type 2 diabetes (574). Diabetes care professionals are encouraged to counsel people with diabetes to use sleep-promoting routines and practices, such as establishing a regular bedtime and rise time, creating a dark, quiet area for sleep with temperature and humidity control, establishing a pre-sleep routine, putting electronic devices (except diabetes management devices) in silent/off mode, exercising during the day,

avoiding daytime naps, limiting caffeine and nicotine in the evening, avoiding spicy foods at night, and avoiding alcohol before bedtime (575). For people with diabetes who have significant sleep difficulties, referral to sleep specialists to address the medical and behavioral aspects of sleep is recommended, ideally in collaboration with the diabetes care team (Fig. 5.2).

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6. Glycemic Goals, Hypoglycemia, and Hyperglycemic Crises: Standards of Care in Diabetes—2026

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American Diabetes Association
Professional Practice Committee for
Diabetes*

The American Diabetes Association (ADA) “Standards of Care in Diabetes” includes the ADA’s current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. Members of the ADA Professional Practice Committee for Diabetes, an interprofessional expert committee, are responsible for updating the Standards of Care annually, or more frequently as warranted. For a detailed description of ADA standards, statements, and reports, as well as the evidence-grading system for ADA’s clinical practice recommendations and a full list of Professional Practice Committee members, please refer to Introduction and Methodology. Readers who wish to comment on the Standards of Care are invited to do so at professional.diabetes.org/SOC.

ASSESSMENT OF GLYCEMIC STATUS

Glycemic status is assessed by A1C measurement, blood glucose monitoring (BGM) by capillary (finger-stick) devices, and different continuous glucose monitoring (CGM) metrics such as time in range (TIR), time below range (TBR), time above range (TAR), glucose management indicator (GMI), coefficient of variation, and mean glucose. Clinical trials of interventions that lower A1C have demonstrated the benefits of improved glycemia with respect to long-term diabetes complications. Glucose monitoring via CGM or BGM (discussed in detail in section 7, “Diabetes Technology”) is useful for diabetes self-management, can provide nuanced information on glucose responses to meals, physical activity, and medication changes, and is particularly useful for optimal medication management and safety in individuals taking insulin. CGM serves an increasingly important role in optimizing the effectiveness and safety of treatment in many people with type 1 diabetes, type 2 diabetes, diabetes in pregnancy, and other forms of diabetes (e.g., cystic fibrosis-related diabetes). Individuals on a variety of insulin treatment plans benefit from CGM with improved glucose levels, decreased hypoglycemia, and enhanced self-efficacy (section 7, “Diabetes Technology”) (1).

Glycemic Assessment

Recommendations

6.1 Assess glycemic status by A1C **A** and/or continuous glucose monitoring (CGM) metrics such as time in range, time above range, and time below range.

B Fructosamine or CGM can be used for glycemic monitoring when an alternative to A1C is required. **B**

6.2 Assess glycemic status at least two times a year, and more frequently (e.g., every 3 months) for individuals not meeting glycemic goals or with recent treatment changes, frequent or severe hypoglycemia or hyperglycemia, or changes in health status, or during periods of rapid growth and development in children and adolescents. **E**

*A complete list of members of the American Diabetes Association Professional Practice Committee for Diabetes can be found at <https://doi.org/10.2337/dc26-SINT>.

Duality of interest information for each contributor is available at <https://doi.org/10.2337/dc26-SDIS>.

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Glycemic Assessment by A1C

The A1C test is the primary tool for assessing glycemic status in both clinical practice and clinical trials, and it is strongly linked to diabetes complications (2–4). A1C reflects average glycemia over approximately 2–3 months. The performance of laboratory tests for A1C is generally excellent for National Glycohemoglobin Standardization Program (NGSP)-certified assays (ngsp.org). Thus, A1C testing should be performed routinely in all people with diabetes at initial assessment and as part of continuing care. Measurement approximately every 3 months determines whether glycemic goals have been reached and maintained. Adults with type 1 or type 2 diabetes who have achieved and are maintaining glucose levels within their goal range may only need A1C testing twice a year. Individuals with less stable glucose levels, those with intensive care plans, or those not meeting their treatment goals may require more frequent testing, typically every 3 months, with additional assessments as needed. Point-of-care A1C testing can offer timely opportunities for treatment adjustments during appointments with health care professionals, although point-of-care tests may be less accurate than laboratory A1C assays (5).

The A1C test is an indirect measure of average glycemia. Factors that affect hemoglobin or red blood cells may affect A1C; see section 2, “Diagnosis and Classification of Diabetes,” for details. For example, conditions that affect red blood cell turnover (e.g., hemolytic anemia and other anemias, glucose-6-phosphate dehydrogenase deficiency, recent blood transfusion, use of drugs that stimulate erythropoiesis, kidney failure, and pregnancy) can interfere with the accuracy of A1C (6). Some hemoglobin variants can interfere with some A1C assays; however, most assays in use in the U.S. are accurate in individuals who are heterozygous for the most common variants (7). A1C cannot be measured in individuals with sickle cell disease (HbSS) or other homozygous hemoglobin variants (e.g., HbEE), since these individuals lack HbA (8). In individuals with conditions that interfere with the interpretation of A1C, alternative approaches to monitoring glycemic status should be used, including self-monitoring of blood glucose, CGM, and/or the use of glycated serum protein assays (discussed below). A1C does not provide a measure of

glycemic variability, real-time glucose levels, or hypoglycemia. For individuals prone to glycemic variability, especially people with type 1 diabetes or type 2 diabetes with insulin deficiency and/or treatment with intensive insulin therapy, glycemic status is best evaluated by the combination of results from BGM or CGM and A1C. Discordant results between A1C and BGM or CGM can occur due to high glycemic variability, inaccurate BGM or CGM measurement, or inaccurate A1C due to the factors discussed above.

As discussed in section 2, “Diagnosis and Classification of Diabetes,” there is controversy regarding the clinical significance of differences in A1C by self-reported race and ethnicity (9–12). There is an emerging understanding of genetic determinants that may modify the association between A1C and glucose levels (13). However, race and ethnicity are not good proxies for these genetic differences that are likely present in a small fraction of individuals of all racial groups. Therefore, race and ethnicity should not be considerations for how A1C is used clinically for glycemic monitoring. Limitations of laboratory tests and within-person variability in glucose and A1C underscore the importance of using multiple approaches to glycemic monitoring and further evaluation of discordant results in all racial or ethnic groups.

Serum Glycated Protein Assays as Alternatives to A1C

Fructosamine and glycated albumin are alternative measures of glycemia that are approved for clinical use for monitoring

glycemic status in people with diabetes. Fructosamine reflects total glycated serum proteins (mostly albumin). Glycated albumin assays reflect the proportion of total albumin that is glycated. Due to the turnover rate of serum protein, fructosamine and glycated albumin reflect glycemia over the past 2–4 weeks, a shorter-term time frame than that of A1C. Fructosamine and glycated albumin are highly correlated in people with diabetes, and the performance of modern assays is typically excellent. Fructosamine and glycated albumin have been linked to long-term complications in epidemiologic cohort studies (14–18). However, there have been few clinical trials, and the evidence base supporting the use of these biomarkers to monitor glycemic status is much weaker than that for A1C. In people with diabetes who have conditions where the interpretation of A1C may be problematic or when A1C cannot be measured (e.g., homozygous hemoglobin variants), fructosamine or glycated albumin may be useful alternatives to monitor glycemic status (8).

Correlation Between A1C and Blood Glucose Monitoring and Continuous Glucose Monitoring

Table 6.1 provides rough equivalents of A1C and mean glucose levels based on data from the international A1C-Derived Average Glucose (ADAG) study. The ADAG study assessed the correlation between A1C and frequent BGM and CGM in 507 adults (83% non-Hispanic White) with type 1, type 2, and no diabetes (19,20). The American Diabetes Association (ADA) and the American Association for Clinical

Table 6.1—Equivalent A1C levels and estimated average glucose (eAG)

A1C (%)	A1C (mmol/mol)	eAG mg/dL*	eAG mmol/L*
5	31	97 (76–120)	5.4 (4.2–6.7)
6	42	126 (100–152)	7.0 (5.5–8.5)
7	53	154 (123–185)	8.6 (6.8–10.3)
8	64	183 (147–217)	10.2 (8.1–12.1)
9	75	212 (170–249)	11.8 (9.4–13.9)
10	86	240 (193–282)	13.4 (10.7–15.7)
11	97	269 (217–314)	14.9 (12.0–17.5)
12	108	298 (240–347)	16.5 (13.3–19.3)

Data in parentheses are 95% CI. A calculator for converting A1C results into eAG, in either mg/dL or mmol/L, is available at professional.diabetes.org/eAG. *These estimates are based on ADAG data of ~2,700 glucose measurements over 3 months per A1C measurement in 507 adults with type 1, type 2, or no diabetes. The correlation between A1C and average glucose was 0.92 (19,20). Adapted from Nathan et al. (19).

Chemistry have determined that the correlation ($r = 0.92$) in the ADAG trial is strong enough to justify reporting both the A1C result and the estimated average glucose (eAG) result when a clinician orders the A1C test. Clinicians should note that the mean plasma glucose numbers in **Table 6.1** are based on ~2,700 readings per A1C measurement in the ADAG trial.

Caveats in interpretation of **Table 6.1** include that these data are from a single study published in 2008. Mean glucose in the ADAG study was calculated from a combination of measurements from an early CGM system and capillary glucose, intermittently, during a 3-month period. This older system required calibration several times a day using a self-monitoring glucose meter. It is unclear how generalizable these estimates are to mean glucose measurements obtained using modern and generally more accurate CGM systems. The comparability of A1C and mean glucose from CGM systems will depend on the number of days of CGM wear, timing of the A1C measurement relative to the CGM wear period, calibration and accuracy of both the glucose meter and the CGM system, the lag time between interstitial glucose and venous glucose (which varies among individuals and within individuals based on physical activity and health status), and any factors that affect A1C or red blood cell turnover (see section 2, “Diagnosis and Classification of Diabetes”).

Glycemic Assessment by Blood Glucose Monitoring

For many people with diabetes, glucose monitoring, either using BGM by capillary (finger-stick) devices and/or CGM in addition to regular A1C testing, is key for achieving glycemic goals. Major clinical trials of insulin-treated individuals have included BGM as part of multifactorial interventions to demonstrate the benefit of intensive glycemic management on diabetes complications (21). BGM is thus an integral component of effective therapy for individuals taking insulin. In recent years, CGM has become a standard method for glucose monitoring for most people with type 1 diabetes and people with type 2 diabetes treated with insulin. Both approaches to glucose monitoring allow people with diabetes to evaluate individual responses to therapy and assess whether glycemic goals are being safely achieved. The specific needs and goals of individuals with diabetes should dictate BGM frequency and timing. Please refer to section 7, “Diabetes Technology,” for a more complete discussion of the use of BGM and CGM.

Glycemic Assessment by Continuous Glucose Monitoring

CGM is particularly useful in people with diabetes who are at risk for hypoglycemia and in people with type 1 diabetes (21). Use of CGM in type 2 diabetes (as well as in several other forms of diabetes) is

growing, especially in people who are taking insulin. TIR is a useful metric of glycemic status. A 10- to 14-day CGM assessment of TIR, with CGM wear of 70% or higher, and other CGM metrics can be used to assess glycemic status and are useful in clinical management (22–26). TIR, and especially mean CGM glucose, correlates with A1C (27–31). TBR (<70 and <54 mg/dL [<3.9 and <3.0 mmol/L]) and TAR (>180 mg/dL [>10.0 mmol/L]) are useful parameters for insulin dose adjustments, reevaluation of the treatment plan, and real-time detection, prevention, and treatment of hypoglycemia and significant hyperglycemia. High coefficient of variation ($>36\%$) has also been related to occurrence of hypoglycemia (32). The international consensus on CGM provides guidance on CGM metrics (**Table 6.2**) and their clinical interpretation (33). To make these metrics actionable, standardized reports with visual summaries have been implemented (33) and help individuals with diabetes and health care professionals interpret the data to guide treatment decisions (27,30). Glucose data can be analyzed remotely to guide adjustment to diabetes therapy (34–36).

Published data from two retrospective studies suggest a strong correlation between TIR and A1C, with a goal of $>70\%$ TIR aligning with an A1C of $\sim 7\%$ (~ 53 mmol/mol) (25,28). Note that the goals of therapy displayed in **Table 6.2**

Table 6.2—CGM metrics for clinical care in nonpregnant individuals with type 1 or type 2 diabetes

Metric	Interpretation	Goals
Metrics for valid CGM wear		
Wear time	Number of days CGM device is worn	≥ 14 -day wear for pattern management
Active percentage time	Percent of time CGM device is active	70% of time active out of 14 days
Glycemic metrics		
Mean glucose	Mean of glucose values	*
Glucose management indicator (GMI)	Calculated value approximating A1C (not always equivalent)	*
Glucose coefficient of variation (CV)	Spread of glucose values	$\leq 36\%+$
TAR >250 mg/dL (>13.9 mmol/L)	Percent of time in level 2 hyperglycemia	$<5\%$ (most adults); $<10\%$ (older adults with complex/intermediate health)
TAR >180 mg/dL (>10 mmol/L)	Percent of time in level 1 hyperglycemia	$<25\%$ (most adults); $<50\%$ (older adults with complex/intermediate health)†
TIR 70–180 mg/dL (3.9–10.0 mmol/L)	Percent of time in range	$>70\%$ (most adults); $>50\%$ (older adults with complex/intermediate health)
TBR <70 mg/dL (<3.9 mmol/L)	Percent of time in level 1 hypoglycemia	$<4\%$ (most adults); $<1\%$ (older adults with complex/intermediate health)§
TBR <54 mg/dL (<3.0 mmol/L)	Percent of time in level 2 hypoglycemia	$<1\%$

CGM, continuous glucose monitoring; TAR, time above range; TBR, time below range; TIR, time in range. *Goals for these values are not standardized. †Some studies suggest that lower coefficient of variation targets ($<33\%$) provide additional protection against hypoglycemia for those receiving insulin or sulfonylureas. ‡Goals are for level 1 and level 2 hyperglycemia combined. §Goals are for level 1 and level 2 hypoglycemia combined. Adapted from Battelino et al. (33).

serve as values to guide changes in therapy. For older adults with complex or intermediate health using CGM, the recommended percent time spent in goal range of 70–180 mg/dL is 50% (or 12 h per day) and the recommended time spent in hypoglycemia of less than 70 mg/dL should not be more than 1%, or 15 min per day, to minimize hypoglycemia risk (33,37–40). In this population, more permissive hyperglycemia is allowed (up to 50% of the time in 24 h) if required to prevent hypoglycemia.

GLYCEMIC GOALS

Recommendations

6.3a An A1C goal of <7% (<53 mmol/mol) is appropriate for many nonpregnant adults without severe hypoglycemia or hypoglycemia affecting health or quality of life. **A**

6.3b A goal time in range of >70% in people using CGM is appropriate for many nonpregnant adults. **B**

6.3c A goal percent time <70 mg/dL (<3.9 mmol/L) of <4% (or <1% for older adults) and a goal percent time <54 mg/dL (<3.0 mmol/L) of <1% are recommended in people using CGM to prevent hypoglycemia. Deintensify or modify therapy if these goals are not met. **B**

6.4 Lower A1C goals (e.g., <6.5% [<48 mmol/mol]) may be appropriate for individuals with diabetes with good health and function and low treatment risks (e.g., hypoglycemia) and burdens (see Fig. 6.1). **B**

6.5 Less stringent glycemic goals may be appropriate for individuals with significant cognitive and/or functional limitations, frailty, or severe comorbidities or where the harms of treatment, including hypoglycemia, are greater than the benefits. **B**

6.6 Deintensify hypoglycemia-causing medications (insulin, sulfonylureas, or meglitinides), or switch to a medication class with lower hypoglycemia risk, for individuals who are at high risk for hypoglycemia, within individualized glycemic goals. **B**

6.7 Deintensify diabetes medications for individuals for whom the harms and/or burdens of treatment may be greater than the benefits, within individualized glycemic goals. **B**

6.8 Reassess glycemic goals based on the individualized criteria shown in Fig. 6.1. **E**

6.9 Set a glycemic goal during consultations to improve outcomes. **A**

For all populations, it is critical that glycemic goals be woven into an individualized, person-centered strategy (41). The glycemic goals for many nonpregnant adults are shown in Table 6.3, and Fig. 6.1 summarizes how A1C and CGM goals should be individualized by each person's health, function, capacity for self-management, potential for the treatment plan to cause hypoglycemia, and other modifying factors. For example, less stringent goals are appropriate for individuals with significant functional and cognitive impairments. For more details regarding glycemic goals in older adults, please refer to section 13, "Older Adults." For glycemic goals in children and adolescents, please refer to section 14, "Children and Adolescents." For glycemic goals during pregnancy, please refer to section 15, "Management of Diabetes in Pregnancy."

Health care professionals should engage in shared decision-making with the individual (as well as with family members and care partners) to establish treatment goals and should adjust goals to improve safety and medication-taking behavior particularly in the setting of changing health status. Setting specific glycemic (and other) treatment goals during clinical consultations has been demonstrated to improve glycemic outcomes for individuals with diabetes (42).

Glucose Lowering and Microvascular Complications

The Diabetes Control and Complications Trial (DCCT) (43), a prospective randomized controlled trial of intensive (mean A1C ~7% [~53 mmol/mol]) versus

standard (mean A1C ~9% [~75 mmol/mol]) glycemic management in people with type 1 diabetes, showed definitively that better glycemic status is associated with 50–76% reductions in rates of development and progression of microvascular complications (retinopathy, neuropathy, and chronic kidney disease). Follow-up of the DCCT cohorts in the Epidemiology of Diabetes Interventions and Complications (EDIC) study (44,45) demonstrated persistence of these microvascular benefits over two decades despite the fact that the glycemic separation between the treatment groups diminished and disappeared during follow-up.

The Kumamoto study (46) and UK Prospective Diabetes Study (UKPDS) (47,48) examined the effects of "intensive glycemic control" among people with short-duration type 2 diabetes, although glycemic lowering in these studies was not intensive by current standards (mean A1C was 7.1% vs. 9.4% in Kumamoto and 7.0% vs. 7.9% in UKPDS). These trials found lower rates of microvascular complications in the intervention arms, with long-term follow-up of the UKPDS cohorts showing enduring effects on most microvascular complications (49). These studies highlight the long-term benefits of early glycemic lowering in type 2 diabetes.

Additionally, the DCCT (43) and UKPDS (50) studies demonstrated a curvilinear relationship between attained A1C level and microvascular complications in type 1 and type 2 diabetes, respectively. Thus, on a population level, the greatest number of complications will be averted by taking individuals with diabetes from very high to moderate A1C levels. These analyses also suggest that further lowering of A1C from 7% to 6% (53 mmol/mol to 42 mmol/mol) is associated with added reduction in the

Table 6.3—Summary of glycemic goals for many nonpregnant adults with diabetes

A1C	<7.0% (<53 mmol/mol)*†
Preprandial capillary plasma glucose	80–130 mg/dL* (4.4–7.2 mmol/L)
Peak postprandial capillary plasma glucose‡	<180 mg/dL* (<10.0 mmol/L)

*More or less stringent glycemic goals may be appropriate for certain individuals. †CGM may be used to assess glycemic status as noted in Recommendations 6.3b and 6.3c. Goals should be individualized based on duration of diabetes, age and life expectancy, comorbid conditions, known cardiovascular disease or advanced microvascular complications, impaired awareness of hypoglycemia, and individual considerations (per Fig. 6.1). ‡Postprandial glucose may warrant special attention if A1C goals are not met despite reaching preprandial glucose goals. Postprandial glucose measurements should be made 1–2 h after the beginning of the meal, which is generally the timing for peak levels in people with diabetes.

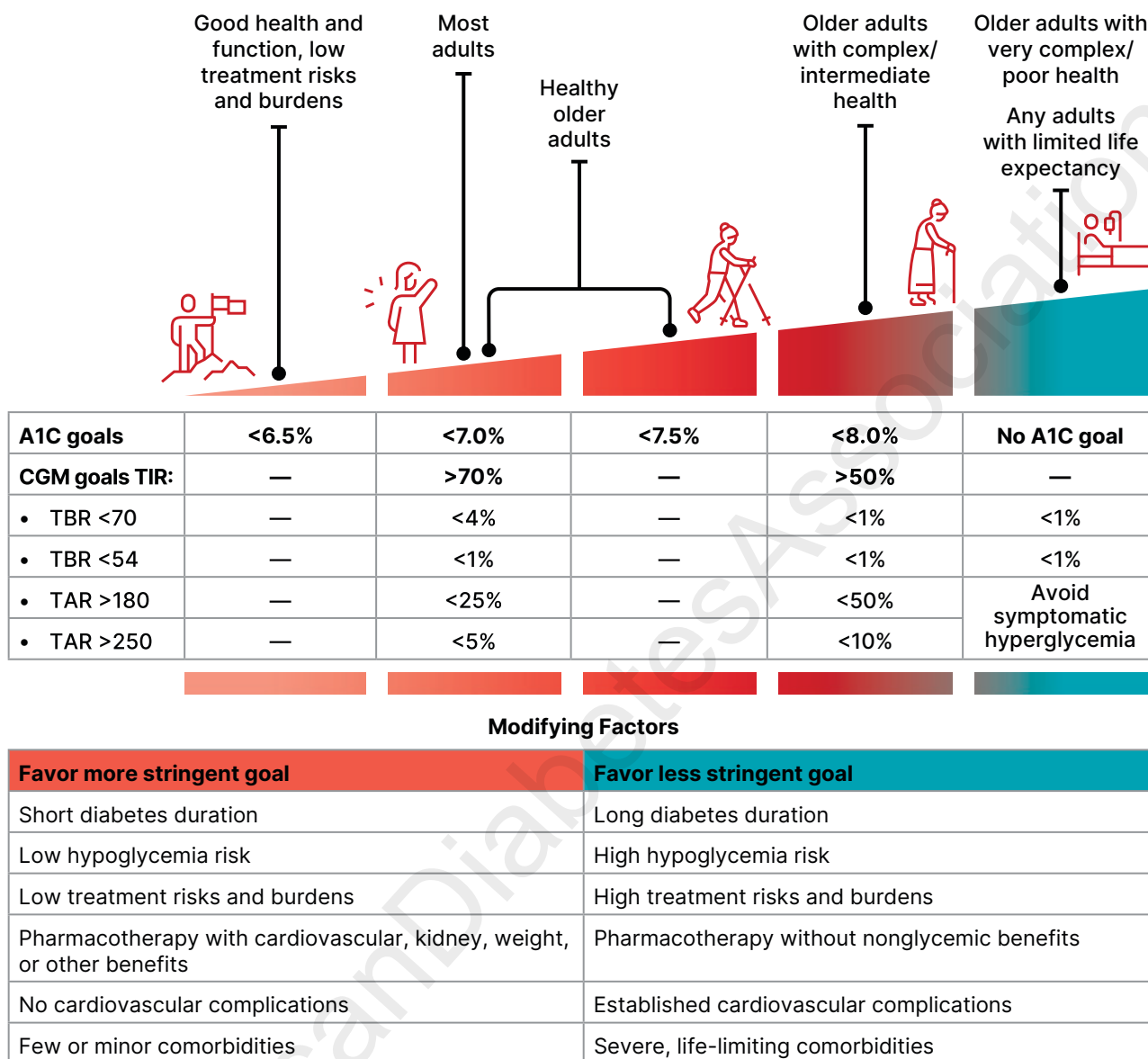


Figure 6.1—Individualized A1C and CGM goals for nonpregnant adults. Select the glycemic goal based on individual health and function as described at the top of the figure. Consider modifying to a more or less stringent goal according to the factors listed in the table. Older adults are classified as healthy (few coexisting chronic illnesses, intact cognitive and functional status), as having complex/intermediate health (multiple coexisting chronic illnesses, two or more instrumental impairments to activities of daily living, or mild to moderate cognitive impairment), or as having very complex/poor health (long-term care or end-stage chronic illnesses, moderate to severe cognitive impairment, or two or more impairments to activities of daily living). Select glycemic goals that avoid symptomatic hypoglycemia and hyperglycemia in all individuals. Consider individuals' resources and support systems to safely achieve glycemic goals. Incorporate the preferences and goals of people with diabetes through shared decision-making. CGM, continuous glucose monitoring; TAR, time above range; TBR, time below range; TIR, time in range.

risk of microvascular complications, but the absolute risk reductions become much smaller and may be outweighed by the increasing risk in hypoglycemia when using medications that cause hypoglycemia (e.g., insulin and insulin secretagogues) or requiring glucose-lowering polypharmacy. The implication of these findings is that A1C goals between 6% and 7% are appropriate, and treatment does not necessarily need to be deintensified, in the setting of low hypoglycemia risk, low treatment risks

and burdens, and long life expectancy (i.e., sufficient time horizon to derive benefit from glucose lowering). Several glucose-lowering medication classes—notably, metformin, glucagon-like peptide 1 receptor agonists (GLP-1 RAs), dual GIP and GLP-1 RA, dual GIP and GLP-1 RA, sodium-glucose cotransporter 2 (SGLT2) inhibitors, and dipeptidyl peptidase 4 inhibitors—are unlikely to cause hypoglycemia, making it possible for many individuals to achieve lower glycemic goals with a low risk for hypoglycemia

(see section 9, “Pharmacologic Approaches to Glycemic Treatment”). Moreover, CGM use was not as common when the DCCT and UKPDS trials were conducted and automated insulin delivery systems were not available; these have been shown to improve glucose levels without increasing hypoglycemia.

Among individuals with type 2 diabetes, three landmark trials (Action to Control Cardiovascular Risk in Diabetes [ACCORD], Action in Diabetes and Vascular Disease:

Preterax and Diamicon MR Controlled Evaluation [ADVANCE], and Veterans Affairs Diabetes Trial [VADT]) were conducted to examine the effects of near normalization of blood glucose on cardiovascular outcomes. The ADVANCE and VADT trials found modest reduction in nephropathy with intensive glycemic management; ACCORD was stopped after a median of 3.5 years due to higher mortality in the intervention arm (51–55). Importantly, these landmark studies were conducted prior to the approval of GLP-1 RAs, dual GIP and GLP-1 RA, and SGLT2 inhibitors, and intensive glucose lowering was achieved predominantly through greater use of insulin and other medications. Findings from these studies, including the concerning increase in mortality in the intensive treatment arm of ACCORD, suggest caution is needed in treating diabetes to near-normal A1C goals in people with long-standing type 2 diabetes using medications with a high risk for hypoglycemia and with other adverse effects and no additional cardiovascular-metabolic benefits.

Glucose Lowering and Cardiovascular Disease Outcomes

The DCCT in individuals with type 1 diabetes and the UKPDS, ACCORD, ADVANCE, and VADT studies in type 2 diabetes all sought to address whether intensive glycemic management reduced cardiovascular disease (CVD) events (43,51,52,54). ACCORD, ADVANCE, and VADT were conducted in relatively older participants with a longer duration of diabetes (mean duration 8–11 years) and either CVD or multiple cardiovascular risk factors. Details of these studies are reviewed extensively in the joint ADA position statement “Intensive Glycemic Control and the Prevention of Cardiovascular Events: Implications of the ACCORD, ADVANCE, and VA Diabetes Trials” (56). No significant reduction in composite CVD events was demonstrated at the end of the intervention in any of these studies, and ACCORD was stopped prematurely at 3.5 years because of an increase in total mortality, particularly sudden CVD deaths. Serious concerns with the intensive glycemic treatment plan used in ACCORD included the rapid escalation of therapies, the early use of large doses of insulin, substantial weight gain, and frequent hypoglycemia. Blood glucose has subsequently been shown to be a weaker independent CVD risk factor compared with

other CVD risk factors, such as hypertension or hypercholesterolemia.

However, a meta-analysis of individual participant data from UKPDS, ACCORD, ADVANCE, and VADT demonstrated a significant reduction in myocardial infarctions and major CVD events but no difference in stroke, heart failure, or mortality between intensive and less intensive glycemic management (57). Additionally, longer-term epidemiological follow-up of these studies also showed a pattern of CVD benefit (58–60). In the post-DCCT follow-up of the EDIC cohort, participants previously randomized to the intensive treatment arm had a significant 57% reduction in the risk of the composite outcome of nonfatal myocardial infarction, nonfatal stroke, or cardiovascular death compared with those previously randomized to the standard treatment arm (58). The benefit of intensive glycemic management in the EDIC cohort of people with type 1 diabetes has been shown to persist for 30 years and was associated with a 32% reduction in CVD events (59).

The UKPDS post-trial 20-year observational follow-up has shown reductions in myocardial infarctions and total mortality both in the group of individuals with overweight treated with metformin and in the group previously treated intensively with sulfonylureas or insulin (49). Post-trial observational follow-up of the VADT over 10 years has also shown a significant reduction in the primary outcome of major CVD events, with myocardial infarctions and heart failure being the most common outcomes (60). In contrast, post-trial observational follow-up of the ADVANCE study in the Action in Diabetes and Vascular Disease Preterax and Diamicon MR Controlled Evaluation Post Trial Observational Study (ADVANCE-ON) demonstrated no significant effect on CVD events at 10 years (61). In the epidemiological follow-up of ACCORD in the Action to Control Cardiovascular Risk in Diabetes Follow-On Study (ACCORDION), the excess increase in total mortality that was seen during 3.5 years of intensive treatment was reduced by returning to conventional management, and therefore there was no difference in total mortality after a total of 9 years of follow-up (62). Collectively, results of these studies suggest that long-term intensive glycemic management may reduce CVD events, particularly myocardial infarctions, with heterogeneity of results

likely driven by differences in study treatments and populations.

Importantly, these landmark studies in individuals with type 2 diabetes did not include GLP-1 RAs, dual GIP and GLP-1 RA, and SGLT2 inhibitors, which are highly beneficial in subgroups like those included in the trials (i.e., individuals with established CVD and those at high risk for cardiovascular and kidney complications). Subsequent cardiovascular and kidney outcomes trials of these agents were not designed to test higher versus lower A1C; therefore, beyond limited post hoc analysis of these trials, there is limited evidence of the independent cardiovascular and kidney effects of glucose lowering when conferred by these medication classes (63). Indeed, beneficial effects of GLP-1 RA, dual GIP and GLP-1 RA, and SGLT2 inhibitor therapies may be mediated by weight loss, hemodynamic effects, blood pressure lowering, and anti-inflammatory changes rather than glucose lowering per se.

As discussed further below, severe hypoglycemia is strongly associated with cardiovascular events and mortality (64). Therefore, health care professionals should be vigilant in preventing hypoglycemia and should not aggressively attempt to achieve near-normal A1C levels in people in whom such goals cannot be safely and reasonably achieved. As discussed in section 9, “Pharmacologic Approaches to Glycemic Treatment,” addition of SGLT2 inhibitors and/or GLP-1–based therapies that have demonstrated CVD and kidney benefits is recommended in individuals with established CVD, chronic kidney disease, and heart failure. As outlined in more detail in section 9, “Pharmacologic Approaches to Glycemic Treatment,” and section 10, “Cardiovascular Disease and Risk Management,” the cardiovascular benefits of SGLT2 inhibitors or GLP-1 RAs are not contingent upon A1C lowering; therefore, initiation should be considered in people with type 2 diabetes and CVD, kidney disease, heart failure, and/or obesity independent of the current A1C, A1C goal, or metformin therapy. Based on these considerations, the following two strategies are offered (65):

1. If already on dual therapy or multiple glucose-lowering therapies and

not on an SGLT2 inhibitor or a GLP-1 RA or dual GIP and GLP-1 RA, consider switching to one of these agents with proven cardiovascular benefit.

2. Introduce SGLT2 inhibitors or GLP-1 RAs or a dual GIP and GLP-1 RA in people with CVD at A1C goal (independent of metformin) for cardiovascular benefit, independent of baseline A1C or individualized A1C goal.

Setting and Modifying Glycemic Goals

Glycemic goals and management should be individualized, with focus on avoiding therapeutic inertia to reduce risks of acute and chronic diabetes complications as well as undue treatment burden and adverse effects of therapy. Multiple factors must be considered when setting a glycemic goal, using shared decision-making to integrate individual needs, goals, and preferences and considering characteristics that influence risks and benefits of therapy. In addition to supporting the establishment of individualized glycemic goals, this approach may optimize engagement and self-efficacy.

The factors to consider in individualizing goals are depicted in **Fig. 6.1**. This figure is not designed to be applied rigidly in the care of a given individual but rather to be used as a framework to guide clinical decision-making (41) and engage people with type 1 and type 2 diabetes in shared decision-making. More aggressive goals may be recommended if they can be achieved safely, with an acceptable burden of therapy (including hypoglycemic risk), and if life expectancy is sufficient to derive benefits of greater glucose lowering. Less stringent goals (e.g., A1C up to 8% [64 mmol/mol]) may be recommended for individuals with complex health status and/or limited life expectancy where benefits of more intensive treatment may not be realized or if the expected risks and burdens of treatment outweigh the potential benefits. Severe or frequent hypoglycemia is an absolute indication for the modification of treatment plans, including setting higher glycemic goals, if the treatment plan requires use of medications associated with high risk for hypoglycemia (i.e., insulin and insulin secretagogues).

Diabetes is a progressive chronic disease; thus, glycemic goals are likely to

change over time. Newly diagnosed individuals and/or those without comorbidities that limit life expectancy may benefit from more intensive glycemic goals proven to prevent microvascular complications. Both DCCT/EDIC and UKPDS suggested that there is metabolic memory, or a legacy effect, in which a finite period of intensive glucose lowering yielded benefits that extended for decades after that period ended (44–48). However, there are no data on the long-term effects of early long-term glucose lowering using modern treatment strategies. Thus, a finite period of intensive treatment to near-normal A1C may yield enduring benefits even if treatment is subsequently deintensified as the individual's situation and needs change, clinical complexity increases, and the treatment plan required to lower glucose levels becomes more complex and/or associated with hypoglycemia. Thus, glycemic goals should be reevaluated over time to balance the individualized risks and benefits.

Hypoglycemia is the major risk to individuals treated with insulin, sulfonylureas, or meglitinides, and it is appropriate to deintensify these medications where there is a high risk for hypoglycemia (see **HYPOGLYCEMIA RISK ASSESSMENT**, below). Switching a high-hypoglycemia-risk medication to lower-hypoglycemia-risk therapy (see section 9, “Pharmacologic Approaches to Glycemic Treatment”) should be considered if needed to achieve individualized glycemic goals or where individuals have evidence-based indications for alternative medications (e.g., use of SGLT2 inhibitors in the setting of heart failure or chronic kidney disease and use of GLP-1 RAs in the setting of CVD or obesity). Clinicians should also consider medication burdens other than hypoglycemia, including tolerability, difficulties of administration, impact on education or employment, and financial cost. These factors should be balanced against benefits from glycemic lowering and disease-specific benefits that may be independent of glycemic lowering (section 9, “Pharmacologic Approaches to Glycemic Treatment”). Multiple trials have shown that deintensification of diabetes treatment can be achieved successfully and safely (66–69). It is important to partner with people with diabetes during the deintensification process to understand their goals of diabetes treatment and agree upon appropriate glycemic monitoring, glucose levels, and goals of care (70).

HYPOGLYCEMIA ASSESSMENT, PREVENTION, AND TREATMENT

Recommendations

6.10 Review history of hypoglycemia at every clinical encounter for all individuals at risk for hypoglycemia, and evaluate hypoglycemic events as indicated. **C**

6.11 Screen individuals at risk for hypoglycemia for impaired hypoglycemia awareness at least annually and when clinically appropriate. **E** Refer to a trained health care professional for evidence-based intervention to improve hypoglycemia awareness. **A**

6.12 Screen individuals at high risk for hypoglycemia or with severe and/or frequent hypoglycemia for fear of hypoglycemia at least annually and when clinically appropriate. **E** Refer to a trained health care professional for evidence-based intervention. **A**

6.13 Consider an individual's risk for hypoglycemia (see **Table 6.5**) when selecting diabetes medications and glycemic goals. **B**

6.14 Use of CGM is beneficial and recommended for individuals at high risk for hypoglycemia. **A**

6.15 Glucose is the preferred treatment for the conscious individual with glucose <70 mg/dL (<3.9 mmol/L), although any form of carbohydrate that contains glucose may be used. Avoid using foods or beverages high in fat and/or protein for initial treatment of hypoglycemia. Fifteen minutes after initial treatment, repeat the treatment if hypoglycemia persists. **B**

6.16 Glucagon should be prescribed for all individuals taking insulin or at high risk for hypoglycemia. **A** Family, caregivers, school personnel, and others providing support to these individuals should know its location and be educated on how to administer it. Glucagon preparations that do not have to be reconstituted are preferred. **B**

6.17 First aid kits should include oral glucose for use in treating hypoglycemia. **C**

6.18 All individuals taking insulin **A** or at risk for hypoglycemia **C** should receive structured education for hypoglycemia prevention and treatment, with ongoing education for those who experience hypoglycemic events.

6.19 One or more episodes of level 2 or 3 hypoglycemia should prompt reevaluation of the treatment plan, including deintensifying or switching diabetes medications if appropriate. **B**

6.20 Regularly assess cognitive function; if impaired or declining cognition is found, the clinician, person with diabetes, and caregiver should increase vigilance for hypoglycemia. **B**

Hypoglycemia Definitions and Event Rates

Hypoglycemia is often the major limiting factor in the glycemic management of type 1 and type 2 diabetes. Recommendations regarding the classification of hypoglycemia are outlined in **Table 6.4** (71). Level 1 hypoglycemia is defined as a measurable glucose concentration <70 mg/dL (<3.9 mmol/L) and ≥54 mg/dL (≥3.0 mmol/L). A blood glucose concentration of 70 mg/dL (3.9 mmol/L) has been recognized as a threshold for adrenergic responses to falling glucose in people without diabetes. Symptoms of hypoglycemia include, but are not limited to, shakiness, irritability, confusion, tachycardia, sweating, and hunger (72). Because many people with diabetes demonstrate impaired counterregulatory responses to hypoglycemia and/or experience impaired hypoglycemia awareness, a measured glucose level <70 mg/dL (<3.9 mmol/L) is considered clinically important, regardless of symptoms. Level 2 hypoglycemia (defined as a blood glucose concentration <54 mg/dL [<3.0 mmol/L]) is the threshold at which neuroglycopenic symptoms begin to occur and requires immediate action to resolve the hypoglycemic event. If an individual has level 2 hypoglycemia without adrenergic or neuroglycopenic symptoms, they likely have impaired hypoglycemia awareness (discussed further in **HYPOGLYCEMIA RISK**

ASSESSMENT, below). This clinical scenario warrants investigation and review of the treatment plan (73,74). Lastly, level 3 hypoglycemia is defined as a severe event characterized by altered mental and/or physical functioning that requires assistance from another person for recovery, irrespective of glucose level.

Hypoglycemia has a broad range of negative health consequences (75). Level 3 hypoglycemia may be recognized or unrecognized and can progress to loss of consciousness, seizure, coma, or death. Level 3 hypoglycemia was associated with mortality in both the standard and the intensive glycemia arms of the ACCORD trial, but the relationships between hypoglycemia, achieved A1C, and treatment intensity were not straightforward (76). An association of level 3 hypoglycemia with mortality was also found in the ADVANCE trial and in clinical practice (77,78). Hypoglycemia can cause acute harm to the person with diabetes or others, especially if it causes falls, motor vehicle accidents, or other injury (79). Hypoglycemia may also cause substantial anxiety that can reduce the quality of life of individuals with diabetes and their caregivers and may contribute to problems with diabetes self-management and treatment (80–82). Recurrent level 2 hypoglycemia and/or level 3 hypoglycemia is an urgent medical issue and requires intervention with treatment plan adjustment, behavioral intervention, delivery of diabetes self-management education and support, and use of technology to assist with hypoglycemia prevention and identification (74,83–86).

Epidemiologic studies of hypoglycemia predominantly rely on claims data to assess hypoglycemia-related hospitalizations and emergency department visits (87–90). These studies do not capture the level 1 and level 2 hypoglycemia that represent the vast majority of hypoglycemic events, and they also substantially underestimate level 3 hypoglycemia (87,91,92).

Nevertheless, they reveal a substantial burden of hypoglycemia-related hospital utilization in the community (87–90). Level 1 and level 2 hypoglycemia can be ascertained from individual self-report (93) and are strong risk factors for subsequent level 3 hypoglycemia.

Hypoglycemia Risk Assessment

Assessment of an individual's risk for hypoglycemia includes evaluating clinical risk factors as well as relevant social, cultural, and economic factors (**Table 6.5**). Recommendations 6.10–6.20 group individuals with diabetes into two hypoglycemia risk categories with clinical significance. Individuals at risk for hypoglycemia are those treated with insulin, sulfonylureas, or meglitinides; clinically significant hypoglycemia is rare among individuals taking other diabetes medication classes (94,95). Individuals at high risk for hypoglycemia are the subset of individuals at risk for hypoglycemia who either have a major hypoglycemia risk factor or have multiple other risk factors (determined by the health care professional incorporating clinical judgment) (**Table 6.5**). This risk stratification is based on epidemiologic studies of hypoglycemia risk (88,89,94,96–100). Validated tools have been developed to estimate hypoglycemia risk using predominantly electronic health record data (101–103). However, these tools do not include all of the important hypoglycemia risk factors, and more research is needed to determine how they can best be incorporated into clinical care.

Among individuals at risk for hypoglycemia, prior hypoglycemic events, especially level 2 or 3 events, are the strongest risk factors for hypoglycemia recurrence (95,98,104–106). Hypoglycemia history should be assessed at every clinical encounter and should include hypoglycemic event frequency, severity, precipitants, symptoms (or lack thereof), and approach to treatment. It is essential to correlate glucose readings, both from glucose meters and CGM systems, with symptoms and treatment, as individuals may experience and treat hypoglycemic symptoms without checking their glucose level (107), treat normal glucose values as hypoglycemic, or tolerate hypoglycemia without treatment either because of lack of symptoms or to avoid hyperglycemia. When low sensor glucose readings occur

Table 6.4—Classification of hypoglycemia

Glycemic criteria/description	
Level 1	Glucose <70 mg/dL (<3.9 mmol/L) and ≥54 mg/dL (≥3.0 mmol/L)
Level 2	Glucose <54 mg/dL (<3.0 mmol/L)
Level 3	A severe event characterized by altered mental and/or physical status requiring assistance for treatment of hypoglycemia, irrespective of glucose level

Adapted from Agiostratidou et al. (71).

Table 6.5—Assessment of hypoglycemia risk among individuals treated with insulin, sulfonylureas, or meglitinides

Clinical and biological risk factors	Social, cultural, and economic risk factors
Major risk factors - Recent (within the past 3–6 months) level 2 or 3 hypoglycemia - Intensive insulin therapy* - Impaired hypoglycemia awareness - Kidney failure - Cognitive impairment or dementia - History of metabolic surgery	Major risk factors - Food insecurity - Low-income status§ - Housing insecurity - Fasting for religious or cultural reasons - Underinsurance
Other risk factors - Multiple recent episodes of level 1 hypoglycemia - Basal insulin therapy* - Age ≥75 years† - Female sex - High glycemic variability‡ - Polypharmacy - Cardiovascular disease - Chronic kidney disease (eGFR <60 mL/min/1.73 m² or albuminuria) - Neuropathy - Retinopathy - Major depressive disorder - Severe mental illness - Gastroparesis - β-Blocker therapy	Other risk factors - Low health literacy - Alcohol or substance use disorder

Major risk factors are those that have a consistent, independent association with a high risk for level 2 or 3 hypoglycemia. Other risk factors are those with less consistent evidence or a weaker association. These risk factors are identified through observational analyses and are intended to be used for hypoglycemia risk stratification. Individuals considered at high risk for hypoglycemia are those with ≥1 major risk factor or who have multiple other risk factors (determined by the health care professional incorporating clinical judgment) (88, 89, 94, 96–99, 117, 119, 122, 190, 191, 88, 89, 94, 96–99, 117, 120, 191, 192). Proximal causes of hypoglycemic events (e.g., exercise and sleep) are not included. eGFR, estimated glomerular filtration rate. *Rates of hypoglycemia are highest for individuals treated with intensive insulin therapy (including multiple daily injections of insulin, continuous subcutaneous insulin infusion, or automated insulin delivery systems), followed by basal insulin, followed by sulfonylureas or meglitinides. Combining treatment with insulin and sulfonylureas further increases hypoglycemia risk. †Accounting for treatment plan and diabetes subtype, the oldest individuals (aged ≥75 years) have the highest risk for hypoglycemia in type 2 diabetes; younger individuals with type 1 diabetes are also at very high risk. ‡Tight glycemic management in randomized trials increases hypoglycemia rates. In observational studies, both low and high A1C are associated with hypoglycemia in a J-shaped relationship. §Includes factors associated with low income, such as living in a socioeconomically deprived area.

in low-risk individuals, or occur without associated symptoms, causes of artifactual hypoglycemia should be investigated, such as compression of a CGM sensor during sleep.

Individuals at risk for hypoglycemia should also be screened for impaired hypoglycemia awareness (also called hypoglycemia unawareness or hypoglycemia-associated autonomic failure) at least yearly. Impaired hypoglycemia awareness is defined as not experiencing the typical counterregulatory hormone release at low glucose levels or the associated symptoms, which often occurs in individuals with long-standing diabetes or

recurrent hypoglycemia (108). Some individuals with impaired hypoglycemia awareness can sense hypoglycemia, but only at lower glucose levels or with fewer symptoms (109). Individuals with impaired hypoglycemia awareness may experience confusion as the first sign of hypoglycemia, which can create fear of hypoglycemia and severely impact quality of life (109). Impaired hypoglycemia awareness dramatically increases the risk for level 3 hypoglycemia (110). Validated questionnaires for assessing impaired hypoglycemia awareness include the single-question Pedersen-Bjergaard (111) and Gold (112) tools; the Clarke (113) and HypoA-Q (114)

tools are longer questionnaires that evaluate multiple domains of impaired hypoglycemia awareness. Comparisons between these tools largely yield good agreement (115,116). To efficiently screen for impaired hypoglycemia awareness in clinical practice, clinicians can ask a single question based on these tools such as “Can you always feel when your blood glucose is low?” and follow “No” responses with a more detailed evaluation.

Other notable clinical and biological risk factors for hypoglycemia are very young age, older age, multimorbidity, cognitive impairment, chronic kidney disease and kidney failure, CVD, depression, neuropathy, and gastroparesis (94,95,117). Female sex has also been found to be an independent risk factor for hypoglycemia in multiple studies, although the mechanisms of this relationship are unclear and require further research (94). Cognitive impairment has a strong bidirectional association with hypoglycemia, and recurrent severe hypoglycemic episodes were associated with a greater decline in psychomotor and mental efficiency after long-term follow-up of the DCCT/EDIC cohort (118). Therefore, cognitive function should be routinely assessed among older adults with diabetes. Hypoglycemia is also a frequent complication for people with diabetes who have undergone metabolic surgery, especially Roux-en-Y gastric bypass (119). Hypoglycemia after metabolic surgery is caused by excessive post-meal endogenous insulin secretion and typically emerges months to years after surgery (120).

There are a number of important social, cultural, and economic hypoglycemia risk factors that should also be considered. Food insecurity is associated with increased risk of hypoglycemia-related emergency department visits and hospitalizations in low-income households, and this was shown to be mitigated by increased federal nutrition program benefits (121). In general, individuals with low annual household incomes (95), individuals who live in socioeconomically deprived areas (98), and individuals who are underinsured (99) or experiencing housing instability (122) experience higher rates of emergency department visits and hospitalizations for hypoglycemia. Clinicians should also be aware of cultural practices that may influence glycemic management (which are discussed in detail in section 5, “Facilitating Positive Health Behaviors and

Well-being to Improve Health Outcomes”), such as fasting as part of religious observance. Fasting may increase the risk for hypoglycemia among individuals treated with insulin or insulin secretagogues if not properly planned for, so clinicians need to engage these individuals to codevelop a diabetes treatment plan that is safe and respectful of their traditions (123).

Young children with type 1 diabetes and older adults, including those with type 1 and type 2 diabetes (124,125), are noted as being particularly vulnerable to hypoglycemia because of their reduced ability to recognize hypoglycemic symptoms and effectively communicate their needs. Individualized glycemic goals, education, nutrition intervention, physical activity management, medication adjustment, glucose monitoring, and routine clinical surveillance may improve outcomes (108). Insulin pumps with automated low-glucose suspend and automated insulin delivery systems have been shown to be effective in reducing hypoglycemia in type 1 diabetes (126). For people with type 1 diabetes with level 3 hypoglycemia and hypoglycemia unawareness that persists despite medical treatment, pancreas transplant alone or human islet transplantation may be an option, but these approaches remain experimental (127,128). Indeed, recent observational data have shown persistence of severe hypoglycemia even among those that used advanced diabetes technologies and management approaches, highlighting the need for ongoing surveillance of hypoglycemic risk (129,130).

Hypoglycemia Treatment

Health care professionals should counsel individuals with diabetes to treat hypoglycemia with fast-acting carbohydrates at the hypoglycemia alert value of 70 mg/dL (3.9 mmol/L) or less (131–133). Individuals should be counseled to recheck their glucose 15 min after ingesting carbohydrates and to repeat carbohydrate ingestion and seek care for ongoing hypoglycemia. Emergency medical services should be called for people who are unalert or unable to administer carbohydrates. These instructions should be reviewed at each clinical visit.

For most individuals, 15 g carbohydrates should be ingested. Individuals using automated insulin delivery systems should typically ingest 5–10 g carbohydrates unless there is hypoglycemia in conjunction with exercise or there has been significant

overestimation of a carbohydrate/meal bolus (134). The acute glycemic response to food correlates better with the glucose content than with the total carbohydrate content. Pure glucose is the preferred initial treatment, but any form of carbohydrate that contains glucose will raise blood glucose. People taking acarbose should treat hypoglycemia with only pure glucose, as acarbose inhibits sucrose breakdown, potentially delaying correction of hypoglycemia if sucrose-containing carbohydrates are used (135). Added fat may slow and then prolong the acute glycemic response. Dietary protein intake may increase insulin secretion and should not be used to treat hypoglycemia (136). Ongoing insulin activity or insulin secretagogues may lead to recurrent hypoglycemia unless more food is ingested after recovery.

Because hypoglycemia may occur in workplaces, schools, and other institutions and public settings (87,91,92,137), first aid kits (both prepackaged and self-made) should include oral glucose for hypoglycemia treatment. Notably, current guidance for first aid kit composition omits glucose (138,139). Options for oral glucose products include glucose tablets, which have the benefits of a long shelf life and easy dosing, and/or glucose gel products, which generally have a shorter shelf life but may be easier to ingest for children and edentulous individuals. Instructions provided with these products should include guidance to only administer oral glucose to an alert person, to check blood glucose before administering oral glucose and 15 min later, and to administer 15 g of glucose as initial treatment.

Glucagon

The use of glucagon is indicated for the treatment of hypoglycemia in people unable or unwilling to consume carbohydrates by mouth. All individuals treated with insulin or who are at high risk of hypoglycemia as discussed above should be prescribed glucagon. For these individuals, clinicians should routinely review their access to glucagon, as appropriate glucagon prescribing is very low in current practice (140–142). An individual does not need to be a health care professional to safely administer glucagon. Those in close contact with, or having custodial care of, individuals with diabetes prescribed glucagon (e.g., family members,

roommates, school personnel, coaches, childcare professionals, correctional institution staff, or coworkers) should be instructed on the use of glucagon, including where the glucagon product is kept and when and how to administer it. It is essential that they be explicitly educated to never administer insulin to individuals experiencing hypoglycemia. Glucagon was traditionally dispensed as a powder that requires reconstitution prior to injection. However, intranasal and ready-to-inject glucagon preparations are now widely available and are preferred due to their ease of administration resulting in more rapid correction of hypoglycemia (143–145). Although the physical and chemical stability of glucagon has improved with newer formulations, care should be taken to replace glucagon products when they reach their expiration date and to store glucagon based on specific product instructions to ensure safe and effective use. For currently available glucagon products and associated costs, see **Table 6.6**. Health insurance providers may prefer only select glucagon products, so it is important to check individuals' insurance coverage and prescribe formulary products whenever possible.

Hypoglycemia Prevention

A multicomponent hypoglycemia prevention plan (**Table 6.7**) is critical to caring for individuals at risk for hypoglycemia. Hypoglycemia prevention begins by establishing an individual's hypoglycemia history and risk factors, as discussed in **HYPOGLYCEMIA RISK ASSESSMENT** above. Structured education for hypoglycemia prevention and treatment is critical and has been shown to improve hypoglycemia outcomes (146,147). Education should ideally be provided through a diabetes self-management education and support program or by a trained diabetes care and education specialist, although these services are not available in many areas (148,149). If structured education is not available, clinicians should educate individuals at risk for hypoglycemia on hypoglycemia definitions, situations that may precipitate hypoglycemia (e.g., fasting, delayed meals, physical activity, and illness), blood glucose self-monitoring, avoidance of driving with hypoglycemia, step-by-step instructions on hypoglycemia treatment as discussed above, and glucagon use as appropriate (146).

CGM can be a valuable tool for detecting and preventing hypoglycemia in many individuals with diabetes, and it is recommended for insulin-treated individuals, especially those using multiple daily insulin injections or continuous subcutaneous insulin infusion. There is clinical trial evidence that CGM reduces rates of hypoglycemia in these populations. CGM can reveal asymptomatic hypoglycemia and help identify patterns and precipitants of hypoglycemic events and provide alarms that can warn individuals of falling glucose so that they can intervene (150,151). CGM may also be helpful to reduce hypoglycemia and improve quality of life in people with hypoglycemia as a complication of metabolic surgery (152,153). For more information on using BGM and CGM for hypoglycemia prevention, see section 7, “Diabetes Technology.”

An essential component of hypoglycemia prevention is appropriate modification to diabetes treatment in the setting of intercurrent illness (discussed in detail below) or to prevent recurrent hypoglycemic events. Level 2 or 3 hypoglycemic events in particular should trigger a reevaluation of the individual’s diabetes treatment plan, with consideration of deintensification of therapy within individualized glycemic goals.

Individuals with impaired hypoglycemia awareness should be offered training to reestablish awareness of hypoglycemia. Fear of hypoglycemia and impaired hypoglycemia awareness often co-occur, so interventions aimed at treating one often benefit both (154). Several evidence-based training programs have been developed for this purpose and have been demonstrated to reduce rates of hypoglycemia and improve quality of life among people with type 1 diabetes and impaired hypoglycemia awareness (74,155,156). However, these programs are not currently available for clinical use. Similar training can be provided through qualified behavioral health professionals, diabetes care and education specialists, or other professionals with experience in this area, although this approach has not been evaluated in clinical trials. In addition, several weeks of avoidance of hypoglycemia, typically accomplished through a temporary relaxation of glycemic goals, can improve counterregulation and hypoglycemia awareness in many people with diabetes (157). Hence, individuals with impaired hypoglycemia

Table 6.6—Median monthly (30-day) AWP and NADAC of glucagon formulations in the U.S.

Product	Form	Median AWP* (min, max)	Median NADAC* (min, max)	Dosage
Glucagon	Injection powder with diluent for reconstitution	\$303 (\$180, \$337)	\$242 (\$207, \$242)	1 mg
Glucagon	Nasal powder	\$357	\$285	3 mg
Glucagon	Prefilled pen, prefilled syringe	\$391	\$303 (\$303, \$304)	0.5 mg, 1 mg
Dasiglucagon	Prefilled pen, prefilled syringe	\$371	\$298	0.6 mg

AWP, average wholesale price; max, maximum; min, minimum; NADAC, National Average Drug Acquisition Cost. AWP and NADAC prices are as of 1 July 2025. *Calculated per unit (AWP [192] or NADAC [193]); median AWP or NADAC is listed alone when only one product and/or price is described).

awareness and recurrent hypoglycemic episodes may benefit from short-term relaxation of glycemic goals.

INTERCURRENT ILLNESS

Stressful events (e.g., illness, trauma, and surgery) increase the risk for both hyperglycemia and hypoglycemia among individuals with diabetes, particularly in the setting of underlying clinical complexity and polypharmacy. In severe cases, they may precipitate hyperglycemic crises, which are life-threatening and require immediate

medical care. Any individuals with diabetes experiencing illness or other stressful events should be assessed for the need for more frequent monitoring of glucose; ketosis-prone individuals also require urine or blood ketone monitoring. Clinicians should reevaluate diabetes treatment during these events and make adjustments as appropriate. Specifically, clinicians should consider holding metformin and SGLT2 inhibitors when oral intake cannot be maintained or if there is concern for acute kidney injury (158). GLP-1 RAs may need to be held for illnesses with significant gastrointestinal

Table 6.7—Components of hypoglycemia prevention for individuals at risk for hypoglycemia at initial, follow-up, and annual visits

Hypoglycemia prevention action	Initial visit	Every follow-up visit	Annual visit
Hypoglycemia history assessment	✓	✓	✓
Hypoglycemia awareness assessment	✓		✓
Cognitive function and other hypoglycemia risk factor assessment	✓		✓
Structured individual education for hypoglycemia prevention and treatment	✓	✓*	✓*
Consideration of diabetes technology needs	✓	✓	✓
Reevaluation of diabetes treatment plan with deintensification, simplification, or agent modification as appropriate	✓	✓†	✓†
Glucagon prescription and training for close contacts for insulin-treated individuals or those at high hypoglycemic risk	✓		✓
Training to improve hypoglycemia awareness	✓‡		✓‡

The listed frequencies are the recommended minimum; actions for hypoglycemia prevention should be taken more often as needed based on clinical judgment. *Indicated with recurrent hypoglycemic events or at initiation of medication with a high risk for hypoglycemia. †Indicated with any level 2 or 3 hypoglycemia, intercurrent illness, or initiating interacting medications. ‡Indicated when impaired hypoglycemia awareness is detected.

symptoms (158). Thiazolidinediones should be held, and their ultimate reinitiation reassessed on an individualized basis, in the setting of heart failure exacerbation or other conditions with hypervolemia (158). In addition, clinicians should be aware of medication interactions that may precipitate hypoglycemia and modify treatment appropriately. Notably, sulfonylureas interact with a number of commonly used antimicrobials (fluoroquinolones, clarithromycin, sulfamethoxazole-trimethoprim, metronidazole, and fluconazole) that can dramatically increase their effective dose, leading to hypoglycemia (159–161). Clinicians should consider temporarily decreasing or stopping sulfonylureas when these antimicrobials are prescribed. It is important to provide specific, individualized guidance to people with diabetes and their caregivers on steps to prevent, detect, and treat significant hypoglycemia, hyperglycemia, and other adverse events during illness and other stressful events as well as to provide guidance on who to call with questions (including during non-clinical hours) and where to seek help for different levels of clinical acuity with the goal of preventing high-risk illness (158).

For further information on management of hyperglycemia in the hospital, see section 16, “Diabetes Care in the Hospital.”

HYPERGLYCEMIC CRISES: DIAGNOSIS, MANAGEMENT, AND PREVENTION

Recommendations

6.21 Review history of hyperglycemic crises (i.e., diabetic ketoacidosis and hyperglycemic hyperosmolar state) at every clinical encounter for all individuals with diabetes at risk for these events. **C**

6.22 Provide structured education on the recognition, prevention, and management of hyperglycemic crisis to all individuals with type 1 diabetes, those with type 2 diabetes who have experienced these events, and people at high risk for these events. **B**

Diabetic ketoacidosis (DKA) and the hyperglycemic hyperosmolar state (HHS) are serious, acute, and life-threatening hyperglycemic emergencies (162). Over the past decade, rates of these hyperglycemic crises have increased in both

type 1 and type 2 diabetes (90,163,164). Both DKA and HHS impart a substantial risk of subsequent morbidity and mortality and high associated health care costs (165). This section focuses on hyperglycemic crisis risk factors, prevention, and outpatient management. The diagnostic criteria, clinical presentation, and inpatient management of DKA and HHS are described in section 16, “Diabetes Care in the Hospital.”

There are a number of clinical factors associated with an increased risk of hyperglycemic crises (**Table 6.8**). In addition, several studies have reported DKA at the presentation of newly diagnosed type 1 diabetes during or after a coronavirus disease 2019 (COVID-19) infection. The precise mechanisms for new-onset diabetes in people with COVID-19 are not known, but several complex interrelated processes may be involved. Some medication classes can affect carbohydrate metabolism and precipitate the development of DKA and HHS, including glucocorticoids, antipsychotic medications, immune checkpoint inhibitors, and SGLT2 inhibitors. The risk of DKA in people with type 1 diabetes using SGLT2 inhibitors can be 5–17 times higher than that in nonusers. In clinical trials of SGLT2 inhibitors in adults with type 1 diabetes, fasting β -hydroxybutyrate of 0.8 mmol/L or higher increased the risk of DKA in the next month by 3.2-fold (166). Given the recognized risk of DKA with SGLT2 inhibitor use in type 1 diabetes, a number of educational initiatives have been suggested for prevention and early intervention to avert progression to severe DKA (167–170). The anticipated availability of continuous ketone monitoring devices may offer a future approach to preventing DKA with and without SGLT2 inhibitor use in type 1 diabetes (171).

In contrast, observational studies and randomized controlled trials have shown that DKA is uncommon in people with type 2 diabetes treated with SGLT2 inhibitors (0.6–4.9 events per 1,000 patient-years) (172). A meta-analysis of four randomized controlled trials found the relative risk of DKA in participants with type 2 diabetes treated with SGLT2 inhibitors versus placebo or active comparator arm to be 2.46 (95% CI 1.16–5.21), while a meta-analysis of five observational studies found the relative risk to be 1.74 (95% CI 1.07–2.83) (173). Risk factors for DKA in

individuals with type 2 diabetes treated with SGLT2 inhibitors include very-low-carbohydrate diets and prolonged fasting, dehydration, excessive alcohol intake, and the presence of autoimmunity, in addition to typical precipitating factors (173,174). Up to 2% of pregnancies with pregestational diabetes (most often type 1 diabetes) are complicated by DKA. The incidence of DKA in gestational diabetes is low (<0.1%) (175). Pregnant individuals may present with euglycemic DKA (glucose <200 mg/dL [11.1 mmol/L]), and the diagnosis of DKA may be hindered by the presence of mixed acid-based disturbances, particularly in the setting of hyperemesis. Due to significant risk of fetomaternal harm, pregnant individuals at risk for DKA should be counseled on the signs and symptoms suggestive of DKA and seek immediate medical attention if concern for DKA is present.

Hyperglycemic crisis should be considered in all individuals presenting with polyuria, polydipsia, weight loss, vomiting, dehydration, and change in cognitive state. Individuals at risk for DKA should be counseled on the early signs and symptoms of DKA, provided with appropriate tools for ketone measurement (urine and/or blood ketone tests), and educated on timely self-management of hyperglycemia and hyperketonemia (“sick day advice”) (176–178) to prevent clinical deterioration and need for acute care. Clinicians should review DKA prevention practices and availability of ketone monitoring tools at each visit. Individuals treated with intensive insulin therapy should not stop or hold their basal insulin even if not eating, and clinicians should provide detailed instructions on insulin dose adjustments in the setting of illness or fasting to prevent DKA occurrence and worsening. Individuals concerned about or experiencing DKA should be encouraged to contact their diabetes care team immediately. Readily available clinical support can help individuals self-manage hyperglycemia during illness and prevent emergency department and hospital care (179). Individuals at risk for DKA should measure ketones in the presence of symptoms and potential precipitating factors (e.g., illness, missed insulin doses, eating disorders), particularly if glucose levels exceed 200 mg/dL (11.1 mmol/L). Use of blood ketone monitoring compared with urine ketone monitoring in a single 6-month randomized controlled clinical

Table 6.8—Risk factors for hyperglycemic crises

Type 1 diabetes/absolute insulin deficiency
Younger age
Prior history of hyperglycemic crises
Prior history of hypoglycemic crises
Presence of other diabetes complications
Presence of other chronic health conditions (particularly in people with type 2 diabetes)
Presence of behavioral health conditions (e.g., depression, bipolar disorder, and eating disorders)
Alcohol and/or substance use
High A1C level
Insulin rationing
SGLT2 (SGLT1/2) inhibitor use
Social determinants of health
SGLT, sodium–glucose cotransporter. Data are from McCoy et al. (194), Gibb et al. (195), Randall et al. (196), Thomas et al. (197), and Borden et al. (198).

trial reduced the risk of hospitalization/emergency room management by approximately 50% (180). When hemodynamically and cognitively intact, able to tolerate oral hydration, and able to administer subcutaneous insulin, individuals may treat mild DKA with frequent blood glucose and urine or blood ketone monitoring, noncaloric hydration, and subcutaneous insulin administration. However, individuals should seek immediate medical attention if they are unable to tolerate oral hydration, they experience ongoing emesis, blood glucose levels and/or ketone levels do not improve with insulin administration, altered mental status is present, or any signs of worsening illness occur. Because HHS is associated with greater volume depletion and is typically triggered by an acute illness, individuals with suspected HHS should be immediately evaluated and treated in the inpatient setting.

A substantial proportion of individuals hospitalized with DKA experience recurrent episodes (181,182), which underscores the importance of engaging individuals experiencing these events to identify triggers and prevent recurrence. Structured diabetes self-management education and support that includes problem-solving is effective at reducing DKA admissions, as are psychological interventions, peer support, individual coaching, and behavioral family systems therapy (183,184). Given that a substantial proportion of DKA in people with established insulin-treated diabetes arises from challenges with self-management, those with recurrent DKA often require extensive multisystemic

behavioral interventions (185). Young people with established diabetes in the pediatric age-group, especially during adolescence, experience greater rates of DKA than adults with diabetes (186). Notably, the majority of DKA cases occur in those with established diabetes compared with those with newly diagnosed diabetes, often in association with psychosocial challenges, such as disordered eating behaviors, and during periods of transition, such as from pediatric to adult health care when there may be gaps in ambulatory care (186–188). In addition to challenges with self-management related to missed or inadequate insulin doses as noted above, a number of factors have been associated with DKA, including female sex, designation as part of an underrepresented group (notably by race and ethnicity or by migration background), higher A1C levels, and higher insulin units/kg/day (likely reflecting an increase in dose in response to a higher A1C that likely resulted from missed insulin) (186–188). Other factors associated with DKA include age 10–14 years, public insurance, and prior episodes of DKA; use of insulin pump therapy does not appear to be associated with increased DKA occurrence in the current era.

Individuals who have experienced DKA or HHS should be screened for social determinants of health that can contribute to or trigger these complications, including inadequate access to insulin, other glucose-lowering medications, and diabetes durable medical equipment (i.e., glucose monitoring and insulin administration

devices), and referred to appropriate health care and/or community services to mitigate these barriers to care (see section 5, “Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes,” for additional details). Access to CGM may also decrease risk of DKA recurrence (189).

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7. Diabetes Technology: Standards of Care in Diabetes—2026

American Diabetes Association
Professional Practice Committee for
Diabetes*

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The American Diabetes Association (ADA) “Standards of Care in Diabetes” includes the ADA’s current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. Members of the ADA Professional Practice Committee for Diabetes, an interprofessional expert committee, are responsible for updating the Standards of Care annually, or more frequently as warranted. For a detailed description of ADA standards, statements, and reports, as well as the evidence-grading system for ADA’s clinical practice recommendations and a full list of Professional Practice Committee members, please refer to Introduction and Methodology. Readers who wish to comment on the Standards of Care are invited to do so at professional.diabetes.org/SOC.

Diabetes technology is the term used to describe the hardware and software that people with diabetes use to assist with self-management, ranging from lifestyle modifications to glucose monitoring and automated therapy adjustments. Historically, diabetes technology has been divided into two main categories: insulin administration (insulin given by syringe, pen, inhalation, patch devices, or pump [also called continuous subcutaneous insulin infusion]) and glucose measurement (assessment by blood glucose monitoring [BGM] or continuous glucose monitoring [CGM]). Diabetes technology now also includes automated insulin delivery (AID) systems that use CGM-informed algorithms to modulate insulin delivery. Furthermore, diabetes technology encompasses connected insulin pens and diabetes self-management support software that serve as medical devices. Diabetes technology, coupled with education, follow-up, pharmacotherapy as needed, and support, can improve the lives and health of people with diabetes; however, the complexity and rapid evolution of the diabetes technology landscape can also be a barrier to implementation for people with diabetes, their care partners, and the health care team.

GENERAL DEVICE PRINCIPLES

Recommendations

7.1 Diabetes devices should be offered to people with diabetes. **A**

7.2 The type(s) and selection of devices should be individualized based on a person’s specific needs, circumstances, preferences, and skill level. In the setting of an individual whose diabetes is partially or wholly managed by someone else (e.g., a young child or a person with cognitive impairment or dexterity, psychosocial issues, and/or physical limitations), the caregiver’s skills and preferences are integral to the decision-making process. **E**

7.3a When prescribing a continuous glucose monitoring (CGM) device, ensure that people with diabetes and caregivers are offered initial and ongoing training and education as indicated by individual circumstances. Education should

*A complete list of members of the American Diabetes Association Professional Practice Committee for Diabetes can be found at <https://doi.org/10.2337/dc26-SINT>.

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include utilization of data, including uploading or sharing data to monitor and adjust therapy. **C**

7.3b When prescribing an automated insulin delivery (AID) system, people with diabetes and their caregivers must receive education on how to use and troubleshoot the system. This education should occur at regular intervals as needed. Education should include utilization of the integrated system and its data, including uploading or sharing data to monitor and adjust therapy. **C**

7.4 Health care professionals working with people with diabetes should be aware of available technologies and seek additional support when needed. **E**

7.5 People with diabetes using CGM, continuous subcutaneous insulin infusion (CSII), and/or AID for diabetes management should have continued access to devices across third-party payors, regardless of age or A1C levels. **E**

7.6 Children and adolescents should be supported at school in the use of diabetes technology, such as CGM systems, CSII, connected insulin pens, and AID systems. **E**

7.7 For adults with diabetes using diabetes technology, reasonable accommodations in educational and work settings should include having sufficient time to manage their devices and respond to high and low glucose levels. **E**

7.8 Consider early initiation, including at diagnosis, of CGM, CSII, and AID depending on a person's or caregiver's needs and preferences. **C**

7.8a There should be no requirement of C-peptide level, **B** the presence of islet autoantibodies, **B** or duration of insulin treatment **C** before initiation of CSII or AID.

7.9 Standardized reports for all CGM, CSII, AID, and connected insulin devices with a minimum of a single-page report, such as the standardized CGM report and weekly summary, should be available and utilized. Options for daily and weekly reports and raw data should be available. **E**

Insurance coverage can lag behind device availability, people's interest in devices and willingness for adoption can vary, and health care teams may have challenges in keeping up with newly released technology. An American Diabetes Association resource, which can be accessed at diabetes.org/living-with-diabetes/treatment-care/diabetes-technology-guide, can help health care professionals and people with diabetes make decisions on the initial choice of device(s). Other sources, including device manufacturers, can help people troubleshoot when difficulties arise (1–7).

Education and Training

In general, no device used in diabetes management works optimally without education, training, and ongoing support. There are multiple resources, including online tutorials and training videos as well as written material, on the use of devices. People with diabetes and their caregivers vary in comfort level with technology, and some prefer in-person training and support. Those with more education regarding device use have better outcomes (1,2); therefore, the need for additional education should be periodically assessed, particularly if treatment goals are not being met.

Training on the use of CGM often differs from that of pump and AID systems. In some settings, CGM training can be done by users themselves with company-provided training materials (for instance, people are able to use the over-the-counter [OTC] CGM brands on their own), although for underresourced, younger (8,9), and older (10) individuals, more repetition and time spent reviewing concepts is often indicated. Additionally, regular monitoring and review of the data obtained from CGM devices is needed to inform and optimize clinical care (8). Education and training should be available to any person who needs it but should not constitute a barrier to device use in a motivated individual.

Insulin pumps and AID systems, on the other hand, generally require training and education for safe use. There are studies where youth with type 1 diabetes have been able to self-initiate tubeless AID systems (11), but for most, training with a certified or trained diabetes educator and education specialist is necessary for full understanding and safe use of the technology.

Health care professionals should be aware of the availability of diabetes devices and their recommended uses and how to access the resources needed to use them. Given the rapidly changing landscape of technology, it is expected that software and/or hardware are being constantly updated; hence, periodic education is helpful to keep health care professionals informed and updated. For those interested in more advanced involvement with device use, there are defined competencies described as basic, fundamental, intermediate, and advanced that are specific to the role of each health care team member (12). The health care team's knowledge and competency are even more critical when people with diabetes are started on advanced diabetes technologies, such as AID systems. In such situations, training of the team is vital and should include a discussion about realistic expectations for the ability of the initiated system to achieve glucose goals, fundamental differences from the previous treatment tools, the system's features and limitations, and the best way to use the new system to maximize the benefits it can offer (13).

Use in Schools for Children and Adolescents

Technology use should be supported in school settings, and instructions for device use should be outlined in the student's diabetes medical management plan (DMMP). A backup treatment plan should be included in the DMMP for potential device failure. School nurses and designees should complete training to stay up to date on diabetes technologies prescribed for use in the school setting. Updated resources to support diabetes care at school, including training materials and a DMMP template, can be found online at (<https://diabetes.org/advocacy/safe-at-school-state-laws/diabetes-medical-management-plan>).

Use for Adults

For adults using devices in educational and employment settings, reasonable accommodations should be provided to allow time and space necessary for safe device use (14). This includes time to respond appropriately to high and low glucose levels and deal with any device notifications and issues.

Technology is rapidly changing, and there is no one-size-fits-all approach to technology use in people with diabetes.

Initiation of Device Use

Diabetes technology should be initiated soon after the time of diagnosis and anytime thereafter, as indicated by the user's needs and wishes. The use of CGM and BGM devices should be started from the outset of the diagnosis of diabetes, particularly in people who require insulin for management (3,4,15,16). CGM use allows for close tracking of glucose levels with adjustment of insulin dosing and lifestyle modifications and removes the burden of frequent BGM. In addition, early CGM initiation after diagnosis of type 1 diabetes in children and adolescents has been shown to decrease A1C levels and is associated with high parental satisfaction and reliance on this technology for diabetes management (5,7). Training on alarm and alert settings when initiating CGM is crucial to avoid alarm fatigue or overload. Interruption of access to CGM is associated with a worsening of outcomes (6,17); therefore, it is important for individuals on CGM to have consistent access to devices. A recent systematic review with meta-analysis also supports the use of CGM in people with type 2 diabetes not using insulin, with observations of improved glycemic outcomes and individual experience, reduced health care resource utilization, and acceptable cost-effectiveness (18).

AID systems are the preferred insulin delivery system in individuals with type 1 diabetes and type 2 diabetes on multiple daily injections (MDI) and people with other forms of insulin-deficient diabetes. They can be considered for use in people on basal insulin who are not reaching their targets. Early initiation of AID therapy has been shown to be beneficial. In an open-label, multicenter, randomized, parallel clinical trial enrolling youth with newly diagnosed type 1 diabetes, initiation of an AID system within 21 days from diagnosis showed 10% higher time in range (TIR) (70–180 mg/dL [3.9–10.0 mmol/L]) and lower A1C at 12 months versus usual care (15). In addition, use of diabetes technology overall improves A1C and increases the number of people achieving an A1C <7% (19). There are no data that the presence or absence of C-peptide or islet autoantibodies is associated with responsiveness to continuous subcutaneous insulin infusion or AID therapy. People with type 2 diabetes who continue to produce insulin

have been shown to benefit from AID therapy (20–23). Similarly, the duration of diabetes is not related to outcomes with the use of technology. Therefore, none of these measures should be used when determining suitability for continuous subcutaneous insulin infusion or AID therapy.

Standardized Reporting

Use of a standardized CGM tracing is helpful for people with diabetes and clinicians (24) and in multiple settings, from connected insulin pens (25) to CGM (26) to AID systems (27). Ideally, both people with diabetes and their health care teams can access and analyze the data, both between and at clinic visits to inform self-management and medication dose titration.

BLOOD GLUCOSE MONITORING

Recommendations

7.10 People with diabetes should be provided with blood glucose monitoring (BGM) devices as indicated by their circumstances, preferences, and treatment. People using CGM devices must also have access to BGM at all times. **A**

7.11 People who are taking insulin and using BGM should be encouraged to check their blood glucose levels when appropriate based on their insulin therapy. This may include checking when fasting, prior to meals and snacks, after meals, at bedtime, in the middle of the night, prior to, during, and after exercise, when hypoglycemia is suspected, after treating low blood glucose levels until achieving normoglycemia, when hyperglycemia is suspected, and prior to and while performing critical tasks such as driving. **B**

7.12 Health care professionals should be aware of the differences in accuracy among blood glucose meters. Only meters approved by the U.S. Food and Drug Administration (FDA) (or comparable regulatory agencies for other geographical locations) with proven accuracy should be used, with unexpired test strips purchased from a pharmacy or licensed distributor and properly stored. **E**

7.13 Although BGM in people on noninsulin therapies has not consistently shown clinically significant reductions in A1C levels, it may be

helpful when modifying meal plans, physical activity plans, and/or medications (particularly medications that can cause hypoglycemia) in conjunction with a treatment adjustment program. **E**

7.14 Consider potential interference of medications and substances on glucose levels measured by blood glucose meters. **B**

Major clinical trials of insulin-treated people with diabetes have included BGM as part of multifactorial interventions to demonstrate the benefit of intensive glycemic management on diabetes complications (28). BGM is thus an integral component of effective therapy for individuals using insulin. In recent years, CGM has emerged as a method for the assessment of glucose levels that improves outcomes compared with BGM in many settings (discussed below). Glucose monitoring (BGM or CGM) allows people with diabetes to evaluate their individual responses to therapy and assess whether glycemic goals are being safely achieved. Integrating glucose testing results into diabetes management can be a useful tool for guiding medical nutrition therapy and physical activity, preventing hypoglycemia, or adjusting medications (particularly prandial insulin doses or correction bolus doses). The specific needs and goals of the person with diabetes should dictate BGM and CGM frequency and timing. As recommended by the device manufacturers and the U.S. Food and Drug Administration (FDA), people with diabetes using CGM must also have access to BGM for multiple reasons, including whenever there is suspicion that the CGM is inaccurate, while waiting for the CGM device to warm up, when there is a disruption in CGM transmission, for calibration (if needed) or if a warning message appears, when CGM supplies are delayed, and in any clinical setting where glucose levels are changing rapidly (>2 mg/dL/min), which could cause a discrepancy between CGM and blood glucose values.

Meter Standards

Glucose meters meeting FDA guidance for meter accuracy provide the most reliable data for diabetes management. There are several current standards for the accuracy of blood glucose meters,

but the two most used are those of the International Organization for Standardization (ISO) (ISO 15197:2013) and the FDA (Table 7.1). In the U.S., currently marketed meters must meet the standard under which they were approved, which may not be the current standard. Moreover, the monitoring of current accuracy postmarketing is left to the manufacturer and not routinely checked by an independent source.

People with diabetes assume their glucose meter is accurate because it is FDA cleared, but that may not be the case. In prior analyses with glucose meters, 14 of 18 glucose meters met the minimum accuracy requirements (29). However, few studies have compared meters head-to-head.

Certain meter system characteristics, such as the use of lancing devices that are less painful (30) and the ability to reapply blood to a strip with an insufficient initial sample, or meters with integrated speech that can read aloud glucose levels for visually impaired individuals (31), may also be beneficial to people with diabetes (32) and may make BGM less burdensome to perform.

Use of Strips From Unlicensed Entities

People with diabetes should be advised against purchasing or reselling preowned or secondhand test strips, as these may give incorrect results. Only unopened and unexpired vials of glucose test strips should be used to ensure BGM accuracy.

Optimizing Blood Glucose Meter Use

Optimal use of BGM devices requires proper review and interpretation of data by both the person with diabetes and the health care professional to ensure

that data are used in an effective and timely manner. In a large cohort analysis of over 24,000 adults with both type 1 and type 2 diabetes, more frequent use of BGM was associated with lower A1C levels, with greater BGM frequency associated with lower A1C in people with type 1 diabetes across the lifespan (33,34). In young adults with type 1 diabetes, there was also a correlation between greater BGM frequency and lower A1C levels (34). Among those who check their blood glucose at least once daily, many reported taking no action when results were high or low (35). Some meters now provide advice to the user in real time when monitoring glucose levels (36), whereas others can be used as a part of integrated health platforms (37). People with diabetes should be taught how to use BGM data to adjust food intake, physical activity, or pharmacologic therapy to achieve their treatment goals. The ongoing need for and frequency of BGM should be reevaluated at each routine visit to ensure its effective use (34,38).

People With Diabetes Treated With Intensive Insulin Therapies

Glucose monitoring is particularly important for people with diabetes treated with insulin therapy to detect and prevent hypoglycemia and hyperglycemia. Most individuals on intensive insulin therapies (MDI or insulin pump therapy) should be encouraged to assess glucose levels using BGM (and preferably CGM with BGM backup) prior to meals and snacks, at bedtime, occasionally postprandially, prior to, during, and after physical activity, when they suspect hypoglycemia or hyperglycemia, after treating hypoglycemia until they are

normoglycemic, and prior to and while performing critical tasks such as driving. For many individuals using BGM alone, this requires doing finger sticks 6–10 times daily, although individual needs may vary. A database study of almost 27,000 children and adolescents with type 1 diabetes showed that, after adjusting for multiple confounders, increased daily frequency of BGM was significantly associated with lower A1C levels (−0.2% per additional check per day) and with fewer acute complications (39).

People With Diabetes Using Basal Insulin and/or Oral Agents and Noninsulin Injectables

The evidence is insufficient regarding when to prescribe BGM and how often monitoring is needed for insulin-treated people with diabetes who do not use intensive insulin therapy, such as those with type 2 diabetes taking basal insulin with or without oral agents and/or noninsulin injectables. However, for those taking basal insulin, assessing fasting glucose with BGM to inform dose adjustments to achieve blood glucose goals results in lower A1C levels (40).

In people with type 2 diabetes not taking insulin, studies have not consistently shown benefit, although the most benefit has been seen in individuals participating in structured clinical programs (41,42). Some individuals find BGM useful to provide insight into the impact of nutrition, physical activity, and medication management on glucose levels. Glucose monitoring may also be useful in assessing hypoglycemia, glucose levels during intercurrent illness, or discrepancies between measured A1C and glucose levels when there is concern an A1C

Table 7.1—Comparison of ISO 15197:2013 and FDA blood glucose meter accuracy standards

Setting	FDA*	ISO 15197:2013*
Hospital use	95% within 12% for BG ≥ 75 mg/dL 95% within 12 mg/dL for BG < 75 mg/dL 98% within 15% for BG ≥ 75 mg/dL 98% within 15 mg/dL for BG < 75 mg/dL	95% within 15% for BG ≥ 100 mg/dL 95% within 15 mg/dL for BG < 100 mg/dL 99% in A or B region of consensus error grid†
Home use	95% within 15% for all BG in the usable BG range‡ 99% within 20% for all BG in the usable BG range‡	

BG, blood glucose; FDA, U.S. Food and Drug Administration; ISO, International Organization for Standardization. To convert mg/dL to mmol/L, see endmemo.com/medical/unitconvert/Glucose.php. *Data shown in the FDA column are from the FDA (191). Data shown in the ISO column are from the FDA (192). †The range of blood glucose values for which the meter has been proven accurate and will provide readings (other than low, high, or error). ‡Values outside of the “clinically acceptable” A and B regions are considered “outlier” readings and may be dangerous to use for therapeutic decisions (193).

result may not be reliable in specific individuals (for more details, see section 2, “Diagnosis and Classification of Diabetes”). A key consideration is that performing BGM alone does not lower blood glucose levels. To be useful, the information must be integrated into clinical and self-management treatment plans. Further, as noted above, a recent systematic review with meta-analysis did support use of CGM in people with type 2 diabetes with benefits to glycemic management, individual experience, health care resource utilization, and cost-effectiveness (18,43).

Glucose Meter Inaccuracy

Although many meters function well under various circumstances, health care professionals and people with diabetes must be aware of factors that impair meter (and CGM) accuracy. A meter reading that seems discordant with the clinical picture needs to be retested or tested in a laboratory. Health care professionals in intensive care unit settings need to be particularly aware of the potential for incorrect meter readings during critical illness, and laboratory-based values should be used if there is any doubt. Some meters give error messages if meter readings are likely to be false (44).

Oxygen. Most currently available glucose monitors use an enzymatic reaction linked to an electrochemical reaction, either glucose oxidase or glucose dehydrogenase (45). Glucose oxidase monitors are sensitive to the oxygen available and should only be used with capillary blood in people with normal oxygen saturation. Higher oxygen tensions (i.e., arterial blood or oxygen therapy) may result in false low-glucose readings, and low oxygen tensions (i.e., high altitude, hypoxia, or venous blood readings) may lead to falsely elevated glucose readings. Glucose dehydrogenase-based monitors are generally not sensitive to oxygen.

Temperature. Because the reaction is sensitive to temperature, all monitors have an acceptable temperature range (45). Most will show an error if the temperature is unacceptable, but a few will provide a reading and a message indicating that the value may be incorrect.

Interfering Substances. There are several physiologic and pharmacologic factors that interfere with glucose readings measured

with either personal blood glucose meters or professional blood glucose meters used in various inpatient settings (neonatal intensive care units, hospital wards, and intensive care units) (45). Meters vary in terms of their sensitivity to interfering substances, and this information should be available in the prescribing information for the meter. Some of the possible interfering substances are listed in **Table 7.2**.

CONTINUOUS GLUCOSE MONITORING DEVICES

See **Table 7.3** for definitions of types of currently available CGM devices.

Recommendations

7.15 Use of CGM is recommended at diabetes onset and anytime thereafter for children, adolescents, and adults with diabetes who are on insulin therapy, **A** on noninsulin therapies that can cause hypoglycemia, **C** and on any diabetes treatment where CGM helps in management. **C** The specific CGM device and method for use should be made based on the individual's circumstances, preferences, and needs. **E**

7.16 In people with diabetes on insulin therapy, CGM devices should be used as close to daily as possible for maximal benefit. **A** People with diabetes should have uninterrupted access to their supplies to minimize gaps in CGM. **A**

7.17 During pregnancy for individuals with type 1 diabetes, CGM can help achieve glycemic goals (e.g., time in range and time above range) **A** and A1C goal **B** and may be beneficial for other types of diabetes in pregnancy. **E** See section 15, “Management of Diabetes in Pregnancy,” for more detail regarding use of technology in pregnancy.

7.18 In circumstances when consistent use of CGM is not feasible, consider periodic use of personal or professional CGM to adjust medication and/or lifestyle. **C**

7.19 Skin reactions, either due to irritation or allergy, should be assessed and addressed to aid in successful use of devices. **E**

7.20 People who wear CGM devices should be educated on potential interfering substances and other factors that may affect accuracy. **C**

CGM measures interstitial glucose (which correlates well with plasma glucose, although at times, it can lag if glucose levels are rising or falling rapidly). Although historically there were two basic types of personal CGM devices, real-time CGM (rtCGM) and intermittently scanned CGM (isCGM), now most available prescribed CGM devices have similar characteristics: no swiping required,

Table 7.2—Some of the more common interfering substances and/or conditions that affect blood glucose meters (for inpatient and outpatient use)

Substance or condition	Potential effects on glucose readings measured by BGMs*
Maltose†	Falsely higher blood glucose readings
Galactose	Falsely higher blood glucose readings
Xylose	Falsely higher blood glucose readings
N-Acetylcysteine	Falsely higher or lower blood glucose readings (depending on BGM design)
Acetaminophen	Falsely higher or lower blood glucose readings (depending on BGM design)
Dopamine	Falsely higher or lower blood glucose readings (depending on BGM design)
Pralidoxime (2-PAM)	Falsely higher or lower blood glucose readings (depending on BGM design)
Hydroxyurea	Falsely higher or lower blood glucose readings (depending on BGM design)
Vitamin C	Falsely higher or lower blood glucose readings (depending on BGM design)
Hematocrit (high)	Falsely lower blood glucose readings
Hematocrit (low)	Falsely higher blood glucose readings

*These are potential effects. There are blood glucose monitors (BGMs) that behave differently than listed in this table. Refer to product labeling for product-specific information. †Unmodified glucose dehydrogenase pyrroloquinoline quinone (GDH/PQQ) enzyme method only. Modern BGM designs do not incorporate unmodified GDH-PQQ enzyme.

Table 7.3—Continuous glucose monitoring devices

Type of device	Brand*	Availability	Alarms
rtCGM	Libre 2 Plus and Libre 3 Plus	Prescription	Yes
	Dexcom G6 and G7	Prescription	Yes
	Eversense 365	Prescription	Yes
	Guardian 4	Prescription	Yes
	Simplera	Prescription	Yes
OTC-CGM	Dexcom Stelo	OTC	No
	Abbott Lingo	OTC	No
Professional CGM	Abbott FreeStyle Libre Pro	In office	No
	Dexcom G6 Pro	In office	No

CGM, continuous glucose monitoring; isCGM, intermittently scanned CGM; OTC, over the counter; rtCGM, real-time CGM. *Generic names not available.

continuous stream of data, and adjustable alarms and alerts. If an individual is still using a CGM that requires scanning, the limitations of those systems should be addressed. There are two categories of CGM devices generally available for personal use: those prescribed for diabetes management (rtCGM) and over-the-counter CGM (OTC-CGM), which lacks alarms and alerts and can be used by people not taking diabetes medications that increase the risk of hypoglycemia. Anyone can purchase the OTC-CGM devices, including those without diabetes or with prediabetes who wish to assess their glycemic responses to their lifestyles, including the effects of food choices and exercise. Finally, there are what has been called professional CGM devices, which are devices owned and applied by health care professionals that generate glucose data (blinded or not) over a short period of time.

Table 7.3 provides definitions for the types of CGM devices. For people with type 1 diabetes using CGM, frequency of sensor use is an important predictor of A1C lowering for all age-groups (46,47).

Few real-time systems require calibration by the user, and the need to recalibrate varies in frequency depending on the device. However, all CGM systems require use of BGM to confirm accuracy, especially in settings where there is perceived discordance between sensor reading and the individual's perceived sense of their clinical situation.

Most CGM systems are designated as integrated CGM (iCGM) and cleared as a class II medical device by the FDA for integration with other digitally connected devices. The exact CGM that integrates with any given device (e.g., automated insulin system or connected insulin pen)

varies, and available options should be explored with individuals when choosing an integrated system.

Benefits of Continuous Glucose Monitoring

Data From Randomized Controlled Trials

Multiple randomized controlled trials (RCTs) have been performed using CGM devices, and the results have largely been positive in terms of reducing A1C levels and/or episodes of hypoglycemia if participants regularly wore the devices (46–53). The benefits of CGM have been shown regardless of age, sex, education or income levels, or baseline diabetes characteristics.

The initial studies were done primarily in adults, children, and adolescents with type 1 diabetes on insulin pump therapy and/or MDI (46,47,50,51,54). The primary outcome was met and showed benefit in adults of all ages (46,55,56), including older individuals (57–59). Data in children show that CGM use in young children with type 1 diabetes reduced hypoglycemia; in addition, behavioral support of parents of young children with diabetes using CGM showed the benefits of reducing hypoglycemia concerns and diabetes distress (46,51,60). Similarly, A1C level reduction was seen in adolescents and young adults with type 1 diabetes using rtCGM (50).

RCT data on CGM use in individuals with type 2 diabetes on MDI (61) or insulin (including basal insulin) plus noninsulin therapies (61–64) show consistent reductions in A1C levels and increases in TIR (70–180 mg/dL [3.9–10 mmol/L]) and time below range but not a reduction in rates of level 3 hypoglycemia (65). RCT data for CGM benefits in people with type 2 diabetes not using insulin are increasing and generally have

shown greater benefits of CGM compared with BGM for A1C, TIR, time below range, and time above range (TAR) as well as greater user-reported satisfaction (66,67). In addition, CGM benefits were reported in a population of adults with type 2 diabetes (on noninsulin and insulin-including therapy) with reduction in A1C levels, increase in TIR, and reduction of time in hyperglycemia (>180 mg/dL [>10 mmol/L] and >250 mg/dL [>13.9 mmol/L]) (62). Although glycemic metrics are improved, patient-reported outcomes have shown less consistent satisfaction in this individual population.

Although short-term use of CGM in youth with type 2 diabetes did not impact short-term glucose changes or A1C improvement, users reported behavioral changes with increased blood glucose measurements, increased insulin administration, and overall improved diabetes management and quality of life (68,69). The improvements in type 2 diabetes have largely occurred without changes in insulin doses or other diabetes medications. CGM discontinuation in individuals with type 2 diabetes on basal insulin caused partial reversal of A1C reduction and TIR improvements, suggesting that continued CGM use achieves the greatest benefits (17).

Observational and Real-world Studies

CGM systems are widely available in many countries for people with diabetes, and this allows for the collection of large amounts of data across groups of people with diabetes.

Data for isCGM in adults with diabetes include results from observational studies, retrospective studies, and analyses of registry and population data (70,71). Glycemic benefits in people with type 1 and type 2 diabetes (on MDI, basal insulin, and noninsulin therapies) have been seen in prospective and retrospective studies (49,72).

Reductions in acute diabetes complications, such as diabetic ketoacidosis (DKA), episodes of severe hypoglycemia or diabetes-related coma, and hospitalizations for hypoglycemia and hyperglycemia, have been observed in adults with type 1 or type 2 diabetes (73–75), with persistent effects observed even after 2 years of CGM initiation (76). Similar reductions of acute diabetes events and all-cause inpatient hospitalizations were seen in a retrospective review of

adults with type 2 diabetes treated with basal insulin or with noninsulin therapy 6 months after initiation of isCGM (77).

Retrospective data from rtCGM use in adults (78) with type 1 or type 2 diabetes treated with insulin showed that the use of rtCGM significantly lowered A1C levels and reduced rates of emergency department visits or hospitalizations for hypoglycemia but did not significantly lower overall rates of emergency department visits, hospitalizations, or hyperglycemia.

Recent data have emerged from a real-world observational analysis of rtCGM use in adults with type 2 diabetes not treated with insulin. In this study, rtCGM benefits were observed at 6 months and 12 months versus baseline, with reduction of mean glucose levels, reduction of glucose management indicator (GMI), increase in TIR, increase in time in tight target range (70–140 mg/dL [3.9–7.8 mmol/L]), and reduction in TAR >180 mg/dL (>10 mmol/L) and >250 mg/dL (>13.9 mmol/L) (79).

Real-time Continuous Glucose Monitoring Device Use in Pregnancy

CGM indication has expanded to include pregnancy for Dexcom G7, FreeStyle Libre 2, and FreeStyle Libre 3, which enhances care in this population (80,81). A discussion of CGM use in pregnancy can be found in section 15, “Management of Diabetes in Pregnancy.”

Use of Professional Continuous Glucose Monitoring and Intermittent Use of Personal Continuous Glucose Monitoring

Professional CGM devices, which provide retrospective data, either blinded or unblinded, for analysis can be used to identify patterns of hypoglycemia and hyperglycemia (82–84). Professional CGM

can be helpful to evaluate an individual's glucose levels when either rtCGM or isCGM is not available to the individual or they prefer a blinded analysis or a shorter experience with unblinded data. It can be particularly useful in individuals using agents that can cause hypoglycemia, as the data can be used to evaluate periods of hypoglycemia and make medication dose adjustments if needed. It can also be useful to evaluate periods of hyperglycemia.

Some data have shown the benefit of intermittent use of CGM (rtCGM or isCGM) in individuals with type 2 diabetes on noninsulin and/or basal insulin therapies (63,85). In these RCTs, people with type 2 diabetes not on intensive insulin therapy used CGM intermittently compared with those randomized to BGM. Both early (63) and late (63,86) improvements in A1C levels were found.

Furthermore, in a real-world study, the use of professional CGM in individuals with type 2 diabetes not on insulin at baseline and at 6 months of follow-up resulted in lower A1C at 6 months as well as a shift toward greater use of glucose-lowering medications with cardiometabolic benefits, such as sodium–glucose transporter 2 inhibitors and glucagon-like peptide 1 receptor agonists (87). Use of professional or intermittent CGM should always be coupled with analysis and interpretation for people with diabetes along with education, as needed, to adjust medication and change lifestyle behaviors (88–90).

Side Effects of Continuous Glucose Monitoring Devices

Contact dermatitis (both irritant and allergic) has been reported with all devices that attach to the skin (91–93). In some cases, this has been linked to

the presence of isobornyl acrylate, a skin sensitizer that can cause an additional spreading allergic reaction (94). It is important to ask CGM users periodically about adhesive reactions, as tape formulations may change over time. Patch testing can sometimes identify the cause of contact dermatitis (95). Identifying and eliminating tape allergens is important to ensure the comfortable use of devices and promote self-care (96–99). The PANTHER Program offers resources in English and Spanish at www.panther-program.org/skin-solutions. In some instances, using an implanted sensor can help avoid skin reactions in those sensitive to tape (100,101).

Substances and Factors Affecting Continuous Glucose Monitoring Accuracy

Sensor interference due to several medications/substances is a known potential source of CGM sensor measurement errors (Table 7.4). While several of these substances have been reported in the various CGM brands' user manuals, additional interferences have been discovered after the market release of these products. Hydroxyurea, used for myeloproliferative disorders and hematologic conditions, is one of the most recently identified interfering substances that cause a temporary increase in sensor glucose values discrepant from actual glucose values (102,103). Similarly, substances such as mannitol and sorbitol, when administered intravenously or as a component of peritoneal dialysis solution, may increase blood mannitol or sorbitol concentrations and cause falsely elevated readings of sensor glucose (104). Therefore, it is crucial to routinely review the medications and supplements used by the person with diabetes to

Table 7.4—Continuous glucose monitoring device interfering substances

Medication	Systems affected	Effect
Acetaminophen >4 g/day Any dose	Dexcom G6, Dexcom G7 Medtronic Guardian 4	Higher sensor readings than actual glucose Higher sensor readings than actual glucose
Ascorbic acid (vitamin C), >500 mg/day	FreeStyle Libre 2, FreeStyle Libre 3	Higher sensor readings than actual glucose
Ascorbic acid (vitamin C), >1,000 mg/day	FreeStyle Libre 2 Plus, FreeStyle Libre 3 Plus	Higher sensor readings than actual glucose
Hydroxyurea	Dexcom G6, Dexcom G7, Medtronic Guardian 4	Higher sensor readings than actual glucose
Mannitol (intravenously or as peritoneal dialysis solution)	Senseonics Eversense365	Higher sensor readings than actual glucose
Sorbitol (intravenously or as peritoneal dialysis solution)	Senseonics Eversense365	Higher sensor readings than actual glucose

identify possible interfering substances and advise them accordingly on the need to use additional BGM if sensor values are unreliable due to these substances.

INSULIN DELIVERY

Insulin Syringes and Pens

Recommendations

7.21 For people with insulin-requiring diabetes on multiple daily injections (MDI), insulin pens are preferred in most cases. Still, insulin syringes may be used for insulin delivery considering individual and caregiver preference, insulin type, availability in vials, dosing therapy, cost, and self-management capabilities. **C**

7.22 Insulin pens or insulin injection aids are recommended for people with dexterity issues or vision impairment or when decided by shared decision making to facilitate the accurate dosing and administration of insulin. **C**

7.23 Offer connected insulin pens for people with diabetes taking multiple daily insulin injections when appropriate. **B**

7.24 FDA-approved insulin dose calculators/decision support systems may be helpful for calculating insulin doses. **B**

Injecting insulin with a syringe or pen (105–111) is the insulin delivery method used by most people with diabetes (112), although inhaled insulin is also available. Others use insulin pumps or AID devices (see INSULIN PUMPS AND AUTOMATED INSULIN DELIVERY SYSTEMS, below). For people with diabetes who use insulin, insulin syringes and pens both can deliver insulin safely and effectively for the achievement of glycemic goals. Individual preferences, cost, insulin type, dosing therapy, and self-management capabilities should be considered when choosing among delivery systems. Trials with insulin pens generally show equivalence or small improvements in glycemic outcomes compared with using a vial and syringe. Many individuals with diabetes prefer using a pen because of its simplicity and convenience. It is important to note that while many insulin types are available for purchase as either pens or vials, others may be available in only one form or the other, and there may be significant cost differences between pens and vials (see **Table 9.4** for a

list of insulin product costs with dosage forms). Insulin pens may allow people with vision impairment or dexterity issues to dose insulin accurately (113–115), and insulin injection aids are also available to help with these issues. (For a helpful list of injection aids, see diabetes.org/living-with-diabetes/treatment-care/diabetes-technology-guide). Inhaled technosphere insulin can be useful for people with diabetes, providing an alternative method of insulin delivery with very fast onset of action.

The most common syringe sizes are 1 mL, 0.5 mL, and 0.3 mL, allowing doses of up to 100 units, 50 units, and 30 units, respectively, of U-100 insulin. Some 0.3-mL syringes have half-unit markings, whereas other syringes have markings in 1- to 2-unit increments. In a few parts of the world, insulin syringes still have U-80 and U-40 markings for older insulin concentrations and veterinary insulin, and U-500 syringes are available for the use of U-500 insulin. Syringes are generally used once but may be reused by the same individual in resource-limited settings with appropriate storage and cleansing (115).

Insulin pens offer added convenience by combining the vial and syringe into a single device. Insulin pens, allowing push-button injections, come as disposable pens with prefilled cartridges or reusable insulin pens with replaceable insulin cartridges. Pens vary with respect to dosing increment and minimal dose, ranging from half-unit doses to 2-unit dose increments, with the latter available in U-200 insulin pens. U-500 pens come in 5-unit dose increments. Some reusable pens include a memory function, which can recall dose amounts and timing. Insulin pens, once started, can be kept in use for variable durations, based on the type of insulin, usually for 28 days, ranging from 14 to 56 days. Needle thickness (gauge) and length are other considerations. Needle gauges range from 22 to 34, with a higher gauge indicating a thinner needle. A thicker needle can give a dose of insulin more quickly, while a thinner needle may cause less pain. Needle length ranges from 4 to 12.7 mm, with some evidence suggesting that shorter needles (4–5 mm) lower the risk of intramuscular injection with erratic absorption and possibly the development of lipohypertrophy. When reused, needles may be duller and thus injections may be more painful. Proper insulin injection technique is a

requisite for receiving the full dose of insulin with each injection. Concerns with technique and use of the proper technique are outlined in section 9, “Pharmacologic Approaches to Glycemic Treatment.”

Connected insulin pens are insulin pens with the capacity to record and/or transmit insulin dose data. Insulin pen caps are also available and are placed on existing insulin pens and may assist with calculating insulin doses and by providing a memory function. Some connected insulin pens and pen caps can be programmed to calculate insulin doses, can be synced with select CGM systems, and can provide downloadable data reports. These pens and pen caps are useful to people with diabetes for real-time insulin dosing and allow clinicians to retrospectively review the insulin delivery times and, in some cases, doses and glucose data to make informed insulin dose adjustments (116). A quantitative study showed that people with diabetes preferred connected pens because of their ability to log insulin doses and glucose levels automatically (116). In a multicenter RCT in people with type 1 diabetes, the use of an insulin pen cap was associated with improved glycemic outcomes at 6 weeks in the insulin cap group, with an increase in TIR and decrease in GMI and TAR (117). A systematic review of connected insulin pens or pen caps showed improvement of glucose outcomes whether as A1C reduction, TIR increase, or hypoglycemia reduction (118). A recent real-world study with multinational data collected from 3,954 adults with diabetes using a connected pen and CGM validated the fact that treatment engagement with a connected insulin pen is positively associated with glycemic outcomes. On the other hand, missing as little as two basal doses or four bolus insulin doses over a 14-day period would be associated with a clinically relevant decrease in TIR of $\geq 5\%$ (119).

Bolus calculators have been developed to aid dosing decisions (120–125). These systems are subject to FDA clearance to ensure safety and efficacy in terms of algorithms used and subsequent dosing recommendations. People interested in using these systems should be encouraged to use those that are FDA approved. Health care professional input and education can be helpful for setting the initial dosing calculations

with ongoing follow-up for adjustments as needed.

Insulin Pumps and Automated Insulin Delivery Systems

Recommendations

7.25a AID systems are the preferred insulin delivery method over MDI, CSII, and sensor-augmented pumps in people with type 1 diabetes, **A** adults with type 2 diabetes, **A** children and adolescents with type 2 diabetes, **E** and those with other forms of insulin-deficient diabetes. **B, C, D, E** Choice of an AID system should be made based on the individual's circumstances, preferences, and needs. **E**

7.25b Consider AID systems for select people with type 2 diabetes treated with basal insulin not achieving individualized glycemic goals. **B** Choice of an AID system should be made based on the individual's circumstances, preferences, and needs. **E**

7.26 Individuals with diabetes who have been using CSII and/or AID should have continued access across third-party payors. **E**

Stand-alone Insulin Pumps and AID Systems

Insulin pumps have been available in the U.S. for over 40 years. These devices deliver rapid-acting insulin throughout the day to manage glucose levels. Most insulin pumps use tubing to deliver insulin through a cannula, while a few attach directly to the skin without tubing (pods or patch pumps), and these systems have been approved for use in type 1 and type 2 diabetes. AID systems, which can adjust insulin delivery rates based on sensor glucose values, are preferred over nonautomated pumps and MDI in people with type 1 diabetes and have largely replaced the use of nonintegrated or standard insulin pumps. Recently, three AID systems were approved for use by people with type 2 diabetes.

Historically, studies that compared MDI with insulin pump therapy were relatively small and of short duration. However, a systematic review and meta-analysis concluded that pump therapy in people with type 1 diabetes has modest advantages for lowering A1C levels (-0.30% [95% CI -0.58 to -0.02]) and for reducing severe hypoglycemia rates in children,

adolescents, and adults (126). Real-world data on insulin pump use in individuals with type 1 diabetes show benefits in A1C levels and hypoglycemia reductions as well as total daily insulin dose reduction (127).

Although AID systems have been shown to improve outcomes compared with MDI and insulin pump therapy alone, the choice of insulin delivery system is up to the individual along with support from their diabetes care team (126). Thus, the choice of insulin delivery method is based on the characteristics of the person with diabetes and which method is most likely to benefit them. Diabetes Wise (diabeteswise.org/), for individuals with diabetes, Diabetes Wise Pro (pro.diabeteswise.org/), for health care professionals, and the PANTHER Program (pantherprogram.org/device-comparison-chart) have helpful websites to assist health care professionals and people with diabetes in choosing diabetes devices based on their individual needs and preferences.

Adoption of AID and pump therapy in the U.S. shows geographical variations, which may be related to health care professional preference or center characteristics (128) and socioeconomic status, as pump therapy is more common in individuals of higher socioeconomic status, as reflected by private health insurance, family income, and education (128). Given the barriers to optimal diabetes care observed in disadvantaged groups (129), addressing the differences in access to insulin pumps and other diabetes technologies may lower health disparities (130).

AID systems preferentially, as well as insulin pump therapy alone or along with CGM, can be successfully started at the time of diagnosis (131) or at any point when they are needed in the course of an individual's diabetes. These devices can be safely used in adults (including older adults), adolescents, and children (15,16). Practical aspects of pump therapy initiation include assessment of readiness of the person with diabetes and their caregivers, if applicable. There is no consensus on which factors are most predictive of success with insulin pump or AID therapy (132). However, an understanding of the technical features of the system and how to troubleshoot if problems are encountered is necessary for safe use.

Complications and Challenges of Infusing Insulin

Complications of infused insulin can be caused by issues with infusion sets (dislodgement and occlusion), which put individuals at risk for ketosis and DKA and thus must be recognized and managed early (133). Other pump skin issues include lipohypertrophy or, less frequently, lipoatrophy (134) and pump site infection. Discontinuation of pump therapy is relatively uncommon today; the frequency has decreased over the past few decades, and its causes have changed (135). Current reasons for discontinuation are problems with cost or wearability, loss of insurance, dislike of the pump, suboptimal glycemic outcomes, or psychosocial considerations (e.g., anxiety or depression) (130). Common barriers to pump therapy adoption in children and adolescents are concerns regarding the physical interference of the device, discomfort with the idea of having a device on the body, therapeutic effectiveness, and financial burden (136–138).

Description of AID Systems

AID systems consist of mainly three components: an insulin pump, a CGM system, and an algorithm that determines insulin delivery. Based on the model and brand of currently FDA-approved and -cleared AID systems, the algorithm can be hosted in the pump body, in an insulin pod, or on a phone app. All AID systems on the market today integrate with one or more CGM systems and adjust insulin delivery either by modulating the preprogrammed basal rates or by replacing the basal rates with microboluses or microdoses of insulin every 5 min.

The modulation of insulin delivery is done by increasing, decreasing, or pausing insulin based on the CGM feedback, the predicted direction of the glucose levels, and the speed with which the glucose levels are changing. Different AID systems modulate insulin based on predicted glucose levels at various times, most commonly 30 min or 1 h. Currently available AID systems have either fixed glucose targets or adjustable glucose targets, ranging from 87 to 180 mg/dL (4.8 to 10 mmol/L), depending on the system. Glucose targets are generally set up for 24 h but can also be adjusted in some systems with up to eight segments per

day. All current AID systems provide automated correction doses, whether embedded in the microdose adjustments every 5 min or by providing additional correction boluses with doses that are dependent on the various types of algorithms, with variable frequency and threshold glucose based on the type of control algorithm. Most AID systems can be used in manual mode, although this is generally not recommended, as the benefits of CGM modulation may be partially or totally lost. However, use of AID in manual mode may be necessary in some circumstances, therefore it is important to review and reassess manual-mode settings periodically. Current AID systems still require manual entry of carbohydrates for meal announcements or qualitative meal estimation announcements to calculate prandial doses.

Adjustments for physical activity are available in most AID systems currently on the market. These can be programmed in various time increments. In general, the glucose target is raised to prespecified levels based on AID systems, and these are often accompanied by more conservative insulin delivery to reduce the risk of hypoglycemia in the setting of increased insulin sensitivity other than physical activity, such as prolonged fasting or NPO status for procedures. Of note, some systems may still give autocorrection boluses if the glucose levels rise above a certain threshold even while the exercise/activity mode has been enabled. Details on the available AID systems and their features can be found at pantherprogram.org/device-type.

AID systems have largely replaced other methods of continuous subcutaneous insulin delivery due to the advantages they offer in insulin modulation to adjust insulin doses and minimize hypoglycemia and hyperglycemia.

Partial Closed-Loop Systems

Sensor-augmented pumps (SAPs) were the precursors of the currently used AID systems. They are discussed here more for historical perspective because they are no longer commonly used, having been replaced by more fully functional AID systems. SAPs consist of three components: an insulin pump, a CGM system, and an algorithm that automates insulin suspension when glucose is low or is predicted to go low within the next 30 min. Predictive low-glucose suspend systems have been shown to reduce time spent with glucose <70 mg/dL

(<3.9 mmol/L) without rebound hyperglycemia during a 6-week randomized crossover trial in people with type 1 diabetes of various ages (139). Similar results were seen in additional studies in adults and children with reduction of hypoglycemia (140–142).

Data from Pivotal Trials

All currently FDA-approved and -cleared AID systems were tested for safety and efficacy in their pivotal trials in children, adolescents, and adults with type 1 diabetes (143–145) as well as in adults with type 2 diabetes (146,147). These studies were conducted by following a variety of methodologies, including observational studies as well as RCTs. Regardless of the study design, all AID system pivotal trials that examined individuals 2 years old or older, including older adults, have consistently demonstrated superiority to either standard insulin delivery or SAP and/or usual care (for the randomized trials), with consistent improvement in A1C, increase in TIR, especially overnight, as well as reduction of time spent in hypoglycemia (in the studies in people with type 1 diabetes). The greatest improvements were seen with AID when used in individuals with the highest baseline A1C or lowest TIR (148). These systems may also lower the risk of exercise-related hypoglycemia (149) and have been shown to have psychosocial benefits (150–155). A review of the literature on the health and economic value of AID systems found that AID systems are cost-effective (156). AID is the standard of care for people with type 1 diabetes who are capable of safely using the device and should be the preferred method of insulin delivery in these individuals. The decision to use AID systems should be made based on the preference of the person with diabetes (and/or caregivers) and the availability of resources to provide necessary training, access, and support for their use.

Data From Real-world Studies

Data from real-world studies on AID systems have become available and continue to increase rapidly. These studies include large numbers of users, at times even 30-fold higher than the number of people studied in AID pivotal trials (157). It is important to emphasize that for some AID systems all data are automatically collected to the database (158), whereas for other systems data

are collected based on voluntary sharing to the database by AID users. A recent systematic review of AID real-world studies, with 20 studies representing 171,209 individuals, substantiated the results observed in the pivotal trials and have confirmed the clinical benefits of AID systems in people with type 1 diabetes. Newer systems have shown increased time spent in automation, and the real-world studies have retrospectively analyzed longer duration of system use compared with their respective pivotal trials, with most analyses occurring for more than 6 months and an average duration of 9 months (157). Benefits include improvement in A1C levels, TIR, and other glucometrics as well as psychosocial benefits (159–164).

Finally, real-world data showed that AID systems provide the same glycemic benefits to Medicare and Medicaid beneficiaries with type 1 and type 2 diabetes, emphasizing that access to this technology should be made available regardless of A1C levels and should be based on the individual's needs (165).

Automated Insulin Delivery Systems in Pregnancy

The use of AID systems in diabetes and pregnancy presents particular challenges, as the current FDA-approved AID systems (except for one that has been FDA approved but is not yet commercially available) have glucose goals that are not pregnancy specific and do not have algorithms designed to achieve pregnancy-specific glucose goals. Initiating or continuing AID systems during pregnancy needs to be assessed carefully. Selected individuals with type 1 diabetes should be evaluated as potential candidates for AID systems in the setting of expert guidance. The details on the use of AID systems in pregnancy are discussed in section 15, "Management of Diabetes in Pregnancy."

Insulin Pumps and Automated Insulin Delivery Systems in People With Type 2 and Other Types of Diabetes

Additional insulin delivery options in people with type 2 diabetes include disposable patch-like devices, which provide either a continuous subcutaneous insulin infusion of rapid-acting insulin (basal) with bolus insulin in 2-unit increments at the press of a button or bolus insulin only, delivered in 2-unit increments, used in

conjunction with basal insulin injections (166–169). Use of a technology as a means of insulin delivery is an individual choice for people with diabetes and should be considered an option in those who are capable of safely using the device.

Open-Source Automated Insulin Dosing

Recommendation

7.27 Support and provide diabetes management advice to people with diabetes who choose to use an open-source AID system. **B**

Open-source automated insulin dosing (OS-AID) algorithms provide the precise code that governs their operation, so health care professionals and people with diabetes can have a more complete understanding of risks and benefits of their use (170). Any commercial entity could provide the source code for their interoperable automated glycemic controller, but most choose not to. OS-AID algorithms are largely designed, maintained, and curated by people with diabetes and their caregivers. Many people with diabetes use these algorithms with cleared CGM systems and insulin pump components. The information on how to set up and manage these systems is freely available online.

OS-AID is the preferred term when referring to any open-source system (commercial or otherwise). It is important to note that the term “DIY” is not reflective of any aspect of these community-driven systems. No individual person has written all the code for these algorithms, and a large percentage of users do not build the software themselves (171). There are two main available algorithms, the OpenAPS algorithm and the Loop algorithm, which have been implemented on a variety of platforms.

The OpenAPS heuristic algorithm (implemented on a system on a chip in OpenAPS, Android smartphones as AndroidAPS, and iPhone as iAPS/Trio) is supported by large real-world studies (172) and a multicenter RCT (173). The OpenAPS algorithm also supports unannounced meals. In a single-center study of adolescents with type 1 diabetes randomized to AndroidAPS with quantitative carbohydrate announcements, qualitative announcements,

and no announcements, TIR was preserved across groups (174).

Loop, an open-source model predictive control algorithm, is implemented on iPhones as an app. Prospective real-world data from 558 adults and children with type 1 diabetes on this system (171) was used to support the FDA clearance of a variant called Tidepool Loop (175), now implemented commercially.

Both the Loop and OpenAPS algorithms offer direct management of algorithm aggressiveness through conventional pump settings. Therefore, it is advisable that health care professionals understand and offer support in tuning settings for these safe and effective technologies (170). This may include, for example, the adjustment of basal rates, insulin-to-carbohydrate ratios, or insulin sensitivity factors. As with any AID system, a backup insulin treatment plan is advisable.

Digital Health Technology

Recommendation

7.28 Consider combining technology (CGM, insulin pump, and/or diabetes apps) with online or virtual licensed coaching to improve glycemic outcomes in individuals with diabetes or prediabetes. **B**

Increasingly, people are turning to the internet for advice, coaching, connection, and health care. Diabetes, partly because it is both common and numeric, lends itself to the development of apps and online programs. Recommendations for developing and implementing a digital diabetes clinic have been published (176). The FDA approves and monitors clinically validated, digital, and usually online health technologies intended to treat a medical or psychological condition; these are known as digital therapeutics, or “digiceuticals” ([fda.gov/medical-devices/digital-health-center-excellence/device-software-functions-including-mobile-medical-applications](https://www.fda.gov/medical-devices/digital-health-center-excellence/device-software-functions-including-mobile-medical-applications)) (177). Other applications, such as those that assist in displaying or storing data, encourage a healthy lifestyle or provide limited clinical data support. Therefore, it is possible to find apps that have been fully reviewed and approved by the FDA and others designed and promoted by people with relatively little skill or knowledge in the clinical treatment of diabetes. There are insufficient data to

provide recommendations for specific apps for diabetes management, education, and support in the absence of RCTs and validation of apps unless they are FDA cleared.

An area of particular importance is that of online privacy and security. Established cloud-based data aggregator programs, such as Tidepool, Glooko, and others, have been developed with appropriate data security features and are compliant with the U.S. Health Insurance Portability and Accountability Act of 1996. These programs can help monitor people with diabetes and provide access to their health care teams (178). Consumers should read the policy regarding data privacy and sharing before entering data into an application and learn how they can manage the way their data will be used (some programs offer the ability to share more or less information, such as being part of a registry or data repository or not).

Many online programs offer lifestyle counseling to achieve weight loss and increased physical activity (179). Many include a health coach and can create small groups of similar participants on social networks. Some programs aim to treat prediabetes and prevent progression to diabetes, often following the model of the Diabetes Prevention Program (180,181). Others assist in improving diabetes outcomes by remotely monitoring clinical data (for instance, wireless monitoring of glucose levels, weight, or blood pressure) and providing feedback and coaching (182–187). There are text messaging approaches that tie into a variety of different types of lifestyle and treatment programs, which vary in terms of their effectiveness (188,189). There are limited RCT data for many of these interventions, and long-term follow-up is lacking. However, in a real-world observational study of individuals with type 2 diabetes treated with basal insulin, noninsulin glucose-lowering medications, or no medications, the use of a digital health solution and rtCGM resulted in reductions of GMI and TAR >180 mg/dL (>10 mmol/L) and >250 mg/dL (>13.9 mmol/L) as well as an increase in TIR by 15% and participation in a least one engagement activity per week (190). Therefore, even with limited data, for an individual with diabetes, opting in to one of these programs can

be helpful in providing support and, for many, is an attractive option.

Inpatient Care

Recommendations

7.29 In people with diabetes wearing personal CGM, the use of CGM should be continued when clinically appropriate during hospitalization, with confirmatory point-of-care glucose measurements for insulin dosing and hypoglycemia assessment and treatment under an institutional protocol. **B**
7.30 Continue use of insulin pump or AID in people with diabetes who are hospitalized when clinically appropriate. This is contingent upon availability of necessary supplies, resources, training, ongoing competency assessments, and implementation of institutional diabetes technology protocols. **C**

For details on technology use in the inpatient setting, see section 16, “Diabetes Care in the Hospital.”

The Future

The pace of development in diabetes technology is extremely rapid. New approaches and tools are available each year. It is difficult for research to keep up with these advances, because newer versions of the devices and digital solutions are already on the market by the time a study is completed. The most important consideration in all these systems is the person with diabetes. Technology selection must be appropriate and safe for the individual. Simply having a device or application does not change outcomes unless the human being engages with it appropriately to create positive health benefits. This underscores the need for the health care team to assist people with diabetes in device and program selection and to support their use through ongoing education and training. Expectations must be tempered by reality—we do not yet have technology that completely eliminates the self-care tasks necessary for managing diabetes, but the tools described in this section can make it easier to manage if disseminated equitably.

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8. Obesity and Weight Management for the Prevention and Treatment of Diabetes: Standards of Care in Diabetes—2026

American Diabetes Association
Professional Practice Committee for
Diabetes*

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The American Diabetes Association (ADA) “Standards of Care in Diabetes” includes the ADA’s current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. Members of the ADA Professional Practice Committee for Diabetes, an interprofessional expert committee, are responsible for updating the Standards of Care annually, or more frequently as warranted. For a detailed description of ADA standards, statements, and reports, as well as the evidence-grading system for ADA’s clinical practice recommendations and a full list of Professional Practice Committee members, please refer to Introduction and Methodology. Readers who wish to comment on the Standards of Care are invited to do so at professional.diabetes.org/SOC.

Obesity is a chronic, often relapsing disease with numerous metabolic, physical, and psychosocial complications, including a substantially increased risk for the development and progression of type 2 diabetes (1). There is strong and consistent evidence that obesity management can delay the progression from prediabetes to type 2 diabetes (2–6) and is highly beneficial in treating type 2 diabetes (7–15). In people with type 2 diabetes and overweight or obesity, modest weight loss improves glycemia and reduces the need for glucose-lowering medications, particularly insulin (7,16,17), and greater weight loss substantially reduces A1C and fasting glucose and may promote sustained diabetes remission (9,18–21). Metabolic surgery, which results in an average >20% body weight loss, greatly improving glycemia and often leading to remission of diabetes, improved quality of life, improved cardiovascular outcomes, and reduced mortality (22,23). Several therapeutic modalities, including intensive behavioral and lifestyle counseling, obesity pharmacotherapy, and metabolic surgery, may aid in achieving and maintaining meaningful weight loss and reducing obesity-associated health risks. This section aims to provide evidence-based recommendations for obesity and weight management, including behavioral, pharmacologic, and surgical interventions, in people with, or at high risk of, diabetes. Additional considerations regarding weight management in older individuals and children and adolescents can be found in section 13, “Older Adults,” and section 14, “Children and Adolescents.”

ASSESSMENT AND MONITORING OF THE INDIVIDUAL WITH OVERWEIGHT OR OBESITY

Recommendations

8.1 Use person-centered, nonjudgmental language that fosters collaboration between individuals and health care professionals, including person-first language

*A complete list of members of the American Diabetes Association Professional Practice Committee for Diabetes can be found at <https://doi.org/10.2337/dc26-SINT>.

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(e.g., “person with obesity” rather than “obese person” and “person with diabetes” rather than “diabetic person”). **E**

8.2a Screen for overweight and obesity using BMI annually. To confirm excess adiposity, additional assessments of body fat using anthropometric assessments (e.g., waist-to-hip ratio) or direct measurements (e.g., dual-energy X-ray absorptiometry, bioelectrical impedance analysis) could be considered where available/feasible. **E**

8.2b Monitor obesity-related anthropometric measurements at least annually to inform treatment considerations. During active weight management treatment, increase monitoring to at least every 3 months. **E**

8.3 Accommodations should be made to provide privacy during anthropometric measurements. **E**

8.4 In people with type 2 diabetes and overweight or obesity, weight management should represent a primary goal of treatment along with glycemic management. **A**

8.5 Provide weight management treatment, aiming for any magnitude of weight loss. Weight loss of 5–7% of baseline weight improves glycemia and other intermediate cardiovascular risk factors. **A** Sustained loss of >10% of body weight usually confers greater benefits, including disease-modifying effects and possible remission of type 2 diabetes **A** and may improve long-term cardiovascular outcomes and mortality. **B**

8.6 Individualize initial treatment approaches for obesity (i.e., lifestyle and nutritional therapy, pharmacologic therapy, or metabolic surgery) **A** based on the person’s medical history, life circumstances, and preferences. **C** Consider combining treatment approaches if appropriate. **C**

Obesity is defined by the World Health Organization as an abnormal or excessive fat accumulation that presents a risk to health (24). BMI (calculated as weight in kilograms divided by the square of height in meters [kg/m^2]) has been used widely to diagnose and stage obesity (overweight: BMI 25–29.9 kg/m^2 ; obesity class 1: BMI 30–34.9 kg/m^2 ; obesity class 2: BMI 35–39.9 kg/m^2 ; obesity class 3: BMI ≥ 40 kg/m^2). Despite its ease of measurement, BMI is not a perfect measure of adipose tissue mass and does not

measure adipose tissue distribution or function, and it does not factor in the presence of weight-related health or well-being consequences (25,26). BMI is especially prone to misclassification in individuals who are very muscular (athletes) or in those with low muscle mass and in populations with different body composition and cardiometabolic risk (27). It is recommended that excess adiposity be confirmed by either direct measurement of body fat, where available, or at least one anthropometric criterion (e.g., waist circumference, waist-to-hip ratio, or waist-to-height ratio) in addition to BMI, using validated methods and cutoff points appropriate to age, sex, and ethnicity and particularly in individuals with BMI 25–34.9 kg/m^2 and in certain populations (South Asian individuals), as these measurements better reflect metabolic disease (28). However, confirming excess adiposity in routine clinical practice may be both challenging and unnecessary in the U.S. adult population aged 20–59 years, in whom the prevalence of obesity by BMI is nearly identical to the obesity prevalence after confirmation of excess adiposity in the vast majority (29). Thus, although BMI is not a perfect measure of adiposity, it remains an acceptable measure for use by clinicians who may not have the resources to obtain additional measures of adiposity on all individuals.

Obesity is a key pathophysiologic driver of diabetes, other cardiovascular risk factors (e.g., hypertension, hyperlipidemia, metabolic dysfunction–associated steatotic liver disease [MASLD], and inflammatory state), and ultimately cardiovascular and kidney disease (30). Diabetes can further exacerbate obesity, including through the use of glucose-lowering therapies that lead to weight gain (e.g., insulin, sulfonylurea, and pioglitazone), and obesity can exacerbate hyperglycemia and diabetes, thereby setting up a vicious cycle that contributes to disease progression and occurrence of microvascular and macrovascular complications. As such, treatment goals for both glycemia and weight are recommended in people with diabetes to address both hyperglycemia and its underlying pathophysiologic driver (obesity) and therefore benefit the person holistically.

Weight stigma, fat bias, and antifat bias are ways to describe the bias toward people living in larger bodies. Fat bias is prevalent among health care professionals and the general public. Health care professionals are strongly encouraged to

increase their awareness of implicit and explicit weight-biased attitudes (31,32). Increasing empathy and understanding about the complexity of weight management among health care professionals is a useful avenue to help reduce weight bias (33). The Obesity Association, a subdivision of the American Diabetes Association, has recently developed guidelines on recognizing and addressing weight bias and stigma (32) and encourages adopting these guidelines to reduce weight bias and stigma.

A person-centered communication style that uses inclusive and nonjudgmental language and active listening to elicit individual preferences and beliefs and assesses potential barriers to care should be used to optimize health outcomes and health-related quality of life. Use person-first language (e.g., “person with obesity” rather than “obese person”) to avoid defining people by their condition (25,32,34,35). Measurement of weight and height (to calculate BMI) and other anthropometric measurements should be performed at least annually to aid the diagnosis of obesity. More frequent assessments (at least every 3 months) should be undertaken to monitor response to treatment during active weight management (36). Clinical considerations, such as the presence of comorbid heart failure or unexplained weight change, may warrant more frequent evaluation (37,38). If such measurements are questioned or declined by the individual, the health care professional should be mindful of possible prior stigmatizing experiences and query for concerns, and the value of monitoring should be explained as a part of the medical evaluation process that helps to inform treatment decisions (39,40). Accommodations should be made to ensure privacy during weighing and other anthropometric measurements, particularly for those individuals who report or exhibit a high level of disease-related distress or dissatisfaction. Anthropometric measurements should be performed and reported nonjudgmentally; such information should be regarded as sensitive health information.

Health care professionals should advise individuals with overweight or obesity and those with increasing weight trajectories that, in general, greater fat accumulation increases the risk of diabetes, cardiovascular disease, and all-cause mortality and has multiple adverse health and quality of life consequences. Health care professionals should also assess readiness to engage in

behavioral changes for weight loss and jointly determine behavioral and weight loss goals and individualized intervention strategies using shared decision-making (41). Strategies may include nutrition and eating pattern changes, physical activity and exercise, behavioral counseling, pharmacotherapy, medical devices, and metabolic surgery. The initial and subsequent therapeutic choices should be individualized based on the person's medical history, life circumstances, and preferences (42).

Among people with type 2 diabetes and overweight or obesity who have inadequate glycemic, blood pressure, and lipid management and/or other obesity-related metabolic complications, modest and sustained weight loss (5–7% of body weight) improves glycemia, blood pressure, and lipids and may reduce the need for disease-specific medications (7,16,17,43). In people with prediabetes, 5–7% weight loss reduces progression to diabetes (2,17,44–47). Greater weight loss produces additional benefits, including a reduction in all-cause mortality and cardiovascular mortality (20,21,48,49). Mounting data have shown that >10% body weight loss usually confers greater benefits on glycemia and improves other metabolic comorbidities, including cardiovascular outcomes, metabolic dysfunction–associated steatohepatitis (MASH), MASLD, adipose tissue inflammation, and sleep apnea, as well as physical comorbidities and quality of life (6,20,21,30,45,49–58). In addition, some studies showed diabetes remission can be maintained for 2–5 years depending on the duration of diabetes (with responders having better β -cell function at baseline) (59).

With the increasing availability of more effective treatments, individuals with diabetes and overweight or obesity should be informed of the potential benefits of both modest and more substantial weight loss and guided in the range of available treatment options, as discussed in the sections below. Shared decision-making should be used when counseling on behavioral changes, intervention choices, and weight management goals.

NUTRITION, PHYSICAL ACTIVITY, AND BEHAVIORAL THERAPY INTERVENTIONS

Recommendations

8.7 Nutrition, physical activity, and behavioral therapy are recommended

for people with type 2 diabetes and overweight or obesity to achieve both weight and health outcome goals. **B**

8.8a Interventions including high frequency of counseling (≥ 16 sessions in 6 months) with focus on nutrition changes, physical activity, and behavioral strategies to achieve a 500–750 kcal/day energy deficit (irrespective of macronutrient composition) should be recommended for weight loss when available. **A**

8.8b If access to such interventions is limited, consider alternative structured programs delivering nutrition changes, physical activity, and behavioral counseling (e.g., remote, telehealth, mobile app). **E**

8.9 Nutrition recommendations should be individualized to the person's preferences and nutritional needs. Use nutritional plans that create an energy deficit, while still following general nutritional guidance, to achieve weight loss. **A**

8.10 When developing a plan of care, consider systemic, structural, cultural, and socioeconomic factors that may impact nutrition patterns and food choices, such as food insecurity and hunger, access to healthful food options, and other social determinants of health. **C**

8.11 For those who achieve weight loss goals, continue to monitor progress, provide ongoing support, and recommend continuing interventions to maintain weight goals long term. **E** Effective long-term (≥ 1 year) weight maintenance programs provide monthly contact and support, include frequent self-monitoring of body weight (weekly or more frequently) and other self-monitoring strategies (e.g., food diaries or wearables), and encourage regular physical activity (200–300 min/week). **A**

8.12 Short-term nutrition intervention using structured, very-low-calorie meals (800–1,000 kcal/day) should be prescribed only to carefully selected individuals by trained practitioners in medical settings with close monitoring. Long-term, comprehensive weight maintenance strategies and counseling should be integrated to maintain weight loss. **B**

8.13 Nutritional supplements are not recommended, as they have not been shown to be effective for weight loss. **A**

8.14 Counsel and regularly monitor individuals pursuing intentional weight loss to ensure adequate nutritional intake, with particular attention to preventing protein insufficiency and micronutrient deficiencies. **E**

For a more detailed discussion of lifestyle management approaches and recommendations, see section 5, “Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes.” For a detailed discussion of nutrition-specific interventions, please refer to “Nutrition Therapy for Adults With Diabetes or Prediabetes: A Consensus Report” (60).

Behavioral Interventions

Numerous behavioral interventions have demonstrated positive effects from reducing energy intake, increasing physical activity, or some combination of these key lifestyle behaviors (61). The Look AHEAD (Action for Health in Diabetes) randomized controlled trial (RCT) demonstrated that people with obesity and type 2 diabetes could achieve and maintain long-term (up to 8 years after trial conclusion) weight loss by participating in a prospective intensive lifestyle intervention (ILI). Approximately half of ILI participants lost and maintained $\geq 5\%$ of their initial body weight (46). Additionally, compared with the diabetes support and education group, ILI participants who lost $\geq 10\%$ at 1 year had a 21% reduced risk of mortality (hazard ratio 0.79 [95% CI 0.67, 0.94]; $P = 0.007$) (62). Culturally tailoring behavioral interventions could be an additional useful tool for improving the impact of interventions (63–65).

To achieve significant weight loss with lifestyle behavior change programs, creating a 500–750 kcal/day energy deficit is recommended. For most women, this is equal to consuming approximately 1,200–1,500 kcal/day, and for most men, this is equal to consuming approximately 1,500–1,800 kcal/day, with adjustment for the individual's baseline body weight. Some RCTs report less than 5% weight loss in adults with diabetes and overweight or obesity following a lifestyle behavioral intervention, but this limited amount of weight loss has not been shown to improve glycemia, lipids, or blood pressure – rather, a minimum weight loss of 5% or more seems necessary to achieve metabolic improvements (66). Weight loss benefits are progressive; more intensive

weight loss goals (>7%, >10%, >15%) can achieve further health improvements if these goals can be feasibly and safely attained. Almost one-third of the Look AHEAD intensive lifestyle group participants lost and maintained $\geq 10\%$ of their initial body weight at 8 years and required fewer glucose-, blood pressure-, and lipid-lowering medications than those randomly assigned to standard care (46).

Nutrition interventions can create the necessary energy deficit to promote weight loss in many ways, and no single way is best (19,67–69). Altering macronutrient content and using meal replacement plans prescribed by trained professionals are two commonly used approaches (70). Reducing processed and ultraprocessed food intake is also an encouraging area of ongoing weight loss research. The Preventing Overweight Using Novel Dietary Strategies (POUNDS) Lost trial reported small but significant improvements when ultraprocessed foods were replaced isocalorically by less processed foods, with improved trunk fat loss ($\beta = 3.9$ [95% CI -7.01 to -0.70]; $P = 0.02$) (71). The specific nutrition and lifestyle choices should be based on the individual's health status, maintaining or improving nutrition status and overall wellness, clinical considerations, social determinants of health, overall preferences, and other cultural and personal circumstances that affect eating and activity patterns (72) (see section 5, "Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes," for more discussion on processed and ultraprocessed foods).

There continues to be debate on the physiological basis of obesity (73,74), and low carbohydrate eating patterns continue to be of interest for people with diabetes and health care professionals. A 2022 meta-analysis of RCTs 12 weeks to 2 years in duration was conducted in people with overweight or obesity and with or without diabetes. Low carbohydrate diets were defined as nonketogenic, >50 g to 150 g carbohydrate per day, or <45% of total energy intake. Both at 3–12 months and up to 2 years after randomization, there were no greater benefits for those consuming low carbohydrate over balanced carbohydrate (defined as carbohydrate intake of 45–65% of total energy) in people with or without diabetes. Additionally, the authors concluded change in A1C was not meaningfully different

among the groups (mean difference -0.14%) (75).

Based on two of the largest RCTs completed in the U.S. investigating lifestyle behavior change—the Diabetes Prevention Program (DPP) and Look AHEAD—proven intensive behavioral interventions generally include ≥ 16 sessions during an initial 6 months and focus on durable nutritional changes, physical activity, and behavioral strategies to achieve a ~ 500 –750 kcal/day energy deficit. Such interventions should be provided by trained individuals and can be conducted face-to-face or remotely and on an individual or group basis (66,76). Assessing a person's motivation level, life circumstances, cultural considerations, socioeconomic factors, and ability to implement behavioral changes to achieve weight loss should be considered along with medical status when such interventions are recommended and initiated (41,77).

Very-low-calorie interventions (usually 800–1,000 kcal/day) are another approach that might be appropriate in some people with diabetes and obesity. As evidenced by findings from the U.K.-based DiRECT (Diabetes Remission Clinical Trial), structured, very-low-calorie eating patterns, using high-protein foods and meal replacement products, may increase the pace and/or magnitude of initial weight loss and glycemic improvements compared with standard behavioral interventions (20,21,78). However, such intensive nutritional interventions should be provided only by trained and experienced professionals in medical settings with close ongoing monitoring and integration with behavioral support and counseling, and only for a short term (generally up to 3 months). Furthermore, due to the high risk of complications (electrolyte abnormalities, severe fatigue, cardiac arrhythmias, etc.), very-low-calorie intensive interventions should be prescribed only to carefully selected individuals, such as those requiring weight loss and/or glycemic management before surgery, if benefits exceed potential risks (79,80). As weight recurrence is common, such interventions should include long-term, comprehensive weight maintenance strategies and counseling to maintain weight loss and behavioral changes (81).

Despite widespread marketing and exorbitant claims, there is no clear evidence that nutrition supplements (e.g., herbs, vitamins and minerals, amino acids, enzymes, and antioxidants) are effective for obesity

management or weight loss (82–84). Several large systematic reviews show that most trials evaluating nutrition supplements for weight loss are of low quality and at high risk of bias. High-quality published studies show little or no weight loss benefits.

It is important to monitor nutrition intake in individuals with diabetes undergoing treatment for obesity to prevent or mitigate nutrition deficiencies (85,86). Multivitamin mineral supplements can be considered for individuals who consume less than 1,200 kcal/day, exclude micronutrient nutrient-rich food groups from their usual intake (e.g., fruits and vegetables, whole grains, proteins, nuts, and seeds), are strict vegetarians, have underlying health conditions that impair nutrient absorption, are older (aged >50 years), or experience excessive weight loss (87). Those experiencing significant (>20%) or rapid (>4% per month) weight loss should be screened for micronutrient deficiencies (88). Screening for micronutrient deficiencies should be guided by general clinical judgment, as there are no universal recommendations for how often to screen. Some micronutrients of concern include iron, calcium, magnesium, zinc, and vitamins A, D, E, K, B1, B12, and C (89).

Monitoring protein and fiber intake is also important for people undergoing weight loss treatment. To preserve lean mass, health care professionals should emphasize the importance of optimizing protein intake alongside resistance training and encourage protein supplementation as needed (90). Also encouraging adequate fiber and water intake to prevent and manage constipation for people consuming very-low-calorie eating patterns can be useful. Referral to a registered dietitian nutritionist can streamline this education.

For a more detailed discussion of nutrition and physical activity in the context of diabetes and weight loss, see section 5, "Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes."

For people undergoing metabolic surgery, it is advised to provide corrective supplementation in cases of documented deficiency (91) and prophylactically (92). See METABOLIC SURGERY, below, for more details on nutrition guidance for people who have undergone metabolic surgery.

Physical activity is beneficial to people with diabetes and overweight or obesity for numerous reasons, primarily for maintaining and improving overall health, and

should be encouraged not only for weight loss. Rather, physical activity should be encouraged because it can improve quality of life, cardiorespiratory fitness, and glyce-mic management efforts and reduce mor-tality (93–96). Like all adults, people with overweight and obesity should be encour-aged to do activities they enjoy, with an eventual goal of getting 150 min of physi-cal activity per week. For a more detailed discussion of physical activity and exercise, see section 5, “Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes.”

Health disparities adversely affect peo-ple who have systematically experienced greater obstacles to health based on their race or ethnicity, socioeconomic status, gender identity, disability, or other factors. Overwhelming research shows that these disparities can significantly affect health outcomes, including increasing the risk for obesity, diabetes, and diabetes-related complications. Health care professionals should evaluate systemic, structural, and socioeconomic factors that may impact food choices, access to healthful foods, and nutrition patterns; behavioral pat-terns, such as neighborhood safety and availability of safe outdoor spaces for physical activity; environmental expo-sures; access to health care; social con-texts; and, ultimately, diabetes risk and outcomes. For a detailed discussion of social determinants of health, refer to “Social Determinants of Health: A Sci-entific Review” (97).

Maintaining weight loss is of paramount importance, and people with type 2 diabe-tes and overweight or obesity who have lost weight should be offered long-term (≥ 1 year) comprehensive weight loss maintenance programs. Weight loss maintenance programs should be delivered by an interprofessional team with appropriate training and experience in implementing long-term weight main-tenance programs. While we acknowl-edge that most insurers, Medicare, and Medicaid are not currently covering many long-term weight maintenance programs, there is evidence to support their effec-tiveness and benefits (46,66,98) on both personal and population levels. Weight maintenance programs should include at least monthly contact with trained indi-viduals and focus on ongoing monitoring of body weight (weekly or more fre-quently) and/or other self-monitoring strategies such as tracking food and

beverage intake and steps, continued fo-cus on nutrition and behavioral changes, and participation in high volume of physi-cal activity (200–300 min/week) (99, 100). Some commercial and proprietary weight loss programs have shown prom-ising weight loss results; however, results vary across programs, most lack evi-dence of effectiveness, many do not satisfy guideline recommendations, and some promote unscientific and possibly dangerous practices (101,102). Along with routine medical management visits, people with obesity and diabetes or predi-abetes should be screened during diabetes self-management education and support and medical nutrition therapy encounters for a history of dieting and past or current disordered eating behaviors. See section 5, “Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes,” for more information on disordered eating and the role of behavioral health counsel-ing in obesity management.

PHARMACOTHERAPY

Recommendations

8.15 Whenever clinically appropriate, engage other care team members to minimize use of weight-promoting med-ications for treatment of other condi-tions among adults with diabetes and obesity. **E**

8.16 When choosing glucose-lowering medications for people with type 2 diabe-tes and overweight or obesity, priori-tize medications with beneficial effect on weight. **B**

8.17 Obesity pharmacotherapy should be considered for people with diabetes and overweight or obesity along with lifestyle changes. Potential benefits and risks must be considered. **A**

8.18 In people with diabetes and over-weight or obesity, the preferred phar-macotherapy should be a glucagon-like peptide 1 receptor agonist or dual glucose-dependent insulinotropic poly-peptide and glucagon-like peptide 1 re-ceptor agonist with greater weight loss efficacy (i.e., semaglutide or tirzapa-tide), especially considering their added weight-independent benefits. **A**

8.19 Obesity pharmacotherapy indi-cated for chronic therapy should be continued beyond reaching weight loss goals to maintain the health ben-efits, as discontinuation often results in recurrence of weight gain and worsening

or reemergence of cardiometabolic risk factors. **B**

8.20 Individualize the dose and the dose titration approach of obesity pharmacotherapy to balance effective-ness, health benefits, and tolerability; the optimal treatment dose may not be the maximum approved dose. **B**

8.21 In people with diabetes not reaching weight treatment goals, mod-ify or intensify treatment with addi-tional approaches, including structured lifestyle management programs, meta-bolic surgery, **A** and additional or alter-native pharmacologic agents. **B**

Glucose-Lowering Therapy

Numerous effective glucose-lowering med-ications are currently available. However, to achieve both glycemic and weight man-agement goals for diabetes treatment, health care professionals should prioritize the use of glucose-lowering medications with a beneficial effect on weight. Agents associated with clinically meaningful weight loss include glucagon-like peptide 1 (GLP-1) receptor agonists (RAs) and a dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 RA (tirzapa-tide), and they are the preferred agents in individuals with stable insurance cov-erage. Sodium–glucose cotransporter 2 inhibitors, metformin, and amylin mim-etics are also associated with weight loss, although the magnitude of weight loss is much smaller ($<5\%$ body weight loss). Di-peptidyl peptidase 4 inhibitors, centrally acting dopamine agonist (bromocriptine), α -glucosidase inhibitors, and bile acid se-questrants (colesevelam) are considered weight neutral. In contrast, insulin secreta-gogues (sulfonylureas and meglitinides), thiazolidinediones, and insulin are often as-sociated with weight gain (see section 9, “Pharmacologic Approaches to Glycemic Treatment”).

Concomitant Medications

Health care professionals should care-fully review the individual’s concomitant medications and, whenever clinically ap-propriate, engage other care team mem-bers to minimize or provide alternatives for medications that promote weight gain (103–106). Examples of medications associated with weight gain include anti-psychotics (e.g., clozapine, olanzapine, and risperidone), some antidepressants (e.g., tricyclic antidepressants, some selective

serotonin reuptake inhibitors, and monoamine oxidase inhibitors), glucocorticoids, injectable progestins, some anticonvulsants (e.g., gabapentin and pregabalin), β -blockers (e.g., atenolol, metoprolol, and propranolol), and possibly sedating antihistamines and anticholinergics (103). The use of weight promoting medication can hinder the effectiveness of lifestyle interventions for weight loss in people with diabetes. Notably, a post hoc analysis of the Look AHEAD study showed a negative association between the use of weight-promoting or obesogenic medications and weight loss outcomes. The association was dose-dependent—participants using two or more obesogenic medications were less likely to achieve the 5% and 10% weight loss benchmarks than those using one medication (106).

Approved Obesity Pharmacotherapy

The U.S. Food and Drug Administration (FDA) has approved several medications for obesity as adjuncts to a reduced-calorie eating pattern and increased physical activity in individuals with BMI ≥ 30 kg/m² or ≥ 27 kg/m² with one or more obesity-associated comorbid conditions (e.g., type 2 diabetes, hypertension, and/or dyslipidemia). Nearly all FDA-approved obesity pharmacotherapies have been shown to improve glycemia in people with type 2 diabetes and delay progression to type 2 diabetes in at-risk individuals (4,5,11–14,54,107–111) and some of these agents (e.g., liraglutide, semaglutide, and tirzepatide) have a dual indication for glucose lowering as well as weight management. Phentermine and other older adrenergic agents are approved for short-term treatment (112), while all others are approved for long-term treatment (Tables 8.1 and 8.2). Refer to section 14, “Children and Adolescents,” for medications approved for adolescents with obesity. In addition, setmelanotide, a melanocortin 4 receptor agonist, is approved for use in cases of rare genetic mutations resulting in severe hyperphagia and extreme obesity, such as leptin receptor deficiency and proopiomelanocortin deficiency.

In people with type 2 diabetes and overweight or obesity, agents with both glucose-lowering and weight loss effects are preferred (refer to section 9, “Pharmacologic Approaches to Diabetes Treatment”) and include agents from the GLP-1 RA class and the dual GIP and

GLP-1 RA class (collectively referred to as nutrient-stimulated hormone-based therapeutics, a class that also includes other investigational agents that act on various nutrient-stimulated hormonal pathways, like glucagon and amylin). Should use of these medications not result in achievement of weight management goals, or if they are not tolerated or are contraindicated, other obesity treatment approaches should be considered. In the Effect and Safety of Semaglutide 2.4 mg Once-Weekly in Subjects With Overweight or Obesity and Type 2 Diabetes (STEP 2) trial, semaglutide 2.4 mg resulted in a body weight loss of 6.2% more than placebo and A1C lowering of 1.2% more than placebo after 68 weeks (54). In the Efficacy and Safety of Tirzepatide Once Weekly in Participants With Type 2 Diabetes Who Have Obesity or Are Overweight: A Randomized, Double-Blind, Placebo-Controlled Trial (SURMOUNT-2), tirzepatide resulted in body weight loss of 9.6% and 11.6% more than placebo and A1C lowering of 1.55% and 1.57% more than placebo after 72 weeks of treatment with the 10 mg and 15 mg doses, respectively, with adverse effects similar to those seen with the GLP-1 RA class (109). The observed weight loss with obesity pharmacotherapy is lower in people with diabetes than in those of similar baseline weight without diabetes; therefore, it is important to appropriately manage expectations of individuals with diabetes and health care professionals. Success should be framed as weight loss plus glycemic improvement, lower insulin needs and cardiovascular benefit. Obesity pharmacotherapy has demonstrated multiple additional benefits beyond weight loss and improvement in glucose management. Some such examples include improvements in cardiovascular risk factors (e.g., blood pressure and lipids), inflammation, obstructive sleep apnea, MASLD and MASH, and symptoms related to heart failure with preserved ejection fraction (113–116). Liraglutide 1.8 mg and semaglutide 1 mg (doses approved for type 2 diabetes, which are lower than those approved for the treatment of obesity) demonstrated reduction in cardiovascular events in people with type 2 diabetes who are either at high risk for cardiovascular disease or have established cardiovascular disease (55,117). Additionally, semaglutide 2.4 mg (dose approved for the treatment of obesity) also demonstrated

reduction in cardiovascular events in people with overweight or obesity and preexistent cardiovascular disease but without diabetes (118).

Health care professionals should be knowledgeable about the dosing, benefits, and risks for each treatment option to balance the potential benefits of successful weight loss against the potential risks for each individual. The high risk and prevalence of cardiovascular disease in people with diabetes must be balanced against the lack of long-term cardiovascular outcomes trial data for agents like combination naltrexone and bupropion and combination phentermine and topiramate. The response to all obesity pharmacotherapies is highly heterogeneous; therefore, their weight loss effectiveness should be reevaluated after initiation and therapy adjustments should be considered, if needed. All these medications are contraindicated in individuals who are pregnant or actively trying to conceive and are not recommended for use in individuals who are nursing. Individuals of childbearing potential should receive counseling regarding the use of reliable methods of contraception while using weight loss medications. Tirzepatide in particular may reduce the efficacy of oral hormonal contraceptives due to delayed gastric emptying, an effect that is largest after the first dose and diminishes over time. Individuals using oral hormonal contraceptives should switch to a nonoral contraceptive method or add a barrier method of contraception for 4 weeks after initiation and for 4 weeks after each dose escalation.

Nutrition deficiencies might be more of a concern in people receiving pharmacotherapy for obesity management. A recent retrospective cohort study quantified nutritional deficiencies among a large cohort of people—461,382 U.S. adults prescribed GLP-1 RAs between 2017 and 2022, in which more than half had obesity or overweight and more than 80% had type 2 diabetes. The analysis showed that nearly 13% of those in the cohort were diagnosed with nutritional deficiencies after 6 months and over 22% after 12 months. Vitamin D deficiency was the most frequently diagnosed subtype (6-month incidence was 7.5%; 12-month incidence was 13.6%) (85). Thus, choice of therapy should be guided by person-centered treatment factors, including comorbidities, considerations of adverse effects and treatment burden, treatment cost and accessibility,

Table 8.1—Obesity pharmacotherapy in individuals with type 2 diabetes

Medication name	Treatment arm: weight loss from baseline	Time frame for weight loss (weeks)*	Common side effects	Possible safety concerns and considerations
Sympathomimetic amine anorectic: approved for short-term use only				
Phentermine (183,184)†	• 15 mg q.d.; 7.4% • 7.5 mg q.d.; 6.6% • Placebo; 2.3%	28	Dry mouth, insomnia, dizziness, irritability, increased blood pressure, elevated heart rate	• Contraindicated for use in combination with monoamine oxidase inhibitors • Contraindicated with a history of cardiovascular disease • Do not use if at high risk for glaucoma due to risk of acute angle-closure glaucoma
Lipase inhibitor				
Orlistat (4,185)‡	• 120 mg t.i.d.; 9.6% • Placebo; 5.6%	52	Abdominal pain, flatulence, fecal urgency	• Contraindicated in cholestasis • Potential malabsorption of fat-soluble vitamins (A, D, E, K) and of certain medications (e.g., cyclosporine, thyroid hormone, anticonvulsants) • Rare cases of severe liver injury reported • Cholelithiasis reported • Nephrolithiasis reported. Monitor renal function and discontinue if oxalate nephropathy occurs
Sympathomimetic amine anorectic/antiepileptic combination				
Phentermine/topiramate ER (54,116)§	• 15 mg/92 mg q.d.; 9.8% • 7.5 mg/46 mg q.d.; 7.8% • Placebo; 1.2%	56	Constipation, paresthesia, insomnia, nasopharyngitis, xerostomia, increased blood pressure, nephrolithiasis	• Contraindicated for use in combination with monoamine oxidase inhibitors • Contraindicated during pregnancy due to risk of fetal harm with topiramate • Cognitive impairment associated with rapid dose titration or high initial doses • Caution with cardiovascular disease • Do not use if at high risk for glaucoma due to risk of acute angle-closure glaucoma
Opioid antagonist/antidepressant combination				
Naltrexone/bupropion ER (13,186)	• 16 mg/180 mg b.i.d.; 5% • Placebo; 1.8%	56	Constipation, nausea, headache, xerostomia, insomnia, elevated heart rate and blood pressure	• Contraindicated in people with unmanaged hypertension and/or seizure disorders • Contraindicated for use with chronic opioid therapy • Acute angle-closure glaucoma may occur • Increased blood pressure and heart rate may occur; monitor in people with cardiovascular and cerebrovascular disease Boxed warning: • Risk of suicidal behavior/ideation in people younger than 24 years old who have depression
GLP-1 receptor agonist				
Liraglutide (14,55,187)	• 3.0 mg q.d.; 6% • 1.8 mg q.d.; 4.7% • Placebo; 2%	56	Gastrointestinal side effects (nausea, vomiting, diarrhea, esophageal reflux, constipation)	The following apply to both GLP-1 receptor agonists: • Provide guidance on discontinuation prior to surgical procedures to mitigate potential for pulmonary aspiration with general anesthesia or deep sedation

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Table 8.1—Continued

Medication name	Treatment arm; weight loss from baseline	Time frame for weight loss (weeks)*	Common side effects	Possible safety concerns and considerations
Semaglutide (54,117,188)	• 2.4 mg weekly; 9.6% • 1.0 mg weekly; 7% • Placebo; 3.4%			• Pancreatitis: acute pancreatitis has been reported, but causality has not been established. Do not initiate if at high risk for pancreatitis and discontinue if pancreatitis is suspected • Biliary disease: evaluate for gallbladder disease if cholelithiasis or cholecystitis is suspected; avoid use in at-risk individuals • Gastrointestinal disorders (severe constipation and small-bowel obstruction/ileus progression) • Diabetic retinopathy: close monitoring of retinopathy in those at high risk (older individuals and those with longer duration of type 2 diabetes [≥ 10 years]) • Nonarteritic anterior ischemic optic neuropathy reported; rare incidence. Monitor for this during eye examinations • Impact on drug absorption: orally administered drug absorption may be impaired during dose titration (including oral contraceptives) • Gastrointestinal side effects: counsel on potential for gastrointestinal side effects; provide guidance on dietary modifications to mitigate gastrointestinal side effects (reduction in meal size, mindful eating practices [e.g., stop eating once full], decreasing intake of high-fat or spicy food); consider slower dose titration for those experiencing gastrointestinal challenges. Not recommended for individuals with gastroparesis • Hypoglycemia (with concomitant use of insulin or sulfonylurea) Boxed warning: • Risk of thyroid C-cell tumors in rodents; human relevance not determined; do not use in individuals with personal or family history of medullary thyroid cancer or multiple endocrine neoplasia type 2
Dual GIP and GLP-1 receptor agonist Tirzepatide (109,189)	• 15 mg weekly; 14.7% • 10 mg weekly; 12.8% • Placebo; 3.2%	72	Gastrointestinal side effects (nausea, vomiting, diarrhea, esophageal reflux, constipation)	Same as for GLP-1 receptor agonists, with addition of the following: • Monitor effects of oral medications with narrow therapeutic index (warfarin) or whose efficacy is dependent on threshold concentration • Advise individuals using oral contraceptives to switch to a nonoral contraceptive method or add a barrier method of contraception for 4 weeks after initiation and for 4 weeks after each dose escalation

Select safety and side effect information is provided; for a comprehensive discussion of safety considerations, please refer to the prescribing information for each agent, b.i.d., twice daily; ER, extended release; GIP, glucose-dependent insulinotropic polypeptide; GLP-1, glucagon-like peptide 1; q.d., every day; Rx, prescription; t.i.d., three times daily, p.o., by mouth. *Time frames used in clinical trials. Medications approved for long-term use should be continued as indicated beyond reaching weight loss goals. †Phentermine was evaluated in a general adult population with obesity. As monotherapy, phentermine is only approved for short-term use. Use lowest effective dose; maximum appropriate dose is 37.5 mg. ‡Enrolled participants had normal (79%) or impaired (21%) glucose tolerance. §Maximum dose, depending on response, is 15 mg/92 mg q.d. Approximately 68% of enrolled participants had type 2 diabetes or impaired glucose tolerance. ||Agent has indication for reduction of cardiovascular events (55,117).

Table 8.2—Median monthly (30-day) AWP and NADAC of maximum or maintenance dose of obesity pharmacotherapies

Medication name	Typical adult maintenance dose	AWP (median and range for 30-day supply)	NADAC (median and range for 30-day supply)
Sympathomimetic amine anorectic: approved for short-term use only Phentermine	8–37.5 mg daily	\$43 (\$3–\$58)*	\$2 (\$2–\$3)*
Lipase inhibitor Orlistat	60 mg t.i.d. (OTC) 120 mg t.i.d. (Rx)	\$58 (\$41–\$90) \$675 (\$520–\$781)	NA \$514 (\$416–\$611)
Sympathomimetic amine anorectic/ antiepileptic combination Phentermine/topiramate ER	7.5 mg/46 mg daily	\$238 (\$238–\$251)	NA
Opioid antagonist/antidepressant combination Naltrexone/bupropion ER	16 mg/180 mg b.i.d.	\$750	NA
GLP-1 receptor agonist Liraglutide Semaglutide	3 mg daily 2.4 mg once weekly	\$1,619 \$1,619	\$1,303 \$1,302
Dual GIP and GLP-1 receptor agonist Tirzepatide	5, 10, or 15 mg once weekly	\$1,304**	\$1,022

The costs listed in this table are representative of costs at a national level. These costs may not be representative of an individual's cost and do not account for medication coverage or available discounts. AWP, average wholesale price; b.i.d., twice daily; ER, extended release; GIP, glucose-dependent insulintropic polypeptide; GLP-1, glucagon-like peptide 1; NA, data not available; NADAC, National Average Drug Acquisition Cost; OTC, over the counter; Rx, prescription; t.i.d., three times daily. AWP and NADAC prices are for a 30-day supply of maximum or maintenance dose as of 15 July 2025 (190,191). *Data are for 37.5 mg q.d. dose. **Pricing listed for tirzepatide is for the pens only, not the cost of vials available from the manufacturer.

and the individual's therapeutic goals and preferences. Medication cost and insurance coverage considerations often influence treatment decisions, and payors should cover evidence-based obesity treatments for people with diabetes and prediabetes to reduce barriers to treatment access. It is also essential that health care teams are knowledgeable about insurance coverage requirements and establish systems to support clinicians in prescribing evidence-based obesity pharmacotherapies and to reduce financial hardship of treatment for individuals, including formulary and medication coverage requirements, eligibility for medication assistance programs, and availability of copayment reduction cards (see section 1, "Improving Care and Promoting Health in Populations").

Assessing and Optimizing Efficacy and Safety of Obesity Pharmacotherapy

Obesity pharmacotherapy should be initiated at the lowest dose and the dose titration based on tolerability and response. Clinicians should evaluate other type 2 diabetes pharmacotherapies to mitigate risk of hypoglycemia and counsel people with diabetes appropriately. When adding a GLP-1 RA or a dual GIP and GLP-1 RA,

sulfonylureas should be discontinued or the dose reduced and insulin dosing should be adjusted to avoid hypoglycemia (e.g., reduce bolus by 10–20%, basal ~10% if A1C <7.5% [58 mmol/mol]). The treatment dose should be individualized to balance achievement of weight loss goals, health benefits, and tolerability and may be less than the maximum approved dose (119). Gradual stepwise up titration of obesity medications is a well-supported clinical strategy used in clinical trials for enhancing drug tolerability, reducing adverse effects, and optimizing medication-taking behavior. In some individuals, dose titration at a slower rate or in smaller dose increments than those recommended by the manufacturer may be needed. A recent open-label RCT of 104 people with type 2 diabetes demonstrated that slower, flexible titration of semaglutide improved medication-taking behavior and reduced adverse events without compromising efficacy as compared with the label-recommended titration protocol (119).

Upon initiating medications for obesity, assess their effectiveness and safety at least monthly for the first 3 months and at least quarterly thereafter. Modeling from published clinical trials consistently shows that early responders have improved long-term outcomes (120,121); however, it is notable

that the response rate with the latest generation of obesity pharmacotherapies is much higher (54,109). Unless clinical circumstances (such as poor tolerability) or other considerations (such as financial expense or individual preference) suggest otherwise, those who achieve sufficient early weight loss upon starting a chronic obesity pharmacotherapy (typically defined as >5% weight loss after 3 months of use) should continue the medication long-term. When early weight loss results are modest (typically <5% weight loss after 3 months of use), the benefits of ongoing treatment need to be examined in the context of the glycemic response, the availability of other potential treatment options, treatment tolerance, and overall treatment burden. Ongoing monitoring of the achievement and maintenance of weight management goals is recommended. Obesity is a chronic, relapsing disease, similar to hypertension, and typically requires continuation of pharmacotherapy after weight reduction goals are achieved to sustain weight loss and health benefits. Clinical trials have shown that sudden discontinuation of semaglutide and tirzepatide results in weight recurrence of one-half to two-thirds of the weight loss within 1 year with reversal of cardiometabolic improvements (122–124). Shared decision-making should be used to

determine the best long-term weight management approach, such as continuing pharmacotherapy on the lowest effective dose for weight loss maintenance using intermittent therapy, or stopping medication followed by close weight monitoring. For individuals stopping GLP-1 RA therapies, regular physical activity (≥ 60 min/day), self-monitoring, and dietary patterns emphasizing minimally processed, nutrient-dense foods are strategies reported by individuals in the National Weight Control Registry who were successful in maintaining long-term weight loss (125) that could potentially mitigate weight recurrence. Notably, these have not been validated in the post-GLP-1 RA therapy setting.

For those not reaching or maintaining weight-related treatment goals, avoid treatment inertia by reevaluating ongoing weight management therapies and intensify treatment with additional approaches (e.g., metabolic surgery, additional or alternative pharmacologic agents, and structured lifestyle management programs).

MEDICAL DEVICES FOR WEIGHT LOSS

While gastric banding devices have fallen out of favor due to their limited long-term efficacy and high rate of complications, several minimally invasive medical devices have been approved by the FDA for short-term weight loss, including implanted gastric balloons, a vagus nerve stimulator, and gastric aspiration therapy (126). High cost, limited insurance coverage, and limited data supporting the efficacy of these devices in the treatment of individuals with diabetes has created uncertainty for their current use and led to the voluntary removal of several of these medical devices from the U.S. market (127).

METABOLIC SURGERY

Recommendations

8.22 Consider metabolic surgery as a weight and glycemic management approach in people with type 2 diabetes with BMI ≥ 30.0 kg/m² (or ≥ 27.5 kg/m² in Asian American individuals) who are otherwise good surgical candidates. **A**

8.23 Metabolic surgery should be performed in high-volume centers with interprofessional teams knowledgeable about and experienced in managing obesity, diabetes, and gastrointestinal surgery. **E**

8.24 People being considered for metabolic surgery should be evaluated for comorbid psychological conditions and social and situational circumstances that have the potential to interfere with surgery outcomes. **B**

8.25 People who undergo metabolic surgery should receive long-term medical and behavioral support and routine micronutrient, nutritional, and metabolic status monitoring. **B**

8.26 If post-metabolic surgery hypoglycemia is suspected, clinical evaluation should exclude other potential disorders contributing to hypoglycemia, and management should include education, medical nutrition therapy with a registered dietitian nutritionist experienced in post-metabolic surgery hypoglycemia, and medication treatment, as needed. **A** In individuals with post-metabolic surgery hypoglycemia, use continuous glucose monitoring to improve safety. **C**

8.27 In people who undergo metabolic surgery, routinely screen for psychosocial and behavioral health changes and refer to a qualified behavioral health professional as needed. **C**

8.28 Monitor individuals who have undergone metabolic surgery for insufficient weight loss or weight recurrence at least every 6–12 months. **E** In those who have insufficient weight loss or experience weight recurrence, assess for potential predisposing factors and, if appropriate, consider additional weight loss interventions (e.g., obesity pharmacotherapy). **C**

Surgical procedures for obesity treatment—often referred to interchangeably as bariatric surgery, weight loss surgery, metabolic surgery, or metabolic/bariatric surgery—can promote significant and durable weight loss and improve glycemic management and long-term outcomes in those with type 2 diabetes. Given the magnitude and rapidity of improvement of hyperglycemia and glucose homeostasis, these procedures have been suggested as treatments for type 2 diabetes even in the absence of severe obesity, hence the current preferred terminology of “metabolic surgery” (128).

A substantial body of evidence, including data from large cohort studies and randomized controlled (nonblinded)

clinical trials, demonstrates that metabolic surgery achieves superior glycemic management and reduction of cardiovascular risk in people with type 2 diabetes and obesity compared with nonsurgical intervention (51). In addition to improving glycemia, metabolic surgery reduces the incidence of microvascular disease (129), improves quality of life (51,130,131), decreases cancer risk, improves cardiovascular disease risk factors and long-term cardiovascular events (131–137), and decreases all-cause mortality (138). Cohort studies that match surgical and nonsurgical subjects strongly suggest that metabolic surgery reduces all-cause mortality (139). Studies have also shown that metabolic surgery can improve liver outcomes among individuals with MASH, including biopsy-proven disease (140,141).

The overwhelming majority of procedures performed in the U.S. are vertical sleeve gastrectomy (VSG) and Roux-en-Y gastric bypass (RYGB). Both procedures result in a smaller stomach pouch and often robust changes in enteroendocrine hormones. In VSG, ~80% of the stomach is removed, leaving behind a long, thin sleeve-shaped pouch. RYGB creates a much smaller stomach pouch (roughly the size of a walnut), which is then attached to the distal small intestine, thereby bypassing the duodenum and jejunum.

Metabolic surgery has been demonstrated to have beneficial effects on type 2 diabetes irrespective of the presurgical BMI (142). The American Society for Metabolic and Bariatric Surgery recommends metabolic surgery for people with type 2 diabetes and a BMI ≥ 30 kg/m² (or ≥ 27.5 kg/m² for Asian American individuals) in surgically eligible individuals. A real-world data analysis through the National Patient-Centered Outcomes Research Network (PCORnet) in the U.S. compared surgical outcomes between 6,233 individuals with type 2 diabetes who underwent RYGB and 3,477 who underwent VSG. At 1 year after surgery, those who had RYGB lost on average 29.1% of their total body weight, while those who had VSG lost on average 22.8% of their total body weight. At 5 years after surgery, the total body weight loss was 24.1% for those who had RYGB and 16.1% for those who had VSG, with 86.1% of individuals experiencing type 2 diabetes remission after RYGB and 83.5% of individuals experiencing type 2 diabetes remission after VSG. Among the 6,141 individuals who experienced type 2 diabetes remission,

the subsequent type 2 diabetes relapse rate was lower for those who had RYGB than for those who had VSG (hazard ratio 0.75 [95% CI 0.67–0.84]). Estimated relapse rates for those who had RYGB and VSG were 33.1% and 41.6%, respectively, at 5 years after surgery. At 5 years, compared with baseline, A1C was reduced, on average, 0.4 percentage points more for individuals who had RYGB than for individuals who had VSG (143). Most notably, the Surgical Treatment and Medications Potentially Eradicate Diabetes Efficiently (STAMPEDE) trial, which randomized 150 participants with type 2 diabetes, A1C >7.0%, and BMI 27–43 kg/m² to receive either metabolic surgery or medical treatment for type 2 diabetes using glucose-lowering agents, found that 29% of those treated with RYGB and 23% of those treated with VSG achieved A1C of ≤6.0% after 5 years (51). In the Alliance of Randomized Trials of Medicine vs. Metabolic Surgery in Type 2 Diabetes (ARMSS-T2D) study, a pooled analysis of four single-center RCTs, the rates of remission at 7 years were 18% in the bariatric surgery group and 6% in the medical/lifestyle group (144). Available data suggest an erosion of diabetes remission over time (52,144); 35–50% of individuals who initially achieve remission of diabetes eventually experience recurrence. Still, the median disease-free period among such individuals following RYGB is 8.3 years (144,145), and the majority of those who undergo surgery maintain substantial improvement of glycemia from baseline for at least 5–15 years (51,130,131,133).

Exceedingly few presurgical predictors of diabetes remission have been identified. However, younger age, shorter duration of diabetes (e.g., <8 years) (120), and lesser severity of diabetes (better glycemic management, not using insulin) are associated with higher rates of diabetes remission (51,131,146). Greater baseline visceral fat area may also predict diabetes remission, especially among Asian American people with type 2 diabetes (147).

Whereas metabolic surgery has greater initial costs than nonsurgical obesity treatments, retrospective analyses and modeling studies suggest that surgery may be cost-effective or even cost-saving for individuals with type 2 diabetes. However, these results largely depend on assumptions about the long-term effectiveness and safety of the procedures, the specific medications being compared,

the time horizon for cost-effectiveness assessments, and the population examined (e.g., duration and severity of diabetes) (148).

The safety of metabolic surgery has improved significantly with continued refinement of minimally invasive (laparoscopic) approaches, enhanced training and credentialing, and involvement of interprofessional teams. Perioperative mortality rates are typically 0.1–0.5%, similar to those for common abdominal procedures such as cholecystectomy and hysterectomy (149,150). Major complications occur in 2–6% of those undergoing metabolic surgery, which compares favorably with the rates for other commonly performed elective operations (150). Postsurgical recovery times and morbidity have also dramatically declined. Minor complications and need for operative reintervention occur in up to 15% (149,151–153). Empirical data suggest that the proficiency of the operating surgeon and surgical team is a key determinant of mortality, complications, reoperations, and readmissions (154). Accordingly, metabolic surgery should be performed in high-volume centers with interprofessional teams experienced in managing diabetes, obesity, and gastrointestinal surgery. Refer to the American College of Surgeons website for information on accreditation and locations of accredited programs (<https://www.facs.org/quality-programs/accreditation-and-verification/metabolic-and-bariatric-surgery-accreditation-and-quality-improvement-program/>).

Beyond the perioperative period, longer-term risks include vitamin and mineral deficiencies, anemia, osteoporosis, dumping syndrome (or rapid gastric emptying), and severe hypoglycemia (92). Nutritional and micronutrient deficiencies and related complications occur with variable frequency depending on the type of surgical procedure and require routine monitoring of micronutrient and nutritional status and lifelong vitamin/nutritional supplementation (92). Dumping syndrome usually occurs shortly (10–30 min) after a meal and may present with diarrhea, nausea, vomiting, palpitations, and fatigue; hypoglycemia is usually not present at the time of symptoms but, in some cases, may develop several hours later. Post-metabolic surgery hypoglycemia can occur with RYGB, VSG, and other gastrointestinal procedures and may severely impact quality of life (155–157). Post-metabolic surgery hypoglycemia is driven in part by altered

gastric emptying of ingested nutrients, leading to rapid intestinal glucose absorption and excessive postprandial secretion of GLP-1 and other gastrointestinal peptides. As a result, overstimulation of insulin release and a sharp drop in plasma glucose occur, most commonly 1–3 h after a high-carbohydrate meal. Symptoms range from sweating, tremor, tachycardia, and increased hunger to impaired cognition, loss of consciousness, and seizures. In contrast to dumping syndrome, which often occurs soon after surgery and improves over time, post-metabolic surgery hypoglycemia typically presents >1 year after surgery. Diagnosis is primarily made by a thorough examination of history, detailed records of food intake, physical activity, and symptom patterns, and exclusion of other potential causes of hypoglycemia (e.g., malnutrition, side effects of medications or supplements, dumping syndrome, and insulinoma). Initial management includes education to facilitate reduced intake of rapidly digested carbohydrates while ensuring adequate intake of protein, healthy fats, and vitamin and nutrient supplements. When available, individuals should be offered medical nutrition therapy with a registered dietitian nutritionist experienced in post-metabolic surgery hypoglycemia and the use of continuous glucose monitoring (ideally real-time continuous glucose monitoring, which can detect dropping glucose levels before severe hypoglycemia occurs), especially for those with impaired hypoglycemia awareness. Medication treatment, if needed, is primarily aimed at slowing carbohydrate absorption (e.g., acarbose) or reducing GLP-1 and insulin secretion (e.g., diazoxide, octreotide) (158).

People who undergo metabolic surgery may be at increased risk for substance use, worsening or new-onset depression and/or anxiety disorders, and suicidal ideation (159–162). Candidates for metabolic surgery should be assessed by a behavioral health professional with expertise in obesity management prior to consideration for surgery (163). Surgery should be postponed in individuals with alcohol or substance use disorders, severe depression, suicidal ideation, or other significant behavioral health conditions until these conditions have been appropriately addressed. Individuals with preoperative or new-onset psychopathology should be assessed regularly following surgery to

optimize behavioral health and post-surgical outcomes.

Finally, no definitive evidence supports the pre- and post-metabolic surgery use of nutrient-stimulated hormone-based therapeutics for chronic obesity. Existing studies suggest that among individuals with a BMI >50 kg/m², GLP-1 RAs are associated with significant weight loss prior to surgery with no increase in complications or time to surgery (164). Nutrient-stimulated hormone-based therapeutics can be considered as adjuvants after metabolic surgery to augment initial weight loss either shortly after surgery or when weight loss has plateaued (165). Studies have also shown that GLP-1 RAs can effectively treat weight recurrence after metabolic surgery and therefore could be considered as an alternative to revisional surgery (166). Long-term outcomes, however, are lacking in terms of durability of weight loss, effect on weight recurrence when medications are stopped, and long-term side effects with use and after discontinuation (167).

TREATMENT OF OBESITY IN TYPE 1 DIABETES

Recommendation

8.29 Apply obesity management strategies used in the general adult population, including GLP-1 RA-based therapy **B** and metabolic surgery, **C** to adults with type 1 diabetes who have obesity (BMI ≥ 30.0 kg/m², or ≥ 27.5 kg/m² in Asian American individuals). Shared decision-making should inform individualized care.

The prevalence of overweight (30–40%) and obesity (15–30%) for people with type 1 diabetes is comparable to that for the general adult population (168–170). In people with type 1 diabetes, obesity portends a higher burden of cardiovascular disease and microvascular complications, when compared with people without obesity (170). In this context, establishing evidence-based interventions for obesity management specifically in type 1 diabetes remains an unmet need. Though preliminary, cross-sectional work and trials (171–178) thus far have shown positive results for people with type 1 diabetes and obesity who are

treated with GLP-1 RA-based therapy or metabolic surgery.

A large electronic health record-based cross-sectional study showed a significant increase in the prescription pattern of GLP-1 RAs and dual GIP and GLP-1 RAs over time, which were prescribed in approximately 6.5% of people with type 1 diabetes in 2023 (179). While people with type 1 diabetes were excluded in most large RCTs testing the efficacy of GLP-1 RA-based therapy on weight loss in people with obesity or type 2 diabetes, real-world data suggest benefits for weight reduction and improvement in A1C in association with lower insulin requirements (172). The ADJUNCT ONE and ADJUNCT TWO randomized placebo-controlled trials investigated safety and efficacy of varying doses of liraglutide for 52 and 26 weeks, respectively, in people with longstanding type 1 diabetes (173,174). While the highest dose of liraglutide (1.8 mg daily) was associated with a $\sim 6\%$ weight reduction in both RCTs, the rates of hypoglycemia increased by 20–30% at all doses and the risk of hyperglycemia with ketosis doubled with liraglutide 1.8 mg when compared with placebo. The appetite suppression and reduction in caloric intake combined with lower insulin requirements appear to be key factors underlying the risk of ketosis associated with GLP-1 RA-based therapy.

For treatment of obesity in people with type 1 diabetes, initiation of GLP-1 RA or dual GIP and GLP-1 RA should follow a detailed review of the drug side effect profiles and a person-centered dialogue about goals and expectations. Thus, it is essential to counsel people with type 1 diabetes who start treatment with a GLP-1 RA or a dual GIP and GLP-1 RA on anticipating an increased risk of hypoglycemia and a reduction in insulin requirements, on maintaining a critical carbohydrate intake, and on testing for excess ketone body production. Notably, dose escalation protocols validated in people with type 2 diabetes should not be extrapolated to people with type 1 diabetes, for whom titration of GLP-1 RA-based therapy should be particularly cautious and accompanied by close monitoring of changes in insulin requirements and in the frequency of episodes of hypoglycemia. In the absence of robust data specific to people with type 1 diabetes regarding therapy discontinuation, the paradigm of maintaining long-term treatment

should be applied to prevent weight recurrence. Also, people with type 1 diabetes who discontinue GLP-1 RA-based treatment, which occurs in $>50\%$ of people with obesity at 1 year (180), should expect a variable increase in insulin requirements.

In this context, the presence of comorbidities such as obstructive sleep apnea, MASH, or coronary artery disease may further guide the selection of people with type 1 diabetes and obesity who would particularly benefit from GLP-1 RA or dual GIP and GLP-1 RA treatment for obesity. Conversely, preexisting gastroparesis, hypoglycemia unawareness, or a recent episode of diabetic ketoacidosis or euglycemic ketoacidosis should generally dissuade from initiating treatment with these medications.

Adjunctive therapy with a GLP-1 RA or a dual GIP and GLP-1 RA in people with type 1 diabetes using automated insulin delivery (AID) systems requires periodic assessment of AID settings, primarily to reduce the risk of hypoglycemia and avoid prolonged insulin delivery suspensions that may predispose to ketosis. As suggested in a recent consensus report (175), deintensification of insulin-to-carbohydrate ratios and sensitivity factor should be expected through the titration process of GLP-1 RA-based therapy. In addition, delayed gastric emptying may require a modification of mealtime insulin dosing to the beginning of or just after the meal to optimally match insulin delivery with food absorption.

In summary, the decision to initiate GLP-1 RA-based therapy in type 1 diabetes should be informed by a detailed conversation of risks and benefits, including the anticipated reduction in insulin requirements, the importance of ketone monitoring and implementation of sick-day rules, and modifications of AID settings, if applicable.

Metabolic surgery represents a highly individualized option for management of obesity in people with type 1 diabetes. In a retrospective analysis of 17 bariatric surgery studies that included 107 individuals with type 1 diabetes (176), 65% of whom underwent RYGB, the average achieved postoperative BMI was 31 kg/m² (reduced from an average preoperative BMI of 41 kg/m²) over the observation period of 1.5–5 years. Other cohort studies have shown similar BMI reductions (177). In contrast, the effects of metabolic surgery on A1C have been inconsistent (177), with

one study noting an increase at 5 years postoperatively (178).

Also, a frequency of diabetic ketoacidosis ranging between 15% and 20% (181,182)—often in the first days after surgery and concomitantly with reduced carbohydrate intake and insulin doses—and enhanced risk of hypoglycemia (182) are key safety issues that should be discussed in detail with people with type 1 diabetes considering metabolic surgery. In addition, long-term surgical complications like dumping syndrome are particularly challenging to manage in people with type 1 diabetes. In conclusion, using a multidisciplinary approach a careful evaluation and extensive counseling is required to select people with type 1 diabetes who would benefit the most from metabolic surgery while individualizing goals and setting realistic expectations.

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9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes—2026

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American Diabetes Association
Professional Practice Committee for
Diabetes*

The American Diabetes Association (ADA) “Standards of Care in Diabetes” includes the ADA’s current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. Members of the ADA Professional Practice Committee for Diabetes, an interprofessional expert committee, are responsible for updating the Standards of Care annually, or more frequently as warranted. For a detailed description of ADA standards, statements, and reports, as well as the evidence-grading system for ADA’s clinical practice recommendations and a full list of Professional Practice Committee members, please refer to Introduction and Methodology. Readers who wish to comment on the Standards of Care are invited to do so at professional.diabetes.org/SOC.

PHARMACOLOGIC THERAPY FOR ADULTS WITH TYPE 1 DIABETES

Recommendations

- 9.1** Treat most adults with type 1 diabetes with continuous subcutaneous insulin infusion or multiple daily doses of prandial (injected or inhaled) and basal insulin. **A**
- 9.2** For most adults with type 1 diabetes, insulin analogs (or inhaled insulin) are preferred over injectable human insulins to minimize hypoglycemia risk. **A**
- 9.3** To improve glycemic outcomes and quality of life and to minimize hypoglycemia risk, most adults with type 1 diabetes should receive education on how to match mealtime insulin doses to carbohydrate intake and fat and protein intake depending on the person’s or caregiver’s needs or preferences. They should also be taught how to modify the insulin dose (correction dose) based on concurrent glycemia, glycemic trends (if available), sick-day management, and anticipated physical activity. **B**
- 9.4** Insulin treatment plans and insulin-taking behaviors should be reevaluated at regular intervals (e.g., every 3–6 months) and adjusted to incorporate specific factors that affect choice of treatment and ensure achievement of individualized glycemic goals. **E**

Insulin Therapy

Insulin treatment is essential for individuals with type 1 diabetes because the hallmark of type 1 diabetes is absent or near-absent β -cell function. In addition to hyperglycemia, insulinopenia can contribute to other metabolic disturbances like hypertriglyceridemia and ketoacidosis as well as tissue catabolism that can be life threatening. Severe metabolic decompensation can be, and was, mostly prevented

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with once- or twice-daily insulin injections for the six or seven decades after the discovery of insulin. Over the past four decades, evidence has accumulated supporting more intensive insulin replacement, using multiple daily injections of insulin or continuous subcutaneous administration through an insulin pump, as providing the best combination of effectiveness and safety for people with type 1 diabetes.

The Diabetes Control and Complications Trial (DCCT) demonstrated that intensive therapy with multiple daily injections or continuous subcutaneous insulin infusion (CSII) reduced A1C and was associated with improved long-term outcomes (1–3). The study was carried out with short-acting (regular) and intermediate-acting (NPH) human insulins. In this landmark trial, lower A1C with intensive management (7.3%) led to ~50% reductions in microvascular complications compared with 9.1% mean A1C in the conventional treatment arm over 6 years of treatment. However, intensive therapy was associated with a higher rate of severe hypoglycemia than

conventional treatment (62 compared with 19 episodes per 100 person-years of therapy) (1). Follow-up of participants from the DCCT demonstrated fewer macrovascular and microvascular complications in the group that received intensive treatment. Achieving intensive glycemic goals during the active treatment period of the study had a persistent beneficial impact over the 20 years after the active treatment component of the study ended (1–3).

Insulin replacement plans typically consist of basal insulin, mealtime insulin, and correction insulin (**Fig. 9.1**) (4). Basal insulin includes NPH insulin, long-acting insulin analogs, and continuous delivery of rapid-acting insulin via an insulin pump. Basal insulin analogs have longer duration of action with flatter, more constant and consistent plasma concentrations and activity profiles than NPH insulin; rapid-acting analogs (RAA) have a quicker onset and peak and shorter duration of action than regular human insulin. In people with type 1 diabetes, treatment with analog insulins is associated with less hypoglycemia and weight gain and lower A1C

compared with injectable human insulins (5–7). Two injectable ultra-rapid-acting analog (URAA) insulin formulations are available that contain excipients that accelerate absorption and provide more activity in the first portion of their profile compared with the other RAA (8,9). Inhaled human insulin has a rapid peak and shortened duration of action compared with RAA (10) (see also subsection ALTERNATIVE INSULIN ROUTES IN PHARMACOLOGIC THERAPY FOR ADULTS WITH TYPE 2 DIABETES). These newer formulations may cause less hypoglycemia while improving postprandial glucose excursions and administration flexibility (in relation to prandial intake) compared with RAA (10–12). In addition, longer-acting basal analogs (U-300 glargine or degludec) may confer a lower hypoglycemia risk compared with U-100 glargine in individuals with type 1 diabetes (13,14).

Despite the advantages of insulin analogs in individuals with type 1 diabetes, the expense and/or complexity of treatment required for their use may be prohibitive (**Table 9.1**). There are multiple approaches to insulin treatment. The

Representative relative attributes of insulin delivery approaches in people with type 1 diabetes

Insulin plans	Greater flexibility	Lower risk of hypoglycemia	Higher costs
MDI with LAA + RAA or URAA	+++	+++	\$\$\$
Less-preferred, alternative injected insulin plans			
MDI with NPH + RAA or URAA	++	++	\$\$
MDI with NPH + short-acting (regular) insulin	++	+	\$
Two daily injections with NPH + short-acting (regular) insulin or premixed	+	+	\$
Continuous insulin infusion plans	Greater flexibility	Lower risk of hypoglycemia	Higher costs
Automated insulin delivery systems	+++++	+++++	\$\$\$\$\$
Insulin pump with threshold/predictive low-glucose suspend	++++	++++	\$\$\$\$\$
Insulin pump therapy without automation	+++	+++	\$\$\$\$

Figure 9.1—Choices of insulin plans in people with type 1 diabetes. Continuous glucose monitoring improves outcomes with injected or infused insulin and is superior to blood glucose monitoring. Inhaled insulin may be used in place of injectable prandial insulin in the U.S. The number of plus or dollar signs is an estimate of relative association of the plan with greater flexibility, lower risk of hypoglycemia, and higher costs between the different plans. Cost symbols are reflective of general costs, which may vary for individuals based on various circumstances: insurance coverage, discounts, rebates, and other price adjustments involved in prescription sales. LAA, long-acting insulin analog; MDI, multiple daily injections; RAA, rapid-acting insulin analog; URAA, injectable ultra-rapid-acting insulin analog or inhaled insulin. Adapted from Holt et al. (4).

Table 9.1—Examples of subcutaneous insulin treatment plans

Plans	Timing and distribution	Advantages	Disadvantages	Adjusting doses
Plans that more closely mimic normal insulin secretion				
Insulin pump therapy, including conventional CSII, sensor-augmented pump, low-glucose suspend; AID systems such as hybrid closed loop	Basal delivery of URAA or RAA; generally 30–50% of TDD. Mealtime and correction: URAA or RAA by bolus based on ICR and/or ISF and target glucose, with premeal insulin ~15 min before eating.	Can adjust basal rates for varying insulin sensitivity by time of day, for exercise, and for sick days. Flexibility in meal timing and content. Pump can deliver insulin in increments of fractions of units. Potential for integration with CGM for AID systems. TIR % highest and TBR % lowest with: hybrid closed-loop > low-glucose suspend > sensor-augmented open-loop > conventional CSII.	Most expensive plan. Must continuously wear one or more devices. Risk of rapid development of ketosis or DKA with interruption of insulin delivery. Potential reactions to adhesives and site infections. Most technically complex approach (harder for people with lower numeracy or literacy skills).	Mealtime insulin: if carbohydrate counting is accurate, change ICR if glucose after meal consistently out of target. Correction insulin: adjust ISF and/or target glucose if correction does not consistently bring glucose into range. Basal rates: adjust based on overnight, fasting or daytime glucose outside of activity of URAA/RAA bolus. AID systems: carbohydrate ratio, insulin on board, targets, and/or ISF may be adjusted, depending on the system; make sure to review and adjust manual mode settings, if available.
MDI: LAA + flexible doses of URAA or RAA at meals	LAA once daily (insulin detemir or insulin glargine may require twice-daily dosing); generally 30–50% of TDD. Mealtime and correction: URAA or RAA based on ICR and/or ISF and target glucose.	Can use pens for all components. Flexibility in meal timing and content. Insulin analogs cause less hypoglycemia than human insulins.	At least four daily injections. Most costly insulins. Smallest increment of insulin is 1 unit (0.5 unit with some pens). LAA may not cover strong dawn phenomenon (rise in glucose in early morning hours) as well as pump therapy.	Mealtime insulin: if carbohydrate counting is accurate, change ICR if glucose after meal consistently out of target. Correction insulin: adjust ISF and/or target glucose if correction does not consistently bring glucose into range. LAA: based on overnight or fasting glucose or daytime glucose outside of activity time course, or URAA or RAA injections.
MDI plans with less flexibility				
Four injections daily with fixed doses of N and RAA	Pre-breakfast: RAA ~20% of TDD. Pre-lunch: RAA ~10% of TDD. Pre-dinner: RAA ~10% of TDD. Bedtime: N ~50% of TDD.	May be feasible if unable to carbohydrate count. All meals have RAA coverage. N is less expensive than LAAs.	Shorter duration RAA may lead to basal deficit during day; may need twice-daily N. Greater risk of nocturnal hypoglycemia with N. Requires relatively consistent mealtimes and carbohydrate intake.	Pre-breakfast RAA: based on BGM after breakfast or before lunch. Pre-lunch RAA: based on BGM after lunch or before dinner. Pre-dinner RAA: based on BGM after dinner or at bedtime. Evening N: based on fasting or overnight BGM.

Continued on p. S186

Table 9.1—Continued

Plans	Timing and distribution	Advantages	Disadvantages	Adjusting doses
Four injections daily with fixed doses of N and R	Pre-breakfast: R ~20% of TDD. Pre-lunch: R ~10% of TDD. Pre-dinner: R ~10% of TDD. Bedtime: N ~50% of TDD.	May be feasible if unable to carbohydrate count. R can be dosed based on ICR and correction. All meals have R coverage. Least expensive insulins.	Greater risk of nocturnal hypoglycemia with N. Greater risk of delayed post-meal hypoglycemia with R. Requires relatively consistent mealtimes and carbohydrate intake. R must be injected at least 30 min before meal for better effect.	Pre-breakfast R: based on BGM after breakfast or before lunch. Pre-lunch R: based on BGM after lunch or before dinner. Pre-dinner R: based on BGM after dinner or at bedtime. Evening N: based on fasting or overnight BGM.
Plans with fewer daily injections				
Three injections daily: N + R or N + RAA	Pre-breakfast: N ~40% TDD + R or RAA ~15% TDD. Pre-dinner: R or RAA ~15% TDD. Bedtime: N ~30% TDD.	Morning insulins can be mixed in one syringe. May be appropriate for those who cannot take injection in middle of day. Morning N covers lunch to some extent. Same advantages of RAAs over R. Least (N + R) or less expensive insulins than MDI with analogs.	Greater risk of nocturnal hypoglycemia with N than LAAs. Greater risk of delayed post-meal hypoglycemia with R than RAAs. Requires relatively consistent mealtimes and carbohydrate intake. Coverage of post-lunch glucose often suboptimal. R must be injected at least 30 min before meal for better effect.	Morning N: based on pre-dinner BGM. Morning R: based on pre-lunch BGM. Morning RAA: based on post-breakfast or pre-lunch BGM. Pre-dinner R: based on bedtime BGM. Pre-dinner RAA: based on post-dinner or bedtime BGM. Evening N: based on fasting BGM.
Twice-daily “split-mixed”: N + R or N + RAA	Pre-breakfast: N ~40% TDD + R or RAA ~15% TDD. Pre-dinner: N ~30% TDD + R or RAA ~15% TDD.	Least number of injections for people with strong preference for this. Insulins can be mixed in one syringe. Least (N + R) or less (N + RAA) expensive insulins vs. analogs. Eliminates need for doses during the day.	Risk of hypoglycemia in afternoon or middle of night from N. Fixed mealtimes and meal content. Coverage of post-lunch glucose often suboptimal. Difficult to reach targets for blood glucose without hypoglycemia.	Morning N: based on pre-dinner BGM. Morning R: based on pre-lunch BGM. Morning RAA: based on post-breakfast or pre-lunch BGM. Evening R: based on bedtime BGM. Evening RAA: based on post-dinner or bedtime BGM. Evening N: based on fasting BGM.

A1D, automated insulin delivery; BGM, blood glucose monitoring; CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion; ICR, insulin-to-carbohydrate ratio; ISF, insulin sensitivity factor; LAA, long-acting analog; MDI, multiple daily injections; N, NPH insulin; R, short-acting (regular) insulin; RAA, rapid-acting analog; TBR, time below range; TDD, total daily insulin dose; TIR, time in range; URAA, ultra-rapid-acting analog (inhaled insulin may be considered if appropriate). Adapted from Holt et al. (4).

central precept in the management of type 1 diabetes is that some form of insulin be given in a defined treatment plan tailored to the individual to prevent diabetic ketoacidosis (DKA) and minimize clinically relevant hypoglycemia while achieving the individual's glycemic goals. Reassessment of insulin-taking behavior and adjustment of treatment plans to account for specific factors, including cost, that affect choice of treatment is recommended at regular intervals (every 3–6 months).

Most studies comparing multiple daily injections with CSII have been relatively small and of short duration. A systematic review and meta-analysis concluded that CSII via pump therapy has modest advantages for lowering A1C (-0.30% [95% CI -0.58 to -0.02]) and for reducing severe hypoglycemia rates in adults (15). Use of CSII is associated with improvement in quality of life, particularly in areas related to fear of hypoglycemia and diabetes distress, compared with multiple daily injections of insulin (16,17). However, there is no consensus to guide the choice of injection or pump therapy in a given individual, and research to guide this decision-making is needed (4).

Integration of continuous glucose monitoring (CGM) into the treatment plan soon after diagnosis improves glycemic outcomes, decreases hypoglycemic events, and improves quality of life for individuals with type 1 diabetes (18–21). Its use is now considered standard of care for most people with type 1 diabetes (4) (see section 7, “Diabetes Technology”). Although nocturnal hypoglycemia is reduced in individuals with type 1 diabetes using sensor-augmented pump therapy with low-glucose suspend and predictive low-glucose suspend (22,23), evidence suggests that automated insulin delivery (AID) systems are superior for increasing percentage of time in range and reducing hypoglycemia (24–26). AID systems, which integrate CSII via an insulin pump, a CGM, and a control algorithm to adjust insulin delivery in real time based on glucose levels, are safe and effective for people with type 1 diabetes. Randomized controlled trials (RCTs) and real-world studies have demonstrated the ability of commercially available systems to improve achievement of glycemic goals while reducing the risk of hypoglycemia (27–32). Data are emerging on the safety and effectiveness of open-source AID systems (33,34). Intensive insulin

management with CSII and CGM should be considered in individuals with type 1 diabetes whenever feasible. AID systems are preferred for individuals with type 1 diabetes who can use them safely (independently or with caregiver support), as they consistently improve time in range, lower A1C, and reduce hypoglycemia (26,28–31,35–38). When choosing among insulin delivery systems, individual preferences, cost, insulin type, dosing plan, and self-management capabilities should be considered. See section 7, “Diabetes Technology,” for a full discussion of insulin delivery devices.

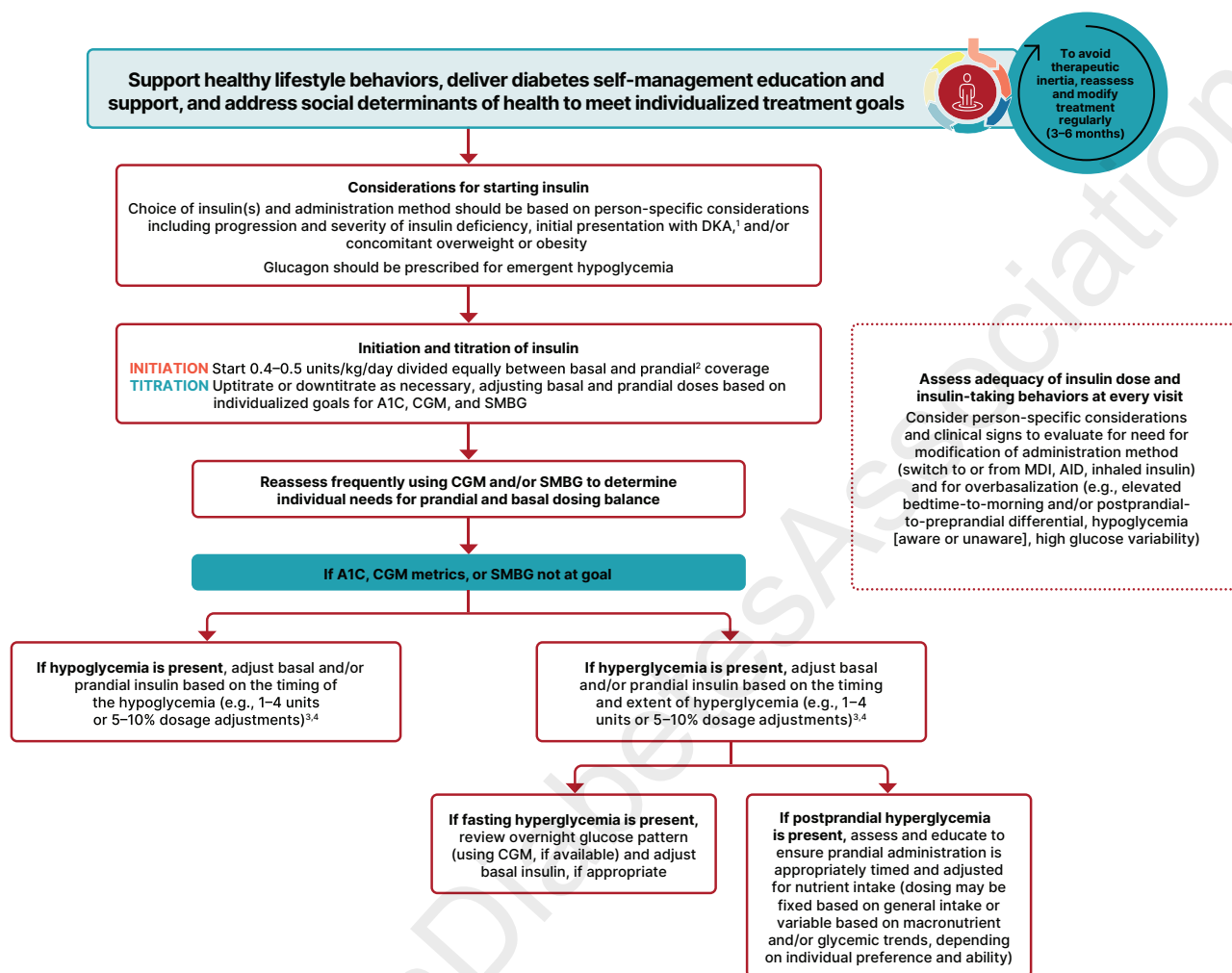
In general, individuals with type 1 diabetes require approximately 30–50% of their daily insulin as basal and the remainder as prandial (39). This proportion depends on several factors, including but not limited to carbohydrate consumption, age, pregnancy status, and puberty stage (4,40–43). Total daily insulin requirements can be estimated based on weight, with typical doses ranging from 0.4 to 1 unit/kg/day. Higher amounts may be required during puberty, the late luteal phase (premenstrual) in menstruating individuals, and illness. The *American Diabetes Association/JDRF Type 1 Diabetes Sourcebook* notes 0.5 units/kg/day as a typical starting dose in adults with type 1 diabetes who are metabolically stable, with approximately one-half administered as prandial insulin given to manage blood glucose after meals and the remaining portion as basal insulin to manage glycemia in the periods between meal absorption (44). In adults newly diagnosed with type 1 diabetes, insulin requirements at initiation typically range from 0.2 to 0.6 units/kg/day, with lower doses often sufficient in those with continued endogenous insulin production (during the partial remission phase or “honeymoon” period, or in people presenting outside of ketoacidosis) (44). This guideline provides an algorithm for insulin use for individuals with type 1 diabetes using insulin injections (**Fig. 9.2**) and detailed information on intensification of therapy to meet individualized needs. In addition, the American Diabetes Association (ADA) position statement “Type 1 Diabetes Management Through the Life Span” provides a thorough overview of type 1 diabetes treatment (45).

Typical multidose insulin treatment plans for adults with type 1 diabetes combine premeal prandial insulin with a longer-acting basal insulin. The long-acting basal

dose is titrated to regulate overnight and fasting glucose. Postprandial glucose excursions are best managed by an appropriately timed injection or inhalation of prandial insulin. Prandial insulin should ideally be administered before meals, although the optimal timing depends on the pharmacokinetics of the formulation (regular, rapid-acting analog, or inhaled), the premeal blood glucose level, and the anticipated carbohydrate intake. Dosing recommendations should therefore be individualized. Because physiologic insulin secretion varies with glycemia, meal size and composition, and tissue demand, strategies have evolved to adjust prandial doses based on predicted needs. Thus, education on how to adjust prandial insulin to account for nutritional intake and the correction dose based on premeal glucose levels, anticipated activity, and sick-day management can be effective and should be offered to most individuals (46–51). Education regarding adjustment of prandial insulin dose for glycemic trends should be provided to individuals who are using CGM alone or an AID system (52–55). Further adjustment of prandial insulin doses for nutritional intake of protein and fat, in addition to carbohydrates, is recommended but may be more feasible for individuals using CSII than for those using multiple daily injections (48). With some AID systems, use of a simplified meal announcement method may be an alternative for prandial insulin dosing (31,56). Assessment and education tailored to improve health literacy and numeracy may be necessary for individuals to effectively use various insulin dosing strategies and tools (57,58) (see section 5, “Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes,” and section 7, “Diabetes Technology”).

The 2021 ADA/European Association for the Study of Diabetes (EASD) consensus report on the management of type 1 diabetes in adults summarizes different insulin plans and glucose monitoring strategies in individuals with type 1 diabetes (**Fig. 9.1** and **Table 9.1**) (4). An individual's treatment plan and insulin-taking behaviors should be frequently reassessed to attain individualized treatment goals and assess risk or progression of complications and comorbidities. The timing of reassessment may vary based on time since diagnosis, ability to attain/maintain treatment goals, health status, comorbidities, and individual needs (4,45,59).

Initiation and adjustment of insulin using multiple daily dosing in individuals with type 1 diabetes



1. Refer to section 16, "Diabetes Care in the Hospital," for information on care during hospitalizations.

2. Prandial insulin options include: injectable rapid-acting and ultra-rapid-acting analog insulins, injectable short-acting human insulin, and inhaled human insulin.

3. Amount of dosage adjustment may vary between individuals depending on their severity of insulin deficiency and/or insulin resistance. Some individuals may require adjustments of 10–20%.

4. Adjustment may be done by their diabetes care team or by individuals, with guidance provided by their diabetes care team, as frequently as once to twice weekly using the lowest levels or average of the previous 3–4 days.

Figure 9.2—Insulin initiation and adjustment for people with type 1 diabetes using multiple daily dosing. AID, automated insulin delivery; CGM, continuous glucose monitoring; DKA, diabetic ketoacidosis; MDI, multiple daily injections; SMBG, self-monitoring of blood glucose.

Insulin Administration Technique

Ensuring that individuals and/or caregivers understand correct insulin administration technique is important to optimize glycemic management and insulin use safety. Advanced insulin injection technique and education with FITTER Forward expert recommendations have been published elsewhere outlining best practices for insulin administration (60). Proper insulin administration technique includes the following: injection, insertion of patch (for bolus patch or fixed-rate patch pump) or infusion set (for CSII or AID systems) into appropriate body areas, or oral inhalation (inhaled human insulin); injection or infusion site rotation; appropriate care of

injection or infusion sites to avoid infection or other complications; avoidance of intramuscular (IM) insulin delivery; and filling of the reservoir (for bolus patch, CSII, or AID systems) or inhaler (for inhaled human insulin) depending on the method of administration. Selection of method of administration (vial and syringe, insulin pen, insulin patch, inhaled insulin, connected insulin pens/devices, or insulin pumps) will depend on a variety of individual-specific factors and needs, cost and coverage, and individual preferences. Reassessment of the appropriate administration technique should be completed during routine follow-up.

Exogenously delivered insulin should be injected or infused into subcutaneous tissue, not intramuscularly. Recommended sites for insulin administration include the abdomen, thigh, buttock, and upper arm. Insulin absorption from IM sites differs from that in subcutaneous sites and is also influenced by the activity of the muscle. Inadvertent IM injection can lead to unpredictable insulin absorption and variable effects on glucose and is associated with frequent and unexplained hypoglycemia. Size 4-mm pen needles should be used to reduce inadvertent IM insulin delivery across ages and body types. IM risk is higher in younger, leaner individuals, with injections into limbs rather than truncal

sites (abdomen, buttocks), and with longer needles. Short needles (e.g., 4-mm) are effective and well tolerated compared with longer needles, including in adults with obesity (61).

Injection or infusion site rotation is necessary to avoid lipohypertrophy, an accumulation of subcutaneous fat in response to the adipogenic actions of insulin at a site of multiple injections. Lipohypertrophy appears as soft, smooth raised areas several centimeters in breadth and can contribute to erratic insulin absorption, increased glycemic variability, and unexplained hypoglycemic episodes. People treated with insulin and/or caregivers should receive education about proper injection or infusion site rotation and how to recognize and avoid injecting in areas of lipohypertrophy (60). As noted in **Table 4.1**, examination of insulin administration sites for the presence of lipohypertrophy, as well as assessment of administration device use and injection technique, are key components of a comprehensive diabetes evaluation and treatment plan. Proper insulin injection, infusion, or inhalation technique may lead to more effective use of this therapy and, as such, holds the potential for improved clinical outcomes.

Noninsulin Treatments for Type 1 Diabetes

Injectable and oral noninsulin glucose-lowering medications have been studied for their efficacy as adjuncts to insulin treatment of type 1 diabetes. Pramlintide is based on the naturally occurring β -cell peptide amylin and is approved for use in adults with type 1 diabetes. Clinical trials have demonstrated a modest reduction in A1C (0.3–0.4%) and modest weight loss (~1–2 kg) with pramlintide (62). Similar results have been reported for several agents currently approved for the treatment of type 2 diabetes. The addition of metformin in adults with type 1 diabetes was associated with small reductions in body weight, insulin dose, and lipid levels but did not sustainably improve A1C (63,64). The largest clinical trials of glucagon-like peptide 1 receptor agonists (GLP-1 RAs) in type 1 diabetes have been conducted with liraglutide 1.8 mg daily, and results showed modest A1C reductions (~0.4%), decreases in weight (~5 kg), and reductions in insulin doses (65,66). Higher rates of DKA and gastrointestinal side effects have limited their use in type 1 diabetes. Liraglutide was also assessed for impact

on C-peptide in individuals with type 1 diabetes and residual β -cell function. During treatment there was no impact on preservation of β -cell function, but with liraglutide discontinuation there was worsening of C-peptide loss compared with placebo (67). Small retrospective case series and pilot studies have revealed potential benefits on body weight and glycemic metrics with addition of semaglutide or tirzepatide for individuals with type 1 diabetes and obesity (68–72). Prospective studies on use of incretin medications (i.e., GLP-1 RAs or a dual glucose-dependent insulinotropic polypeptide [GIP] and GLP-1 RA) for individuals with type 1 diabetes are ongoing and include evaluation of cardiovascular and kidney outcomes and other aspects of care (73–76).

Sodium–glucose cotransporter 2 (SGLT2) inhibitors have been studied in clinical trials in people with type 1 diabetes, and results showed improvements in A1C, reduced body weight, and improved blood pressure (77); however, SGLT2 inhibitor use in type 1 diabetes was associated with an increased rate of DKA (78). The SGLT1/2 inhibitor sotagliflozin has been studied in clinical trials in people with type 1 diabetes, and results showed improvements in A1C and body weight (79); however, sotagliflozin use was associated with an eightfold increase in DKA compared with placebo (80). The studies that led to the approved indication for heart failure (HF) excluded individuals with type 1 diabetes or a history of DKA (81,82). Sotagliflozin is therefore approved for HF and chronic kidney disease (CKD) but contraindicated in type 1 diabetes due to DKA risk. See SGLT INHIBITION AND RISK OF KETOSIS, later in this section, and PREVENTION AND TREATMENT OF HEART FAILURE in section 10, “Cardiovascular Disease and Risk Management,” for information on risk mitigation with the use of SGLT inhibitors in those with type 1 diabetes. The risks and benefits of adjunctive agents continue to be evaluated, with consensus statements providing guidance on selection of candidates for treatment and precautions (83).

There are currently no approved therapies for preservation of C-peptide or prolongation of the partial remission (honeymoon) phase in individuals with established stage 3 type 1 diabetes. Teplizumab was approved by the U.S. Food and Drug Administration (FDA) in 2022 for delay of the progression from stage 2 to stage 3 type 1 diabetes (for additional guidance for use in early stage

type 1 diabetes, refer to section 3, “Prevention or Delay of Diabetes and Associated Comorbidities”), but it is not indicated for those with established stage 3 type 1 diabetes (84). Higher C-peptide levels have been associated with better A1C, lower risk of retinopathy, lower risk of nephropathy, and lower risk of severe hypoglycemia (85). Various therapies, including verapamil, menin inhibitors, Janus kinase inhibitors, antithymocyte globulin, several monoclonal antibodies including teplizumab, and cell therapies, are currently under active investigation (86).

SURGICAL TREATMENT OF TYPE 1 DIABETES

Pancreas and Islet Transplantation

Successful pancreas and islet transplantation can normalize glucose levels and mitigate microvascular complications of type 1 diabetes. However, people receiving these treatments require lifelong immunosuppression to prevent graft rejection and/or recurrence of autoimmune islet destruction. Given the potential adverse effects of immunosuppressive therapy, pancreas transplantation should be reserved for people with type 1 diabetes undergoing simultaneous kidney transplantation, following kidney transplantation, or for those with recurrent ketoacidosis or severe hypoglycemia despite optimized glycemic management (87). In much of the world, allogeneic islet transplantation is regulated as an organ transplant. However, in the U.S., allogeneic islet transplantation is regulated as a cell therapy, and the first such allogeneic islet cell therapy, donislecel-juv, was approved in 2023. Donislecel is indicated for the treatment of adults with type 1 diabetes who are unable to reach their A1C goals because of repeated episodes of severe hypoglycemia despite intensive diabetes management and education (88). Alternative islet sources are currently under active investigation.

The 2021 ADA/EASD consensus report on the management of type 1 diabetes in adults offers a simplified overview of indications for β -cell replacement therapy in people with type 1 diabetes (**Fig. 9.3**) (4).

PHARMACOLOGIC THERAPY FOR ADULTS WITH TYPE 2 DIABETES

Recommendations

9.5 A person-centered shared decision-making approach should guide the

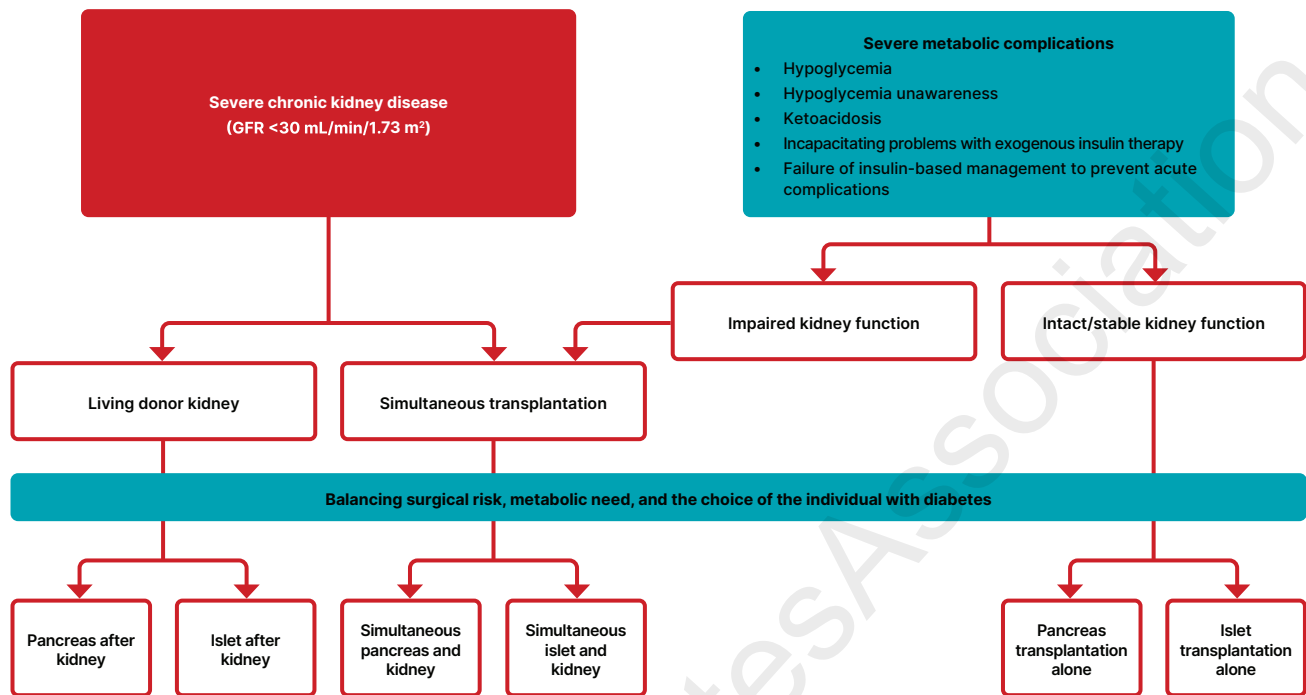
Simplified overview of indications for β -cell replacement therapy in people with type 1 diabetes

Figure 9.3—Simplified overview of indications for β -cell replacement therapy in people with type 1 diabetes. The two main forms of β -cell replacement therapy are whole-pancreas transplantation and islet cell transplantation. β -Cell replacement therapy can be combined with kidney transplantation if the individual has kidney failure, which may be performed simultaneously or after kidney transplantation. All decisions about transplantation must consider the surgical risk, metabolic need, and the choices of the individual with diabetes. GFR, glomerular filtration rate. Adapted from Holt et al. (4).

choice of glucose-lowering medications for adults with type 2 diabetes. Use medications that provide sufficient effectiveness to achieve and maintain intended treatment goals with consideration of the effects on cardiovascular, kidney, weight, and other relevant comorbidities; hypoglycemia risk; cost and access; risk for adverse reactions and tolerability; and individual preferences (Fig. 9.4 and Table 9.2). **E**

9.6 Consider combination therapy in adults with type 2 diabetes for initial treatment to shorten time to attainment of individualized glycemic goals. **A**

9.7 In adults with type 2 diabetes and established or high risk of atherosclerotic cardiovascular disease, the treatment plan should include medications with demonstrated benefits to reduce cardiovascular events (e.g., glucagon-like peptide 1 receptor agonist [GLP-1 RA] and/or sodium-glucose cotransporter 2 [SGLT2] inhibitor) for glycemic management and comprehensive cardiovascular risk reduction (irrespective of A1C) (Fig. 9.4 and Table 9.2). **A**

9.8 In adults with type 2 diabetes who have heart failure (HF) (with either reduced or preserved ejection fraction), an SGLT2 inhibitor is recommended for both glycemic management and prevention of HF hospitalizations (irrespective of A1C) (Fig. 9.4). **A**

9.9a In adults with type 2 diabetes, obesity, and symptomatic heart failure with preserved ejection fraction (HFpEF), the glucose-lowering treatment plan should include a dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 RA with demonstrated benefits for HF-related symptoms and reduction in HF events (irrespective of A1C). **A**

9.9b In adults with type 2 diabetes, obesity, and symptomatic HFpEF, the glucose-lowering treatment plan should include a GLP-1 RA with demonstrated benefits for HF-related symptoms **A** and/or reduction in HF events (irrespective of A1C). **B**

9.10 In adults with type 2 diabetes who have chronic kidney disease (CKD) (with confirmed estimated glomerular filtration rate [eGFR] 20–60 mL/min/

1.73 m² and/or albuminuria), an SGLT2 inhibitor or GLP-1 RA with demonstrated benefit in this population should be used for both glycemic management and for slowing progression of CKD and reduction in cardiovascular events (irrespective of A1C) (Fig. 9.4). The glycemic benefits of SGLT2 inhibitors are reduced at eGFR <45 mL/min/1.73 m². **A**

9.11 In adults with type 2 diabetes and advanced CKD (eGFR <30 mL/min/1.73 m²), a GLP-1 RA is preferred for glycemic management due to lower risk of hypoglycemia and for cardiovascular event reduction. **B** Individuals on dialysis can be safely initiated or continued on GLP-1–based therapy (that is not dependent on kidney clearance) to reduce cardiovascular risk and mortality. **C**

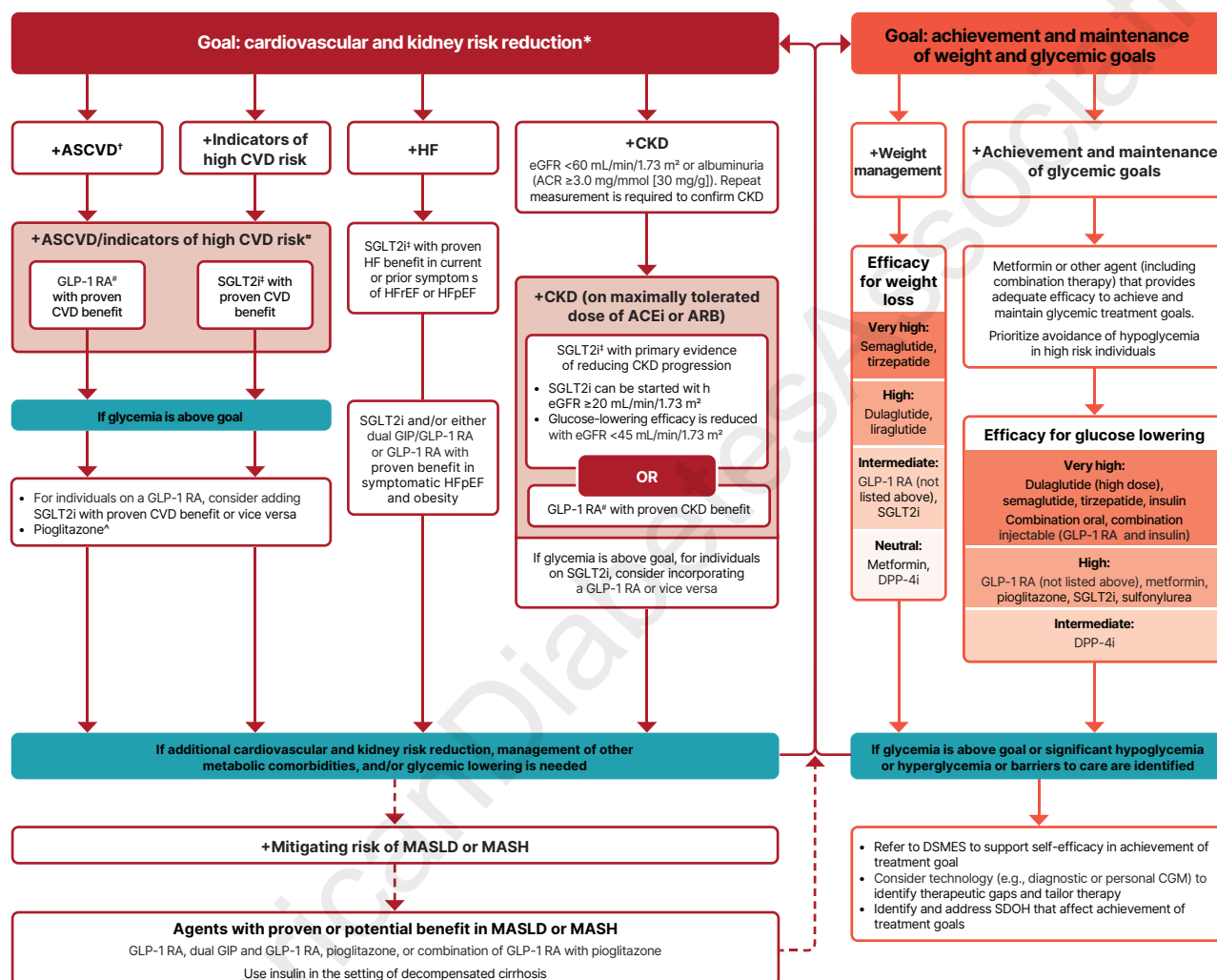
9.12 In adults with type 2 diabetes, metabolic dysfunction–associated steatotic liver disease (MASLD), and overweight or obesity, consider using a GLP-1 RA with demonstrated benefits in metabolic dysfunction–associated steatohepatitis (MASH) **A** or a dual

Use of glucose-lowering medications in the management of type 2 diabetes

(For recommendations for specific conditions, including non-glucose-lowering medications, refer to pertinent sections)

To avoid therapeutic inertia, reassess and modify treatment regularly (3–6 months)

Healthy lifestyle behaviors; diabetes self-management education and support; social determinants of health



* In people with HF, CKD, established CVD, or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be made irrespective of attainment of glycemic goal.

† ASCVD: Defined differently across CVOTs but all included individuals with established CVD (e.g., MI, stroke, and arterial revascularization procedure) and variably included conditions such as transient ischemic attack, unstable angina, amputation, and symptomatic or asymptomatic coronary artery disease. Indicators of high risk: While definitions vary, most comprise ≥55 years of age with two or more additional risk factors (including obesity, hypertension, smoking, dyslipidemia, or albuminuria).

≈ A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high risk CVD. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details.

For GLP-1 RAs, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke, and kidney end points in individuals with T2D with established or high risk of CVD. One kidney outcome trial demonstrated benefit in reducing persistent eGFR reduction and CV death for a GLP-1 RA in individuals with CKD and T2D.

‡ For SGLT2is, CV and kidney outcomes trials demonstrate their efficacy in reducing the risks of composite MACE, CV death, all-cause mortality, MI, HFrEF, and kidney outcomes in individuals with T2D and established or high risk of CVD.

^ Low-dose pioglitazone may be better tolerated and similarly effective as higher doses.

Figure 9.4—Use of glucose-lowering medications in the management of type 2 diabetes. The left side of the algorithm prioritizes mitigation of diabetes-related complications and end-organ effects, while the right side addresses weight and glucose management goals. ACEi, angiotensin-converting enzyme inhibitor; ACR, albumin-to-creatinine ratio; ARB, angiotensin receptor blocker; ASCVD, atherosclerotic cardiovascular disease; CGM, continuous glucose monitoring; CKD, chronic kidney disease; CV, cardiovascular; CVD, cardiovascular disease; CVOT, cardiovascular outcomes trial; DPP-4i, dipeptidyl peptidase 4 inhibitor; DSMES, diabetes self-management education and support; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide 1 receptor agonist; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HHF, hospitalization for heart failure; MACE, major adverse cardiovascular events; MASH, metabolic dysfunction-associated steatohepatitis; MASLD, metabolic dysfunction-associated steatotic liver disease; MI, myocardial infarction; SDOH, social determinants of health; SGLT2i, sodium–glucose cotransporter 2 inhibitor; T2D, type 2 diabetes. Adapted from Davies et al. (90).

GIP and GLP-1 RA with potential benefits in MASH **B** for glycemic management and as an adjunctive therapy to interventions for weight loss.

9.13a In adults with type 2 diabetes and biopsy-proven MASH or those at high risk for liver fibrosis (based on noninvasive tests), a GLP-1 RA is preferred for glycemic management due to beneficial effects on MASH. **A** Pioglitazone or a dual GIP and GLP-1 RA **B** can be considered for glycemic management due to potential beneficial effects on MASH. **B**

9.13b Combination therapy with pioglitazone plus a GLP-1 RA can be considered for the treatment of hyperglycemia in adults with type 2 diabetes with biopsy-proven MASH or those at high risk of liver fibrosis (identified with noninvasive tests) due to potential beneficial effects on MASH. **B**

9.14 Medication plan and medication-taking behavior should be reevaluated at regular intervals (e.g., every 3–6 months) and adjusted as needed to incorporate specific factors that affect choice of treatment and ensure achievement of individualized glycemic goals (Fig. 4.1 and Table 9.2). **E**

9.15 Treatment modification (including intensification or deintensification) for adults not meeting individualized treatment goals should not be delayed. **A**

9.16 Choice of glucose-lowering therapy modification should take into consideration individualized glycemic and weight goals, presence of comorbidities (cardiovascular, kidney, liver, and other metabolic comorbidities), and the risk of hypoglycemia. **A**

9.17 When initiating a new glucose-lowering medication, reassess the need for and/or dose of medications with higher hypoglycemia risk (i.e., sulfonylureas, meglitinides, and insulin) to minimize the risk of hypoglycemia and treatment burden. **A**

9.18 Concurrent use of dipeptidyl peptidase 4 (DPP-4) inhibitors with a GLP-1 RA or a dual GIP and GLP-1 RA is not recommended due to lack of additional glucose lowering beyond that of a GLP-1-based therapy. **B**

9.19 In adults with type 2 diabetes who have not achieved their individualized weight goals, additional weight management interventions (e.g., intensification of lifestyle modifications,

structured weight management programs, pharmacologic agents, or metabolic surgery, as appropriate) are recommended. **A**

9.20 In adults with type 2 diabetes, initiation of insulin should be considered regardless of background glucose-lowering therapy or disease duration if symptoms of hyperglycemia are present or when A1C or blood glucose levels are very high (i.e., A1C >10% [>86 mmol/mol] or blood glucose ≥ 300 mg/dL [≥ 16.7 mmol/L]). **E**

9.21 In adults with type 2 diabetes without severe hyperglycemia or hyperglycemic crisis, GLP-1–based therapy is preferred to insulin for initial or add-on glucose-lowering therapy (Fig. 9.4). **A**

9.22 If insulin is used, combination therapy with a GLP-1 RA, including a dual GIP and GLP-1 RA, is recommended for greater glycemic effectiveness as well as beneficial effects on weight and hypoglycemia risk for adults with type 2 diabetes. Insulin dosing should be reassessed upon addition or dose escalation of a GLP-1 RA or dual GIP and GLP-1 RA. **A**

9.23 In adults with type 2 diabetes who are initiating insulin therapy, continue glucose-lowering agents (unless contraindicated or not tolerated) for ongoing glycemic and metabolic benefits (i.e., weight, cardiometabolic, or kidney benefits). **A**

A holistic, multifaceted, person-centered approach that accounts for the complexity of managing type 2 diabetes and its complications across the life span is recommended. Person-specific factors that affect choice of treatment include individualized glycemic goals (see section 6, “Glycemic Goals, Hypoglycemia, and Hyperglycemic Crises”), individualized weight goals (see section 8, “Obesity and Weight Management for the Prevention and Treatment of Diabetes”), the individual’s risk for hypoglycemia, and the individual’s history of or risk factors for cardiovascular, kidney, liver, and other comorbidities and complications of diabetes (see section 4, “Comprehensive Medical Evaluation and Assessment of Comorbidities,” section 10, “Cardiovascular Disease and Risk Management,” and section 11, “Chronic Kidney Disease and Risk Management”). In addition, treatment

decisions must consider the tolerability and side effect profiles of medications, complexity of the medication plan and the individual’s capacity to implement it given their specific situation and context, and the access, cost, and availability of medications. Lifestyle modifications and health behaviors that improve health (see section 5, “Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes”) should be emphasized along with any pharmacologic therapy. Section 13, “Older Adults,” and section 14, “Children and Adolescents,” have recommendations specific for older adults and for children and adolescents with type 2 diabetes, respectively. Section 10, “Cardiovascular Disease and Risk Management,” and section 11, “Chronic Kidney Disease and Risk Management,” have recommendations for the use of glucose-lowering drugs in the management of cardiovascular disease and kidney disease, respectively.

Choice of Glucose-Lowering Therapy

Healthy lifestyle behaviors, diabetes self-management education and support (DSMES), avoidance of therapeutic inertia, and social determinants of health should be considered in the glucose-lowering management of type 2 diabetes. Pharmacologic therapy should be guided by person-centered treatment factors, including comorbidities, considerations of adverse effects (including hypoglycemia), treatment burden, and treatment goals and preferences. Shared decision-making can be facilitated during clinical encounters through use of decision aides and has been shown to improve A1C in adults with type 2 diabetes, though in clinical trials the benefits of shared decision-making were limited to face-to-face discussions (not online encounters) and to individuals with elevated A1C ($>8\%$) (89). Pharmacotherapy should be started at the time type 2 diabetes is diagnosed, without delay, unless there are contraindications. Medication plans should have adequate efficacy to achieve and maintain individualized treatment goals with respect to glucose lowering, reduction of cardiovascular and kidney disease risks, weight management, and effects on other health conditions and treatment burden. In adults with type 2 diabetes and established or high risk of atherosclerotic cardiovascular disease (ASCVD), HF, and/or CKD, the

Table 9.2—Features of medications for lowering glucose in type 2 diabetes

Medication (route of administration)	Glucose-lowering efficacy ¹	Hypoglycemia risk	CV effects			Kidney effects			Clinical considerations and adverse effects
			Weight effects ²	Effect on MACE	Effect on HF	Progression of CKD	Dosing/use considerations*	MASH effects	
Metformin (oral)	High	No	Neutral (potential for modest loss)	Potential benefit	Neutral	Neutral	Contraindicated with eGFR <30 mL/min/1.73 m²	Neutral	- GI side effects: mitigate with slow dose titration, extended-release formulations, and administration with food - Potential for vitamin B12 deficiency: monitor and replete as appropriate
SGLT2 inhibitors (oral)	Intermediate to high	No	Loss (intermediate)	Benefit: canagliflozin, empagliflozin	Benefit: canagliflozin, dapagliflozin, empagliflozin, ertugliflozin	Benefit: canagliflozin, empagliflozin, dapagliflozin	- See labels of individual agents for dosage considerations for kidney function - Glucose-lowering effect is minimal at eGFR <45 mL/min/1.73 m² and lower; continue or start for cardiovascular and kidney benefit if eGFR >20 mL/min/1.73 m². May continue until dialysis or transplantation	Unknown	- DKA risk in individuals with insulin deficiency (rare in T2D); discontinue, evaluate, and treat promptly if suspected; be aware of predisposing risk factors and clinical presentations (including euglycemic DKA); mitigate risk with sick-day planning; discontinue before scheduled surgery (e.g., 3–4 days), during critical illness, or during prolonged fasting - Genital mycotic infections: mitigate risk with genital hygiene and avoid use in high-risk individuals - Urosepsis and pyelonephritis: evaluate individuals for signs and symptoms of urinary tract infections and treat promptly - Necrotizing fasciitis in the perineum (Fournier gangrene): rare; prompt treatment if suspected - Intravascular volume depletion: attention to volume status and blood pressure, particularly when ill or fasting; adjust other volume-contracting agents as applicable; monitor kidney function upon initiation

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Table 9.2—Continued

Medication (route of administration)	Glucose-lowering efficacy ¹	Hypoglycemia risk	CV effects		Kidney effects			Clinical considerations and adverse effects
			Weight effects ²	Effect on MACE	Effect on HF	Progression of CKD	Dosing/use considerations*	
GLP-1 RAs (SQ; semaglutide also available in oral formulation)	High to very high	No	Loss (intermediate to very high)	Benefit: dulaglutide, liraglutide, semaglutide (SQ and oral)	Benefit: semaglutide (SQ)	Benefit for kidney end points in CVOTs, driven by albuminuria outcomes: dulaglutide, liraglutide, semaglutide (SQ)	- See labels of individual agents for dosage considerations for kidney function - No dose adjustment for dulaglutide, liraglutide, or semaglutide - Monitor kidney function when initiating or escalating doses in individuals with kidney impairment reporting severe adverse GI reactions	- Thyroid C-cell tumors identified in rodents; human relevance not determined - Provide guidance on discontinuation prior to surgical procedures to mitigate potential for pulmonary aspiration with general anesthesia or deep sedation - Pancreatitis: acute pancreatitis has been reported, but causality has not been established; do not initiate if at high risk for pancreatitis, and discontinue if pancreatitis is suspected - Biliary disease: evaluate for gallbladder disease if cholelithiasis or cholecystitis is suspected; avoid use in at-risk individuals - Ileus: reported, but risk level is not well established - Diabetic retinopathy: close monitoring of retinopathy in those at high risk (older individuals and those with longer duration of T2D [≥10 years]) - Nonarteritic anterior ischemic optic neuropathy (NAION) reported (rare incidence); monitor for NAION during eye examinations - Impact on drug absorption: orally administered drug absorption may be impaired during dose titration (including oral contraceptives) - GI side effects: counsel on potential for GI side effects; provide guidance on dietary modifications to mitigate GI side effects (reduction in meal size, mindful eating practices [e.g., stop eating
Dual GIP and GLP-1 RA (SQ)	Very high	No	Loss (very high)	Under investigation	Benefit: tirzepatide	Potential benefit	- See labels of individual agents for dosage considerations for kidney function - No dose adjustment - Monitor kidney function when initiating or escalating doses in individuals with kidney impairment reporting severe adverse GI reactions	Potential benefit

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Table 9.2—Continued

Medication (route of administration)	Glucose-lowering efficacy ¹	Hypoglycemia risk	CV effects			Kidney effects		Clinical considerations and adverse effects
			Weight effects ²	Effect on MACE	Effect on HF	Progression of CKD	Dosing/use considerations*	
DPP-4 inhibitors (oral)	Intermediate	No	Neutral	Neutral	Neutral (potential risk: saxagliptin)	Neutral	- Dose adjustment required based on kidney function (sitagliptin, saxagliptin, alogliptin) - No dose adjustment required for linagliptin	- Pancreatitis has been reported but causality has not been established; discontinue if pancreatitis is suspected - Postmarketing concerns about joint pain (consider discontinuing if debilitating and other treatment options are feasible) and bullous pemphigoid (discontinue if suspected) reversible upon discontinuation
Pioglitazone (oral)	High	No	Gain	Potential benefit	Increased risk	Neutral	- No dose adjustment required - Generally not recommended in kidney impairment due to potential for fluid retention	- Increased risk of HF and fluid retention; do not use in setting of HF - Risk of bone fractures - Bladder cancer: do not use in individuals with active bladder cancer, and use caution in those with prior history of bladder cancer; association observed with higher cumulative exposure (e.g., longer duration, higher doses)
Sulfonylureas (2nd generation) (oral)	High	Yes	Gain	Neutral	Neutral	Neutral	- Glyburide: generally not recommended in CKD - Glipizide and glimepiride: initiate conservatively to avoid hypoglycemia	- FDA Special Warning on increased risk of CV mortality based on studies of an older sulfonylurea (tolbutamide); glimepiride shown to be CV safe (see text) - Use with caution in individuals at risk for hypoglycemia, particularly if in combination with insulin

Continued on p. S196

Table 9.2—Continued

Medication (route of administration)	Glucose-lowering efficacy ¹	Hypoglycemia risk	Weight effects ²		CV effects		Progression of CKD	Kidney effects		MASH effects	Clinical considerations and adverse effects
			Gain	Neutral	Effect on MACE	Effect on HF		Effect on MACE	Effect on HF		
Insulin (human) (SQ, regular insulin also available as inhaled formulation) Insulin (analogs) (SQ)	High to very high	Yes	Gain	Neutral	Neutral	Neutral	Neutral	Lower insulin doses required with a decrease in eGFR; titrate per clinical response	Unknown	Unknown	- Injection site reactions - Higher risk of hypoglycemia with human insulin (NPH or premixed formulations) vs. analogs - Risk of hypoglycemia and duration of activity increases with severity of impaired kidney function - Refer to device-specific instructions for insulins compatible with different delivery systems (i.e., pens, connected insulin pumps, insulin patches)

CKD, chronic kidney disease; CV, cardiovascular; DKA, diabetic ketoacidosis; DPP-4, dipeptidyl peptidase 4; eGFR, estimated glomerular filtration rate; FDA, U.S. Food and Drug Administration; GI, gastrointestinal; GIP, glucose-dependent insulinotropic polypeptide; GLP-1 RA, glucagon-like peptide 1 receptor agonist; HF, heart failure; MACE, major adverse cardiovascular events; MASH, metabolic dysfunction-associated steatohepatitis; SGLT2, sodium-glucose cotransporter 2; SQ, subcutaneous; T2D, type 2 diabetes. *For agent-specific dosing recommendations, please refer to manufacturers' prescribing information. ¹Tsapas et al. (107). ²Tsapas et al. (317). Adapted from Davies et al. (90).

treatment plan should include agents that reduce cardiovascular and kidney disease risk (**Fig. 9.4** and **Table 9.2**) (see also section 10, "Cardiovascular Disease and Risk Management," and section 11, "Chronic Kidney Disease and Risk Management").

In individuals without ASCVD, HF, or CKD, choice of therapy should be informed by considerations of weight management (see section 8, "Obesity and Weight Management for the Prevention and Treatment of Diabetes"), mitigation of metabolic dysfunction–associated steatotic liver disease (MASLD) or metabolic dysfunction–associated steatohepatitis (MASH) risk (see section 4, "Comprehensive Medical Evaluation and Assessment of Comorbidities"), and achievement and maintenance of individualized glycemic goals. In general, higher-efficacy approaches, including combination therapy, have greater likelihood of achieving treatment goals. Weight management is a distinct treatment goal, along with glycemic management, as it has multifaceted benefits, including reduction of A1C, reduction in hepatic steatosis, and improvement in cardiovascular risk factors (90–92). For individuals with type 2 diabetes who require initiation or intensification of glucose-lowering therapy to achieve and/or maintain individualized glycemic goals and who do not have additional considerations informing choice of therapy beyond need for glucose lowering, metformin is a commonly used medication that historically has been the first-line treatment for type 2 diabetes (93,94). Metformin is effective and safe, is inexpensive and widely available, and reduces risks of microvascular complications, cardiovascular events, and death (93,95,96). Metformin is available in an immediate-release form for twice-daily dosing or as an extended-release form that can be given once daily. Compared with sulfonylureas, metformin as first-line therapy has beneficial effects on A1C, is weight neutral, does not cause hypoglycemia, and reduces cardiovascular mortality (97). Metformin is also more effective than dipeptidyl peptidase 4 (DPP-4) inhibitors in lowering A1C and weight when used as monotherapy (98).

The principal side effects of metformin are gastrointestinal intolerance due to bloating, abdominal discomfort, and diarrhea; these can be mitigated by gradual dose titration and/or using extended-

release formulation. The drug is cleared by kidney filtration, and metformin may be safely used in people with estimated glomerular filtration rate ≥ 30 mL/min/1.73 m² (99). Very high circulating levels (e.g., as a result of overdose or acute kidney injury) have been associated with lactic acidosis (100). However, the occurrence of this complication is very rare (101) and primarily occurs when the estimated glomerular filtration rate (eGFR) is <30 mL/min/1.73 m² (102). For people with an eGFR of 30–45 mL/min/1.73 m², there is an increased risk for periodic decreases of eGFR to ≤ 30 mL/min/1.73 m² which heightens the risk of lactic acidosis. Metformin use is also associated with increased risk of vitamin B12 deficiency and worsening of symptoms of neuropathy (103,104), suggesting periodic testing of vitamin B12 levels (see section 3, “Prevention or Delay of Diabetes and Associated Comorbidities”).

The comparative glucose-lowering efficacy of different pharmacologic agents has been examined primarily in network meta-analyses, as few prospective clinical trials have compared multiple drug classes head-to-head. In general, the largest reductions in A1C levels are achieved by treatment plans that include insulin, select GLP-1 RAs (particularly semaglutide), and tirzepatide, while DPP-4 inhibitors resulted in the smallest reductions in A1C (105–107). The Glycemia Reduction Approaches in Type 2 Diabetes: A Comparative Effectiveness (GRADE) trial compared use of insulin glargine U-100, liraglutide, sitagliptin, and glimepiride as add-on treatments to metformin monotherapy among individuals with type 2 diabetes and baseline A1C 6.8–8.5% (108). It found that at 5 years, all therapies decreased A1C levels but glargine and liraglutide were modestly more effective in achieving and maintaining A1C below 7%, while sitagliptin was least effective. Severe hypoglycemia was significantly more common in those prescribed glargine or glimepiride. An observational study that emulated many of GRADE’s design features and included canagliflozin as a comparator arm, but did not include insulin glargine, found that liraglutide was more effective at achieving and maintaining A1C below 7% than sitagliptin, canagliflozin, or glimepiride, which all had comparable effectiveness (108).

Thus, when choosing a glucose-lowering medication to achieve individualized glycemic goals, we recommend engaging in

shared decision-making and considering factors such as glucose-lowering efficacy, the side effect profile, and medication accessibility and affordability (108). In all cases, treatment plans need to be continuously reviewed for efficacy, side effects, hypoglycemia, and treatment burden (Table 9.2).

When A1C is $\geq 1.5\%$ above the individualized glycemic goal (see section 6, “Glycemic Goals, Hypoglycemia, and Hyperglycemic Crises,” for appropriate goals), many individuals will require dual-combination therapy or a more potent glucose-lowering agent to achieve and maintain their goal A1C level (90) (Fig. 9.4 and Table 9.2). Insulin should be considered as part of any combination medication plan when hyperglycemia is severe, especially if catabolic features (weight loss, hypertriglyceridemia, and ketosis) are present. It is common practice to initiate insulin therapy for people who present with blood glucose levels ≥ 300 mg/dL (≥ 16.7 mmol/L) or A1C $>10\%$ (>86 mmol/mol) or if the individual has symptoms of hyperglycemia (i.e., polyuria or polydipsia) or evidence of catabolism (unexpected weight loss) (Fig. 9.5). As glucose toxicity resolves, simplifying the medication plan and/or changing to noninsulin agents is possible. Additionally, there is evidence that people with type 2 diabetes and severe hyperglycemia can also be effectively treated with a sulfonylurea, a GLP-1 RA, or a dual GIP and GLP-1 RA, though evidence is scarce for individuals with baseline A1C above 10–12% (105,109–111). GLP-1 RAs and tirzepatide have additional benefits over insulin and sulfonylureas, specifically lower risks for hypoglycemia (both) and favorable weight (both), cardiovascular (GLP-1 RAs), kidney (GLP-1 RAs), and liver (both) end points.

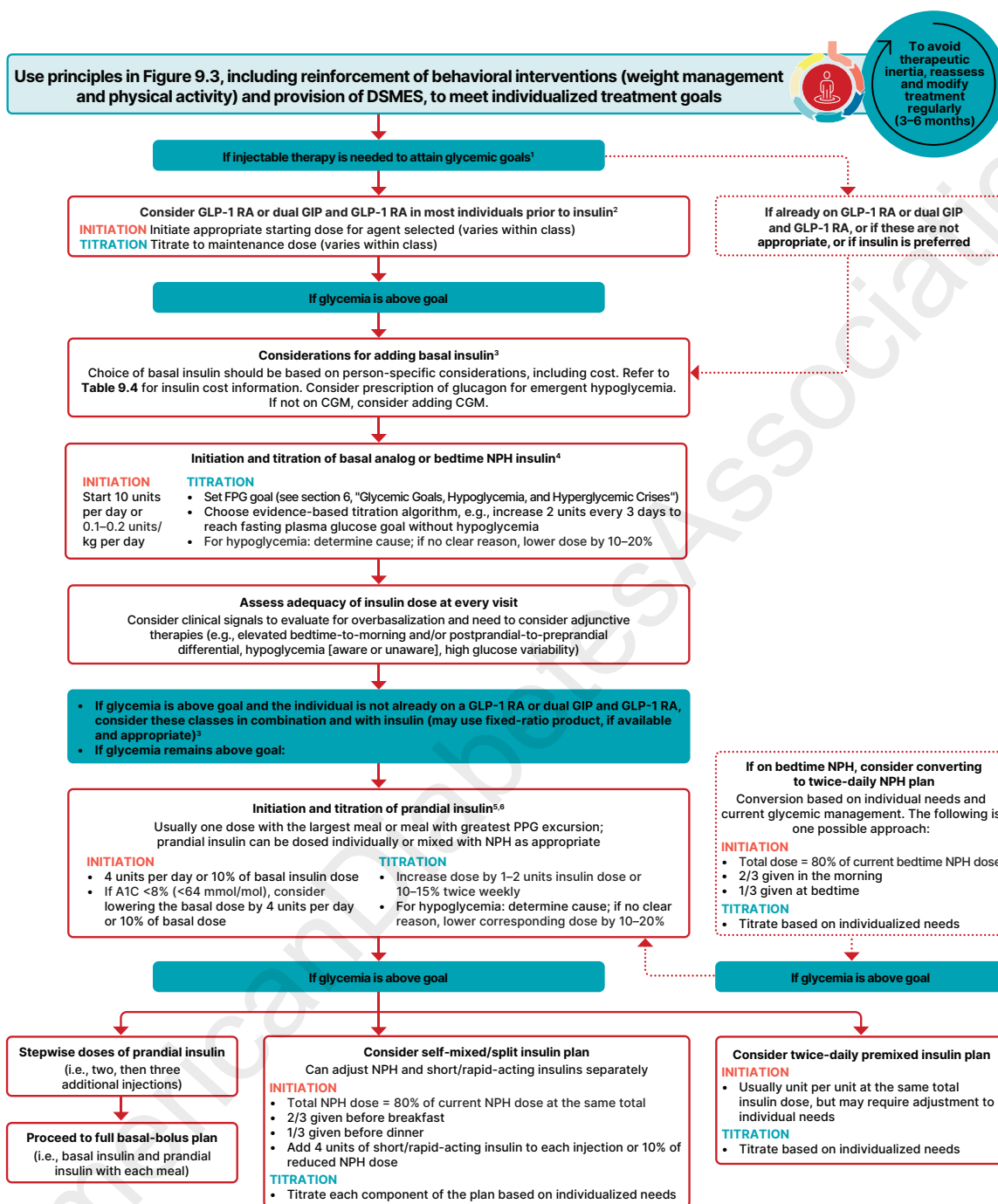
Combination Therapy

Because type 2 diabetes is a progressive disease, maintenance of glycemic goals often requires combination therapy. Traditional recommendations have called for the use of stepwise addition of medications to metformin to maintain A1C goals. The advantage of this is to provide a clear assessment of the positive and negative effects of new drugs and reduce potential side effects and expense (112). However, some data support initial combination therapy for more rapid attainment of glycemic goals (113,114) and later combination therapy for longer durability of glycemic

effect (115). Initial combination therapy should be considered in people presenting with A1C levels 1.5–2.0% above their individualized goal or in those at high risk for cardiovascular disease (CVD) or with established CVD irrespective of A1C levels (GLP-1 RA and SGLT2 inhibitor combination therapy) (see section 10, “Cardiovascular Disease and Risk Management”). The incorporation of high-glycemic-efficacy therapies or therapies for cardiovascular and kidney disease risk reduction (e.g., GLP-1 RAs, a dual GIP and GLP-1 RA, and SGLT2 inhibitors) may reduce the need for agents that increase the risks of hypoglycemia and weight gain or are less well tolerated. Thus, treatment intensification requires purposeful selection of medications in alignment with multiple individualized person-centered treatment goals simultaneously (Fig. 9.4).

Treatment intensification, deintensification, or modification, as appropriate, for people not meeting individualized treatment goals should not be delayed (therapeutic inertia) (116). Results from comparative effectiveness meta-analyses suggest that each new class of oral noninsulin agents when added to metformin generally lowers A1C by approximately 0.7–1.0% (8–11 mmol/mol). Addition of GLP-1 RAs or the dual GIP and GLP-1 RA to metformin usually results in 1% to $\geq 2\%$ lowering of A1C (105,117,118) (Fig. 9.4 and Table 9.2). Use of GLP-1 RAs (or the dual GIP and GLP-1 RA) together with a DPP-4 inhibitor is not recommended, as there is no added glucose-lowering benefit beyond that of the GLP-1 RA alone (119–121).

When even greater potency of glucose reduction is needed, basal insulin, either human NPH or a long-acting insulin analog, should be initiated. However, if the individual is not already receiving GLP-1 RA or dual GIP and GLP-1 RA therapy, an agent from these classes should be started first, as it may be sufficient for achieving individualized A1C goals but with lower risk of hypoglycemia and with favorable weight, cardiovascular, kidney, and liver profiles. While most GLP-1 RAs are injectable medications, an oral formulation of semaglutide is commercially available (122). In trials analyzing the addition of an injectable GLP-1 RA, dual GIP and GLP-1 RA, or insulin in people needing further glucose lowering, glycemic efficacies of GLP-1 RAs and the dual GIP and GLP-1 RA were similar to or greater than



1. Consider insulin as the first injectable if symptoms of hyperglycemia are present, when A1C or blood glucose levels are very high (i.e., A1C >10% [>86 mmol/mol] or blood glucose ≥ 300 mg/dL [≥ 16.7 mmol/L]), or when a diagnosis of type 1 diabetes is a possibility.
2. When selecting GLP-1 RAs, consider individual preference, glycemic lowering, weight-lowering effect, and frequency of injection. If CVD is present, consider GLP-1 RA with proven CVD benefit; oral or injectable GLP-1 RAs are appropriate.
3. For people on GLP-1 RA and basal insulin combination, consider use of a fixed-ratio combination product (IDegLira or iGlarLixi).
4. Consider switching from evening NPH to a basal analog if the individual develops hypoglycemia and/or frequently forgets to administer NPH in the evening and would be better managed with a morning dose of a long-acting basal insulin. Consider dosing NPH in the morning for steroid-induced hyperglycemia.
5. Prandial insulin options include injectable rapid- and ultra-rapid-acting analog insulins, injectable short-acting human insulin, or inhaled human insulin.
6. If adding prandial insulin to NPH, consider initiation of a self-mixed or premixed insulin plan to decrease the number of injections required.

Figure 9.5—Intensifying to injectable therapies in type 2 diabetes. CGM, continuous glucose monitoring; DSMES, diabetes self-management education and support; FPG, fasting plasma glucose; GLP-1 RA, glucagon-like peptide 1 receptor agonist; GIP, glucose-dependent insulintropic polypeptide; PPG, postprandial glucose. Adapted from Davies et al. (318).

that of basal insulin (123–130). GLP-1 RAs and dual GIP and GLP-1 RA in these trials also had a lower risk of hypoglycemia and beneficial effects on body weight compared with insulin, albeit with greater gastrointestinal side effects. Thus, trial results support high-potency GLP-1 RAs and dual GIP and GLP-1 RA as the preferred options for individuals requiring more intensive glucose management (Fig. 9.5).

In individuals who are intensified to insulin therapy, combination therapy with a GLP-1 RA or a dual GIP and GLP-1 RA has been shown to have greater efficacy and durability of glycemic treatment effects, as well as weight and hypoglycemia benefits, than treatment intensification with insulin alone (90,131). However, cost, accessibility, and tolerability are important considerations for GLP-1 RA and dual GIP and GLP-1 RA use.

In all cases, treatment plans need to be continuously reviewed for efficacy, side effects (including hypoglycemia), and treatment burden (Table 9.2). In some instances, the individual will require medication reduction or discontinuation. Common reasons for this include ineffectiveness, hypoglycemia, intolerable side effects, new contraindications, expense, or a change in glycemic goals (e.g., in response to development of comorbidities). See below for cost considerations of glucose-lowering therapies (MEDICATION COSTS AND AFFORDABILITY). Section 13, “Older Adults,” has a full discussion of treatment considerations in older adults. Treatment deintensification may also be needed in the setting of weight loss and/or optimization of lifestyle behaviors, when fewer pharmacologic agents are needed to maintain A1C goals. In this case, we recommend preferential deescalation of therapies that are most likely to cause side effects, hypoglycemia, and/or treatment burden and do not have cardiovascular, kidney, or metabolic benefits for continued use.

Glucose-Lowering Therapy for People With Cardiovascular Disease or Risk Factors for Cardiovascular Disease

For people with type 2 diabetes and established ASCVD or indicators of high ASCVD risk, HF, or CKD, an SGLT2 inhibitor and/or GLP-1 RA with demonstrated cardiovascular benefit (Table 9.2) is recommended independent of A1C, with or without metformin use, and in consideration of person-specific factors (Fig. 9.4).

GLP-1 RAs or a dual GIP and GLP-1 RA with demonstrated benefits are recommended for people with type 2 diabetes, obesity, and symptomatic HF with preserved ejection fraction (132–135) (Table 9.2 and Fig. 9.4). Individuals with these comorbidities already achieving their individualized glycemic goals with other medications may benefit from switching to these preferred medications to reduce risk of ASCVD, HF, and/or CKD in addition to achieving glycemic goals (see section 10, “Cardiovascular Disease and Risk Management,” and section 11, “Chronic Kidney Disease and Risk Management”). This is particularly important because SGLT2 inhibitors and GLP-1 RAs are associated with lower risk of hypoglycemia and individuals with ASCVD, HF, and CKD have higher hypoglycemia risk than individuals without these conditions (136).

Individuals at lower risk for ASCVD may still benefit from GLP-1 RA therapy to reduce their risk of future cardiovascular events. The GRADE trial, which was designed to examine the comparative effectiveness of insulin glargine U-100, glimepiride, liraglutide, and sitagliptin in individuals with relatively short duration of diabetes (and without established CVD) with respect to achieving and maintaining A1C below 7%, found that individuals treated with liraglutide had a lower risk of cardiovascular events than individuals receiving the other three treatments (hazard ratio 0.7 [95% CI 0.6–0.9]), although no significant differences were found between individual treatment groups for major adverse cardiovascular events, hospitalization for HF, or cardiovascular death (137). Individuals with type 2 diabetes and moderate levels of CVD risk appear to derive cardiovascular and mortality benefits with preferential use of GLP-1 RA and SGLT2 inhibitors compared with sulfonylurea or DPP-4 inhibitors (138). Similarly, while greater reductions in HF hospitalization risk are observed with SGLT2 inhibitor therapy in individuals with higher baseline HF risk, some benefit is observed across the full range of HF risk (139).

Glucose-Lowering Therapy for People With Chronic Kidney Disease

For individuals with type 2 diabetes and CKD, considerations for selection of glucose-lowering medications include their effectiveness and safety when eGFR is reduced as well as the potential to affect CKD progression, CVD risk, and hypoglycemia (140). Preferred medications for glucose

management in individuals with CKD are GLP-1 RAs and SGLT2 inhibitors (can be initiated if eGFR is above 20 mL/min/1.73 m²). GLP-1 RAs are effective in lowering glucose levels, regardless of kidney function, with a low risk for hypoglycemia, and a recent clinical trial suggests that the GLP-1 RA semaglutide has a beneficial effect on CVD, mortality, and kidney outcomes among people with CKD, leading to the recommendation that semaglutide can be used as another first-line agent for people with CKD (141,142). Other GLP-1 RAs (liraglutide and dulaglutide) may also have CKD benefits, but no other dedicated kidney trials have been published. Similarly, no dedicated kidney outcomes studies for the dual GIP and GLP-1 RA (tirzepatide) have been published, although post hoc analyses of clinical trials in people with type 2 diabetes have shown that tirzepatide slowed the rate of eGFR decline and reduced albuminuria (143,144). The GLP-1 RAs lixisenatide and exenatide, which require the kidneys for elimination, should be avoided in individuals with eGFR ≤30 mL/min/1.73 m² or with creatinine clearance ≤30 mL/min, respectively (145–147).

Dedicated kidney outcomes trials in people with CKD and type 2 diabetes have shown that the SGLT2 inhibitors empagliflozin, canagliflozin, and dapagliflozin have beneficial effects on slowing progression of CKD and CV outcomes in this population (148–150). However, their ability to lower glucose levels declines when the eGFR falls below 45 mL/min/1.73 m² (151–153). Metformin is also a therapeutic agent for those with CKD due to its well-documented efficacy and safety profile for people with type 2 diabetes. However, there is no documented direct kidney benefit. Importantly, metformin should not be started in those whose eGFR is <45 mL/min/1.73 m². For those already treated with metformin, the dose of metformin should be reduced once eGFR is <45 mL/min/1.73 m² and should be stopped once eGFR is <30 mL/min/1.73 m² (99). A secondary analysis of the GRADE trial found that insulin glargine, liraglutide, sitagliptin, and glimepiride did not prevent the development of CKD when added to metformin monotherapy in individuals without underlying CKD (154).

Individuals with CKD, particularly advanced CKD and kidney failure, are at high risk for hypoglycemia (136). If treated with insulin and/or sulfonylureas, treatment needs

to be closely monitored and adjusted as eGFR declines and individuals need to be educated about and closely monitored for hypoglycemia occurrence (140). See section 11, "Chronic Kidney Disease and Risk Management," for more details about prevention and treatment of CKD in individuals with diabetes.

Glucose-Lowering Therapy for People With Metabolic Comorbidities

Many adults with diabetes, either type 2 diabetes or type 1 diabetes, with obesity are at high risk of developing MASLD or MASH as well as MASH cirrhosis. Hence, the presence of MASLD or MASH should be a consideration when choosing glucose-lowering therapies. Accruing randomized clinical trial data suggest that pioglitazone, GLP-1 RAs, and a dual GIP and GLP-1 RA have favorable outcomes in terms of decreasing hepatic steatosis and in the resolution of MASH without worsening of fibrosis in individuals with biopsy-proven MASH or those at higher risk of clinically significant liver fibrosis identified with noninvasive tests (155–160). Combination therapy with pioglitazone plus GLP-1 RA should also be considered for treatment of hyperglycemia in adults with type 2 diabetes with biopsy-proven MASH or those at higher risk of clinically significant liver fibrosis identified with noninvasive tests, as such therapy is safe and effective and has been shown to reduce hepatic steatosis (161–163). It is important to note that these studies are based on phase 2 clinical trials and that only semaglutide has recently shown benefit in a phase 3 clinical trial with histological outcomes in MASH, including improvements in steatohepatitis and fibrosis (156); this subsequently led to its approval by the FDA for the treatment of MASH with moderate to advanced liver fibrosis, while the other therapies await further phase 3 confirmation of evidence. However, these plans are preferred as they offer potential benefit compared with lack of histological benefit (or clinical trial data) from other glucose-lowering therapies in MASLD. Further details regarding liver health in diabetes can be found in section 4, "Comprehensive Medical Evaluation and Assessment of Comorbidities."

Obesity is present in over 90% of people with type 2 diabetes, and in these individuals weight management is a key treatment goal, along with glucose lowering. In the setting of obesity, the choice of glucose-lowering medications should take

into consideration their effects on weight. Insulins, sulfonylureas, and thiazolidinediones can promote weight gain and should be used judiciously and at the lowest possible dose. Glucose-lowering medications that promote weight loss should be prioritized. Of the currently available agents, tirzepatide and semaglutide have the highest efficacy in terms of glucose lowering as well as weight loss, followed by dulaglutide, liraglutide, and extended-release exenatide (164–168). Other glucose-lowering medications (metformin, SGLT2 inhibitors, DPP-4 inhibitors, dopamine agonists, bile acid sequestrants, and α -glucosidase inhibitors) are weight neutral or have a modest beneficial effect on weight. These medications can be used as add-on therapies in people with type 2 diabetes and obesity who require additional glucose lowering or if the more effective medications are not tolerated, are contraindicated, or are unavailable. Metabolic surgery, especially Roux-en-Y gastric bypass and sleeve gastrectomy, are very effective interventions to achieve both weight and glycemic goals and have additional health benefits beyond improving metabolism (169). Further details regarding treatment of obesity can be found in section 8, "Obesity and Weight Management for the Prevention and Treatment of Diabetes."

Insulin Therapy

Many adults with type 2 diabetes eventually require and benefit from insulin therapy (Fig. 9.5). See INSULIN ADMINISTRATION TECHNIQUE, above, for guidance on how to administer insulin safely and effectively. The progressive nature of type 2 diabetes should be regularly and objectively explained to individuals with diabetes, and clinicians should avoid using insulin as a threat or describing it as a sign of personal failure. The utility and importance of insulin to achieve and maintain glycemic goals once progression of the disease overcomes the effect of other agents as well as for temporary use for acute situations (such as hospitalization, acute illness, or high-dose glucocorticoid therapy) should be emphasized. Educating and involving people with diabetes in insulin management is beneficial. For example, instruction of individuals with type 2 diabetes initiating insulin on self-titration of insulin doses based on glucose monitoring improves glycemic management (170). Comprehensive education regarding

glucose monitoring, nutrition, physical activity, contingency planning (for illness, fasting, or medication unavailability), and the prevention and appropriate treatment of hypoglycemia are critically important for all individuals using insulin. Assessment and education tailored to improve health literacy and numeracy may be necessary for individuals to effectively use various insulin dosing strategies and tools (57,58). See section 5, "Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes," for guidance on diabetes self-management education.

Basal Insulin

Basal insulin alone is the most convenient initial insulin treatment and can be added to noninsulin glucose-lowering medications. For individuals with type 2 diabetes, starting doses can be estimated based on body weight (0.1–0.2 units/kg/day) and the degree of hyperglycemia, with individualized titration over time as needed to achieve and maintain glycemic goals. The principal action of basal insulin is to restrain hepatic glucose production and limit hyperglycemia overnight and between meals (171,172). Attainment of fasting glucose goals can be achieved with human NPH insulin or a long-acting insulin analog. In clinical trials, long-acting basal analogs (U-100 glargine) have been demonstrated to reduce the risk of level 2 hypoglycemia and nocturnal hypoglycemia compared with NPH insulin (173). Longer-acting basal analogs (U-300 glargine or degludec) convey a lower nocturnal hypoglycemia risk than U-100 glargine (174,175). It is important to understand how to convert individuals from one basal insulin to another, as switching insulins may be required due to the availability of more clinically appropriate insulin alternatives, removal of a product from the market (i.e., insulin detemir), or changes to insurance coverage. Often doses can be converted unit for unit and subsequently adjusted based on glucose monitoring; however, an initial dose reduction of 10–20% can be used for individuals in very tight management or at high risk for hypoglycemia and is typically needed when switching from human NPH insulin or U-300 glargine to another insulin (176). Clinicians should also be aware of the potential for overbasalization with insulin therapy (i.e., use of higher than clinically necessary and appropriate dose of basal insulin, typically masking insufficient

mealtime insulin). Clinical signals that should prompt evaluation for overbasalization include high bedtime-to-morning or postprandial-to-preprandial glucose differential (e.g., bedtime-to-morning glucose differential ≥ 50 mg/dL [≥ 2.8 mmol/L]), hypoglycemia (aware or unaware), and high glucose variability. Evidence of over-basalization should prompt reevaluation of the glucose-lowering treatment plan to better address postprandial hyperglycemia (177).

Combination Injectable Therapy and Prandial Insulin

If basal insulin has been titrated to an acceptable fasting blood glucose level and A1C remains above goal, if there is evidence of significant postprandial hyperglycemia, or if signs of overbasalization are present, advancement to combination injectable therapy is necessary (Fig. 9.5). This approach can use a GLP-1 RA or dual GIP and GLP-1 RA added to basal insulin or multiple doses of prandial insulin (131,178). If an individual is not already being treated with a GLP-1 RA or dual GIP and GLP-1 RA, a GLP-1 RA (either as an individual product or in a fixed-ratio combination with a basal insulin product) or dual GIP and GLP-1 RA should be considered prior to starting prandial insulin to address prandial management and to lower the risks of hypoglycemia and weight gain associated with insulin therapy (131,178).

Further intensification of insulin therapy entails adding doses of prandial insulin to basal insulin. Starting with a single prandial dose with the largest meal of the day is simple and effective, and it can be advanced to a plan with multiple prandial doses if necessary (179). We suggest starting with a prandial insulin dose of 4 units or 10% of the amount of basal insulin at the largest meal or the meal with the greatest postprandial excursion. The prandial insulin plan can then be intensified based on individual needs (Fig. 9.5). Alternatively, for an individual treated with basal insulin in whom additional prandial coverage is desired but administering insulin prior to one or more meals is not feasible, the medication plan can be converted to two doses of a premixed insulin. Each approach has advantages and disadvantages. For example, basal-prandial plans offer greater flexibility for individuals who eat on irregular schedules, have variable meal content, or otherwise benefit from greater individualization and flexibility in insulin administration. On the other hand,

two doses of premixed insulin is a simple, convenient means of spreading insulin across the day. Moreover, human insulins, separately, self-mixed, or as premixed NPH/regular (for example, 70/30) formulations, are often less costly alternatives to insulin analogs.

Individuals with type 2 diabetes are generally more insulin resistant than those with type 1 diabetes, require higher daily doses (~ 1 unit/kg), and have lower rates of hypoglycemia (180). Meta-analyses of trials comparing rapid-acting insulin analogs with human regular insulin in type 2 diabetes have not reported meaningful differences in A1C or hypoglycemia (181). Titration of prandial insulin can be based on home self-monitored blood glucose or CGM. When significant additions to the prandial insulin dose are made, particularly with the evening meal, consideration should be given to decreasing basal insulin to reduce risk of hypoglycemia. When initiating intensification of insulin therapy, metformin, SGLT2 inhibitors, and GLP-1 RAs (or a dual GIP and GLP-1 RA) should be maintained, unless adverse effects (including significant treatment burden) or contraindications are present. Use of sulfonylureas, meglitinides, and DPP-4 inhibitors should be limited or discontinued, as these medications do not have additional beneficial effects on cardiovascular, kidney, weight, or liver outcomes, and sulfonylureas and meglitinides increase risk of hypoglycemia and weight gain. Adjunctive use of pioglitazone may help to improve glycemia and reduce the amount of insulin needed, although potential side effects should be considered and may limit its use.

Once a basal-bolus insulin plan is initiated, dose titration is important, with adjustments made in both prandial and basal insulins based on blood glucose levels and an understanding of the pharmacodynamic profile of each formulation (also known as pattern control or pattern management). In some people with type 2 diabetes with significant clinical complexity, multimorbidity, and/or treatment burden, it may become necessary to simplify or deintensify complex insulin plans to decrease risk of hypoglycemia and improve quality of life (see section 13, "Older Adults").

Concentrated Insulins

Concentrated preparations may be more convenient (fewer injections to achieve goal dose) and comfortable (less volume

to inject the desired dose and/or less injection effort) for individuals and may improve treatment plan engagement in those with insulin resistance who require large doses of insulin. Several concentrated insulin preparations are currently available. U-500 regular insulin is, by definition, five times more concentrated than U-100 regular insulin. U-500 regular insulin has distinct pharmacokinetics with similar onset but a delayed, blunted, and prolonged peak effect and longer duration of action compared with U-100 regular insulin; thus, it has characteristics more like a premixed intermediate-acting (NPH) and regular insulin product and can be used as two or three daily injections (182,183). U-300 glargine and U-200 degludec are three and two times, respectively, as concentrated as their U-100 formulations and allow higher doses of basal insulin administration per volume used. U-300 glargine has a longer duration of action than U-100 glargine but modestly lower efficacy per unit administered (184–186). The U-200 formulations of insulin degludec, insulin lispro, and insulin lispro-aabc have pharmacokinetics similar to those of their U-100 counterparts (187–189). While U-500 regular insulin is available in both prefilled pens and vials, other concentrated insulins are available only in prefilled pens to minimize the risk of dosing errors. If U-500 regular insulin vials are prescribed, the prescription should be accompanied by a specific prescription for U-500 syringes to minimize the risk of dosing errors.

Alternative Insulin Routes

Insulin is primarily administered via subcutaneous injection or infusion. Administration devices provide some additional variation in the subcutaneous delivery beyond vial and syringe versus insulin pen. Those devices include continuous insulin pumps (programmable or automated basal and bolus settings and fixed basal and bolus settings) and bolus-only insulin patch pump. In addition, prandial or correction insulin doses may be administered using inhaled human insulin. Inhaled insulin is available as monomers of regular human insulin; studies in individuals with type 1 diabetes suggest that inhaled insulin has pharmacokinetics faster than those of RAA (190). Studies comparing inhaled insulin with injectable insulin have demonstrated its faster onset and shorter duration compared with the RAA insulin lispro as well as clinically meaningful A1C reductions and

weight reductions compared with the RAA insulin aspart over 24 weeks (190–192). Use of inhaled insulin may result in a decline in lung function (reduced forced expiratory volume in 1 s [FEV₁]). Inhaled insulin is contraindicated in individuals with chronic lung disease, such as asthma and chronic obstructive pulmonary disease, and is not recommended in individuals who smoke or who recently stopped smoking. All individuals require spirometry (FEV₁) testing to identify potential lung disease prior to and after starting inhaled insulin therapy.

ADDITIONAL RECOMMENDATIONS FOR ALL INDIVIDUALS WITH DIABETES

Recommendations

9.24 Include healthy behaviors, diabetes self-management education and support, avoidance of therapeutic inertia, and social determinants of health as essential components of the glucose-lowering management of diabetes. **A**

9.25 Use of continuous glucose monitoring (CGM) is recommended at diabetes onset and anytime thereafter for adults with diabetes who are on insulin therapy, **A** on noninsulin therapies that can cause hypoglycemia, **B** and on any diabetes treatment where CGM aids in management. **B** The choice of CGM device and method for use should be made based on the individual's circumstances, preferences, and needs.

9.26 Monitor for signs of overbasalization during insulin therapy, such as significant bedtime-to-morning or postprandial-to-preprandial glucose differential, occurrences of hypoglycemia (aware or unaware), and high glycemic variability. When overbasalization is suspected, a thorough reevaluation should occur promptly to further tailor therapy to the individual's needs. **E**

9.27 Automated insulin delivery systems should be offered to all adults with type 1 and 2 diabetes on insulin depending on the person's or caregiver's needs and preferences. **A**

9.28 Glucagon should be prescribed for all individuals taking insulin or at high risk for hypoglycemia. **A** Family, caregivers, school personnel, and others providing support to these individuals should know its location and be educated on how to administer it. Glucagon preparations that

do not require reconstitution are preferred. **B**

9.29 Routinely assess all people with diabetes for financial obstacles that could impede their diabetes management. Clinicians, members of the diabetes care team, and social services professionals should work collaboratively, as appropriate and feasible, to support these individuals by implementing strategies to reduce costs, thereby improving their access to evidence-based care. **E**

9.30 In adults with diabetes and cost-related barriers, consider use of lower-cost medications for glycemic management (i.e., metformin, sulfonylureas, thiazolidinediones, and human insulin) within the context of their risks for hypoglycemia, weight gain, cardiovascular and kidney events, and other adverse effects. **E**

Several key aspects of insulin management that are relevant to all people with diabetes requiring insulin therapy, including available formulations, insulin plans and delivery systems, administration technique, and overbasalization, were discussed earlier in this section. Additional essential components for the glucose-lowering management plan that are relevant to people with all types of diabetes include encouraging healthy behaviors and diabetes self-management education and support (see section 5, "Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes"), considering social determinants of health (see section 1, "Improving Care and Promoting Health in Populations"), avoiding and preventing therapeutic inertia, and prescribing glucagon and affordable diabetes treatments.

Diabetes Technology and Glycemic Management

The use of continuous glucose monitoring (CGM) in adults with diabetes improves glycemic outcomes (e.g., A1C, time in range) and reduces episodes of hypoglycemia in adults with diabetes who are on insulin therapy or other noninsulin therapies that can induce hypoglycemia (193–209). In addition, the use of AID systems should be offered to adults with type 1 or type 2 diabetes who are on insulin therapy to improve glycemic management and glycemic outcomes (26,28–32,35–37,210–215). The decision

of which CGM and/or AID system to use should be based on the preference of the individual with diabetes and their caregivers, availability of resources to provide the needed training and education, and available support. As the diabetes technology landscape is rapidly evolving and individuals require a tailored approach, health care teams may encounter challenges with determining the best technology for people with diabetes. An ADA resource, which can be found at diabetes.org/living-with-diabetes/treatment-care/diabetes-technology-guide, can provide helpful information for health care professionals and individuals with diabetes in making decisions regarding technology. For more information on diabetes technology, see section 7, "Diabetes Technology."

Glucagon

Due to the risk of hypoglycemia with insulin treatment, all individuals treated with insulin or who are at high risk for hypoglycemia should be prescribed glucagon. Individuals with diabetes who are prescribed glucagon and those in close contact with them should be educated on the use and administration of the individual's prescribed glucagon product. The glucagon product available to individuals may differ based on coverage and cost; however, products that do not require reconstitution are preferred for ease of administration (216,217). Clinicians should routinely review the individual's access to glucagon, as appropriate glucagon prescribing is low (218–220). See section 6, "Glycemic Goals, Hypoglycemia, and Hyperglycemic Crises," for additional information on hypoglycemia and glucagon in individuals with diabetes.

Medication Costs and Affordability

Costs for noninsulin and insulin diabetes medications have increased dramatically over the past two decades, and an increasing proportion of cost is now passed on to people with diabetes and their families (221). **Table 9.3** provides cost information for currently approved noninsulin therapies, while **Table 9.4** provides these data for insulin. Of note, prices listed are average wholesale prices (AWP) (222) and National Average Drug Acquisition Costs (NADAC) (223); these estimates allow for a comparison of drug prices but do not represent the actual costs to

Table 9.3—Median monthly (30-day) AWP and NADAC of maximum approved daily dose of noninsulin glucose-lowering agents in the U.S.

Class	Compound	Dosage strength/ product (if applicable)	Maximum approved daily dose†	Median AWP (min, max)*	Median NADAC (min, max)*
Biguanides	• Metformin	500 mg (IR)	2,000 mg	\$85 (\$3, \$216)	\$2
		500 mg (ER)	2,000 mg	\$89 (\$5, \$6,719)	\$3
		850 mg (IR)	2,550 mg	\$108 (\$3, \$189)	\$2
		1,000 mg (IR)	2,000 mg	\$87 (\$2, \$144)	\$1
		1,000 mg (ER)	2,000 mg	\$1,884 (\$242, \$7,214)	\$26 (\$24, \$28)
		500 mg (Sol)	2,000 mg	\$810 (\$810, \$1,478)	\$417
Sulfonylureas (2nd generation)	• Glimepiride	4 mg	8 mg	\$73 (\$71, \$198)	\$2
		10 mg (IR)	40 mg	\$72 (\$67, \$91)	\$6
	• Glipizide	10 mg (XL/ER)	20 mg	\$48	\$9
		6 mg (micronized)	12 mg	\$54 (\$48, \$71)	\$13
		5 mg	20 mg	\$88 (\$63, \$432)	\$7
Thiazolidinedione	• Pioglitazone	45 mg	45 mg	\$348 (\$7, \$349)	\$4
α-Glucosidase inhibitors	• Acarbose	100 mg	300 mg	\$106 (\$104, \$378)	\$22
	• Miglitol	100 mg	300 mg	\$294 (\$241, \$346)	\$183
Meglitinides	• Nateglinide	120 mg	360 mg	\$104	\$16
	• Repaglinide	2 mg	16 mg	\$878 (\$799, \$1,728)	\$28
DPP-4 inhibitors	• Alogliptin	25 mg	25 mg	\$234	\$143
	• Linagliptin	5 mg	5 mg	\$630	\$504
	• Saxagliptin	5 mg	5 mg	\$524 (\$523, \$524)	\$179
	• Sitagliptin	100 mg	100 mg	\$341	\$303
		25 mg/mL	100 mg	\$354	NA
SGLT2 inhibitors	• Bexagliflozin	20 mg	20 mg	\$47	NA
	• Canagliflozin	300 mg	300 mg	\$718	\$575
	• Dapagliflozin	10 mg	10 mg	\$664	\$345
	• Empagliflozin	25 mg	25 mg	\$629	\$604
	• Ertugliflozin	15 mg	15 mg	\$428	\$343
GLP-1 RAs	• Dulaglutide	4.5 mg pen	4.5 mg‡	\$1,185	\$953
	• Liraglutide	18 mg/3 mL pen	1.8 mg	\$929 (\$845, \$929)	\$577
	• Semaglutide	2 mg pen	2 mg‡	\$1,197	\$966
		14 mg (tablet)	14 mg	\$1,197	\$965
Dual GIP and GLP-1 RA	• Tirzepatide	15 mg pen	15 mg‡	\$1,296	\$1,041
Bile acid sequestrant	• Colesevelam	625 mg tabs	3.75 g	\$692 (\$674, \$712)	\$56
		3.75 g suspension	3.75 g	\$674 (\$673, \$675)	\$93
Dopamine-2 agonist	• Bromocriptine	0.8 mg	4.8 mg	\$1,188	\$957

AWP, average wholesale price; DPP-4, dipeptidyl peptidase 4; ER and XL, extended release; GIP, glucose-dependent insulintropic polypeptide; GLP-1 RA, glucagon-like peptide 1 receptor agonist; IR, immediate release; max, maximum; min, minimum; NA, data not available; NADAC, National Average Drug Acquisition Cost; SGLT2, sodium–glucose cotransporter 2; Sol, solution. AWP and NADAC prices as of 15 July 2025.

*Calculated for 30-day supply (AWP [222] or NADAC [223] unit price × number of doses required to provide maximum approved daily dose × 30 days); median AWP or NADAC listed alone when only one product and/or price. †Used to calculate median AWP and NADAC (min, max); generic prices used, if available commercially. ‡Administered once weekly.

people with diabetes because they do not account for various discounts, rebates, and other price adjustments often involved in prescription sales that affect the actual cost incurred by the individual. Medication costs can be a major source of stress for people with diabetes and contribute to worse medication-taking behavior (224); cost-reducing strategies may improve medication-taking behavior in some cases (225).

Caps on out-of-pocket costs for insulin have been implemented for individuals with Medicare insurance (to \$35 per

insulin prescription per month) and individuals with state-regulated commercial insurance plans who live in 26 states and the District of Columbia that implemented such legislation (to either \$35 per insulin prescription per month or \$100 per total monthly insulin payment) (226–228). Additionally, insulin manufacturers have introduced cost reductions and copayment assistance programs; however, these do not cover all insulins, and the copayment assistance programs have variable eligibility requirements and reduce out-of-pocket payments to variable degrees (229) (see

section 1, “Improving Care and Promoting Health in Populations”). Individuals with high-deductible health plans and those without insurance coverage can incur very high out-of-pocket expenses for glucose-lowering therapies. Moreover, no such caps exist for diabetes medical equipment (i.e., equipment for glucose monitoring and insulin administration) or for noninsulin medications. It is therefore essential to screen all people with diabetes for financial concerns and cost-related barriers to care and to engage members of the health care team, including

Table 9.4—Median cost of insulin products in the U.S. calculated as AWP and NADAC per 1,000 units of specified dosage form/product

Insulins	Compounds	Dosage form/product	Median AWP (min, max)*	Median NADAC (min, max)*
Rapid-acting	• Aspart	U-100 vial	\$87+	\$70+
		U-100 cartridge	\$107+	\$86+
		U-100 prefilled pen	\$112+	\$90+
	• Aspart biosimilars#	U-100 vial	\$83	NA
		U-100 prefilled pen	\$107	NA
		U-100 vial	\$347	\$278
	• Aspart ("faster acting product")	U-100 cartridge	\$430	\$344
		U-100 prefilled pen	\$447	\$358
	• Glulisine	U-100 vial	\$102	\$82
		U-100 prefilled pen	\$132	\$105
	• Inhaled insulin	Inhalation cartridges	\$1,578	\$1,265
		U-100 vial	\$30+	\$24+
	• Lispro	U-100 cartridge	\$123	\$98
		U-100 prefilled pen	\$127+	\$102+
		U-200 prefilled pen	\$424	\$339
Short-acting	• Human regular	U-100 vial	\$56 (\$54, \$58)‡	\$44 (\$43, \$46)‡
		U-100 prefilled pen	\$73	\$58
	• Human NPH	U-100 vial	\$58 (\$54, \$58)‡	\$45 (\$43, \$46)‡
		U-100 prefilled pen	\$93 (\$73, \$113)	\$74 (\$58, \$91)
		U-500 vial	\$178	\$143
		U-500 prefilled pen	\$230	\$183
Concentrated human regular insulin	• U-500 human regular insulin	U-500 vial	\$178	\$143
		U-500 prefilled pen	\$230	\$183
	• Degludec	U-100 vial	\$142+	\$114+
		U-100 prefilled pen	\$142+	\$114+
		U-200 prefilled pen	\$142+	\$114+
		U-100 vial	\$77	\$62
	• Glargine	U-100 prefilled pen	\$77	\$62
		U-300 prefilled pen	\$152	\$122+
Long-acting	• Glargine biosimilar/follow-on products	U-100 vial	\$76+	\$61+
		U-100 prefilled pen	\$74 (\$74, † \$261)	\$59 (\$59, † \$209)
	• Aspart 70/30	U-100 vial	\$87+†	\$69+†
		U-100 prefilled pen	\$112+†	\$90+†
	• Lispro 50/50	U-100 vial	\$102	NA
		U-100 prefilled pen	\$127	\$102
Premixed insulin products	• Lispro 75/25	U-100 vial	\$102	\$82
		U-100 prefilled pen	\$127+	\$102+
	• NPH/regular 70/30	U-100 vial	\$56 (\$54, \$58)	\$45 (\$43, \$46)
		U-100 prefilled pen	\$93 (\$73, \$113)‡	\$74 (\$58, \$90)‡
	• Degludec/liraglutide	100/3.6 mg prefilled pen	\$1,073	\$859
		100/33 mg prefilled pen	\$713	\$571
Premixed insulin/GLP-1 RA products	• Glargine/lixisenatide	100/3.6 mg prefilled pen	\$1,073	\$859
		100/33 mg prefilled pen	\$713	\$571

AWP, average wholesale price; GLP-1 RA, glucagon-like peptide 1 receptor agonist; NA, data not available; NADAC, National Average Drug Acquisition Cost. AWP (222) and NADAC (223) prices as of 15 July 2025. *AWP or NADAC calculated as in **Table 9.3**. †Unbranded product prices used when available. ‡AWP and NADAC data presented do not include human insulins (approximately \$25/vial or \$43/box of 5 pens) or select analog insulins (approximately \$73/vial or \$86/box of 5 pens) available at Walmart; median listed alone when only one product and/or price. #Pricing for aspart-xjhz not available on 15 July 2025.

pharmacists, certified diabetes care and education specialists, social workers, community health workers, community paramedics, and others, to identify cost-saving opportunities for medications, diabetes durable medical equipment, and glucagon (230).

SPECIAL CIRCUMSTANCES AND POPULATIONS

Recommendations

9.31a Use of compounded products that are not approved by the U.S. Food and Drug Administration (FDA) is

not recommended due to uncertainty about their content and resulting concerns about safety, quality, and effectiveness. **C**

9.31b If a glucose-lowering medication is unavailable (e.g., in shortage), it is

recommended to switch to a different FDA-approved medication with similar efficacy, as clinically appropriate. **E**

9.31c Upon resolution of the unavailability (e.g., shortage), reassess the appropriateness of resuming the original FDA-approved medication. **E**

9.32a Individuals of childbearing potential with diabetes should be counseled on contraception options **A** and the impact of some glucose-lowering medications on contraception efficacy. **C**

9.32b A person-centered shared decision-making approach to preconception planning is essential for all individuals of childbearing potential with diabetes.

A Preconception planning should address attainment of glycemic goals, **A** the time frame for discontinuing noninsulin glucose-lowering medications, **E** and optimal glycemic management in preparation for pregnancy. **A**

9.33 Individuals who develop hyperglycemia during treatment with immunotherapy (including anti-PD-1 or anti-PD-L1 therapy, e.g., nivolumab, pembrolizumab, or avelumab) should be assessed for the immediate need for initiation of insulin therapy due to the potential risk of diabetic ketoacidosis while additional testing is completed to determine if the hyperglycemia is related to immunotherapy-associated diabetes. Close monitoring, education, and dose adjustment are needed if insulin is started. **C**

9.34 Consider metformin as the first-line treatment of hyperglycemia due to mTOR inhibitors. **E**

9.35a Consider metformin as the first-line treatment of hyperglycemia due to phosphoinositide 3-kinase (PI3K) inhibitors that affect the α isoform (e.g., alpelisib and inavolisib). **E**

9.35b Use of insulin should be reserved for severe hyperglycemia and hyperglycemic crises due to its potential impact on the efficacy of PI3K inhibitors. **E**

9.36 Adjust or initiate additional glucose-lowering therapies to maintain individualized glycemic goals based on the specific glucocorticoid treatment plan, with frequent reassessment of glucose levels and glucocorticoid treatment plans. **C**

9.37 In adults with posttransplantation diabetes mellitus (PTDM) or preexisting type 2 diabetes, insulin is preferred for

the management of hyperglycemia in the postoperative setting. **A** A DPP-4 inhibitor can be considered for mild hyperglycemia. **A**

9.38a In adults with PTDM or preexisting type 2 diabetes, noninsulin pharmacotherapy can be used for long-term glycemic management, **C** and medication selection may differ depending on the transplanted organ(s). **E**

9.38b In adults with PTDM or preexisting type 2 diabetes, a GLP-1 RA can be considered for long-term glycemic management due to additional cardiometabolic benefits (e.g., cardiovascular, kidney, weight, and liver benefits). **C**

9.38c If long-term individualized glycemic goals cannot be achieved or maintained with noninsulin pharmacotherapy in adults with PTDM or preexisting type 2 diabetes, consider adding insulin. **C**

9.39 Educate individuals with diabetes who are at risk for developing diabetic ketoacidosis and who are treated with SGLT inhibition on the risks and signs of ketoacidosis and methods of risk mitigation management, provide them with appropriate tools for ketone measurement (i.e., serum β -hydroxybutyrate), and discourage a ketogenic eating pattern. **E**

Therapeutic Strategies With Medication Unavailability

Health care professionals and people with diabetes struggle when medication supplies are insufficient to meet the demand. Examples of such circumstances include recalls involving a number of metformin products and the marked increase in demand for agents from the GLP-1 RA and dual GIP and GLP-1 RA classes. The latter circumstance led to such a low level of availability that products were determined by the FDA to be in shortage (231). To assist with supply of medications during the time they are in shortage (as signaled by their inclusion on the FDA Drug Shortages Database), compounding pharmacies and outsourcing compounding facilities are allowed to make copies, or products that are essentially duplicates of the marketed FDA-approved product (232). A significant number of concerning reports regarding safety and efficacy of compounded incretin products have emerged, including using salt forms of the FDA-approved product's

active ingredient that are not proven safe or effective for use in humans, incorporation of additional ingredients not clinically tested when mixed with incretin products (e.g., vitamin B12 and vitamin B6), products provided in nonstandard concentrations and doses and/or multidose vials and prefilled syringes not accompanied by education or labeling to mitigate administration errors, and the emergence of counterfeit products that pose significant risk to individuals taking these products (233–236). Due to safety, quality, and effectiveness concerns, use of non-FDA-approved compounded products is not recommended (237). Instead, consider switching to a different FDA-approved medication as clinically appropriate (238). Once the desired FDA-approved product becomes available, individuals should be reassessed to determine the appropriateness of resuming the product based on their current care needs, preferences, and priorities.

Care Considerations for Individuals of Childbearing Potential

The impact of glycemia during pregnancy is well understood; however, evidence for the safe use of noninsulin glucose-lowering medications is limited (see section 15, "Management of Diabetes in Pregnancy"). Studies on the efficacy and safety of glucose-lowering medications exclude individuals who are pregnant and require individuals of childbearing potential to use one or two forms of contraception. It is recommended that individuals of childbearing potential use a form of contraception when also taking glucose-lowering medications with unknown risks, limited evidence on safety, or known risks during pregnancy, regardless of the individual's intention to become pregnant, as many pregnancies are unplanned. The options for contraception should be discussed with all individuals of childbearing potential with diabetes and should include information regarding the potential impact of glucose-lowering medications on the effectiveness of contraception. Medications that affect gastrointestinal emptying time (e.g., GLP-1 RAs or dual GIP and GLP-1 RA) may affect the absorption of orally administered medications, including oral contraception. The impact on gastric emptying with GLP-1 RAs and the dual GIP and GLP-1 RA is highest at initiation and with dosage increases and then diminishes with continued administration (239). Tirzepatide, the

dual GIP and GLP-1 RA, was shown to affect the levels of oral contraception during the time of its highest impact on gastric emptying; the GLP-1 RAs may affect the levels of oral contraception as well but to a lesser extent than tirzepatide (240,241). Thus, individuals starting or increasing doses of tirzepatide who also take oral contraception should use a second form of contraception until the maintenance dose of tirzepatide is achieved and used for at least 4 weeks (242).

Preconception counseling should be part of the routine care of individuals with diabetes who have childbearing potential. Counseling should include the known benefits and risks of glucose-lowering medications as well as other medications (e.g., lipid-lowering and antihypertensive therapies) during pregnancy and recommendations for when changes in medications should occur prior to pregnancy. Individuals planning pregnancy should be counseled that a period of several months is usually needed and adjustment of therapy approved for use in pregnancy to achieve preconception glycemic goals prior to pregnancy (see section 15, "Management of Diabetes in Pregnancy," for more information on preconception counseling and glucose-lowering treatment during pregnancy).

Therapeutic Strategies for Individuals Receiving Cancer Treatment

Hyperglycemia due to chemotherapy may either be transient (improving upon treatment cessation) or represent permanent diabetes. Immune checkpoint inhibitors (ICIs) impair regulatory components of the immune system, allowing for immunogenic response against cancer cells, which can result in autoimmune toxicities, including an autoimmune form of diabetes that results in β -cell destruction (incidence approximately $\leq 1\%$) (243–246). This form of diabetes is most common after exposure to ICIs that target programmed cell death protein 1 (PD-1) (i.e., nivolumab and pembrolizumab) and those that target programmed cell death protein ligand 1 (PD-L1) (i.e., durvalumab and avelumab). ICIs that target cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) (i.e., ipilimumab) have also been implicated in this process, but much less commonly (247).

Hyperglycemia as a result of ICIs can occur at any time after the initiation of therapy—as quickly as 1 week after the

first dose to up to 12 months after. Insulin therapy is the cornerstone of management, as individuals typically present with rapid-onset, severe hyperglycemia or DKA (248). Early initiation of therapy can prevent these drastic presentations, and the initiation of basal insulin should be considered in individuals with blood glucose >250 mg/dL while further evaluation takes place. Prandial insulin is often required as well, if insulinopenia is confirmed. ICI treatment should not be discontinued in the event of severe hyperglycemia, as the β -cell destruction associated with this process is irreversible. Lifelong insulin therapy is generally required (249).

Phosphatidylinositol 3-kinase (PI3K) inhibitors are small molecules that inhibit intracellular signaling, interfering with cancer cell proliferation and survival. Four isoforms have been identified as therapeutic targets, with both pan-PI3K inhibitors and isoform-specific inhibitors in clinical use. The α isoform of this enzyme (PI3K α) is also involved in insulin signaling, and the inhibition of this pathway by either pan-PI3K inhibitors (i.e., copanlisib and duvelisib) or specific PI3K α inhibitors (i.e., alpelisib and inavolisib) can lead to hyperglycemia (250). Hyperglycemia typically occurs within the first 2 weeks of therapy, with an incidence of approximately 60% (251–254). Risk factors include preexisting dysglycemia, BMI >25 kg/m², and age >65 years. Adequate management is crucial, as uncontrolled hyperglycemia can lead to discontinuation and/or reduction in medication dose, which can negatively affect the efficacy of the therapy (254–256).

Metformin is the first-line oral agent to treat PI3K inhibitor-induced hyperglycemia, with uptitration of the dose as tolerated (256). Pioglitazone is also an option as monotherapy or in combination with metformin, but its slow onset of action can limit its effectiveness (257). SGLT2 inhibitors have also shown efficacy, but close monitoring is needed, as ketoacidosis has been reported (258). Insulin and sulfonylureas should be considered only as a last resort, as increased insulin levels may reactivate the PI3K pathway, counteracting the antitumor effects of PI3K inhibition (256,259). There is no direct evidence for the use of GLP-1 RAs for PI3K inhibitor-induced hyperglycemia. They should not be considered for treatment in this circumstance at this time due to their uncertain effect on PI3K inhibitor

efficacy (based on their increase in insulin secretion) and the potential to cause nausea and vomiting.

mTOR kinase inhibitors, including everolimus, cause hyperglycemia by interfering with insulin signaling, leading to impaired insulin secretion and increased insulin resistance. Metformin is the first-line treatment of hyperglycemia secondary to mTOR inhibitor treatment because of its efficacy and safety profile. Due to its ability to reduce insulin resistance, pioglitazone may be considered as a second-line treatment, depending on the risks of its adverse effects to the individual. There is no direct evidence regarding the efficacy of GLP-1 RAs or SGLT2 inhibitors for mTOR inhibitor-induced hyperglycemia; however, there is also no evidence that they impair the efficacy of the mTOR inhibitor. Thus, evaluation of their use as second- or third-line treatments for this circumstance should be made based on their overall benefits and risks. Insulin is typically reserved for cases of refractory hyperglycemia after noninsulin treatments are used, in the presence of intolerance or contraindications to noninsulin treatments, or for severe hyperglycemia (260–262).

Glucocorticoids (including prednisone and dexamethasone), which are often used as part of acute, adjunctive, and chronic treatment of cancer and inflammatory conditions (e.g., rheumatoid arthritis and inflammatory bowel disease) as well as posttransplantation, cause hyperglycemia primarily by increased insulin resistance and hepatic glucose production. Other contributing effects include increased appetite, decreased production/secretion of insulin, and enhanced effects of counterregulatory hormones (such as epinephrine) (263–266). The timing and extent of hyperglycemia vary based on the dose, duration, route of administration (i.e., intravenous, oral, or intraarticular) and the specific glucocorticoid used (265–271). For example, with morning administration of prednisone (with the first meal of the day), glucose starts rising after the first meal, with peak effects in the afternoon and evening, and declines to baseline by the next morning; in contrast, with a single dose of dexamethasone, glucose elevations may last more than 24 h with some decline overnight. The extent of the elevation is dependent on the dose, so as the glucocorticoid is tapered, the extent of hyperglycemia will

decline. Monitoring glucose levels solely in the morning may miss the extent of the hyperglycemia experienced due to glucocorticoid use and prevent appropriate management (263,265–267,272). Thus, glucose-lowering medication adjustments or additions should match the timing and extent of hyperglycemia and allow for rapid adjustment as the dose of the glucocorticoid dose changes to minimize the likelihood of hyperglycemia and hypoglycemia. Insulin is the most frequently used glucose-lowering medication to manage hyperglycemia secondary to glucocorticoid use. The selection of insulin type and dose depends on the dose and duration of the glucocorticoid (265,266,269, 272–275). Additions or dose adjustments of sulfonylureas, including meglitinides, have also been used for those with type 2 diabetes or no previous diagnosis of diabetes. Due to lack of direct evidence and the time needed to achieve the glucose-lowering effect, additions or dose adjustments of other glucose-lowering medications are reserved for when stable doses of glucocorticoids are chronically administered and are not for acute management (265,266,269,272, 275,276).

Pancreatic Diabetes and Cystic Fibrosis–Related Diabetes

Individuals with pancreatic diabetes may require early insulin initiation to achieve and maintain glycemic goals. In individuals with a history of pancreatitis, use of incretin medications (i.e., GLP-1 RAs, a dual GIP and GLP-1 RA, and DPP-4 inhibitors) should be avoided (see section 2, “Diagnosis and Classification of Diabetes”). Individuals with cystic fibrosis–related diabetes should be treated with insulin therapy; insulin pump therapy, including AID systems, should be considered when appropriate (277).

Posttransplantation Diabetes Mellitus

The diagnosis of posttransplantation diabetes mellitus (PTDM) relies on the same glycemic characteristics as other forms of diabetes. However, due to the unique effects of immunosuppressant drugs, an oral glucose tolerance test (OGTT) is the preferred and most accurate method for diagnosis (compared with A1C or fasting plasma glucose) (278). In 2024, an update from the 3rd International PTDM Consensus Meeting recommended screening for diabetes risk factors with a

pretransplant OGTT while the individual is on the waitlist, followed by early OGTT at 3 months posttransplantation to diagnose PTDM and a late OGTT at 1 year and onward as appropriate (279).

As with all strategies in metabolic management, lifestyle modifications remain a mainstay of long-term management. The Comparing Glycaemic Benefits of Active Versus Passive Lifestyle Intervention in Kidney Allograft Recipients (CAVIAR) study compared active and passive lifestyles after kidney transplantation using behavior therapy and found a statistically significant reduction in fat mass and weight loss with active lifestyle. However, there were no changes in the primary outcomes of glucose metabolism (i.e., insulin secretion, insulin sensitivity, or disposition index). The rate of PTDM was halved in the active group, but this finding was not statistically significant (280).

In early postoperative periods, insulin is the preferred drug for glycemic management due to its lack of interactions with other transplant medications, immediate efficacy, and added potential to prevent PTDM, albeit with the expected risk of hypoglycemia (281–283). Sulfonylureas may also be used for individuals with stable kidney function with similar precautions of hypoglycemia, but they may not confer any added metabolic benefits outside of glucose management (284).

Although still limited, data are increasing to inform the optimal pharmacologic management of PTDM and preexisting type 2 diabetes at the time of transplant (285,286) (for diagnosis and classification of PTDM, see section 2, “Diagnosis and Classification of Diabetes”). While many individuals require insulin therapy immediately posttransplantation, noninsulin therapies can be used for long-term management. Studies of metformin, DPP-4 inhibitors, SGLT2 inhibitors, GLP-1 RAs, and pioglitazone in individuals who have undergone solid organ transplantation have demonstrated effectiveness and safety but are limited by small sample sizes, short follow-up, and risk of bias due to retrospective, single-center, or single-arm prospective designs (287). The majority of studies are in individuals who have undergone kidney transplantation, but studies in liver and heart transplantation are available to a lesser degree as well. Selection of pharmacotherapeutic classes should take into account organ-specific physiology, immunosuppressant plan, and

general metabolic and cardiovascular circumstances.

Metformin can be used but with caution; it should not be initiated if eGFR is <45 mL/min/1.73 m², and it should be discontinued with eGFR <30 mL/min/1.73 m². Limitations in metformin use include the risk of lactic acidosis with fluctuating kidney function, either with graft dysfunction or rejection in kidney transplantation or acute kidney injury in other solid organ transplantation. Metformin use may be associated with lower risks of cardiac allograft vasculopathy after heart transplantation (288) and all-cause, malignancy-related, and infection-related mortality after kidney transplantation (289).

DPP-4 inhibitors have been shown to be safe and effective posttransplantation in RCTs, even in the immediate posttransplant period for mild hyperglycemia or impaired glucose tolerance, and have the potential to decrease progression to PTDM (290).

GLP-1 RA therapy may be preferred for many individuals, as shown by increasing evidence from large retrospective studies on the benefits of GLP-1 RAs on cardiovascular, kidney, weight loss, and glucose lowering outcomes. Studies have not found any concern for negative interaction with immunosuppressants, which would necessitate changes in dosing (291–303). However, caution should be used when gastrointestinal side effects occur, particularly if individuals have this additive effect to the side effects of the immunosuppressants. Additionally, in lung transplant recipients, gastroparesis and gastroesophageal reflux are of particular concern, as these conditions may induce allograft lung damage and are frequent side effects of GLP-1 RAs. A gastric emptying study may be useful in identifying ideal candidates before initiation.

SGLT2 inhibitors may be similarly preferred for individuals with ASCVD, HF, and CKD and appear to be safe and effective in PTDM (304–309). However, there is increased risk of genitourinary tract infection, which is of particular concern in immunosuppressed individuals. Of note, kidney transplant recipients have an innate anatomical increased risk of urinary tract infections (UTIs), particularly immediately posttransplant when the ureteral stent is still in place. Prior history of UTIs and individual risk of UTIs should be considered when using this class after kidney transplant.

It is essential that diabetes management posttransplantation is implemented in the setting of an interprofessional team. The transplant physicians and the endocrinologists should work collaboratively to monitor for medication toxicity and deleterious side effects that may affect allograft function and to optimize cardiovascular and metabolic outcomes.

Maturity-Onset Diabetes of the Young

Individuals with maturity-onset diabetes of the young due to *HNF1A* and *HNF4A* mutations can be treated with low-dose sulfonylurea therapy but may ultimately require insulin therapy (310) (see section 2, “Diagnosis and Classification of Diabetes”) (Table 2.7). For those with *HNF1A* mutations, addition of a DPP-4 inhibitor to the sulfonylurea may help improve glycemic variability and attainment of glycemic goals (311). Individuals with neonatal diabetes due to *KCNJ22* and *ABCC8* mutations can be treated with high-dose sulfonylureas, while those with *INS*, *GATA6*, *EIF2AK3*, and *FOXP3* mutations require insulin therapy (310).

SGLT Inhibition and Risk of Ketosis

Individuals with type 1 diabetes (83,312) and insulin-deficient type 2 diabetes are at increased risk for DKA with SGLT inhibitor therapy (SGLT2 inhibitors or the SGLT1/2 inhibitor). SGLT inhibitor-associated DKA occurs in approximately 4% of people with type 1 diabetes; the risk can be 5–17 times higher than that in people with type 1 diabetes not treated with SGLT inhibitors (313). It is important to note that SGLT2 inhibitors are not approved for use in people with type 1 diabetes. In contrast, DKA is uncommon in people with type 2 diabetes treated with SGLT inhibitors, with an estimated incidence of 0.6–4.9 events per 1,000 person-years (314). Risk factors for DKA in individuals with either type 1 or type 2 diabetes treated with SGLT inhibitors include very-low-carbohydrate eating patterns, prolonged fasting, dehydration, excessive alcohol intake, and other common precipitating factors (83,312). Up to a third of people treated with SGLT2 inhibitors who developed DKA present with glucose levels <200 mg/dL (<11.1 mmol/L) (315), and in one study 71% presented with glucose levels ≤250 mg/dL (≤13.9 mmol/L) (316); therefore, it is important to educate at-risk individuals about the signs and symptoms of DKA and DKA mitigation

and management and to prescribe accurate tools for ketone measurement. Individuals who have experienced DKA should not be treated with SGLT inhibition. Additional guidance on DKA risk mitigation is available in section 6, “Glycemic Goals, Hypoglycemia, and Hyperglycemic Crises.”

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10. Cardiovascular Disease and Risk Management: Standards of Care in Diabetes—2026

American Diabetes Association
Professional Practice Committee for
Diabetes*

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The American Diabetes Association (ADA) “Standards of Care in Diabetes” includes the ADA’s current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. Members of the ADA Professional Practice Committee for Diabetes, an interprofessional expert committee, are responsible for updating the Standards of Care annually, or more frequently as warranted. For a detailed description of ADA standards, statements, and reports, as well as the evidence-grading system for ADA’s clinical practice recommendations and a full list of Professional Practice Committee members, please refer to Introduction and Methodology. Readers who wish to comment on the Standards of Care are invited to do so at professional.diabetes.org/SOC.

For prevention and management of diabetes complications in children and adolescents, please refer to section 14, “Children and Adolescents.”

Cardiovascular disease (CVD) is a broad term that includes atherosclerotic cardiovascular disease (ASCVD) and heart failure, two CVDs common among people with diabetes. ASCVD broadly refers to a history of acute coronary syndrome, myocardial infarction (MI), stable or unstable angina or coronary or other arterial revascularization, stroke, or peripheral artery disease (PAD) including aortic aneurysm and is the leading cause of morbidity and mortality in people with diabetes (1). Diabetes itself confers independent ASCVD risk, and among people with diabetes, all major cardiovascular risk factors, including hypertension, hyperlipidemia, and obesity, are clustered and common (2). Numerous studies have shown the efficacy of managing individual cardiovascular risk factors in preventing or slowing ASCVD in people with diabetes. Furthermore, large benefits are seen when multiple cardiovascular risk factors (glycemic, blood pressure, and lipid management) are addressed simultaneously, with evidence for long-lasting benefits (3–5). Notably, most of the evidence supporting interventions to reduce cardiovascular risk in diabetes comes from trials of people with type 2 diabetes. No randomized trials have been specifically designed to assess the impact of cardiovascular risk reduction strategies in people with type 1 diabetes. Therefore, the recommendations for cardiovascular risk factor modification for people with type 1 diabetes are extrapolated from data obtained in people with type 2 diabetes and are similar to those for people with type 2 diabetes.

Under the current paradigm of comprehensive risk factor modification, cardiovascular morbidity and mortality have notably decreased in people with both type 1 and type 2 diabetes (1). Indeed, when all major cardiovascular risk factors are treated to within the target ranges, people with type 2 diabetes have risk of death, MI, or stroke similar to that of the general population (6). Despite these encouraging opportunities to reduce morbidity and mortality, only a minority of people with

*A complete list of members of the American Diabetes Association Professional Practice Committee for Diabetes can be found at <https://doi.org/10.2337/dc26-S010>.

This section has received endorsement from the American College of Cardiology.

Duality of interest information for each contributor is available at <https://doi.org/10.2337/dc26-S010>.

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type 2 diabetes achieve recommended risk factor goals and are treated with guideline-recommended therapy (7–9). Therefore, continued focus on delivering high-quality comprehensive cardiovascular care and on addressing barriers to risk factor management are required to implement the treatment recommendations (1,10) outlined in this section.

CVD also includes heart failure, and diabetes is a risk factor for incident heart failure, which is at least twofold more prevalent in people with diabetes compared with those without diabetes and is a major cause of morbidity and mortality (11). People with diabetes may present with a wide spectrum of heart failure, including heart failure with preserved ejection fraction (HFpEF), heart failure with mildly reduced ejection fraction (HFmrEF), or heart failure with reduced ejection fraction (HFrEF) (12,13). Comorbid conditions including overweight and obesity and hypertension often precede the development of HFpEF and have been implicated in the pathophysiology of HFpEF (14). Coronary artery disease is a major risk factor and a cause of myocardial injury in ischemic heart disease leading to HFrEF. In addition, people with diabetes are at risk for developing structural heart disease and HFrEF in the absence of obstructive coronary artery disease (15). The pathophysiology of heart failure in people with diabetes and further details of screening, diagnosis, and treatment of people with heart failure and diabetes are also outlined in a previous consensus statement by the American Diabetes Association (ADA) (16).

There is an increasing appreciation of the common pathophysiology and interrelationship of cardiometabolic risk factors leading to both adverse cardiovascular and adverse kidney outcomes in people with diabetes, including ASCVD, heart failure, and chronic kidney disease (CKD) (17,18). These three comorbidities are frequently caused by metabolic risk, which is frequently driven by obesity and its associated risk factors, and the incidence of all three conditions rises with increasing A1C levels (19). Collectively, this combination of comorbidities has been termed cardiorenal metabolic disease or cardiovascular-kidney-metabolic health (20–22). Reasons to concurrently consider cardiovascular and kidney comorbidities in the management of people with diabetes include not only the common metabolic risk but also the major benefit observed across the spectrum of CVD,

heart failure, and kidney outcomes in people with type 2 diabetes treated with sodium–glucose cotransporter (SGLT) inhibitors or glucagon-like peptide 1 receptor agonists (GLP-1 RAs). Therefore, in addition to the management of hyperglycemia, hypertension, and hyperlipidemia, treatment with SGLT inhibitors and/or GLP-1 RAs that have demonstrated cardiovascular and kidney benefit is considered a fundamental element of risk reduction and a core pharmacological strategy to improve cardiovascular and kidney outcomes in people with type 2 diabetes (Fig. 10.1). In addition to the standards of care for the prevention and treatment of CVD outlined below, the reader is referred to section 9, “Pharmacologic Approaches to Glycemic Treatment,” and section 11, “Chronic Kidney Disease and Risk Management,” for a comprehensive review of pharmacological management of hyperglycemia and kidney benefit from SGLT2 inhibitors, SGLT1/2 inhibitors, and GLP-1 RAs.

HYPERTENSION AND BLOOD PRESSURE MANAGEMENT

An elevated blood pressure is defined as a systolic blood pressure 120–129 mmHg with a diastolic blood pressure <80 mmHg (23). Hypertension is defined as a systolic blood pressure ≥ 130 mmHg or a diastolic blood pressure ≥ 80 mmHg (23). This is in agreement with the definition of hypertension by the American College of Cardiology and American Heart Association (23). Hypertension is common among people with type 1 and type 2 diabetes. Hypertension is a major risk factor for ASCVD, heart failure, and microvascular complications. Moreover, numerous studies have shown that antihypertensive therapy reduces ASCVD events, heart failure, and microvascular complications. Please refer to the ADA position statement “Diabetes and Hypertension” for a detailed review of the epidemiology, diagnosis, and treatment of hypertension (24) and hypertension guideline recommendations (25–28). For blood pressure goals and management in individuals with diabetes who are pregnant, see section 15, “Management of Diabetes in Pregnancy” for details.

Screening and Diagnosis

Recommendations

10.1 Blood pressure should be measured at every routine clinical visit, or at

least every 6 months. Individuals found to have elevated blood pressure without a diagnosis of hypertension (systolic blood pressure 120–129 mmHg and diastolic blood pressure <80 mmHg) should have blood pressure confirmed using multiple readings, including measurements on a separate day, to diagnose hypertension. **A** Hypertension is defined as a systolic blood pressure ≥ 130 mmHg or a diastolic blood pressure ≥ 80 mmHg based on an average of two or more measurements obtained on two or more occasions. **A** Individuals with blood pressure $\geq 180/110$ mmHg and cardiovascular disease could be diagnosed with hypertension at a single visit. **E**

10.2 Counsel all people with hypertension and diabetes to monitor their blood pressure at home after appropriate education. **A**

Blood pressure should be measured at every routine clinical visit or at least every 6 months by a trained individual who should follow the guidelines established for the general population: measurement in the seated position, with feet on the floor and arm supported at heart level, after 5 min of rest. Cuff size should be appropriate for the upper-arm circumference (29). Individuals identified to have elevated blood pressure or hypertension should have blood pressure confirmed using multiple readings, including measurements on a separate day, to diagnose hypertension. However, in individuals with CVD and blood pressure $\geq 180/110$ mmHg, it is reasonable to diagnose hypertension at a single visit (25). Postural changes in blood pressure and pulse may be evidence of autonomic neuropathy and therefore require adjustment of blood pressure goals. Lying, sitting, and standing blood pressure measurements should be checked on initial visit and as indicated.

Home blood pressure self-monitoring and 24-h ambulatory blood pressure monitoring may provide evidence of white coat hypertension, masked hypertension, or other discrepancies between office and true blood pressure (30,31). In addition to confirming or refuting a diagnosis of hypertension, home blood pressure assessment may be useful to monitor antihypertensive treatment. A systematic review and meta-analysis of prospective

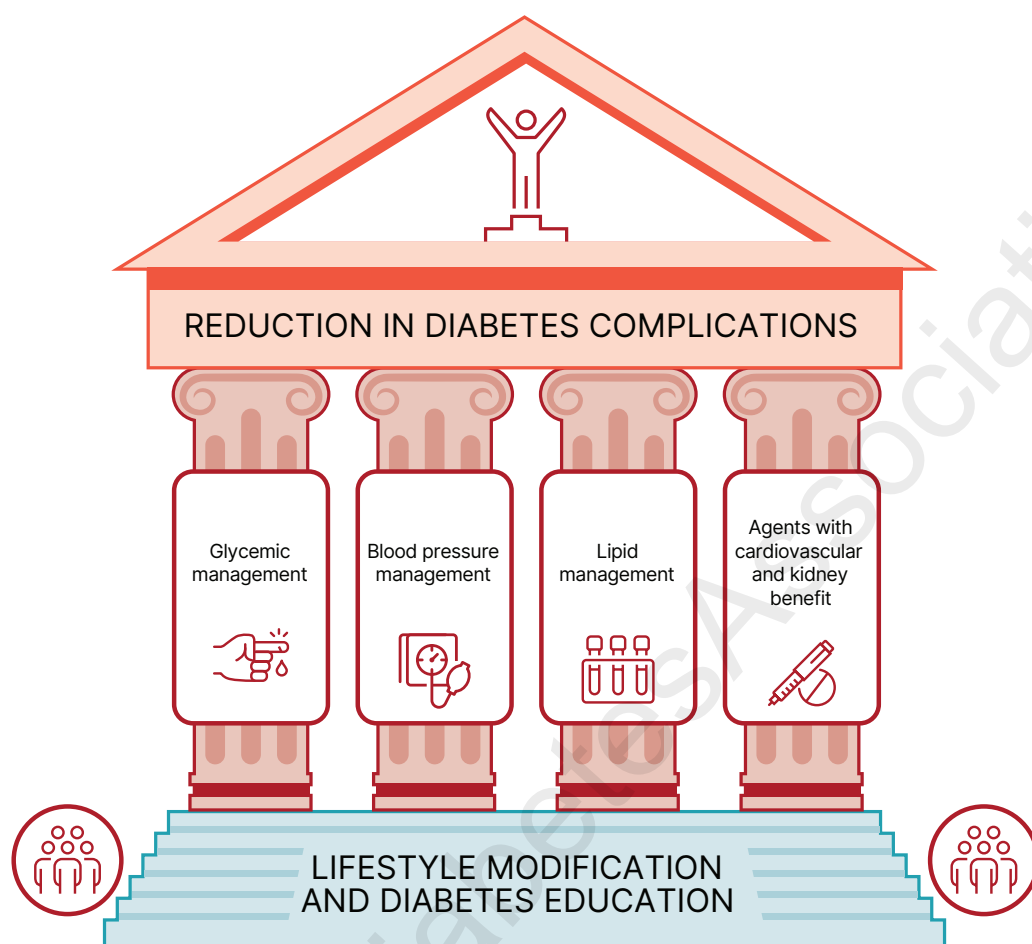


Figure 10.1—Multifactorial approach to reduction in risk of diabetes complications.

studies concluded that blood pressure measurements from either 24-h ambulatory or home blood pressure measurements can predict cardiovascular risk (30–32). Moreover, home blood pressure monitoring may improve medication-taking behavior and thus help reduce cardiovascular risk (33).

Treatment Goals

Recommendations

10.3 For people with diabetes and hypertension, blood pressure goals should be individualized through a shared decision-making process that addresses cardiovascular risk, potential adverse effects of antihypertensive medications, and individual preferences. **B**

10.4 If it can be safely attained, the on-treatment blood pressure goal is <130/80 mmHg; a systolic blood pressure goal <120 mmHg should be encouraged in individuals with high cardiovascular or kidney risk. **A**

Randomized clinical trials have demonstrated unequivocally that treatment of hypertension reduces cardiovascular events as well as microvascular complications (34–40). There has been controversy on the recommendation of a specific blood pressure goal in people with diabetes. The recommendation to support a blood pressure goal of <130/80 mmHg in people with diabetes is consistent with guidelines from the American College of Cardiology and American Heart Association (24), the International Society of Hypertension, and the European Society of Cardiology/European Society of Hypertension Blood Pressure/Hypertension Guidelines (26). Participants with diabetes comprised nearly 20% of the Strategy of Blood Pressure Intervention in the Elderly Hypertensive Patients (STEP) trial, which noted decreased cardiovascular events with treatment of hypertension to a systolic blood pressure goal of <130 mmHg (41). A systolic blood pressure goal of <120 mmHg is encouraged in those

individuals with high cardiovascular or kidney risk because of the results of Blood Pressure Control Target in Diabetes (BPROAD) and the Effects of Intensive Systolic Blood Pressure Lowering Treatment in Reducing Risk of Vascular Events (ESPRIT) trials. BPROAD was an open-label trial that randomized individuals with diabetes and elevated CVD risk to an intensive systolic blood pressure goal of <120 mmHg and noted a 21% reduction in nonfatal stroke, nonfatal MI, heart failure, or cardiovascular death compared with the group receiving standard systolic blood pressure goal of <140 mmHg (42). ESPRIT also compared an intensive systolic blood pressure goal of <120 mmHg to a standard goal of <140 mmHg in individuals with diabetes (39%), prior stroke, or elevated cardiovascular risk. ESPRIT noted a significant 12% reduction in the primary outcome, a composite of MI, revascularization, hospitalization for heart failure, stroke, or cardiovascular death (43). The results of BPROAD and ESPRIT are supported

by the Systolic Blood Pressure Intervention Trial (SPRINT), which demonstrated that treatment to a goal systolic blood pressure of <120 mmHg decreases cardiovascular event rates by 25% in high-risk individuals, although people with diabetes were excluded from this trial (44). While the relatively underpowered ACCORD (Action to Control Cardiovascular Risk in Diabetes) blood pressure trial (ACCORD BP) did not demonstrate that aiming for a systolic blood pressure <120 mmHg in people with diabetes results in decreased cardiovascular event rates, the prespecified secondary outcome of stroke was reduced by 41% with intensive treatment (45). Notably, there is an absence of high-quality data available to guide blood pressure goals in people with type 1 diabetes, but a similar blood pressure goal of <130/80 mmHg is recommended in people with type 1 diabetes. As discussed below, treatment should be individualized. For more information on individualized blood pressure goals in older individuals, please see section 13, "Older Adults."

Randomized Controlled Trials of Intensive Versus Standard Blood Pressure Management

BPROAD provides the strongest evidence to support a systolic blood pressure treatment goal of <120 mmHg, as it enrolled people with type 2 diabetes and increased cardiovascular risk with a baseline systolic blood pressure ≥ 140 mmHg (or 130–180 mmHg if already taking antihypertensive medication). Increased cardiovascular risk was defined as a history of CVD at least 3 months before enrollment, subclinical CVD, two or more cardiovascular risk factors, and CKD (estimated glomerular filtration rate [eGFR] 30 to <60 mL/min/1.72 m²). The 12,821 participants with type 2 diabetes were randomized to a goal systolic blood pressure <120 mmHg or standard treatment (goal systolic blood pressure <140 mmHg). The primary outcome of nonfatal stroke, nonfatal MI, treatment or hospitalization for heart failure, or death from cardiovascular causes was reduced by 21% in the intensive treatment group (hazard ratio [HR] 0.79, 95% CI 0.69–0.90), with an achieved mean systolic blood pressure in the intensive group of 121.6 mmHg vs. 133.2 mmHg in the standard therapy group. Adverse event rates were similar in the two groups, although symptomatic hypotension and hyperkalemia were more frequent in the intensive therapy group (42).

A second, large blood pressure trial including a substantial number of people with diabetes was published since the development of the 2025 "Standards of Care in Diabetes." The ESPRIT trial randomized 11,255 individuals with high cardiovascular risk (established CVD or two risk factors), of whom 39% had type 2 diabetes, to intensive treatment (goal systolic blood pressure of <120 mmHg) versus standard treatment (goal systolic blood pressure <140 mmHg). The primary outcome, a composite of MI, revascularization, hospitalization for heart failure, stroke, or cardiovascular death, was significantly reduced by 12% in the intensive therapy group (HR 0.88, 95% CI 0.78–0.99) irrespective of the diagnosis of diabetes at baseline. The investigators reported a modest increase in adverse events, including syncope (0.4% vs. 0.1%, HR 3.00, 95% CI 1.35–6.68) (43).

Although SPRINT excluded people with type 2 diabetes, it provides evidence to support the BPROAD and ESPRIT findings that lower blood pressure goals in individuals at increased cardiovascular risk improve outcome (44). The trial enrolled 9,361 individuals with a systolic blood pressure of ≥ 130 mmHg and increased cardiovascular risk and treated to a systolic blood pressure goal of <120 mmHg (intensive treatment) versus a goal of <140 mmHg (standard treatment). The primary composite outcome of MI, acute coronary syndromes, stroke, heart failure, or death from cardiovascular causes was reduced by 25% in the intensive treatment group. The achieved systolic blood pressures in the trial were 121 mmHg and 136 mmHg in the intensive versus standard treatment group, respectively. Adverse outcomes, including hypotension, syncope, electrolyte abnormality, and acute kidney injury (AKI), were more common in the intensive treatment arm; risk of adverse outcomes therefore needs to be weighed against the cardiovascular benefit of more intensive blood pressure lowering.

The STEP trial assigned 8,511 individuals aged 60–80 years with hypertension to a systolic blood pressure goal of 110 to <130 mmHg (intensive treatment) or 130 to <150 mmHg (40). In this trial, in which approximately 19% of participants had diabetes, the primary composite outcome of stroke, acute coronary syndrome, acute decompensated heart failure, coronary revascularization, atrial fibrillation, or death from cardiovascular causes occurred in 3.5% of individuals in the intensive

treatment group versus 4.6% in the standard treatment group (HR 0.74 [95% CI 0.60–0.92]; $P = 0.007$). Hypotension occurred more frequently in the intensive treatment group (3.4%) compared with the standard treatment group (2.6%) without significant differences in other adverse events, including dizziness, syncope, or fractures. For more information on blood pressure goals in older adults, please see section 13, "Older Adults."

ACCORD BP randomized 4,733 individuals with type 2 diabetes to intensive therapy (aiming for a systolic blood pressure <120 mmHg) or standard therapy (aiming for a systolic blood pressure <140 mmHg) (45). The mean achieved systolic blood pressures were 119 mmHg and 133 mmHg in the intensive and standard groups, respectively. The primary composite outcome of nonfatal MI, nonfatal stroke, or death from cardiovascular causes was not significantly reduced in the intensive treatment group, although the prespecified secondary outcome of stroke was significantly reduced by 41% in the intensive treatment group. Adverse events attributed to blood pressure treatment, including hypotension, syncope, bradycardia, hyperkalemia, and elevations in serum creatinine, occurred more frequently in the intensive treatment arm than in the standard therapy arm. ACCORD BP has been viewed as underpowered due to the composite primary end point being less sensitive to blood pressure intervention (44,45).

In the Action in Diabetes and Vascular Disease: Preterax and Diamicon MR Controlled Evaluation (ADVANCE) trial, 11,140 people with type 2 diabetes were randomized to receive either treatment with a fixed combination of perindopril and indapamide or matching placebo (46). The primary end point, a composite of cardiovascular death, nonfatal stroke or MI, or new or worsening kidney or eye disease, was reduced by 9% in the combination treatment. The achieved systolic blood pressure was ~ 135 mmHg in the treatment group and 140 mmHg in the placebo group.

The Hypertension Optimal Treatment (HOT) trial enrolled 18,790 individuals and aimed for a diastolic blood pressure <90 mmHg, <85 mmHg, or <80 mmHg (47). The cardiovascular event rates, defined as fatal or nonfatal MI, fatal and nonfatal strokes, and all other cardiovascular events, were not significantly different between diastolic blood pressure goals (≤ 90 mmHg,

≤ 85 mmHg, and ≤ 80 mmHg), although the lowest incidence of cardiovascular events occurred with an achieved diastolic blood pressure of 82 mmHg. However, in people with diabetes, there was a significant 51% reduction in MI, stroke, and cardiovascular death in the treatment group with a goal diastolic blood pressure

of < 80 mmHg compared with a goal diastolic blood pressure of < 90 mmHg.

Individualization of Treatment Goals

People with diabetes and clinicians should engage in a shared decision-making process to determine individual blood pressure goals (23). A thorough review of the

benefits and risks of intensive blood pressure goals is consistent with a person-focused approach to care that values individual priorities and health care professional judgment (48). Secondary analyses of ACCORD BP and SPRINT suggest that clinical factors can help identify individuals more likely to benefit from and less likely

Recommendations for the treatment of confirmed hypertension in nonpregnant people with diabetes

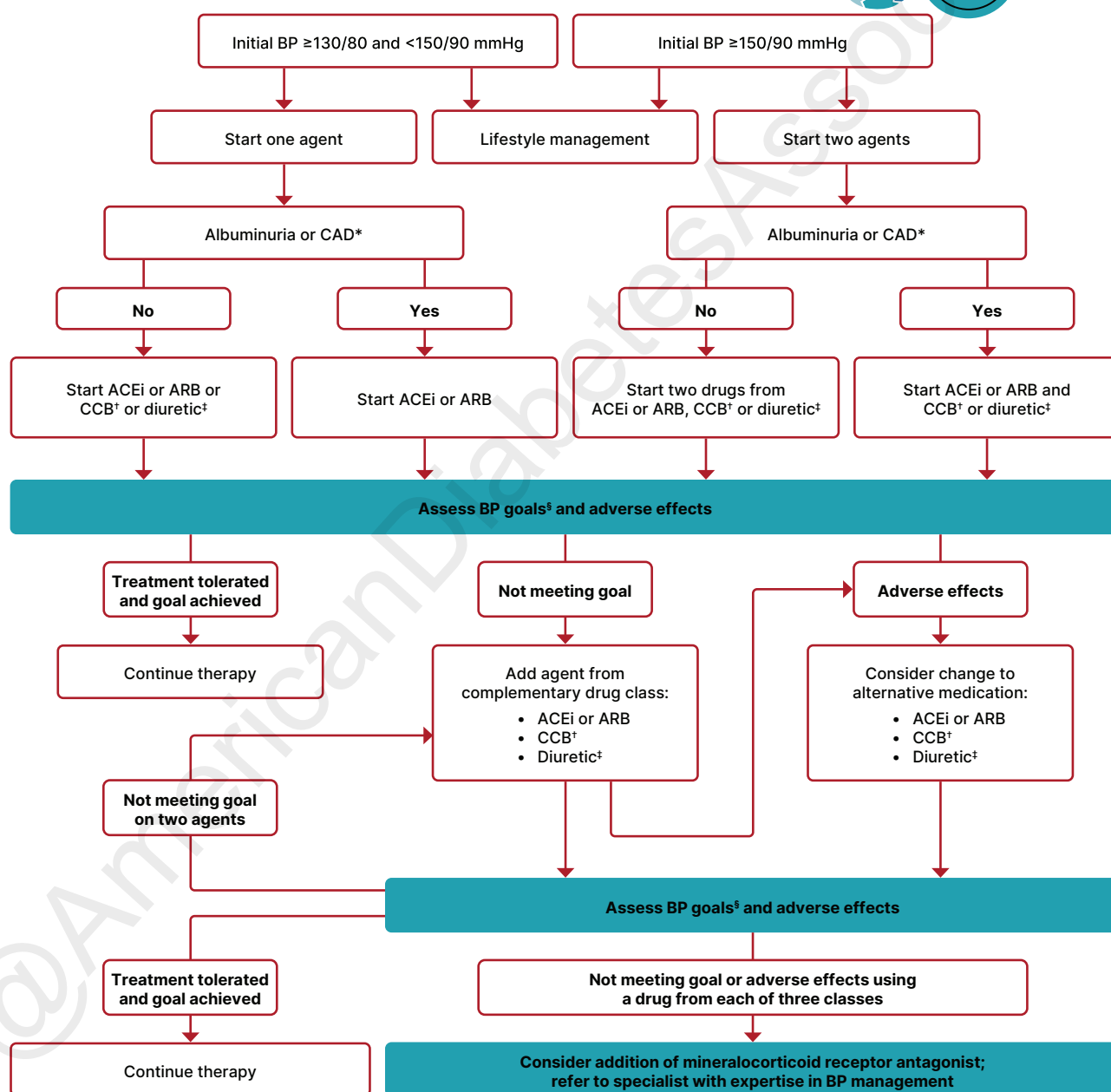


Figure 10.2—Recommendations for the treatment of confirmed hypertension in nonpregnant people with diabetes. *An ACE inhibitor (ACEi) or angiotensin receptor blocker (ARB) is suggested for the treatment of hypertension in people with coronary artery disease (CAD) or urine albumin-to-creatinine ratio 30–299 mg/g creatinine and is strongly recommended for individuals with urine albumin-to-creatinine ratio ≥ 300 mg/g creatinine. †Dihydropyridine calcium channel blocker (CCB). ‡Thiazide-like diuretic; long-acting agents shown to reduce cardiovascular events, such as chlorthalidone and indapamide, are preferred. §If it can be safely attained, the on-treatment blood pressure goal is $< 130/80$ mmHg; a systolic blood pressure goal < 120 mmHg should be encouraged in individuals with high cardiovascular or kidney risk. BP, blood pressure. Adapted from de Boer et al. (24).

to be harmed by intensive blood pressure management (49,50).

Absolute benefit from blood pressure reduction correlated with absolute baseline cardiovascular risk in SPRINT and in earlier clinical trials conducted at higher baseline blood pressure levels (50,51). The results of BPROAD and ESPRIT highlight that targeting an on-treatment systolic blood pressure goal of <120 mmHg in people with high cardiovascular risk is associated with reduction in cardiovascular events compared with systolic blood pressure <140 mmHg. These benefits should be weighed against treatment-related adverse events such as hypotension and syncope, which may be particularly relevant in older individuals with orthostatic hypotension, substantial comorbidity, functional limitations, or polypharmacy and some individuals who may prefer higher blood pressure goals to enhance quality of life.

Treatment Strategies

Lifestyle Intervention

Recommendation

10.5 For people with diabetes and blood pressure >120/80 mmHg, advise lifestyle behaviors including weight loss when indicated, a Dietary Approaches to Stop Hypertension (DASH)-style eating pattern including reducing sodium, limiting or avoiding alcohol consumption, increased physical activity, and smoking cessation. **A**

Lifestyle management is an important component of hypertension treatment because it lowers blood pressure, enhances the effectiveness of some antihypertensive medications, promotes other aspects of metabolic and vascular health, and generally leads to few adverse effects. Lifestyle therapy consists of reducing excess body weight through caloric restriction (see section 8, "Obesity and Weight Management for the Prevention and Treatment of Diabetes"), at least 150 min of moderate-intensity aerobic activity per week (see section 3, "Prevention or Delay of Diabetes and Associated Comorbidities"), restricting sodium intake (<2,300 mg/day), increasing consumption of fruits and vegetables (8–10 servings per day) and low-fat dairy products or nondairy alternatives (2–3 servings per day), avoiding excessive alcohol consumption (no more than 2 servings per day in men and no more than 1 serving

per day in women) (52), and increasing activity levels (53) (see section 5, "Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes"). A systematic review of 10 randomized controlled trials reported that compared with control diet, the modified Dietary Approaches to Stop Hypertension (DASH) eating pattern could reduce mean systolic (−3.26 mmHg [95% CI −5.58 to −0.94 mmHg]; $P = 0.006$) and diastolic (−2.07 mmHg [95% CI −3.68 to −0.46 mmHg]; $P = 0.01$) blood pressure (54).

These lifestyle interventions are reasonable for individuals with diabetes and mildly elevated blood pressure (systolic >120 mmHg and diastolic <80 mmHg) and should be initiated along with pharmacologic therapy when hypertension is diagnosed (Fig. 10.2) (53). A lifestyle therapy plan should be developed in collaboration with the person with diabetes and discussed as part of diabetes management. Use of internet or mobile-based digital platforms to reinforce healthy behaviors may be considered as a component of care, as these interventions have been found to enhance the efficacy of medical therapy for hypertension (55,56).

PHARMACOLOGIC INTERVENTIONS

Recommendations

10.6 In individuals with confirmed office-based blood pressure $\geq 130/80$ mmHg, pharmacologic therapy should be initiated and titrated to achieve their individualized blood pressure goal. **A**

10.7 Individuals with confirmed office-based blood pressure $\geq 150/90$ mmHg should, in addition to lifestyle therapy, have prompt initiation and timely titration of two drugs or a single-pill combination of drugs for hypertension that have also been demonstrated to reduce cardiovascular events in people with diabetes. **A**

10.8 Treatment for hypertension should include drug classes demonstrated to reduce cardiovascular events in people with diabetes. **A** ACE inhibitors or angiotensin receptor blockers (ARBs) are recommended first-line therapy for hypertension in people with diabetes and albuminuria or coronary artery disease. **A**

10.9 Multiple-drug therapy is generally required to achieve blood pressure goals. However, avoid any combination

of ACE inhibitors, ARBs (including ARBs and neprilysin inhibitors), and direct renin inhibitors. **A**

10.10 In nonpregnant people with diabetes and hypertension, either an ACE inhibitor or ARB is recommended for those with moderately increased albuminuria (UACR 30–299 mg/g creatinine) **B** and is strongly recommended for those with severely increased albuminuria (UACR ≥ 300 mg/g creatinine) and/or estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m² to maximally tolerated dose to prevent the progression of kidney disease and reduce cardiovascular events. **A** If one class is not tolerated, the other should be substituted. **B**

10.11 Monitor for drop in eGFR and for increase in serum potassium levels at initiation and periodically as clinically appropriate when ACE inhibitors, ARBs, and mineralocorticoid receptor antagonists (MRAs) are used. **B** Monitor for hypokalemia when diuretics are used at routine visits and 7–14 days after initiation or after a dose change and periodically as clinically appropriate. **B**

10.12 In sexually active individuals of childbearing potential who are not using reliable contraception, avoid ACE inhibitors, ARBs, MRAs, direct renin inhibitors, and neprilysin inhibitors, as they are contraindicated in pregnancy. **A**

Initial Number of Antihypertensive Medications. Initial treatment for people with diabetes depends on the severity of hypertension (Fig. 10.2). Those with blood pressure between 130/80 mmHg and 150/90 mmHg may begin with a single drug. For individuals with blood pressure $\geq 150/90$ mmHg, initial pharmacologic treatment with two antihypertensive medications is recommended to more effectively achieve blood pressure goals (57–59). Single-pill antihypertensive combinations may improve medication-taking behavior in some individuals (60,61).

Classes of Antihypertensive Medications. Initial treatment for hypertension should include any of the drug classes demonstrated to reduce cardiovascular events in people with diabetes (27): ACE inhibitors (62), angiotensin receptor blockers (ARBs) (62), thiazide-like diuretics (63), or dihydropyridine calcium channel blockers (64).

In people with diabetes and established coronary artery disease, ACE inhibitors or ARBs are recommended first-line therapy for hypertension (65–67). For individuals with albuminuria (urine albumin-to-creatinine ratio [UACR] ≥ 30 mg/g), initial treatment should include an ACE inhibitor or ARB to reduce the risk of progressive kidney disease (24) (**Fig. 10.2**). In individuals receiving ACE inhibitor or ARB therapy, continuation of those medications as kidney function declines to eGFR < 30 mL/min/1.73 m² may provide cardiovascular benefit without significantly increasing the risk of kidney failure (68). In the absence of albuminuria, risk of progressive kidney disease is low, and ACE inhibitors and ARBs have not been found to afford superior cardioprotection compared with thiazide-like diuretics or dihydropyridine calcium channel blockers (69). β -Blockers are indicated in the setting of prior MI, active angina, or HFrEF but have not been shown to reduce mortality as blood pressure-lowering agents in the absence of these conditions (36,70,71).

Pregnancy and Antihypertensive Medications. Please refer to section 15, “Management of Diabetes in Pregnancy,” for additional information on pregnancy blood pressure goals and treatment. During pregnancy, treatment with ACE inhibitors, ARBs, direct renin inhibitors, mineralocorticoid receptor antagonists (MRAs), and neprilysin inhibitors are contraindicated, as they may cause fetal damage. Special consideration should be taken for individuals of childbearing potential, and people intending to become pregnant should switch from an ACE inhibitor or ARB, renin inhibitor, MRA, or neprilysin inhibitor to an alternative antihypertensive medication approved for use during pregnancy. Antihypertensive drugs known to be effective and safe in pregnancy include methyldopa, labetalol, and long-acting nifedipine, while hydralazine may be considered in the acute management of hypertension in pregnancy or severe preeclampsia (72). Diuretics are not recommended for blood pressure management in pregnancy but may be used during late-stage pregnancy if needed for volume management (72). The American College of Obstetricians and Gynecologists also recommends that, postpartum, individuals with gestational hypertension, preeclampsia, or both have their blood pressures observed for 72 h in the hospital and 7–10 days postpartum.

Long-term follow-up is recommended for these individuals, as they have increased lifetime cardiovascular risk (73).

Multiple-Drug Therapy. Multiple-drug therapy is often required to achieve blood pressure goals (**Fig. 10.2**), particularly in the setting of CKD in people with diabetes. However, the use of both ACE inhibitors and ARBs in combination, or the combination of an ACE inhibitor or ARB and a direct renin inhibitor, is contraindicated given the lack of added ASCVD benefit and increased rate of adverse events—namely, hyperkalemia, syncope, and AKI (74–76). Titration of and/or addition of further blood pressure medications should be made in a timely fashion to overcome therapeutic inertia in achieving blood pressure goals.

Hyperkalemia and Acute Kidney Injury. Treatment with ACE inhibitors and ARBs or MRAs can cause AKI and hyperkalemia, while diuretics can cause AKI and either hypokalemia or hyperkalemia (depending on mechanism of action) (77,78). Elevations in serum creatinine (up to 30% from baseline) with ACE inhibitors or ARBs must not be confused with AKI (79). AKI is defined as a rapid decline in kidney function, typically within a short period (hours to days), characterized by increase in serum creatinine and/or decrease in urine output (80). Serum creatinine and potassium should be monitored after initiation of treatment with an ACE inhibitor or ARB, MRA, or diuretic and monitored during treatment and following uptitration of these medications, particularly among individuals with reduced glomerular filtration (77,78,81). For more information on AKI, see section 11, “Chronic Kidney Disease and Risk Management.”

RESISTANT HYPERTENSION

Recommendation

10.13 Individuals with hypertension who are not meeting blood pressure goals on three classes of antihypertensive medications (including a diuretic) should be considered for MRA therapy. **A**

Resistant hypertension is defined as blood pressure $\geq 130/80$ mmHg despite a therapeutic strategy that includes appropriate lifestyle management plus a diuretic and two other antihypertensive drugs with complementary mechanisms of action at

maximally tolerated doses. Prior to diagnosing resistant hypertension, a number of other conditions should be excluded, including missed doses of antihypertensive medications, white coat hypertension, and primary and secondary hypertension. Difficulty following the care plan may also be a reason for resistant hypertension. International Society of Hypertension guidelines put a strong emphasis on screening for care plan difficulties in management of hypertension and recommend using objective measures such as review of pharmacy records, pill counting, and the chemical analysis of blood or urine rather than subjective methods of detecting inconsistencies in care plan engagement in routine clinical practice. However, this may not be feasible in all practice settings (25).

People with diabetes and confirmed resistant hypertension should be evaluated for secondary causes of hypertension, including primary aldosteronism, renal artery stenosis, CKD, and obstructive sleep apnea. In general, barriers to medication taking (such as cost and side effects) should be identified and addressed (**Fig. 10.2**). MRAs, including spironolactone and eplerenone, are effective for management of resistant hypertension in people with type 2 diabetes when added to existing treatment with an ACE inhibitor or ARB, thiazide-like diuretic, or dihydropyridine calcium channel blocker (82). In addition, MRAs reduce albuminuria in people with diabetic nephropathy (83–85). However, adding an MRA to a treatment plan that includes an ACE inhibitor or ARB may increase the risk for hyperkalemia, emphasizing the importance of regular monitoring for serum creatinine and potassium in these individuals, and long-term outcome studies are needed to better evaluate the role of MRAs in blood pressure management.

LIPID MANAGEMENT

Lifestyle Intervention

Recommendations

10.14 Lifestyle modification focusing on weight loss (if indicated); application of a Mediterranean or DASH eating pattern; reduction of saturated fat and trans fat; increase of dietary n-3 fatty acids, soluble fiber, and plant stanol and sterol intake; and increased physical activity should be recommended to improve the lipid profile and reduce the risk of developing atherosclerotic

cardiovascular disease (ASCVD) in people with diabetes. **A**

10.15 Intensify lifestyle therapy and optimize glycemic management for people with diabetes with elevated triglyceride levels (≥ 150 mg/dL [≥ 1.7 mmol/L]) and/or low HDL cholesterol (< 40 mg/dL [< 1.0 mmol/L] for men and < 50 mg/dL [< 1.3 mmol/L] for women). **C**

Lifestyle intervention, including weight loss in people with overweight or obesity (when appropriate) (22,86), increased physical activity, and medical nutrition therapy, allows some individuals to reduce ASCVD risk factors such as hypertension, dyslipidemia, or obesity. Nutrition intervention should be tailored according to each person's age, pharmacologic treatment, lipid levels, and medical conditions.

Recommendations should focus on application of a Mediterranean (87) or DASH eating pattern, reducing saturated and *trans* fat intake, and increasing plant stanol and sterol, n-3 fatty acid, and viscous fiber (such as in oats, legumes, and citrus) intake (22,86). Glycemic management may also beneficially modify plasma lipid levels, particularly in people with very high triglycerides and poor glycemic management. See section 5, "Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes," for additional nutrition information.

Ongoing Therapy and Monitoring With Lipid Panel

Recommendations

10.16 In adults with prediabetes or diabetes not taking statins or other lipid-lowering therapy, it is reasonable to obtain a lipid profile at the time of diagnosis, at an initial medical evaluation, annually thereafter, or more frequently if indicated. **E**

10.17 Obtain a lipid profile at initiation of statins or other lipid-lowering therapy, 4–12 weeks after initiation or a change in dose, and annually thereafter, as it facilitates monitoring the response to therapy and informs medication-taking behavior. **A**

In adults with diabetes, it is reasonable to obtain a lipid profile (total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides) at the time of diagnosis, at the initial medical evaluation, and

at least every 5 years thereafter in individuals < 40 years of age. In younger people with longer duration of disease (such as those diagnosed in childhood or adolescence), more frequent lipid profiles may be reasonable. A lipid panel should also be obtained immediately before initiating statin therapy. Once an individual is taking a statin, LDL cholesterol levels should be assessed 4–12 weeks after initiation of statin therapy, after any change in dose, and annually (e.g., to monitor for medication taking and efficacy). Monitoring lipid profiles after initiation of statin therapy and during therapy increases the likelihood of dose titration and following the statin treatment plan (88–90). Clinicians should attempt to find a dose or alternative statin that is tolerable if side effects occur. There is evidence for benefit from even extremely low, less-than-daily statin doses (91).

STATIN TREATMENT

Primary Prevention

Recommendations

10.18 For people with diabetes aged 40–75 years without ASCVD, use moderate-intensity statin therapy in addition to lifestyle therapy. **A**

10.19 For people with diabetes aged 20–39 years with additional ASCVD risk factors, it may be reasonable to initiate statin therapy in addition to lifestyle therapy. **C**

10.20 For people with diabetes aged 40–75 years at higher cardiovascular risk, including those with one or more additional ASCVD risk factors, high-intensity statin therapy is recommended to reduce LDL cholesterol by $\geq 50\%$ of baseline and to obtain an LDL cholesterol goal of < 70 mg/dL (< 1.8 mmol/L). **A**

10.21 For people with diabetes aged 40–75 years at higher cardiovascular risk, especially those with multiple additional ASCVD risk factors and an LDL cholesterol ≥ 70 mg/dL (≥ 1.8 mmol/L), it may be reasonable to add ezetimibe or a proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor to maximum tolerated statin therapy. **B**

10.22 In adults with diabetes aged > 75 years already on statin therapy, it is reasonable to continue statin treatment. **B**

10.23 In adults with diabetes aged > 75 years, it may be reasonable to

initiate moderate-intensity statin therapy after discussion of potential benefits and risks. **C**

10.24 In people with diabetes intolerant to statin therapy, treatment with bempedoic acid is recommended to reduce cardiovascular event rates as an alternative cholesterol-lowering plan. **A**

10.25 In most circumstances, lipid-lowering agents should be stopped prior to conception and avoided in sexually active individuals of childbearing potential who are not using reliable contraception. **B** In some circumstances (e.g., familial hypercholesterolemia, familial hypertriglyceridemia, prior ASCVD event, or history of pancreatitis), lipid-lowering therapy may be continued when the benefits outweigh risks. **E**

Secondary Prevention

Recommendations

10.26 For people of all ages with diabetes and ASCVD, high-intensity statin therapy should be added to lifestyle therapy. **A**

10.27 For people with diabetes and ASCVD, treatment with high-intensity statin therapy is recommended to obtain an LDL cholesterol reduction of $\geq 50\%$ from baseline and an LDL cholesterol goal of < 55 mg/dL (< 1.4 mmol/L). Addition of ezetimibe or a PCSK9 inhibitor with proven benefit in this population is recommended if this goal is not achieved on maximum tolerated statin therapy. **B**

10.28a For individuals who do not tolerate the intended statin intensity, the maximum tolerated statin dose should be used. **E**

10.28b For people with diabetes and ASCVD intolerant to statin therapy, PCSK9 monoclonal antibody therapy, **A** bempedoic acid therapy, **A** or PCSK9 inhibitor therapy with inclisiran siRNA **E** should be considered as an alternative cholesterol-lowering therapy.

Initiating Statin Therapy

People with type 2 diabetes have an increased prevalence of lipid abnormalities, contributing to their high risk of ASCVD. Multiple clinical trials have demonstrated

the beneficial effects of statin therapy on ASCVD outcomes in subjects with and without established ASCVD (92,93). Subgroup analyses of people with diabetes in larger trials (94–98) and trials in people with diabetes (99,100) showed significant primary and secondary prevention of ASCVD events and coronary heart disease (CHD) death in people with diabetes. Meta-analyses including data from >18,000 people with diabetes from 14 randomized trials of statin therapy (mean follow-up 4.3 years) demonstrated a 9% proportional reduction in all-cause mortality and 13% reduction in vascular mortality for each 1 mmol/L (39 mg/dL) reduction in LDL cholesterol (101). The cardiovascular benefit in this large meta-analysis did not depend on baseline LDL cholesterol levels and was linearly related to the LDL cholesterol reduction without a low threshold beyond which there was no benefit observed (101). It is important to note that the effects of statin therapy do not differ based on sex (92).

Accordingly, statins are the drugs of choice for LDL cholesterol lowering and cardioprotection. **Table 10.1** shows the two statin dosing intensities that are recommended for use in clinical practice. High-intensity statin therapy will achieve an approximately $\geq 50\%$ reduction in LDL cholesterol, and moderate-intensity statin plans achieve 30–49% reductions in LDL cholesterol. Low-dose statin therapy is generally not recommended in people with diabetes but is sometimes the only dose of statin that an individual can tolerate. For individuals who do not tolerate the intended intensity of statin, the maximum tolerated statin dose should be used.

As in those without diabetes, absolute reductions in ASCVD outcomes (CHD death and nonfatal MI) are greatest in people with high baseline ASCVD risk (known ASCVD and/or very high LDL cholesterol

levels), but the overall benefits of statin therapy in people with diabetes at moderate or even low risk for ASCVD are convincing (102,103). The relative benefit of lipid-lowering therapy has been uniform across most subgroups tested (101,104), including subgroups that varied with respect to age and other risk factors.

Primary Prevention (People Without ASCVD)

For primary prevention, moderate-dose statin therapy is recommended for those aged ≥ 40 years (22,105,106), although high-intensity therapy should be considered in the context of additional ASCVD risk factors, such as older age, hypertension, dyslipidemia, smoking, CKD, or obesity (**Fig. 10.3**). The evidence is strong for people with diabetes aged 40–75 years, an age-group well represented in statin trials showing benefit. Since cardiovascular risk is enhanced in people with diabetes, as noted above, individuals who also have multiple other coronary risk factors have increased risk, equivalent to that of those with ASCVD. Therefore, current guidelines recommend that in people with diabetes who are at higher cardiovascular risk, especially those with one or more ASCVD risk factors such as older age, hypertension, dyslipidemia, smoking, CKD, or obesity, high-intensity statin therapy should be prescribed to reduce LDL cholesterol by $\geq 50\%$ from baseline and to obtain an LDL cholesterol of <70 mg/dL (<1.8 mmol/L) (107–109). Since, in clinical practice, it is frequently difficult to ascertain the baseline LDL cholesterol level prior to statin therapy initiation, in those individuals, a focus on an LDL cholesterol goal of <70 mg/dL (<1.8 mmol/L) rather than percent reduction in LDL cholesterol is recommended. In those individuals, it may also be reasonable to add ezetimibe or proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor therapy to maximum

tolerated statin therapy if needed to reduce LDL cholesterol levels by $\geq 50\%$ and to achieve the recommended LDL cholesterol goal of <70 mg/dL (<1.8 mmol/L) (110). While there are no randomized controlled trials specifically assessing cardiovascular outcomes of adding ezetimibe or PCSK9 inhibitors to statin therapy in primary prevention, a portion of the participants without established CVD were included in some studies, which also included participants with established CVD. A meta-analysis suggests that there is a cardiovascular benefit of adding ezetimibe or PCSK9 inhibitors to treatment for people at high risk (111). Less evidence is available for individuals aged >75 years, as few older people with diabetes have been enrolled in primary prevention trials. However, heterogeneity by age has not been seen in the relative benefit of lipid-lowering therapy in trials that included older participants (100,101,104), and because older age confers higher risk, the absolute benefits are actually greater (104,112). Moderate-intensity statin therapy is recommended in people with diabetes who are ≥ 75 years of age. However, the risk-benefit profile should be routinely evaluated in this population, with downward titration of dose performed as needed. See section 13, “Older Adults,” for more details on clinical considerations for this population.

Age <40 Years and/or Type 1 Diabetes.

Very little clinical trial evidence exists for people with type 2 diabetes under the age of 40 years or for people with type 1 diabetes of any age. For pediatric recommendations, see section 14, “Children and Adolescents.” In the Heart Protection Study (lower age limit 40 years), the subgroup of ~ 600 people with type 1 diabetes had a reduction in risk proportionately similar, although not statistically significant, to that in people with type 2 diabetes (95). Even though the data are not definitive, similar statin treatment approaches should be considered for people with type 1 or type 2 diabetes, particularly in the presence of other cardiovascular risk factors. Individuals <40 years of age have lower risk of developing a cardiovascular event over a 10-year period; however, their lifetime risk of developing CVD and experiencing an MI, stroke, or cardiovascular death is high. For people who are <40 years of age and/or have type 1 diabetes with other ASCVD risk factors (such as older age, hypertension,

Table 10.1—High-intensity and moderate-intensity statin therapy

High-intensity statin therapy (lowers LDL cholesterol by $\geq 50\%$)	Moderate-intensity statin therapy (lowers LDL cholesterol by 30–49%)
Atorvastatin 40–80 mg	Atorvastatin 10–20 mg
Rosuvastatin 20–40 mg	Rosuvastatin 5–10 mg
	Simvastatin 20–40 mg
	Pravastatin 40–80 mg
	Lovastatin 40 mg
	Fluvastatin XL 80 mg
	Pitavastatin 1–4 mg

Once-daily dosing. XL, extended release.

Lipid management for primary prevention of atherosclerotic cardiovascular disease events in people with diabetes in addition to healthy behavior modification

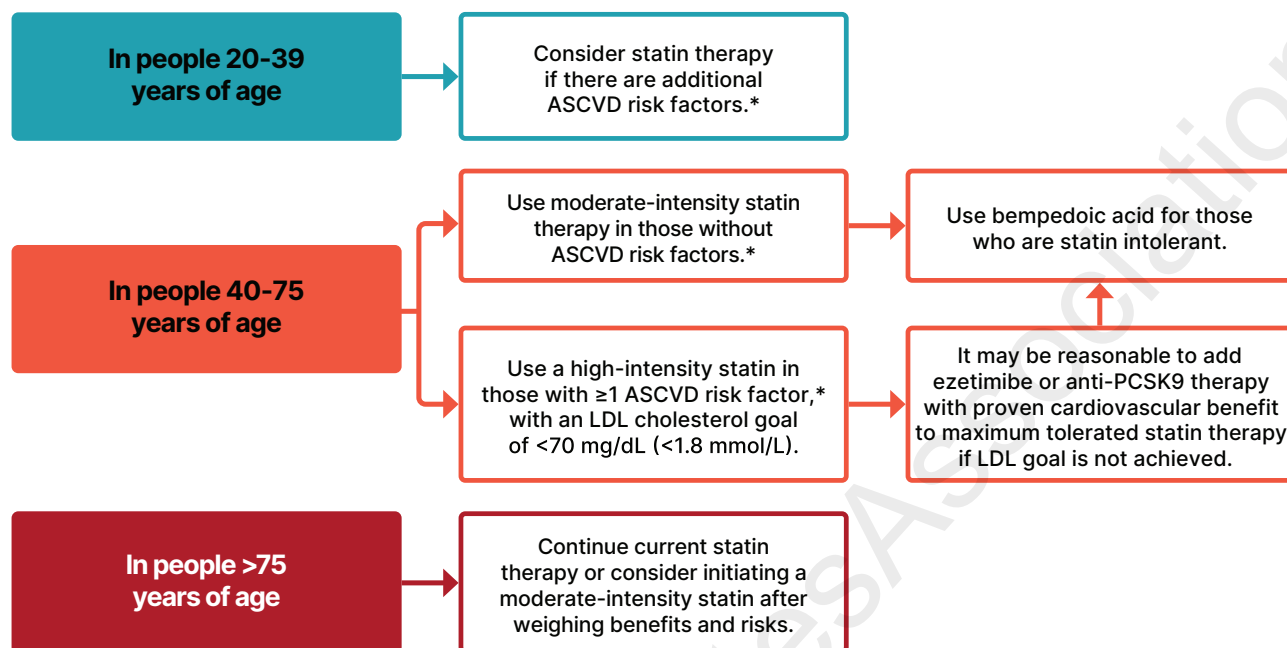


Figure 10.3—Recommendations for primary prevention of atherosclerotic cardiovascular disease (ASCVD) in people with diabetes using cholesterol-lowering therapy. *ASCVD risk factors include older age, hypertension, dyslipidemia, smoking, chronic kidney disease, or obesity. Adapted from “Standards of Care in Diabetes—2024 Abridged for Primary Care Professionals” (315).

dyslipidemia, smoking, CKD, or obesity), it is recommended that the individual and health care professional discuss the relative benefits and risks and consider the use of moderate-intensity statin therapy. Please refer to “Type 1 Diabetes Mellitus and Cardiovascular Disease: A Scientific Statement From the American Heart Association and American Diabetes Association” (113) for additional discussion. Recent data from the PCSK9 inhibitor trial FOURIER (Further Cardiovascular Outcomes Research With PCSK9 Inhibition in Subjects With Elevated Risk) suggest that LDL cholesterol-lowering benefit has important cardiovascular risk reduction benefits in people with type 1 diabetes and established CVD, as discussed in SECONDARY PREVENTION (PEOPLE WITH ASCVD), below (114).

Secondary Prevention (People With ASCVD)

Intensive therapy is indicated because cardiovascular event rates are increased in people with diabetes and established ASCVD, and it has been shown to be of benefit in multiple large meta-analyses and randomized cardiovascular outcomes trials (93,101,104,112,115). High-intensity statin therapy is recommended for all people with diabetes and ASCVD to obtain an LDL cholesterol reduction of $\geq 50\%$ from baseline and an LDL cholesterol goal of < 55 mg/dL (< 1.4 mmol/L) (Fig. 10.4). The addition of ezetimibe or a PCSK9 inhibitor is recommended if this goal is not achieved on maximum tolerated statin therapy. These recommendations are based on the observation that high-intensity versus moderate-intensity statin therapy reduces cardiovascular event rates in high-

risk individuals with established CVD in randomized trials (93). The Cholesterol Treatment Trialists’ Collaboration, involving 26 statin trials, of which 5 compared high-intensity versus moderate-intensity statins, showed a 21% reduction in major cardiovascular events in people with diabetes for every 39 mg/dL (1 mmol/L) of LDL cholesterol lowering, irrespective of baseline LDL cholesterol or individual characteristics (101). The evidence to support lower LDL cholesterol goals in people with diabetes and established CVD derives from multiple large, randomized trials investigating the benefits of adding nonstatin agents to statin therapy, including combination treatment with statins and ezetimibe (112,116) or PCSK9 inhibitors (115,117–119). Each trial found a large benefit in reducing ASCVD events that was directly

Lipid management for secondary prevention of atherosclerotic cardiovascular disease events in people with diabetes

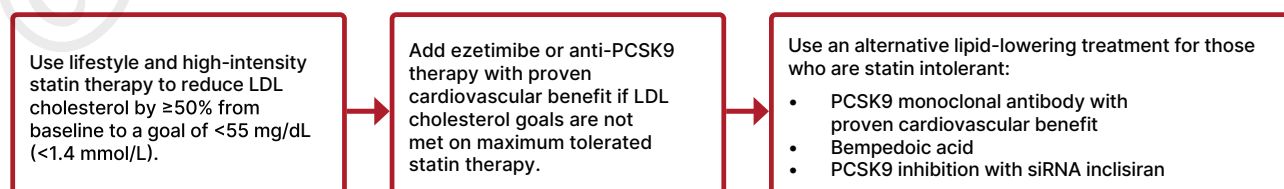


Figure 10.4—Recommendations for secondary prevention of atherosclerotic cardiovascular disease (ASCVD) in people with diabetes using cholesterol-lowering therapy. Adapted from “Standards of Care in Diabetes—2024 Abridged for Primary Care Professionals” (315).

related to the degree of further LDL cholesterol lowering. A large number of participants with diabetes were included in these trials, and prespecified analyses were completed to evaluate cardiovascular outcomes in people with and without diabetes (116,118,119). The decision to add a non-statin agent should be made following a discussion between a clinician and a person with diabetes about the net benefit, safety, and cost of combination therapy.

Combination Therapy for LDL Cholesterol Lowering

Statins and Ezetimibe

The best evidence for combination therapy of statins and ezetimibe comes from the IMPROVED Reduction of Outcomes: Vytorin Efficacy International Trial (IMPROVE-IT). The trial showed the addition of ezetimibe to a moderate-intensity statin led to a 6.4% relative benefit and a 2% absolute reduction in major adverse cardiovascular events (atherosclerotic cardiovascular events), with the degree of benefit being directly proportional to the change in LDL cholesterol (112). A subanalysis of participants with diabetes (27% of the 18,144 participants) showed a significant reduction of major adverse cardiovascular events with the combination treatment over moderate-intensity statin alone (116).

Statins and PCSK9 Inhibitors

The addition of the PCSK9 monoclonal antibodies evolocumab and alirocumab to maximum tolerated doses of statin therapy in participants who were at high risk for ASCVD demonstrated an average reduction in LDL cholesterol ranging from 52% to 65% (120,121). No cardiovascular outcome trials have been performed to assess whether PCSK9 inhibitor therapy reduces ASCVD event rates in individuals at low or moderate risk for ASCVD (primary prevention). The evidence on the effect of PCSK9 monoclonal antibodies on ASCVD outcomes is from studies of treatment with alirocumab and evolocumab. When added to a maximally tolerated statin, these agents reduced LDL cholesterol by ~60% (115) and significantly reduced the risk of major adverse cardiovascular events by 15–20% in the FOURIER (evolocumab) and ODYSSEY OUTCOMES (Evaluation of Cardiovascular Outcomes After an Acute Coronary Syndrome During Treatment With Alirocumab) trials (115,117,122). In the subanalyses of the participants with diabetes (40% in FOURIER and 28.8% in

ODYSSEY OUTCOMES), similar benefits were seen compared with those for individuals without diabetes in FOURIER (119), whereas a greater absolute risk reduction was seen for participants with diabetes (2.3% [95% CI 0.4–4.2]) than for those with prediabetes (1.2% [0.0–2.4]) or normoglycemia (1.2% [−0.3–2.7]) in the ODYSSEY OUTCOMES trial (118). While clinical outcome data for the effects of LDL cholesterol lowering in people with type 1 diabetes are scarce, a stratified analysis of FOURIER provided insights on the background risk of cardiovascular events in people with type 1, type 2, or no diabetes (114). Of the 27,564 participants in FOURIER, 197 (0.7%) had type 1 diabetes and 10,834 (39.3%) had type 2 diabetes. Participants with type 1 diabetes randomly assigned to placebo had a higher rate of major cardiovascular events (Kaplan-Meier event rate 20.4%) than those with type 2 diabetes (15.2%) and those without diabetes (11.0%). The relative reduction in the risk of the primary major adverse cardiovascular event outcome with active compared with placebo evolocumab was similar across different types or statuses of diabetes (type 1 diabetes HR 0.66, 95% CI 0.32–1.38; type 2 diabetes HR 0.84, 95% CI 0.75–0.93; no diabetes HR 0.87, 95% CI 0.79–0.96). These observations suggest that the absolute risk reduction of major cardiovascular events with evolocumab in individuals with type 1 diabetes was at least as large, if not larger, than that seen for type 2 diabetes or no diabetes. These data support the use of PCSK9 inhibitors in the achievement of aggressive LDL cholesterol lowering in people with type 1 diabetes and established ASCVD (114).

In addition to the monoclonal antibodies, an siRNA, inclisiran, which also targets PCSK9 and is referred to as a PCSK9 siRNA in this section, has demonstrated the ability to reduce LDL cholesterol by 49–52% in trials evaluating individuals with established CVD or ASCVD risk equivalent (123). Cardiovascular outcome trials using inclisiran in people with established CVD (124,125) and for primary prevention in those at high risk for CVD (126) are currently ongoing. For this reason, therapy with the PCSK9 monoclonal antibodies (alirocumab and evolocumab) is preferred to therapy with PCSK9 siRNA (inclisiran).

Intolerance to Statin Therapy

Statin therapy is a cornerstone of CVD prevention and treatment; however, a

subset of individuals experience partial (inability to tolerate sufficient dosage necessary to achieve therapeutic objectives due to adverse effects) or complete (inability to tolerate any dose) intolerance to statin therapy (127). Although the definition of statin intolerance differs between organizations and across clinical study methods, these individuals will require an alternative treatment approach. Initial steps in people intolerant to statins may include switching to a different high-intensity statin if a high-intensity statin is indicated, switching to moderate-intensity or low-intensity statin, lowering the statin dose, or using nondaily dosing with statins. While considering these alternative treatment plans, the addition of nonstatin treatment plans to maximum tolerated statin therapy should be considered, as these are frequently associated with improved medication-taking behavior and achievement of LDL cholesterol goals (127).

PCSK9-Directed Therapies

The PCSK9 monoclonal antibodies alirocumab and evolocumab both have been shown to be effective for LDL cholesterol reduction and fewer skeletal muscle-related adverse effects when studied in populations considered statin intolerant. The Study of Alirocumab in Patients With Primary Hypercholesterolemia and Moderate, High, or Very High Cardiovascular Risk, Who Are Intolerant to Statins (ODYSSEY ALTERNATIVE) trial studied the reduction in LDL cholesterol with alirocumab compared with ezetimibe or 20 mg atorvastatin in individuals at moderate to very high cardiovascular risk for 24 weeks. The proportion of the study population with type 2 diabetes was ~24%. After the 24 weeks, alirocumab lowered LDL cholesterol levels by 54.8% versus 20.1% with ezetimibe. There were similar rates of any adverse event for all treatments; however, fewer events that led to treatment discontinuation and few skeletal muscle-related adverse events occurred with alirocumab (128).

The Goal Achievement After Utilizing an Anti-PCSK9 Antibody in Statin Intolerant Subjects 1, 2, and 3 (GAUSS 1, 2, and 3) trials, as well as the Open-Label Study of Long-term Evaluation Against LDL Cholesterol (OSLER) open-label extension of the GAUSS 1 and 2 trials, evaluated the safety and LDL cholesterol reduction of evolocumab plus ezetimibe compared with

ezetimibe alone in individuals with statin intolerance.

Reductions in LDL cholesterol ranged from 55% and 56% for evolocumab biweekly and monthly plus daily oral placebo, respectively, to 19% and 16% for ezetimibe daily plus biweekly or monthly subcutaneous placebo, respectively. Fewer musculoskeletal adverse effects occurred in those treated with evolocumab or ezetimibe than in those treated with ezetimibe plus placebo, although rates of discontinuation due to these effects were similar. Use of low-dose statins was allowed in these studies and was associated with an increase in the incidence of musculoskeletal adverse effects (129,130). Similar LDL cholesterol reductions were demonstrated in the GAUSS 3 trial after 24 weeks (54.5% with evolocumab compared with 16.7% with ezetimibe), with slightly higher rates of musculoskeletal adverse events (20.7% with evolocumab and 28.8% with ezetimibe). The higher rates of these adverse events may be due in part to the first phase of this trial, which randomized individuals to a statin rechallenge with either atorvastatin or placebo (131).

Inclisiran, a PCSK9 siRNA, has also been proposed as an option for individuals with statin intolerance. Although most of the individuals in studies of inclisiran were on statin therapy, one short-term study (Trial to Evaluate the Effect of ALN-PCSSC Treatment on Low-density Lipoprotein Cholesterol [ORION-1]) included individuals with documented statin intolerance (132) and could continue into an open-label extension trial (Extension Trial of Inclisiran in Participants With Cardiovascular Disease and High Cholesterol [ORION-3]), where an LDL cholesterol reduction of ~45% was maintained through the end of year 4 (133). It is important to note that of the ORION-3 participants, 23% had diabetes and 33% were not taking statin therapy. Although it may be expected that those with statin intolerance experienced a response similar to the response of those on statin therapy, evaluation of response based on background lipid-lowering therapy was not described.

Bempedoic Acid

Bempedoic acid, a newer LDL cholesterol-lowering agent targeting the same pathway as statins but without activity in skeletal muscle, thus limiting muscle-related adverse effects, lowers LDL cholesterol levels by 15% for those on statins and

24% for those not taking statins (134). Use of this agent with ezetimibe results in an additional 19% reduction in LDL cholesterol (134). The Evaluation of Major Cardiovascular Events in Patients With, or at High Risk for, Cardiovascular Disease Who Are Statin Intolerant Treated With Bempedoic Acid or Placebo (CLEAR Outcomes) trial found a reduction in four-point major adverse cardiovascular events by 13% compared with placebo for individuals with established ASCVD (70% of population) or at high risk for ASCVD (30% of population) and considered to be intolerant to statin therapy. It is important to note that ~19% of individuals were on very-low-dose statin therapy at baseline (135). Prespecified subanalyses evaluated the impact for individuals with diabetes and showed a 17% reduction in four-point major adverse cardiovascular events when treated with bempedoic acid (136). For individuals requiring primary prevention, the use of bempedoic acid resulted in a 30% reduction in primary composite outcome compared with placebo (137).

Lipid-Lowering Care Considerations for Individuals of Childbearing Potential

Individuals of childbearing potential are less likely to be treated with statins or achieve their LDL cholesterol goals based on their cardiovascular risk (138–140). This is likely related to concerns and lack of familiarity with the use of lipid-lowering agents during pregnancy. The trials evaluating the efficacy and safety of lipid-lowering medications exclude individuals who are pregnant and require individuals of childbearing potential to use contraception (some requiring two forms). Therefore, for many pregnant individuals, it is recommended that they discontinue lipid-lowering therapies during gestation. However, for individuals at higher risk for cardiovascular events (e.g., those with familial hypercholesterolemia or preexisting ASCVD), the risk of discontinuing all lipid-lowering therapy during preconception and pregnancy should be reviewed and weighed against an increased risk for cardiovascular events. Consideration of initiating statin therapy during pregnancy should occur with these high-risk individuals. Although the evidence is limited, statins did not increase teratogenic effects for individuals with familial hypercholesterolemia (141,142), and a meta-analysis of pravastatin in pregnant individuals showed a reduction in preeclampsia,

premature birth, and neonatal intensive care unit admissions (143). There is limited information regarding the use of lipid-lowering therapies (other than bile acid sequestrants) during pregnancy. Thus, it is recommended that individuals of childbearing potential use a form of contraception when also using lipid-lowering medications with unknown risks, limited evidence on safety, or known risks during pregnancy regardless of intention to become pregnant, as many pregnancies are unplanned, and preconception counseling should be part of the routine care of individuals with diabetes who have childbearing potential. Counseling should include the known benefits and risks of lipid-lowering medications versus the risks and benefits of not treating the conditions for which they are prescribed, as well as other medications (e.g., noninsulin glucose-lowering therapies and antihypertensive agents), during pregnancy and recommendations for when changes in medications should occur prior to pregnancy (138) (see section 15, “Management of Diabetes in Pregnancy,” for more information on preconception counseling and lipid-lowering treatment during pregnancy).

Treatment of Other Lipoprotein Fractions or Goals

Recommendations

10.29 For individuals with fasting triglyceride levels ≥ 500 mg/dL (≥ 5.7 mmol/L), evaluate for secondary causes of hypertriglyceridemia and consider medical therapy to reduce the risk of pancreatitis. **C**

10.30 In adults with hypertriglyceridemia (fasting triglycerides >150 mg/dL [>1.7 mmol/L] or nonfasting triglycerides >175 mg/dL [>2.0 mmol/L]), clinicians should address and treat lifestyle factors (obesity and metabolic syndrome), secondary factors (diabetes, chronic liver or kidney disease and/or nephrotic syndrome, and hypothyroidism), and medications that raise triglycerides. **C**

10.31 In individuals with ASCVD or other cardiovascular risk factors on a statin with managed LDL cholesterol but elevated triglycerides (150–499 mg/dL [1.7–5.6 mmol/L]), the addition of icosapent ethyl can be considered to reduce cardiovascular risk. **B**

Hypertriglyceridemia should be addressed with nutritional and lifestyle

changes, including weight loss and abstinence from alcohol (144). Severe hypertriglyceridemia (fasting triglycerides ≥ 500 mg/dL [≥ 5.7 mmol/L] and especially $> 1,000$ mg/dL [> 11.3 mmol/L]) may warrant pharmacologic therapy (fibric acid derivatives and/or fish oil) and reduction in fat intake to reduce the risk of acute pancreatitis (145). Moderate- or high-intensity statin therapy should also be used as indicated to reduce risk of cardiovascular events (see *STATIN TREATMENT*, above) (144,146). In people with hypertriglyceridemia (fasting triglycerides > 150 mg/dL [> 1.7 mmol/L] or nonfasting triglycerides > 175 mg/dL [> 2.0 mmol/L]), lifestyle interventions, treatment of secondary factors, and avoidance of medications that might raise triglycerides are recommended.

For individuals with established CVD or with risk factors for CVD with elevated triglycerides (150–499 mg/dL [1.7–5.6 mmol/L]) after maximizing statin therapy, icosapent ethyl may be added to reduce cardiovascular risk. The Reduction of Cardiovascular Events with Icosapent Ethyl-Intervention Trial (REDUCE-IT) showed that the addition of icosapent ethyl to statin therapy in this population resulted in a 25% relative risk reduction ($P < 0.001$) for the primary end point composite of cardiovascular death, nonfatal MI, nonfatal stroke, coronary revascularization, or unstable angina compared with placebo. This risk reduction was seen in individuals with or without diabetes at baseline. The composite of cardiovascular death, nonfatal MI, or nonfatal stroke was reduced by 26% ($P < 0.001$). Additional ischemic end points were significantly lower in the icosapent ethyl group than in the placebo group, including cardiovascular death, which was reduced by 20% ($P = 0.03$). The proportions of individuals experiencing adverse events and serious adverse events were similar between the active and placebo treatment groups. Current evidence from randomized trials does not support cardiovascular risk reduction for other n-3 fatty acids, and results of the REDUCE-IT trial should not be extrapolated to other products (147). As an example, the addition of 4 g per day of a carboxylic acid formulation of the n-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) (n-3 carboxylic acid) to statin therapy in individuals with atherogenic dyslipidemia and high cardiovascular risk, 70% of whom had diabetes, did not reduce the risk of major

adverse cardiovascular events compared with the inert comparator of corn oil (148).

Low levels of HDL cholesterol, often associated with elevated triglyceride levels, are the most prevalent pattern of dyslipidemia in people with type 2 diabetes. However, the evidence for the use of drugs that target these lipid fractions is substantially less robust than that for statin therapy (149). Neither the ACCORD-lipid trial nor the Pemafibrate to Reduce Cardiovascular Outcomes by Reducing Triglycerides in Patients with Diabetes (PROMINENT) trial, both conducted in people with type 2 diabetes on statin therapy, found that the fibrate fenofibrate or pemafibrate improved cardiovascular outcomes (150,151).

Other Combination Therapy

Recommendations

10.32 In individuals receiving statin therapy, the addition of fibrate, niacin, or dietary supplements containing n-3 fatty acids is not recommended as they do not provide additional cardiovascular risk reduction. **A**

Statin and Fibrate Combination Therapy

Combination therapy (statin and fibrate) is associated with an increased risk for abnormal transaminase levels, myositis, and rhabdomyolysis. The risk of rhabdomyolysis is more common with higher doses of statins and renal insufficiency and appears to be higher when statins are combined with gemfibrozil (compared with fenofibrate) (152).

In the ACCORD study, in people with type 2 diabetes who were at high risk for ASCVD, the combination of fenofibrate and simvastatin did not reduce the rate of fatal cardiovascular events, nonfatal MI, or nonfatal stroke compared with simvastatin alone (153). In the PROMINENT trial, in people with type 2 diabetes and elevated triglycerides (≥ 200 mg/dL and low HDL [≤ 40 mg/dL]), pemafibrate 0.2 mg twice daily reduced triglycerides by 26% but did not reduce the risk of the primary outcome of nonfatal MI, nonfatal stroke, hospitalization for unplanned coronary revascularization, or cardiovascular death (151). Therefore, combination therapy with statin and fibrate is not recommended for cardiovascular risk reduction.

Statin and Niacin Combination Therapy

Combination therapy with a statin and niacin is not recommended, given the lack of efficacy on major ASCVD outcomes and increased side effects. Monotherapy with niacin is also not recommended. Large clinical trials, including the Atherothrombosis Intervention in Metabolic Syndrome With Low HDL/High Triglycerides: Impact on Global Health Outcomes (AIM-HIGH) and Heart Protection Study 2—Treatment of HDL to Reduce the Incidence of Vascular Events (HPS2-THRIVE) trials, failed to demonstrate a benefit of adding niacin to individuals on appropriate statin therapy. In fact, there was a possible increased risk of ischemic stroke in the AIM-HIGH trial (154) and an increased incidence of new-onset diabetes (absolute excess, 1.3 percentage points; $P < 0.001$) and disturbances in diabetes management among those with diabetes in the HPS2-THRIVE trial in those on combination therapy (155).

Diabetes Risk With Statin Use

Several studies have reported a modestly increased risk of incident type 2 diabetes with statin use (156,157), which may be limited to those with diabetes risk factors and/or impaired glucose tolerance. An analysis of one of the initial studies suggested that although statin use was associated with diabetes risk, the cardiovascular event rate reduction with statins far outweighed the risk of incident diabetes, even for individuals at highest risk for diabetes (158). The absolute risk increase was small (over 5 years of follow-up, 1.2% of participants on placebo developed diabetes and 1.5% on rosuvastatin developed diabetes) (158). A meta-analysis of 13 randomized statin trials with 91,140 participants showed an odds ratio of 1.09 for a new diagnosis of diabetes, so that (on average) treatment of 255 individuals with statins for 4 years resulted in one additional case of diabetes while simultaneously preventing 5.4 vascular events among those 255 individuals (157).

Lipid-Lowering Agents and Cognitive Function

Although concerns regarding a potential adverse impact of lipid-lowering agents on cognitive function have been raised, several lines of evidence argue against this association, as detailed in a 2018 European Atherosclerosis Society Consensus

Panel statement (159). First, there are three large, randomized trials of statin versus placebo where specific cognitive tests were performed, and no differences were seen between statin and placebo (160–163). In addition, no change in cognitive function has been reported in studies with the addition of ezetimibe (112) or PCSK9 monoclonal antibodies (115,164) to statin therapy, including among individuals treated to very low LDL cholesterol levels. In addition, systematic reviews of randomized controlled trials and prospective cohort studies evaluating cognition in individuals receiving statins found that published data do not reveal an adverse effect of statins on cognition (165,166). Therefore, a concern that statins or other lipid-lowering agents might cause cognitive dysfunction or dementia is not currently supported by evidence and should not deter their use in individuals with diabetes at high risk for ASCVD (167).

ANTIPLATELET AGENTS

Recommendations

10.33 Use aspirin therapy (75–162 mg/day) as a secondary prevention strategy in those with diabetes and a history of ASCVD. **A**

10.34a For individuals with ASCVD and documented aspirin allergy, clopidogrel (75 mg/day) should be used. **B**

10.34b The length of treatment with dual antiplatelet therapy using low-dose aspirin and a P2Y₁₂ inhibitor in individuals with diabetes after an acute coronary syndrome, acute ischemic stroke, or transient ischemic attack should be determined by an interprofessional team approach that includes a cardiovascular or neurological specialist, respectively. **E**

10.35 Combination therapy with 81 mg aspirin daily plus 2.5 mg rivaroxaban twice daily should be considered for individuals with stable coronary and/or peripheral artery disease (PAD) and low bleeding risk to prevent major adverse limb and cardiovascular events. **A**

10.36 Aspirin therapy (75–162 mg/day) may be considered as a primary prevention strategy in those with diabetes who are at increased cardiovascular risk after a comprehensive discussion with the individual on the benefits versus the comparable increased risk of bleeding. **A**

Risk Reduction

Aspirin has been shown to be effective in reducing cardiovascular morbidity and mortality in high-risk individuals with previous MI or stroke (secondary prevention) and is strongly recommended. In primary prevention, however, among individuals with no previous cardiovascular events, its net benefit is more controversial (156,168).

Previous randomized controlled trials of aspirin, specifically in people with diabetes, failed to consistently show a significant reduction in overall ASCVD end points, raising questions about the efficacy of aspirin for primary prevention in people with diabetes, although some sex differences were suggested (169–171).

The Antithrombotic Trialists' Collaboration published an individual participant-level meta-analysis (172) of six large trials of aspirin for primary prevention in the general population. These trials collectively enrolled over 95,000 participants, including almost 4,000 with diabetes. Overall, they found that aspirin reduced the risk of serious vascular events by 12% (relative risk 0.88 [95% CI 0.82–0.94]). The largest reduction was for nonfatal MI, with little effect on CHD death (relative risk 0.95 [95% CI 0.78–1.15]) or total stroke.

Most recently, the ASCEND (A Study of Cardiovascular Events in Diabetes) trial randomized 15,480 people with diabetes but no evident CVD to aspirin 100 mg daily or placebo (173). The primary efficacy end point was vascular death, MI, stroke, or transient ischemic attack. The primary safety outcome was major bleeding (i.e., intracranial hemorrhage, sight-threatening bleeding in the eye, gastrointestinal bleeding, or other serious bleeding). During a mean follow-up of 7.4 years, there was a significant 12% reduction in the primary efficacy end point (8.5% vs. 9.6%; $P = 0.01$). In contrast, major bleeding was significantly increased from 3.2 to 4.1% in the aspirin group (rate ratio 1.29; $P = 0.003$), with most of the excess being gastrointestinal bleeding and other extracranial bleeding. There were no significant differences by sex, weight, or duration of diabetes or other baseline factors, including ASCVD risk score.

Two other large, randomized trials of aspirin for primary prevention, in people without diabetes (ARRIVE [Aspirin to Reduce Risk of Initial Vascular Events]) (174) and in the elderly (ASPREE [Aspirin in Reducing Events in the Elderly]) (175), in

which 11% of participants had diabetes, found no benefit of aspirin on the primary efficacy end point and an increased risk of bleeding. In ARRIVE, with 12,546 individuals over a period of 60 months of follow-up, the primary end point occurred in 4.29% vs. 4.48% of individuals in the aspirin versus placebo groups (HR 0.96 [95% CI 0.81–1.13]; $P = 0.60$). Gastrointestinal bleeding events (characterized as mild) occurred in 0.97% of individuals in the aspirin group vs. 0.46% in the placebo group (HR 2.11 [95% CI 1.36–3.28]; $P = 0.0007$). In ASPREE, which included 19,114 individuals, for CVD (fatal CHD, MI, stroke, or hospitalization for heart failure) after a median of 4.7 years of follow-up, the rates per 1,000 person-years were 10.7 vs. 11.3 events in aspirin vs. placebo groups (HR 0.95 [95% CI 0.83–1.08]). The rate of major hemorrhage per 1,000 person-years was 8.6 events versus 6.2 events, respectively (HR 1.38 [95% CI 1.18–1.62]; $P < 0.001$).

Thus, aspirin appears to have a modest effect on ischemic vascular events, with the absolute decrease in events depending on the underlying ASCVD risk. The main adverse effect is an increased risk of gastrointestinal bleeding. The excess risk may be as high as 5 per 1,000 per year in real-world settings. However, for adults with ASCVD risk $>1\%$ per year, the number of ASCVD events prevented will be similar to the number of episodes of bleeding induced, although these complications do not have equal effects on long-term health (176).

Recommendations for using aspirin as primary prevention include both men and women aged ≥ 50 years with diabetes and at least one additional major risk factor (hypertension, dyslipidemia, smoking, obesity, or CKD) who are not at increased risk of bleeding (e.g., older age, anemia, or kidney disease) (177–180). Noninvasive imaging techniques such as coronary calcium scoring may help further tailor aspirin therapy, particularly in those at low risk (181,182). For people >70 years of age (with or without diabetes), the balance appears to have greater risk than benefit (173,175). Thus, for primary prevention, the use of aspirin needs to be carefully considered and generally may not be recommended. Aspirin may be considered in the context of high cardiovascular risk with low bleeding risk but generally not in older adults. Aspirin therapy for primary prevention may be considered in the context of shared

decision-making, which carefully weighs the cardiovascular benefits against the increase in risk of bleeding.

For people with documented ASCVD, use of aspirin for secondary prevention has far greater benefit than risk; for this indication, aspirin is still recommended (168).

Aspirin Use in People <50 Years of Age

Aspirin is not recommended for those at low risk of ASCVD (such as men and women aged <50 years with diabetes with no other major ASCVD risk factors), as the low benefit is likely to be outweighed by the risk of bleeding. Clinical judgment should be used for those at intermediate risk (younger individuals with one or more risk factors or older individuals with no risk factors) until further research is available. ASCVD risk factors include older age, hypertension, dyslipidemia, smoking, CKD, or obesity. Individuals' willingness to undergo long-term aspirin therapy should also be considered in shared decision-making (183). Aspirin use in individuals aged <21 years is generally contraindicated due to the associated risk of Reye syndrome.

Aspirin Dosing

Average daily dosages used in most clinical trials involving people with diabetes ranged from 50 to 650 mg but were mostly in the range of 100–325 mg/day. There is little evidence to support any specific dose, but using the lowest possible dose may help to reduce side effects (184). In the ADAPTABLE (Aspirin Dosing: A Patient-Centric Trial Assessing Benefits and Long-term Effectiveness) trial of individuals with established CVD, 38% of whom had diabetes, there were no significant differences in cardiovascular events or major bleeding between individuals assigned to 81 mg and those assigned to 325 mg aspirin daily (185). In the U.S., the most common low-dose tablet is 81 mg, and it appears that 75–162 mg/day is optimal.

Indications for P2Y₁₂ Receptor Antagonist Use

Combination dual antiplatelet therapy with aspirin and a P2Y₁₂ receptor antagonist is indicated after acute coronary syndromes and coronary revascularization with stenting (186). Evidence supports use of either ticagrelor or clopidogrel if no percutaneous coronary intervention was performed

and clopidogrel, ticagrelor, or prasugrel if a percutaneous coronary intervention was performed (187). In people with diabetes and prior MI (1–3 years before), adding ticagrelor to aspirin significantly reduces the risk of recurrent ischemic events, including cardiovascular and CHD death (188). Similarly, the addition of ticagrelor to aspirin reduced the risk of ischemic cardiovascular events compared with aspirin alone in people with diabetes and stable coronary artery disease (189,190). However, a higher incidence of major bleeding, including intracranial hemorrhage, was noted with dual antiplatelet therapy. The net clinical benefit (ischemic benefit vs. bleeding risk) was improved with ticagrelor therapy in the large prespecified subgroup of individuals with history of percutaneous coronary intervention, while no net benefit was seen in individuals without prior percutaneous coronary intervention (190). However, early aspirin discontinuation compared with continued dual antiplatelet therapy after coronary stenting may reduce the risk of bleeding without a corresponding increase in the risks of mortality and ischemic events, as shown in a prespecified analysis of people with diabetes enrolled in the TWILIGHT (Ticagrelor With Aspirin or Alone in High-Risk Patients After Coronary Intervention) trial and a meta-analysis (191,192).

Current guidelines recommend short-term dual antiplatelet therapy after high-risk transient ischemic attack and minor stroke (193). The indications for dual antiplatelet therapy and length of treatment are rapidly evolving and should be determined by an interprofessional team approach that includes a cardiovascular or neurological specialist, as appropriate.

Combination Antiplatelet and Anticoagulation Therapy

Combination therapy with aspirin plus low-dose rivaroxaban may be considered for people with stable coronary and/or PAD to prevent major adverse limb and cardiovascular complications. In the COMPASS (Cardiovascular Outcomes for People Using Anticoagulation Strategies) trial of 27,395 individuals with established coronary artery disease and/or PAD, aspirin plus rivaroxaban 2.5 mg twice daily was superior to aspirin plus placebo in the reduction of cardiovascular ischemic events, including major adverse limb events. The absolute benefits of combination therapy appeared larger in people with diabetes,

who comprised 10,341 of the trial participants (194,195). A similar treatment strategy was evaluated in the Vascular Outcomes Study of ASA (acetylsalicylic acid) Along with Rivaroxaban in Endovascular or Surgical Limb Revascularization for Peripheral Artery Disease (VOYAGER PAD) trial (196), in which 6,564 individuals with PAD who had undergone revascularization were randomly assigned to receive rivaroxaban 2.5 mg twice daily plus aspirin or placebo plus aspirin. Rivaroxaban treatment in this group of individuals was also associated with a significantly lower incidence of ischemic cardiovascular events, including major adverse limb events. However, an increased risk of major bleeding was noted with rivaroxaban added to aspirin treatment in both COMPASS and VOYAGER PAD.

The risks and benefits of dual antiplatelet or antiplatelet plus anticoagulant treatment strategies should be thoroughly discussed with eligible individuals, and shared decision-making should be used to determine an individually appropriate treatment approach. This field of cardiovascular risk reduction is evolving rapidly, as are the definitions of optimal care for individuals with differing types and circumstances of cardiovascular complications.

CARDIOVASCULAR DISEASE

Screening

Recommendations

10.37a In asymptomatic individuals, routine screening for coronary artery disease is not recommended, as it does not improve outcomes as long as ASCVD risk factors are treated. **A**

10.37b Consider investigations for coronary artery disease in the presence of any of the following: signs or symptoms of cardiac or associated vascular disease, including carotid bruits, transient ischemic attack, stroke, claudication, or PAD; or electrocardiographic abnormalities (e.g., pathological Q waves). **E**

10.38a Adults with diabetes are at increased risk for the development of asymptomatic cardiac structural or functional abnormalities (stage B heart failure) or symptomatic (stage C) heart failure. Consider screening adults with diabetes by measuring a natriuretic peptide (B-type natriuretic peptide [BNP] or N-terminal pro-BNP [NT-proBNP]) to facilitate prevention of stage C heart failure. **B**

10.38b In asymptomatic individuals with diabetes and abnormal natriuretic peptide levels, echocardiography is recommended to identify stage B heart failure. **A**

10.39 In asymptomatic individuals with diabetes and age ≥ 65 years, microvascular disease in any location, or foot complications or any end-organ damage from diabetes, screening for PAD with ankle-brachial index testing is recommended if a PAD diagnosis would change management. **B**

Treatment

Recommendations

10.40a Among people with type 2 diabetes who have established ASCVD or chronic kidney disease (CKD), a sodium–glucose cotransporter 2 (SGLT2) inhibitor or glucagon-like peptide 1 receptor agonist (GLP-1 RA) with demonstrated cardiovascular disease benefit is recommended as part of the comprehensive cardiovascular risk reduction and/or glucose-lowering treatment plans. **A**

10.40b In people with type 2 diabetes and established ASCVD or multiple ASCVD risk factors, or CKD, an SGLT2 inhibitor with demonstrated cardiovascular benefit is recommended to reduce the risk of cardiovascular events. **A**

10.40c In people with type 2 diabetes and established ASCVD or multiple risk factors for ASCVD, or CKD, a GLP-1 RA with demonstrated cardiovascular benefit is recommended to reduce the risk of cardiovascular events. **A**

10.40d In people with type 2 diabetes and established ASCVD or multiple risk factors for ASCVD, combined therapy with an SGLT2 inhibitor with demonstrated cardiovascular benefit and a GLP-1 RA with demonstrated cardiovascular benefit may be considered for additive reduction of the risk of adverse cardiovascular and kidney events. **B**

10.41a In people with type 2 diabetes and established heart failure with either preserved or reduced ejection fraction, an SGLT2 inhibitor (including SGLT1/2 inhibitor) with proven benefit in this population is recommended to reduce the risk of worsening heart failure and cardiovascular death. **A**

10.41b In people with type 2 diabetes and established heart failure with either preserved or reduced ejection fraction, an SGLT2 inhibitor with proven benefit in this population is recommended to improve quality of life. **A**

10.42 For individuals with type 2 diabetes and CKD with albuminuria treated with maximum tolerated doses of ACE inhibitor or ARB, recommend treatment with a nonsteroidal MRA with demonstrated benefit to improve cardiovascular outcomes and reduce the risk of CKD progression. **A**

10.43 In individuals with diabetes aged ≥ 55 years with established ASCVD or multiple ASCVD risk factors, ACE inhibitor or ARB therapy is recommended to reduce the risk of cardiovascular events. **A**

10.44a In individuals with diabetes and asymptomatic (stage B) heart failure, an interprofessional approach to optimize guideline-directed medical therapy, which should include a cardiovascular disease specialist, is recommended to reduce the risk for progression to symptomatic (stage C) heart failure. **A**

10.44b In individuals with diabetes and asymptomatic (stage B) heart failure, ACE inhibitors or ARBs and β -blockers are recommended to reduce the risk for progression to symptomatic (stage C) heart failure. **A**

10.44c In individuals with type 2 diabetes and asymptomatic (stage B) heart failure or with high risk of or established cardiovascular disease, treatment with an SGLT inhibitor with proven heart failure prevention benefit **A** or a GLP-1 RA with heart failure prevention benefit **B** is recommended to reduce the risk of hospitalization for heart failure.

10.44d In adults with type 2 diabetes, obesity, and symptomatic heart failure with preserved ejection fraction (HFpEF), the treatment plan should include a dual GIP/GLP-1 RA **A** or a GLP-1 RA **B** with demonstrated benefit for reduction in heart failure events.

10.44e In adults with type 2 diabetes, obesity, and symptomatic HFpEF, the treatment plan should include a dual GIP/GLP-1 RA or a GLP-1 RA with demonstrated benefit for reduction in heart failure symptoms. **A**

10.44f In individuals with type 2 diabetes and CKD, recommend treatment with a nonsteroidal MRA with demonstrated benefit to reduce the risk of hospitalization for heart failure. **A**

10.44g In individuals with diabetes, guideline-directed medical therapy for myocardial infarction and symptomatic stage C heart failure is recommended with ACE inhibitors or ARBs (including ARBs and neprilysin inhibitors), MRAs, β -blockers, and SGLT2 inhibitors. **A**

10.44h In individuals with diabetes and symptomatic stage C heart failure with ejection fraction $>40\%$, a nonsteroidal MRA with proven benefit in reducing worsening heart failure events is recommended. **A** A nonsteroidal MRA should not be used with an MRA.

10.45 In people with type 2 diabetes with stable heart failure, metformin may be continued for glucose lowering if eGFR remains >30 mL/min/1.73 m² but should be avoided in unstable or hospitalized individuals with heart failure. **B**

10.46 Educate individuals with diabetes who are at risk for developing diabetic ketoacidosis and who are treated with SGLT inhibition on the risks and signs of ketoacidosis and methods of risk mitigation management, provide them with appropriate tools for ketone measurement (i.e., serum β -hydroxybutyrate), and discourage a ketogenic eating pattern. **E**

Cardiac Testing

Candidates for advanced or invasive cardiac testing include those with 1) symptoms or signs of cardiac or vascular disease and 2) an abnormal resting electrocardiogram (ECG). Exercise ECG testing without or with echocardiography may be used as the initial test. In adults with diabetes ≥ 40 years of age, measurement of coronary artery calcium is also reasonable for cardiovascular risk assessment. Pharmacologic stress echocardiography or nuclear imaging should be considered in individuals with diabetes in whom resting ECG abnormalities preclude exercise stress testing (e.g., left bundle branch block or ST-T abnormalities). In addition, individuals who require stress testing and are unable to exercise should undergo

pharmacologic stress echocardiography or nuclear imaging.

Screening Asymptomatic Individuals for Atherosclerotic Cardiovascular Disease

The screening of asymptomatic individuals with high ASCVD risk is not recommended, in part because these high-risk people should already be receiving intensive medical therapy—an approach that provides benefits similar to those of invasive revascularization (197,198). A randomized trial demonstrated no clinical benefit of routine screening with adenosine-stress radionuclide myocardial perfusion imaging in asymptomatic people with type 2 diabetes and normal ECGs (199). Another randomized study showed that routine screening with coronary computed tomography angiography did not reduce the composite rate of all-cause mortality, nonfatal MI, or unstable angina in asymptomatic people with type 1 or type 2 diabetes (200). Studies have also found that a risk factor–based approach to the initial diagnostic evaluation and subsequent follow-up for coronary artery disease fails to identify which people with type 2 diabetes who will have silent ischemia on screening tests (201,202).

Any benefit of noninvasive coronary artery disease screening methods, such as computed tomography calcium scoring, to identify subgroups for different treatment strategies remains unproven in asymptomatic people with diabetes, though research is ongoing. Coronary calcium scoring in asymptomatic people with diabetes may help in risk stratification (203,204) and provide reasoning for treatment intensification and/or guiding informed individual decision-making and willingness for medication initiation and participation. However, their routine use leads to radiation exposure and may result in unnecessary invasive testing, such as coronary angiography and revascularization procedures. The ultimate balance of benefit, cost, and risk of such an approach in asymptomatic individuals remains controversial, particularly in the modern setting of aggressive ASCVD risk factor management.

Screening for Asymptomatic Heart Failure in People With Diabetes

People with diabetes are at an increased risk for developing heart failure, as shown in multiple longitudinal, observational studies

(205,206). This association is not only observed in people with type 2 diabetes but also evident in people with type 1 diabetes (205,206). In a large multinational cohort of 750,000 people with diabetes without established CVD, heart failure and CKD were the most frequent first manifestations of cardiovascular or kidney disease (207). For a detailed review of screening, diagnosis, and treatment recommendations of heart failure in people with diabetes, the reader is further referred to the ADA report “Heart Failure: An Underappreciated Complication of Diabetes. A Consensus Report of the American Diabetes Association” (16).

People with diabetes are at particularly high risk for progression from asymptomatic stage A and B to symptomatic stage C and D heart failure (208,209). Identification, risk stratification, and early treatment of risk factors in people with diabetes and asymptomatic stages of heart failure reduce the risk for progression to symptomatic heart failure (210,211). In people with type 2 diabetes, measurement of natriuretic peptides, including B-type natriuretic peptide (BNP) or N-terminal pro-BNP (NT-proBNP), identifies people at risk for heart failure development, progression of symptoms, and heart failure–related mortality (212–214). A similar association and prognostic values of increased NT-proBNP with increased cardiovascular and all-cause mortality has been reported in people with type 1 diabetes (215). Results from several randomized controlled trials revealed that more intensive treatment of risk factors in people with increased levels of natriuretic peptides reduces the risk for symptomatic heart failure, heart failure hospitalization, and newly diagnosed left ventricular dysfunction (211,216,217).

Consider screening asymptomatic adults with diabetes for the development of cardiac structural or functional abnormalities (stage B heart failure) by measuring BNP or NT-proBNP. The biomarker threshold for abnormal values is BNP level ≥ 50 pg/mL and NT-proBNP level ≥ 125 pg/mL. Use clinical judgement when evaluating abnormal levels of natriuretic peptide and consider possible competing diagnoses that may lead to increased levels of natriuretic peptide, such as renal insufficiency, pulmonary hypertension, chronic obstructive lung disease, obstructive sleep apnea, ischemic and hemorrhagic stroke, and anemia. Conversely, natriuretic peptide levels may be decreased in people

with obesity, which impairs sensitivity of testing.

In people with diabetes and an abnormal natriuretic peptide level, echocardiography is recommended as the next step to screen for structural heart disease and echocardiographic Doppler indices for evidence of diastolic dysfunction and increased filling pressures (218). At this stage, an interprofessional approach, which should include a CVD specialist, is recommended to implement a guideline-directed medical treatment strategy, which may reduce the risk of progression to symptomatic stages of heart failure (210). The recommendations for screening and treatment of heart failure in people with diabetes discussed in this section are consistent with the ADA consensus report on heart failure (16) and with current American Heart Association/American College of Cardiology/Heart Failure Society of America guidelines for the management of heart failure (219).

Screening for Asymptomatic Peripheral Artery Disease in People With Diabetes

The risk for PAD in people with diabetes is higher than that in people without diabetes (220–222). In the PAD Awareness, Risk, and Treatment: New Resources for Survival (PARTNERS) program, 30% of people aged 50–69 years with a history of cigarette smoking or diabetes, or aged ≥ 70 years regardless of risk factors, had PAD (223). Similarly, in other screening studies, 26% of people with diabetes have been shown to have PAD (224), and diabetes increased the odds of having PAD by 85% (225). Notably, classical symptoms of claudication are uncommon, and almost half of people with newly diagnosed PAD were asymptomatic (223). Many individuals with PAD remain asymptomatic either because they limit physical activity to avoid claudication symptoms or because a comorbid condition prevents them from reaching a threshold of activity to provoke symptoms. Risk factors associated with an increased risk for PAD in people with diabetes include age, smoking, hypertension, dyslipidemia, worse glycemic management, longer duration of diabetes, neuropathy, and retinopathy as well as a prior history of CVD (226,227). In addition, the presence of microvascular disease is associated with adverse outcomes in people with PAD, including an increased risk for future limb amputation (228,229). While

a positive screening test for PAD in an asymptomatic population has been associated with increased cardiovascular event rates (230,231), prospective, randomized studies addressing whether screening for PAD in people with diabetes improves long-term limb outcomes and cardiovascular event rates are limited. In the randomized controlled Viborg Vascular (VIVA) trial, 50,156 participants, of whom approximately 10% had diabetes, were randomized to combined vascular screening for abdominal aortic aneurysm, PAD, and hypertension or to no screening. Although the number needed to invite for screening to prevent one death was close to 170, vascular screening was associated with increased pharmacologic therapy (antiplatelet, lipid-lowering, and antihypertensive therapy), reduced in-hospital time for PAD and coronary artery disease, and reduced mortality (232). Therefore, screening is recommended for asymptomatic PAD using ankle-brachial index in people with diabetes in whom a diagnosis of PAD may help further intensify pharmacologic therapies and improve cardiovascular and limb outcomes, such as the intensification of LDL-lowering therapies (233), the initiation of low-dose rivaroxaban therapy (234), or the initiation of GLP-1 RA, as recent clinical trial evidence supports a symptomatic benefit of GLP-1 RA in people with diabetes and PAD (235). These people include those with age ≥ 65 years, diabetes with duration ≥ 10 years, microvascular disease, clinical evidence of foot complications, or any end-organ damage from diabetes.

Lifestyle and Pharmacologic Interventions

Intensive lifestyle intervention focusing on weight loss through decreased caloric intake and increased physical activity, as performed in the Look AHEAD (Action for Health in Diabetes) trial, may be considered for improving glucose management, fitness, and some ASCVD risk factors (236). Individuals at increased ASCVD risk should receive statin, ACE inhibitor, or ARB therapy if the individual has hypertension, and possibly aspirin, unless there are contraindications to a particular drug class.

Clear cardiovascular benefits exist for ACE inhibitor or ARB therapy in people with diabetes. The Heart Outcomes Prevention Evaluation (HOPE) study randomized 9,297 individuals aged ≥ 55 years with a history of vascular disease or

diabetes plus one other cardiovascular risk factor to either ramipril or placebo. Ramipril significantly reduced cardiovascular and all-cause mortality, MI, and stroke (237). ACE inhibitors or ARB therapy also have well-established long-term benefit in people with diabetes and CKD or hypertension, and these agents are recommended for hypertension management in people with known ASCVD (particularly coronary artery disease) (66,67,238). People with type 2 diabetes and CKD should be considered for treatment with finerenone to reduce cardiovascular outcomes and the risk of CKD progression (239–242). β -Blockers should be used in individuals with active angina or HFrEF and for 3 years after MI in those with preserved left ventricular function (243,244).

Glucose-Lowering Therapies and Cardiovascular Outcomes

In 2008, the U.S. Food and Drug Administration (FDA) issued guidance for industry to perform cardiovascular outcomes trials for all new medications for the treatment of type 2 diabetes amid concerns of increased cardiovascular risk (245). Diabetes medications approved prior to 2008 were not subject to the guidance. This guidance was revised in May 2023 (246).

SGLT2 Inhibitors

Results of large cardiovascular outcome trials of empagliflozin (10 mg or 25 mg daily) and canagliflozin (100 or 300 mg daily) showed that treatment with either drug reduced rates of MI, stroke, or cardiovascular death. While there was an increased risk of lower-limb amputation with canagliflozin in one trial (247), no significant increase in lower-limb amputations, fractures, AKI, or hyperkalemia was seen in other trials of canagliflozin (248). The major cardiovascular outcome trial of dapagliflozin (10 mg daily) did not show a reduction in the coprimary outcome of MI, stroke, or cardiovascular death but did show a significantly lower rate of the coprimary composite outcome of hospitalization for heart failure or cardiovascular death, which was driven by its effect on hospitalization for heart failure. Cardiovascular outcome trials of ertugliflozin and bexagliflozin have not demonstrated evidence of cardiovascular risk reduction (249,250).

GLP-1 Receptor Agonists

Results of trials with the GLP-1 RAs liraglutide (once daily) and semaglutide,

albiglutide, efpeglenatide, and dulaglutide (once weekly) have all shown evidence of a reduction in major atherosclerotic cardiovascular outcomes (MI, stroke, or cardiovascular death) (251–256). An oral formulation of semaglutide has also demonstrated cardiovascular benefit (257–259). Lixisenatide and extended-release exenatide were not superior to placebo with respect to the primary end point of cardiovascular outcomes (260) and therefore are not recommended for CVD risk reduction.

In summary, the numerous large randomized controlled trials report statistically significant reductions in cardiovascular events for three of the FDA-approved SGLT2 inhibitors (empagliflozin, canagliflozin, and dapagliflozin) and four FDA-approved GLP-1 RAs (liraglutide, albiglutide [although that agent was removed from the market for business reasons], semaglutide [subcutaneous and oral formulations], and dulaglutide). Cardiovascular outcome trials of the dual glucose-dependent insulinotropic polypeptide (GIP)/GLP-1 RA tirzepatide are ongoing (261).

Meta-analyses of the trials reported to date suggest that GLP-1 RAs and SGLT2 inhibitors reduce risk of atherosclerotic major adverse cardiovascular events to a comparable degree in people with type 2 diabetes and established ASCVD (262,263). SGLT2 inhibitors and GLP-1RA also reduce risk of heart failure hospitalization and progression of kidney disease in people with established ASCVD, multiple risk factors for ASCVD, or albuminuric kidney disease (264,265). In people with type 2 diabetes and established ASCVD, multiple ASCVD risk factors, or CKD, an SGLT2 inhibitor with demonstrated cardiovascular benefit or a GLP-1 RA with demonstrated cardiovascular benefit or both is recommended to reduce the risk of major adverse cardiovascular events and/or heart failure hospitalization. Emerging data suggest that use of both classes of drugs will provide an additive cardiovascular and kidney outcomes benefit; thus, combination therapy with an SGLT2 inhibitor and a GLP-1 RA may be considered to provide the complementary outcomes benefits associated with these classes of medication (254), which are largely independent of glycemic management. The efficacy and safety of SGLT2 inhibitors for reduction of cardiovascular and kidney events in people with type 1 diabetes is being investigated and is not currently recommended due to a significant increase of

diabetic ketoacidosis and euglycemic ketoacidosis (266).

Other Classes

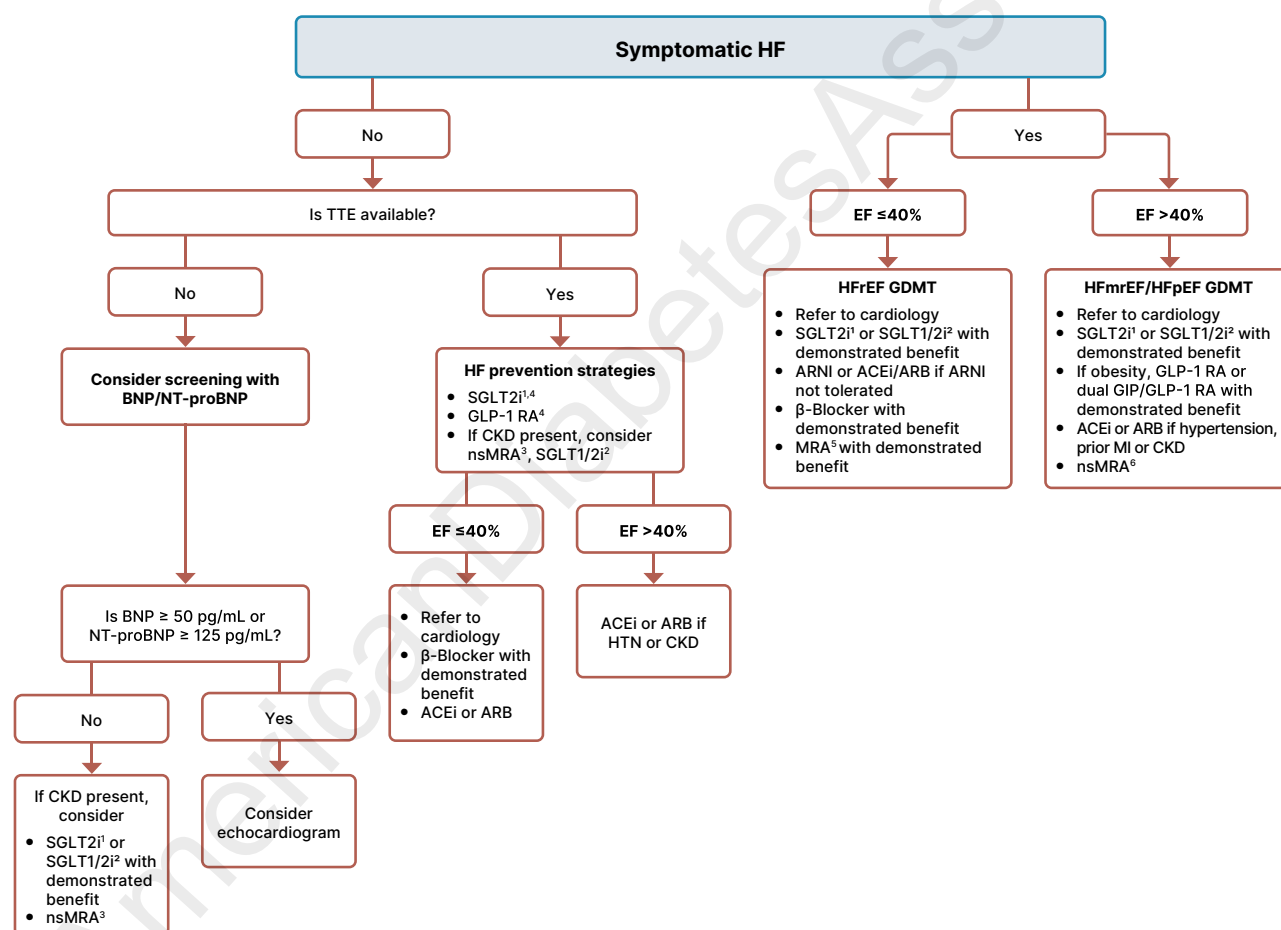
Cardiovascular outcomes trials of dipeptidyl peptidase 4 (DPP-4) inhibitors have not shown cardiovascular benefits relative to placebo. The CAROLINA (Cardiovascular Outcome Study of Linagliptin Versus Glimepiride in Type 2 Diabetes) study demonstrated noninferiority between a DPP-4 inhibitor, linagliptin, and a sulfonylurea, glimepiride, on cardiovascular outcomes despite lower rates of hypoglycemia in the linagliptin treatment group (267).

Prevention and Treatment of Heart Failure

Prevention of Symptomatic Heart Failure

ACE Inhibitors or ARBs and β -Blockers. Early primary prevention strategies and treatment of associated risk factors reduce incident, symptomatic heart failure and should include lifestyle intervention with nutrition, physical activity, weight management, and smoking cessation (268–271) (Fig. 10.5). The vast majority of incident heart failure is preceded by hypertension; up to 91% of all new heart failure development in the Framingham cohort occurred in people with a previous diagnosis of

hypertension (272). Therefore, management of hypertension constitutes a key goal in people with diabetes and stage A or B heart failure. For example, in the UK Prospective Diabetes Study (UKPDS) trial, intensive blood pressure management in people with type 2 diabetes reduced the risk for heart failure by 56% (273). Intensive treatment of hypertension in people with diabetes in the BROAD trial led to a 34% reduction in treatment or hospitalization for heart failure (HR 0.66, 95% CI 0.41–1.04), a finding that parallels observations from the SPRINT trial where the risk for development of incident heart



1. SGLT2i parameters: if eGFR ≥ 20 mL/min/1.73 m²

2. SGLT1/2i can be used as an alternative to SGLT2i if eGFR ≥ 30 mL/min/1.73 m²

3. If UACR ≥ 30 mg/g, K+ < 5.0 mEq/L (< 5.0 mmol/L)

4. The absolute benefit of SGLT2i and GLP-1RA in preventing symptomatic HF will be greatest among those at the highest absolute risk.

5. If eGFR ≥ 30 mL/min/1.73 m², K+ < 5.0 mEq/L (< 5.0 mmol/L)

6. If eGFR ≥ 25 mL/min/1.73 m², K+ < 5.0 mEq/L (< 5.0 mmol/L)

Figure 10.5—Overview of recommendations for the prevention and treatment of symptomatic heart failure in people with diabetes. ACEi, ACE inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor; BNP, B-type natriuretic peptide; NT-proBNP, N-terminal pro-B-type natriuretic peptide; CKD, chronic kidney disease; CVD, cardiovascular disease; EF, ejection fraction; eGFR, estimated glomerular filtration rate; GDMT, guideline-directed medical therapy; GIP/GLP-1 RA, glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 receptor agonist; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HF, heart failure; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFReEF, heart failure with reduced ejection fraction; HTN, hypertension; MI, myocardial infarction; MRA, mineralocorticoid receptor antagonist; nsMRA, nonsteroidal mineralocorticoid receptor antagonist; SGLT1/2i, sodium–glucose cotransporter 1 and 2 inhibitor; SGLT2i, sodium–glucose cotransporter 2 inhibitor; TTE, transthoracic echocardiography; UACR, urine albumin-to-creatinine ratio.

failure decreased by 36% (42,274). As discussed in the HYPERTENSION AND BLOOD PRESSURE MANAGEMENT section above, use of ACE inhibitors or ARBs is the preferred treatment strategy for management of hypertension in people with diabetes, particularly in the presence of albuminuria or coronary artery disease. People with diabetes and stage B heart failure who remain asymptomatic but have evidence of structural heart disease, including history of MI, acute coronary syndrome, or left ventricular ejection fraction (LVEF) $\leq 40\%$, should be treated with ACE inhibitors or ARBs plus β -blockers according to current treatment guidelines (219). In the landmark Studies of Left Ventricular Dysfunction (SOLVD) study, in which 15% of people had diabetes, treatment with enalapril reduced incident heart failure in people with asymptomatic left ventricular dysfunction by 20% (275). In the Survival and Ventricular Enlargement (SAVE) study, which enrolled asymptomatic people with reduced LVEF after MI, including 23% people with diabetes, treatment with captopril reduced the development of heart failure by 37% (276). Subsequent retrospective analyses from both trials revealed that concomitant use of β -blockers was associated with decreased risk of progression to symptomatic heart failure (277,278). The Carvedilol Post-Infarct Survival Control in Left Ventricular Dysfunction (CAPRICORN) study randomized people with a history of MI and reduced LVEF to treatment with carvedilol (279). Approximately half of the study participants were asymptomatic, and 23% of study participants had a history of diabetes. Treatment with carvedilol reduced mortality by 23%, and there was a 14% risk reduction for heart failure hospitalization. Finally, in the Reversal of Ventricular Remodeling With Toprol-XL (REVERT) trial, in which 45% of the people enrolled had diabetes, metoprolol improved adverse cardiac remodeling in asymptomatic individuals with an LVEF $< 40\%$ and mild left ventricular dilatation (280).

SGLT Inhibitors. SGLT2 inhibitors constitute a key treatment approach to reduce ASCVD and heart failure outcomes in people with diabetes. People with type 2 diabetes and increased cardiovascular risk or established CVD should be treated with an SGLT2 inhibitor to prevent the development of incident heart failure. In the EMPA-REG OUTCOME trial, only 10%

of study participants had a prior history of heart failure, and treatment with empagliflozin reduced the relative risk for hospitalization from heart failure by 35% (281). In the CANVAS Program, hospitalization from heart failure was reduced by 33% in people allocated to canagliflozin, and only 14% of individuals enrolled had a prior history of heart failure (247). In the DECLARE-TIMI 58 study, only 10% of study participants had a prior history of heart failure, and dapagliflozin reduced cardiovascular mortality and hospitalization for heart failure by 17%, which was consistent across multiple study subgroups regardless of a prior history of heart failure (282). Finally, in the Effect of Sotagliflozin on Cardiovascular and Renal Events in Participants With Type 2 Diabetes and Moderate Renal Impairment Who Are at Cardiovascular Risk (SCORED) trial, randomization to the SGLT1/2 inhibitor sotagliflozin reduced the primary outcome of death from cardiovascular causes, hospitalizations for heart failure, and urgent visits for heart failure in people with type 2 diabetes, CKD, and risk for CVD (283). Therefore, SGLT inhibitor treatment is recommended in asymptomatic people with type 2 diabetes at risk or with established CVD to prevent incident heart failure and hospitalization from heart failure.

GLP-1 Receptor Agonists. A recently published meta-analysis of GLP-1 RA registration trials, including those for the commonly used medications dulaglutide, liraglutide, and semaglutide (both subcutaneous and oral), demonstrated a 14% relative reduction in the risk of hospitalization for heart failure (HR 0.86, 95% CI 0.79–0.93) (255). The trials included in these meta-analyses included people with type 2 diabetes and established ASCVD or at high risk for ASCVD but were not designed as trials of individuals with established heart failure. In addition, heart failure was a prespecified outcome of the randomized, placebo-controlled trial of semaglutide in people with type 2 diabetes and CKD and found a significant reduction in the risk of heart failure among those randomized to active semaglutide (284). Thus, there is sufficient evidence to recommend the use of GLP-1 RAs to prevent the development of heart failure in individuals with type 2 diabetes and risk factors for ASCVD. Individuals at even higher risk of heart failure, such as those with established ASCVD or

CKD, are likely to see a larger absolute risk reduction than healthier individuals at relatively lower cardiovascular and kidney risk.

Finerenone. Finerenone is a nonsteroidal MRA and has recently been studied in people with diabetes and CKD, including the Finerenone in Reducing Kidney Failure and Disease Progression in Diabetic Kidney Disease (FIDELIO-DKD) and the Efficacy and Safety of Finerenone in Subjects With Type 2 Diabetes Mellitus and the Clinical Diagnosis of Diabetic Kidney Disease (FIGARO-DKD) studies. In FIDELIO-DKD, finerenone was compared with placebo for the primary outcome of kidney failure, a sustained decrease of at least 40% in the eGFR from baseline, or death from renal causes in people with type 2 diabetes and CKD (285). A prespecified secondary outcome was death from cardiovascular causes, nonfatal MI, nonfatal stroke, or hospitalization for heart failure, which was reduced by 13% in the finerenone group. The incidence of heart failure hospitalization occurred less in the finerenone-treated group, and only 7.7% of study participants had a prior history of heart failure. In the FIGARO-DKD trial, finerenone reduced the primary outcome of death from cardiovascular causes, nonfatal MI, nonfatal stroke, or hospitalization for heart failure (HR 0.87 [95% CI 0.76–0.98]; $P = 0.03$) in people with type 2 diabetes and CKD (240). Only 7.8% of all participants had a prior history of heart failure, and the incidence of hospitalization for heart failure was reduced in the finerenone-allocated treatment arm (HR 0.71 [95% CI 0.56–0.90]). Owing to these observations, treatment with finerenone is recommended in people with type 2 diabetes and CKD to reduce the risk of progression from stage A heart failure to symptomatic incident heart failure.

Treatment of Symptomatic Heart Failure

In general, current guideline-directed medical therapy for a history of MI and symptomatic stage C and D heart failure in people with diabetes is similar to that for people without diabetes. At these symptomatic stages of heart failure, a collaborative approach with a cardiovascular specialist is recommended. The treatment recommendations are detailed in current 2022 American Heart Association/American College of Cardiology/Heart Failure

Society of America guidelines for the management of heart failure (12,13).

SGLT Inhibitors

The SGLT2 inhibitors empagliflozin, canagliflozin, and dapagliflozin reduce the incidence of heart failure and improve heart failure–related outcomes, including hospitalization for heart failure and heart failure–related symptoms, in people with diabetes with preserved or reduced ejection fraction (242,247,248,281,286–294). The results of these clinical trials have been extensively outlined in the 2024 ADA “Standards of Care in Diabetes” (295). These results led to trials of empagliflozin and dapagliflozin in individuals with symptomatic heart failure (both HFpEF and HFrEF), often in populations with and without diabetes.

The DAPA-HF trial specifically evaluated the effects of dapagliflozin 10 mg daily on the primary outcome of a composite of worsening heart failure or cardiovascular death in individuals with New York Heart Association (NYHA) class II, III, or IV heart failure and an ejection fraction of 40% or less (287). Dapagliflozin treatment had a lower risk of the primary outcome (HR 0.74 [95% CI 0.65–0.85]), lower risk of first worsening heart failure event (HR 0.70 [95% CI 0.59–0.83]), and lower risk of cardiovascular death (HR 0.82 [95% CI 0.69–0.98]) compared with placebo. The effect of dapagliflozin on the primary outcome was consistent regardless of the presence or absence of type 2 diabetes (287). Similar results were obtained in clinical trials with empagliflozin (291). In Empagliflozin Outcome Trial in Patients With Chronic Heart Failure With Preserved Ejection Fraction (EMPEROR-Preserved), the primary outcome of cardiovascular death or hospitalization for heart failure was reduced in adults with NYHA functional class I–IV and chronic HFpEF (LVEF >40%), extending the previously seen benefit in people with heart failure to those with preserved ejection fraction irrespective of the presence of type 2 diabetes (242). A similar benefit for heart failure outcomes was seen in the Dapagliflozin Evaluation to Improve the Lives of Patients with Preserved Ejection Fraction Heart Failure (DELIVER) trial for dapagliflozin in people with mildly reduced or preserved ejection fraction (290). In the Effect of Sotagliflozin on Cardiovascular Events in Patients With Type 2 Diabetes Post Worsening Heart Failure

(SOLOIST-WHF) trial, sotagliflozin, a combined SGLT1/2 inhibitor, initiated during or shortly after hospitalization for heart failure in people with diabetes, also reduced the risk for the primary end point of deaths from cardiovascular causes and hospitalizations and urgent visits for heart failure (296). A large meta-analysis (297) including the EMPEROR-Reduced, EMPEROR-Preserved, DAPA-HF, DELIVER, and SOLOIST-WHF trials included 21,947 individuals and demonstrated reduced risk for the composite of cardiovascular death or hospitalization for heart failure, cardiovascular death, first hospitalization for heart failure, and all-cause mortality. The findings on the studied end points were consistent in both trials of heart failure with mildly reduced or preserved ejection fraction and in all five trials combined. In addition to the hospitalization and mortality benefit in people with heart failure, SGLT2 inhibitors improve clinical stability and functional status in individuals with heart failure (289,292–294). Collectively, these studies indicate that SGLT2 inhibitors reduce the risk for heart failure hospitalization and cardiovascular death in a wide range of people with heart failure independently of glucose-lowering activity. Therefore, in people with type 2 diabetes and established HFpEF or HFrEF, an SGLT2 inhibitor with proven benefit in this population is recommended to reduce the risk of worsening heart failure and cardiovascular death. In addition, an SGLT2 inhibitor is recommended in this population to improve symptoms, physical limitations, and quality of life.

One concern with expanded use of SGLT inhibition is the infrequent but serious risk of diabetic ketoacidosis, including the atypical presentation of euglycemic ketoacidosis. While multiple pathways have been proposed to explain the propensity to excess ketone body production with SGLT2 inhibitors (e.g., increases in glucagon levels), generally the occurrence of other risk factors or situations is needed to precipitate the onset of diabetic ketoacidosis or euglycemic ketoacidosis, including, but not limited to, a systemic illness, insulin pump malfunctions, significant reduction in insulin doses, and prolonged periods of fasting or carbohydrate restriction. Although there were low rates of ketoacidosis in the cardiovascular and heart failure outcomes trials evaluating SGLT inhibition, these studies excluded individuals with type 1 diabetes and/or recent

history of diabetic ketoacidosis (296,298). To decrease the risk of ketoacidosis when using SGLT inhibition in people with diabetes, it is recommended that clinicians assess the underlying susceptibility; provide education regarding the risks, symptoms, and prevention strategies; and prescribe home monitoring supplies for β -hydroxybutyrate (299,300). Assessment of susceptibility, education, and provision of monitoring supplies should reoccur throughout the duration of SGLT inhibitor treatment as core preventative strategies to minimize the risk of ketoacidosis (301,302).

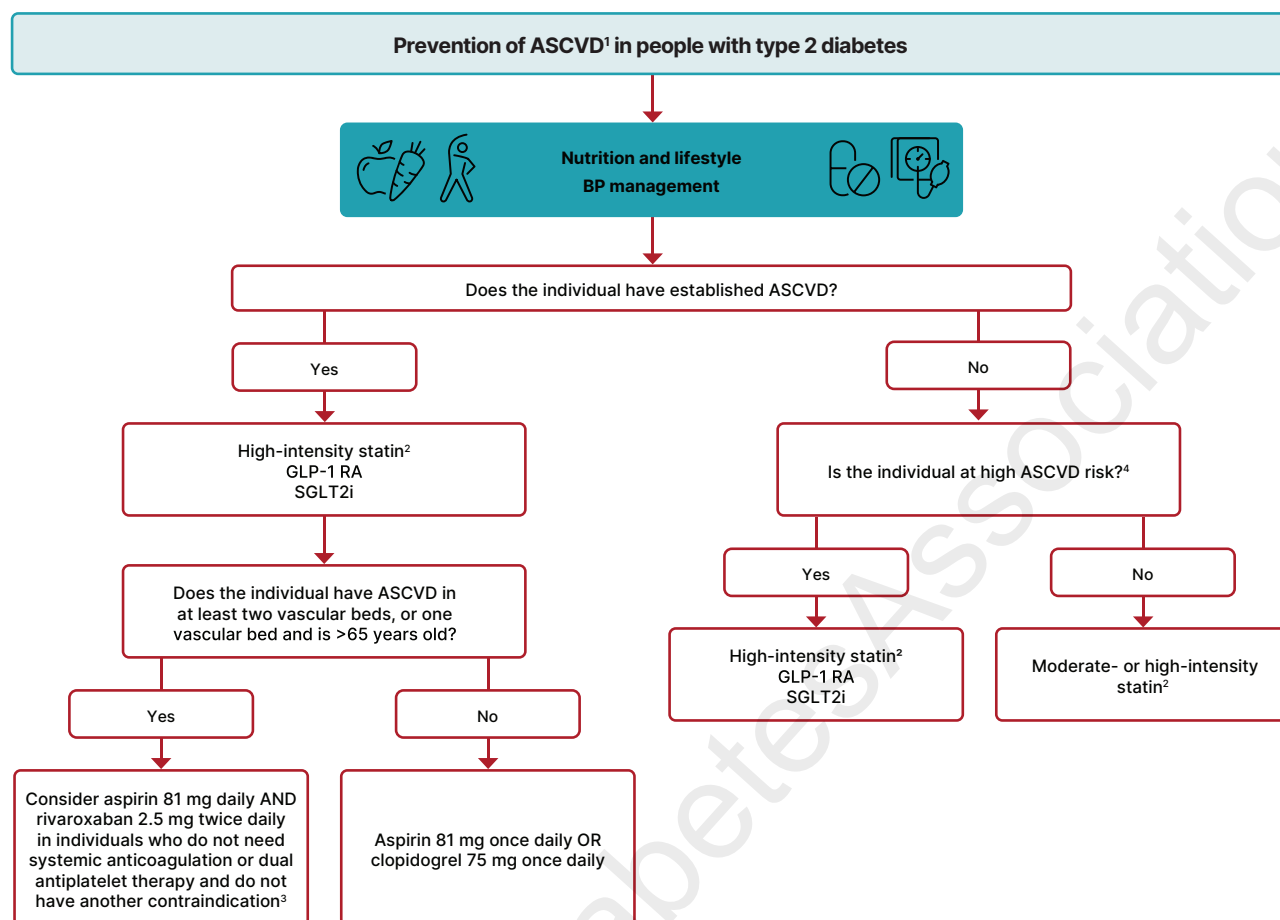
Mineralocorticoid Receptor Antagonists

Consistent with heart failure guidelines, an MRA like spironolactone or eplerenone is recommended in people with HFpEF (ejection fraction $\leq 40\%$) and type 2 diabetes (12,13).

The selective nonsteroidal MRA finerenone was examined in the Study to Evaluate the Efficacy (Effect on Disease) and Safety of Finerenone in Participants With Heart Failure and Left Ventricular Ejection Fraction (Proportion of Blood Expelled Per Heart Stroke) Greater or Equal to 40% (FINEARTS-HF) trial of people with symptomatic HFpEF (ejection fraction $\geq 40\%$) and was found to reduce the risk of total number of worsening heart failure events or cardiovascular death by 16% (rate ratio 0.84, 95% CI 0.74–0.95) (303). Of the enrolled participants, 41% had type 2 diabetes. Thus, finerenone improves cardiovascular and kidney outcomes in people with type 2 diabetes. Addition of finerenone can be considered to improve heart failure outcomes in individuals with symptomatic HFpEF. In people with type 2 diabetes and CKD with albuminuria treated with maximum tolerated doses of ACE inhibitor or ARB, the addition of finerenone should be considered to improve cardiovascular outcomes, including the risk for heart failure hospitalization, and to reduce the risk of CKD progression.

GLP-1 RA and Dual GIP/GLP-1 RA

Increasing evidence has demonstrated the benefits of GLP-1 RA or dual GIP/GLP-1 RA on symptoms and outcomes for people with HFpEF and obesity, and while most people with HFpEF have obesity, approximately 45% have diabetes (304,305). The Semaglutide Treatment Effect in People with Obesity and HFpEF and Diabetes Mellitus (STEP-HFpEF DM) trial evaluated whether the GLP-1 RA semaglutide



1. ASCVD is defined as a history of an acute coronary syndrome or myocardial infarction, angina, coronary heart disease with or without revascularization, other arterial revascularization, stroke, or peripheral artery disease assumed to be atherosclerotic in origin.

2. Non-statin with demonstrated benefit should be considered in those with statin intolerance.

3. Consider low-dose rivaroxaban in people with atherosclerotic disease in at least two vascular beds, or in one bed and are older than 65 years, who do NOT have an increased risk of bleeding, recent (<1 year) stroke, renal failure, LVEF <30%, or need for dual antiplatelet therapy or systemic anticoagulation.

4. Individuals at high risk for ASCVD include those with end-organ damage such as left ventricular hypertrophy or retinopathy or with multiple CV risk factors (e.g., older age, hypertension, smoking, dyslipidemia, CKD, and obesity).

Figure 10.6—Approach to prevent ASCVD in people with type 2 diabetes. ASCVD, atherosclerotic cardiovascular disease; BP, blood pressure; CKD, chronic kidney disease; CV, cardiovascular; GLP-1 RA, glucagon-like peptide 1 receptor agonist; LVEF, left ventricle ejection fraction; SGLT2i, sodium–glucose cotransporter 2 inhibitor.

improves symptoms related to heart failure in people with type 2 diabetes (306). In the study, 616 people with type 2 diabetes and a BMI of 30 or greater with HFpEF were assigned to receive once-weekly semaglutide at a dose of 2.4 mg or placebo. The primary end point was the change in the Kansas City Cardiomyopathy Questionnaire clinical summary score (KCCQ-CSS) (range from 0 to 100) and the change in weight. After 1 year of treatment, the mean change in the score was 13.7 points with semaglutide and 6.4 points with placebo, and the mean body weight was reduced by 9.8% in the group assigned to semaglutide compared with 3.4% with placebo. In addition, in the confirmatory secondary end point, semaglutide treatment improved 6-min walk distance. SUMMIT [A Study of Tirzepatide

(LY3298176) in Participants With Heart Failure With Preserved Ejection Fraction (HFpEF) and Obesity] was a randomized, double-blind, placebo-controlled trial of tirzepatide, a dual GIP and GLP-1 RA, in individuals with established HFpEF and obesity (48% with diabetes). The coprimary outcomes were death from cardiovascular causes or a worsening heart failure event and a change in the KCCQ-CSS. Worsening heart failure or cardiovascular death was less frequent in individuals receiving tirzepatide (9.9% of individuals) versus placebo (15.3% of individuals; HR 0.62, 95% CI 0.41–0.95). In addition, the mean KCCQ-CSS improved significantly more in those on active tirzepatide (19.5) than in the placebo group (12.7) (307). Because of the results of these trials, treatment with a GLP-1 RA or GIP/GLP-1 RA for a reduction in heart

failure events and heart failure symptoms in people with symptoms of heart failure is recommended.

Other Glucose-Lowering Therapies in Heart Failure

Thiazolidinediones have a strong and consistent relationship with increased risk of heart failure (308,309) and should be avoided in people with heart failure. Metformin may be used for the management of hyperglycemia in people with stable heart failure as long as kidney function remains within the recommended range for use (310). DPP-4 inhibitors are generally considered safe to use in heart failure, though in The Saxagliptin Assessment of Vascular Outcomes Recorded in Patients with Diabetes Mellitus–Thrombolysis in Myocardial Infarction 53 (SAVOR-TIMI 53)

study, participants randomized to saxagliptin were more likely to be hospitalized for heart failure than those given placebo (311). However, three other cardiovascular outcomes trials—Examination of Cardiovascular Outcomes with Alogliptin versus Standard of Care (EXAMINE) (312), Trial Evaluating Cardiovascular Outcomes with Sitagliptin (TECOS) (313), and the Cardiovascular and Renal Microvascular Outcome Study With Linagliptin (CARMELINA) (314)—did not find a significant increase in risk of heart failure hospitalization with DPP-4 inhibitor use compared with placebo.

Clinical Approach

As has been carefully outlined in **Fig. 9.4** in section 9, “Pharmacologic Approaches to Glycemic Treatment,” people with type 2 diabetes with or at high risk for ASCVD, heart failure, or CKD should be treated with a cardioprotective SGLT inhibitor and/or GLP-1 RA as part of the comprehensive approach to cardiovascular and kidney risk reduction. Importantly, these agents should be included in the plan of care irrespective of the need for additional glucose lowering and irrespective of metformin use. **Figure 10.6** outlines the approach to risk reduction with SGLT2 inhibitor and GLP-1 RA therapy in conjunction with other traditional, guideline-based preventive medical therapies for blood pressure, lipids, and glycemia and antiplatelet therapy.

Adoption of these agents should be reasonably straightforward in people with type 2 diabetes and established cardiovascular or kidney disease. Incorporation of SGLT2 inhibitor or GLP-1 RA therapy in the care of individuals with diabetes may need to replace some or all of their existing medications to minimize risks of hypoglycemia and adverse side effects and potentially to minimize medication costs. Close collaboration between primary and specialty care professionals and other members of the health care team (advanced practice professionals, pharmacists, nutritionists, and others) can help facilitate these transitions in clinical care and, in turn, improve outcomes for people with type 2 diabetes who are at high risk for ASCVD, heart failure, or CKD.

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11. Chronic Kidney Disease and Risk Management: Standards of Care in Diabetes—2026

American Diabetes Association
Professional Practice Committee for
Diabetes*

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The American Diabetes Association (ADA) “Standards of Care in Diabetes” includes the ADA’s current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. Members of the ADA Professional Practice Committee for Diabetes, an interprofessional expert committee, are responsible for updating the Standards of Care annually, or more frequently as warranted. For a detailed description of ADA standards, statements, and reports, as well as the evidence-grading system for ADA’s clinical practice recommendations and a full list of Professional Practice Committee members, please refer to Introduction and Methodology. Readers who wish to comment on the Standards of Care are invited to do so at professional.diabetes.org/SOC.

For prevention and management of diabetes complications in children and adolescents, please refer to section 14, “Children and Adolescents.”

EPIDEMIOLOGY OF DIABETES AND CHRONIC KIDNEY DISEASE

Chronic kidney disease (CKD) is diagnosed by the persistent elevation of urinary albumin excretion (albuminuria), estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m², or other manifestations of kidney damage (1). In this section, the focus is on CKD attributed to diabetes in adults, which occurs in 20–40% of people with diabetes (1–4). CKD in people with diabetes typically develops after a duration of 10 years in type 1 diabetes (the most common presentation is 5–15 years after the diagnosis of type 1 diabetes) but may be present at diagnosis of type 2 diabetes. CKD can progress to kidney failure requiring dialysis or kidney transplantation and is the leading cause of kidney failure in the U.S. (5). In addition, among people with type 1 or type 2 diabetes, the presence of CKD markedly increases cardiovascular risk and health care costs (6). The incidence of CKD in people with diabetes has decreased over the last decade but remains high in the U.S. (3) and around the world (7). For details on the management of CKD in children and adolescents with diabetes, please see section 14, “Children and Adolescents.”

ASSESSMENT OF ALBUMINURIA AND ESTIMATED GLOMERULAR FILTRATION RATE

Recommendations

11.1a Assess kidney function with random urine albumin-to-creatinine ratio (UACR) and estimated glomerular filtration rate (eGFR) at least annually in people with type 1 diabetes with duration of ≥ 5 years and in all people with type 2 diabetes regardless of treatment. **B**

11.1b In people with chronic kidney disease (CKD), monitor urinary albumin (e.g., spot UACR) and eGFR 1–4 times per year depending on the stage of kidney disease (**Fig. 11.1**). **B**

*A complete list of members of the American Diabetes Association Professional Practice Committee for Diabetes can be found at <https://doi.org/10.2337/dc26-SINT>.

This section has received endorsement from the National Kidney Foundation.

Duality of interest information for each contributor is available at <https://doi.org/10.2337/dc26-SDIS>.

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CKD is classified based on:				Albuminuria categories		
				Description and range		
				A1	A2	A3
				Normal to mildly increased <30 mg/g <3 mg/mmol	Moderately increased 30-299 mg/g 3-29 mg/mmol	Severely increased ≥300 mg/g ≥30 mg/mmol
GFR categories (mL/min/1.73 m ²) Description and range	G1	Normal or high	≥90	Screen 1	Treat 1	Treat and refer 2
	G2	Mildly decreased	60-89	Screen 1	Treat 1	Treat and refer 2
	G3a	Mildly to moderately decreased	45-59	Treat 1	Treat 2	Treat and refer 3
	G3b	Moderately to severely decreased	30-44	Treat 2	Treat and refer 3	Treat and refer 3
	G4	Severely decreased	15-29	Treat and refer 3	Treat and refer 3	Treat and refer 4+
	G5	Kidney failure	<15	Treat and refer 4+	Treat and refer 4+	Treat and refer 4+

■ Low risk (if no other markers of kidney disease, no CKD) ■ High risk
■ Moderately increased risk ■ Very high risk

Figure 11.1—Risk of CKD progression, cardiovascular disease risk, and mortality; frequency of visits; and referral to nephrology according to GFR and albuminuria. The numbers in the boxes are a guide to the frequency of screening or monitoring (number of times per year). Green reflects no evidence of CKD by estimated GFR or albuminuria, with screening indicated once per year. For monitoring of prevalent CKD, suggested monitoring varies from once per year (yellow) to four times or more per year (i.e., every 1–3 months [deep red]) according to risks of CKD progression and CKD complications (e.g., cardiovascular disease, anemia, and hyperparathyroidism). These are general parameters based only on expert opinion and underlying comorbid conditions, and disease state must be taken into account, as should the likelihood of impacting a change in management for any individual. CKD, chronic kidney disease; GFR, glomerular filtration rate. Adapted from de Boer et al. (1).

Screening for albuminuria can be most easily performed by urine albumin-to-creatinine ratio (UACR) in a random spot urine collection (1). Timed or 24-h collections are more burdensome, and in many clinical scenarios it is preferable to measure UACR. Measurement of a spot urine sample for albumin alone (whether by immunoassay or by using a sensitive dipstick test specific for albuminuria) without simultaneously measuring urine creatinine is less expensive but susceptible to false-negative and false-positive determinations as a result of variation in urine concentration due to hydration (8). Thus, semiquantitative or qualitative (dipstick) screening will need to be confirmed by UACR values in an accredited laboratory (9,10). Hence, it is better to simply collect a spot urine sample for UACR because it will ultimately need to be done.

Normal to mildly increased level of urine albumin excretion is defined as <30 mg/g creatinine, moderately elevated albuminuria is defined as ≥30 to

<300 mg/g creatinine, and severely elevated albuminuria is defined as ≥300 mg/g creatinine. However, UACR is a continuous measurement, and differences within the normal and abnormal ranges are associated with kidney and cardiovascular outcomes (6,11,12). Furthermore, because of high biological variability of >20% between measurements in urinary albumin excretion, two of three specimens of UACR collected within a 3- to 6-month period should be abnormal before considering an individual to have moderately or severely elevated albuminuria (1,13,14). Exercise within 24 h, infection, fever, heart failure, marked hyperglycemia, menstruation, and marked hypertension may elevate UACR independently of kidney damage (15). A recent analysis showed variability in the measurement of UACR when measured weekly over a 1-month period. Thus, repeated measurements and tracking of trending over time are needed to properly follow changes in UACR (13).

Traditionally, eGFR is calculated from serum creatinine in steady state using a validated formula. eGFR is routinely reported by laboratories along with serum creatinine, and eGFR calculators are available online at www.kidney.org/professionals/gfr_calculator. The 2021 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation should be used to estimate GFR for everyone (16,17). An eGFR persistently <60 mL/min/1.73 m² and/or a urinary albumin value of >30 mg/g creatinine is considered abnormal, though optimal thresholds for clinical diagnosis are debated in older adults over the age of 70 years (1,18). Cystatin C, a low-molecular-weight protein produced by all nucleated cells, can be used to calculate the eGFR particularly in individuals with alterations in the generation of creatinine such as amputation, frailty, low muscle mass, and liver disease. However, cystatin C may also be confounded by non-kidney function factors such as inflammation, age, sex, body size, thyroid function, and

diabetes. The combination of both filtration markers (creatinine and cystatin C) is more accurate and would support better clinical decisions than either marker alone (16,19).

DIAGNOSIS OF CHRONIC KIDNEY DISEASE IN PEOPLE WITH DIABETES

CKD in people with diabetes is usually a clinical diagnosis made based on the presence of albuminuria and/or reduced eGFR in the absence of signs or symptoms of other primary causes of kidney damage. The typical presentation of CKD in people with diabetes is considered to include long-standing duration of diabetes, retinopathy, albuminuria without gross hematuria, and gradually progressive loss of eGFR. However, signs of CKD may be present at diagnosis or without retinopathy in type 2 diabetes. Reduced eGFR without albuminuria has been frequently reported in type 1 and type 2 diabetes and is becoming more common over time as the prevalence of diabetes increases in the U.S. (2,3,18,20,21). An active urinary sediment (containing red or white blood cells or cellular casts), rapidly increasing albuminuria or total proteinuria, the presence of nephrotic syndrome, rapidly decreasing eGFR, or the absence of retinopathy (particularly in type 1 diabetes) suggests alternative or additional causes of kidney disease. For individuals with these features, referral to a nephrologist for further diagnosis, including the possibility of kidney biopsy, should be considered. It is rare for people with type 1 diabetes to develop kidney disease without retinopathy. In type 2 diabetes, retinopathy is only moderately sensitive and specific for CKD caused by diabetes, as confirmed by kidney biopsy (22). It cannot be definitively stated that a person with diabetes and CKD has CKD related to diabetes unless the person has a

kidney biopsy, as there may be another cause or multiple causes. Hence, without a biopsy, it is recommended to state that the individual has CKD in a person with diabetes or presumed diabetic nephropathy. Refer to a nephrologist if there are any reasons to consider another cause of CKD in a person with diabetes with atypical features or multiple comorbidities (Table 11.1).

STAGING OF CHRONIC KIDNEY DISEASE

CKD is defined in stages by level of eGFR and albuminuria, with stage G1 and stage G2 CKD defined by evidence of high albuminuria with $\text{eGFR} \geq 90 \text{ mL/min/1.73 m}^2$ and $\text{eGFR} \geq 60$ but $< 90 \text{ mL/min/1.73 m}^2$, respectively. Stages G3-G5 CKD are defined by progressively lower ranges of eGFR (23). Stage G5 is kidney failure (Fig. 11.1). At any eGFR, the degree of albuminuria is associated with risk of cardiovascular disease (CVD), CKD progression, and mortality (6). Therefore, there is an additional subclassification by level of urine albumin (Fig. 11.1) (1). Thus, based on the current classification system, both eGFR and albuminuria must be quantified to guide treatment decisions. Quantification of eGFR levels is essential for modifications of medication dosages or restrictions of use (Fig. 11.1) (23,24), and the degree of albuminuria should influence the choice of antihypertensive medications (see section 10, "Cardiovascular Disease and Risk Management") or glucose-lowering medications (see below). Observed history of eGFR loss (which is also associated with risk of CKD progression and other adverse health outcomes) and cause of kidney damage (including possible causes other than diabetes) may also affect these decisions (25).

ACUTE KIDNEY INJURY

Acute kidney injury (AKI) is defined as a rapid decline in kidney function, typically within a short period (hours to days), characterized by increase in serum creatinine and/or decrease in urine output (26). People with diabetes are at higher risk of AKI than those without diabetes (27). The rates of hospitalizations for AKI requiring dialysis are five times higher in adults with diabetes compared with adults without diabetes (risk ratio 5.0; 95% CI 4.8–5.1) (28). Other risk factors for AKI include preexisting CKD, the use of medications that cause kidney injury (e.g., nonsteroidal anti-inflammatory drugs), certain intravenous dyes (e.g., iodinated radiocontrast agents), and the use of medications that alter kidney blood flow and intrakidney hemodynamics. In particular, many antihypertensive medications (e.g., diuretics, ACE inhibitors, and angiotensin receptor blockers [ARBs]) can reduce intravascular volume, kidney blood flow, and/or glomerular filtration. There was concern that sodium–glucose cotransporter 2 (SGLT2) inhibitors may promote AKI through volume depletion, particularly when combined with diuretics or other medications that reduce glomerular filtration; however, this has not been found to be true in randomized controlled trials of advanced kidney disease (29) or high CVD risk with normal kidney function (30–32). Nonsteroidal mineralocorticoid receptor antagonists (nsMRAs) do not increase the risk of AKI when used to slow kidney disease progression (33). Timely identification and treatment of AKI is important because AKI is associated with increased risks of progressive CKD and other poor health outcomes (34).

Elevations in serum creatinine (up to 30% from baseline) with renin-angiotensin system (RAS) blockers (such as ACE inhibitors and ARBs) must not be confused with AKI (35). An analysis of the Action to Control Cardiovascular Risk in Diabetes Blood Pressure (ACCORD BP) trial demonstrated that participants randomized to intensive blood pressure lowering with up to a 30% increase in serum creatinine did not have any increase in mortality or progressive kidney disease (36,37). Urine biomarkers of tubule function (β_2 -microglobulin, α_1 -microglobulin, and uromodulin), injury (interleukin-18, kidney injury molecule 1, and neutrophil gelatinase-associated lipocalin), inflammation (monocyte chemoattractant protein 1), and repair (human

Table 11.1—Reasons to consider nondiabetic kidney diseases in a person with chronic kidney disease and diabetes

- Type 1 diabetes duration < 5 years or no retinopathy
- Active urine sediment (e.g., containing red blood cells or cellular casts)
- Chronically well-managed blood glucose
- Rapidly declining eGFR
- Rapidly increasing or very high UACR ($> 300 \text{ mg/g}$) or urine protein/creatinine level ($> 500 \text{ mg/g}$)

Information adapted from Liang et al. (133). eGFR, estimated glomerular filtration rate; UACR, urine albumin-to-creatinine ratio.

cartilage glycoprotein 40) did not increase in individuals assigned to intensive blood pressure control in the Systolic Blood Pressure Intervention Trial (SPRINT) trial despite decrease in eGFR (37).

Accordingly, ACE inhibitors and ARBs should not be discontinued for increases in serum creatinine (<30%) in the absence of volume depletion. Similar rises in creatinine are seen at the initiation of SGLT2 inhibitors and glucagon-like peptide 1 receptor agonists (GLP-1 RA) due to hemodynamic changes in the tubuloglomerular feedback, and the medication should not be discontinued.

SURVEILLANCE

Recommendation

11.2 Aim to reduce urinary albumin by $\geq 30\%$ in people with CKD and albuminuria ≥ 300 mg/g to slow CKD progression. **B**

Both albuminuria and eGFR should be monitored annually to enable timely diagnosis of CKD, monitor progression of CKD, detect superimposed kidney diseases including AKI, assess risk of CKD complications, dose medications appropriately, and determine whether nephrology referral is needed. Among people with existing kidney disease, albuminuria and eGFR may change due to progression of CKD, development of a separate superimposed cause of kidney disease, AKI, or other effects of medications, as noted above. Serum potassium should also be monitored in individuals treated with diuretics because these medications can cause hypokalemia, which is associated with cardiovascular risk and mortality (38–40). Individuals with eGFR < 60 mL/min/1.73 m² receiving ACE inhibitors, ARBs, or mineralocorticoid receptor antagonists (MRAs) should have serum potassium measured periodically to assess for hyperkalemia. Additionally, people with this lower range of eGFR should have their medication dosing verified, their exposure to nephrotoxins (e.g., nonsteroidal anti-inflammatory drugs and iodinated contrast) should be minimized, and they should be evaluated for potential CKD complications (**Table 11.2**).

Annual quantitative assessment of UACR is needed for diagnosis of albuminuria, institution of ACE inhibitor or ARB therapy to maximum tolerated doses,

Table 11.2—Screening for selected complications of chronic kidney disease

Complication	Physical and laboratory evaluation
Blood pressure $> 130/80$ mmHg	Blood pressure, weight, BMI
Volume overload	History, physical examination, weight
Electrolyte abnormalities	Serum electrolytes
Metabolic acidosis	Serum electrolytes
Anemia	Hemoglobin; iron, iron saturation, ferritin testing if indicated
Metabolic bone disease	Serum calcium, phosphate, PTH, vitamin 25(OH)D

Complications of chronic kidney disease (CKD) generally become prevalent when estimated glomerular filtration rate falls below 60 mL/min/1.73 m² (stage G3 CKD or greater) and become more common and severe as CKD progresses. Evaluation of elevated blood pressure and volume overload should occur at every clinical contact possible; laboratory evaluations are generally indicated every 6–12 months for stage G3 CKD, every 3–5 months for stage G4 CKD, and every 1–3 months for stage G5 CKD, or as indicated to evaluate symptoms or changes in therapy. 25(OH)D, 25-hydroxyvitamin D; PTH, parathyroid hormone.

and achievement of blood pressure goals. Early changes in kidney function may be detected by increases in albuminuria before changes in eGFR (41), and this also significantly affects cardiovascular risk. Continued surveillance can assess both response to therapy and disease progression and may aid in assessing participation in ACE inhibitor or ARB therapy. In addition, in clinical trials of ACE inhibitor or ARB therapy in people with type 2 diabetes, reducing albuminuria to levels < 300 mg/g creatinine or by $> 30\%$ from baseline has been associated with improved kidney and cardiovascular outcomes, leading to the recommendation that medications should be titrated to maximize reduction in UACR as residual risk persists with elevated UACR (9). Reduction in albuminuria is also important to evaluate the efficacy of medications prescribed for kidney protection, as both SGLT2 inhibitors and finerenone have shown that the majority of their beneficial effect is mediated by reduction in albuminuria (42,43). See **Table 11.3** for interventions that lower albuminuria.

Real-world data demonstrate less benefit on cardiovascular and kidney outcomes

at submaximal of RAS blockade (44). Remission of albuminuria may occur spontaneously, and cohort studies evaluating associations of change in albuminuria with clinical outcomes have overall reported cardiovascular and kidney outcome benefits (9,45,46).

The prevalence of CKD complications correlates with eGFR (40). When eGFR is < 60 mL/min/1.73 m², screening for complications of CKD is indicated (**Table 11.2**). Early vaccination against hepatitis B virus is indicated in individuals likely to progress to kidney failure (see section 4, “Comprehensive Medical Evaluation and Assessment of Comorbidities,” for further information on immunization).

Prevention

The only proven primary prevention interventions for CKD in people with diabetes are blood glucose (A1C goal of 7%) and blood pressure management ($< 130/80$ mmHg). There is no evidence that RAS inhibitors or any other interventions prevent the development of CKD in the absence of hypertension or albuminuria. Thus, the American Diabetes

Table 11.3—Interventions that lower albuminuria

- Blood glucose management
- Blood pressure management
- Treatment with ACE inhibitors or ARBs
- Smoking cessation
- Weight loss
- Changes in eating patterns (decreased salt intake and/or protein intake)
- Physical activity
- Treatment with SGLT2 inhibitors, MRAs, or GLP-1 RAs

ARB, angiotensin receptor blocker; GLP-1 RA, glucagon-like peptide 1 receptor agonist; MRA, mineralocorticoid receptor antagonist; SGLT2, sodium–glucose cotransporter 2.

Association does not recommend routine use of these medications solely for the purpose of prevention of the development of CKD. In 2023, the Glycemia Reduction Approaches in Diabetes: A Comparative Effectiveness Study (GRADE) was published (47). This large prospective study compared liraglutide, sitagliptin, glimeperide, and insulin glargine with respect to achieving and maintaining A1C goals in people with type 2 diabetes treated with metformin monotherapy; kidney and cardiovascular end points were examined as secondary outcomes. A total of 5,047 participants were enrolled from July 2013 to August 2017 and were followed for an average of 5 years. Almost all participants did not have signs of kidney disease at the time of enrollment. No differences between the examined medications were observed for kidney-protective effects among these medications for prevention. Of note, SGLT2 inhibitors were not included in the study, as these medications were not routinely available at the time the study started.

INTERVENTIONS

Nutrition

Recommendation

11.3 For people with CKD stage G3 or higher, protein intake should be 0.8 g/kg body weight per day, as for the general population. **A** For individuals on dialysis, protein intake of 1.0–1.2 g/kg/day should be considered, since protein energy wasting is a major problem for some individuals on dialysis. **B**

For people with stage G3–G5 non-dialysis-dependent CKD, protein intake should be ~0.8 g/kg body weight per day (the recommended daily allowance) (1). Compared with higher levels of protein intake, this level slowed GFR decline with evidence of a greater effect over time. Higher levels of protein intake (>20% of daily calories from protein or >1.3 g/kg/day) have been associated with increased albuminuria, more rapid kidney function loss, and CVD mortality and therefore should be avoided. In people with CKD and diabetes, consuming protein below the recommended daily allowance of 0.8 g/kg/day is not recommended, because it does not alter blood glucose levels, cardiovascular risk measures, or the

course of GFR decline (48). The National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI) (49) and the International Society of Renal Nutrition and Metabolism (50) recommend a lower protein intake level (0.6–0.8 g/kg/day) for kidney protection and state that this lower level is relatively safe. However, for CKD in diabetes, the expert grade is “opinion” only. Low-protein eating patterns should only be followed alongside guidance from a health care professional experienced in managing nutrition for people with CKD.

Restriction of dietary sodium (to <2,300 mg/day) may be useful to manage blood pressure and reduce cardiovascular risk (51,52), and individualization of potassium intake may be necessary to manage serum potassium concentrations (27,38,39). These interventions may be most important for individuals with reduced eGFR, for whom urinary excretion of sodium and potassium may be impaired. For individuals on dialysis, higher levels of protein intake should be considered since protein-energy wasting is a major problem for some individuals on dialysis (53). Recommendations for sodium and potassium intake should be individualized based on comorbid conditions, medication use, blood pressure, and laboratory data. Medical nutrition therapy by a registered dietitian nutritionist is highly successful in achieving the sodium and protein intake goals in individuals with CKD.

Glycemic Goals

Recommendation

11.4 Optimize glucose management to reduce the risk or slow the progression of CKD (Fig. 9.4). **A**

Intensive lowering of blood glucose with the goal of achieving near-normoglycemia has been shown in large, randomized studies to delay the onset and progression of albuminuria and reduce eGFR in people with type 1 diabetes (54,55) and type 2 diabetes (1,56,57). Insulin alone was used to lower blood glucose in the Diabetes Control and Complications Trial (DCCT)/Epidemiology of Diabetes Interventions and Complications (EDIC) study of type 1 diabetes, while a variety of agents were used in clinical trials of type 2 diabetes, supporting the conclusion that lowering blood glucose itself helps prevent CKD and its progression. The effects of

glucose-lowering therapies on CKD have helped define A1C goals.

The presence of CKD affects the risks and benefits of intensive lowering of blood glucose and a number of specific glucose-lowering medications. Adverse effects of intensive management of blood glucose levels (hypoglycemia and mortality) were increased among people with kidney disease at baseline (58). Moreover, there is a lag time of at least 2 years in type 2 diabetes to over 10 years in type 1 diabetes for the effects of intensive glucose control to manifest as improved eGFR outcomes (59–61). Therefore, in some people with prevalent CKD and substantial comorbidity, treatment may be less intensive (i.e., A1C goals may be higher) to decrease the risk of hypoglycemia (1,62). A1C levels are also less reliable at advanced CKD stages (63,64). Therefore, glycated albumin and fructosamine, which reflect average glycemia over a shorter time (15–30 days), are helpful in clinical management (65,66).

Blood Pressure and Use of ACE Inhibitors and Angiotensin Receptor Blockers

Recommendations

11.5 If it can be safely attained, the on-treatment blood pressure goal for people with CKD is <130/80 mmHg; a systolic blood pressure goal <120 mmHg and/or reduction in blood pressure variability should be encouraged. **A**

11.6a In nonpregnant people with diabetes and hypertension, either an ACE inhibitor or an angiotensin receptor blocker (ARB) is recommended for those with moderately increased albuminuria (UACR 30–299 mg/g creatinine) **B** and is strongly recommended for those with severely increased albuminuria (UACR ≥300 mg/g creatinine) and/or eGFR <60 mL/min/1.73 m² to maximally tolerated dose to prevent the progression of kidney disease and reduce cardiovascular events. **A** If one class is not tolerated, the other should be substituted. **B**

11.6b Monitor for drop in eGFR and increase in serum potassium levels at initiation and periodically as clinically appropriate when ACE inhibitors, ARBs, and mineralocorticoid receptor antagonists (MRAs) are used. **B** Monitor for hypokalemia when diuretics are used

at routine visits and 7–14 days after initiation or after a dose change and periodically as clinically appropriate. **B**

11.6c An ACE inhibitor or an ARB is not recommended for the primary prevention of CKD in people with diabetes who have normal blood pressure, normal UACR (<30 mg/g creatinine), and normal eGFR. **A**

11.6d Continue renin-angiotensin system blockade for mild to moderate increases in serum creatinine ($\leq 30\%$) in individuals who have no signs of extracellular fluid volume depletion. **A**

ACE inhibitors and ARBs remain a mainstay of management for people with CKD with albuminuria and for the treatment of hypertension in people with diabetes (with or without CKD in people with diabetes). Indeed, all the trials that evaluated the benefits of SGLT2 inhibition, GLP-1 RA, or nSMA effects were conducted in individuals who were being treated with an ACE inhibitor or ARB, in some trials up to maximum tolerated doses.

Hypertension is a strong risk factor for the development and progression of CKD (67). Antihypertensive therapy reduces the risk of albuminuria (68–71), and among people with type 1 or 2 diabetes with established CKD (eGFR <60 mL/min/1.73 m² and UACR ≥ 300 mg/g creatinine), ACE inhibitor or ARB therapy reduces the risk of progression to kidney failure (72–81). Moreover, antihypertensive therapy reduces the risk of cardiovascular events (68).

A blood pressure level $<130/80$ mmHg is recommended to reduce CVD mortality and slow CKD progression among all people with diabetes. Lower blood pressure goals (e.g., systolic blood pressure [SBP] <120 mmHg) should be considered based on individual anticipated benefits and risks (82). People with CKD are at increased risk of CKD progression (particularly those with albuminuria) and CVD; therefore, lower blood pressure goals may be suitable in some cases, especially in individuals with severely elevated albuminuria (≥ 300 mg/g creatinine) (83).

Blood pressure variability or the intra-individual fluctuation in blood pressure levels over time is more frequent and of higher magnitude in individuals with CKD. Blood pressure variability was associated with 47% greater risk of kidney failure (hazard ratio [HR] 1.47; 95% CI

1.09–1.99) for each 10-mmHg increase after adjustment for demographic and traditional risk factors (84,85).

Blood Pressure Control Target in Diabetes (BPROAD), an open-label trial that randomized 12,821 individuals with diabetes and elevated CVD risk to an intensive SBP goal of ≤ 120 mmHg or standard treatment that targeted an SBP of ≤ 140 mmHg for up to 5 years, noted a 21% reduction in nonfatal stroke, nonfatal myocardial infarction, heart failure, or cardiovascular death in the intensive SBP group (82). Incident albuminuria was also reduced in the intensive-treatment group compared with the standard-treatment group (11.29 vs. 13.84 events per 100 person-years) (HR 0.87; 95% CI 0.77–0.97). There were similar incidences of CKD progression and CKD development.

In an observational study of male veterans there was a beneficial effect of lowering SBP, but only if diastolic blood pressure was not <70 mmHg (86).

ACE inhibitors or ARBs are the preferred first-line agents for blood pressure treatment among people with diabetes, hypertension, eGFR <60 mL/min/1.73 m², and UACR ≥ 300 mg/g creatinine because of their proven benefits for prevention of CKD progression (72,73,75). ACE inhibitors and ARBs are considered to have similar benefits (76,77,83) and risks. In the setting of lower levels of albuminuria (30–299 mg/g creatinine), ACE inhibitor or ARB therapy at maximum tolerated doses in trials has reduced progression to more advanced albuminuria (≥ 300 mg/g creatinine), slowed CKD progression, and reduced cardiovascular events but has not reduced progression to kidney failure (75,78). While ACE inhibitors or ARBs are often prescribed for moderately increased albuminuria (30–299 mg/g creatinine) without hypertension, outcome trials have not been performed in this setting to determine whether they improve kidney outcomes. Moreover, two long-term, double-blind studies demonstrated no kidney-protective effect of either ACE inhibitors or ARBs among people with type 1 and type 2 diabetes who were normotensive with or without high albuminuria (formerly microalbuminuria, 30–299 mg/g creatinine) (79,80).

ACE inhibitors and ARBs are commonly not dosed at maximum tolerated doses because of concerns that serum creatinine will rise. In all clinical trials demonstrating efficacy of ACE inhibitors and ARBs in slowing kidney disease

progression, the maximum tolerated doses were used, so the drugs should be uptitrated as tolerated. Moreover, there are now studies demonstrating outcome benefits on both mortality and slowed CKD progression in people with diabetes who have an eGFR <30 mL/min/1.73 m² (81). Additionally, when increases in serum creatinine reach 30% without associated hyperkalemia, RAS blockade should be continued (36,87).

Among individuals with diabetes and/or CKD receiving an ACE inhibitor or ARB therapy, SGLT2 inhibitor initiation was associated with a lower risk of hyperkalemia (HR 0.89 [95% CI 0.82–0.96]) and ACE inhibitor or ARB therapy discontinuation compared with nonusers (36% vs. 45%; $P < 0.001$) (88). In a joint analysis of two randomized, double-blind, placebo-controlled, event-driven trials of SGLT2 inhibitors in individuals with albuminuric CKD, the relative effect on ACE inhibitor or ARB blockade discontinuation was more pronounced among individuals with baseline UACR $\geq 1,000$ mg/g (pooled HR 0.77; 95% CI 0.63–0.94; P -heterogeneity = 0.009) (89).

Two recent large retrospective analyses provide additional support for the use of ACE inhibitors and ARBs at the maximum tolerated dose in individuals with CKD. Ku et al. (90) reviewed 17 trials that included 11,800 individuals with CKD (defined as eGFR <60 mL/min/1.73 m²); 82% had diabetes. The authors reported that a $<13\%$ decline in eGFR over a 3-month period or a $<21\%$ decline in a 1-month period was associated with better long-term kidney outcomes. Hattori et al. (91) evaluated 6,065 participants between 2005 and 2021 ($\sim 40\%$ had diabetes) with eGFR ranging from 10 to 60 mL/min/1.73 m² who had ACE inhibitors or ARBs stopped (usually due to hyperkalemia or AKI) and found that those who restarted the ACE inhibitor or ARB had better long-term kidney outcomes and lower mortality (there was no significant difference in hyperkalemia in those who restarted ACE inhibitors or ARBs). There is also an accompanying editorial that details the strengths and weaknesses of the studies (92).

In the absence of kidney disease, ACE inhibitors or ARBs are useful to manage blood pressure but have not proven superior to alternative classes of antihypertensive therapy, including thiazide-like diuretics and dihydropyridine calcium channel blockers (93). In a trial of people with type 2

diabetes and normal urinary albumin excretion, an ARB reduced or suppressed the development of albuminuria but increased the rate of cardiovascular events (94). In a trial of people with type 1 diabetes exhibiting neither albuminuria nor hypertension, ACE inhibitors or ARBs did not prevent the development of glomerulopathy assessed by kidney biopsy (79). This was further supported by a similar trial in people with type 2 diabetes (80).

Two clinical trials studied the combinations of ACE inhibitors and ARBs and found no benefits on CVD or CKD, and the medication combination had higher adverse event rates (hyperkalemia and/or AKI) (95,96). Therefore, the combined use of ACE inhibitors and ARBs should be avoided.

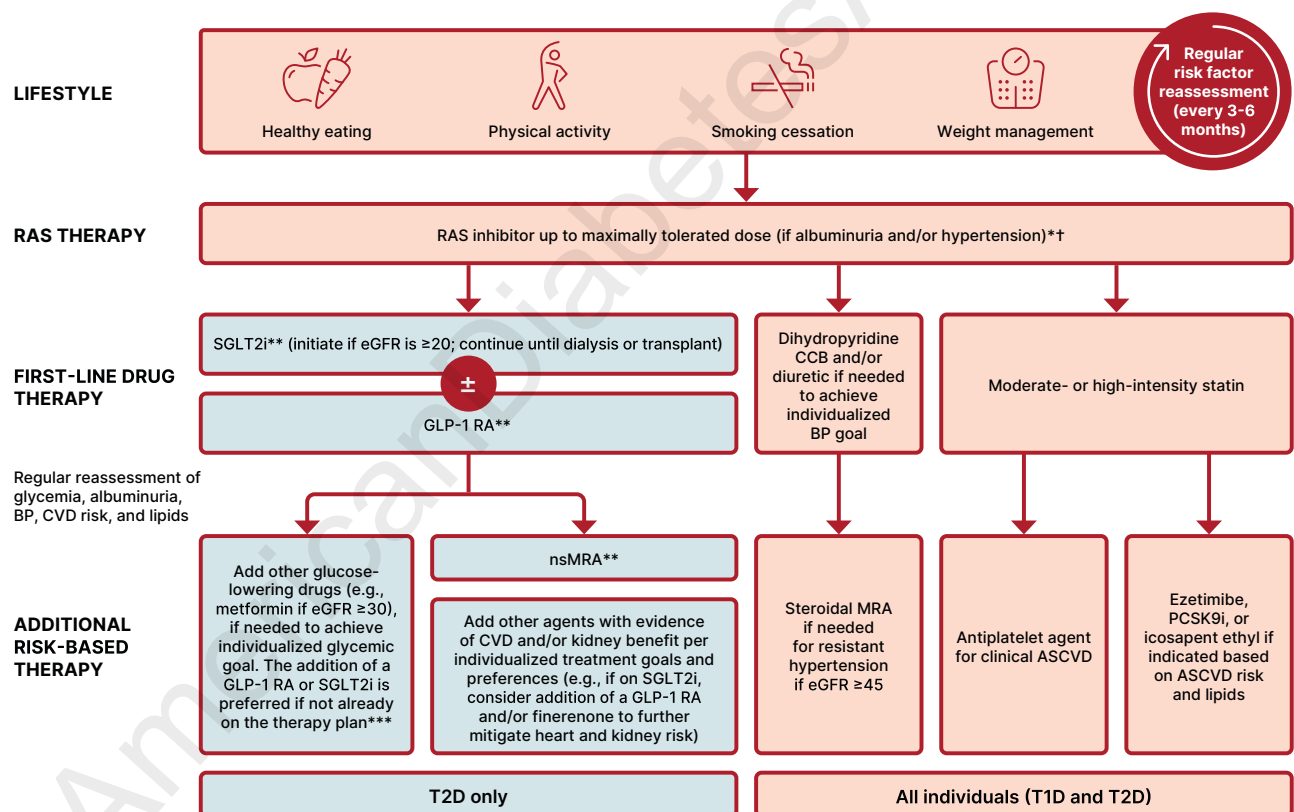
Direct Kidney Effects of Glucose-Lowering Medications

Recommendations

11.7a For people with type 2 diabetes and CKD, use of a sodium–glucose cotransporter 2 (SGLT2) inhibitor with demonstrated benefit to reduce CKD progression and cardiovascular events is recommended. SGLT2 inhibitors should be initiated in individuals with eGFR ≥ 20 mL/min/1.73 m² but can safely continue until kidney failure. **A**

11.7b To reduce kidney disease progression and cardiovascular risk in people with type 2 diabetes and CKD, a glucagon-like peptide 1 agonist with demonstrated benefit in this population is recommended. **A**

Some glucose-lowering medications also have effects on the kidney that are direct, i.e., not mediated through glycemia. For example, SGLT2 inhibitors reduce kidney tubular glucose reabsorption, weight, systemic blood pressure, intraglomerular pressure, and albuminuria and slow GFR loss through mechanisms that appear independent of glycemia (31,97–101). Moreover, recent data support the notion that SGLT2 inhibitors reduce oxidative stress in the kidney by $>50\%$ and blunt increases in angiotensinogen as well as reduce NLRP3 inflammasome activity (100,102,103). GLP-1 RAs have also been shown to improve kidney outcomes (104–109). Nonmetabolic mechanisms by which GLP-1 RAs are believed to protect the kidney include anti-inflammatory,



*The majority of participants in SGLT2i, GLP-1 RA and nsMRA kidney outcome trials were receiving background optimized RAS inhibitor therapy.

**With demonstrated benefit in this population

***Glucose-lowering efficacy of GLP-1 RAs is preserved at low eGFR; glucose-lowering efficacy of SGLT2i is diminished at lower eGFR.

Figure 11.2—Holistic approach for improving outcomes in people with diabetes and CKD. Icons presented indicate the following benefits: BP cuff, BP lowering; glucose meter, glucose lowering; heart, cardioprotection; kidney, kidney protection; scale, weight management. eGFR is presented in units of mL/min/1.73 m². †ACEi or ARB (at maximal tolerated doses) should be first-line therapy for hypertension when albuminuria is present. Otherwise, dihydropyridine calcium channel blocker or diuretic can also be considered; all three classes are often needed to attain BP targets. †Finerenone is currently the only nsMRA with proven clinical kidney and cardiovascular benefits. ACEi, angiotensin-converting enzyme inhibitor; ACR, albumin-to-creatinine ratio; ARB, angiotensin receptor blocker; ASCVD, atherosclerotic cardiovascular disease; BP, blood pressure; CCB, calcium channel blocker; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide 1 receptor agonist; HTN, hypertension; MRA, mineralocorticoid receptor antagonist; nsMRA, nonsteroidal mineralocorticoid receptor antagonist; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor; RAS, renin-angiotensin system; SGLT2i, sodium–glucose cotransporter 2 inhibitor; T1D, type 1 diabetes; T2D, type 2 diabetes.

antioxidative, and immunomodulatory actions (110,111). Kidney beneficial effects should be considered when selecting agents for glucose lowering (see section 9, "Pharmacologic Approaches to Glycemic Treatment").

Selection of Glucose-Lowering Medications for People With Chronic Kidney Disease

For people with type 2 diabetes and established CKD, special considerations for the selection of glucose-lowering medications include limitations to available medications when eGFR is diminished (such as increased risk for hypoglycemia) and a desire to mitigate risks of CKD progression, CVD, and hypoglycemia (112,113). Medication dosing may require modification with eGFR <60 mL/min/1.73 m² (1). **Figure 11.2** shows the algorithm for medications in people with diabetes and CKD.

The U.S. Food and Drug Administration (FDA) revised its guidance for the use of metformin in CKD in 2016 (114), recommending use of eGFR instead of serum creatinine to guide treatment and expanding the pool of people with kidney disease for whom metformin treatment should be considered. The revised FDA guidance states that 1) metformin is contraindicated in individuals with an eGFR <30 mL/min/1.73 m², 2) eGFR should be monitored while taking metformin, 3) the benefits and risks of continuing treatment should be reassessed when eGFR falls to <45 mL/min/1.73 m² (115,116), 4) metformin should not be initiated for individuals with an eGFR <45 mL/min/1.73 m², and 5) metformin should be temporarily discontinued at the time of or before iodinated contrast imaging procedures in individuals with eGFR 30–60 mL/min/1.73 m².

Several studies have shown cardiovascular and kidney protection from SGLT2 inhibitors and GLP-1 RAs. Selection of which glucose-lowering medications to use should be based on the usual criteria of an individual's risks (cardiovascular and kidney in addition to glucose management) as well as considerations of effects on weight, other adverse effects, other key comorbidities, individual preferences, and cost.

SGLT2 inhibitors are recommended for people with eGFR ≥20 mL/min/1.73 m² and type 2 diabetes, as they slow CKD progression and reduce heart failure risk independent of their effects on glucose

(117). GLP-1 RAs are suggested for cardiovascular risk reduction if such risk is a predominant problem, as they reduce risks of CVD events and slow progression of CKD (109,118–122).

A number of large cardiovascular outcomes trials in people with type 2 diabetes at high risk for CVD or with existing CVD examined kidney effects as secondary outcomes. These trials include EMPA-REG OUTCOME [BI 10773 (Empagliflozin) Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients], CANVAS (Canagliflozin Cardiovascular Assessment Study), LEADER (Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results), REWIND (Researching Cardiovascular Events With a Weekly Incretin in Diabetes), and SUSTAIN-6 (Trial to Evaluate Cardiovascular and Other Long-term Outcomes With Semaglutide in Subjects With Type 2 Diabetes) (99,104,107,123). Specifically, compared with placebo, empagliflozin reduced the risk of incident or worsening nephropathy (a composite of progression to UACR >300 mg/g creatinine, doubling of serum creatinine, kidney failure, or death from kidney failure) by 39% and the risk of doubling of serum creatinine accompanied by eGFR ≤45 mL/min/1.73 m² by 44%; canagliflozin reduced the risk of progression of albuminuria by 27% and the risk of reduction in eGFR, kidney failure, or death from kidney failure by 40%; liraglutide reduced the risk of new or worsening nephropathy (a composite of persistent macroalbuminuria, doubling of serum creatinine, kidney failure, or death from kidney failure) by 22%; dulaglutide reduced the composite kidney outcome (risk of ≥40% sustained decline in eGFR, kidney failure, or kidney-related death) by 25%; and semaglutide reduced the risk of new or worsening nephropathy (a composite of persistent UACR >300 mg/g creatinine, doubling of serum creatinine, or kidney failure) by 36% (each $P < 0.01$). These analyses were limited by evaluation of study populations not selected primarily for CKD and examination of kidney effects as secondary outcomes.

Three large clinical trials of SGLT2 inhibitors have focused on people with CKD and assessment of primary kidney outcomes. Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation (CRENDENCE), a placebo-controlled trial of canagliflozin among 4,401 adults with type 2 diabetes, UACR ≥300–5,000

mg/g creatinine, and eGFR range 30–90 mL/min/1.73 m² (mean eGFR 56 mL/min/1.73 m² with a mean albuminuria level of >900 mg/day), had a primary composite end point of kidney failure doubling of serum creatinine, or kidney or cardiovascular death (29,124). It was stopped early due to positive efficacy and showed a 32% risk reduction for development of kidney failure over placebo (29). Additionally, the development of the primary end point, which included dialysis for ≥30 days, kidney transplantation or eGFR <15 mL/min/1.73 m² sustained for ≥30 days by central laboratory assessment, doubling from the baseline serum creatinine average sustained for ≥30 days by central laboratory assessment, or kidney death or cardiovascular death, was reduced by 30%. This benefit was on background ACE inhibitor or ARB therapy in >99% of the participants (29). Moreover, in this advanced CKD group, there were clear benefits on cardiovascular outcomes demonstrating a 31% reduction in cardiovascular death or heart failure hospitalization and a 20% reduction in cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke (29,125,126).

A second trial in advanced CKD in people with diabetes was the Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease (DAPA-CKD) study (127). This trial examined a cohort similar to that in CRENDENCE except 67.5% of the participants had type 2 diabetes and CKD (the other one-third had CKD without type 2 diabetes), and the end points were slightly different. The primary outcome was time to the first occurrence of any of the components of the composite, including ≥50% sustained decline in eGFR or reaching kidney failure or cardiovascular death, or kidney death. Secondary outcome measures included time to the first occurrence of any of the components of the composite kidney outcome (≥50% sustained decline in eGFR or reaching kidney failure or kidney death), time to the first occurrence of either of the components of the cardiovascular composite (cardiovascular death or hospitalization for heart failure), and time to death from any cause. The trial had 4,304 participants with a mean eGFR at baseline of 43.1 ± 12.4 mL/min/1.73 m² (range 25–75 mL/min/1.73 m²) and a median UACR of 949 mg/g (range 200–5,000 mg/g). There was a significant benefit by dapagliflozin for the primary end point (HR 0.61 [95% CI

0.51–0.72]; $P < 0.001$) (127). The HR for the kidney composite of a sustained decline in eGFR of $\geq 50\%$, kidney failure, or death from kidney causes was 0.56 (95% CI 0.45–0.68; $P < 0.001$). The HR for the composite of death from cardiovascular causes or hospitalization for heart failure was 0.71 (95% CI 0.55–0.92; $P = 0.009$). Finally, all-cause mortality was decreased in the dapagliflozin group compared with the placebo group ($P < 0.004$).

The EMPA-KIDNEY (Study of Heart and Kidney Protection with Empagliflozin) (128) study enrolled participants with kidney disease with an eGFR of at least 20 but less than 45 mL/min/1.73 m² or who had an eGFR of at least 45 but less than 90 mL/min/1.73 m² with a UACR of at least 200 mg/g creatinine. Approximately one-half of the 6,609 participants had diabetes. The empagliflozin-treated participants had lower risk of progression of kidney disease and lower risk of death from cardiovascular causes (HR 0.72 [95% CI 0.64–0.82]; $P < 0.001$).

With respect to cardiovascular outcomes, SGLT2 inhibitors have demonstrated reduced risk of heart failure hospitalizations and some also demonstrated cardiovascular risk reduction. GLP-1 RAs have clearly demonstrated cardiovascular benefits. (See section 10, “Cardiovascular Disease and Risk Management,” for further detailed discussion.)

Of note, while the glucose-lowering effects of SGLT2 inhibitors are blunted with eGFR < 45 mL/min/1.73 m², the kidney and cardiovascular benefits were still seen at eGFR levels as low as 20 mL/min/1.73 m² even with no significant change in glucose (4,29,31,107,123,127,129,130). Most participants with CKD in these trials also had diagnosed atherosclerotic cardiovascular disease (ASCVD) at baseline, although $\sim 28\%$ of CANVAS participants with CKD did not have diagnosed ASCVD (32).

Cardiovascular and kidney events are reduced with SGLT2 inhibitor use in individuals with severe CKD independent of glucose-lowering effects (126,131). The six-year kidney benefits of SGLT2 inhibitors are comparable between empagliflozin and dapagliflozin for AKI, albuminuria, and CKD progression (132).

The FLOW study demonstrated that the GLP-1 RA semaglutide had kidney-protective effects in people with type 2 diabetes and CKD (109). The study enrolled 3,533 participants with significant kidney

disease defined by level of eGFR and/or by level of albuminuria (of note, all participants had an albuminuria level of at least 100 mg/g). The primary outcome was defined as the first major kidney disease event (onset of $> 50\%$ in eGFR, onset of persistent eGFR of < 15 mL/min/1.73 m², initiation of dialysis or transplant, kidney death, and cardiovascular death). The study was stopped early due to reaching a prespecified outcome. There was a 24% lower HR for those taking semaglutide compared with the placebo group. Of note, cardiovascular deaths comprised about 38% of the events. When the cardiovascular deaths are removed from the analysis, the HR for kidney-specific events was 21% lower in those taking semaglutide. Thus, this kidney outcome study supports a beneficial effect of semaglutide in slowing decline in kidney function as well as being cardioprotective in people with CKD and type 2 diabetes. Of note, the participants who took semaglutide had lower A1C, lower blood pressure, and more weight loss—all of which are beneficial for slowing decline in kidney function and reducing cardiovascular adverse events. Whether this beneficial combination of effects was the primary cause for the kidney-protective outcomes or whether there is a unique kidney-protective effect of semaglutide remains to be determined.

While there is no published randomized controlled trial demonstrating the kidney outcomes of tirzepatide, a dual glucose-dependent insulinotropic polypeptide and GLP-1 RA, the SURMOUNT-2 (Tirzepatide Once Weekly for the Treatment of Obesity in People With Type 2 Diabetes) trial of 938 participants with overweight or obesity with type 2 diabetes showed that tirzepatide reduced albuminuria without adverse changes in eGFR compared with placebo. However, only 5% of the participants had eGFR < 60 mL/min/1.73 m², and 31% had albuminuria at baseline.

Adverse event profiles of these agents also must be considered. Please refer to **Table 9.2** for medication-specific factors, including adverse event information, for these agents. Additional clinical trials focusing on CKD and cardiovascular outcomes in people with CKD are ongoing and will be reported in the next few years.

For people with type 2 diabetes and CKD, the selection of specific agents may depend on comorbidity and CKD stage. SGLT2 inhibitors are recommended for

individuals at high risk of CKD progression (i.e., with albuminuria or a history of documented eGFR loss) (**Fig. 9.4**). For people with type 2 diabetes and CKD, use of an SGLT2 inhibitor in individuals with eGFR ≥ 20 mL/min/1.73 m² is recommended to reduce CKD progression and cardiovascular events. The reason for the limit of eGFR is as follows. The major clinical trials for SGLT2 inhibitors that showed benefit for CKD in people with diabetes are CREDENCE, DAPA-CKD, and EMPA-KIDNEY. CREDENCE enrollment criteria included eGFR > 30 mL/min/1.73 m² and UACR > 300 mg/g (29,125). DAPA-CKD enrolled individuals with eGFR > 25 mL/min/1.73 m² and UACR > 200 mg/g. Subgroup analyses from DAPA-CKD (133) and analyses from the EMPEROR heart failure trials suggest that SGLT2 inhibitors are safe and effective at eGFR levels of > 20 mL/min/1.73 m². The Empagliflozin Outcome Trial in Patients With Chronic Heart Failure With Preserved Ejection Fraction (EMPEROR-Preserved) enrolled 5,998 participants (134), and the Empagliflozin Outcome Trial in Patients With Chronic Heart Failure and a Reduced Ejection Fraction (EMPEROR-Reduced) enrolled 3,730 participants (135); enrollment criteria included eGFR > 60 mL/min/1.73 m², but efficacy was seen at eGFR > 20 mL/min/1.73 m² in people with heart failure. Most recently, the EMPA-KIDNEY trial showed efficacy in participants with eGFR as low as 20 mL/min/1.73 m² (128). Hence, the recommendation is to use SGLT2 inhibitors in individuals with eGFR as low as 20 mL/min/1.73 m². In addition, the DECLARE-TIMI 58 trial suggested effectiveness in participants with normal urinary albumin levels (136). In sum, for people with type 2 diabetes and CKD, use of an SGLT2 inhibitor is recommended to reduce CKD progression and cardiovascular events in people with an eGFR ≥ 20 mL/min/1.73 m². However, SGLT2 inhibitors should be continued if tolerated until an individual starts dialysis.

Of note, most GLP-1 RAs may also be used at low eGFR for cardiovascular protection but may require dose adjustment (125). Lixisenatide and exenatide, which require the kidneys for elimination, result in higher exposure to the medication and have limited data in individuals with eGFR < 30 mL/min/1.73 m² or creatinine clearance < 30 mL/min, respectively (137–139).

Kidney and Cardiovascular Outcomes of Mineralocorticoid Receptor Antagonists in Chronic Kidney Disease

Recommendation

11.8 To reduce CKD progression and cardiovascular events in people with CKD and albuminuria, a nonsteroidal MRA that has been shown to be effective in clinical trials is recommended (if eGFR is ≥ 25 mL/min/1.73 m²). Potassium levels should be monitored 1 month after initiation. **A**

MRAs historically have not been well studied in people with diabetes and CKD because of the risk of hyperkalemia (140,141). However, data that do exist suggest sustained benefit on albuminuria reduction. There are two different classes of MRAs, steroidal and nonsteroidal, with one group not extrapolatable to the other (142). Late in 2020, the results of the first of two trials, the Finerenone in Reducing Kidney Failure and Disease Progression in Diabetic Kidney Disease (FIDELIO-DKD) trial, which examined the kidney effects of finerenone, an nsMRA, demonstrated a significant reduction in CKD progression and cardiovascular events in people with diabetes and advanced CKD (33,143). This trial had a primary end point of time to first occurrence of the composite end point of onset of kidney failure, a sustained decrease of eGFR $>40\%$ from baseline over at least 4 weeks, or kidney death. A prespecified secondary outcome was time to first occurrence of the composite end point of cardiovascular death or nonfatal cardiovascular events (myocardial infarction, stroke, or hospitalization for heart failure). Other secondary outcomes included all-cause mortality, time to all-cause hospitalizations, and change in UACR from baseline to month 4, and time to first occurrence of the following composite end point: onset of kidney failure, a sustained decrease in eGFR of $\geq 57\%$ from baseline over at least 4 weeks, or kidney death.

The double-blind, placebo-controlled trial randomized 5,734 people with CKD and type 2 diabetes to receive finerenone or placebo. Eligible participants had a UACR of 30 to <300 mg/g, an eGFR of 25 to <60 mL/min/1.73 m², and diabetic retinopathy, or a UACR of 300–5,000 mg/g and an eGFR of 25 to <75 mL/min/1.73 m². The potassium level had to be ≤ 4.8 mmol/L. The mean

age of participants was 65.6 years, and 30% were female. The mean eGFR was 44.3 mL/min/1.73 m², and the mean albuminuria was 852 mg/g (interquartile range 446–1,634 mg/g). The primary end point was reduced with finerenone compared with placebo (HR 0.82 [95% CI 0.73–0.93]; $P = 0.001$), as was the key secondary composite of cardiovascular outcomes (HR 0.86 [95% CI 0.75–0.99]; $P = 0.03$). Hyperkalemia resulted in 2.3% discontinuation in the study group compared with 0.9% in the placebo group. However, the study was completed, and there were no deaths related to hyperkalemia. Of note, 4.5% of the total group were being treated with SGLT2 inhibitors.

The Finerenone in Reducing Cardiovascular Mortality and Morbidity in Diabetic Kidney Disease (FIGARO-DKD) trial assessed the safety and efficacy of finerenone in reducing cardiovascular events among people with type 2 diabetes and CKD with elevated UACR (30 to <300 mg/g creatinine) and eGFR 25–90 mL/min/1.73 m² (144). The potassium level had to be ≤ 4.8 mmol/L. The study randomized eligible subjects to either finerenone ($n = 3,686$) or placebo ($n = 3,666$). Participants with an eGFR of 25–60 mL/min/1.73 m² at the screening visit received an initial dose at baseline of 10 mg once daily, and if eGFR at screening was ≥ 60 mL/min/1.73 m², the initial dose was 20 mg once daily. An increase in the dose from 10 to 20 mg once daily was encouraged after 1 month, provided the serum potassium level was ≤ 4.8 mmol/L and eGFR was stable. The mean age of participants was 64.1 years (31% were female), and the median follow-up duration was 3.4 years. The median A1C was 7.7%, the mean SBP was 136 mmHg, and the mean GFR was 67.8 mL/min/1.73 m². People with heart failure with a reduced ejection fraction and uncontrolled hypertension were excluded.

The primary composite outcome was cardiovascular death, myocardial infarction, stroke, and hospitalization for heart failure. The finerenone group showed a 13% reduction in the primary end point compared with the placebo group (12.4% vs. 14.2%; HR 0.87 [95% CI 0.76–0.98]; $P = 0.03$). This benefit was primarily driven by a reduction in heart failure hospitalizations: 3.2% vs. 4.4% in the placebo group (HR 0.71 [95% CI 0.56–0.90]).

Of the secondary outcomes, the most noteworthy was a 36% reduction in kidney failure: 0.9% vs. 1.3% in the placebo

group (HR 0.64 [95% CI 0.41–0.99]). There was a higher incidence of hyperkalemia in the finerenone group, 10.8% vs. 5.3%, although only 1.2% of the 3,686 individuals on finerenone stopped the study due to hyperkalemia.

The FIDELITY prespecified pooled efficacy and safety analysis incorporated individuals from both the FIGARO-DKD and FIDELIO-DKD trials ($n = 13,171$) to allow for evaluation across the spectrum of severity of CKD, since the populations were different (with a slight overlap) and the study designs were similar (145). The analysis showed a 14% reduction in composite cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, and hospitalization for heart failure for finerenone vs. placebo (12.7% vs. 14.4%; HR 0.86 [95% CI 0.78–0.95]; $P = 0.002$).

It also demonstrated a 23% reduction in the composite kidney outcome, consisting of sustained $\geq 57\%$ decrease in eGFR from baseline over ≥ 4 weeks, or kidney death, for finerenone versus placebo (5.5% vs. 7.1%; HR 0.77 [95% CI 0.67–0.88]; $P < 0.001$).

The pooled FIDELITY trial analysis confirms and strengthens the positive cardiovascular and kidney outcomes with finerenone across the spectrum of CKD, irrespective of baseline ASCVD history (with the exclusion of those with heart failure with reduced ejection fraction).

Combination Therapy Considerations to Optimize Kidney and Cardiovascular Risk Reduction

Recommendation

11.9 Simultaneous initiation of an SGLT2 inhibitor and a nonsteroidal MRA (finerenone) can be considered in adults with type 2 diabetes and UACR ≥ 100 mg/g with eGFR 30–90 mL/min/1.73 m² on a renin-angiotensin system inhibitor due to evidence of safety and beneficial effects on albuminuria. **B**

All of the recent kidney and cardiovascular outcomes studies for individuals with diabetes and CKD were completed in the setting of maximally tolerated RAS blockade. Thus, all individuals should have their treatment for RAS blockade adjusted to the maximally tolerated dose, even when considering combination therapy with other treatments. Although there have been no studies directly comparing SGLT2 inhibitors, GLP-1 RAs, or MRAs, the

mechanisms of action of these medications are different and independent from glucose lowering. Therefore, it has been proposed and there is increasing evidence that combination therapy is likely to be beneficial for both cardiovascular and kidney outcomes.

A population-based cohort study compared individuals on either a GLP-1 RA or SGLT2 inhibitor with those who added a treatment from the other class (SGLT2 inhibitor added to GLP-1 RA or vice versa). The addition of a GLP-1 RA on top of SGLT2 inhibitor treatment was associated with a 30% lower risk of major adverse cardiovascular events and 57% lower risk of serious kidney events compared with GLP-1 RA therapy alone after a median follow-up of 9 months. The addition of an SGLT2 inhibitor on top of GLP-1 RA was associated with a 29% lower risk of major adverse cardiovascular events compared with SGLT2 inhibitor alone. When stratified based on history of kidney disease, the use of combination treatment by individuals with a history of kidney disease was associated with a lower risk of major adverse cardiovascular events compared with those without kidney disease (146). Concomitant use of SGLT2 inhibitor with GLP-1 RA did not affect the overall benefits of semaglutide on kidney and cardiovascular outcomes in participants with type 2 diabetes and CKD in a prespecified analysis of the FLOW trial; however, the limited use of SGLT2 inhibitors at baseline may have affected these results (147).

The recent CONFIDENCE (Combination Effect of Finerenone and Empagliflozin in Participants With Chronic Kidney Disease and Type 2 Diabetes Using a Urinary Albumin-to-Creatinine Ratio End Point) trial is the first published combination trial. There were three randomized arms: finerenone alone, empagliflozin alone, or the combination of the two therapies. Participants had CKD (eGFR >30 and <90 mL/min per 1.73 m²) with albuminuria (UACR >100 and <5,000 mg/g) and type 2 diabetes. Simultaneous initiation of finerenone and empagliflozin led to a reduction in the UACR at 180 days of 52% with combination therapy, which was 32% greater than that with empagliflozin alone and 29% greater than that with finerenone alone (148). This trial provides support for initial combination therapy in the setting of type 2 diabetes and CKD to slow kidney disease progression.

Health care professionals should use their best judgement, considering the individuals' comorbidities and preferences, as to which medication to prescribe initially (SGLT2 inhibitor or GLP-1 RA) and whether combination therapy is warranted. As noted, all of these studies included participants taking either an ACE inhibitor or an ARB, often at maximally tolerated doses. In addition, while current evidence of kidney benefit is limited to CKD in type 2 diabetes, multiple studies are in progress to determine if these therapies also improve kidney outcomes in people with type 1 diabetes (149,150).

Use of Kidney-Protective Medications in Pregnancy

Recommendation

11.10 Kidney-protective medications that are potentially harmful in pregnancy should be avoided in sexually active individuals of childbearing potential who are not using reliable contraception and, if used, should be switched prior to conception to kidney-protective medications considered safer during pregnancy. **B**

During pregnancy, treatment with ACE inhibitors, ARBs, direct renin inhibitors, MRAs, SGLT2 inhibitors, and neprilysin inhibitors is contraindicated, as they may cause fetal damage. Special consideration should be taken for individuals of childbearing potential, and people intending to become pregnant should switch from an ACE inhibitor or ARB, renin inhibitor, MRA, or neprilysin inhibitor to an alternative antihypertensive medication approved during pregnancy. Antihypertensive drugs known to be effective and safe in pregnancy include methyldopa, labetalol, and long-acting nifedipine, while hydralazine may be considered in the acute management of hypertension in pregnancy or severe preeclampsia (151). Diuretics are not recommended for blood pressure management in pregnancy but may be used during late-stage pregnancy if needed for volume management (151). The American College of Obstetricians and Gynecologists also recommends that, postpartum, individuals with gestational hypertension, preeclampsia, and superimposed preeclampsia have their blood pressures observed for 72 h in the hospital and 7–10 days postpartum. Long-term follow-up is recommended for

these individuals, as they have increased lifetime cardiovascular risk (152). See section 15, "Management of Diabetes in Pregnancy," for additional information.

Treatment for Severe Chronic Kidney Disease and Kidney Failure

Recommendation

11.11a Individuals with eGFR <20 mL/min/1.73 m² and not on dialysis can be safely continued on SGLT2 inhibitors to reduce the risk of CKD progression **B** and for cardiovascular benefits. **C**

11.11b Individuals on dialysis can be safely initiated or continued on GLP-1–based therapy that is not dependent on kidney clearance to reduce cardiovascular risk and mortality. **C**

SGLT2 inhibitors have non-kidney effects in multiple organs, including the cardiovascular system. For individuals who tolerate the medication, therapy should be continued unless kidney failure develops. A post hoc analysis of the DAPA-CKD trial demonstrated that in individuals with stage G4 CKD and albuminuria, the effects of dapagliflozin were consistent with those observed in the trial overall, with no evidence of increased risks (133). However, we will learn more about the safety and efficacy in kidney failure when results of the ongoing Renal Lifecycle trial are published. This study aims to investigate the effects of an SGLT2 inhibitor compared with placebo on the incidence of kidney failure, heart failure, mortality, and safety in individuals with an eGFR ≤25 mL/min/1.73 m² or kidney failure (153).

Small randomized controlled trials have demonstrated that GLP-1–based therapy has beneficial effects in body weight and glycemic management in individuals on dialysis. Idorn et al. (154) demonstrated that GLP-1 levels are increased in individuals on dialysis compared with individuals in the control group not on dialysis, and individuals on dialysis were more likely to experience gastrointestinal symptoms. In individuals receiving peritoneal dialysis, Hiramatsu et al. (155) found over a 12-month period that left ventricular mass index decreased and left ventricular ejection fraction increased. Vanek et al. (156), in a prospective 12-week open-label trial of 13 individuals on dialysis who had been denied transplant due to

high BMI, demonstrated an average weight reduction of 4.6 ± 2.4 kg with semaglutide.

In a national cohort study of 151,649 individuals with type 2 diabetes initiating dialysis between 2013 and 2021, GLP-1–based therapy was associated with a 23% lower mortality and 66% higher chance of transplant waitlisting (157).

In an observational study, use of GLP-1–based therapy at the onset of dialysis was associated with a decreased risk of major cardiovascular events (adjusted HR 0.65, $P < 0.001$) and all-cause mortality (adjusted HR 0.63, $P < 0.001$) during a median follow-up of 1.4 years. However, this study had methodological issues, including the likely inclusion of individuals with AKI (158). As mentioned before, exenatide and lixisenatide should not be used in individuals on dialysis.

Referral to a Nephrologist

Recommendations

11.12a Individuals should be referred for evaluation by a nephrologist if they have rapidly increasing urinary albumin levels and/or rapidly decreasing eGFR and/or if the eGFR is <30 mL/min/ 1.73 m². **A**

11.12b Refer to a nephrologist for uncertainty about the etiology of kidney disease or difficult management issues. **B**

Health care professionals should consider referral to a nephrologist if the individual with diabetes has continuously rising UACR levels and/or continuously declining eGFR, if there is uncertainty about the etiology of kidney disease, for difficult management issues (anemia, secondary hyperparathyroidism, significant increases in albuminuria despite good blood pressure management, metabolic bone disease, resistant hypertension, or electrolyte disturbances), or when there is advanced kidney disease (eGFR <30 mL/min/ 1.73 m²) requiring discussion of kidney replacement therapy for kidney failure (1). The threshold for referral may vary depending on the frequency with which a health care professional encounters people with diabetes and kidney disease. Consultation with a nephrologist when stage G4 CKD develops (eGFR <30 mL/min/ 1.73 m²) has been found to reduce cost, improve quality of care, and delay the need for dialysis (159).

However, other specialists and health care professionals should also educate

people with diabetes about the progressive nature of CKD, the kidney preservation benefits of proactive treatment of blood pressure and blood glucose, and the potential need for kidney replacement therapy.

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12. Retinopathy, Neuropathy, and Foot Care: Standards of Care in Diabetes—2026

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American Diabetes Association
Professional Practice Committee for
Diabetes*

The American Diabetes Association (ADA) “Standards of Care in Diabetes” includes the ADA’s current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. Members of the ADA Professional Practice Committee for Diabetes, an interprofessional expert committee, are responsible for updating the Standards of Care annually, or more frequently as warranted. For a detailed description of ADA standards, statements, and reports, as well as the evidence-grading system for ADA’s clinical practice recommendations and a full list of Professional Practice Committee members, please refer to Introduction and Methodology. Readers who wish to comment on the Standards of Care are invited to do so at professional.diabetes.org/SOC.

Diabetes is defined by hyperglycemia (1). Chronic hyperglycemia is the best-established concomitant risk factor associated with microvascular complications (e.g., diabetic retinopathy and neuropathy). Optimizing glycemic management has the beneficial impact of preventing or delaying microvascular disease in diabetes. For example, the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) study in people with type 1 diabetes showed that the early beneficial effects of intensive (A1C ~7% [~53 mmol/mol]) versus conventional (A1C ~9% [~75 mmol/mol]) therapy on microvascular complications persisted for ~10 years after the convergence of A1C levels in the two groups during the EDIC follow-up—a novel concept, termed metabolic memory, in which a period of near-normal glycemia produces long-term beneficial effects on complications, with such effects persisting even though subsequent levels of glycemia may have risen (2,3). Many mechanisms may mediate the effects of chronic hyperglycemia on complications, including glycation, lipoxidation, inflammation, apoptosis, and epigenetic and other intracellular processes (4).

DIABETIC RETINOPATHY

Recommendations

12.1 Implement strategies to help people with diabetes reach glycemic goals to reduce the risk or slow the progression of diabetic retinopathy. **A**

12.2 Implement strategies to help people with diabetes reach blood pressure and lipid goals to reduce the risk or slow the progression of diabetic retinopathy. **A**

Diabetic retinopathy is a highly specific neurovascular complication of diabetes, with prevalence strongly related to both the duration of diabetes and the level of chronic

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hyperglycemia (5). Diabetic retinopathy is characterized by microaneurysms in the earliest stage, followed by retinal hemorrhages and ischemia. In response to ischemia, neovascularization can occur; this is proliferative diabetic retinopathy (PDR). At any point along this spectrum, the retina vasculature can leak fluid (and exudates) leading to diabetic macular edema (DME). Other ocular complications include vitreous hemorrhage and tractional retinal detachment. Diabetic retinopathy is the most frequent cause of new cases of blindness among adults aged 20–74 years in high-income countries (1). Glaucoma and cataracts occur earlier and more frequently in people with diabetes.

In addition to diabetes duration, factors that increase the risk of, or are associated with, retinopathy include chronic hyperglycemia (6,7), nephropathy (8), hypertension (9), and dyslipidemia (10–12). Intensive diabetes management with the goal of achieving early and/or subsequent near-normoglycemia has been shown in large prospective randomized studies to prevent and/or delay the onset and progression of diabetic retinopathy, reduce the need for future ocular procedures, and potentially improve self-reported visual function (6,10,13–15).

There are conflicting data on the impact of glucagon-like peptide 1 receptor agonist (GLP-1 RA) treatment on various facets of eye health, including development of nonarteritic anterior ischemic optic neuropathy, glaucoma, neovascular age-related macular degeneration (AMD), and diabetic retinopathy progression (16). GLP-1 RAs including liraglutide, semaglutide, and dulaglutide have been shown to be associated with a risk of mildly worsening diabetic retinopathy in randomized trials (17,18). Further data from clinical studies with longer follow-up purposefully designed for diabetic retinopathy risk assessment, particularly including individuals with established diabetic retinopathy, are needed. Retinopathy status should be assessed when glucose-lowering therapies are intensified, such as those using GLP-1 RAs, since rapid reductions in A1C have been shown to be associated with a risk of initial worsening of retinopathy (19). There have been matched cohort studies linking GLP-1 RAs with various ocular complications such as nonarteritic anterior ischemic optic neuropathy (20,21) and AMD (22) in people with diabetes, but data are limited and further studies are needed.

In contrast, GLP-1 RAs may have ocular benefits. For example, several studies have shown an association with GLP-1 RAs and lower intraocular pressure (23) as well as a reduced risk of glaucoma (24,25).

Screening

Recommendations

12.3 Adults with type 1 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist 5 years after the onset of diabetes. **B**

12.4 People with type 2 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist at the time of the diabetes diagnosis. **B**

12.5 If there is no evidence of retinopathy from one or more annual eye exams and glycemic indicators are within the goal range, then screening every 1–2 years may be considered. If any level of diabetic retinopathy is present, subsequent dilated retinal examinations should be repeated at least annually by an ophthalmologist or optometrist. If retinopathy is progressing or sight-threatening, then examinations by an ophthalmologist will be required more frequently. **B**

12.6 Programs that use retinal photography with remote reading or the use of U.S. Food and Drug Administration–approved artificial intelligence algorithms to improve access to diabetic retinopathy screening are appropriate screening strategies for diabetic retinopathy. Such programs need to provide pathways for timely referral for a comprehensive eye examination when indicated. **B**

12.7 Counsel individuals of childbearing potential with preexisting type 1 or type 2 diabetes who are planning pregnancy or who are pregnant on the risk of development and/or progression of diabetic retinopathy. **B**

12.8 Individuals with preexisting type 1 or type 2 diabetes should receive an eye exam before pregnancy as well as in the first trimester and may need to be monitored every trimester and for 1 year postpartum as indicated by the degree of retinopathy. **B**

Identifying individuals with diabetes-related eye disease is important because

people with vision-threatening retinopathy may be asymptomatic. Additionally, current therapies can not only prevent vision loss but also help improve vision for many individuals. Prompt diagnosis allows triage of people with diabetes and timely intervention that may prevent vision loss in individuals who are asymptomatic despite advanced diabetes-related eye disease.

Diabetic retinopathy screening should be performed using validated approaches and methodologies. Children and adolescents with type 1 or type 2 diabetes are also at risk for complications and need to be screened for diabetic retinopathy (26–28) (see section 14, “Children and Adolescents”). If diabetic retinopathy is evident on screening, prompt referral to an ophthalmologist is recommended. Subsequent examinations for individuals with type 1 or type 2 diabetes are generally repeated annually for individuals without or with mild retinopathy. Exams every 1–2 years may be cost-effective after one or more normal eye exams. In a population with well-managed type 2 diabetes, there was little risk of development of significant retinopathy within a 3-year interval after a normal examination (29), and less frequent intervals have been found in simulated modeling to be potentially effective in screening for diabetic retinopathy in individuals without diabetic retinopathy (30). However, it is important to adjust screening intervals based on the presence of specific risk factors for retinopathy onset and worsening retinopathy. More frequent examinations by the ophthalmologist will be required if retinopathy is progressing or risk factors such as not meeting glycemic goals, advanced retinopathy, or DME are present.

Retinal photography with remote reading by experts has great potential to provide screening services in areas where qualified eye care professionals are not readily available (31,32). High-quality fundus photographs can detect most clinically significant diabetic retinopathy. Interpretation of the images should be performed by a trained eye care professional or reading center technician or by artificial intelligence (AI) programs that are U.S. Food and Drug Administration (FDA) approved for this purpose. Retinal photography may also enhance efficiency and reduce costs when the expertise of ophthalmologists can be used for more complex examinations and for treatment (31,33,34). In-person exams

are still necessary when the retinal photographs are of unacceptable quality and for follow-up if abnormalities are detected. Retinal photographs are not a substitute for dilated comprehensive eye exams, which should be performed at least initially and at yearly intervals thereafter or more frequently as recommended by an eye care professional. AI systems that detect more than mild diabetic retinopathy and DME that have been authorized for use by the FDA represent an alternative to traditional screening approaches (35). Three AI platforms have been approved by the FDA for diabetic retinopathy screening and examination: AEYE diagnostic screening technology, or AEYE-DS (AEYE Health); EyeArt AI screening system (Eyenuk); and LumineticsCore, formerly IDX-DR (Digital Diagnostics). These services are covered by most insurance plans. Prospective multicenter clinical trials on diagnostic accuracy have been published for each platform (36). However, the benefits and optimal utilization of this type of screening have yet to be fully determined. Results of all screening eye examinations should be documented and transmitted to the referring health care professional.

Type 1 Diabetes

Because retinopathy is estimated to take at least 5 years to develop after the onset of hyperglycemia, people with type 1 diabetes should have an initial dilated and comprehensive eye examination 5 years after the diagnosis of diabetes (30).

Type 2 Diabetes

People with type 2 diabetes who may have had undiagnosed hyperglycemia for years and have a significant risk of prevalent diabetic retinopathy at the time of diabetes diagnosis should have an initial dilated and comprehensive eye examination at the time of diagnosis.

Pregnancy

Individuals who develop gestational diabetes mellitus do not require eye examinations during pregnancy, since they do not appear to be at increased risk of developing diabetic retinopathy during pregnancy (37). However, individuals of childbearing potential with preexisting type 1 or type 2 diabetes who are planning pregnancy or who have become pregnant should be counseled on the baseline prevalence and risk of development and/or

progression of diabetic retinopathy. In a systematic review and meta-analysis of 18 observational studies of pregnant individuals with preexisting type 1 or type 2 diabetes, the prevalence of any diabetic retinopathy and PDR in early pregnancy was 52.3% and 6.1%, respectively. The pooled progression rate per 100 pregnancies for new diabetic retinopathy development was 15.0 (95% CI 9.9–20.8), worsened nonproliferative diabetic retinopathy was 31.0 (95% CI 23.2–39.2), pooled sight-threatening progression rate from nonproliferative diabetic retinopathy to PDR was 6.3 (95% CI 3.3–10.0), and worsened PDR was 37.0 (95% CI 21.2–54.0), demonstrating that close follow-up should be maintained during pregnancy to prevent vision loss (38). In addition, rapid implementation of intensive glyce-mic management in the setting of retinopathy may be associated with early worsening of retinopathy (similar to what has been seen with GLP-1 RA therapy in nonpregnancy settings), and these individuals may also benefit from more frequent follow-up initially (39).

A systematic review and meta-analysis and a randomized controlled trial demonstrate that pregnancy in individuals with type 1 diabetes may aggravate retinopathy and threaten vision, especially when glycemic management is suboptimal or retinopathy severity is advanced at the time of conception (38,39). Laser photocoagulation can minimize the risk of vision loss during pregnancy for individuals with high-risk PDR or center-involved DME (39). The use of anti-vascular endothelial growth factor (anti-VEGF) injections in pregnant individuals may be justified if the potential benefit outweighs the potential risk to the fetus and only if clearly indicated (40). Current anti-VEGF medications have been assigned to pregnancy category C by the FDA (animal studies have revealed evidence of embryo-fetal toxicity, but there are no controlled data in human pregnancy), and caution should be used in pregnant individuals with diabetes because of theoretical risks to the vasculature of the developing fetus.

Treatment

Two of the main motivations for screening for diabetic retinopathy are to prevent loss of vision and to intervene with treatment when vision loss can be prevented or reversed.

Recommendations

12.9 Promptly refer individuals with any level of diabetic macular edema, moderate or worse nonproliferative diabetic retinopathy (a precursor of proliferative diabetic retinopathy [PDR]), or any PDR to an ophthalmologist who is knowledgeable and experienced in the management of diabetic retinopathy. **A**

12.10 Panretinal laser photocoagulation therapy is indicated to reduce the risk of vision loss in individuals with high-risk PDR and, in some cases, severe nonproliferative diabetic retinopathy. **A**

12.11 Intravitreal injections of anti-vascular endothelial growth factor (anti-VEGF) are a reasonable alternative to traditional panretinal laser photocoagulation for some individuals with PDR and also reduce the risk of vision loss in these individuals. **A**

12.12 Intravitreal injections of anti-VEGF are indicated as first-line treatment for most eyes with diabetic macular edema that involves the foveal center and impairs visual acuity. **A**

12.13 Macular focal/grid photocoagulation and intravitreal injections of corticosteroid are reasonable treatments in eyes with persistent diabetic macular edema despite previous anti-VEGF therapy or eyes that are not candidates for this first-line approach. **A**

12.14 The presence of retinopathy is not a contraindication to aspirin therapy for cardioprotection, as aspirin does not increase the risk of retinal hemorrhage. **A**

Photocoagulation Therapy

Two large trials, the Diabetic Retinopathy Study (DRS) in individuals with PDR and the Early Treatment Diabetic Retinopathy Study (ETDRS) in individuals with macular edema, provide the strongest support for the therapeutic benefits of laser photocoagulation therapy. The DRS (41) showed that panretinal photocoagulation reduced the risk of severe vision loss from PDR from 15.9% in untreated eyes to 6.4% in treated eyes with the greatest benefit ratio in those with more advanced baseline disease (disc neovascularization or vitreous hemorrhage). Later, the ETDRS verified the benefits of panretinal photocoagulation for high-risk PDR and in

older-onset individuals with severe non-proliferative diabetic retinopathy or less-than-high-risk PDR (42). Panretinal laser photocoagulation is still commonly used to manage PDR. A macular focal/grid laser photocoagulation technique was shown in the ETDRS to be effective in treating eyes with clinically significant macular edema from diabetes (42), but this is now largely considered a second-line treatment of DME.

Anti-VEGF Treatment

Data from the DRCR Retina Network (formerly the Diabetic Retinopathy Clinical Research Network) and others demonstrate that intravitreal injections of anti-VEGF agents are effective at regressing proliferative disease and lead to noninferior or superior visual acuity outcomes compared with panretinal laser over 2 years of follow-up (43,44). In addition, it was observed that individuals treated with ranibizumab tended to have less peripheral visual field loss, fewer vitrectomy surgeries for secondary complications from their proliferative disease, and a lower risk of developing DME (43). However, a potential drawback in using anti-VEGF therapy to manage proliferative disease is that individuals were required to have a greater number of visits and received a greater number of treatments than is typically required for management by panretinal laser, which may not be optimal for some individuals. Additionally, unlike panretinal laser, anti-VEGF therapy requires participation in scheduled follow-up. Individuals with nonintentional lapses in treatment are at risk for worse visual acuity and anatomic outcomes (45). Subsequently, there is variability in treatment patterns among eye specialists, with treatment plans tailored to the individual person.

The FDA has approved aflibercept and ranibizumab for the treatment of eyes with diabetic retinopathy. Other emerging therapies for retinopathy that may use sustained intravitreal delivery of pharmacologic agents are currently under investigation. Anti-VEGF treatment of eyes with nonproliferative diabetic retinopathy has been demonstrated to reduce subsequent development of retinal neovascularization and DME but has not been shown to improve visual outcomes over 2 years of therapy and therefore has not been widely adopted for this indication (46).

While the ETDRS (42) established the benefit of focal laser photocoagulation

therapy in eyes with clinically significant macular edema (defined as retinal edema located at or threatening the macular center), current data from well-designed clinical trials demonstrate that intravitreal anti-VEGF agents provide more effective treatment of center-involved DME than monotherapy with laser (47,48). Five anti-VEGF agents currently are used to treat eyes with center-involved DME, namely, bevacizumab (used off-label) and the on-label medications ranibizumab, aflibercept (2 mg and 8 mg), brolucizumab, and faricimab (5). A comparative effectiveness study demonstrated that aflibercept provides vision outcomes superior to those of bevacizumab when eyes have moderate visual impairment (vision of 20/50 or worse) from DME (49). With ranibizumab and aflibercept, most individuals require administration of intravitreal therapy with anti-VEGF agents every 4–8 weeks during the first 12 months of treatment, with fewer injections needed in subsequent years to maintain remission from center-involved DME. The more recently approved medications faricimab and aflibercept 8 mg can achieve visual acuity and anatomic gains similar to those of aflibercept 2 mg with adjustable dosing up to every 16 weeks (50,51). For eyes that have good vision (20/25 or better) despite DME, close monitoring with initiation of anti-VEGF therapy if vision worsens provides 2-year vision outcomes similar to those of immediate initiation of anti-VEGF therapy (52).

Eyes that have persistent DME despite anti-VEGF treatment may benefit from macular laser photocoagulation or intravitreal therapy with corticosteroids (53). Both of these therapies are also reasonable first-line approaches for individuals who are not candidates for anti-VEGF treatment due to systemic considerations such as pregnancy.

Adjunctive Therapy

Lowering blood pressure has been shown to decrease retinopathy progression, although strict goals (systolic blood pressure <120 mmHg) do not impart additional benefit (10). The presence of retinopathy is not a contraindication to aspirin therapy for cardioprotection, as aspirin does not increase the risk of retinal hemorrhage (54). In individuals with dyslipidemia, retinopathy progression may be slowed by the addition of fenofibrate, particularly with early diabetic retinopathy at baseline

(55–57). Statins are widely used to reduce the risk of vascular disease, including diabetic retinopathy. Their beneficial role in type 2 diabetes is well established even in individuals with retinopathy at diagnosis. In particular, the sight-threatening types of retinopathy, including DME and PDR, are reduced with statin use (58). Pioglitazone and rosiglitazone treatment might be associated with development or worsening of DME, although the evidence is conflicting (59).

Visual Rehabilitation

Recommendations

12.15 People who experience diabetes-related vision loss should be counseled on the availability and scope of vision rehabilitation care and provided, or referred for, a comprehensive evaluation of their visual impairment by a practitioner experienced in vision rehabilitation. **E**

12.16 People with diabetes-related vision loss should receive educational materials and resources for eye care support in addition to self-management education (e.g., glycemic management and hypoglycemia awareness). **E**

In the U.S., ~12% of adults with diabetes have some level of vision impairment (60). They may have difficulty reaching their diabetes treatment goals and performing many other activities of daily living, which can lead to depression, anxiety, social isolation, and difficulties at home, in the workplace, or at school (61).

People with diabetes are at increased risk of chronic vision loss, subsequent functional decline, and resulting disability. Vision impairment has physical, psychological, behavioral, and social consequences that affect people with diabetes, their families, friends, and caregivers. Health care professionals and stakeholders may not be aware of the overall impact of vision loss on an individual's health and well-being. People with diabetes-related vision loss should be evaluated to determine their potential to benefit from comprehensive vision restoration. Vision rehabilitation can help people with vision loss achieve maximum function, independence, and quality of life.

NEUROPATHY

Diabetic neuropathies are a heterogeneous group of disorders with diverse clinical

manifestations (4). The early recognition and appropriate management of neuropathy in people with diabetes is important (62). Points to be aware of include the following:

1. Diabetic neuropathy is a diagnosis of exclusion. Nondiabetic neuropathies may be present in people with diabetes and may be treatable.
2. Up to 50% of diabetic peripheral neuropathy (DPN) cases may be asymptomatic (63). If not recognized and if preventive foot care is not implemented, people with diabetes are at risk for injuries as well as diabetic foot ulcers (DFUs) and amputations. DFUs can be defined as a break of the epidermis and at least part of the dermis, below the ankle, in a person with diabetes. Consequences of DFUs include decline in functional status and reduced independence with daily activities, decreased quality of life, cost of wound care, infection, hospitalization, lower-extremity amputation, and death.
3. Recognition and treatment of autonomic neuropathy may improve symptoms, reduce sequelae, and improve quality of life (63). Cardiovascular autonomic neuropathy (CAN) can be a serious complication, as it can exacerbate cardiovascular disease and contribute to heart failure and sudden cardiac death (62).

Screening

Recommendations

12.17 All people with diabetes should be assessed for diabetic peripheral neuropathy starting at diagnosis of type 2 diabetes and 5 years after the diagnosis of type 1 diabetes and at least annually thereafter. **B**

12.18 Assessment for distal symmetric polyneuropathy should include a careful history and assessment of either temperature or pinprick sensation (small-fiber function) and vibration sensation using a 128-Hz tuning fork (large-fiber function). All people with diabetes should have annual 10-g monofilament testing to identify feet at risk for ulceration and amputation. **B**

12.19 Symptoms and signs of autonomic neuropathy should be assessed in people with diabetes starting at diagnosis of type 2 diabetes and 5 years after the diagnosis of type 1 diabetes, and at least annually thereafter, and

with evidence of other microvascular complications, particularly kidney disease and diabetic peripheral neuropathy. Screening can include asking about orthostatic dizziness, syncope, early satiety, erectile dysfunction, changes in sweating patterns, or dry cracked skin in the extremities. Signs of autonomic neuropathy include orthostatic hypotension, a resting tachycardia, or evidence of peripheral dryness or cracking of skin. **E**

Diagnosis

Diabetic Peripheral Neuropathy

Individuals who have had type 1 diabetes for 5 years and all individuals with type 2 diabetes should be assessed annually for DPN using medical history and simple clinical tests (63). Symptoms and signs of DPN vary according to the class of sensory fibers involved. The most common early symptoms are induced by the involvement of small fibers and include pain and dysesthesia (unpleasant sensations of burning and tingling). The involvement of large fibers may cause balance issues (including falls), numbness, and loss of protective sensation (LOPS). LOPS is a risk factor for DFU due to predisposition to unrecognized minor trauma. The following clinical tests may be used to assess small- and large-fiber function and protective sensation:

1. Small-fiber function: pinprick and temperature sensation
2. Large-fiber function: lower-extremity reflexes, vibration perception, proprioception, and 10-g monofilament
3. Protective sensation: 10-g monofilament, Ipswich touch test (64,65)

These tests not only screen for the presence of dysfunction but also predict future risk of complications. Electrophysiological testing, magnetic resonance imaging (MRI) scan of the spine (66), or referral to a neurologist is rarely needed, except in situations where the clinical features are atypical (acute or subacute presentation, non-length dependent, asymmetric, and/or motor involvement) or the diagnosis is unclear.

In all people with diabetes and DPN, causes of neuropathy other than diabetes should be considered, including toxins (e.g., alcohol), neurotoxic medications (e.g., chemotherapy), vitamin B12 (especially in

those treated chronically with metformin) and other nutritional deficiencies (e.g., acquired copper deficiency after metabolic surgery), hypothyroidism, kidney disease, malignancies (e.g., multiple myeloma, bronchogenic carcinoma), infections (e.g., HIV, hepatitis C), chronic inflammatory demyelinating neuropathy, inherited neuropathies, and vasculitis (67). See the American Diabetes Association position statement "Diabetic Neuropathy" for more details (63).

Diabetic Autonomic Neuropathy

Individuals who have had type 1 diabetes for 5 years and all individuals with type 2 diabetes should be assessed annually for autonomic neuropathy (63). The symptoms and signs of autonomic neuropathy should be elicited carefully during the history and physical examination. Major clinical manifestations of diabetic autonomic neuropathy include resting tachycardia, orthostatic hypotension, gastroparesis, constipation, diarrhea, fecal incontinence, erectile dysfunction, neurogenic bladder, and sudomotor dysfunction with either increased or decreased sweating. Screening for symptoms of autonomic neuropathy includes asking about symptoms of orthostatic intolerance (dizziness, lightheadedness, or weakness with standing), syncope, exercise intolerance, constipation, diarrhea, urinary retention, urinary incontinence, or changes in sweat function. Further testing can be considered if symptoms are present and will depend on the end organ involved but might include cardiovascular autonomic testing, sweat testing, urodynamic studies, gastric emptying, endoscopy or colonoscopy. Impaired counterregulatory responses to hypoglycemia in type 1 and type 2 diabetes can lead to impaired hypoglycemia awareness but are not directly linked to autonomic neuropathy.

Cardiovascular Autonomic Neuropathy

CAN is associated with mortality independent of other cardiovascular risk factors (68,69). In its early stages, CAN may be completely asymptomatic and detected only by decreased heart rate variability with deep breathing. Advanced disease may be associated with resting tachycardia (>100 bpm) and orthostatic hypotension (a fall in systolic or diastolic blood pressure by >20 mmHg or >10 mmHg, respectively, upon standing without an appropriate increase in heart rate).

Gastrointestinal Neuropathies

Gastrointestinal neuropathies are a diagnosis of exclusion (including consideration of gastrointestinal adverse effects due to medications such as metformin and/or GLP-1–based therapy). They may involve any portion of the gastrointestinal tract, with manifestations including esophageal dysmotility, gastroparesis, biliary dysfunction, constipation, diarrhea, and fecal incontinence (70). Gastroparesis should be suspected in individuals with erratic glycemic management or with upper gastrointestinal symptoms without another identified cause. Exclusion of reversible/iatrogenic causes such as medications (e.g., certain GLP-1–based therapies, opioids) or organic causes of gastric outlet obstruction or peptic ulcer disease (endoscopy and/or imaging) is needed before considering a diagnosis of or specialized testing for gastroparesis. The diagnostic gold standard for gastroparesis is the measurement of gastric emptying with scintigraphy of digestible solids at 15-min intervals for 4 h after food intake. The use of ^{13}C octanoic acid breath test is an approved alternative.

Genitourinary Disturbances

Diabetic autonomic neuropathy may also cause genitourinary disturbances, including sexual dysfunction and bladder dysfunction. In men, diabetic autonomic neuropathy may cause erectile dysfunction and/or retrograde ejaculation (63). Female sexual dysfunction occurs more frequently in those with diabetes and presents as decreased sexual desire, increased pain during intercourse, decreased sexual arousal, and inadequate lubrication (71). Lower urinary tract symptoms manifest as urinary incontinence and bladder dysfunction (nocturia, frequent urination, urinary urgency, and weak urinary stream). Evaluation of bladder function should be performed for individuals with diabetes who have recurrent urinary tract infections, pyelonephritis, incontinence, or a palpable bladder.

Treatment

Specific treatment to reverse the underlying nerve damage in diabetes is currently not available. Optimal glycemic management can effectively prevent DPN and CAN in type 1 diabetes (72,73) and may modestly slow their progression in type 2 diabetes (74), but it does not reverse

neuronal loss. Treatments of other modifiable risk factors (including obesity, lipids, and blood pressure) can aid in prevention of DPN progression in type 2 diabetes and may reduce disease progression in type 1 diabetes (75–78). Therapeutic strategies (pharmacologic and nonpharmacologic) for the relief of painful DPN and symptoms of autonomic neuropathy can potentially reduce pain (63) and improve quality of life. CAN treatment is generally focused on alleviating symptoms.

Recommendations

12.20 Optimize glucose management to prevent or delay the development of neuropathy in people with type 1 diabetes **A** and to slow the progression of neuropathy in people with type 2 diabetes. **C** Optimize weight, blood pressure, and lipid management to reduce the risk or slow the progression of diabetic neuropathy. **B**

12.21 Assess and treat pain related to diabetic peripheral neuropathy **B** and symptoms of autonomic neuropathy to improve quality of life. **E**

12.22 Gabapentinoids, serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants, and sodium channel blockers are recommended as initial pharmacologic treatments for neuropathic pain in diabetes. **A** Combinations of these medications can provide additional relief of neuropathic pain. **A** Opioids, including tramadol and tapentadol, should not be used for neuropathic pain treatment in diabetes given the potential for adverse events except in rare circumstances. **B**

Glycemic Management

Optimal glycemic management, implemented early in the course of diabetes, has been shown to effectively delay or prevent the development of DPN and CAN in people with type 1 diabetes (6,79–82). Although the evidence for the benefit of optimal glycemic management is not as strong for type 2 diabetes, some studies have demonstrated a modest slowing of progression without reversal of neuronal loss (74,83). Specific glucose-lowering strategies may have different effects. In a post hoc analysis, participants, particularly men, in the Bypass Angioplasty Revascularization Investigation in Type 2 Diabetes (BARI 2D) trial treated

with insulin sensitizers had a lower incidence of distal symmetric polyneuropathy over 4 years than those treated with insulin or sulfonylurea (84). Additionally, evidence from the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial showed benefit of intensive glucose and blood pressure management on the prevention of CAN in type 2 diabetes (85).

Weight Management

Obesity is consistently associated with neuropathy in cross-sectional and longitudinal studies (86). While obesity has been established as a risk factor for neuropathy, including in those with diabetes, the treatment of obesity and its impact on neuropathy outcomes are less well studied. The Look AHEAD (Action for Health in Diabetes) randomized trial found that a lifestyle intervention primarily focused on dietary weight loss led to improvements in neuropathy symptoms but not neuropathy examination scores (75). Observational studies of metabolic surgery have also revealed improvements in neuropathy outcomes, but randomized trials are lacking (77,78). Studies are emerging regarding weight loss medications and neuropathy; however, results have been conflicting and further studies are needed (87). Clinical evidence of potential benefits of GLP-1 RA agents on DPN is still controversial and limited (88). In contrast, altered skin sensation, including allodynia (i.e., pain evoked by contact, e.g., with socks, shoes, and bedclothes), has been described with use of either GLP-1 RA (89) or dual glucose-dependent insulinotropic polypeptide and GLP-1 RA agents (90). Exercise often leads to a small reduction in weight and may also have positive effects on diabetic neuropathy. Two systematic reviews have shown that exercise interventions improve diabetic neuropathy outcomes, including symptoms, examination findings, balance, and functional assessments, but the strength of the evidence is low (91,92).

Lipid Management

Dyslipidemia is a key factor in the development of neuropathy in people with type 2 diabetes and may contribute to neuropathy risk in people with type 1 diabetes (93,94). Although the evidence for a relationship between lipids and neuropathy development has become increasingly clear in type 2 diabetes (with high triglycerides showing the strongest relationship),

the optimal therapeutic intervention has not been identified. Positive effects of physical activity, weight loss, and metabolic surgery have been reported in individuals with DPN, but use of conventional lipid-lowering pharmacotherapy (such as statins or fibrates) does not appear to be effective in treating or preventing DPN development (95).

Blood Pressure Management

There are multiple reasons for blood pressure management in people with diabetes, and neuropathy progression (especially in type 2 diabetes) has now been added to this list. Although data from many studies have supported the role of hypertension in the risk of neuropathy development, a meta-analysis of data from 14 countries in the International Prevalence and Treatment of Diabetes and Depression (INTERPRET-DD) study revealed hypertension as an independent risk factor for DPN development with an odds ratio of 1.58 (95% CI 1.18–2.12) (96). In the ACCORD trial, intensive blood pressure intervention also decreased CAN risk by 25% (85).

Neuropathic Pain Management

Neuropathic pain can be severe and can impact quality of life, affect sleep, limit mobility, and contribute to depression and anxiety (97). No compelling evidence exists in support of glycemic or lifestyle management as therapies for neuropathic pain in diabetes or prediabetes, which leaves only pharmaceutical interventions (98). A recent guideline by the American Academy of Neurology (AAN) recommends that the initial treatment of pain should also focus on the concurrent treatment of both sleep and mood disorders because of increased frequency of these problems in individuals with DPN (99).

Several pharmacologic therapies exist for treatment of pain in diabetes (100). The AAN guideline update suggested that gabapentinoids, serotonin-norepinephrine reuptake inhibitors (SNRIs), sodium channel blockers, and tricyclic antidepressants (TCAs) all could be considered in the treatment of pain in DPN (99). These AAN recommendations offer a supplement to the American Diabetes Association pain monograph (101). A head-to-head trial suggested therapeutic equivalency for TCAs, SNRIs, and gabapentinoids in the treatment of pain in DPN (102). The trial also supported the role of combination therapy in those who did not respond well to monotherapy

for the treatment of pain in DPN. For those with severe painful symptoms not responding to a single agent, combination therapy with two to three agents may be effective at much lower doses, and pharmacological and nonpharmacological approaches may also be effective (63).

Gabapentinoids. Gabapentinoids include several calcium channel $\alpha 2\text{-}\delta$ subunit ligands. Several high-quality and medium-quality studies support the role of pregabalin in treatment of pain in DPN (103). One high-quality study and many small studies support the role of gabapentin in the treatment of pain in DPN. Medium-quality studies suggest that mirogabalin has a small effect on pain in DPN (99). Adverse effects may be more severe in older individuals (104) and may be attenuated by lower starting doses and more gradual titration.

SNRIs. SNRIs include duloxetine, venlafaxine, and desvenlafaxine, all selective SNRIs. Two high-quality studies and five medium-quality studies support the role of duloxetine in the treatment of pain in DPN. A high-quality study supports the role of venlafaxine in the treatment of pain in DPN. Only one medium-quality study supports a possible role for desvenlafaxine for treatment of pain in DPN (99). Adverse events may be more severe in older people but may be attenuated with lower doses and slower titration of duloxetine.

Tricyclic Antidepressants. TCAs have been studied for treatment of pain. Most of the relevant data were acquired from trials of amitriptyline and include two high-quality studies and two medium-quality studies supporting the effectiveness of amitriptyline in the treatment of painful DPN (99,102). Anticholinergic side effects may be dose limiting, especially in individuals ≥ 65 years of age.

Sodium Channel Blockers. Sodium channel blockers include lamotrigine, lacosamide, carbamazepine, oxcarbazepine, and valproic acid. Five medium-quality studies support the role of sodium channel blockers in treating pain in DPN (99).

Capsaicin. Capsaicin has received FDA approval for treatment of pain in DPN using an 8% patch, with one high-quality study reported (105). One medium-quality study

of 0.075% capsaicin cream has been reported (105). In individuals with contraindications to oral pharmacotherapy or who prefer topical treatments, the use of topical capsaicin can be considered.

Lidocaine 5% Plaster/Patch. Lidocaine patches have limited data supporting their use in DPN and are not effective in more widespread distribution of pain (although they may be of use in individuals with nocturnal neuropathic foot pain). Lidocaine patches cannot be used for more than 12 h in a 24-h period (106).

Opioids. Several randomized controlled trials (RCTs) have demonstrated that opioids (dextromethorphan, oxycodone, morphine sulfate) can reduce pain in individuals with DPN (106). However, evidence for the long-term efficacy of opioids in neuropathic pain is lacking. In fact, the Centers for Disease Control and Prevention (CDC) performed a systematic review that found no studies of opioids for chronic pain have evaluated long-term outcomes, including pain, function, and quality of life (107). Moreover, CDC and AAN reviews have documented the long-term harms from opioids, including abuse, addiction, fractures, heart attacks, motor vehicle accidents, overdose, and mortality (107,108). The current evidence balancing risks and benefits has led AAN to recommend against opioids for the treatment of painful DPN except in rare circumstances (99).

Tapentadol and Tramadol. Tapentadol and tramadol exert their analgesic effects through both μ -opioid receptor agonism (opioid) and norepinephrine and serotonin reuptake inhibition. Given that opioids and SNRIs are both effective for painful DPN, it is not surprising that these SNRI and opioid agents are effective in the treatment of pain in DPN too (99). However, the effect size is similar to that of other effective therapies, such as SNRIs, and these medications have the same risks as other opioids listed above. In fact, tramadol has been shown to be associated with all-cause mortality with an effect size similar to that of codeine (109). Similar to other opioids, risks likely outweigh benefits, and the AAN guidelines also recommend against their use for painful DPN except in rare circumstances (99).

Orthostatic Hypotension Management

Treating orthostatic hypotension is challenging. The therapeutic goal is to minimize

postural symptoms rather than to restore normotension. Most individuals require both nonpharmacologic measures (e.g., ensuring adequate salt intake, avoiding medications that aggravate hypotension, or using compressive garments over the legs and abdomen) and pharmacologic measures. Physical activity and exercise should be encouraged to avoid deconditioning, which is known to exacerbate orthostatic intolerance, and volume repletion with fluids and salt is critical. Additionally, supine blood pressure tends to be much higher in these individuals, often requiring treatment of blood pressure at bedtime with shorter-acting drugs that also affect baroreceptor activity such as guanfacine or clonidine, shorter-acting calcium blockers (e.g., isradipine), or shorter-acting β -blockers such as atenolol or metoprolol tartrate. Alternatives can include enalapril if an individual is unable to tolerate preferred agents (110–112). Midodrine and droxidopa are approved by the FDA for the treatment of orthostatic hypotension.

Gastroparesis Management

Treatment of diabetic gastroparesis may be very challenging. A small-particle eating pattern may provide some symptom relief (113–115). In addition, foods with small particle size may improve key symptoms (116). Withdrawing drugs with adverse effects on gastrointestinal motility, including opioids, anticholinergics, TCAs, GLP-1 RAs, and pramlintide, may also improve intestinal motility (113,117). However, the risk of removal of GLP-1–based therapies should be balanced against their potential benefits. In cases of severe gastroparesis, pharmacologic interventions are needed. Only metoclopramide, a prokinetic agent, is approved by the FDA for the treatment of gastroparesis (118). However, the level of evidence regarding the benefits of metoclopramide for the management of gastroparesis is weak, and given the risk for serious adverse effects (extrapyramidal signs such as acute dystonic reactions, drug-induced parkinsonism, akathisia, and tardive dyskinesia), its use in the treatment of gastroparesis beyond 12 weeks is no longer recommended by the FDA. It should be reserved for severe cases that are unresponsive to other therapies (117). Other treatment options include domperidone (available outside the U.S.) and erythromycin, which is only effective for short-term use due to tachyphylaxis (118). Gastric electrical stimulation

using a surgically implantable device has received approval from the FDA, although there are very limited data on DPN and the results do not support gastric stimulation as an effective therapy in diabetic gastroparesis (119).

Erectile Dysfunction Management

In addition to treatment of hypogonadism if present, treatments for erectile dysfunction may include phosphodiesterase type 5 inhibitors, intracorporeal or intra-urethral prostaglandins, vacuum devices, or penile prostheses (63). As with DPN treatments, these interventions do not change the underlying pathology and natural history of the disease process but may improve a person's quality of life.

FOOT CARE

Recommendations

12.23 Perform a comprehensive foot evaluation at least annually to identify risk factors for ulcers and amputations. **A**

12.24 The examination should include inspection of the skin, assessment of foot deformities, neurological assessment (10-g monofilament testing or Ipswich touch test with at least one additional assessment: pinprick, temperature, or vibration), and vascular assessment, including pulses in the legs and feet. **B**

12.25 Individuals with evidence of sensory loss or prior ulceration or amputation should have their feet inspected at every visit. **A**

12.26 Obtain a prior history of ulceration, amputation, Charcot foot, angioplasty or vascular surgery, cigarette smoking, retinopathy, and renal disease and assess current symptoms of neuropathy (e.g., pain, burning, numbness) and vascular disease (e.g., leg fatigue, claudication). **B**

12.27 Initial screening for peripheral artery disease (PAD) should include assessment of lower-extremity pulses, capillary refill time, rubor on dependency, pallor on elevation, and venous filling time. Individuals with a history of leg fatigue, claudication, and rest pain relieved with dependency or decreased or absent pedal pulses should be referred for ankle-brachial index with toe pressures and for further vascular assessment as appropriate. **B**

12.28 An interprofessional approach facilitated by a podiatrist in conjunction

with other appropriate team members is recommended for individuals with foot ulcers and high-risk feet (e.g., those on dialysis, those with Charcot foot, those with a history of prior ulcers or amputation, and those with PAD). **B**

12.29 Refer individuals who smoke and have a history of prior lower-extremity complications, loss of protective sensation (LOPS), structural abnormalities, or PAD to foot care specialists for ongoing preventive care and lifelong surveillance. **B** These individuals should also be provided with information on the importance of smoking cessation and referred for counseling on smoking cessation. **A**

12.30 Provide general preventive foot self-care education to all people with diabetes, including those with LOPS, on appropriate ways to examine their feet (palpation or visual inspection with an unbreakable mirror) for daily surveillance of early foot problems. **B**

12.31 The use of specialized therapeutic footwear is recommended for people with diabetes at high risk for ulceration, including those with LOPS, foot deformities, ulcers, callous formation, poor peripheral circulation, or history of amputation. **B**

12.32 For chronic diabetic foot ulcers that have failed to heal with optimal standard care alone, adjunctive treatment with randomized controlled trial-proven advanced agents should be considered (e.g., negative-pressure wound therapy, several skin substitutes, or topical oxygen therapy). **A**

Foot ulcerations, infections, and amputations are common complications associated with diabetes. These may be the consequences of several factors, including peripheral neuropathy, peripheral artery disease (PAD), and foot deformities. They represent major causes of morbidity and mortality in people with diabetes. Early recognition of at-risk feet and preulcerative lesions as well as prompt treatment of ulcerations and other lower-extremity complications can delay or prevent adverse outcomes. Infection can proceed rapidly in the neuroischemic extremity, often without signs or symptoms commensurate with its severity. Infection is usually the final precipitating cause of lower-extremity amputations (120).

Prevention and management of diabetic foot complications is a centerpiece of diabetes care. Early recognition requires an understanding of those factors that put people with diabetes at increased risk for ulcerations and amputations. Factors that are associated with the at-risk foot include the following:

- Chronic hyperglycemia
- Peripheral neuropathy/LOPS
- PAD
- Foot deformities (bunions, hammer-toes, Charcot joint, etc.)
- Preulcerative corns or calluses
- Prior ulceration
- Prior amputation
- Smoking
- Retinopathy
- Nephropathy (particularly individuals on dialysis or posttransplant)
- Social determinants of health such as socioeconomic status and access-to-care factors (121)

Identifying the at-risk foot begins with a detailed history documenting diabetes management, smoking history, exercise tolerance, history of claudication or rest pain, and prior ulcerations or amputations. A thorough examination of the feet should be performed annually in all people with diabetes and more frequently in at-risk individuals (122). The examination should include assessment of skin integrity, assessment for LOPS using the 10-g monofilament or Ipswich touch test (64,65) along with at least one other neurological assessment tool, pulse examination of the dorsalis pedis and posterior tibial arteries, and assessment for foot deformities such as bunions, hammertoes, and prominent

metatarsals, which increase plantar foot pressures and increase risk for ulcerations. At-risk individuals should be assessed at each visit and should be referred to foot care specialists for ongoing preventive care and surveillance. The physical examination can stratify people with diabetes into different categories and determine the frequency of these visits (123) (**Table 12.1**).

Evaluation for Loss of Protective Sensation

The presence of peripheral sensory neuropathy is the single most common component cause for foot ulceration. In a multicenter trial, peripheral neuropathy was found to be a component cause in 78% of people with diabetes with ulcerations and that the triad of peripheral sensory neuropathy, minor trauma, and foot deformity was present in >63% of participants (124). All people with diabetes should undergo a comprehensive foot examination at least annually or more frequently for those in higher-risk categories (122,123).

LOPS is vital to risk assessment and the identification of the foot at risk for ulceration. One of the most useful tests to determine LOPS is the 10-g monofilament test. The monofilament test should be performed with at least one other neurologic assessment tool (e.g., pinprick, temperature perception, ankle reflexes, or vibratory perception with a 128-Hz tuning fork or similar device). Absent monofilament sensation and one other abnormal test confirm the presence of LOPS (123). Notably, while the 10-g monofilament test alone allows for detection of more advanced DPN and risk for ulcerations, it does not reliably identify those individuals

with early disease that would benefit most from therapeutic intervention to prevent progression (62). Thus, the clinician should not use it as the sole method for DPN diagnosis. In the U.K. and several other countries, the Ipswich touch test is preferred to monofilament testing to identify at-risk feet and uses finger touch to assess for LOPS (64,65). Further neurological testing, such as nerve conduction studies, electromyography, nerve biopsy, or intraepidermal nerve fiber density biopsies, are not routinely indicated for the diagnosis of peripheral sensory neuropathy (63).

Evaluation for Peripheral Artery Disease

Initial screening for PAD should include a history of leg fatigue, claudication, and rest pain relieved with dependency. Physical examination for PAD should include assessment of lower-extremity pulses, capillary refill time, rubor on dependency, pallor on elevation, and venous filling time (122,125). Any individual exhibiting signs and symptoms of PAD should be referred for noninvasive arterial studies in the form of Doppler ultrasound with pulse volume recordings. While ankle-brachial indices will be calculated, they should be interpreted carefully, as they are known to be inaccurate in people with diabetes due to non-compressible vessels. Toe systolic blood pressure tends to be more accurate. Toe systolic blood pressure <30 mmHg is suggestive of PAD and an inability to heal foot ulcerations (126). Individuals with abnormal pulse volume recording tracings and toe pressures <30 mmHg with foot ulcers should be referred for formal vascular evaluation and angiography. Due to the high prevalence of PAD in people

Table 12.1—International Working Group on Diabetic Foot risk stratification system and corresponding foot screening frequency

Category	Ulcer risk	Characteristics	Examination frequency*
0	Very low	No LOPS and no PAD	Annually
1	Low	LOPS or PAD	Every 6–12 months
2	Moderate	LOPS + PAD, or LOPS + foot deformity, or PAD + foot deformity	Every 3–6 months
3	High	LOPS or PAD and one or more of the following: • History of foot ulcer • Amputation (minor or major) • Kidney failure	Every 1–3 months

Adapted with permission from Schaper et al. (123). LOPS, loss of protective sensation; PAD, peripheral artery disease. *Examination frequency suggestions are based on expert opinion and person-centered requirements.

with diabetes, the Society for Vascular Surgery and the American Podiatric Medical Association guidelines recommend that all people with diabetes >50 years of age should undergo screening via non-invasive arterial studies (125,127). If normal, these should be repeated every 5 years (125). The Wound Ischemia foot Infection (WIFI) staging system for diabetic foot lesions is being increasingly used not only to stage PAD severity and amputation risk but also to predict DFU healing (128–130).

Foot Care Education for People With Diabetes

All people with diabetes (and their caregivers), particularly those with the aforementioned high-risk conditions, should receive general foot care education, including appropriate management strategies (131–133). This education should be provided to all newly diagnosed people with diabetes as part of an annual comprehensive examination and to individuals with high-risk conditions at every visit. Recent studies have shown that while education improves knowledge of diabetic foot problems and self-care of the foot, it does not improve behaviors associated with active participation in their overall diabetes care and the achievement of personal health goals (134). Evidence also suggests that while education for people with diabetes and their families is important, the knowledge is quickly forgotten and needs to be reinforced regularly (135).

Individuals considered at risk should understand the implications of foot deformities, LOPS, and PAD; the proper care of the foot, including nail and skin care; and the importance of daily foot inspections. Individuals with LOPS should be educated on appropriate ways to examine their feet (palpation or visual inspection with an unbreakable mirror) for daily surveillance of early foot problems. People with diabetes should also be educated on the importance of referrals to foot care specialists. A recent study showed that people with diabetes and foot disease lacked awareness of their risk status and why they were being referred to an interprofessional team of foot care specialists. Further, they exhibited a variable degree of interest in learning further about foot complications (136).

Individuals' understanding of these issues and their physical ability to conduct proper foot surveillance and care should

be assessed. Those with visual difficulties, physical constraints preventing movement, or cognitive problems that impair their ability to assess the condition of the foot and to institute appropriate responses will need other people, such as family members, to assist with their care. Although not yet widely adopted, self-monitoring of foot temperatures with smart mats, smart insoles, or socks as indicators of inflammation have promise in the early identification of impending ulceration when incorporated into an interactive prevention protocol (137,138).

The selection of appropriate footwear and footwear behaviors at home should also be discussed (e.g., no walking barefoot, avoiding open-toed shoes). Therapeutic footwear with custom-made orthotic devices have been shown to reduce peak plantar pressures (133). Most studies use reduction in peak plantar pressures as an outcome as opposed to ulcer prevention. Certain design features of the orthoses, such as rocker soles and metatarsal accommodations, can reduce peak plantar pressures more significantly than insoles alone. A systematic review, however, showed there was no significant reduction in ulcer incidence after 18 months compared with standard insoles and extradePTH shoes. Further, it was also noted that evidence to prevent first ulcerations was nonexistent.

Treatment

Management recommendations for foot care for people with diabetes will be determined by their risk category. No-risk or low-risk individuals often can be managed with education and self-care. People in the moderate- to high-risk category should be referred to foot care specialists for further evaluation and regular surveillance as outlined in **Table 12.1**. This category includes individuals with LOPS, PAD, and/or structural foot deformities, such as Charcot foot, bunions, or hammertoes. Individuals with any open ulceration or unexplained swelling, erythema, or increased skin temperature should be referred urgently to a foot care specialist or interprofessional team.

Initial management recommendations should include daily foot inspection, use of moisturizers for dry, scaly skin, and avoidance of self-care of ingrown nails and calluses. Well-fitted athletic or walking shoes with customized pressure-relieving orthoses should be part of initial

recommendations for people with increased plantar pressures (as demonstrated by plantar calluses). Individuals with deformities such as bunions or hammertoes may require specialized footwear such as extradePTH shoes. Those with even more significant deformities, as in Charcot joint disease, may require custom-made footwear. For recalcitrant deformities or for recurrent ulcerations not amenable to conservative footwear therapy alone, appropriate surgical reconstruction by an experienced diabetic foot surgeon should be considered (133,139).

Special consideration should be given to individuals with neuropathy who present with a warm, swollen, red foot with or without a history of trauma and without an open ulceration. These individuals require a thorough workup for possible Charcot neuroarthropathy (140,141). Foot and ankle X-rays should be performed in all individuals presenting with the above clinical findings. Early diagnosis and treatment of this condition is of paramount importance in preventing deformities and instability that can lead to ulceration and amputation. These individuals require total non-weight-bearing and urgent referral to a foot care specialist for further management. Surgical reconstruction of these complex limb-threatening deformities has assumed an important role with many surgeries yielding high levels of success and limb salvage (139,142,143). Nonetheless, such procedures need to be approached by experienced surgeons with an appreciation not only for the complexities of deformity but also for the complexities of the individuals themselves.

Management of people with diabetes and PAD requires not only careful assessment but also both holistic and interventional approaches. See section 10, "Cardiovascular Disease and Risk Management," for details on the multifactorial management of PAD. Optimal management of glycemia, hypertension, dyslipidemia, smoking cessation, weight management, and antiplatelet agents and addressing other modifiable risk factors are important to prevent or slow any progression of microvascular and macrovascular complications. People with diabetes who have a major lower-limb amputation have a decreased 5-year survival rate. One study showed a 67% 5-year mortality rate in people with diabetes who had a major limb amputation compared with a 57% 5-year mortality rate in those

without diabetes (144). Most of the excess morbidity and mortality in these individuals is related to cardiovascular disease and emphasizes the need for good glycemic and cardiovascular risk management.

Emerging glucose-lowering therapies with PAD (and other cardiovascular disease) benefits include GLP-1 RA agents. Treatment with GLP-1 RAs may reduce risk of lower-extremity amputations, DFUs, and all-cause mortality compared with sodium-glucose cotransporter 2 (SGLT2) inhibitors (145). For example, oral semaglutide had a significantly lower rate of major adverse limb events (e.g., hospitalization for acute and chronic limb ischemia) in the designated cardiovascular outcome trial (146). In addition, the Semaglutide and Walking Capacity in People with Symptomatic Peripheral Artery Disease and Type 2 Diabetes (STRIDE) study investigated the impact of injectable semaglutide in individuals with type 2 diabetes and PAD who were identified at the earliest symptomatic stage of PAD (Fontaine stage IIa) (147). Semaglutide significantly improved minimal and pain-free walking distance, quality of life, and disease progression based on composite outcomes of rescue therapy initiation, all-cause death, or major adverse limb events within the 52-week study period. Post hoc subgroup analyses showed that the benefits of semaglutide were independent of baseline diabetes duration, A1C levels, BMI status, or concomitant SGLT2 inhibitor treatment. In contrast, the SGLT2 inhibitor canagliflozin was associated with an increased risk of lower-limb amputation (mostly affecting toes) in the Canagliflozin Cardiovascular Assessment Study (CANVAS) cardiovascular outcome trial (148). The mechanism by which canagliflozin may increase the risk of amputations is unknown. As a precaution, stopping canagliflozin should be considered if an individual develops a significant lower-limb complication (e.g., DFU, osteomyelitis, or gangrene), at least until the condition has resolved.

Individuals diagnosed with or suspected of having PAD, especially when associated with DFU, infection, or gangrene, require referral to vascular interventionists or vascular surgeons for appropriate angiography and revascularization (125). Time is often of the essence, since delays in treatment can lead to further tissue loss. Although there is still some debate over the benefits of endovascular versus open surgical revascularization, it is clear that

treatment needs to be individualized to the specific individual-level comorbidities as well as vascular anatomy and patterns of arterial insufficiency.

Infection is a potentially limb-threatening complication and must not only be diagnosed at earliest presentation but also treated promptly and aggressively (149). Not all ulcers are clinically infected, but when exhibiting clinical signs of infection or when bone is exposed or probed, appropriate diagnostic measures must be used. Tissue samples for culture and sensitivity and radiologic or other imaging should be undertaken to ascertain the presence of bone erosions/osteomyelitis, abscesses, or gas. When equivocal findings on radiographs are present, computed tomography scans, MRI, or other advanced imaging techniques should be considered. Abscesses need to be drained promptly, either at chairside or in a formal operating room setting depending upon the extent and severity of infection. Necrotizing soft tissue infections and wet gangrene are surgical emergencies and need immediate surgical referral for wide incision and drainage, often including amputation to manage the source of infection. Underlying osteomyelitis often complicates deep or long-standing ulcers. MRI is most useful for determining the extent of bone infection and is often used for preoperative planning. While not generally presenting as acute infections, osteomyelitis needs to be properly diagnosed with bone cultures and histopathology and managed with either conservative, surgical, or combined approaches. The International Working Group on the Diabetic Foot (IWGDF) and the Infectious Diseases Society of America (IDSA), in their combined intersociety guideline, fully discuss the diagnosis, classification, and treatment of diabetes-related foot infections, including general recommendations for antimicrobial therapies (149). Most importantly, treatment of diabetes-related foot infections needs to be individualized based upon its severity as well as upon important individual-level comorbidities (including PAD).

Most DFUs should heal if pressure is removed from the ulcer site, the arterial circulation is sufficient, and infection is managed and treated aggressively. In addition, there have been a number of developments in the treatment of ulcerations over the years (150). These include negative-pressure therapy, growth factors, bioengineered tissue, acellular matrix tissue,

stem cell therapy, hyperbaric oxygen therapy, and topical oxygen therapy (151–153). While there is literature to support many modalities currently used to treat diabetic foot wounds, robust RCTs are often lacking. However, it is agreed that the initial treatment and evaluation of ulcerations include the following five basic principles of ulcer treatment:

- Offloading or pressure relief of ulcerations
- Debridement of hyperkeratotic, necrotic, or nonviable tissue
- Revascularization of ischemic wounds when necessary
- Management of infection: soft tissue or bone
- Use of wound-appropriate topical dressings

However, despite following the above principles, some ulcerations will become chronic and fail to heal. Careful evaluation is necessary to determine if there are associated deformities predisposing to high plantar pressures that need to be addressed with surgical offloading procedures to expedite healing (139,154–156). Additionally, underlying osteomyelitis must be ruled out as a cause for the nonhealing ulcer and treated as necessary. Once these complicating factors have been addressed, adjunctive advanced wound therapy can play an important role. When to use advanced wound therapy has been the subject of much discussion, as the therapy is often quite expensive. It has been determined that if a wound fails to show a reduction of 50% or more after 4 weeks of appropriate wound management (i.e., the five basic principles above), consideration should be given to the use of advanced wound therapy (157). Treatment of these chronic wounds is best managed in an interprofessional setting.

Evidence to support advanced wound therapy is challenging to produce and to assess. Randomization of trial participants is difficult, as there are many variables that can affect wound healing. In addition, many RCTs exclude certain cohorts of people, e.g., individuals with chronic kidney disease and especially those on dialysis. Finally, blinding of participants and clinicians is not always possible. Meta-analyses and systematic reviews of observational studies are used to determine the clinical

effectiveness of these modalities. Such studies can augment formal RCTs by including a greater variety of participants in various clinical settings who are typically excluded from the more rigidly structured clinical trials. Nonetheless, use of those products or agents with robust RCTs or systematic reviews should generally be preferred over those without grade A evidence (158).

Advanced wound therapy can be classified into several broad categories (150). Topical growth factors, acellular matrix tissues, placental tissues, and bioengineered cellular therapies are commonly used in offices and wound care centers to expedite healing of chronic, more superficial ulcerations. Over the years, there has been increased evidence to support the use of these modalities.

Negative-pressure wound therapy was first introduced in the early to mid-1990s. It has become especially useful in wound preparation for skin grafts and flaps and assists in the closure of deep, large wounds (159). A variety of types exist in the marketplace and range from electrically powered to mechanically powered in different sizes depending upon the specific wound requirements.

Electrical stimulation, pulsed radiofrequency energy, and extracorporeal shock-wave therapy are biophysical modalities that are believed to upregulate growth factors or cytokines to stimulate wound healing, while low-frequency noncontact ultrasound is used to debride wounds. However, most of the studies advocating the use of these modalities have been retrospective observational studies or poor-quality RCTs (152).

Hyperbaric oxygen therapy is the delivery of oxygen through a chamber, either individual or multiperson, with the intention of increasing tissue oxygenation to increase tissue perfusion and neovascularization, combat resistant bacteria, and stimulate wound healing. While there had been great interest in this modality being able to expedite healing of chronic DFUs, there has only been one RCT with positive results that reported increased healing rates at 9 and 12 months compared with control participants (160). Several other studies with significant design deficiencies and participant dropouts have failed to provide corroborating evidence that hyperbaric oxygen therapy should be widely used for managing nonhealing DFUs (161,162). While there may be some

benefit in prevention of amputation in selected chronic neuroischemic ulcers, studies have shown no benefit in healing DFUs in the absence of ischemia and/or infection (152,163).

Topical oxygen therapy has been studied rather vigorously, with several high-quality RCTs and systematic reviews and meta-analyses all supporting its efficacy in healing chronic DFUs at 12 weeks (151,153,164–168). Three types of topical oxygen devices are available, including continuous-delivery, low-constant-pressure, and cyclical-pressure modalities. Importantly, topical oxygen therapy devices provide for home-based therapy and replace the need for daily visits to specialized centers. Very high participation with very few reported adverse events combined with improved healing rates makes this therapy another attractive option for advanced wound care (164–168).

If DFUs fail to heal despite appropriate standard or surgical wound care, adjunctive advanced therapies should be instituted and are best managed in an interprofessional manner. Those products with grade A evidence to support their efficacy should be considered over those with less robust or no evidence at all. FDA-approved products for DFUs include living, bioengineered skin substitutes like Apligraf and Derma-graft, along with growth factor products like becaplermin. Once healed, all individuals should be enrolled in a formal comprehensive prevention program focused on reducing the incidence of recurrent ulcerations and subsequent amputations (122,133,169). These principles are outlined in the above section, foot care education for people with diabetes.

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13. Older Adults: Standards of Care in Diabetes—2026

American Diabetes Association
Professional Practice Committee for
Diabetes*

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The American Diabetes Association (ADA) “Standards of Care in Diabetes” includes the ADA’s current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. Members of the ADA Professional Practice Committee for Diabetes, an interprofessional expert committee, are responsible for updating the Standards of Care annually, or more frequently as warranted. For a detailed description of ADA standards, statements, and reports, as well as the evidence-grading system for ADA’s clinical practice recommendations and a full list of Professional Practice Committee members, please refer to Introduction and Methodology. Readers who wish to comment on the Standards of Care are invited to do so at professional.diabetes.org/SOC.

Recommendations

13.1 Assess the medical, psychological, functional (self-management abilities), and social domains in older adults with diabetes using a comprehensive approach to determine goals and therapeutic approaches for diabetes management. **B**

13.2 Screen at least annually for geriatric syndromes (e.g., cognitive impairment, depression, urinary incontinence, falls, persistent pain, and frailty), hypoglycemia, and polypharmacy in older adults with diabetes, as they may affect diabetes management and diminish quality of life. **B**

Diabetes is a highly prevalent health condition in the aging population. Over 29% of people over the age of 65 years have diabetes (1,2). The number of older adults living with diabetes is expected to increase rapidly in the coming decades as the population ages and the effects of increasing obesity rates manifest in this population (3). Importantly, diabetes in older adults is a highly heterogeneous condition. While type 2 diabetes predominates in the older population (as in the younger population), improvements in insulin delivery, technology, and care over the last few decades have led to increasing numbers of people with childhood and adult-onset type 1 diabetes surviving and thriving into their later decades. Type 1 diabetes is increasingly diagnosed in older adulthood as well, with greater awareness of and attention to appropriate diabetes classification across the life course, with higher incidence in Western countries (4).

Diabetes management in older adults requires regular assessment of medical, psychological, functional, and social domains. When assessing older adults with diabetes, it is important to accurately categorize the type of diabetes, diabetes duration, the presence of complications and comorbidities, the individual’s capacity for self-management and availability of support systems, treatment burden, and treatment-related concerns, such as fear of hypoglycemia, polypharmacy, and financial barriers. Screening for

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diabetes complications in older adults should be individualized and periodically revisited, as this may affect treatment goals and therapeutic approaches (5–7). Older adults with diabetes have higher rates of functional disability, accelerated muscle loss, mobility impairment, frailty, and coexisting illnesses, such as hypertension, chronic kidney disease, coronary heart disease, stroke, and premature death than those without diabetes (2,8). They also have higher rates of common geriatric syndromes such as cognitive impairment, depression, urinary incontinence, falls, persistent pain, frailty, and polypharmacy (1). These conditions may affect older adults' diabetes self-management abilities and quality of life, particularly if unaddressed, and older adults with diabetes often require greater caregiver support than those without diabetes (2,9–11). See section 4, "Comprehensive Medical Evaluation and Assessment of Comorbidities," for the full range of issues to consider when caring for older adults with diabetes.

The Institute for Healthcare Improvement has developed an evidence-based "4Ms" framework for age-friendly health care that is being adopted by many health systems caring for older adults. The key elements of this approach are Mentation,

Medications, Mobility, and What Matters Most, with each element affecting the others (12). The 4Ms framework provides a helpful conceptual model to address person-specific issues that may be interrelated and affect diabetes management in older individuals (Fig. 13.1) and offers a framework to establish individualized treatment goals and approaches (13–15), including delivery of diabetes self-management education (particularly when complicating factors arise or when transitions in care occur) and whether the current plan is too complex for the individual's self-management ability or for the care partners providing care (16). Particular attention should be paid to complications that can develop over short periods of time and/or would significantly impair functional status, such as visual and lower-extremity complications. Table 13.1 suggests a structured approach to screening for common geriatric syndromes and other causes of functional impairment using key screening questions, followed by validated screening tools when specific geriatric syndromes are suspected, as well as resources for scoring. These tools should be used when clinically indicated and can be performed by any member of the diabetes care team. Importantly, the general care principles discussed here apply

to all individuals with complex health needs and are not limited to older adults.

NEUROCOGNITIVE FUNCTION

Recommendation

13.3 Screening for early detection of mild cognitive impairment or dementia should be performed for adults 65 years of age or older at the initial visit, annually, and as appropriate. **B**

Older adults with diabetes are at higher risk of cognitive decline and institutionalization than older adults without diabetes (17–19). Presentation of cognitive impairment ranges from subtle executive dysfunction to memory loss to overt dementia. People with diabetes have higher incidences of all-cause dementia, Alzheimer disease, and vascular dementia than people without diabetes (20). People with Alzheimer disease or other dementias are more likely to develop diabetes than those without it; this possible link emphasizes critical metabolic processes that contribute to neurodegeneration (21). Both hyperglycemia and hypoglycemia are associated with a decline in cognitive function (22,23), and longer duration of diabetes is associated with worsening cognitive function. A newly

Using the 4Ms framework of age-friendly health systems to address person-specific issues that can affect diabetes management

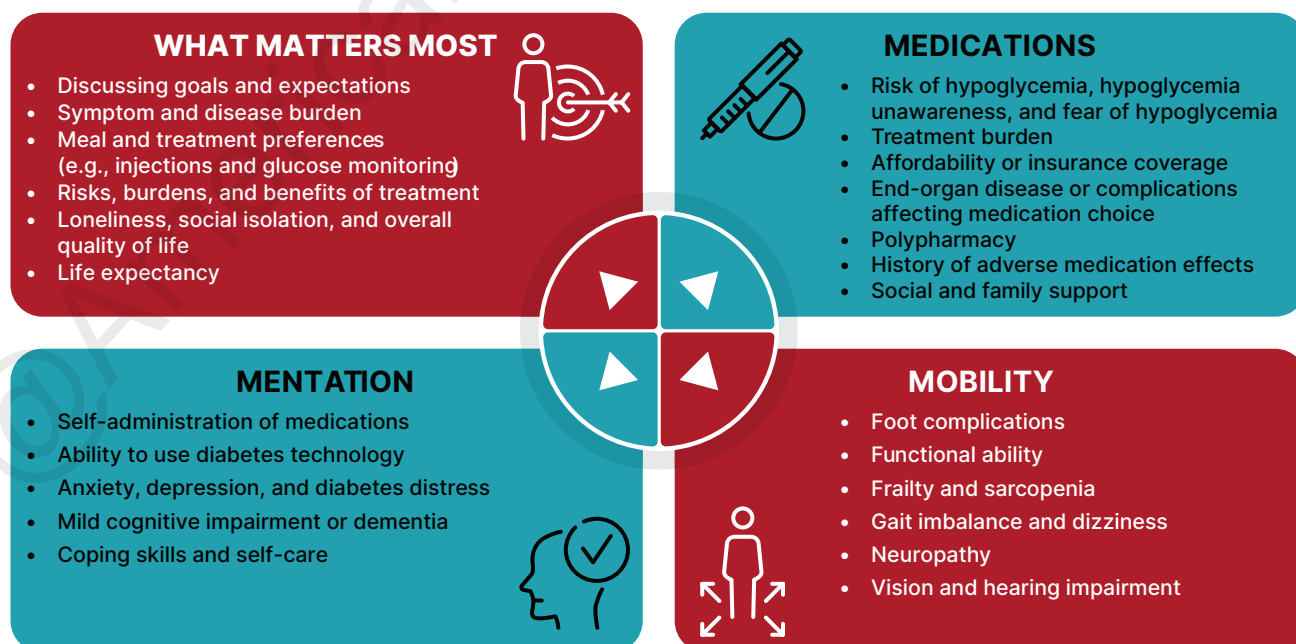


Figure 13.1—Using the 4Ms framework of age-friendly health systems to address person-specific issues that can affect diabetes management.

Table 13.1—Geriatric syndromes and other functional impairments: key symptoms and suggested screening approaches

Domain	Sample screening questions	Suggested screening measure	No. of items	Score range	Cut points	Time to complete	Measure translated languages
Geriatric syndromes							
Cognitive impairment or dementia	Have you noticed any changes in your memory or ability to think clearly?	Mini-Cog (31)	5	0–5	<3 validated for dementia screening	3 min	Multiple
Delirium	What day of the week is it?	4AT (182)	4	0–12	≥4 possible delirium	2 min	Multiple
Depression	During the past month, have you often been bothered by feeling down, depressed, or hopeless?	Geriatric Depression Scale 5 (GDS-5) (183,184)	5	0–5	≥2 possible depression	2 min	Multiple
Falls and risk of falling	Have you fallen in the past year or are you afraid of falling due to a balance or walking problem?	STEADI tool (185)	3	0–3	A single “yes” response to any question indicates an increased risk of falling	1–2 min	Multiple
Frailty	Have you felt unusually tired recently or had difficulty walking up steps without resting?	Clinical Frailty Scale (CFS) (186)	1	1–9	≥5 clinically meaningful frailty	1–2 min	Multiple
Malnutrition	Have you unintentionally lost weight in the last 6 months?	Mini Nutritional Assessment Short Form (MNA-SF) (187)	6	0–14	12–14, normal nutritional status; 8–11, at risk for malnutrition; 0–7, malnourished	5 min	Multiple
Pain	Are you currently experiencing any pain?	Numeric Pain Rating Scale	1	0–10	1–3, mild; 4–6, moderate; 7–10, severe	1–2 min	NA
Polypharmacy	Are you taking more medications than you think you should, or are you experiencing side effects?	Beers Criteria or review all prescription and nonprescription medications (188)	List review	NA	The presence of any medication on the list warrants review, especially if the risk outweighs the benefit	Varies	Multiple
Sarcopenia	Have you had difficulty walking across a room or climbing a flight of stairs in the past year?	SARC-F Questionnaire (189)	5	0–10	≥4 sarcopenia risk	2–3 min	Multiple
Sensory impairment: hearing	Do you have difficulty hearing, even when using a hearing aid?	Whisper test (190)	6	NA	Possible hearing loss: unable to repeat at least 3 of the random letters and numbers	2–3 min	NA

Continued on p. S280

Table 13.1—Continued

Domain	Sample screening questions	Suggested screening measure	No. of items	Score range	Cut points	Time to complete	Measure translated languages
Sensory impairment: vision	Do you have difficulty seeing, even when wearing your glasses?	Snellen chart	1	NA	20/40 or worse indicates vision impairment	2–3 min	NA
Sleep disorders: insomnia	Do you have trouble falling asleep, staying asleep, or waking up too early and not being able to fall back asleep?	Insomnia Severity Index 7 (ISI-7) (191)	7	0–28	≥8 insomnia	3 min	Multiple
Urinary incontinence	Do you have trouble with bladder control or accidental leakage?	3 Incontinence Questions (3IQ) (192)	3	NA	The tool classifies type of incontinence based on responses	1–2 min	Multiple
Functional impairments							
Dexterity	Do you have trouble using your hands for everyday tasks like buttoning clothes?	Button and coin test: button and unbutton a shirt button and pick up a small coin from a flat surface	2	0–2	0, significant impairment; 1, mild to moderate impairment; 2, limited to no impairment	1–2 min	NA
Dizziness	Do you experience dizziness, feeling lightheaded, or a feeling of spinning (vertigo)? Have you noticed any changes in your balance or steadiness?	Orthostatic vital signs; neurological examination (e.g., assessment of gait, balance, reflexes, sensory loss, vestibular function); medical evaluation	NA	NA	NA	NA	NA
Executive functioning	Do you find it hard to plan or organize your daily activities?	Trail Making Test B	25	Time to finish	≥180 s indicates impairment in executive function	3–5 min	Multiple

This table summarizes key symptoms and suggested screening approaches for common geriatric syndromes and other functional impairments that can be present in older adults with diabetes. NA, not applicable.

recognized clinical entity, diabetes-related dementia, is emerging as distinct from Alzheimer disease and vascular dementia. Diabetes-related dementia is characterized by a slower progression of dementia, absence of typical neuroimaging findings, advanced age, elevated A1C levels, long duration of diabetes, high frequency of insulin use, frailty, sarcopenia, and dynapenia (loss of muscle strength not caused by neurologic or muscular diseases) (23). Ongoing studies are evaluating whether lifestyle interventions may help to maintain cognitive function in older adults (24). However, studies on diabetes prevention or intensive glycemic and blood pressure management have not demonstrated a reduction in cognitive decline (25,26). Several glucose-lowering drugs, such as thiazolidinediones, glucagon-like peptide 1 receptor agonists (GLP-1 RAs) and sodium-glucose cotransporter 2 (SGLT2) inhibitors, have shown small benefits on slowing progression of cognitive decline (27). A systematic review and meta-analysis found that although cardioprotective glucose-lowering therapies were not associated with a reduction in all-cause dementia, GLP-1 RAs were associated with a statistically significant reduction in all-cause dementia (28). Notably, cardiovascular risk factors are also associated with an increased risk of cognitive decline and dementia. Management of blood pressure and cholesterol lowering with statins have been associated with a reduced risk of incident dementia and are, thus, particularly important in older adults with diabetes.

Older adults with diabetes should be carefully screened and monitored for cognitive impairment (2). Several assessment tools are available to screen for cognitive impairment (29,30), such as the Mini-Cog (31), Mini-Mental State Examination (32), and the Montreal Cognitive Assessment (33), which may help identify individuals with dementia (who are experiencing memory loss, a decrease in executive function, and declines in their basic and instrumental activities of daily living) or those requiring neuropsychological evaluation when dementia is suspected. Annual screening is indicated for adults 65 years of age or older for early detection of mild cognitive impairment or dementia (6,34). Screening for cognitive impairment should also be performed when an individual presents with a significant decline in clinical status due to increased problems with self-care

activities and medication management, such as errors in calculating insulin dose, difficulty counting carbohydrates, skipped meals, skipped insulin doses, and difficulty recognizing, preventing, or treating hypoglycemia. People who screen positive for cognitive impairment should receive diagnostic assessment as appropriate, including referral to a behavioral health professional for formal cognitive and neuropsychological evaluation if indicated and feasible (35).

Identifying cognitive impairment early has important implications for diabetes care. The presence of cognitive impairment can make it challenging to reach individualized glycemic, blood pressure, and lipid goals. Cognitive dysfunction may make it difficult for individuals to perform complex self-care tasks (29), such as monitoring glucose, administering and adjusting insulin doses, and maintaining the timing and nutritional content of meals. These factors increase risk for hypoglycemia, which, in turn, can worsen cognitive function and have multiple other adverse effects in older individuals with diabetes. When cognitive dysfunction is identified, it is therefore essential to simplify care plans and engage the appropriate support structure to assist aging individuals with diabetes in all aspects of their care.

HYPOGLYCEMIA

Recommendations

13.4 Ascertain and address episodes of hypoglycemia at routine visits because older adults with diabetes have a greater risk of hypoglycemia, especially when treated with hypoglycemic agents (e.g., sulfonylureas, meglitinides, and insulin). **B**

13.5 Recommend continuous glucose monitoring (CGM) for older adults with type 1 diabetes **A** and type 2 diabetes on insulin therapy **B** to improve glycemic outcomes, reduce hypoglycemia, and reduce treatment burden.

13.6 Consider the use of automated insulin delivery systems **B** and other advanced insulin delivery devices such as connected pens **E** to reduce risk of hypoglycemia for older adults, based on individual ability and support system.

Older adults may be at higher risk of hypoglycemia for many reasons, including irregular meal intake, particularly in the

setting of requiring insulin therapy, and worsening kidney function (36). As described above, older adults have higher rates of cognitive impairment and dementia, leading to difficulties in performing complex self-care activities (e.g., glucose monitoring, insulin administration and dose adjustment). Cognitive decline has been associated with increased risk of hypoglycemia, and conversely, severe hypoglycemia has been linked to increased risk of dementia (37–39). Therefore, as discussed in Recommendation 13.3, it is important to routinely screen older adults for cognitive impairment and dementia and discuss findings with the individuals and their care partners.

People with diabetes and their care partners should be routinely queried about any history of hypoglycemic events, impaired hypoglycemia awareness, and fear of hypoglycemia as discussed in section 6, “Glycemic Goals, Hypoglycemia, and Hyperglycemic Crises.” Symptoms and signs of hypoglycemia are also discussed in section 6 and are of value to care partners of individuals with cognitive impairment who may not be able to report hypoglycemia symptoms. Older adults can also be stratified for future risk for hypoglycemia with validated risk calculators (e.g., Kaiser Hypoglycemia Model for adults with type 2 diabetes) (40) and with consideration of hypoglycemia risk factors (**Table 6.5**). An important step to mitigate hypoglycemia risk is to determine whether the person with diabetes is skipping meals or has difficulty correctly taking and dosing their glucose-lowering medications. Glycemic goals and pharmacologic treatments may need to be adjusted to minimize the occurrence of hypoglycemic events, prioritizing use of medications at low risk for hypoglycemia and other adverse effects (41). This recommendation is also supported by results from multiple randomized controlled trials (RCTs), such as the Action to Control Cardiovascular Risk in Diabetes (ACCORD) study and the Veterans Affairs Diabetes Trial (VADT), which showed that intensive treatment protocols aimed to achieve an A1C <6.0% with complex drug plans significantly increased the risk for hypoglycemia requiring assistance compared with standard treatment (42,43). However, these intensive treatment plans included extensive use of insulin and minimal use of GLP-1 RAs, and they preceded the availability of SGLT2 inhibitors. Hypoglycemia

may also be precipitated by acute illness and other stressful events such as trauma or surgery. During these events, older adults and their care partners should be provided individualized guidance on glycemic monitoring and adjustment of glucose-lowering medications to prevent hypoglycemia. See **INTERCURRENT ILLNESS** in section 6, “Glycemic Goals, Hypoglycemia, and Hyperglycemic Crises,” for more details.

Use of Continuous Glucose Monitoring and Advanced Insulin Delivery Devices

Continuous glucose monitoring (CGM) devices have been shown to be effective at improving glycemic management and acceptable to people of all age-groups, including older individuals with type 1 diabetes (44–48) or insulin-requiring type 2 diabetes (49,50). Additionally, benefits have been shown with CGM use in older individuals not treated with insulin, particularly for reducing hypoglycemia and improving other glycemic outcomes. Importantly, it may take longer for older adults to learn and gain facility with new technology and it may be beneficial to engage their caregivers in the process. Moreover, it is important to assess a person’s cognitive and functional capacity for using technology and to ensure availability of engagement and support of the care partner, if appropriate (51). CGM may also be useful for glucose monitoring in older adults with physical and/or cognitive limitations who require monitoring of blood glucose by a surrogate and in those who reside in group homes, assisted living facilities, or other post-acute long-term care settings.

Advanced insulin delivery devices have similarly been shown to improve glycemic outcomes in small studies conducted among older adults. The Older Adult Closed Loop (ORACL) trial in 30 older adults (mean age 67 years) with type 1 diabetes found that an automated insulin delivery (AID) strategy was associated with significant improvements in time in range (TIR), as well as modest improvements in hypoglycemia, compared with sensor-augmented pump therapy (52). In a different open-label, crossover design clinical trial in 37 older adults (aged ≥ 60 years), 16 weeks of treatment with a hybrid closed-loop advanced insulin delivery system improved TIR and reduced time above range compared with sensor-augmented pump therapy; however, in contrast to the ORACL study,

no significant differences in hypoglycemia were observed (53). Both studies enrolled older individuals whose blood glucose was relatively well managed at baseline (mean A1C $\sim 7.4\%$). A later RCT of older adults with type 2 diabetes using multiple daily injections who were unable to manage insulin therapy on their own demonstrated an increase of TIR of 27% over 12 weeks of AID use in addition to tailored home health care services (54). More recently, in the Automated Insulin Delivery in Elderly With Type 1 Diabetes (AIDE T1D) study that included 82 adults aged 65 years and older, participants randomized to AID use experienced less hypoglycemia than those randomized to hybrid closed loop, predictive low glucose suspend, and sensor-augmented pump therapy in a crossover design (55). In the extension phase of the study, 91% of the participants chose the AID system (55). Finally, a real-world evidence analysis of a Medicare population (4,243 individuals, 89% with type 1 diabetes, mean age 67.4 years) also indicated that initiating hybrid closed-loop insulin delivery was associated with improvements in mean glucose and a 10% increase in TIR (56). These studies provide evidence that older individuals with type 1 and type 2 diabetes can successfully use advanced insulin delivery technologies to improve glycemic outcomes, as has been seen in younger populations.

TREATMENT GOALS

Recommendations

13.7a Older adults with diabetes with few and stable coexisting chronic illnesses, and intact cognitive and functional status, should have lower glycemic goals (such as A1C <7.0 – 7.5% [<53 – 58 mmol/mol]) and/or time in range [TIR] 70 – 180 mg/dL [3.9 – 10.0 mmol/L] of $\geq 70\%$ and time below range ≤ 70 mg/dL [≤ 3.9 mmol/L] of $\leq 4\%$ if CGM is used. **C**

13.7b Older adults with diabetes and intermediate or complex health are clinically heterogeneous with variable life expectancy. Selection of glycemic goals should be individualized and should prioritize avoidance of hypoglycemia, with less stringent goals (such as A1C $<8.0\%$ [<64 mmol/mol] and/or TIR 70 – 180 mg/dL [3.9 – 10.0 mmol/L] of $\geq 50\%$ and time below range

<70 mg/dL [3.9 mmol/L] of $<1\%$) for those with significant cognitive and/or functional limitations, frailty, severe comorbidities, and a less favorable risk-to-benefit ratio of diabetes medications. **C**

13.7c Older adults with very complex or poor health receive minimal benefit from stringent glycemic goals. Clinicians should focus on avoiding hypoglycemia and symptomatic hyperglycemia. **C**

13.8 Screening for diabetes complications should be individualized in older adults with diabetes. Prioritize screening for complications that would lead to impairment of functional status or quality of life. **C**

13.9 The on-treatment blood pressure goal for most older adults with diabetes is $<130/80$ mmHg when it can be achieved safely, **A** and more a relaxed blood pressure goal (e.g., $<140/90$ mmHg) may be used for people with poor health, limited life expectancy, or high risk for adverse effects of hypertensive therapy. **E**

13.10 Treatment of other cardiovascular risk factors should be individualized in older adults with diabetes, considering the time frame of benefit. Lipid-lowering therapy and antiplatelet agents may benefit those with life expectancies at least equal to the time frame of primary prevention or secondary intervention trials. **A**

As for all people with diabetes, diabetes self-management education and ongoing diabetes self-management support are vital components of diabetes care for older adults and their caregivers. Self-management knowledge and skills should be reassessed following a significant clinical change or hospitalization, when treatment plan changes are made, or when an individual’s functional abilities diminish. In addition, declining or impaired ability to perform diabetes self-care behaviors may be an indication that an older person with diabetes needs a referral for cognitive and physical functional assessment, using age-normalized evaluation tools, as well as help establishing a support structure for diabetes care (5,35). See **Table 13.1** for screening and evaluation tools for geriatric syndromes and other functional impairments.

The care of older adults with diabetes is complicated by their clinical, cognitive, and functional heterogeneity and their

varied prior experience with disease management. Some older individuals may have developed diabetes years earlier and have significant complications, others are newly diagnosed and may have had years of undiagnosed diabetes with resultant complications, and still, other older adults may have truly recent-onset disease with few or no complications (57). Some older adults with diabetes have other underlying chronic conditions, substantial diabetes-related comorbidity, limited cognitive or physical functioning, or frailty (58,59). Other older individuals with diabetes have little comorbidity and intact cognitive and physical functioning.

Life expectancy is affected by the age of the individual, disease burden, and degrees of frailty and disability. Multiple prognostic tools for life expectancy for older adults are available (60,61). The Life Expectancy Estimator for Older Adults with Diabetes (LEAD) tool was developed and validated among older adults with diabetes, and a high risk score was strongly associated with having a life expectancy of <5 years (62). These data may be a useful starting point to inform decisions about selecting less stringent glycemic goals, particularly when more stringent goals may necessitate use of pharmacotherapies with higher risk of hypoglycemia and other adverse effect profiles (62,63). Older adults also vary in their preferences for the intensity and mode of glucose management (64). Health care professionals caring for older adults with diabetes must take this heterogeneity into consideration when engaging people with diabetes in shared decision-making to establish treatment goals (14,15,41) (**Table 13.2**). In addition, older adults with diabetes should be assessed for disease treatment and self-management knowledge, health literacy, and mathematical literacy (numeracy) at the onset and throughout treatment. Limited time for medical visits, and competing priorities such as acute problems or change in living situation or social support, can make implementation of these recommendations challenging. See **Fig. 6.1** for individual/disease-related factors to consider when determining individualized glycemic goals.

A1C results may be inaccurate in those who have received blood transfusions and who have medical conditions that affect red blood cell turnover (see section 2, “Diagnosis and Classification of Diabetes,”

for additional details on the limitations of A1C) (65). Conditions affecting red blood cell turnover that are common in older adults include kidney failure, recent significant blood loss, and erythropoietin therapy. In these instances, blood glucose monitoring and/or CGM should be used for glycemic goal setting (**Table 13.2**). Serum glycated protein assays such as fructosamine may also be useful for glycemic monitoring in conjunction with other measures (see section 6, “Glycemic Goals, Hypoglycemia, and Hyperglycemic Crises”) (66–68).

Older Adults With Good Functional Status and Without Complications

There are few long-term studies in older adults demonstrating the benefits of intensive glycemic, blood pressure, and lipid management. Older adults who can be expected to live long enough to realize the benefits of long-term intensive diabetes management, who have good cognitive and physical function, and who experience little (or acceptable to them) burden of treatment may be treated using therapeutic interventions and goals similar to those for younger adults with diabetes (**Table 13.2**).

Older Adults With Complications and Reduced Functionality

Older adults with diabetes categorized as having complex or intermediate health (**Table 13.2**) are still heterogeneous with respect to their function and life expectancy (69–71). Based on concepts of competing mortality and time to benefit, individuals with shorter life expectancy, advanced diabetes complications, life-limiting comorbid illnesses, frailty, or substantial cognitive or functional impairments will have less benefit from glucose lowering and should have less stringent glycemic goals (72). These individuals may not only not derive benefit from intensive glucose lowering but are also more likely to experience serious adverse effects of treatment, such as hypoglycemia (73). However, significant hyperglycemia should also be avoided—even in the setting of complex health status—as elevated glucose levels (>180 mg/dL [>10 mmol/L]) increase risks of dehydration, weakness, infection, poor wound healing, and hyperglycemic crises (74). Glycemic goals should, at a minimum, avoid these consequences. Factors to consider for individualizing glycemic goals are outlined in **Fig. 6.1** and **Fig. 13.1**.

Clinicians should also consider the balance of risks and benefits of an individual's diabetes medications, including disease-specific benefits (such as reducing symptomatic heart failure or stabilizing chronic kidney disease) and burdens such as hypoglycemia risk, tolerability, difficulties of administration, inadequate support system, and financial cost. In addition, attention to oral health, vision and hearing loss, foot care, fall prevention, and early detection of depression will improve quality of life.

While **Table 13.2** provides overall guidance for identifying individuals with complex and very complex health needs, there is no global consensus on the optimal classification strategy. Empiric research on the classification of older adults with diabetes based on comorbid illness has suggested three broad classes of individuals: a healthy, a geriatric, and a cardiovascular class (14,69,75). The geriatric class has the highest prevalence of obesity, hypertension, arthritis, and incontinence, while the cardiovascular class has the highest prevalence of myocardial infarctions, heart failure, and stroke. Compared with the healthy class, the cardiovascular class has the highest risk of frailty and subsequent mortality. Additional research is needed to develop a reproducible classification scheme to distinguish the natural history of disease as well as differential response to glucose management and specific glucose-lowering agents (76).

Older Adults at the End of Life

For people with diabetes receiving palliative care and end-of-life care, the focus should be to avoid hypoglycemia and symptomatic hyperglycemia while reducing the burdens of glycemic management. Thus, as organ failure develops, the treatment plan should be deintensified. At the end of life, most agents for type 2 diabetes may be removed (77). There is, however, no consensus for the end-of-life management of type 1 diabetes (78). Consultation with a geriatric or palliative care specialist might be warranted to assist with complex medical and functional issues as well as advance care planning. See **END-OF-LIFE CARE**, below, for additional information.

Beyond Glycemic Management

Although minimizing hyperglycemia may be important in older individuals with

Table 13.2—Framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes

Characteristics and health status of person with diabetes	Rationale	Reasonable A1C goal*	Reasonable CGM goals	Fasting or preprandial glucose	Bedtime glucose	Blood pressure	Lipids
Healthy (few coexisting chronic illnesses, intact cognitive and functional status)	Longer remaining life expectancy	<7.0–7.5% (<53–58 mmol/mol)	TIR 70–180 mg/dL (3.9–10.0 mmol) of ≥70%, and TBR ≤70 mg/dL (≤3.9 mmol/L) of ≤4%	80–130 mg/dL (4.4–7.2 mmol/L)	80–180 mg/dL (4.4–10.0 mmol/L)	<130/80 mmHg	Statin, unless contraindicated or not tolerated
Complex/intermediate (multiple coexisting chronic illnesses† or two or more ADL impairments or mild to moderate cognitive impairment)	Variable life expectancy. Individualize goals, considering: • Severity of comorbidities • Cognitive and functional limitations • Frailty • Risk-to-benefit ratio of diabetes medications • Individual preference	<8.0% (<64 mmol/mol)	TIR 70–180 mg/dL (3.9–10.0 mmol) of ≥50% and TBR <70 mg/dL (<3.9 mmol/L) of <1%	90–150 mg/dL (5.0–8.3 mmol/L)	100–180 mg/dL (5.6–10.0 mmol/L)	<130/80 mmHg	Statin, unless contraindicated or not tolerated
Very complex/poor health (PALTC or end-stage chronic illnesses‡ or moderate to severe cognitive impairment or two or more ADL impairments)	Limited remaining life expectancy makes benefit minimal	Avoid reliance on A1C; glucose management decisions should be based on avoiding hypoglycemia and symptomatic hyperglycemia		100–180 mg/dL (5.6–10.0 mmol/L)	110–200 mg/dL (6.1–11.1 mmol/L)	<140/90 mmHg	Consider likelihood of benefit with statin

This table represents a consensus framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes. The characteristic categories are general concepts. Not every individual will clearly fall into a particular category. Consideration of individual and care partner preferences, care partner engagement, abilities, and resources is an important aspect of treatment individualization. Additionally, an individual's health status and preferences may change over time. ADL, activities of daily living; CGM, continuous glucose monitoring; PALTC, post-acute and long-term care; TBR, time below range; TIR, time in range. *A lower A1C goal may be set for an individual if achievable without recurrent or severe hypoglycemia or undue treatment burden. †Coexisting chronic illnesses are conditions serious enough to require medications or lifestyle management and may include arthritis, cancer, heart failure, depression, emphysema, falls, hypertension, incontinence, stage 3 or worse chronic kidney disease, myocardial infarction, and stroke. "Multiple" means at least three, but many individuals may have five or more (193). ‡The presence of a single end-stage chronic illness, such as stage 3–4 heart failure or oxygen-dependent lung disease, chronic kidney disease requiring dialysis, or uncontrolled metastatic cancer, may cause significant symptoms or impairment of functional status and significantly reduce life expectancy. Adapted from Kirkman et al. (5).

diabetes, greater reductions in morbidity and mortality are likely to result from a clinical focus on comprehensive cardiovascular risk factor modification. There is strong evidence from clinical trials of the value of treating hypertension in older adults (79–81), with treatment of hypertension to individualized blood pressure goals indicated in most. There is less evidence for lipid-lowering therapy and aspirin therapy, although the benefits of these interventions for primary and secondary prevention are likely to apply to older adults whose life expectancies equal or exceed the time frames of the clinical trials (82). In the case of statins, the follow-up time of clinical trials ranged from 2 to 6 years. While the time frame of trials can be used to inform treatment decisions, a more specific concept is the time to benefit for a therapy, which, for statins, is 2.5 years (83).

LIFESTYLE MANAGEMENT

Recommendations

13.11a Recommend healthful eating with adequate protein intake (at least 0.8 g/kg body weight/day) for older adults with diabetes to maintain and potentially higher, individualized amounts to regain lean body mass and function. **B**

13.11b Recommend regular physical activity, including aerobic activity, weight-bearing exercise, and resistance training as tolerated in those who can safely engage in such activities, particularly to maintain lean body mass, especially in those pursuing weight loss. **B**

13.12 For older adults with type 2 diabetes, overweight or obesity, and the capacity to exercise safely, an intensive lifestyle intervention focused on dietary changes, physical activity, and weight loss (e.g., 5–7%) should be considered for its benefits on quality of life, mobility and physical functioning, and cardiometabolic risk. **A**

Lifestyle management in older adults should be tailored to frailty status. Diabetes in the aging population is associated with reduced muscle strength, poor muscle quality, and accelerated loss of muscle mass, which may result in sarcopenia or dynapenia (84) and/or osteopenia (85). Diabetes is also recognized as an independent risk factor for frailty. Frailty is

characterized by a decline in physical performance and an increased risk of negative health outcomes due to physiological vulnerability and functional or psychosocial stressors. Inadequate nutritional intake, particularly inadequate protein intake, can increase the risk of sarcopenia and frailty in older adults. There is no current evidence showing that adjusting protein intake beyond the general recommendations (0.8–1.5 g/kg body weight/day or 15–20% of calories) improves glycemic management or cardiovascular outcomes in individuals with diabetes (86,87). Nevertheless, individualized protein goals may be beneficial, as some research suggests that moderately higher protein intake (20–30%) can support diabetes management by enhancing satiety (88). In populations with sarcopenia, interventions combining protein supplementation with resistance exercise have resulted in increases in muscle mass and muscle strength (89). Special attention should be paid to malnutrition or the risk of malnutrition in older adults with diabetes given its association with sarcopenia (90,91). Malnutrition is also associated with decreases in activities of daily living, grip strength, physical performance of lower limbs, cognition, and quality of life (92–94). See section 5, “Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes,” for a description of malnutrition and screening recommendations. Management of malnutrition, sarcopenia, and frailty in diabetes includes optimal nutrition with adequate protein intake combined with a physical activity program that includes aerobic, weight-bearing, and resistance training. The benefits of a structured physical activity program (as in the Lifestyle Interventions and Independence for Elders [LIFE] study) in frail older adults include reducing sedentary time, preventing mobility disability, and reducing frailty (95). The goal of these programs is not weight loss but enhanced functional status. For nonfrail older adults with type 2 diabetes and overweight or obesity, an intensive lifestyle intervention designed to reduce weight is beneficial across multiple outcomes. The Look AHEAD (Action for Health in Diabetes) trial is described in section 8, “Obesity and Weight Management for the Prevention and Treatment of Diabetes.” Look AHEAD specifically excluded individuals with a low functional status. It enrolled people between 45 and 74 years of age and

required that they be able to perform a maximal exercise test (96,97). Although the Look AHEAD trial did not achieve its primary outcome of reducing cardiovascular events, the intensive lifestyle intervention produced multiple clinical benefits, including weight loss, improved physical fitness, increased HDL cholesterol, lowered systolic blood pressure, reduced A1C levels, reduced waist circumference, and reduced need for medications (98). Subgroup analyses found improved cardiovascular outcomes among participants who lost at least 10% of baseline body weight in the first year (99). Risk factor management improved with reduced use of antihypertensive medications, statins, and insulin (100). Age-stratified analyses showed that older adults in the trial (aged 60–70 years) experienced benefits similar to those seen for younger participants (101,102). The lifestyle intervention also produced benefits on aging-relevant outcomes, including reductions in multimorbidity, improved physical function, and enhanced quality of life (103–106).

PHARMACOLOGIC THERAPY

Recommendations

13.13 Select medications with low risk of hypoglycemia in older adults with type 2 diabetes, specifically for those with hypoglycemia risk factors. **B**

13.14a Deintensify hypoglycemia-causing medications (e.g., insulin, sulfonylureas, or meglitinides) or switch to a medication class with low hypoglycemia risk for individuals who are at high risk for hypoglycemia, using individualized glycemic goals. **B**

13.14b In older adults with diabetes, deintensify diabetes medications for individuals for whom the harms and/or burdens of treatment may be greater than the benefits, within individualized glycemic goals. **E**

13.14c Simplify complex treatment plans (especially insulin) to reduce the risk of hypoglycemia and polypharmacy and to decrease treatment burden. **B**

13.14d In older adults with type 2 diabetes and established or high risk of atherosclerotic cardiovascular disease, heart failure, and/or chronic kidney disease, the treatment plan should include agents that reduce cardiovascular and kidney disease risk, irrespective of glycemia. **A**

13.15 Consider costs of care and coverage when developing treatment plans to reduce risk of cost-related barriers to taking medication and performing self-management behaviors. **B**

Special care is required in prescribing and monitoring pharmacologic therapies in older adults, who are at high risk of polypharmacy and its adverse sequelae, often have nuanced considerations for choice of specific medication classes, and may have cognitive and/or functional impairments that affect the capacity for safe self-management. Therapeutic choices should also take into consideration whether older adults with diabetes live independently, have an engaged and available caregiver, or live in a skilled nursing facility, assisted living facility, or group home (and what level of assistance for medication taking and glucose monitoring is available in these facilities). It is important to match complexity of the treatment plan to the self-management ability of older adults with diabetes and their available social and medical support. Cost may be an especially important consideration, as older adults are often treated with multiple medications and live on fixed incomes. Accordingly, the costs of care and insurance coverage rules should be considered when developing treatment plans to reduce the risk of cost-related barriers to use (107,108). See **Fig. 9.4** for general recommendations regarding glucose-lowering treatment for adults with type 2 diabetes, **Table 9.2** for person-and drug-specific factors to consider when selecting glucose-lowering agents, and **Table 9.3** and **Table 9.4** for median monthly cost in the U.S. of noninsulin glucose-lowering agents and insulin, respectively.

Intensive glycemic management in older adults, particularly those with complex health status, with medication plans that increase the risk of hypoglycemia through use of insulin and/or sulfonylureas has been identified as overtreatment, is common in clinical practice (109–113), and may increase the risk of mortality (42). High treatment burden is another indicator of potential overtreatment. Deintensification of glucose-lowering plans can be achieved by either lowering the dose or discontinuing some medications, as long as individualized glycemic goals are maintained (114,115). Multiple studies evaluating

deintensification protocols in diabetes and hypertension have shown that deintensification is safe and possibly beneficial for older adults (114). Using the 4S pathway (41), **Fig. 13.2** offers a road map for assessing treatment difficulty; reevaluating glyce-mic goals through shared decision-making; deintensifying, simplifying, or modifying treatments; and reassessing treatment engagement and burdens.

Metformin

Metformin is a good treatment option for glucose lowering in older adults with type 2 diabetes due to its low risk for hypoglycemia and simple administration profile, but prescription guidelines must be followed carefully and regularly reassessed. Metformin may be used safely in individuals with an estimated glomerular filtration rate (eGFR) ≥ 30 mL/min/1.73 m² (116), although lower doses should be used in those with eGFR 30–45 mL/min/1.73 m². eGFR should be monitored every 3–6 months in those at risk for decline in kidney function. However, metformin is contraindicated in those with advanced kidney disease and should be used with caution in those with hypoperfusion, hypoxemia, and impaired hepatic function due to potential risk of lactic acidosis. Metformin may be temporarily discontinued before procedures including imaging studies using iodinated contrast, during hospitalizations, and when acute illness may compromise kidney or liver function. Additionally, metformin can cause gastrointestinal side effects (this risk can be minimized through slow uptitration at initiation) and a reduction in appetite that can be problematic for some older adults. Extended-release formulation may be used as an alternative to immediate-release formulation in older adults experiencing difficulties in maintaining medication plans or experiencing gastrointestinal effects. For those taking metformin long term (>4 years), vitamin B12 levels should be monitored annually (117).

Pioglitazone

Pioglitazone has low risk for hypoglycemia but should be used cautiously and in select individuals due to risks for heart failure, fluid retention, weight gain, osteoporosis, and/or macular edema (118,119). Adverse effect risks are reduced with lower doses of pioglitazone and when it is used as part of combination therapy. There may also be

the beneficial effect of stroke reduction (120).

Insulin Secretagogues

Sulfonylureas are associated with hypoglycemia, bone loss (121), and fracture risk (122) and should be used with caution. Similarly, meglitinides (repaglinide and nateglinide) increase the risk of hypoglycemia and fracture risk (123,124). If used, sulfonylureas with a shorter duration of action, such as glipizide, may be preferred, although a recent analysis found that the risk of major adverse cardiovascular events was highest with glipizide (125). Glyburide is a longer-acting sulfonylurea with multiple active metabolites and should be avoided in older adults due to its hypoglycemia risk (126). Many antimicrobials (most commonly fluoroquinolones and sulfamethoxazole-trimethoprim) interact with sulfonylureas to increase the effective sulfonylurea dose, which may precipitate hypoglycemia (127–129). Sulfonylureas should be reduced or temporarily discontinued in these circumstances. Consistent and adequate eating patterns are essential to reducing hypoglycemia risk, and insulin secretagogues may need to be dose-reduced or held in the setting of illness, fasting, or when eating is otherwise impaired. Older adults treated with insulin secretagogues should be routinely screened for hypoglycemia, hypoglycemia awareness should be assessed, and prevention and treatment strategies should be reinforced.

DPP-4 Inhibitors

Dipeptidyl peptidase 4 (DPP-4) inhibitors have few side effects and minimal risk of hypoglycemia, but their cost may be a barrier to some older adults. DPP-4 inhibitors are relatively weak glucose-lowering agents and do not reduce cardiovascular or kidney disease risks like GLP-1 RAs and SGLT2 inhibitors (130). In general, these medications may be useful in older adults with mild hyperglycemia or with high risk of hypoglycemia when a GLP-1 RA or a dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 RA is not tolerated. DPP-4 inhibitors may be used as an alternative to metformin in older adults with low eGFR; linagliptin does not require renal dose adjustment.

GLP-1–Based Therapies

GLP-1 RAs and the GIP/GLP-1 RA tirzepatide are highly effective glucose-lowering

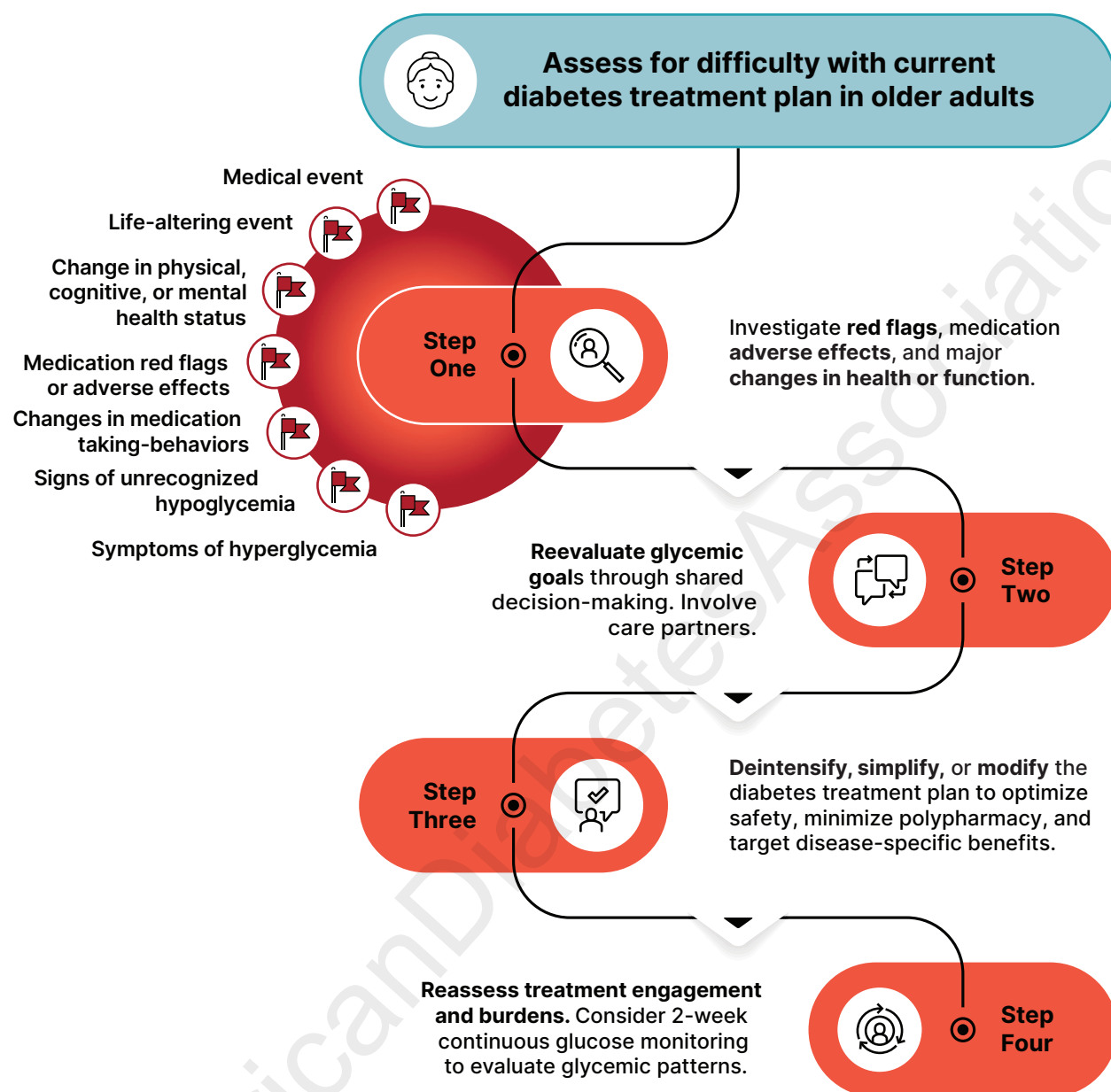


Figure 13.2—Stepwise approach for assessing difficulties in the diabetes treatment plan; reevaluating glycemic goals through shared decision-making; deintensifying, simplifying, or modifying the treatment plan; and reassessing the safety and burdens of any interventions. Created using recommendations from Munshi et al. (41).

medications with low risk for hypoglycemia and can be used in the setting of reduced eGFR, including during dialysis. GLP-1 RAs have demonstrated additional cardiovascular benefits among people with diabetes and established atherosclerotic cardiovascular disease (ASCVD) and those at higher ASCVD risk, with chronic kidney disease, and with symptomatic heart failure with preserved ejection fraction in the setting of obesity. See section 9, “Pharmacologic Approaches to Glycemic Treatment,” section 10, “Cardiovascular Disease and Risk Management,” and section 11, “Chronic Kidney Disease and Risk Management,”

for more extensive discussion. In a systematic review and meta-analysis of GLP-1 RA trials, these agents have been found to reduce major adverse cardiovascular events, cardiovascular deaths, stroke, and myocardial infarction to the same degree for people over and under 65 years of age (131). Weight loss achieved with use of GLP-1 RAs and the GIP/GLP-1 RA is also beneficial for obstructive sleep apnea (132), knee osteoarthritis (133), and metabolic dysfunction-associated steatohepatitis (MASH) (134–136). While the evidence for this class of agents for older adults continues to grow, there are a number of

practical issues that should be considered specifically for older people. These drugs are injectable agents (with the exception of oral semaglutide) (137), which require visual, motor, and cognitive skills for appropriate administration, although most have a weekly dosing schedule. GLP-1 RAs may also be associated with nausea, vomiting, diarrhea, and/or constipation, and doses should be titrated slowly. GLP-1 RAs are therefore not preferred in older adults experiencing unexplained weight loss or undernutrition or with problematic constipation, significant gastroparesis, recurrent ileus, or bowel obstruction.

Individuals should be monitored regularly for dehydration and excessive weight loss, which may lead to significant loss of muscle mass (sarcopenia) and bone density. The risk for sarcopenia can be mitigated with adequate protein intake and resistance or strength training (89).

SGLT2 Inhibitors

SGLT2 inhibitors are administered orally, which may be convenient for older adults with diabetes. In those with established ASCVD, these agents have shown cardiovascular benefits (138). This class of agents has also been found to be beneficial for people with heart failure and to slow the progression of chronic kidney disease. See section 9, "Pharmacologic Approaches to Glycemic Treatment," section 10, "Cardiovascular Disease and Risk Management," and section 11, "Chronic Kidney Disease and Risk Management," for a more extensive discussion regarding the indications for this class of agents. Stratified analyses of the trials of this drug class indicate that older adults have similar or greater benefits than younger people (139–141). SGLT2 inhibitors are generally well tolerated among older adults, although thoughtful selection is needed to avoid adverse effects in individuals at elevated risk (142). SGLT2 inhibitors may cause clinically significant volume depletion, for which older adults are at greater risk, and should be used cautiously in older adults who are frail or prone to orthostasis (143). SGLT2 inhibitors cause a higher rate of genital mycotic infections, especially in women, and may need to be discontinued if this effect becomes burdensome (144). Their use may also be associated with a small increase in urinary tract infections; caution should be used in people with recurrent or severe urinary tract infections (144). Because SGLT2 inhibitors typically increase urine volume, symptoms of urinary incontinence should be queried before and after SGLT2 inhibitor initiation (145,146). Euglycemic diabetic ketoacidosis (DKA) is a rare but potentially serious phenomenon associated with treatment with SGLT2 inhibitors, especially in those with multimorbidity who reside in post-acute and long-term care (PALTC) settings, with infection being the most common trigger (145,147).

Insulin Therapy

The use of insulin therapy requires that individuals or their caregivers have good visual and motor skills and cognitive ability to manage insulin dosing and administration and to recognize and treat hypoglycemia. Insulin doses, times of administration, and treatment plans should be tailored to meet individualized glycemic goals and to avoid hypoglycemia. Age alone does not limit the utility of technology, and older adults who are capable of using CGM devices or an automated insulin delivery system should be encouraged to use them as long as they help to provide safe and effective glycemic management (see discussion above).

Once-daily basal insulin injection therapy may be a reasonable option in many older adults, although noninsulin therapies are preferred due to lower risk of hypoglycemia and other potential benefits as discussed above. When choosing basal insulin, the prescriber should take into account that long-acting insulin analogs have been associated with a lower risk of emergency department visits and hospitalizations for hypoglycemia than NPH insulin in the Medicare population (148). Multiple daily injections of insulin may be too complex for many older individuals with advanced diabetes complications, life-limiting coexisting chronic illnesses, cognitive or functional impairment, or limited functional status or social support. If affordable, use of insulin pens should be preferred to syringes, mostly in older adults with functional impairment.

Studies suggest that simplification of the insulin plan to match an individual's self-management abilities and their available social and medical support is associated with reduced hypoglycemia and disease-related distress without worsening glycemic outcomes (149–152). **Figure 13.3** depicts an algorithm, and potential approach, that can be used to simplify the insulin administration plan (151), and **Table 13.3** provides examples of and rationale for situations where deintensification and/or insulin plan simplification may be appropriate in older adults.

Other Factors to Consider

The needs of older adults with diabetes and their care partners should be evaluated to construct a tailored care plan. Inadequate social support and reduced access to long-term services and support may

reduce these individuals' quality of life and increase the risk of functional dependency (10). The living situation must be considered as it may affect diabetes management and support needs. Social and instrumental support networks (e.g., adult children and care partners) that provide instrumental or emotional support for older adults with diabetes should be included in diabetes management discussions and shared decision-making.

The need for ongoing support of older adults becomes even greater when transitions to PALTC become necessary. Unfortunately, these transitions can lead to discontinuity in goals of care, errors in dosing, and changes in nutrition and activity (153). Older adults in assisted living facilities may not have support to administer their own medications, whereas those living in a nursing home for short-term rehabilitation or PALTC may rely on first-line care partners including nursing and care professionals with variable clinical expertise. Those receiving palliative care (with or without hospice) may require an approach that emphasizes comfort and symptom management while deemphasizing strict metabolic and blood pressure management.

SPECIAL CONSIDERATIONS FOR OLDER ADULTS WITH TYPE 1 DIABETES

Due in part to the success of modern diabetes management, people with type 1 diabetes are living longer, and the population of people over 65 years with type 1 diabetes is growing (154–156). Many of the recommendations in this section regarding comprehensive geriatric assessment and personalization of goals and treatments are directly applicable to older adults with type 1 diabetes; however, this population has unique challenges and requires distinct treatment considerations (157). Insulin is an essential life-preserving therapy for people with type 1 diabetes. To avoid DKA, older adults with type 1 diabetes need some form of basal insulin even when they are unable to ingest meals. Insulin may be delivered through injection, with an AID system, or with an insulin pump alone depending on individual preference, capability, and circumstances. CGM should be used in conjunction with any insulin delivery system. CGM is approved for use by Medicare and can play a critical role in improving A1C, reducing

Simplification of complex insulin therapy in people with type 2 diabetes on insulin

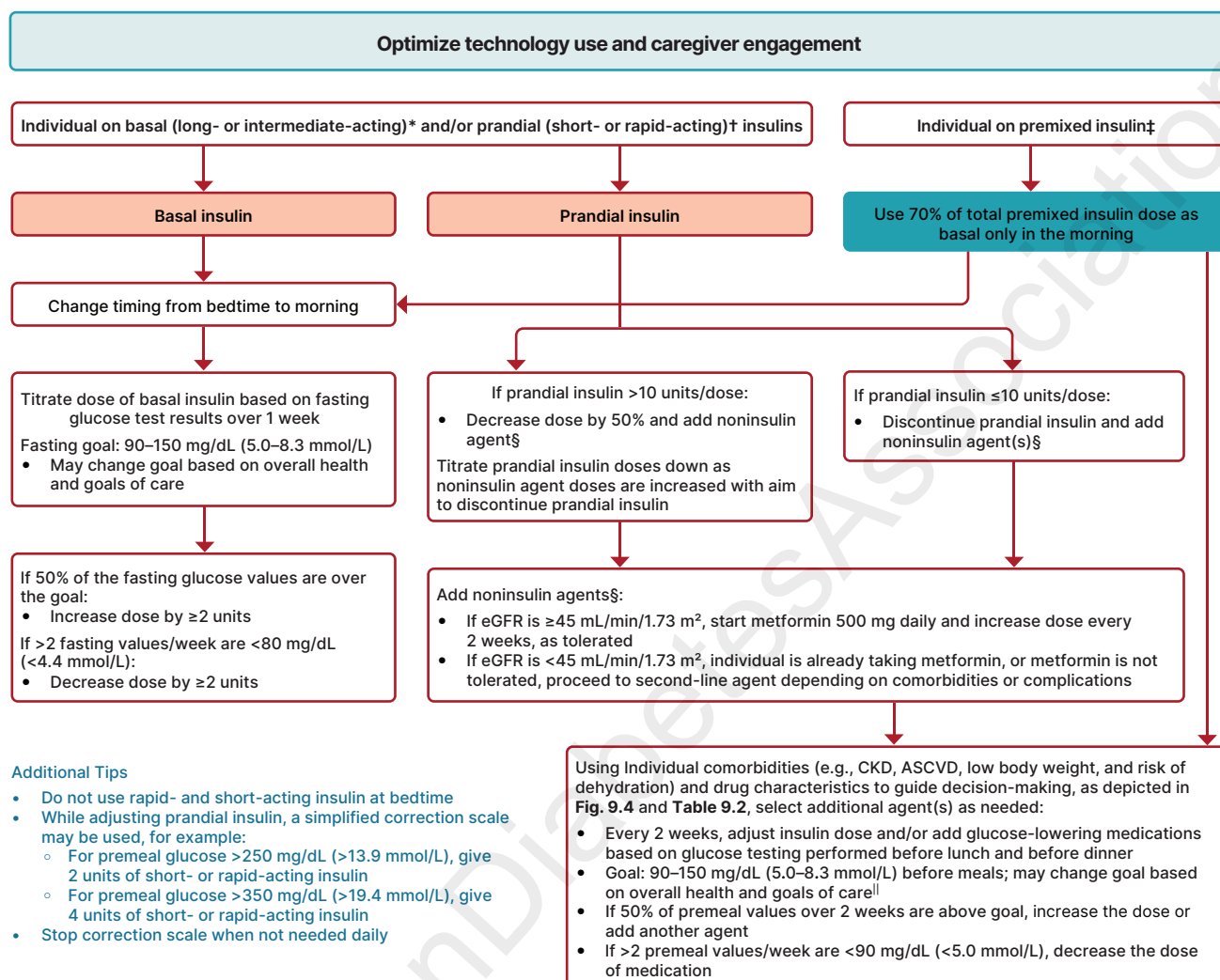


Figure 13.3—Algorithm to simplify insulin administration plans in older individuals. ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate. *Basal insulins: glargine U-100 and U-300, degludec, and human NPH. †Prandial insulins: short-acting (regular human insulin) or rapid-acting (lispro, aspart, and glulisine). ‡Premixed insulins: 70/30, 75/25, and 50/50 products. §Examples of noninsulin agents include metformin, sodium-glucose cotransporter 2 inhibitors, dipeptidyl peptidase 4 inhibitors, glucagon-like peptide 1 receptor agonists (GLP1-RAs), and dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 RAs. ||See Table 13.2. Adapted with permission from Munshi et al. (151).

glycemic variability, and reducing risk of hypoglycemia (49) (see section 7, “Diabetes Technology,” and section 9, “Pharmacologic Approaches to Glycemic Treatment”). In older people with type 1 diabetes, administration of insulin may become more difficult as complications, cognitive impairment, and functional impairment arise. This increases the importance of care partners in the lives of these individuals. Older people with type 1 diabetes may require placement in PALTC settings (i.e., nursing homes and skilled nursing facilities), and unfortunately staff in these settings continue to be less familiar with CGM devices, insulin pumps, or advanced insulin delivery devices. Nevertheless, a feasibility study in

PALTC facilities showed that CGM can be useful in older adults with diabetes, although it requires substantial staff training (158). Additional studies of older adults with diabetes living in PALTC facilities using CGM revealed a high prevalence of hypoglycemia both in people using insulin and in those using sulfonylureas, thus showing that this population of older adults in PALTC facilities are at increased risk for hypoglycemia (159,160). Using CGM can provide useful and more prompt information on hypoglycemia as well as time spent in severe hyperglycemia (as noted in a study of 65 residents in 8 long-term facilities) in this population (161). Of note, a recent RCT in PALTC facilities

showed that real-time CGM use for up to 60 days was safe and effective in guiding insulin doses compared with BGM by point of care. There were no differences in TIR, time below range, or mean glucose levels (162). Some staff may be less knowledgeable about the differences between type 1 and type 2 diabetes. DKA may be mistaken for sepsis, end-organ failure, or other electrolyte abnormalities. In these instances, the individual or their family may be more familiar with their current diabetes management plan than the staff or health care professionals. Education of relevant support staff and health care professionals in rehabilitation and PALTC settings regarding insulin dosing and use of pumps and CGM

Table 13.3—Considerations for treatment plan simplification and deintensification/deprescribing in older adults with diabetes

Characteristics and health status of person with diabetes	Reasonable glycemic goal	Rationale/considerations	When may medication plan simplification be required?	When may treatment deintensification be required?
Healthy (few chronic illnesses, intact cognitive and functional status)	A1C <7.0–7.5% (<53–58 mmol/mol)	• Healthy individuals can usually perform complex tasks for glycemic management • During acute illness, individuals may be at risk for medication administration errors	• Severe or recurrent hypoglycemia on insulin regardless of A1C • Wide glucose excursions • Cognitive or functional decline following acute illness	• Severe or recurrent hypoglycemia on insulin or sulfonylureas, regardless of A1C • Wide glucose excursions • Polypharmacy
Complex/intermediate (multiple chronic illnesses or ≥ 2 ADL impairments or mild to moderate cognitive impairment)	A1C <8.0% (<64 mmol/mol)	• Comorbidities may affect self-management abilities and capacity to avoid hypoglycemia	• Severe or recurrent hypoglycemia on insulin therapy, regardless of A1C • Difficulty managing insulin plan • Significant change in social circumstances, (e.g., loss of care partner or change in living situation or finances)	• Severe or recurrent hypoglycemia on insulin or sulfonylureas, regardless of A1C • Wide glucose excursions • Polypharmacy
Community-dwelling individuals receiving short-term care in a skilled nursing facility	Avoid reliance on A1C; glucose goal 100–200 mg/dL (5.6–11.1 mmol/L)	• Glycemic management is important for recovery, wound healing, and avoidance of infections • Recovery from acute illness may impair cognitive function • More support may be needed on transition to home	• Consider reinstating prehospitalization treatment if it increased in complexity during hospitalization	• Weight loss, anorexia, short-term cognitive decline, and/or loss of physical functioning
Very complex/poor health (PALTC or end-stage chronic illnesses or moderate to severe cognitive impairment or ≥ 2 ADL impairments)	Avoid reliance on A1C and avoid hypoglycemia and symptomatic hyperglycemia	• No benefits of tight glycemic goals in this population • Hypoglycemia should be avoided • Most important outcomes are maintenance of cognitive and functional status	• The individual would like to decrease the number of injections and finger-stick blood glucose monitoring • The individual has an inconsistent eating pattern	• Cognitive dysfunction, depression, anorexia, or inconsistent eating pattern while taking sulfonylureas or meglitinides • Taking any diabetes medications without clear benefits
At the end of life	Avoid hypoglycemia and symptomatic hyperglycemia	• Goal is to provide comfort and avoid tasks or interventions that cause pain or discomfort • Care partners are important in providing medical care and maintaining quality of life	• Pain or discomfort caused by treatment (e.g., injections or finger sticks) • Excessive stress of care partners due to treatment complexity	• Taking any diabetes medications without clear benefits in improving symptoms and/or comfort

Treatment plan simplification refers to changing strategy to decrease the complexity of a medication plan (e.g., fewer administration times and fewer blood glucose checks) and decreasing the need for calculations (such as sliding-scale insulin calculations or insulin-carbohydrate ratio calculations). Deintensification/deprescribing refers to decreasing the dose or frequency of administration of a treatment or discontinuing a treatment altogether. ADL, activities of daily living; PALTC, post-acute and long-term care. Created using information from Munshi et al. 2016 (151) and 2017 (194).

is recommended as part of general diabetes education (see Recommendations 13.16 and 13.17).

TREATMENT IN POST-ACUTE AND LONG-TERM CARE SETTINGS

Recommendations

13.16 Recommend diabetes education/training (including that for CGM devices, insulin pumps, and advanced insulin delivery systems) for the staff of post-acute and long-term care settings to improve the management of older adults with diabetes. **E**

13.17 People with diabetes residing in post-acute and long-term care settings need careful assessment of mobility, mentation, medications, and management preferences to establish individualized glycemic goals and to make appropriate choices of glucose-lowering agents and devices (including CGM devices, insulin pumps, and advanced insulin delivery systems) based on their clinical and functional status. **E**

Management of diabetes in the PALTC setting has multiple unique and nuanced considerations. Individualization of health care is important for all people with diabetes; however, practical guidance for feasible and sustainable care delivery is needed for health care professionals, PALTC staff, and care partners (163,164). Training should include diabetes detection, identification of complications, glycemic monitoring, determination of individualized glycemic goals, medication and nutritional considerations, oral care and regular foot assessment, wound and infection concerns, and institutional quality assessment. PALTC facilities should develop their own policies and procedures for prevention, recognition, and management of hypoglycemia and symptomatic hyperglycemia. For more information, see the ADA position statement “Management of Diabetes in Long-term Care and Skilled Nursing Facilities” and diabetes management guidelines for the PALTC setting (153,163,164). With the increased longevity of populations, the care of people with diabetes and its complications in PALTC is an area that warrants greater study.

Nutritional Considerations

An older adult residing in a PALTC facility may have irregular and unpredictable meal

consumption, undernutrition, diminished appetite, and impaired swallowing. Furthermore, therapeutic nutrition plans or modified food consistencies may inadvertently lead to decreased food intake and contribute to unintentional weight loss and undernutrition. Meals tailored to a person's culture, preferences, and personal goals may increase quality of life, satisfaction with meals, and nutrition status (165). It may be helpful to give insulin immediately after meals to ensure that the dose is appropriate for the amount of carbohydrate the individual consumed in the meal. However, postprandial insulin administration needs to be balanced against the potential for hypoglycemia, ensuring that prandial insulin is rapid-acting (not short-acting) and is given as soon as possible after eating. It is similarly important that insulin not be given too early before meals and that preprandial glucose monitoring, insulin administration, and eating occur as close to each other as possible.

Hypoglycemia

Older adults with diabetes in PALTC are especially vulnerable to hypoglycemia. They have a disproportionately high number of health conditions that can increase hypoglycemia risk: impaired cognitive and renal function, slowed hormonal regulation and counter-regulation, suboptimal hydration, variable appetite and nutritional intake, requirement for feeding assistance, polypharmacy, and slowed intestinal absorption (166). Oral agents may achieve glycemic outcomes similar to those for basal insulin in PALTC residents with type 2 diabetes (109,167). CGM may be a useful approach to monitoring for and preventing hypoglycemia among individuals treated with insulin in PALTC (160,161,168).

Another consideration for the PALTC setting is that unlike in the hospital setting, health care professionals are not required to evaluate individuals daily. According to federal guidelines, at a minimum, assessments should be done at least every 30 days for the first 90 days after admission and then at least once every 60 days and as clinically indicated for acute medical problems or worsening of existing conditions. Although in practice some individuals may be seen more frequently, individuals may have poorly managed glucose levels or wide excursions without the practitioner being

notified. Health care professionals may adjust treatment plans by telephone, fax, or in person directly at the PALTC facilities, provided they are given timely notification of blood glucose management issues from a standardized alert system. It is important for individuals with significant and/or persistent dysglycemia to be reassessed and their treatment modified without delay to prevent recurrence of hypoglycemia and significant hyperglycemia.

The following alert strategy could be considered:

1. Call a health care professional immediately in cases of low blood glucose levels (<70 mg/dL [<3.9 mmol/L]). However, treatment of hypoglycemia should not be delayed.
2. Call as soon as possible when
 - a. glucose values are 70–100 mg/dL (3.9–5.6 mmol/L) (treatment plan may need to be adjusted),
 - b. two or more blood glucose values >250 mg/dL (>13.9 mmol/L) are observed within a 24-h period accompanied by a significant change in clinical status,
 - c. glucose values are consistently >250 mg/dL (>13.9 mmol/L) within a 24-h period,
 - d. glucose values are consistently >300 mg/dL (>16.7 mmol/L) over 2 consecutive days,
 - e. any reading is too high for the glucose monitoring device, or
 - f. the individual is sick, with symptomatic hyperglycemia, vomiting, fever, lethargy, or poor oral intake.

END-OF-LIFE CARE

Recommendations

13.18 When palliative care is needed in older adults with diabetes, health care professionals should discuss goals and intensity of care with people with diabetes and their care partners. Strict glucose, blood pressure, and lipid management are not necessary; consider deintensification or simplification of medication plans and prioritize symptom management. **E**

13.19 Prioritize the overall comfort, prevention of distressing symptoms, and preservation of quality of life and dignity as primary goals for diabetes management at the end of life. **C**

Management of diabetes in the setting of palliative medicine or hospice care at the end of life is a unique situation. The goal of palliative medicine is to promote comfort, symptom management and prevention (pain, hypoglycemia, hyperglycemia, and dehydration), and preservation of dignity and quality of life in the setting of limited life expectancy (169,170).

In the setting of palliative care, health care professionals should initiate conversations with people with diabetes and their care partners regarding the goals and intensity of diabetes care; strict glucose and blood pressure management may not be consistent with achieving comfort and quality of life. Avoidance of severe hypertension and hyperglycemia aligns with the goals of palliative care. In a multicenter trial, withdrawal of statins among people with diabetes in palliative care was found to improve quality of life (171–173). The evidence for the safety and efficacy of deintensification protocols in older adults is growing for both glucose and blood pressure management (113,174) and is clearly relevant for palliative care. An individual has the right to refuse testing and treatment, whereas health care professionals may consider withdrawing treatment and limiting diagnostic testing, including a reduction in the frequency of blood glucose monitoring (175,176). CGM could be considered when frequent blood glucose monitoring is burdensome but monitoring for hypoglycemia and hyperglycemia is needed. Glycemic goals should aim to prevent hypoglycemia (blood glucose <70 mg/dL) and severe hyperglycemia (blood glucose >250 mg/dL when symptom burden increases), although individuals vary in their response (177). Treatment interventions need to be mindful of quality of life. Careful monitoring of oral intake is warranted. The clinical decision-making process may need to involve the individual, family, and care partners, leading to a care plan that is safe, effective, and goal-concordant (178). Pharmacologic therapy for type 2 diabetes may include oral agents with low likelihood of causing hypoglycemia as first line, followed by a simplified insulin plan such as basal insulin. Agents that can cause gastrointestinal and other adverse symptoms may not be good choices in this setting. As symptoms progress, some agents may be slowly tapered and discontinued.

Different categories have been proposed for diabetes management in those at the end of life (77).

1. A stable individual: Continue with the person's previous medication plan, with a focus on 1) the prevention of hypoglycemia and 2) the management of hyperglycemia using blood glucose monitoring, keeping levels below the renal threshold of glucose, and hyperglycemia-mediated dehydration. There is no role for A1C monitoring.
2. An individual with organ failure: Preventing hypoglycemia is of greatest significance. Dehydration must be prevented and treated. In people with type 1 diabetes, insulin administration may be reduced as the oral intake of food decreases but should not be stopped. For those with type 2 diabetes, agents that may cause hypoglycemia should be reduced in dose. The main goal is to avoid hypoglycemia, allowing for glucose values in the upper level of the desired goal range.
3. A dying individual: For people with type 2 diabetes, the discontinuation of all medications may be a reasonable approach, as these individuals are unlikely to have any oral intake. In people with type 1 diabetes, there is no consensus, but a small amount of basal insulin may maintain glucose levels and prevent acute hyperglycemic complications and symptom burden.

Diabetes health care professionals are well positioned to support people with diabetes in advance care planning. Health care professionals can assist people with diabetes in clarifying and documenting their values, preferences, and goals for care in an advanced care plan (172). Advance care plans are guides to help health care professionals and care partners make difficult treatment decisions when the person with diabetes is no longer able to make decisions for themselves. Research shows that people with diabetes want to discuss end-of-life care plans with their health care professional (179). Two validated tools exist to support health care professionals in this process: the Supportive and Palliative Care Indicators Tool (180) and the Gold Standards Framework Proactive Identification Guidance (181).

In conclusion, the management of diabetes in older adults at the end of life necessitates a person-centered approach that prioritizes attainment of individualized treatment goals, comfort, symptom management, quality of life, and the preservation of dignity.

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14. Children and Adolescents: Standards of Care in Diabetes—2026

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American Diabetes Association
Professional Practice Committee for
Diabetes*

The American Diabetes Association (ADA) “Standards of Care in Diabetes” includes the ADA’s current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. Members of the ADA Professional Practice Committee for Diabetes, an interprofessional expert committee, are responsible for updating the Standards of Care annually, or more frequently as warranted. For a detailed description of ADA standards, statements, and reports, as well as the evidence-grading system for ADA’s clinical practice recommendations and a full list of Professional Practice Committee members, please refer to Introduction and Methodology. Readers who wish to comment on the Standards of Care are invited to do so at professional.diabetes.org/SOC.

The management of diabetes in children and adolescents cannot simply be derived from care routinely provided to adults with diabetes. The epidemiology, pathophysiology, developmental considerations, and response to therapy in pediatric diabetes are often different from those of adult diabetes. There are also differences in recommended care for children and adolescents with type 1 diabetes, type 2 diabetes, and other forms of diabetes.

This section is organized into four major parts: the first part introduces type 1 and type 2 diabetes in children and adolescents. The second part addresses care for children and adolescents with all types of diabetes, including diabetes self-management education and support (DSMES) and nutrition therapy; the third part addresses care specifically for children and adolescents with type 1 diabetes, and the fourth part addresses care specifically for children and adolescents with type 2 diabetes. Monogenic diabetes (neonatal diabetes and maturity-onset diabetes of the young) and cystic fibrosis–related diabetes, which are often present in children and adolescents, are discussed in section 2, “Diagnosis and Classification of Diabetes.” **Table 14.1** provides recommendations for screening and treatment of complications and related conditions in pediatric type 1 diabetes and type 2 diabetes. In addition to comprehensive diabetes care, children and adolescents with diabetes should receive age-appropriate and developmentally appropriate pediatric care, including immunizations as recommended by the American Academy of Pediatrics (AAP) (1). To ensure continued care as a person with diabetes becomes an adult, guidance is provided at the end of this section on the transition from pediatric to adult diabetes care.

Expert opinion and a review of available and relevant experimental data are summarized in the American Diabetes Association (ADA) position statements “Type 1 Diabetes in Children and Adolescents” (2) and “Evaluation and Management of Youth-Onset Type 2 Diabetes” (3). Finally, other sections in the Standards of Care

*A complete list of members of the American Diabetes Association Professional Practice Committee for Diabetes can be found at <https://doi.org/10.2337/dc26-SINT>.

This section has received endorsement from The International Society for Pediatric and Adolescent Diabetes.

Duality of interest information for each contributor is available at <https://doi.org/10.2337/dc26-SDIS>.

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may have recommendations that apply to children and adolescents with diabetes and are referenced in the narrative of this section.

INTRODUCTION TO TYPE 1 DIABETES IN CHILDREN AND ADOLESCENTS

Type 1 diabetes is the most common form of diabetes in children and adolescents (4), although there are more adults living with and diagnosed with type 1 diabetes (5). Nearly 4 in every 1,000 children and adolescents in the U.S. were reported to have type 1 diabetes from 2019 through 2022 (6). The health care professional must consider the unique aspects of care and management of children and adolescents with type 1 diabetes, such as changes in insulin sensitivity related to physical growth and sexual maturation, ability to provide self-care, supervision in the childcare and school and athletic environments, emerging independence in adolescents, neurological vulnerability to hypoglycemia and hyperglycemia in young children, and adverse neurocognitive effects of diabetic ketoacidosis (DKA) (7). Attention to family dynamics, developmental stages, and physiologic differences related to sexual maturity is essential in developing and implementing an optimal diabetes treatment plan (8). Additionally, more people (adults, children, and adolescents) with type 1 diabetes are living with obesity than in the past, which adds to the complexity of living with and managing type 1 diabetes (9). Information addressing issues specific to children and adolescents with type 1 diabetes (e.g., glycemic goals, DKA, pumps and automated insulin dosing, autoimmunity) is provided in TYPE 1 DIABETES IN CHILDREN AND ADOLESCENTS, below.

INTRODUCTION TO TYPE 2 DIABETES IN CHILDREN AND ADOLESCENTS

The prevalence of type 2 diabetes in children and adolescents has continued to increase over the past 20 years (4). The U.S. Centers for Disease Control and Prevention published projections for type 2 diabetes prevalence using the SEARCH for Diabetes in Youth (SEARCH) study database. Assuming a 2.3% annual increase, the prevalence among those under 20 years of age will quadruple in 40 years (10,11). Information addressing issues specific to children and adolescents with type 2 diabetes is

provided in TYPE 2 DIABETES IN CHILDREN AND ADOLESCENTS, below.

Evidence suggests that type 2 diabetes in children and adolescents is different not only from type 1 diabetes but also from type 2 diabetes in adults and has unique features, such as a more rapidly progressive decline in β -cell function and accelerated development of diabetes complications (3,12). Long-term follow-up data from the Treatment Options for Type 2 Diabetes in Adolescents and Youth (TODAY) study reported most individuals with type 2 diabetes diagnosed as children or adolescents had microvascular complications by young adulthood (13). Type 2 diabetes disproportionately impacts youth from historically marginalized communities and can occur in complex psychosocial and cultural contexts which may make it difficult to implement and sustain healthy lifestyle changes and self-management behaviors (9,14,15). Additional risk factors include obesity and excess adiposity (16), family history of diabetes possibly mediated by shared genetics, lifestyle, and environmental factors (17), female sex, maternal gestational diabetes mellitus (18), and adverse social determinants of health (12). Information addressing issues specific to children and adolescents with type 2 diabetes (e.g., glycemic goals) is provided in TYPE 2 DIABETES IN CHILDREN AND ADOLESCENTS, below.

GUIDELINES FOR ALL CHILDREN AND ADOLESCENTS WITH DIABETES

Diabetes Self-Management Education and Support

An interprofessional team trained in pediatric diabetes management and sensitive to the challenges of diabetes management in children and adolescents, as well as their family members, should provide diabetes-specific care for this population. It is essential that DSMES, medical nutrition therapy, and psychosocial and behavioral support be provided at diagnosis and routinely (e.g., at each follow-up visit) thereafter in a developmentally appropriate format that builds on prior knowledge by a team of health care professionals experienced with the biological, educational, nutritional, behavioral, and emotional needs of the growing child and adolescent along with family members. Children and adolescents with diabetes spend much of the day in school. Therefore, close

communication with and the cooperation of school personnel are essential for optimal diabetes management and safety and maximal academic and athletic opportunities. The diabetes team should ask about and discuss diabetes management responsibilities with children, adolescents, and parents or caregivers on an ongoing basis, taking into account developmental and psychosocial needs.

Recommendation

14.1 Children and adolescents with diabetes, and their parents or caregivers (for individuals aged <18 years), should receive comprehensive, culturally sensitive, and developmentally appropriate individualized diabetes self-management education and support according to reference standards at diagnosis and routinely thereafter. **B**

Pediatric DSMES, whether for type 1 or type 2 diabetes, involves both children and adolescents and their parents or caregivers. Family involvement is a vital component of optimal diabetes management throughout childhood and adolescence. However, no matter how sound the medical plan is, self-management will only be effective if the affected individuals and/or family can implement it. In a 2024 meta-analysis of 42 randomized controlled trials (RCTs) conducted across the globe, in children and adolescents with type 1 diabetes, both educational DSMES and psychological support were found to improve A1C (19). While there are no DSMES meta-analyses on children or adolescents with type 2 diabetes, a 2024 systematic review and meta-analysis of 55 family-based type 2 diabetes prevention studies reported that lifestyle behaviors, body weight, and body fat percentage all improved following family participation in prevention-focused programs (20).

Diabetes care requires an approach that places the child or adolescent with diabetes and their parents or caregivers at the center of the care model. The care team must be capable of evaluating the educational, behavioral, emotional, and psychosocial factors that affect treatment plan implementation and must work with the children, adolescents, and family members to overcome barriers or redefine goals as appropriate. As the child with diabetes enters the

adolescent years, part of the clinical visit should include time for the health care professional to meet alone with the adolescent to begin the process of increasing autonomy.

As a child or adolescent with diabetes grows, develops, and acquires the need and desire for greater independent self-care skills, DSMES requires periodic and routine (e.g., at each follow-up visit) reassessment. The pediatric diabetes care team should work with children and adolescents with diabetes and their parents or caregivers to ensure there is not a premature transfer of self-management tasks to children and adolescents during this time. In addition, it is important to assess the educational needs and skills of, and provide training to, daycare workers, school nurses, and school personnel who are responsible for the care and supervision of the child with diabetes (21). An interprofessional diabetes team, including a physician or advanced practice health care professional (e.g., nurse practitioner, physician assistant), certified diabetes care and education specialist (CDCES), registered dietitian nutritionist, and behavioral health specialist or social worker, is essential. For children and adolescents with type 2 diabetes, initial treatment must include management of comorbidities such as obesity, dyslipidemia, hypertension, and microvascular complications along with assessment of social needs.

For children and adolescents with all types of diabetes, providing education on healthy lifestyle behaviors is critically important, and typically this is done through DSMES. For those with type 1 diabetes, insulin therapy is paramount, alongside DSMES. For treatment of type 2 diabetes in children and adolescents, lifestyle management, also taught through DSMES, is foundational, and pharmacologic treatment with or without insulin is necessary. For children and adolescents with obesity and diabetes, it should be noted that diabetes type is often uncertain in the first few weeks of treatment due to overlap in presentation and that a substantial percentage will present with clinically significant ketoacidosis (22). Therefore, initial therapy should address the hyperglycemia and associated metabolic derangements irrespective of ultimate diabetes type, with adjustment of therapy once metabolic compensation has been established and subsequent information, such as islet

autoantibody results, becomes available. **Figure 14.1** provides an approach to the initial treatment of new-onset diabetes in children and adolescents with overweight or obesity with clinical suspicion of type 2 diabetes.

Nutrition Therapy

Recommendations

14.2 Provide individualized medical nutrition therapy for children and adolescents with prediabetes or diabetes, emphasizing key nutrition principles (i.e., more nonstarchy vegetables, whole fruits, legumes, whole grains, nuts and seeds, and low-fat dairy products and less sugar-sweetened beverages, sweets, meat, refined grains, and processed or ultraprocessed foods), **B** as an essential component of the overall treatment plan.

14.3 Monitor carbohydrate intake, whether by carbohydrate counting or experience-based estimation, as a key component to optimizing glycemic and weight management for children and adolescents with diabetes. **B**

14.4 Educate children and adolescents and their caregivers on the potential need to adjust insulin with high-fat and high-protein meals. Meal composition affects postprandial glucose excursions. **A**

14.5 In children and adolescents with diabetes, provide comprehensive nutrition education at diagnosis, and at least annually and ideally more frequently, by an experienced registered dietitian nutritionist to assess the eating pattern in relation to weight status, age-appropriate growth, risk for disordered eating behaviors, and cardiovascular disease risk factors. **E**

Nutrition management for all types of diabetes in children and adolescents should be individualized and needs to consider family habits, food preferences, religious or cultural needs, finances, schedules, physical activity, and the individual's and family's abilities in numeracy, literacy, and self-management strategies. Routine visits with a registered dietitian nutritionist, preferably experienced in working with pediatric populations with diabetes, are recommended and should include assessment for changes in food preferences over time, access to food, growth and development, weight status,

cardiovascular risk, and potential for disordered eating.

Consuming an evidence-based eating pattern is associated with better glyce-mic outcomes in children and adolescents with type 1 and type 2 diabetes (23–25), although the evidence in type 2 diabetes is less robust. Education on healthy, culturally aligned eating should be provided for all children and adolescents with diabetes and their families. For children and adolescents taking meal-time insulin, carbohydrate content is the primary variable for calculation of meal-time insulin doses. Meals with higher fat and protein content, however, can cause early hypoglycemia and delayed postprandial hyperglycemia. Some adjustments in insulin dosing, including a split dose or an increase in calculated dose or use of an extended bolus feature when available to account for proteins and fats, can improve postprandial glucose management (26,27). Additionally, considering that carbohydrate counting in pregnant adults with type 1 diabetes has been reported to aid in weight management, as it contributes to portion management, so it is reasonable to consider it as a useful tool for both glycemic and weight management in children and adolescents (28).

Given the complex social and environmental context surrounding children and adolescents with prediabetes and diabetes, individual-level lifestyle interventions may not be sufficient to address the multifaceted interplay of family dynamics, behavioral health, community readiness, and the broader environmental system (3). In these cases, referrals to members of the care team with expertise in behavioral health and social work might be beneficial where available.

Physical Activity and Exercise

Recommendations

14.6 Physical activity is recommended for all children and adolescents with diabetes with the goal of 60 min of moderate- to vigorous-intensity aerobic activity daily, with vigorous muscle-strengthening and bone-strengthening activities at least 3 days per week. **B**

14.7 Children and adolescents with diabetes using insulin therapy and their parents should monitor glucose levels before, during, and after physical activity and receive education about personalized glycemic goals

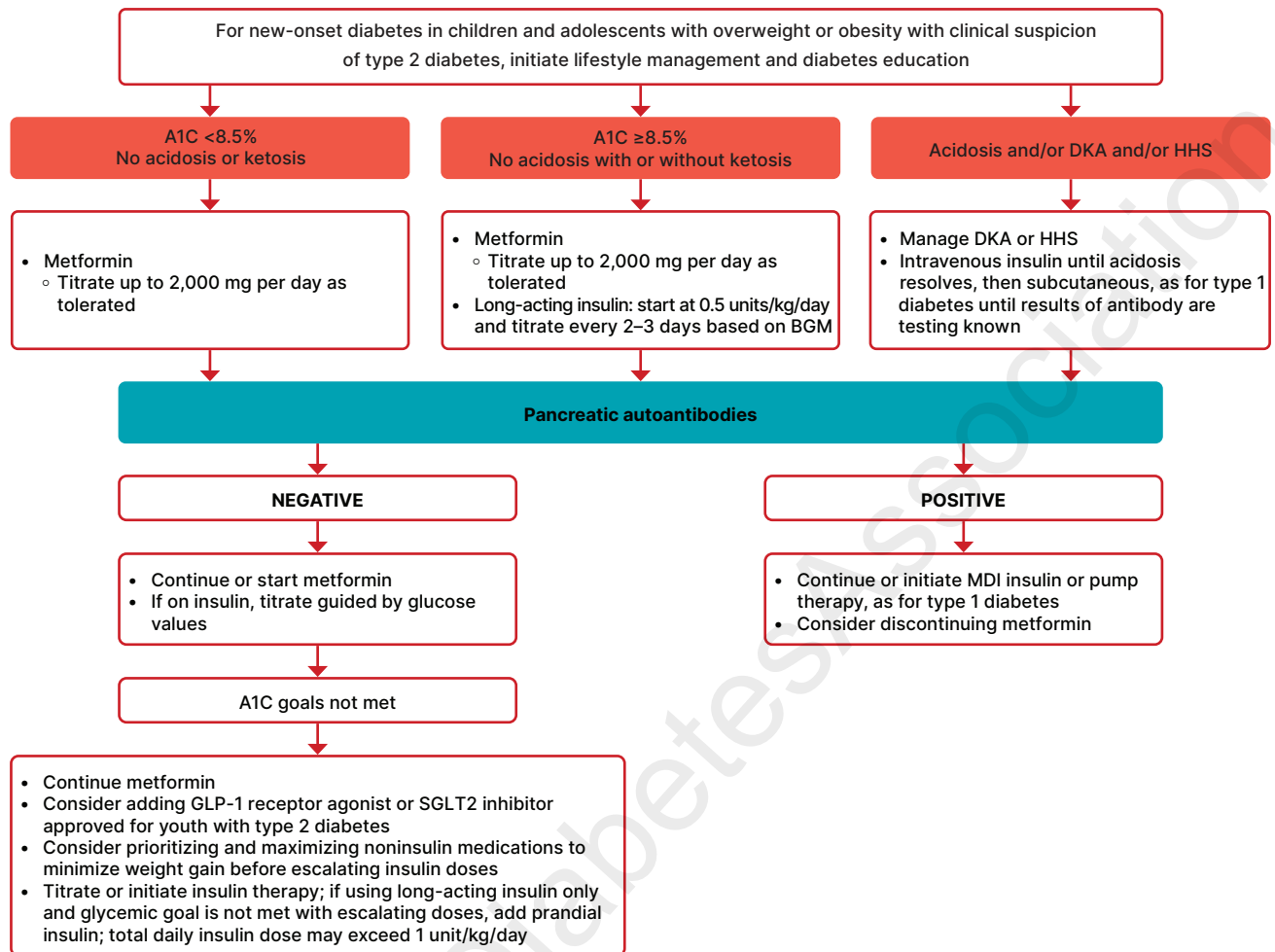


Figure 14.1—Management of new-onset diabetes in youth with overweight or obesity with clinical suspicion of type 2 diabetes. A1C 8.5% = 69 mmol/mol. BGM, blood glucose monitoring; CGM, continuous glucose monitoring; DKA, diabetic ketoacidosis; GLP-1, glucagon-like peptide 1; HHS, hyperosmolar hyperglycemic state; MDI, multiple daily injections; SGLT2, sodium–glucose cotransporter 2. Adapted from the ADA position statement “Evaluation and Management of Youth-Onset Type 2 Diabetes” (3).

according to the type and intensity of the planned physical activity. **C**
14.8 Children and adolescents with diabetes and their parents or caregivers should be educated on strategies to prevent hypoglycemia during, after, and overnight following physical activity or exercise. Treatment for hypoglycemia should be accessible before, during, and after engaging in activity. **C**

Like for all children and adolescents, physical activity and structured exercise positively impact metabolic and psychological health in children with type 1 diabetes (23,29–31), prediabetes, and type 2 diabetes (25,32–34). Exercise can have positive effects on insulin sensitivity, strength, cardiorespiratory fitness, weight management, social interaction, mood, self-esteem building, and perhaps most

importantly, the creation of healthful habits for adulthood. However, for children and adolescents using insulin, exercise also has the potential to cause both hypoglycemia and hyperglycemia, so providing education on those effects is warranted.

See below for strategies to mitigate hypoglycemia risk and minimize hyperglycemia associated with exercise in children and adolescents with type 1 diabetes or those using insulin. For an in-depth discussion, see previously published reviews and guidelines (35–37).

Overall, it is recommended that all children and adolescents, including those with prediabetes and diabetes, should participate in 60 min of moderate-intensity (e.g., brisk walking, dancing) to vigorous-intensity (e.g., running, jumping rope, soccer) aerobic activity daily, including resistance and flexibility training (34). Although

uncommon in the pediatric population, they should be evaluated for comorbid conditions or diabetes complications that may restrict participation in an exercise program.

School and Child Care

As the majority of waking hours for most children and adolescents can be spent in school and/or daycare, training of school or daycare personnel as well as athletic coaches to provide care in accordance with the individualized diabetes medical management plan is essential for optimal diabetes management and safe access to all school- or daycare-sponsored opportunities (38–40). This is of particular importance for those children and adolescents who require insulin. In addition, federal and state laws require schools, daycare facilities, and other entities to provide needed diabetes care to enable the child

to safely access the school or daycare environment. Refer to the ADA position statements “Diabetes Care in the School Setting” (38) and “Care of Young Children with Diabetes in the Childcare and Community Setting” (40) and the ADA’s Safe at School website (diabetes.org/resources/know-your-rights/safe-at-school-state-laws) for additional details.

Psychosocial Care

Recommendations

14.9 At diagnosis and during routine follow-up care, screen children and adolescents with type 1 diabetes, **B** type 2 diabetes, **B** and other forms of diabetes **E** for psychosocial concerns (e.g., diabetes distress, depressive symptoms, anxiety, disordered eating behaviors), family factors, and behavioral health concerns that could affect diabetes management with age-appropriate standardized and validated tools. Refer to a qualified behavioral health professional, preferably experienced in childhood diabetes, when indicated.

14.10 Behavioral health professionals should be considered integral members of the pediatric diabetes interprofessional team. **E**

14.11 Encourage developmentally appropriate family involvement in diabetes management tasks for children and adolescents with type 1 diabetes, type 2 diabetes, **B** and other forms of diabetes, **E** recognizing that premature or unsupportive transfer of diabetes care responsibility to children and adolescents can contribute to diabetes distress, lower engagement in diabetes self-management behaviors, and deterioration in glycemia.

14.12 Health care professionals should screen for food insecurity, housing stability, health literacy, financial barriers, and social or community support and apply that information to treatment decisions. **E**

14.13 Health care professionals should consider asking school-aged children and adolescents with type 1 diabetes, **B** type 2 diabetes, **E** and other forms of diabetes, **E** along with their parents or caregivers, about social adjustment (peer relationships) and school performance to determine whether further intervention is needed.

14.14 Offer adolescents with diabetes time by themselves with their health care professional(s) at a developmentally appropriate age. **E**

14.15 During adolescence, generally during the stage of pubertal growth and development, incorporate reproductive health and preconception counseling into routine diabetes clinic visits for all individuals of childbearing potential because of the risk of adverse pregnancy outcomes in this population. **A**

Rapid and dynamic cognitive, developmental, and emotional changes occur during childhood, adolescence, and emerging adulthood. Diabetes management places substantial burdens on the child, adolescent, and family, necessitating ongoing assessment of psychosocial status and social determinants of health during routine diabetes visits (41,42). Consider the impact of diabetes on quality of life as well as the development of behavioral health problems related to diabetes distress, symptoms of depression, symptoms of anxiety, fear of hypoglycemia and hyperglycemia, disordered eating behaviors, and eating disorders (41,43). Further, consideration of the sociocultural context and efforts to personalize diabetes management are of critical importance to minimize barriers to care, enhance participation, and maximize response to treatment. Screening for food insecurity, housing instability, and other barriers related to the social determinants of health should be part of routine pediatric diabetes care (44).

Children and adolescents with type 1 diabetes, type 2 diabetes, and other forms of diabetes experience high rates of diabetes distress, depression, anxiety disorders, disordered eating behaviors, and eating disorders (45–50). For this reason, routine psychosocial screening is recommended for children and adolescents with type 1, type 2, and other forms of diabetes. Diabetes distress is the emotional response to living with and managing a demanding chronic condition. Approximately 30% of children and adolescents with type 1 diabetes (45) and 24% of children and adolescents with type 2 diabetes (51) report clinically significant levels of diabetes distress. Screening for diabetes distress may begin as early as 7 or 8 years of age (43), using validated tools for

children, adolescents, and their parents or caregivers (52). The pooled prevalence of depression is 22.2% in children and adolescents with type 1 and type 2 diabetes (53). This high rate highlights the importance of routine depression screening in this population, beginning at age 12 years and continuing thereafter (54), particularly when treatment goals are not being met or when there are significant changes in medical status or life circumstances. The pooled prevalence of anxiety is 17.7% in children and adolescents with type 1 and type 2 diabetes (53), supporting routine screening for anxiety in children and adolescents aged 8 years and above (54). For children and adolescents experiencing severe and/or frequent hypoglycemia as well as substantial hyperglycemia, it is important to screen both their parents or caregivers and the individual with diabetes for fear of hypoglycemia (55). Children as young as 6 years old can provide reliable self-reports for fear of hypoglycemia (55). Lastly, screening for disordered eating behaviors is recommended when signs and symptoms (e.g., unexplained weight loss, hyperglycemia, and DKA) and/or behavioral and emotional indicators (e.g., secrecy around eating and excessive concern about weight) are present using validated screening tools (56). Children and adolescents with type 1 diabetes are at increased risk for disordered eating behaviors and clinical eating disorders, which can lead to serious short- and long-term complications affecting diabetes outcomes and overall health. A particularly dangerous behavior in this population is insulin omission for weight loss (57). In the SEARCH study, disordered eating behaviors and insulin omission were also common among adolescents and young adults with type 2 diabetes, with 50.3% reporting disordered eating behaviors and 23% reporting insulin omission (58).

Given the complexity of psychosocial concerns in the management of diabetes in children and adolescents, collaboration between the diabetes health care team and a behavioral health professional is recommended. Early detection of diabetes distress, depression, anxiety, fear of hypoglycemia, and disordered eating behaviors can facilitate effective treatment options and help minimize adverse effects on diabetes management and health outcomes (41,43). When psychological symptoms are identified, referral to a behavioral health professional, ideally with experience in

pediatric diabetes, may be warranted. Such professionals can provide individualized, evidence-based behavioral health care services, including cognitive-behavioral therapy, mindfulness-based approaches, and other interventions, to improve psychosocial functioning in children and adolescents with diabetes (59–61).

The complexities of diabetes management require ongoing caregiver involvement in care throughout childhood and adolescence. Developmentally appropriate, supportive family teamwork between the growing child or adolescent and their parent(s) can help increase parent involvement in diabetes management and maintain or improve A1C in children and adolescents with A1C $\geq 8.0\%$ (62). It is appropriate to inquire about diabetes-specific family relationships, including family teamwork and conflict, during visits; health care professionals can both help families negotiate a plan and refer to an appropriate behavioral health professional for more in-depth support (63). Such professionals can conduct further assessments and deliver evidence-based behavioral interventions to support developmentally appropriate, collaborative family involvement in diabetes self-management (64,65). Monitoring of social adjustment (peer relationships) and school performance can facilitate both well-being and academic achievement (66,67). Diabetes management and glycemic levels may be associated with and impact academic progress and students' functioning in the school setting, which highlights the need for appropriate accommodations and access to diabetes-related support in school (68).

Decision-making involvement with children and adolescents regarding the adoption of management plan components can improve participation in diabetes self-management, technology adoption, and glycemic outcomes (69,70). Use of well-designed decision aids can engage children and adolescents in comprehensive, unbiased conversations with their diabetes care team about treatment options (71). Creating self-care contracts (72) and integrating technology that shares glucose data with the care team may facilitate shared decision-making and enhance care (73). Importantly, health care professionals working with children and adolescents who are not yet able to provide legal consent must balance clinical oversight with promoting developmentally appropriate independence. Recommendations include

providing education tailored to the developmental stage, encouraging gradual transfer of responsibility with self-care, guiding parental involvement as responsibilities change, teaching self-advocacy to prepare for transitions in care, and incorporating psychosocial support at all stages (67,74). Although cognitive abilities vary, the ethical position often adopted is the "mature minor rule," whereby children after age 12 or 13 years who can make an informed decision have the right to consent or withhold consent to general medical treatment, except in cases in which refusal would significantly endanger health (75). Importantly, not all children aged 12 or 13 years will be cognitively or emotionally prepared for transfer of daily self-care responsibilities. In these cases, emphasize assent to help ensure they are engaged in decision-making and to encourage them to take an active role in their self-management alongside caregivers.

Beginning at the onset of puberty or at diagnosis of diabetes for pubertal and postpubertal children and adolescents, all individuals with childbearing potential should receive education about the effective use of contraception to prevent unplanned pregnancy, as risks of fetal malformations are associated with elevated A1C. The TODAY study documented high rates of maternal complications during pregnancy and low rates of pre-conception counseling and contraception use in adolescents and young adults with type 2 diabetes (76). Preconception counseling using developmentally appropriate educational and behavioral strategies enables individuals of childbearing potential to make well-informed decisions (77). Preconception counseling resources tailored for adolescents are available at no cost through the ADA (78). Refer to the ADA position statement "Psychosocial Care for People With Diabetes" for further details (43).

The presence of behavioral health professionals on pediatric interprofessional teams emphasizes the importance of psychosocial care. These psychosocial factors are significantly related to self-management difficulties, elevated A1C, reduced quality of life, and higher rates of acute and chronic diabetes complications. A proactive, team-based approach to psychosocial screening, referral, and intervention is essential to support the health of children and adolescents with diabetes.

Glycemic Monitoring, Insulin Delivery, and Goals

Recommendations

14.16 Continuous glucose monitoring (CGM) should be offered for diabetes management at diagnosis or as soon as possible in children and adolescents with diabetes who are capable of using the device safely (either by themselves or with caregivers). **A** The choice of device should be made based on the individual's and family's circumstances, desires, and needs.

14.17 Offer automated insulin delivery (AID) systems for diabetes management to children and adolescents with type 1 diabetes who are capable of using the device safely (either by themselves or with caregivers). Choice of device should be made based on the individual's and family's circumstances, desires, and needs. **A**

14.18 Offer open-loop insulin pump therapy for type 1 diabetes management to children and adolescents on multiple daily injections who are capable of using the device safely (either by themselves or with caregivers) if unable to use AID systems. Choice of device should be made based on the individual's and family's circumstances, desires, and needs. **A**

14.19 Students with diabetes must be supported at school in the use of diabetes technology, including CGM, insulin pumps, connected insulin pens, and AID systems, as prescribed by their diabetes care team. **C**

14.20 A1C goals must be individualized and reassessed over time. An A1C of $<7\%$ (<53 mmol/mol) is appropriate for most children and adolescents with diabetes. **B**

14.21 Less stringent A1C goals (such as $<7\%$ [<53 mmol/mol] or $<7.5\%$ [<58 mmol/mol]) may be appropriate for children and adolescents with diabetes who cannot articulate symptoms of hypoglycemia; have hypoglycemia unawareness; cannot access advanced insulin delivery technology and/or CGM; cannot check blood glucose regularly; or have nonglycemic factors that increase A1C. **B**

14.22 Even less stringent A1C goals may be appropriate for children and adolescents with diabetes and a history of severe hypoglycemia or limited life expectancy or where the harms of

treatment are greater than the benefits. **B**

14.23 Health care professionals may reasonably suggest more stringent A1C goals (such as <6.5% [<48 mmol/mol]) for selected children and adolescents with diabetes if they can be achieved without significant hypoglycemia, excessive weight gain, negative impacts on well-being or mental health, or undue burden of care or in those who have nonglycemic factors that decrease A1C (e.g., lower erythrocyte life span). Lower goals may also be appropriate during the honeymoon phase. **B**

14.24 For children and adolescents with diabetes, CGM metrics derived from CGM use over the most recent 14 days (or longer) are recommended to be used in conjunction with or without A1C whenever possible. **B**

Current standards for diabetes management reflect the need to minimize hyperglycemia as safely as possible. The Diabetes Control and Complications Trial (DCCT) (79), which did not enroll children <13 years of age, demonstrated that near normalization of blood glucose levels was more difficult to achieve in adolescents than in adults. Nevertheless, the increased use of continuous glucose monitoring (CGM) and AID systems, goal setting, and improved education have been associated with more children and adolescents reaching the blood glucose goals recommended by the ADA (80–82), particularly in families in which the parent or caregiver as well as the child or adolescent with diabetes participate jointly to perform the required diabetes-related tasks.

TYPE 1 DIABETES IN CHILDREN AND ADOLESCENTS

Lower A1C in adolescence and young adulthood is associated with a lower risk and rate of microvascular and macrovascular complications (83–85) and demonstrates the effects of metabolic memory (86–89). While an A1C goal of <7% (<53 mmol/mol) is appropriate for most children and adolescents with type 1 diabetes, as AID algorithms continue to improve and access to these systems expands, children and adolescents who can attain a goal of <6.5% (<48 mmol/mol) without adverse effects should be encouraged to do so. In

addition, achieving lower A1C levels is likely facilitated by setting lower A1C goals (80,90). Lower goals may be possible during the honeymoon phase of type 1 diabetes and in those with access to CGM and AID. The honeymoon phase, also referred to as partial remission, refers to a transient period of increased endogenous insulin secretion shortly after diagnosis when initiation of insulin therapy resolves glucotoxicity and allows for improved insulin secretion from residual β -cells. Recent data with newer devices indicate that the risk of hypoglycemia at lower A1C is less than it was before (81,82,91–94). However, special consideration should be given to the risk of hypoglycemia in young children (aged <6 years) who are often unable to recognize, articulate, and/or manage hypoglycemia. Registry data indicate that lower A1C goals can be achieved in children, including those aged <6 years, without increased risk of severe hypoglycemia (91). Please refer to section 6, “Glycemic Goals, Hypoglycemia, and Hyperglycemic Crisis,” for more information on glycemic assessment.

A strong relationship exists between the frequency of glucose monitoring and glycemic outcomes (95,96). Glucose levels for all children and adolescents with type 1 diabetes should be monitored multiple times daily using CGM whenever possible. For those who cannot access CGM and in case of inaccurate CGM readings, access to finger-stick blood glucose monitoring remains essential. Use of CGM soon after type 1 diabetes diagnosis is associated with improved A1C (97–99). Parents, caregivers, and children and adolescents should be offered initial and ongoing education and support for CGM use. Behavioral support may further improve ongoing CGM use (100). Metrics derived from CGM include percent time in range (TIR), time below target range (<70 mg/dL and <54 mg/dL), and time above target range (>180 mg/dL and >250 mg/dL) (101). While studies indicate a relationship between TIR and A1C (102,103), it is still uncertain what the ideal goal TIR should be for children, and further studies are needed. Though 14 days of CGM data has long been considered the gold standard, recent data indicate that 10 or more days of CGM data provides a reliable assessment of glycemia and that ≥ 7 days of data may be sufficient for children and adolescents attaining TIR goals (104,105). Please refer to section 7,

“Diabetes Technology,” for more information on the use of blood glucose meters, CGM, and insulin pumps. More information on insulin injection technique can be found in section 9, “Pharmacologic Approaches to Glycemic Treatment.”

In addition, type 1 diabetes and chronic hyperglycemia are associated with adverse effects on cognition during childhood and adolescence (7,106,107). Several factors, including young age, severe hypoglycemia at <6 years of age, DKA, and chronic hyperglycemia (106,108,109), may contribute to adverse effects on brain development and function. Attaining higher CGM TIR is associated with better structural brain development and better neurocognitive outcomes (108), further emphasizing the importance of achieving glycemic goals (7,108).

Key Concepts in Setting Glycemic Goals

- Glycemic goals should be individualized, and lower goals may be reasonable based on a benefit-risk assessment.
- Blood glucose goals should be modified in children with frequent hypoglycemia or hypoglycemia unawareness.

Exercise Needs Specific to Children and Adolescents With Type 1 Diabetes

Real-world data from the Type 1 Diabetes Exercise Initiative Pediatric (T1DEXIP) study reported that glucose levels tended to drop during exercise, most particularly in those with lower A1C, shorter diabetes duration, and less fear of hypoglycemia (110). Furthermore, glucose levels tended to be lowest at about 8–16 h postexercise in those with similar characteristics, and nocturnal hypoglycemia was more frequent when activity levels were higher and longer in duration (111). These data underscore the need for individualized management strategies for children and adolescents using insulin, including common sense precautions and understanding how to make insulin dose adjustments when undertaking exercise and physical activity. Accessible rapid-acting carbohydrates and frequent blood glucose monitoring before, during, and after exercise, with or without CGM maximize safety with exercise. As hyperglycemia can occur before, during, and after physical activity, it is important to ensure the elevated glucose level is not related to insulin deficiency, as that can lead to worsening hyperglycemia with exercise and DKA risk. Intense

activity should be postponed with marked hyperglycemia (glucose ≥ 350 mg/dL [≥ 19.4 mmol/L]), moderate to large urine ketones, and/or β -hydroxybutyrate > 1.5 mmol/L in the setting of insulin deficiency. Caution may be needed when β -hydroxybutyrate levels are ≥ 0.6 mmol/L in association with absence of insulin (112,113).

Prevention and treatment of hypoglycemia associated with physical activity includes decreasing prandial insulin for the meal or snack before and after exercise, and/or increasing carbohydrate intake. Children and adolescents using insulin pumps without automated insulin delivery (AID) can lower basal rates by ~ 10 – 50% or more or suspend for 1–2 h during exercise (111). Decreasing basal rates or long-acting insulin doses by $\sim 20\%$ after exercise may reduce delayed exercise-induced hypoglycemia (110). Using AID systems may improve TIR (70–180 mg/dL) during exercise, and children and adolescents can use device-specific settings that are more conservative or increase the glucose goal to prevent hypoglycemia with exercise (114).

Blood glucose goals prior to physical activity and exercise are 126–180 mg/dL (7.0–10.0 mmol/L) but should be individualized based on the insulin plan and type, intensity, and duration of activity (36,115). The accuracy of CGM systems varies depending on the type of exercise (116). Consider additional carbohydrate intake during and/or after exercise, depending on duration and intensity of physical activity, to prevent hypoglycemia. For low-to moderate-intensity aerobic activities (30–60 min), and if the child or adolescent is fasting, 10–15 g of carbohydrate may prevent hypoglycemia (36). The timing of carbohydrate intake before exercise is of great importance for children and adolescents using AID systems, as a rise in glucose may result in increased automated insulin delivery with a subsequent increase in the risk for hypoglycemia (113). After insulin boluses (relative hyperinsulinemia), consider 0.5–1.0 g of carbohydrates/kg per h of exercise (~ 30 – 60 g), similar to carbohydrate requirements for optimizing performance in athletes without type 1 diabetes (117,118).

For children and adolescents with type 1 diabetes and obesity, physical activity is a key component of diabetes care. Obesity is equally common in children and adolescents with or without type 1 diabetes.

Living with obesity is associated with a higher frequency of cardiovascular risk factors, and it disproportionately affects children and adolescents from racial and ethnic minoritized groups (e.g., Black and Latino children and adolescents) (9,119). Therefore, diabetes health care professionals should monitor weight status and encourage a healthy eating pattern, physical activity, and healthy weight as key components of pediatric type 1 diabetes care.

TYPE 2 DIABETES IN CHILDREN AND ADOLESCENTS

For information on risk-based screening for type 2 diabetes and prediabetes in children and adolescents, please refer to section 2, “Diagnosis and Classification of Diabetes.” For additional support for these recommendations, see the ADA position statement “Evaluation and Management of Youth-Onset Type 2 Diabetes” (3).

Screening and Diagnosis of Type 2 Diabetes in Children and Adolescents

Recommendations

14.25 Consider risk-based screening for prediabetes and/or type 2 diabetes after the onset of puberty or after 10 years of age, whichever occurs earlier, in children with overweight (BMI ≥ 85 th to < 95 th percentile) or obesity (BMI ≥ 95 th percentile) and who have one or more additional risk factor for diabetes (see **Table 2.5** for evidence grading of other risk factors).

14.26 If screening is normal, repeat screening at a minimum of 2-year intervals **E** or more frequently if BMI is increasing. **C**

14.27 Fasting plasma glucose, 2-h plasma glucose during a 75-g oral glucose tolerance test, elevated random glucose with symptoms of hyperglycemia, and/or A1C can be used to test for prediabetes or type 2 diabetes in children and adolescents. **B**

14.28 Children and adolescents with overweight or obesity with hyperglycemia in whom the diagnosis of type 2 diabetes is being considered should have a panel of pancreatic autoantibodies tested to exclude the possibility of autoimmune type 1 diabetes. **B**

In recent years, incidence and prevalence of type 2 diabetes in children and

adolescents have increased dramatically, especially in historically marginalized communities (120). A few studies suggest oral glucose tolerance tests or fasting plasma glucose values as more suitable diagnostic tests than A1C in the pediatric population, especially among certain ethnicities (121), while fasting glucose alone may overdiagnose diabetes in children and adolescents (122,123). In addition, many studies that compare A1C to fasting plasma glucose or oral glucose tolerance test do not consider that diabetes diagnostic criteria are based on long-term health outcomes, and validations are not currently available in the pediatric population (124). An analysis of National Health and Nutrition Examination Survey (NHANES) data suggests using A1C for screening of high-risk children and adolescents due to association with cardiometabolic risk (125). While the ADA acknowledges there are limitations in the data supporting A1C for diagnosing type 2 diabetes in children and adolescents, the ADA continues to recommend its use in this population (121). A1C is not recommended for diagnosis of diabetes in children and adolescents with cystic fibrosis or symptoms suggestive of acute onset of type 1 diabetes, and only A1C assays without interference are appropriate for children and adolescents with hemoglobinopathies.

Diagnostic Challenges: Overlap of Type 1 and Type 2 Diabetes

Given the current obesity epidemic, distinguishing between type 1 and type 2 diabetes in children can be difficult. Overweight and obesity are common in children with type 1 diabetes (126), and diabetes-associated autoantibodies and ketosis may be present in pediatric individuals with clinical features of type 2 diabetes (including obesity and acanthosis nigricans) (122). The presence of islet autoantibodies has been associated with faster progression to insulin deficiency (122). At the onset of diabetes, DKA occurs in $\sim 11\%$ of children and adolescents aged 10–19 years with type 2 diabetes (127). Although uncommon, type 2 diabetes has been observed in prepubertal children under the age of 10 years, thus it should be part of the differential in children with suggestive symptoms (128). Finally, obesity contributes to the development of type 1 diabetes in some individuals (129), which further blurs

the lines between diabetes types. We must acknowledge that people with type 1 diabetes can also experience weight gain and insulin resistance. However, accurate diagnosis is critical, as treatment plans, educational approaches, nutrition advice, and outcomes differ markedly between individuals with predominantly insulin resistance versus absolute insulinopenia phenotypes. It must also be acknowledged that overlap between type 1 and type 2 diabetes can exist, and both insulin resistance and absolute insulinopenia should be treated appropriately (130). The significant diagnostic difficulties posed by maturity-onset diabetes of the young are discussed in section 2, “Diagnosis and Classification of Diabetes.” In addition, there are rare and atypical diabetes cases that represent a challenge for clinicians and researchers.

Management

Lifestyle Management

Recommendations

14.29 Provide children and adolescents with overweight or obesity and type 2 diabetes and their families with developmentally and culturally appropriate comprehensive lifestyle programs integrated with diabetes management to achieve at least a 7–10% decrease in excess weight. **B**

14.30 Given the necessity of long-term weight management for children and adolescents with diabetes, lifestyle intervention should be based on a chronic care model and offered in the context of diabetes care. **E**

Glycemic Goals

Recommendations

14.31 For children and adolescents with type 2 diabetes, glycemic status should be assessed at least every 3 months or as frequently as clinically indicated. **E**

14.32 Consider setting an A1C goal of <6.5% (<48 mmol/mol) for most children and adolescents with type 2 diabetes who have a low risk of hypoglycemia. For those at higher risk of hypoglycemia, A1C goals should be individualized as clinically appropriate. **C**

Exercise Needs Specific to Children and Adolescents With Type 2 Diabetes

Children and adolescents with type 2 diabetes and their families should receive education and support for physical activity, including achieving and maintaining a healthy weight (34). Family-based interventions have been reported to be effective on physical activity behavior (25,131). A family-centered approach to lifestyle modification, including those aspects focused on physical activity, is essential in children and adolescents with type 2 diabetes, and recommendations should be culturally appropriate and sensitive to family resources (see section 5, “Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes”).

Pharmacologic Management

Recommendations

14.33 Initiate pharmacologic therapy with consideration of multiple add-on therapies early on, in addition to behavioral counseling for healthful nutrition and physical activity changes, at diagnosis of type 2 diabetes. **A**

14.34 In individuals with incidentally diagnosed type 2 diabetes (A1C <8.5% [<69 mmol/mol] and asymptomatic), metformin is the initial pharmacologic treatment of choice unless contraindicated by kidney function. **A**

14.35 Children and adolescents with marked hyperglycemia (A1C $\geq 8.5\%$ [≥ 69 mmol/mol]) without acidosis at diagnosis should be treated initially with long-acting insulin while metformin is initiated and titrated. **B**

14.36 Initiate subcutaneous or intravenous insulin treatment in individuals with ketoacidosis to rapidly correct the hyperglycemia and the metabolic derangement. Once acidosis is resolved, metformin should be initiated while subcutaneous insulin therapy is continued. **A**

14.37 In individuals presenting with severe hyperglycemia (blood glucose ≥ 600 mg/dL [≥ 33.3 mmol/L]), consider assessment and treatment as needed for hyperglycemic hyperosmolar state. **A**

14.38 If individualized glycemic goals are not achieved or maintained with metformin (with or without long-acting insulin), glucagon-like peptide 1 receptor agonist (GLP-1 RA) and/or sodium–glucose cotransporter 2 inhibitor

(SGLT2i) should be considered in children and adolescents with type 2 diabetes of approved ages. **A**

14.39 For children and adolescents with type 2 diabetes not meeting individualized glycemic goals, consider maximizing noninsulin therapies (metformin, GLP-1 RA, and SGLT2i) before initiating and/or intensifying the insulin therapy plan. **E**

14.40 In individuals with type 2 diabetes initially treated with insulin and metformin and/or other glucose-lowering medications who are meeting glucose goals based on blood glucose monitoring or CGM, reducing or discontinuing insulin should be considered. **B**

Glycemic goals should be individualized, taking into consideration the long-term health benefits of more stringent goals and risk for adverse effects, such as hypoglycemia. A lower A1C goal of <6.5% in children and adolescents with type 2 diabetes compared with <7% recommended in type 1 diabetes is justified by a lower risk of hypoglycemia and higher risk of complications in children and adolescents with type 2 diabetes (13,132–136). Blood glucose monitoring plans should be individualized, taking into consideration the pharmacologic treatment of the person. Although data on CGM in children and adolescents with type 2 diabetes are sparse (137,138), CGM could be considered in individuals requiring frequent blood glucose monitoring for diabetes management as well as for those on insulin who are capable of using the device safely (either by themselves or with caregivers).

Current pharmacologic treatment options for children and adolescents with type 2 diabetes are limited to four approved drug classes: insulin, metformin, glucagon-like peptide 1 (GLP-1) receptor agonists, and sodium–glucose cotransporter 2 inhibitors (SGLT2is). Presentation with ketoacidosis or marked ketosis requires a period of insulin therapy until fasting and postprandial glycemia have been restored to normal or near-normal levels. Insulin pump therapy should be considered for those on long-term multiple daily injections who are able to safely manage the device. Initial treatment should also be with insulin when the distinction

between type 1 diabetes and type 2 diabetes is unclear and in individuals who have random blood glucose concentrations ≥ 250 mg/dL (≥ 13.9 mmol/L) and/or A1C $\geq 8.5\%$ (≥ 69 mmol/mol) (139). Metformin therapy should be added after resolution of ketosis or ketoacidosis.

When initial insulin treatment is not required, initiation of metformin is recommended as first-line therapy. The TODAY study found that metformin alone provided durable glycemic management (A1C $< 8\%$ [< 64 mmol/mol] for 6 months) only in approximately half of the participants (140). The Restoring Insulin Secretion (RISE) Consortium study did not demonstrate differences in measures of glucose or β -cell function preservation between metformin and insulin, but there was more weight gain with insulin (141).

To date, the TODAY study is the only trial combining lifestyle and metformin therapy in children and adolescents with type 2 diabetes; the combination did not perform better than metformin alone in achieving durable glycemic levels (139).

RCTs in children and adolescents have shown that GLP-1 receptor agonists are safe and effective for decreasing A1C (142–146) and promoting weight loss at higher doses approved for obesity (147). Use of GLP-1 receptor agonists can increase the frequency of gastrointestinal side effects and should not be used in individuals with a family history of medullary thyroid cancer. A recently published RCT of the dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 receptor agonist tirzepatide at doses of 5 mg and 10 mg weekly demonstrated clinically meaningful and statistically significant improvements in both A1C and weight at 30 weeks in the pooled tirzepatide group versus placebo with benefits sustained at 52 weeks (148). The most common adverse events were gastrointestinal, as seen in adult trials (148). There is no regulatory approval to date for pediatric use of tirzepatide.

In addition to GLP-1 receptor agonists, SGLT2is are well-studied drugs in adults with type 2 diabetes, and now empagliflozin, dapagliflozin, and canagliflozin are approved for use in children and adolescents aged 10–17 years with type 2 diabetes based on clinical trials showing clinically relevant decreases in A1C (149–152). These agents are well tolerated in children and adolescents with type 2 diabetes with a low risk of severe hypoglycemia and

DKA. Individuals should be counseled on the increased risk of genitourinary infections.

In a multicenter double-blind, placebo-controlled trial of children and adolescents randomized at baseline to 10 mg empagliflozin, 5 mg linagliptin, or placebo, there was a significant reduction in A1C in the empagliflozin pooled group at 6 months (empagliflozin dose increased to 25 mg in a random manner in those with A1C $\geq 7\%$ at 14 weeks) compared with the placebo group; the linagliptin group did not demonstrate A1C benefit versus placebo (149). In a multicenter double-blind, placebo-controlled trial of dapagliflozin (151), children and adolescents with type 2 diabetes were randomized at baseline to 5 mg dapagliflozin, 2.5 mg saxagliptin, or placebo (with doses of dapagliflozin and saxagliptin increased in a random manner at week 14, namely, 10 mg dapagliflozin or 5 mg saxagliptin in those with A1C $\geq 7\%$). After 6 months, the pooled dapagliflozin versus placebo group had a significant reduction in A1C with no significant difference between the saxagliptin and placebo groups. Similarly, in the third SGLT2i randomized controlled clinical trial (152), children and adolescents with type 2 diabetes were randomized at baseline to 100 mg canagliflozin or placebo (with those in the canagliflozin group not achieving A1C $< 7\%$ at week 12 further randomized to continue at 100 mg or increase to 300 mg). After 6 months, the pooled canagliflozin versus placebo group demonstrated a significant reduction in A1C. In all three clinical trials of the SGLT2is, safety outcomes were assessed over 12 months and demonstrated safety profiles in children and adolescents matching those found in studies of adults with type 2 diabetes (149,151,152).

Metabolic Surgery

Recommendations

14.41 Consider metabolic surgery for the treatment of adolescents with type 2 diabetes who have class 2 obesity or higher (BMI 35 to < 40 kg/m² or 120% to $< 140\%$ percentile for age and sex, whichever is lower) and who have elevated A1C and/or serious comorbidities despite lifestyle and pharmacologic intervention. **A**

14.42 Metabolic surgery for adolescents with type 2 diabetes should

be performed only by an experienced surgeon working as part of a well-organized and engaged interprofessional team, including a surgeon, endocrinologist, registered dietitian nutritionist, behavioral health specialist, and nurse. **A**

The results of weight loss and lifestyle interventions for obesity in children and adolescents have been modest, and treatment options as adjuncts to lifestyle therapy are limited, although these findings do not include a more recently available dual GIP and GLP-1 receptor agonist. Recent U.S. Food and Drug Administration–approved medications for individuals age 12 years and older include phentermine and topiramate extended-release capsules and GLP-1 receptor agonists (147,153–155), with no pediatric regulatory approval of the dual GIP and GLP-1 receptor agonist. Metabolic surgery is now increasingly performed in adolescents with obesity. Small retrospective analyses and a prospective multicenter, non-randomized study suggest that bariatric or metabolic surgery have benefits in adolescents with obesity and type 2 diabetes like those observed in adults. Early follow-up studies indicate that adolescents experience similar degrees of weight loss compared with adults and even higher rates of type 2 diabetes and hypertension remission (156). A secondary data analysis from the Teen-Longitudinal Assessment of Bariatric Surgery (Teen-LABS) and TODAY studies suggests surgical treatment of adolescents with severe obesity and type 2 diabetes is associated with improved glycemia compared with the agents used in the TODAY study (157); however, no randomized trials have compared the effectiveness and safety of surgery with those of current treatment options in adolescents and particularly with the vertical sleeve gastrectomy, which is the most widely performed metabolic surgery in adolescents (158). The guidelines used as an indication for metabolic surgery in adolescents generally include class 2 obesity or higher (BMI 35 to < 40 kg/m² or 120% to $< 140\%$ of the 95th percentile for age and sex, whichever is lower), with comorbidities or BMI 40 kg/m² or higher with or without comorbidities (159–163). A number of groups, including the Pediatric Bariatric Study Group and Teen-LABS study, have

demonstrated the effectiveness of metabolic surgery in adolescents (159–163). The 10-year follow up data from Teen-LABS also demonstrates long-term durability of weight loss and comorbidity remission in adolescents (164). Additional long-term data on the rates of complications, reoperations, nutritional deficiencies, and diabetes recurrence are still needed. Furthermore, newer obesity pharmacotherapy trials are being performed in children and adolescents with the anticipation that positive results for weight loss in association with safety, including the recently published trial of tirzepatide (148), may supplant the need for metabolic surgery.

Prevention and Management of Diabetes Complications Among All Children and Adolescents With Diabetes

Recommendations **14.43–14.79**, regarding type 1 and type 2 diabetes complications, are presented in **Table 14.1** to facilitate direct comparison.

Autoimmune Conditions

Because of the increased frequency of other autoimmune diseases in type 1 diabetes, screening for thyroid dysfunction and celiac disease should be considered (165–169). Periodic screening in asymptomatic individuals has been recommended, but the optimal frequency of screening is unclear.

Although much less common than thyroid dysfunction and celiac disease, other autoimmune conditions, such as Addison disease (primary adrenal insufficiency), autoimmune hepatitis, autoimmune gastritis, dermatomyositis, premature ovarian failure, and myasthenia gravis, occur more commonly in the population with type 1 diabetes than in the general pediatric population and should be assessed and monitored as clinically indicated. In addition, relatives of individuals with type 1 diabetes should be offered testing for islet autoantibodies through research studies (e.g., Type 1 Diabetes TrialNet) and national programs for early diagnosis of preclinical type 1 diabetes (stages 1 and 2).

Thyroid Disease

Autoimmune thyroid disease is the most common autoimmune disorder associated with diabetes, occurring in 17–30% of individuals with type 1 diabetes (166,

170,171). At the time of diagnosis, ~25% of children with type 1 diabetes have thyroid autoantibodies (172), the presence of which is predictive of thyroid dysfunction—most commonly hypothyroidism, although hyperthyroidism occurs in ~0.5% of people with type 1 diabetes (173,174). For thyroid autoantibodies, a study from Sweden indicated that antithyroid peroxidase antibodies were more predictive of autoimmune thyroid disease than antithyroglobulin antibodies in multivariate analysis (175). Thyroid function tests may be misleading (nonthyroidal illness) if performed at the time of diagnosis owing to the effect of previous hyperglycemia, ketosis or ketoacidosis, weight loss, etc. Therefore, if performed at diagnosis and slightly abnormal, thyroid function tests should be repeated soon after a period of metabolic stability and achievement of glycemic goals. Subclinical hypothyroidism may be associated with an increased risk of symptomatic hypoglycemia and dyslipidemia (176,177) and a reduced linear growth rate. Hyperthyroidism alters glucose metabolism and usually causes deterioration of glycemia.

Celiac Disease

Celiac disease is an immune-mediated disorder that occurs with increased frequency in people with type 1 diabetes (1.6–16.4% of individuals compared with 0.3–1% in the general population) (165,168,169, 178–181). Screening people with type 1 diabetes for celiac disease is further justified by its association with osteoporosis, vitamin D deficiency, iron deficiency, growth failure, erratic glucose levels due to altered food absorption, and potential increased risk of retinopathy and albuminuria (182–184).

Screening for celiac disease includes measuring serum levels of IgA and tissue transglutaminase (tTG) IgA antibodies, or, with IgA deficiency, screening can include measuring tTG IgG antibodies or deamidated gliadin peptide IgG antibodies. Because most cases of celiac disease are diagnosed within the first 5 years after the diagnosis of type 1 diabetes, screening should be considered soon after diagnosis and repeated at 2 and then 5 years (179) or if clinical symptoms arise, such as poor growth or increased hypoglycemia (182).

Although celiac disease can be diagnosed more than 10 years after diabetes

diagnosis, there are insufficient data after 5 years to determine the optimal screening frequency. Gastroenterology guidelines on screening for celiac disease in children (not specific to children with type 1 diabetes) suggest that biopsy may not be necessary in symptomatic children with high antibody titers (i.e., >10 times the upper limit of normal) provided that further testing is performed (verification of endomysial antibody positivity on a separate blood sample) (185). About 95% of people with type 1 diabetes (186) and almost 99% of people with celiac disease carry HLA-DQ2 and/or HLA-DQ8 (187), so genetic testing may not be needed. In symptomatic children with type 1 diabetes and confirmed celiac disease, gluten-free eating patterns reduce symptoms and rates of hypoglycemia (188). The challenging eating plan restrictions associated with having both type 1 diabetes and celiac disease place an added burden on individuals. Therefore, a biopsy to confirm the diagnosis of celiac disease is recommended when the diagnosis is in question, especially in asymptomatic children and adolescents, before establishing a diagnosis of celiac disease and endorsing significant eating plan changes.

Management of Cardiovascular Risk Factors

Hypertension

Blood pressure measurements should be performed using the appropriate size cuff and with arm at heart level with the child or adolescent seated and relaxed. Elevated blood pressure should be confirmed on at least three separate days, and ambulatory blood pressure monitoring should be considered. Evaluation of secondary causes of hypertension should proceed as clinically indicated (189,190). Treatment is generally initiated with an ACE inhibitor, but an angiotensin receptor blocker can be used if the ACE inhibitor is not tolerated (e.g., due to cough) (191).

Dyslipidemia

Population-based studies estimate that 14–45% of children and adolescents with type 1 diabetes have two or more atherosclerotic cardiovascular disease (CVD) risk factors (192–194), and the prevalence of CVD risk factors increases with age (194) and among racial and ethnic minoritized groups (119), with girls having a higher risk burden than boys (193).

Table 14.1—Recommendations for diabetes-associated conditions in children and adolescents

	Type 1 diabetes recommendations	Type 2 diabetes recommendations	Type 1 and 2 diabetes recommendations
Dyslipidemia	14.43 For children and adolescents with type 1 diabetes, lipid screening should be performed soon after diagnosis, preferably after glycemia has improved and age is ≥ 2 years. If initial LDL cholesterol is ≤ 100 mg/dL (≤ 2.6 mmol/L), subsequent testing should be performed at 9–11 years of age B and repeated every 3 years. E	14.44 In children and adolescents with type 2 diabetes, lipid screening should be performed soon after diagnosis, preferably after glycemia has improved and annually thereafter. B	14.45 The LDL cholesterol goal is <100 mg/dL (<2.6 mmol/L). E 14.46 In children and adolescents with diabetes, if lipids are abnormal, initial therapy should consist of optimizing glycemia and medical nutritional therapy to limit calories from fat to 25–30% and saturated fat to $<7\%$, limit cholesterol to <200 mg/day, avoid <i>trans</i> fats, and aim for $\sim 10\%$ calories from monounsaturated fats for elevated LDL. For elevated triglycerides, MNT should also focus on decreasing carbohydrate intake and increasing foods rich in n-3 fatty acids in addition to the above changes. A 14.47 In children and adolescents with diabetes, if LDL cholesterol remains >130 mg/dL (>3.4 mmol/L) after 6 months of nutrition intervention, initiate therapy with a statin, with a goal of LDL <100 mg/dL (<2.6 mmol/L). Due to the potential teratogenic effects, individuals of childbearing potential should receive reproductive counseling, and statins should be avoided in individuals of childbearing potential who are not using reliable contraception. B 14.48 In children and adolescents with diabetes, if triglycerides are >400 mg/dL (>4.7 mmol/L) fasting or $>1,000$ mg/dL (>11.6 mmol/L) nonfasting, optimize glycemia and begin fibrate, with a goal of <400 mg/dL (<4.7 mmol/L) fasting to reduce risk for pancreatitis. C
Hypertension			14.49 In children and adolescents with diabetes, BP should be measured at every clinic visit. In children and adolescents with high BP (BP ≥ 90th percentile for age, sex, and height or, in adolescents aged ≥ 13 years, $\geq 120/80$ mmHg) on three separate measurements, ambulatory BP monitoring should be strongly considered. B 14.50 Excess weight increases cardiovascular event rates among people with diabetes and should be addressed with MNT, intensive lifestyle interventions focusing on dyslipidemia, hypertension, hyperglycemia along with adjunct pharmacotherapy, and/or bariatric surgery as appropriate. C 14.51 In children and adolescents with diabetes, after excluding secondary hypertension, treatment of elevated BP (defined as 90th to <95th percentile for age, sex, and height or, in adolescents aged ≥ 13 years, 120–129/<80 mmHg) is lifestyle modification focused on healthy nutrition, physical activity, sleep, and, if appropriate, weight management. C 14.52 For children and adolescents with diabetes, after excluding other causes, in addition to lifestyle modification, ACE inhibitors or ARBs should be started for treatment of

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Table 14.1—Continued

	Type 1 diabetes recommendations	Type 2 diabetes recommendations	Type 1 and 2 diabetes recommendations
Nephropathy	14.54 For children and adolescents with type 1 diabetes, nephropathy screening should be obtained at puberty or at age ≥ 11 years, whichever is earlier, once the youth have had diabetes for 5 years and annually thereafter. B	14.55 In children and adolescents with type 2 diabetes, nephropathy screening should be performed at the time of diagnosis and annually thereafter. An elevated UACR (>30 mg/g creatinine) should be confirmed on two of three samples. B	confirmed hypertension (defined as BP consistently ≥ 95th percentile for age, sex, and height or, in adolescents aged ≥ 13 years, BP $\geq 130/80$ mmHg). Due to the potential teratogenic effects, individuals of childbearing potential should receive reproductive counseling, and ACE inhibitors and ARBs should be avoided in individuals of childbearing potential who are not using reliable contraception. B 14.53 For children and adolescents the goal of hypertension treatment is BP <90th percentile for age, sex, and height or, in adolescents aged ≥ 13 years, BP $<130/80$ mmHg. C 14.56 In children and adolescents with diabetes, nephropathy screening should be performed with a random spot urine sample. Consider obtaining a morning sample if there are effects of exercise or orthostatic changes. An elevated UACR (>30 mg/g creatinine) should be confirmed on two of three samples over a 6-month period. B 14.57 Determine eGFR at the time of diagnosis and annually thereafter. E 14.58 In nonpregnant children and adolescents with diabetes, either an ACE inhibitor or an ARB is recommended for those with moderately increased albuminuria (UACR 30–299 mg/g creatinine) B and is strongly recommended for those with severely increased albuminuria (UACR ≥ 300 mg/g creatinine) and/or eGFR <60 mL/min/1.73 m² to maximally tolerated dose to prevent the progression of kidney disease and reduce cardiovascular events. A If one class is not tolerated, the other should be substituted. B Due to the potential teratogenic effects, individuals of childbearing potential should receive reproductive counseling, and ACE inhibitors and ARBs should be avoided in individuals of childbearing potential who are not using reliable contraception. B 14.59 For children and adolescents with nephropathy, continue monitoring (every 3–6 months and/or as indicated by UACR and eGFR) to detect disease progression. E 14.60 Refer to nephrology in case of uncertainty of etiology, worsening UACR, or decrease in eGFR. E 14.63 Optimizing glycemia is recommended to decrease the risk or slow the progression of retinopathy. B
Retinopathy	14.61 An initial dilated and comprehensive diabetes eye examination is recommended once youth have had type 1 diabetes for 3–5 years, provided they are aged ≥ 11 years or puberty has started, whichever is earlier. B	14.62 Retinopathy screening in children and adolescents with type 2 diabetes should be performed at or soon after diagnosis and annually thereafter. C	

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Table 14.1—Continued

	Type 1 diabetes recommendations	Type 2 diabetes recommendations	Type 1 and 2 diabetes recommendations
Neuropathy	14.64 For children and adolescents with type 1 diabetes, after the initial examination, repeat dilated and comprehensive eye examination or retinal photography is recommended every 2 years. Less frequent examinations, every 4 years, may be acceptable on the advice of an eye care professional and based on risk factor assessment, including a history of A1C <8% (<64 mmol/mol). B 14.67 For children and adolescents with type 1 diabetes, consider an annual comprehensive foot exam at the start of puberty or at age ≥11 years, whichever is earlier, once the youth have had type 1 diabetes for 5 years. The examination should include inspection, assessment of foot pulses, pinprick, 10-g monofilament sensation tests, testing of vibration sensation using a 128-Hz tuning fork, and ankle reflex tests. B	14.65 Less frequent examination (every 2 years) using dilated eye examination or retinal photography may be considered if achieving glycemic goals and a normal eye exam. C 14.68 Screen children and adolescents with type 2 diabetes for the presence of neuropathy by foot examination at diagnosis and annually. The examination could include inspection, assessment of foot pulses, pinprick, 10-g monofilament sensation tests, testing of vibration sensation using a 128-Hz tuning fork, and ankle reflex tests. C	14.66 Programs that use nondilated retinal photography (with remote reading or use of a validated assessment tool) can be appropriate screening strategies for diabetic retinopathy. B
MASLD	14.69 Evaluate children and adolescents with type 2 diabetes for MASLD (by measuring AST and ALT) at diagnosis and annually thereafter. B 14.70 Consider referral to gastroenterology for persistently elevated or worsening transaminases. B		
Obstructive sleep apnea			14.71 In children and adolescents with diabetes, screening for symptoms of sleep apnea should be done at least annually, and referral to a pediatric sleep specialist is recommended for evaluation and a polysomnogram, if indicated. Obstructive sleep apnea should be treated when documented. B
Polycystic ovary syndrome			14.72 Evaluate for polycystic ovary syndrome in adolescent girls with diabetes, including laboratory studies, when clinically indicated. B 14.73 Metformin, in addition to lifestyle modification, is likely to improve the menstrual cyclicity and hyperandrogenism in adolescent girls with diabetes. E
Cardiovascular disease			14.74 Excessive weight gain increases cardiovascular event rates among children and adolescents with diabetes and should be addressed with lifestyle and obesity pharmacotherapy as appropriate. C

Continued on p. S311

Table 14.1—Continued

	Type 1 diabetes recommendations	Type 2 diabetes recommendations	Type 1 and 2 diabetes recommendations
Autoimmune conditions	14.75 In children and adolescents with type 1 diabetes, assess for autoimmune conditions outside of critical illness if clinically indicated. B		
Thyroid disease	14.76 In children and adolescents with type 1 diabetes, measure thyroid-stimulating hormone concentrations at diagnosis when clinically stable or soon after optimizing glycemia. If normal, suggest rechecking every 1–2 years or sooner if the individual has positive thyroid antibodies or develops symptoms or signs suggestive of thyroid dysfunction, thyromegaly, an abnormal growth rate, or unexplained glycemic variability. B		
Celiac disease	14.77 Screen children and adolescents with type 1 diabetes outside of critical illness for celiac disease by measuring IgA tissue tTG antibodies, with documentation of acceptable serum IgA levels for the local assay, soon after the diagnosis of diabetes, or IgG tTG and deamidated gliadin antibodies if IgA is deficient. B 14.78 Repeat screening for celiac disease within 2 years of type 1 diabetes diagnosis and then again after 5 years and consider more frequent screening in children and adolescents who have symptoms or a first-degree relative with celiac disease. B 14.79 Prescribe a gluten-free eating pattern for children and adolescents with confirmed celiac disease to avoid nutritional complications. Refer children and adolescents and their caregivers to a registered dietitian nutritionist experienced in managing both diabetes and celiac disease. B		

ARB, angiotensin receptor blocker; BP, blood pressure; eGFR, estimated glomerular filtration rate; MASLD, metabolic dysfunction–associated steatotic liver disease; MNT, medical nutrition therapy; tTG, tissue transglutaminase; UACR, urinary albumin-to-creatinine ratio.

Pathophysiology. The atherosclerotic process begins in childhood, and although atherosclerotic CVD events are not expected to occur during childhood, observations using a variety of methodologies show that children and adolescents with type 1 diabetes may have subclinical CVD within the first decade of diagnosis (195–197). Studies of carotid intima media thickness have yielded inconsistent results (190,191).

Screening. Diabetes predisposes the individual to the development of accelerated arteriosclerosis. Lipid evaluation for these individuals contributes to risk assessment and identifies an important proportion of those with dyslipidemia. Therefore, initial screening should be done soon after diagnosis. If the initial screen is normal, subsequent screening may be done at 9–11 years of age, which is a stable time for lipid assessment in children (198). Children and adolescents with a primary lipid disorder (e.g., familial hyperlipidemia) should be referred to a lipid specialist. Non-HDL cholesterol level has been identified as a significant predictor of the presence of atherosclerosis—as powerful as any other lipoprotein cholesterol measure in children and adolescents. For people with diabetes, non-HDL cholesterol level seems to be more predictive of persistent dyslipidemia and, therefore, atherosclerosis and future events than total cholesterol, LDL cholesterol, or HDL cholesterol level alone. A major advantage (199) of non-HDL cholesterol is that it can be accurately calculated in a nonfasting state and therefore is practical to obtain in clinical practice as a screening test (200). Youth with type 1 diabetes have a high prevalence of lipid abnormalities (192,199). Even if normal, screening should be repeated within 3 years, as A1C and other cardiovascular risk factors can change dramatically during adolescence (201).

Treatment. Pediatric lipid guidelines provide some guidance relevant to children and adolescents with type 1 diabetes and secondary dyslipidemia (190,191,202); however, there are few studies on modifying lipid levels in children and adolescents with type 1 diabetes. A 6-month trial of nutritional counseling produced a significant improvement in lipid levels (203); likewise, a lifestyle intervention trial with 6 months of exercise in adolescents demonstrated improvement in lipid levels (204). Data from the SEARCH study show

that improved glucose over a 2-year period is associated with a more favorable lipid profile; however, improved glycemia alone will not normalize lipids in children and adolescents with type 1 diabetes and dyslipidemia (205,206).

Although intervention data are sparse, the American Heart Association categorizes children and adolescents with type 1 diabetes in the highest tier for cardiovascular risk and recommends both lifestyle and pharmacologic treatment for those with elevated LDL cholesterol levels (207,208). Initial therapy should include a nutrition plan that restricts saturated fat to 7% of total calories and dietary cholesterol to 200 mg/day (198). Data from randomized clinical trials in children as young as 7 months of age indicate that this nutrition plan is safe and does not interfere with normal growth and development.

Long-term safety and cardiovascular outcome efficacy of statin therapy have been established for children with familial hypercholesterolemia (209). At the time of this writing, rosuvastatin is indicated for children as young as 6 years old (210). Statins should be avoided in individuals of childbearing age who are not using reliable contraception (see section 15, “Management of Diabetes in Pregnancy,” for more information). The multicenter, randomized, placebo-controlled Adolescent Type 1 Diabetes Cardio-Renal Intervention Trial (AdDIT) provides safety data on pharmacologic treatment with an ACE inhibitor and statin in adolescents with type 1 diabetes (190).

Microvascular Complications

Nephropathy

Data from 7,549 individuals <20 years of age in the T1D Exchange clinic registry emphasize the importance of meeting glycemic and blood pressure goals, particularly as diabetes duration increases, to reduce the risk of chronic kidney disease. The data also underscore the importance of routine screening to ensure early diagnosis and timely treatment of albuminuria (211). An estimation of glomerular filtration rate (GFR), calculated with GFR-estimating equations using serum creatinine, height, age, and sex (212), should be considered at baseline and repeated as indicated based on clinical status, age, diabetes duration, and therapies. Improved methods are needed to screen for early GFR loss, since estimated GFR is inaccurate

at $\text{GFR} > 75 \text{ mL/min/1.73 m}^2$ (212,213). The AdDIT study in adolescents with type 1 diabetes demonstrated the safety of ACE inhibitor treatment, but the treatment did not change the albumin-to-creatinine ratio over the course of the study (190).

Retinopathy

Retinopathy (like albuminuria) most commonly occurs after the onset of puberty and after 5–10 years of diabetes duration (214). It is currently recognized that there is a low risk of development of vision-threatening retinal lesions prior to 12 years of age (215,216). A 2019 publication based on the follow-up of the DCCT adolescent cohort supports a lower frequency of eye examinations than previously recommended, particularly in adolescents with A1C closer to the goal range (217,218). Autonomous artificial intelligence screening for diabetic retinopathy has been shown to increase access to this routine health maintenance (219). Referrals should be made to eye care professionals with expertise in diabetic retinopathy and experience in counseling pediatric individuals and families on the importance of prevention, early detection, and intervention.

Neuropathy

Diabetic neuropathy rarely occurs in prepubertal children or after only 1–2 years of diabetes (214), although data suggest a prevalence of distal peripheral neuropathy of 7% among 1,734 adolescents with type 1 diabetes in the SEARCH for Diabetes in Youth study and association with the presence of CVD risk factors (220,221). A comprehensive foot exam, including inspection, palpation of dorsalis pedis and posterior tibial pulses, and determination of proprioception, vibration, and monofilament sensation, should be performed annually along with an assessment of symptoms of neuropathic pain (221). Foot inspection can be performed at each visit to educate youth regarding the importance of foot care and often detects concurrent, unreported medical issues like tinea pedis or paronychia that would require treatment (see section 12, “Retinopathy, Neuropathy, and Foot Care”).

Type 2 Diabetes Comorbidities

Comorbidities may already be present at the time of diagnosis of type 2 diabetes in children and adolescents (12,222).

Therefore, blood pressure measurement, a fasting lipid panel, assessment of random urine albumin-to-creatinine ratio, foot examination for neuropathy, and a dilated eye examination should be performed at diagnosis. Additional medical conditions that may need to be addressed include polycystic ovary disease and other comorbidities associated with pediatric obesity, such as sleep apnea, hepatic steatosis, orthopedic complications, and psychosocial concerns. The ADA position statement “Evaluation and Management of Youth-Onset Type 2 Diabetes” (3) provides guidance on the prevention, screening, and treatment of type 2 diabetes and its comorbidities in children and adolescents.

Type 2 diabetes in children and adolescents is associated with significant microvascular and macrovascular risk burden and a substantial increase in the risk of cardiovascular morbidity and mortality at an earlier age than in those diagnosed later in life (13,223). The higher complication risk in earlier-onset type 2 diabetes is likely related to prolonged lifetime exposure to hyperglycemia and other atherogenic risk factors, including insulin resistance, dyslipidemia, hypertension, and chronic inflammation. There is a low risk of hypoglycemia in children and adolescents with type 2 diabetes, even if they are being treated with insulin (224), and there are high rates of chronic complications (133–135,224). These diabetes comorbidities also appear to be higher than those found in children and adolescents with type 1 diabetes despite shorter diabetes duration and lower A1C (222). In addition, the progression of vascular abnormalities appears to be more pronounced in children and adolescents-onset type 2 diabetes than with type 1 diabetes of similar duration, including ischemic heart disease and stroke (223).

In adolescents with type 2 diabetes and polycystic ovary syndrome, oral contraceptives are appropriate agents.

SUBSTANCE USE AMONG ALL CHILDREN AND ADOLESCENTS WITH DIABETES

Tobacco, Electronic Cigarettes, Alcohol, and Cannabis

Recommendations

14.80 Screen children and adolescents with diabetes for tobacco/nicotine vaping, substance use, and alcohol use

at diagnosis and regularly thereafter, **C** discourage use and provide appropriate referrals to cessation programs as needed. **A**

14.81 Advise all children, adolescents, and young adults with diabetes not to use cannabis recreationally in any form. **E**

The adverse health effects of smoking and use of tobacco products are well recognized with respect to future cancer and CVD risk. Despite this, rates of tobacco use are significantly higher among adolescents and young adults with type 1 and type 2 diabetes than those without diabetes (225,226). In children and adolescents with diabetes, it is important to avoid additional CVD risk factors. Smoking increases the risk of the onset of albuminuria; therefore, smoking avoidance is important to prevent both microvascular and macrovascular complications (199). Discouraging use of tobacco products, including vaping and electronic cigarettes (227,228), is an important part of routine diabetes care. Individuals with diabetes should be advised to avoid vaping and using electronic cigarettes, either as a way to stop smoking tobacco or as a recreational drug. In younger children, it is important to assess exposure to cigarette smoke in the home because of the adverse effects of secondhand smoke and to discourage them from ever smoking.

Alcohol use has implications for glycemic management and safety in adolescents and young adults with diabetes. Alcohol consumption can cause delayed hypoglycemia, typically 6 to 12 h after drinking (229). Further, alcohol increases the risk of hypoglycemia unawareness because symptoms of alcohol intoxication (e.g., slurred speech, drowsiness, confusion, difficulty walking) mimic symptoms of hypoglycemia (230). An untreated hypoglycemic event can result in loss of consciousness, seizure, and even death (230). For this reason, efforts are warranted to reduce alcohol use and increase education about the risks of alcohol use and strategies to minimize risks. A psychoeducational intervention for adolescents with chronic medical conditions, including type 1 diabetes, has demonstrated benefits for knowledge, understanding of perceived risks, and reduced use in some subgroups (231). See also section 5, “Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes.”

Increased legalization and multiple formulations of cannabis products have increased the availability of these products. Among adolescents with type 1 diabetes, reported cannabis use ranged from 17.1% for past-month use to 23% for past 3-month use to 30.9% for lifetime use (231,232). Cannabis use increases the risk for hyperglycemic ketosis-cannabis hyperemesis syndrome in adults with type 1 diabetes (233,234), and emerging evidence in adolescents suggests a similar pattern (235). Hyperglycemic ketosis-cannabis hyperemesis syndrome is characterized by nausea that progresses to severe vomiting, leading to ketosis and alkalosis, and subsequently hyperglycemia (236). For adolescents with type 1 diabetes presenting with hyperglycemic emergencies, health care professionals should consider hyperglycemic ketosis-cannabis hyperemesis syndrome in individuals with pH ≥ 7.4 and bicarbonate >15 mmol/L in the presence of ketosis (236). Routine diabetes care should discourage the use of recreational cannabis in all forms. See section 5, “Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes,” for more information about smoking cessation, tobacco, electronic cigarettes, and cannabis use in people with diabetes.

TRANSITION FROM PEDIATRIC TO ADULT CARE FOR ALL CHILDREN AND ADOLESCENTS WITH DIABETES

Recommendations

14.82 Diabetes care teams should implement transition preparation programs beginning in early adolescence and, at the latest, at least 1 year before the anticipated transfer from pediatric to adult health care. **E**

14.83 Interprofessional adult and pediatric health care teams should provide support and resources for adolescents, young adults, and their families prior to and during the transfer process from pediatric to adult health care. **C**

14.84 Pediatric diabetes specialists should partner with adolescents with diabetes and their caregivers to engage in shared decision-making for the timing of transfer to an adult diabetes specialist. There is no age-specific cutoff for young people with diabetes to transfer to an adult diabetes specialist. **E**

Care and close supervision of diabetes management are increasingly shifted from parents and other adults to the young people with type 1 or type 2 diabetes throughout childhood and adolescence. The shift from pediatric to adult health care professionals, however, often occurs abruptly as the older teen enters the next developmental stage, referred to as emerging adulthood (237), which is a critical period for young people who have diabetes. During this period of major life transitions, adolescents and young adults may begin to move out of their parents' or caregivers' homes and become increasingly responsible for their diabetes care. Their new responsibilities include self-management of their diabetes, scheduling and attending medical appointments, ensuring timely prescription refills, and financing health care once they are no longer covered by their parents' health insurance plans (ongoing coverage until age 26 years is currently available under provisions of the U.S. Affordable Care Act). In addition to lapses in health care, this is also a period associated with deterioration in glycemic stability; increased occurrence of acute complications; psychosocial, emotional, and behavioral challenges; and the emergence of chronic complications (238,239). The transfer period from pediatric to adult care is prone to fragmentation in health care delivery, which may adversely impact health care quality, cost, and outcomes (240). Worsening diabetes health outcomes during the transition to adult care and early adulthood have been documented (241,242).

Comprehensive and coordinated planning that begins in early adolescence is necessary to facilitate a seamless transition from pediatric to adult health care (238). Research on effective interventions to promote successful transition to adult care is limited, although there are promising developments that may improve attendance at follow-up appointments and lower hospitalizations (243,244). Use of transition coordinators, technology to support communication with young adults, and other interventions may be useful in addressing the identified needs and preferences of young adults for transition (245) and in supporting successful establishment in adult care settings (246–249). Given the behavioral, psychosocial, and developmental factors that relate to this transition, diabetes care teams addressing

transition should include clinicians certified diabetes care and education specialists, nurses, behavioral health professionals, registered dietitian nutritionists, and social workers (64,250). Resources to enhance social and peer support during the transition process may also be valuable (251). A comprehensive discussion regarding the challenges faced during this period, including specific recommendations, is found in the ADA position statement "Diabetes Care for Emerging Adults: Recommendations for Transition From Pediatric to Adult Diabetes Care Systems" (238). Ultimately, there is no age cutoff for adolescents and young adults with diabetes to transfer to adult diabetes care. The decision to transfer should be a collaborative process in which the young person with diabetes, their caregivers, and pediatric diabetes specialists discuss readiness, preferences, and concerns to ensure that the transfer aligns with the young person's needs and circumstances (244).

The Endocrine Society, in collaboration with the ADA and other organizations, has developed transition tools for clinicians and young people with diabetes and their families (238).

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15. Management of Diabetes in Pregnancy: Standards of Care in Diabetes—2026

American Diabetes Association
Professional Practice Committee for
Diabetes*

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The American Diabetes Association (ADA) “Standards of Care in Diabetes” includes the ADA’s current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. Members of the ADA Professional Practice Committee for Diabetes, an interprofessional expert committee, are responsible for updating the Standards of Care annually, or more frequently as warranted. For a detailed description of ADA standards, statements, and reports, as well as the evidence-grading system for ADA’s clinical practice recommendations and a full list of Professional Practice Committee members, please refer to Introduction and Methodology. Readers who wish to comment on the Standards of Care are invited to do so at professional.diabetes.org/SOC.

DIABETES IN PREGNANCY

The prevalence of diabetes in pregnancy has been increasing in the U.S. in parallel with the worldwide epidemic of obesity. Not only is the prevalence of type 1 diabetes and type 2 diabetes increasing in individuals of reproductive age but there is also a dramatic increase in the reported rates of gestational diabetes mellitus (GDM). Diabetes confers significantly greater maternal and fetal risk that is largely related to the degree of hyperglycemia but also is related to chronic complications and comorbidities of diabetes. In general, specific risks of diabetes in pregnancy include spontaneous abortion, fetal anomalies, preeclampsia, fetal demise, macrosomia, neonatal hypoglycemia, neonatal hyperbilirubinemia, and neonatal respiratory distress syndrome. In addition, exposure to hyperglycemia in utero increases the risks of obesity, hypertension, and type 2 diabetes in offspring later in life (1,2).

Preconception Counseling

Recommendations

15.1 Starting at puberty and continuing in all people with diabetes and child-bearing potential, preconception counseling should be incorporated into routine diabetes care. **A**

15.2 Family planning should be discussed, and effective contraception (with consideration of long-acting, reversible contraception) should be prescribed and used until an individual’s treatment plan and A1C are optimized for pregnancy. **A**

15.3 Preconception counseling should address the importance of achieving glucose levels as close to normal as is safely possible without excessive hypoglycemia, ideally A1C <6.5% (<48 mmol/mol), to reduce the risk of congenital anomalies, preeclampsia, macrosomia, preterm birth, and other complications. **A**

*A complete list of members of the American Diabetes Association Professional Practice Committee for Diabetes can be found at <https://doi.org/10.2337/dc26-SINT>.

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15.4 Individuals with a history of gestational diabetes mellitus (GDM) should seek preconception screening for diabetes and preconception care to identify and treat hyperglycemia and prevent congenital malformations and other adverse maternal and fetal outcomes. **E**

Preconception counseling for pregnant people with preexisting type 1 or type 2 diabetes is highly effective in reducing the risk of congenital malformations and decreasing the risk of preterm delivery and admission to neonatal intensive care units (NICU). Preconception counseling is also associated with reductions in perinatal mortality and small-for-gestational-age birth weight (3). A key point is the need to incorporate a question about plans for pregnancy into the routine primary and gynecologic care of people with diabetes.

There are opportunities at any health care visit to educate all adults and adolescents with diabetes and childbearing potential about the risks of unplanned pregnancies and about improved maternal and fetal outcomes with pregnancy planning (4). Education and counseling should be offered, even when individuals already use contraception or do not intend to conceive (5). Effective preconception counseling could avert substantial health and associated cost burdens related to the offspring (6). Family planning should be discussed, including the benefits of long-acting, reversible contraception, and effective contraception should be prescribed and used until the individual is prepared and ready to become pregnant (7–12).

All individuals with diabetes and childbearing potential should be informed about the importance of achieving and maintaining as near euglycemia as safely possible prior to conception and throughout pregnancy. Observational studies show an increased risk of diabetic embryopathy, especially anencephaly, microcephaly, congenital heart disease, kidney anomalies, and caudal regression, directly proportional to elevations in A1C during the first 10 weeks of pregnancy (13). Although observational studies are confounded by the association between elevated periconceptional A1C and other engagement in self-care behaviors, the quantity and consistency of data are convincing and support the recommendation to optimize glycemia prior to conception with an A1C <6.5% (<48 mmol/mol), as this is associated with the lowest risk of

congenital anomalies (given that organogenesis occurs primarily at 5–8 weeks of gestation), preeclampsia, and preterm birth (13–17). In a systematic review and meta-analysis of observational studies, preconception care for pregnant individuals with preexisting diabetes was associated with lower A1C and reduced risks of birth defects, preterm delivery, perinatal mortality, small-for-gestational-age births, and neonatal intensive care unit admissions (18).

To minimize the occurrence of complications, beginning at the onset of puberty or at diagnosis, all adults and adolescents with diabetes of childbearing potential should receive education about 1) the risks of malformations associated with unplanned pregnancies, even with mild hyperglycemia, and 2) the use of effective contraception at all times when trying to prevent a pregnancy. Preconception counseling using developmentally appropriate educational tools enables adolescents with childbearing potential to make well-informed decisions (4). Preconception counseling resources tailored to adolescents are available at no cost through the American Diabetes Association (ADA) (19).

Individuals with prediabetes or a history of GDM will need preconception evaluation for as long as they have childbearing potential. Individuals with a history of GDM who are planning pregnancy should undergo screening for type 2 diabetes or prediabetes prior to conception, and if not screened preconception, testing should be performed before 15 weeks of gestation, as outlined in section 2, “Diagnosis and Classification of Diabetes.” In the nonpregnant state, evaluation may be performed with any glycemic test recommended in section 2, “Diagnosis and Classification of Diabetes.” Should type 2 diabetes be diagnosed preconception, the individual should initiate treatment with a goal to achieve and maintain an A1C of <6.5% (<48 mmol/mol) prior to conception using therapies approved for use in pregnancy.

Risks for GDM are characterized by an increased risk of large-for-gestational-age birth weight and neonatal and pregnancy complications and an increased risk of long-term maternal type 2 diabetes and abnormal glucose metabolism of offspring in childhood (20). These associations with maternal oral glucose tolerance test (OGTT) results are continuous with no clear inflection points (21,22). Offspring with exposure to untreated GDM have

reduced insulin sensitivity and β -cell compensation and are more likely to have impaired glucose tolerance in childhood (23). In other words, short-term and long-term risks increase with progressive maternal hyperglycemia.

Weight should be assessed at the preconception evaluation. Counseling on the specific risks of obesity in pregnancy and lifestyle interventions to prevent and treat obesity, including referral to a registered dietitian nutritionist (RDN), is recommended regardless of diabetes status (24). In a randomized trial of individuals with overweight or obesity and a history of GDM, weight loss prior to a subsequent pregnancy was associated with a lower risk of GDM recurrence, especially when weight loss was $\geq 5\%$ (odds ratio [OR] 0.18, 95% CI 0.04–0.88) (25). Counseling on weight management should include the known benefits and risks of different strategies for achieving and maintaining weight loss. For strategies that include pharmacotherapy, recommendations should be given for when changes in medications should occur prior to pregnancy. The risk for associated hypertension and other comorbidities may be as high or higher with type 2 diabetes as it is with type 1 diabetes, even if diabetes is better managed and of shorter apparent duration, with pregnancy loss appearing to be more prevalent in the third trimester in those with type 2 diabetes compared with the first trimester in those with type 1 diabetes (26,27).

Preconception Care

Recommendations

15.5 Individuals with preexisting diabetes who are planning a pregnancy should ideally begin receiving interprofessional care prior to conception, which includes an endocrinology health care professional, maternal-fetal medicine specialist, registered dietitian nutritionist, and diabetes care and education specialist, when available. **B**

15.6 In addition to focused attention on achieving glycemic goals, **A** standard preconception care should be augmented with extra focus on nutrition, physical activity, diabetes self-care education, and screening for diabetes comorbidities and complications. **B**

15.7 Individuals with preexisting diabetes who are planning a pregnancy or who have become pregnant should be counseled on the risk of development

and/or progression of diabetic retinopathy. Dilated eye examinations should occur ideally before pregnancy as well as in the first trimester, and then pregnant individuals should be monitored every trimester and for 1 year postpartum as indicated by the degree of retinopathy and as recommended by the eye care health care professional. **B**

The importance of preconception care for all pregnant people is highlighted by American College of Obstetricians and Gynecologists (ACOG) Committee Opinion 762, “Prepregnancy Counseling” (5). Preconception care for people with prediabetes and diabetes should include the standard screening and care recommended for any person planning pregnancy (5). Prescription of prenatal vitamins with at least 400–800 µg of folic acid (28) and 150 µg of potassium iodide (29) is recommended prior to conception. Review and counseling on abstaining from nicotine products, alcohol, and recreational drugs, including cannabis, is important. Standard care includes screening for sexually transmitted infections and thyroid disease, recommended vaccinations, routine genetic screening, a careful review of all prescription and nonprescription medications, herbal supplements, and nonherbal supplements used and a review of travel history and plans with special attention on areas known to have relevant endemic viruses, as outlined by ACOG. See **Table 15.1** for additional details on elements of preconception care (5,28,30).

Due to the complexity of insulin management in pregnancy, referral to a specialized center offering team-based care (with team members including a maternal-fetal medicine specialist, endocrinologist or other health care professional experienced in managing pregnancy and preexisting diabetes, RDN, diabetes care and education specialist, and social worker, as needed) is recommended if this resource is available. When a single specialized center is not available, providing an interprofessional team approach through interprofessional team members at different centers may still be beneficial.

The most important diabetes-specific component of preconception care is the attainment of glycemic goals prior to conception. Diabetes-specific counseling should include an explanation of the risks to mother and fetus related to pregnancies

Table 15.1—Checklist for preconception care for people with prediabetes, diabetes, or a history of gestational diabetes mellitus

Preconception education should include:

- ☐ Comprehensive nutrition assessment and recommendations for:
 - Overweight and obesity or underweight
 - Meal planning
 - Correction of nutritional deficiencies
 - Caffeine intake
 - Safe food preparation technique
- ☐ Lifestyle recommendations for:
 - Regular moderate exercise
 - Avoidance of hyperthermia (hot tubs)
 - Adequate sleep
- ☐ Comprehensive diabetes self-management education
- ☐ Counseling on diabetes in pregnancy per current standards, including natural history of insulin resistance in pregnancy and postpartum; preconception glycemic goals; avoidance of DKA or severe hyperglycemia; avoidance of severe hypoglycemia; progression of retinopathy in individuals with preexisting diabetes; PCOS (if applicable); fertility in people with diabetes; genetics of diabetes; risks to pregnancy including miscarriage, stillbirth, congenital malformations, macrosomia, preterm labor and delivery, hypertensive disorders in pregnancy
- ☐ Supplementation
 - Folic acid supplement (400–800 µg/day routine)
 - Appropriate use of over-the-counter medications and supplements

Health assessment and plan should include:

- ☐ General evaluation of overall health
- ☐ Evaluation of diabetes and its comorbidities and complications, including DKA or severe hyperglycemia; severe hypoglycemia/hypoglycemia unawareness; barriers to care; comorbidities such as hyperlipidemia, hypertension, MASLD, PCOS, and thyroid dysfunction; complications such as macrovascular disease in individuals with preexisting diabetes, nephropathy, neuropathy (including autonomic bowel and bladder dysfunction), and retinopathy
- ☐ Evaluation of obstetric or gynecologic history, including a history of cesarean section, congenital malformations or fetal loss, current methods of contraception, hypertensive disorders of pregnancy, postpartum hemorrhage, preterm delivery, previous macrosomia, Rh incompatibility, and thrombotic events (DVT/PE)
- ☐ Review of current medications and appropriateness during pregnancy

Screening should include:

- ☐ Diabetes complications and comorbidities, including comprehensive foot exam; comprehensive ophthalmologic exam; ECG in individuals starting at age 35 years who have cardiac signs or symptoms or risk factors and, if abnormal, further evaluation; lipid panel; serum creatinine; TSH; and urine albumin-to-creatinine ratio
- ☐ Anemia
- ☐ Genetic carrier status (based on history):
 - Cystic fibrosis
 - Sickle cell anemia
 - Tay-Sachs disease
 - Thalassemia
 - Others if indicated
- ☐ Infectious disease (per ACOG guidelines)

Preconception plan should include:

- ☐ Immunizations (per ACOG guidelines) (203–205)
- ☐ Nutrition and medication plan to achieve glycemic goals prior to conception, including appropriate implementation of blood glucose monitoring, continuous glucose monitoring (if indicated and appropriate), and pump technology (if indicated and appropriate)
- ☐ Contraceptive plan to prevent pregnancy until glycemic goals are achieved
- ☐ Management plan for general health, gynecologic concerns, comorbid conditions, or complications, if present, including hypertension, nephropathy, retinopathy; Rh incompatibility; and thyroid dysfunction

Created using information from American College of Obstetricians and Gynecologists (ACOG) (5) and others (28,30). DKA, diabetic ketoacidosis; DVT/PE, deep vein thrombosis/pulmonary embolism; ECG, electrocardiogram; MASLD, metabolic dysfunction-associated steatotic liver disease; PCOS, polycystic ovary syndrome; TSH, thyroid-stimulating hormone.

associated with diabetes and the ways to reduce risks, including glycemic goal setting, lifestyle and behavioral management, and medical nutrition therapy (3). Prior to conception, it is recommended to achieve glucose levels as close to normal as is safely possible without excessive hypoglycemia, ideally A1C <6.5% (<48 mmol/mol), and preconception glycemic goals should be achieved using therapies approved for use in pregnancy. Setting preconception glucose goals is helpful in guiding insulin dose adjustments. The following preconception glucose goals have been advised: preprandial glucose 80–110 mg/dL (4.4–6.1 mmol/L) and 2 h postprandial glucose <155 mg/dL (<8.6 mmol/L) (31). Prandial insulin dose should be reduced for postprandial glucose <100 mg/dL (5.6 mmol/L).

For individuals with preexisting diabetes, the presence of microvascular complications is associated with higher risk of disease progression and adverse pregnancy outcomes (32). Diabetes-specific testing should include A1C, creatinine, and urinary albumin-to-creatinine ratio. Special attention should be paid to the review of the medication list for potentially harmful drugs, e.g., ACE inhibitors (33), angiotensin receptor blockers (33), and lipid-lowering medications including statins in some cases (34). For individuals using medications that are not approved for use in pregnancy (such as some glucose-lowering, lipid-lowering, and antihypertensive agents), preconception care should include recommendations for when changes in medications should occur to stabilize the conditions and risk factors managed by these medications (such as glucose levels, weight, lipids, and blood pressure) on alternate therapies prior to pregnancy. Glucagon-like peptide 1 receptor agonists (GLP-1 RAs) and dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 RAs should be discontinued prior to pregnancy, and contraception should be used while taking them (see section 9, “Pharmacologic Approaches to Glycemic Treatment”). The manufacturer prescribing information recommends discontinuation of semaglutide at least 2 months before a planned pregnancy due to its long half-life (35). No recommendation is included in the U.S. prescribing information for tirzepatide, although the Canadian manufacturer prescribing information recommends tirzepatide discontinuation at least 1 month before pregnancy (36). Importantly, before attempting conception, preconception glycemic goals should be

achieved following discontinuation of GLP-1 RA therapy or dual GIP and GLP-1 RA therapy, with initiation and titration of insulin therapy when needed to achieve preconception glycemic goals. Thus, individuals planning pregnancy should be counseled that a period of several months is usually needed to allow for both elimination of the medication and adjustment of therapy approved for use in pregnancy to achieve preconception glycemic goals prior to pregnancy. Individuals should additionally be counseled about the risk of weight recurrence after discontinuation of these agents.

A referral for a comprehensive eye exam is recommended. Individuals with preexisting diabetic retinopathy need close monitoring during pregnancy to assess for stability or progression of retinopathy and provide treatment if indicated (37).

GLYCEMIC GOALS IN PREGNANCY

Recommendations

15.8 Fasting, preprandial, and postprandial blood glucose monitoring are recommended in individuals with diabetes in pregnancy to achieve optimal glucose levels. Glucose goals are fasting plasma glucose <95 mg/dL (<5.3 mmol/L) and either 1-h postprandial glucose <140 mg/dL (<7.8 mmol/L) or 2-h postprandial glucose <120 mg/dL (<6.7 mmol/L). **B**

15.9 Due to increased red blood cell turnover, A1C is slightly lower during pregnancy in people with and without diabetes. Ideally, the A1C goal in pregnancy is <6% (<42 mmol/mol) if this can be achieved without significant hypoglycemia, but the goal may be relaxed to <7% (<53 mmol/mol) if necessary to prevent hypoglycemia. **B**

15.10 Continuous glucose monitoring (CGM) can help to achieve glycemic goals (e.g., time in range, time above range) **A** and A1C goal **B** in type 1 diabetes and pregnancy and may be beneficial for other types of diabetes in pregnancy. **E**

15.11 Recommend CGM to pregnant individuals with type 1 diabetes. **A** In conjunction with aims to achieve traditional pre- and postprandial glycemic goals, CGM can reduce the risk for large-for-gestational-age infants and neonatal hypoglycemia in pregnancy complicated by type 1 diabetes. **A**

15.12 CGM metrics may be used in combination with blood glucose monitoring to achieve optimal pre- and postprandial glycemic goals. **E**

15.13 Commonly used estimated A1C and glucose management indicator calculations should not be used in pregnancy as estimates of A1C. **C**

Insulin Physiology

Pregnancy in people with normal glucose metabolism is characterized by fasting glucose levels that are lower than those in the nonpregnant state due to insulin-independent glucose uptake by the fetus and placenta and by mild postprandial hyperglycemia and carbohydrate intolerance as a result of diabetogenic placental factors. Early pregnancy may be a time of enhanced insulin sensitivity and lower glucose levels and is followed by progressive insulin resistance in the second and third trimesters (38–40). Insulin resistance drops rapidly with the delivery of the placenta. In people with normal pancreatic function, insulin production is sufficient to meet the challenge of this physiological insulin resistance and to maintain normal glucose levels. However, in people with diabetes, hyperglycemia occurs if treatment is not adjusted appropriately.

Glucose Monitoring

Reflecting this physiology, fasting and postprandial blood glucose monitoring (BGM) is recommended to achieve glycemic goals in pregnant people with diabetes. Preprandial testing is also recommended when using insulin pumps or basal-bolus therapy so that the premeal rapid-acting insulin dosage can be adjusted. Postprandial monitoring is associated with better glycemic outcomes and a lower risk of preeclampsia (41,42). There are no adequately powered randomized trials comparing different fasting and postmeal glycemic goals for preexisting diabetes in pregnancy.

Similar to the glycemic goals recommended by ACOG (11), the ADA-recommended goals for pregnant people with type 1 or type 2 diabetes are shown in **Table 15.2**. Lower limits are based on the mean of normal blood glucose in pregnancy (43) but do not apply to individuals with type 2 diabetes treated with nutrition alone. Hypoglycemia in pregnancy is as defined and discussed in Recommendations 6.10–6.19 (see section 6, “Glycemic

Table 15.2—Blood glucose goals in pregnancies associated with diabetes

Glucose measurement	Blood glucose goal		
	Type 1 diabetes or type 2 diabetes [^]	GDM treated with insulin	GDM not treated with insulin
Fasting glucose	70–95 mg/dL (3.9–5.3 mmol/L)	70–95 mg/dL (3.9–5.3 mmol/L)	<95 mg/dL (<5.3 mmol/L)
1-h postprandial glucose	110–140 mg/dL* (6.1–7.8 mmol/L)	110–140 mg/dL* (6.1–7.8 mmol/L)	<140 mg/dL* (<7.8 mmol/L)
2-h postprandial glucose	100–120 mg/dL (5.6–6.7 mmol/L)	100–120 mg/dL (5.6–6.7 mmol/L)	<120 mg/dL (<6.7 mmol/L)

Gestational diabetes mellitus (GDM) blood glucose goals shown are recommended by the Fifth International Workshop-Conference on Gestational Diabetes Mellitus (45). [^]Lower glucose limits do not apply to individuals with type 2 diabetes treated with nutrition alone. Aim for less stringent goals if these cannot be achieved without significant hypoglycemia, based on clinical experience and individualization of care.

*Optimal goal includes either a 1-h postprandial glucose level or 2-h postprandial glucose level within column of type of diabetes.

Goals, Hypoglycemia, and Hyperglycemic Crises”). The most appropriate hypoglycemia threshold level in pregnancy has not been validated but has ranged from <60 to <70 mg/dL (<3.3 to <3.9 mmol/L) in the past. Current recommendations for hypoglycemia thresholds include blood glucose <70 mg/dL (<3.9 mmol/L) and sensor glucose <63 mg/dL (<3.5 mmol/L) (43,44). These fasting or premeal and postprandial glucose values represent optimal levels if they can be achieved safely. In practice, it may be challenging for a person with type 1 diabetes to achieve these goals without hypoglycemia, particularly those with a history of recurrent hypoglycemia or impaired awareness of hypoglycemia. If an individual cannot achieve these goals without significant hypoglycemia, aim for less stringent goals based on clinical experience and individualization of care.

For individuals with GDM, the glucose goals recommended by the Fifth International Workshop-Conference on Gestational Diabetes Mellitus should be used (45) (Table 15.2).

For individuals found to have hyperglycemia less than overt diabetes on early pregnancy screening, the benefits of treatment remain uncertain, controversy exists regarding optimal management strategies, and professional society guidance is conflicting (46,47). While hyperglycemia less than overt diabetes in early pregnancy has been associated with increased risk of adverse pregnancy and neonatal outcomes and higher risk of a later GDM diagnosis (see Recommendation 2.32b) (48–52), it has not been established that universal treatment in early pregnancy (prior to the usual time of GDM diagnosis and treatment at 24–28 weeks’ gestation) is beneficial for all individuals in this group.

Most randomized controlled trials (RCTs) of treatment of early abnormal glucose

metabolism have been underpowered for outcomes. One large multicenter RCT (Treatment of Booking Gestational Diabetes Mellitus [TOBOGM] trial), which enrolled pregnant individuals with at least one risk factor for hyperglycemia, administered early screening (mean 15.6 ± 2.5 weeks) for GDM with a 75-g OGTT (53). Individuals who met World Health Organization criteria for GDM were randomized to receive early treatment or a repeat OGTT at 24–28 weeks (with deferred treatment if indicated). The first primary outcome measure was an adverse neonatal composite outcome including birth <37 weeks, birth weight ≥4.5 kg, birth trauma, neonatal respiratory distress within 24 h of birth, phototherapy, stillbirth neonatal death, or shoulder dystocia. Early GDM treatment resulted in a modest improvement in the composite adverse neonatal outcome (24.9% early treatment vs. 30.5% control group, relative risk 0.82 [0.68–0.98]), although this was driven primarily by differences in rates of neonatal respiratory distress between groups that included neonates requiring ≥4 h of supplemental oxygen who may not have required a higher level of respiratory care. In prespecified subgroup analyses, there was a suggestion of more benefit among individuals who had the OGTT at <14 weeks and among those with OGTT glycemic values in higher glycemic ranges (53).

Subsequent secondary analyses have shed additional light on which subgroups may derive greatest benefit from treatment. Importantly, almost one-third of individuals randomized to observation demonstrated regression of GDM when retested at 24–28 weeks’ gestation. Pregnancy outcomes among participants with regression were similar to those of individuals without GDM (54), and these individuals are therefore unlikely to benefit from treatment in

early gestation. Continuous positive associations were observed between 1- and 2-h postload glucose measurements and the perinatal composite outcome as well as large for gestational age (55). Among those who were randomized to observation, treatment initiation at 24–28 weeks’ gestation normalized large-for-gestational-age risk but not risk of preterm birth and neonatal jaundice (56). Systematic reviews and meta-analyses of RCTs have not shown consistent benefits of early GDM treatment (57,58). Taken together with the observation of possible increased risk of small-for-gestational-age infants among TOBOGM participants with OGTT results in the lower glycemic range who were randomized to treatment (53), it appears that treatment benefits are not universal across this population, with suggestion of benefit in some groups and harm in others.

Professional society guidance regarding early pregnancy treatment of hyperglycemia less than overt diabetes sharply differs (46,47). Future studies are needed to refine identification of those individuals with early abnormal glucose metabolism in whom hyperglycemia will persist and in whom early treatment will afford incremental benefit beyond that afforded by treatment for GDM diagnosed at the usual time in late pregnancy. Importantly, the TOBOGM investigators excluded individuals with fasting glucose ≥110 mg/dL (≥6.1 mmol/L) for safety reasons (53), and thus the risk-benefit balance in pregnant individuals with fasting glucose 110–125 mg/dL (6.1–6.9 mmol/L) was not evaluated in this study. While RCT data to guide clinical practice in this subgroup are lacking, it is possible that selective treatment of early pregnancy hyperglycemia within this subgroup would lead to more pronounced reductions in adverse pregnancy and neonatal outcomes.

Therefore, the benefits of treatment of early abnormal glucose metabolism remain uncertain. Nutrition counseling and periodic testing of fasting glucose levels (e.g., 3–4 times per week) are suggested. Testing frequency may proceed to daily, and treatment may be intensified, if fasting plasma glucose is predominantly ≥ 110 mg/dL (≥ 6.1 mmol/L) prior to 15 weeks of gestation. Individualized discussion of areas of uncertainty and the option to treat for fasting glucose ≥ 110 mg/dL (≥ 6.1 mmol/L) via shared decision-making is reasonable. When treatment for early abnormal glucose metabolism is initiated, fasting and postprandial glucose levels should be monitored and the standard glucose goals recommended in pregnancies associated with diabetes (**Table 15.2**) should be used.

A1C in Pregnancy

In studies of individuals without preexisting diabetes, increasing A1C levels within the normal range are associated with adverse outcomes (59). In the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study, increasing levels of glycemia were also associated with worsening outcomes (21). Observational studies in preexisting diabetes and pregnancy show the lowest rates of adverse fetal outcomes in association with A1C $< 6.5\%$ (< 42 – 48 mmol/mol) early in gestation (14,15,17, 60). Clinical trials have not evaluated the risks and benefits of achieving these goals, and treatment goals should account for the risk of maternal hypoglycemia in setting an individualized goal of $< 6\%$ (< 42 mmol/mol) to $< 7\%$ (< 53 mmol/mol). Due to physiological increases in red blood cell turnover, A1C levels fall during normal pregnancy (61,62). Additionally, as A1C represents an integrated measure of glucose, it may not fully capture postprandial hyperglycemia, which drives macrosomia. Thus, although A1C may be useful, it should be used as a secondary measure of glycemia in pregnancy, after glucose monitoring.

In the second and third trimesters, A1C $< 6\%$ (< 42 mmol/mol) has the lowest risk of large-for-gestational-age infants (60,63,64), preterm delivery (65), and preeclampsia (1,66). Taking all of this into account, a goal of $< 6\%$ (< 42 mmol/mol) is optimal during pregnancy if it can be achieved without significant hypoglycemia, which, in addition to the usual adverse sequelae, may increase the risk of low birth weight (67,68). Given the

alteration in red blood cell kinetics during pregnancy and physiological changes in glycemic parameters, A1C levels may need to be monitored more frequently than usual (e.g., monthly).

Continuous Glucose Monitoring in Pregnancy

The Continuous Glucose Monitoring in Pregnant Women With Type 1 Diabetes Trial (CONCEPTT) was an RCT of real-time CGM in addition to standard care, including optimization of pre- and postprandial glucose goals, versus standard care for pregnant people with type 1 diabetes. It demonstrated the value of using real-time CGM in pregnant individuals with type 1 diabetes by showing a mild improvement in A1C and significant improvements in the maternal glucose time in range (TIR) and time above range (TAR), without an increase in hypoglycemia, and reductions in large-for-gestational-age births, length of infant hospital stays, and severe neonatal hypoglycemia (69). An observational cohort study that evaluated the glycemic variables reported using CGM systems found that lower mean glucose, lower SD, and higher percentage of TIR were associated with lower risks of large-for-gestational-age births and other adverse neonatal outcomes (70). Data from one study suggest that use of the CGM-reported mean glucose is superior to use of estimated A1C, glucose management indicator, and other calculations to estimate A1C, given the changes to A1C that occur in pregnancy (71). One RCT and several observational studies have found that a 5% increase in CGM TIR was associated with improvements in neonatal morbidity, including large-for-gestational-age births and neonatal intensive care unit admissions (69,70, 72,73). CGM TIR can be used for assessment of glycemic outcomes in people with type 1 diabetes, but it does not provide actionable data to address fasting and postprandial hypoglycemia or hyperglycemia. The cost of CGM use by pregnant individuals with type 1 diabetes is offset by improved maternal and neonatal outcomes (74).

At this time, there are insufficient data to support the use of CGM in all people with type 2 diabetes or GDM (75–79). One RCT evaluating use of CGM or standard BGM in GDM found no significant difference in the primary end point, a composite of adverse perinatal and neonatal outcomes (79). TIR was lower in the CGM group, though CGM use was preferred by participants. In contrast, another

RCT of CGM plus adjunctive BGM versus BGM alone in GDM found that 24-h TIR was higher and 24-h mean glucose was lower with CGM use (80). Adequately powered RCTs exclusively evaluating CGM use in pregnant individuals with type 2 diabetes are not currently available. Additionally, it is important to note that optimal targets for CGM metrics during pregnancy affected by type 2 diabetes or GDM have not been defined to date, which confounds interpretation of the limited data available evaluating CGM use in these populations. The decision of whether to use CGM in pregnant individuals with type 2 diabetes or GDM should be individualized based on treatment plan, circumstances, preferences, and needs.

The international consensus on TIR (44) endorses pregnancy glucose goal ranges and goals for TIR for people with type 1 diabetes using CGM as reported on the ambulatory glucose profile. The international consensus on TIR (44) endorses the same sensor glucose goal ranges for individuals with type 2 diabetes in pregnancy and GDM but could not quantify the goal of amount of time spent within each category because of insufficient data. However, the consensus does not specify the type or accuracy of the CGM device or need for alarms and alerts. The accuracy of one CGM system among pregnant individuals with type 1 diabetes, type 2 diabetes, and GDM has been demonstrated, supporting its use in pregnancy without confirmatory capillary blood glucose measurements (81). The proportion of CGM values within 20% or 20 mg/dL of comparator values ≥ 100 mg/dL or < 100 mg/dL, respectively (%20/20 agreement rates), was 78.6% on day 1 of sensor wear, increased to 96.3% on days 4 and 7, and increased to 97.3% on day 10. Although CGM systems for use in pregnancy do not require calibrations and are approved for nonadjunctive use, determination of glucose levels by finger stick is advised in certain circumstances, such as following correction of hypoglycemia (due to the time lag between change in plasma vs. interstitial glucose values), when symptoms do not match sensor glucose reading, and on the first day of use when sensor accuracy may be lower (81). Selection of CGM device should be based on an individual's circumstances, preferences, and needs.

Goals for sensor glucose ranges in pregnancy are:

- Goal sensor glucose range 63–140 mg/dL (3.5–7.8 mmol/L): TIR, goal >70%
- Time below range (TBR) (<63 mg/dL [<3.5 mmol/L]): level 1 TBR, goal <4%
- TBR (<54 mg/dL [<3.0 mmol/L]): level 2 TBR, goal <1%
- TAR (>140 mg/dL [>7.8 mmol/L]): TAR, goal <25%

Goals for time spent in each range are specific for pregnant individuals with type 1 diabetes.

MANAGEMENT OF DIABETES IN PREGNANCY

Recommendations

15.14 Nutrition counseling before and during pregnancy should promote an eating pattern including fruits, vegetables, legumes, whole grains, nuts, seeds, fish, and other lean protein, which will provide a balance of macronutrients and healthy n-3 fatty acids. **C**

15.15 Lifestyle behavior change is an essential component of management of GDM and may suffice as treatment for many individuals. Insulin should be added if needed to achieve glycemic goals. **A**

15.16 Telehealth visits used in combination with in-person visits for pregnant people with GDM can improve outcomes compared with standard in-person care alone. **A**

15.17 Insulin should be used to manage type 1 diabetes in pregnancy **A** and is the preferred agent for the management of GDM **A** and type 2 diabetes in pregnancy. **B**

15.18 Either multiple daily injections or insulin pump technology can be used in pregnancy complicated by type 1 diabetes. **C**

15.19 Automated insulin delivery (AID) systems with pregnancy-specific glucose targets are recommended for pregnant individuals with type 1 diabetes. **A**

15.20 AID systems without pregnancy-specific glucose targets or a pregnancy-specific algorithm may be considered for select pregnant individuals with type 1 diabetes when used with assistive techniques and working with experienced health care teams. **B**

15.21 Metformin and glyburide, individually or in combination, should not be used as first-line agents for management of diabetes in pregnancy, as both cross the placenta to the fetus **A** and

may not be sufficient to achieve glycemic goals. **B** Other oral and noninsulin injectable glucose-lowering medications lack long-term safety data and are not recommended. **E**

15.22 Metformin, when used to treat polycystic ovary syndrome and induce ovulation, should be discontinued by the end of the first trimester. **A**

The management of pregnancies associated with diabetes includes appropriate nutrition, lifestyle and behavior management, physical activity goals, and pharmacotherapy to support the maternal, fetal, and placental needs and reach glycemic goals regardless of the diabetes type.

Medical Nutrition Therapy

In people with preexisting diabetes, glycemic goals are usually achieved through a combination of insulin administration and medical nutrition therapy. Because glycemic goals in pregnant individuals are stricter than in nonpregnant individuals, it is important that pregnant people with diabetes consume consistent amounts of carbohydrates to match their prandial insulin dosages or use insulin-to-carbohydrate ratios to match prandial insulin dosages to the carbohydrates being consumed in order to minimize postprandial hyperglycemia or hypoglycemia. Referral to an RDN is important to establish a food plan and to determine weight gain goals. The quality of the carbohydrates should be evaluated. A subgroup analysis of the CONCEPTT study demonstrated that the food choices of individuals planning pregnancy and currently pregnant assessed during the run-in phase prior to randomization were characterized by high-fat, low-fiber, and poor-quality carbohydrate intakes. Fruit and vegetable consumption was inadequate, with one in four participants at risk for micronutrient deficiencies, highlighting the importance of medical nutrition therapy (82).

An expert panel on nutrition in pregnancy and the U.S. Department of Health and Human Services recommend a balance of macronutrients. An eating pattern that severely restricts any macronutrient class should be avoided, specifically the ketogenic eating pattern that lacks carbohydrates, the paleo eating pattern because of dairy restriction, and any eating pattern characterized by excess saturated fats (83). Pregnant individuals with diabetes are recommended to consume whole foods,

including fruits, vegetables, legumes, whole grains, lean protein, and healthy fats with n-3 fatty acids, which includes nuts and seeds and fish, which are less likely to promote excessive weight gain (84). Processed foods, fatty red meat, and sweetened foods and beverages should be limited (83,84).

The recommended dietary reference intake for all pregnant people is a minimum of 175 g of carbohydrate (~35% of a 2,000-calorie diet), a minimum of 71 g of protein, and 28 g of fiber (85). The nutrition plan should emphasize monounsaturated and polyunsaturated fats while limiting saturated fats and avoiding *trans* fats. As is true for all nutrition therapy in people with diabetes, the amount and type of carbohydrate will impact glucose levels. Promoting higher-quality, nutrient-dense carbohydrates results in improved fasting or postprandial glucose levels, lower free fatty acids, improved insulin action, and vascular benefits, and it may reduce excess infant adiposity. Individuals who substitute fat for carbohydrates may unintentionally enhance lipolysis, promote elevated free fatty acids, and worsen maternal insulin resistance (86,87). Fasting ketone testing may be useful to identify those who are severely restricting carbohydrates to manage blood glucose. Carbohydrate restriction can increase the risk of higher dietary fat consumption, which may lead to fetal overgrowth (83). Simple carbohydrates will result in higher postmeal excursions.

Medical nutrition therapy for GDM is an individualized nutrition plan developed between the pregnant person and an RDN familiar with the management of GDM (88, 89). The food plan should provide adequate calorie intake to promote fetal, neonatal, and maternal health, achieve glycemic goals, and promote appropriate weight gain, according to the 2009 National Academy of Medicine recommendations (90). There is no definitive research that identifies a specific optimal calorie intake for people with GDM or suggests that their calorie needs are different from those of pregnant individuals without GDM. The food plan should be based on a nutrition assessment with dietary reference intake guidance from the National Academy of Medicine.

Lifestyle and Behavioral Management

Although there is some heterogeneity, many RCTs and a Cochrane review suggest that the risk of GDM may be reduced by appropriate nutrition, exercise, and

lifestyle counseling, particularly when interventions are started during the first trimester or early in the second trimester (91–93).

After diagnosis of GDM, treatment starts with medical nutrition therapy, physical activity, and weight management, depending on pregestational weight, as outlined in this section. Depending on the population, studies suggest that 70–85% of people diagnosed with GDM under Carpenter-Coustan criteria can manage GDM with lifestyle modification alone; it is anticipated that this proportion will be even higher if the lower International Association of the Diabetes and Pregnancy Study Groups (94) diagnostic thresholds are used.

Physical Activity

It is recommended that generally healthy people do at least 150 min of moderate-intensity aerobic activity each week during pregnancy and postpartum, preferably spread throughout the week (95). Adjustments to a physical activity routine or plan should be done in consultation with a health care professional, especially if someone is considering a big change in physical activity intensity (95). Such activity improves cardiorespiratory fitness and reduces the risk for excessive gestational weight gain or postpartum weight retention (95).

Regular exercise has been reported to reduce the odds of developing GDM, gestational hypertension, and preeclampsia by 38%, 39%, and 41%, respectively (96), and acute and long-term prenatal exercise can positively affect glycemia, with a larger effect noted in people with diabetes (97). With respect to GDM, a systematic review demonstrated improvements in glucose outcomes and reductions in need to start insulin or insulin dose requirements with an exercise intervention. However, there was heterogeneity in the types of effective exercise (aerobic, resistance, or both) and duration of exercise (20–50 min/day, 2–7 days/week of moderate intensity) (98), so there is insufficient evidence about which specific type of exercise program has the biggest impact on these diabetes-related outcomes in pregnancy.

Health Care Delivery for People With Diabetes in Pregnancy

As discussed in PRECONCEPTION CARE, team-based care is recommended either through a single specialized center (when available) or multiple centers with interprofessional team members as part of the care plan

during pregnancy. A meta-analysis of 32 RCTs evaluating the effectiveness of telehealth interventions, which ranged from telehealth visits to the use of health apps, used in combination with in-person visits for GDM, demonstrated reduced incidences of cesarean delivery, premature rupture of membranes, pregnancy-induced hypertension or preeclampsia, preterm birth, neonatal asphyxia, and polyhydramnios compared with standard in-person care alone (99).

Pharmacologic Therapy

Insulin

Insulin should be used to manage type 1 diabetes in pregnancy and is preferred for the management of type 2 diabetes in pregnancy and GDM. The physiology of pregnancy necessitates frequent titration of insulin to match changing requirements and underscores the importance of daily and frequent glucose monitoring. In early pregnancy, many people with type 1 diabetes will have lower insulin requirements and an increased risk for hypoglycemia (38). At around 16 weeks, insulin resistance begins to increase, and total daily insulin doses increase linearly by ~5% per week through week 36. This usually results in a doubling of daily insulin dose compared with the prepregnancy requirement. While there is an increase in both basal and bolus insulin requirements, bolus insulin requirements take up a larger proportion of overall total daily insulin needs in individuals with preexisting diabetes as pregnancy progresses (39,40). The insulin requirement levels off toward the end of the third trimester. A rapid and significant reduction in insulin requirements may indicate the development of placental insufficiency (100), although data are conflicting (101).

Optimal glycemic goals are often easier to achieve during pregnancy with type 2 diabetes than with type 1 diabetes but can require much higher doses of insulin, sometimes necessitating concentrated insulin formulations. It is recommended that insulin management be performed with interprofessional team members with relevant expertise.

None of the currently available human insulin preparations have been demonstrated to cross the placenta (102–107). Insulins studied in RCTs are preferred (108–110) over those studied in cohort studies (111), which are preferred over

those studied in case reports only. Basal insulin options in pregnancy include insulin glargine (long-acting), NPH insulin (intermediate-acting), and insulin degludec (ultralong-acting). Insulin detemir (the only basal insulin with RCT data supporting its use during pregnancy) was removed from the market by the manufacturer and is no longer available. Observational studies of glargine use during pregnancy have not shown evidence of increased adverse fetal outcomes with use of insulin glargine versus NPH insulin (111), and insulin glargine is widely used during pregnancy. Although the data on insulin degludec are still limited and emerging, insulin degludec was shown in an RCT to be noninferior to detemir (108), noting that this study was not powered to detect differences in maternal safety or pregnancy outcomes. The prolonged duration of action of insulin degludec (at least 42 h) may present challenges in pregnancy. The need for slower dose titration due to its longer half-life (recommended interval between dose changes is 3–4 days [112]) may impede the frequent dose adjustments often needed in response to the rapidly changing insulin requirements of pregnancy, and hypoglycemia could occur postpartum when insulin requirements decrease sharply. Regarding rapid-acting insulins options, insulin aspart and insulin lispro are widely considered safe and effective for use during pregnancy (113–115). Use of faster-acting insulin aspart (faster aspart) among pregnant women with type 1 or type 2 diabetes led to similar fetal growth and A1C relative to insulin aspart (116); a secondary analysis of women with type 1 diabetes showed that faster-acting aspart use resulted in higher TIR and less severe hypoglycemia compared with aspart (117).

Both multiple daily insulin injections and continuous subcutaneous insulin infusion are reasonable delivery strategies in pregnancy, with neither showing superiority over the other (106,118).

Automated insulin delivery (AID) systems have been studied in pregnancy and postpartum. The use of AID systems in pregnancy affected by diabetes presents particular challenges, as the current U.S. Food and Drug Administration (FDA)-approved AID systems (except for one that has been FDA approved but is not yet commercially available in the U.S.) do not have algorithms designed to achieve pregnancy-specific glucose goals,

and the lowest glucose target available for most systems is higher than the fasting glucose target range recommended during pregnancy. Initiating or continuing AID systems during pregnancy therefore needs to be assessed carefully. Selected individuals with type 1 diabetes should be evaluated as potential candidates for AID systems in the setting of expert guidance.

Recent data have shown the clinical benefits and safety of AID use, though only one study used an AID system with a pregnancy-specific glucose target. In the Automated insulin Delivery Among Pregnant women with Type 1 diabetes [AiDAPT] trial, 124 pregnant individuals with type 1 diabetes were randomized to either an AID system with glucose targets that could be set near or in the pregnancy-specific fasting glucose range or standard of care (CGM with either multiple daily injections or standard insulin pump therapy) (119). Investigators recommended pump glucose targets of 100 mg/dL in early pregnancy and 81–90 mg/dL from 16 to 20 weeks onward. The AID group had a higher TIR (10.5% difference between groups, $P < 0.001$), lower TAR (−10.2% [95% CI −13.8 to −6.6]), and lower A1C (−0.31% [−0.50 to −0.12]), and a subset of participants who were interviewed reported benefits with AID use during pregnancy (e.g., more enjoyment of pregnancy, better sleep, less worry) (119, 120). The AID system evaluated in this study is FDA approved but is not currently available in the U.S.

There have additionally been RCTs examining AID systems that do not have either pregnancy-specific glucose targets in the algorithms or algorithms that adapt specifically to pregnancy but were used with assistive techniques. In a study with 95 pregnant individuals with type 1 diabetes, participants used an AID system set to a glucose target of 100 mg/dL or to standard of care. The 24-h TIR was similar between groups, but the nocturnal TIR was higher (6.58%, $P = 0.003$), the 24-h TBR was lower (−1.34%, $P = 0.002$), and the nocturnal TBR was lower (−1.86%, $P = 0.0005$) in the AID group (121). AID users reported higher diabetes treatment satisfaction and had less hypoglycemia unawareness (per Gold scores) (121). In a pilot study ($n = 23$) where participants were randomized in the second trimester to AID with a system whose glucose target is 120 mg/dL or sensor-augmented pump (SAP) therapy with the same system, time spent

<63 mg/dL (<3.5 mmol/L) decreased significantly in the AID group from baseline to third trimester (7.5% first trimester vs. 2.8% third trimester, $P < 0.05$), but the average sensor glucose was higher in the AID group in the third trimester (mean [SE] 119 [4] SAP vs. 132 [4] AID, $P = 0.0475$) without significant differences between groups in other CGM metrics (122). These two studies used assistive techniques, such as administration of fake carbohydrate insulin boluses for carbohydrates that were not consumed, and pump management was determined by expert guidance from an experienced interprofessional team (121–123). Thus, it may be appropriate to continue or initiate AID therapy with systems that do not have pregnancy-specific glucose targets or algorithms in carefully selected pregnant individuals with type 1 diabetes in the setting of using assistive techniques with expert guidance (121–123). Some pregnant individuals may derive glycemic benefit from use of an AID system that is not approved for use in pregnancy (for example, decreased hypoglycemia and/or improved TIR in automated vs. manual mode in that individual); decisions regarding AID use during pregnancy should be informed by careful consideration of individualized risks and benefits. Assessment of potential candidates for AID use in pregnancy should include relevant parameters such as glycemic levels, presence or absence of severe hypoglycemic or hyperglycemic events, ability or comfort in engaging with diabetes technology, psychosocial determinants, cost, individual preference, and other factors as relevant. If the decision is made to use AID systems without pregnancy-specific targets in selected pregnant individuals, then using assistive techniques, such as the combination of SAP mode (or manual mode) and automated mode at different time points in pregnancy or throughout the day, should be considered and applied as needed to achieve intended goals (123).

Continuous subcutaneous insulin infusion was compared with intravenous insulin infusion in an RCT of 70 participants during labor and delivery. There was no difference between groups in the primary outcome of neonatal hypoglycemia or in secondary outcomes (e.g., mean neonatal glucose in first 24 h of life, severe neonatal hypoglycemia) (124). In an RCT of 18 participants using AID or SAP therapy for 12 weeks postpartum (125), those in the AID group had fewer hypoglycemia

episodes. One prespecified observational analysis of individuals who continued AID intrapartum and/or early postpartum found improved TIR intrapartum and similar TIR early postpartum in the AID group compared with the standard insulin therapy group, without severe hypoglycemia (126). In a prespecified extension to the AiDAPT trial, in which participants continued either AID or standard insulin therapy for 6 months postpartum, TIR was higher and mean glucose lower in the AID group, without significant differences in hypoglycemia (127). Suggested strategies for postpartum adjustment of AID pump settings have been described (128).

Treatment of GDM with lifestyle and insulin has been demonstrated to improve perinatal outcomes in two large RCTs, as summarized in a U.S. Preventive Services Task Force review (129). Insulin is the first-line agent recommended for the treatment of GDM in the U.S. While individual studies support limited efficacy of metformin (130,131) and glyburide (132) in reducing glucose levels for the treatment of GDM, these agents are not recommended as the first-line treatment of GDM because they are known to cross the placenta and data on long-term safety for offspring is of some concern (20). Furthermore, in separate RCTs, glyburide and metformin failed to achieve adequate glycemic outcomes in 23% and 25–28% of participants with GDM, respectively (133,134).

Sulfonylureas

Sulfonylureas are known to cross the placenta and have been associated with increased neonatal hypoglycemia. Concentrations of glyburide in umbilical cord plasma are approximately 50–70% of maternal levels (133,134). In systematic reviews and meta-analyses, compared with insulin or metformin, glyburide was associated with a higher rate of neonatal hypoglycemia and macrosomia and an increased neonatal abdominal circumference (135,136).

Glyburide was not found to be noninferior to insulin based on a composite outcome of neonatal hypoglycemia, macrosomia, and hyperbilirubinemia among individuals with GDM (137). In a randomized noninferiority trial evaluating insulin compared with an oral glucose-lowering medication strategy (metformin with addition of glyburide and then insulin substitution for glyburide if glycemic goals were not met) in GDM, the oral glucose-lowering medication strategy failed to meet criteria for noninferiority compared with insulin in

preventing large-for-gestational-age infants (138). In addition, the oral glucose-lowering strategy was associated with increased risk of maternal hypoglycemia compared with insulin (138). Long-term safety data for offspring exposed to glyburide are not available (137,138).

Metformin

Metformin was associated with a lower risk of neonatal hypoglycemia and less maternal weight gain than insulin in systematic reviews and RCTs for GDM treatment, but treatment monotherapy failure occurred in 14–46% of individuals (135, 139–142). A meta-analysis of 11 RCTs demonstrated that metformin treatment in pregnancy does not reduce the risk of GDM in high-risk individuals with obesity, polycystic ovary syndrome, or preexisting insulin resistance (143). RCTs of individuals with preexisting type 2 diabetes treated either with insulin alone or insulin plus metformin did not show differences in composite neonatal health outcomes between groups (144,145), and one of these also included individuals diagnosed with diabetes early in gestation (145). Neonatal birth weights were smaller in the metformin groups of these studies, but the metformin group experienced more drug intolerance in one study and there was a doubling of small-for-gestational-age neonates in the other (144,145). RCTs comparing metformin with other therapies for ovulation induction in individuals with polycystic ovary syndrome have not demonstrated benefit in preventing spontaneous abortion or GDM (146), and there is no evidence-based need to continue metformin in these individuals (147–149).

Of note, metformin readily crosses the placenta, resulting in umbilical cord blood levels of metformin as high or higher than simultaneous maternal levels (150,151). In a primate model, metformin initiated early in gestation led to fetal bioaccumulation of metformin, growth restriction, and renal dysmorphology (152). In the Metformin in Gestational Diabetes: The Offspring Follow-Up (MiG TOFU) study's analyses of 7- to 9-year-old offspring, the 9-year-old offspring exposed to metformin for the treatment of GDM in the Auckland cohort (but not the Adelaide cohort) were heavier and had a higher waist-to-height ratio and waist circumference than those exposed to insulin (153). In one RCT of metformin use in pregnancy for polycystic ovary syndrome, follow-up of 4-year-old offspring

demonstrated higher BMI and increased obesity in the offspring exposed to metformin (154). A follow-up study at 5–10 years showed that the offspring had higher BMI, weight-to-height ratios, and waist circumferences and a borderline increase in fat mass (155,156). A meta-analysis demonstrated that metformin exposure resulted in smaller neonates with an acceleration of postnatal growth, resulting in higher BMI in childhood (155). Follow-up of offspring from the Metformin in Women with Type 2 Diabetes in Pregnancy (MiTy Kids) trial showed no differences in anthropometrics of children at 24 months (157). When prepregnancy metformin use is continued in early pregnancy, it can be discontinued at the end of the first trimester (after organogenesis) to avoid sudden deterioration of glycemia and an associated increased risk of malformations due to hyperglycemia (158). Continuation of metformin in early pregnancy is considered safe, as first-trimester metformin use has not been associated with increased risk of major congenital malformations (159,160), and there is minimal maternal-to-fetal transfer of metformin in early gestation (161,162).

There are some people with GDM requiring medical therapy who may not be able to use insulin safely or effectively during pregnancy due to cost, comprehension, or cultural influences. Oral agents may be an alternative for these individuals after discussing the known risks and the need for more long-term safety data in offspring. However, due to the potential for growth restriction or acidosis in the setting of placental insufficiency, metformin should not be used in pregnant people with hypertension or preeclampsia or those at risk for intrauterine growth restriction (157,161,162).

Special Considerations for Management of Pregnancies With Diabetes

Pregnant individuals with type 1 diabetes have an increased risk of hypoglycemia in the first trimester and after delivery, and like all pregnant people, they have altered counterregulatory response in pregnancy that may decrease hypoglycemia awareness. Education for people with diabetes and family members about the prevention, recognition, and treatment of hypoglycemia is important before, during, and after pregnancy to help prevent and manage hypoglycemia risk.

Pregnancy is a ketogenic state, and people with type 1 diabetes and, to a

lesser extent, those with type 2 diabetes are at risk for diabetic ketoacidosis (DKA) at lower blood glucose levels than in the nonpregnant state. Pregnant people with type 1 diabetes should be advised to obtain ketone test strips and receive education on DKA prevention and detection. DKA carries a high risk of stillbirth. Those in DKA who are unable to eat often require intravenous fluid containing dextrose with an insulin drip to adequately meet the higher carbohydrate demands of the placenta and fetus in the third trimester to resolve their ketosis.

Retinopathy is a special concern in pregnancy. The necessary rapid implementation of euglycemia in the setting of retinopathy is associated with worsening of retinopathy (163). Meta-analyses have also demonstrated a high risk of new-onset retinopathy and progression of existing retinopathy in pregnant individuals with type 1 or type 2 diabetes (37,164). Therefore, it is recommended that individuals with preexisting diabetes have dilated eye examinations before pregnancy, in each trimester of pregnancy, and for 1 year postpartum as indicated by the degree of retinopathy and as recommended by the eye care health care professional.

Recommended weight gain during pregnancy for people with overweight status is 15–25 lbs (6.8–11.3 kg) and for those with obesity is 10–20 lbs (4.5–9.1 kg) (90). There are no adequate data on optimal weight gain versus weight maintenance in pregnant people with BMI >35 kg/m²; however, losing weight is not recommended because of the increased risk of small-for-gestational-age infants (24).

PREECLAMPSIA AND ASPIRIN

Recommendation

15.23 Pregnant individuals with type 1 or type 2 diabetes should be prescribed low-dose aspirin 100–150 mg/day starting at 12–16 weeks of gestation to lower the risk of preeclampsia. **E** A dosage of 162 mg/day may be acceptable; **E** currently, in the U.S., low-dose aspirin is available in 81-mg tablets.

Diabetes in pregnancy is associated with an increased risk of preeclampsia (165). The U.S. Preventive Services Task Force recommends that blood pressure measurements be obtained throughout gestation to screen for hypertensive disorders of pregnancy

(166). The Task Force also recommends using low-dose aspirin (81 mg/day) as a preventive medication at 12 weeks of gestation in individuals at high risk for preeclampsia, such as those with type 1 or type 2 diabetes (167). However, a meta-analysis and an additional trial demonstrate that low-dose aspirin <100 mg is not effective in reducing preeclampsia, so a dose of >100 mg is required (168–170). A cost-benefit analysis has concluded that this approach would reduce morbidity, save lives, and lower health care costs (171). There are insufficient data about whether the use of aspirin specifically in pregnant people with preexisting diabetes ultimately reduces the incidence of preeclampsia (172,173), although a meta-analysis showed that preeclampsia reductions occurred with aspirin administration in high-risk groups overall (165). Individuals with GDM may be candidates for aspirin therapy for preeclampsia prevention if they have a single high-risk factor, such as chronic hypertension or an autoimmune disease, or multiple moderate risk factors, such as being nulliparous, having obesity, being age ≥ 35 years, or other factors per the U.S. Preventive Services Task Force (167). More studies are needed to assess the long-term effects of prenatal aspirin exposure on offspring (172).

PREGNANCY AND NON-GLUCOSE-LOWERING DRUG CONSIDERATIONS

Recommendations

15.24 In pregnant individuals with diabetes and chronic hypertension, a blood pressure threshold <140/90 mmHg is recommended for initiation and titration of therapy for better pregnancy outcomes. **A** Therapy should be deintensified if blood pressure is <90/60 mmHg. **E**

15.25a Potentially harmful medications in pregnancy (e.g., ACE inhibitors, angiotensin receptor blockers, mineralocorticoid receptor antagonists) should be stopped prior to conception and avoided in sexually active individuals of childbearing potential who are not using reliable contraception. **B**

15.25b In most circumstances, lipid-lowering medications should be stopped prior to conception and avoided in sexually active individuals of childbearing potential with diabetes who are not using reliable contraception. **B**

B In some circumstances (familial

hypercholesterolemia, severe hypertriglyceridemia, prior atherosclerotic cardiovascular disease event), lipid-lowering therapy may be continued when the benefits outweigh risks. **E**

In normal pregnancy, blood pressure is lower than in the nonpregnant state. The Chronic Hypertension and Pregnancy (CHAP) Trial Consortium's RCT on treatment of mild chronic hypertension during pregnancy demonstrated that a blood pressure of 140/90 mmHg, as the threshold for initiation or titration of treatment, reduces the incidence of adverse pregnancy outcomes without compromising fetal growth (174). The CHAP Consortium's study mitigates concerns about small-for-gestational-age birth weight. Attained mean $\pm$ SD blood pressure measurements in the treated versus untreated groups were systolic 129.5 ± 10.0 vs. 132.6 ± 10.1 mmHg (between-group difference -3.11 [95% CI -3.95 to 2.28]) and diastolic 79.1 ± 7.4 vs. 81.5 ± 8.0 mmHg (-2.33 [95% CI -2.97 to 0.04]), respectively (174). Individuals with diabetes had an even better composite outcome score than those without diabetes (174).

A secondary analysis of the CHAP trial evaluated 434 individuals with both diabetes and chronic hypertension to determine the effect of a lower blood pressure goal (<130/80 mmHg) on pregnancy and neonatal outcomes (175). Participants with lower blood pressure were more likely to be on antihypertensive medications at the start of pregnancy and more likely to have newly diagnosed diabetes prior to 20 weeks. Average blood pressure attained was systolic 122.0 ± 5.7 mmHg vs. 134.9 ± 7.4 mmHg and diastolic 74.4 ± 4.0 mmHg vs. 81.7 ± 5.7 mmHg in the <130/80 mmHg vs. 130–139/80–89 mmHg groups, respectively. Participants with an average blood pressure <130/80 mmHg were less likely to have the primary composite adverse perinatal outcome (19.3% vs. 46.5%, adjusted relative risk 0.43, 95% CI 0.30–0.61) and its components: preeclampsia with severe features (14.0 vs. 40.5%, adjusted risk ratio 0.35, 95% CI 0.23–0.54) and indicated preterm birth <35 weeks (8.0% vs. 20.1%, adjusted risk ratio 0.44, 95% CI 0.24–0.79), $P < 0.01$ for both. They were less likely to have adverse perinatal outcomes: birth weight <10th percentile (3.3% vs. 8.8%, adjusted risk ratio 0.37, 95% CI 0.14–0.96,

$P = 0.04$), NICU admission (36.0% vs. 51.4%, adjusted risk ratio 0.74, 95% CI 0.59–0.94, $P = 0.01$), and days in NICU (7.0 vs. 11.0, adjusted risk ratio 0.54, 95% CI 0.49–0.59, $P < 0.01$) (175). As participants were not randomized to a blood pressure goal of <130/80 mmHg, there is uncertainty as to whether the improved outcomes were attributable to the lower attained blood pressures or to other underlying differences in participant characteristics. There was no evidence of worse outcomes in the group with blood pressure <130/80 mmHg.

As a result of the CHAP study, ACOG issued a Practice Advisory recommending a blood pressure of 140/90 mmHg as the threshold for initiation or titration of medical therapy for chronic hypertension in pregnancy (176) rather than their previously recommended threshold of 160/110 mmHg (177).

During pregnancy, treatment with ACE inhibitors and angiotensin receptor blockers is contraindicated because they may cause fetal renal dysplasia, oligohydramnios, pulmonary hypoplasia, and intrauterine growth restriction (33). A large study found that after adjusting for confounders, first-trimester ACE inhibitor exposure does not appear to be associated with congenital malformations (178). ACE inhibitors and angiotensin receptor blockers should be stopped prior to pregnancy or as soon as possible in the first trimester to avoid second- and third-trimester fetopathy (178). Antihypertensive drugs known to be effective and safe in pregnancy include methyldopa, nifedipine, labetalol, and clonidine. Atenolol is not recommended, but other β -blockers may be used, if necessary. Diuretic use during pregnancy is generally not recommended, although it may be used safely when prescribed at lower doses for individuals in certain circumstances (e.g., chronic kidney disease and reduced glomerular filtration rate) (179).

For most individuals, lipid-lowering medications (e.g., bempedoic acid, PCSK9 therapies, fibrates) should be stopped prior to pregnancy or at the first pregnancy visit (34). Based on available evidence, statins should also be avoided in pregnancy in most circumstances (34). The risk of teratogenicity with statins appears to be low, but data are limited (34). Statins can be considered in a shared decision-making process between pregnant people with diabetes and their health care teams, including

discussion of risks and benefits in pregnant individuals at high risk, such as those with a history of atherosclerotic cardiovascular disease or familial hypercholesterolemia (homozygous or severe heterozygous) (34). Hydrophilic statins, such as pravastatin, may be associated with less fetal harm than lipophilic statins (180). Pravastatin has been studied in multiple pregnancy trials administering therapy at various time points in gestation with the aim to reduce preeclampsia risk, and although its ability to do so is inconclusive to date, there does not appear to be increased neonatal mortality or morbidity associated with its use during gestation (34). In pregnant individuals with a history of severe hypertriglyceridemia, triglyceride levels should be monitored, and nutrition interventions with or without pharmacologic therapy for severe hypertriglyceridemia should be instituted when indicated to reduce pancreatitis risk (34).

POSTPARTUM CARE

Recommendations

15.26 Insulin requirements need to be evaluated and adjusted for individuals requiring insulin after delivery because insulin resistance decreases dramatically immediately postpartum. **C**

15.27 A contraceptive plan should be discussed and implemented with all people with diabetes of childbearing potential. **A**

15.28 Breastfeeding efforts are recommended for all individuals with diabetes. **A** Breastfeeding is recommended for individuals with a history of GDM for multiple benefits, **A** including a reduced risk for type 2 diabetes later in life. **B**

15.29 Postpartum care should include psychosocial assessment and support for self-care. **E**

15.30 Screen individuals with a recent history of GDM at 4–12 weeks postpartum, using the 75-g oral glucose tolerance test and clinically appropriate nonpregnancy diagnostic criteria. **B**

15.31 Individuals with a history of GDM should have lifelong screening for the development of type 2 diabetes or prediabetes every 1–3 years. **B**

15.32 Individuals with overweight or obesity and a history of GDM found to have prediabetes should receive

intensive lifestyle interventions and/or metformin to prevent diabetes. **A**

Diabetes Treatment Postpartum

For individuals requiring insulin after delivery, insulin sensitivity increases dramatically with the delivery of the placenta. In one study, insulin requirements in the immediate postpartum period were roughly 34% lower than prepregnancy insulin requirements (181). Insulin sensitivity then returns to prepregnancy levels over the following 1–2 weeks. For individuals taking insulin, particular attention should be directed to hypoglycemia prevention in the setting of breastfeeding and erratic sleep and eating schedules (182). Individuals with GDM usually do not require diabetes medications in the postpartum period.

Contraception

A major barrier to effective preconception care is the fact that many pregnancies are unplanned (183). Planning pregnancy is critical in individuals with preexisting diabetes to achieve the optimal glycemic goals necessary to prevent congenital malformations and reduce the risk of other complications. Therefore, all individuals with diabetes of childbearing potential should have family planning options reviewed at regular intervals to make sure that effective contraception is implemented and maintained. This applies to individuals in the immediate postpartum period. Individuals with diabetes have the same contraception options and recommendations as those without diabetes, although the existence of diabetes complications or other vascular disease may modify recommended options (12). Long-acting, reversible contraception may be ideal for individuals with diabetes and childbearing potential. The risk of an unplanned pregnancy outweighs the risk of any currently available contraception option.

Lactation

Considering the immediate nutritional and immunological benefits of breastfeeding for the baby, all mothers, including those with diabetes, should be supported in attempts to breastfeed. An analysis of 28 systematic reviews and meta-analyses of associations between breastfeeding and outcomes in children found that breastfeeding was associated with numerous health benefits for children,

such as reduced infant mortality due to infectious diseases at <6 months of age (OR 0.22–0.59 across studies), reduced respiratory infections in children aged <2 years, and reduced asthma or wheezing in children and adolescents aged 5–18 years (OR 0.91, 0.85–0.98) (184). The same analysis found that breastfeeding was associated with improved maternal health outcomes, including reduced risks of breast cancer (OR 0.81 [95% CI 0.77–0.86]), ovarian cancer (OR 0.70 [95% CI 0.64–0.75]), and type 2 diabetes (OR 0.68 [95% CI 0.57–0.82]). Breastfeeding may also confer longer-term metabolic benefits to both mother (185) and offspring (186). Breastfeeding reduces the risk of developing type 2 diabetes in mothers with previous GDM (185). It may improve the metabolic risk factors of offspring, but more studies are needed (187). However, lactation can increase the risk of overnight hypoglycemia, and insulin dosing may need to be adjusted.

Special Postpartum Considerations for Individuals With Gestational Diabetes Mellitus

Because GDM often represents previously undiagnosed prediabetes, type 2 diabetes, maturity-onset diabetes of the young, or even developing type 1 diabetes, individuals with GDM should be tested for persistent diabetes or prediabetes at 4–12 weeks postpartum with a fasting 75-g OGTT using nonpregnancy criteria as outlined in section 2, “Diagnosis and Classification of Diabetes,” specifically **Tables 2.1** and **2.2**. The OGTT is recommended over A1C at 4–12 weeks postpartum, because A1C may be persistently impacted (lowered) by the increased red blood cell turnover related to pregnancy, by blood loss at delivery, or by the preceding 3-month glucose profile. The OGTT is more sensitive at detecting glucose intolerance, including both prediabetes and diabetes, and has been examined as a screening tool for these conditions in the first 12 weeks after delivery in individuals who had a recent pregnancy with GDM (188,189). OGTT testing immediately postpartum, while still hospitalized, has demonstrated improved engagement in testing but also variably reduced sensitivity to the diagnosis of impaired fasting glucose, impaired glucose tolerance, and type 2 diabetes (190,191). In a small subset of individuals who are unable to tolerate or who decline the postpartum glucose

tolerance test, an A1C performed at 6–12 months postpartum may be considered. A retrospective study aimed to evaluate the performance of A1C as a postpartum screening test (192). The study included 677 out of 9,118 individuals with a recent GDM diagnosis who had both A1C and 2-h 75-g OGTT testing performed for clinical purposes between delivery and 12 months postpartum. A1C level of 5.7% had 80% sensitivity and 80.8% specificity for the detection of a 2-h plasma glucose value ≥ 200 mg/dL (≥ 11.1 mmol/L). A weakness of this study is the likelihood of selection bias, as it is not standard of care to perform both tests unless there is higher concern for a diagnosis of diabetes.

Individuals with a history of GDM should have ongoing screening for prediabetes or type 2 diabetes every 1–3 years, even if results of the initial 75-g OGTT at 4–12 weeks postpartum are normal. Ongoing evaluation may be performed with any recommended glycemic test (see section 2, “Diagnosis and Classification of Diabetes”).

Individuals with a history of GDM have an increased lifetime maternal risk for diabetes estimated at 50–60% (193,194), and those with GDM have a 10-fold increased risk of developing type 2 diabetes compared with those without GDM (193). Absolute risk of developing type 2 diabetes after GDM increases linearly through a person's lifetime, being ~20% at 10 years, 30% at 20 years, 40% at 30 years, 50% at 40 years, and 60% at 50 years (194). Hazard ratios for incident diabetes were significantly elevated for a history of GDM in a single pregnancy but were even higher for a history of two GDM pregnancies in a large retrospective cohort study (hazard ratios ranged from 4.35- to 15.8-fold based on number of pregnancies with GDM and which pregnancy the individual had GDM (first or second) (195). In the prospective Nurses' Health Study II (NHS II), subsequent diabetes risk after a history of GDM was significantly lower in those who followed healthy eating patterns (196). Adjusting for BMI moderately attenuated this association. Interpregnancy weight gain is associated with increased risk of adverse pregnancy outcomes (197) and higher risk of GDM, while in people with BMI >25 kg/m², weight loss is associated with lower risk of developing GDM in the subsequent pregnancy (198). Development of type 2 diabetes is 18% higher

per unit of BMI increase from prepregnancy BMI at follow-up, highlighting the importance of effective weight management after GDM (199). In addition, postdelivery lifestyle interventions are effective in reducing risk of type 2 diabetes (200).

Both metformin and intensive lifestyle intervention prevent or delay progression to diabetes in individuals with prediabetes and a history of GDM. Only five to six individuals with prediabetes and a history of GDM need to be treated with either intervention to prevent one case of diabetes over 3 years (201). In these individuals, lifestyle intervention and metformin reduced progression to diabetes by 35% and 40%, respectively, over 10 years compared with placebo (202). If pregnancy has motivated the adoption of healthy nutrition, building on these gains to support weight loss is recommended in the postpartum period (see section 3, “Prevention or Delay of Diabetes and Associated Comorbidities”).

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16. Diabetes Care in the Hospital: Standards of Care in Diabetes—2026

American Diabetes Association
Professional Practice Committee for
Diabetes*

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The American Diabetes Association (ADA) “Standards of Care in Diabetes” includes the ADA’s current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. Members of the ADA Professional Practice Committee for Diabetes, an interprofessional expert committee, are responsible for updating the Standards of Care annually, or more frequently as warranted. For a detailed description of ADA standards, statements, and reports, as well as the evidence-grading system for ADA’s clinical practice recommendations and a full list of Professional Practice Committee members, please refer to Introduction and Methodology. Readers who wish to comment on the Standards of Care are invited to do so at professional.diabetes.org/SOC.

Among hospitalized individuals, hyperglycemia, hypoglycemia, and glucose variability are associated with adverse outcomes, including increased morbidity and mortality (1,2). Identification and careful management of people with diabetes and dysglycemia during hospitalization has direct and immediate benefits. Diabetes management in the inpatient setting includes identification and treatment of hyperglycemia and hypoglycemia, diagnosing and managing hyperglycemic crises, perioperative care planning, and a proactive transition plan for outpatient diabetes care with timely scheduled follow-up appointments. These steps can improve outcomes, shorten hospital stays, and reduce the need for readmission and emergency department visits. For older individuals or for people with diabetes in post-acute and long-term care settings, please see section 13, “Older Adults.”

HOSPITAL CARE DELIVERY STANDARDS

Recommendations

- 16.1** Perform an A1C test on all people with diabetes or hyperglycemia (random blood glucose >140 mg/dL [>7.8 mmol/L]) at the time of admission to the hospital if no A1C test result is available from the prior 3 months. **B**
- 16.2** Institutions should implement protocols using validated written or computerized provider order entry sets for management of dysglycemia in the hospital that allow for a personalized approach. **B**

Considerations on Admission

Initial evaluation should state the type of diabetes (i.e., type 1, type 2, gestational, pancreatogenic, stress hyperglycemia, drug related, or nutrition related [e.g., enteral or parenteral nutrition]) when it is known. To identify people with undiagnosed diabetes, and

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because inpatient treatment and discharge planning are more effective when preadmission glycemia is considered, A1C should be measured for all people with diabetes or dysglycemia at the time of admission to the hospital or soon after if no A1C test result is available from the previous 3 months (3–5). Incorporating A1C into the glucose management order set may help increase frequency of A1C testing (6). In addition, diabetes self-management knowledge and behaviors should be assessed on admission, and diabetes self-management education should be provided throughout the hospital stay, especially if a new treatment plan is being considered. Diabetes self-management education should include the knowledge and skills needed after discharge, such as medication dosing and administration, meal planning, glucose monitoring, and recognition and treatment of hypoglycemia (7). For individuals residing in group homes or institutional settings (8), information on site capabilities related to diabetes management should be obtained and the therapeutic plan should be adjusted accordingly.

High-quality hospital care for diabetes requires clear and actionable standards for care delivery, which are best implemented using structured order sets with computerized provider order entry (CPOE) as well as quality improvement strategies for process improvement (9). The National Academy of Medicine recommends CPOE to prevent medication-related errors and to increase medication administration efficiency (10). Systematic reviews of randomized controlled trials using computerized assistance to improve glycemic outcomes in the hospital found significant improvement in the percentage of time individuals spent in the glycemic goal range, lower mean blood glucose levels, and no increase in hypoglycemia (11). Where feasible, the structured order set should provide computerized guidance for glycemic management, including initial weight-based insulin dosing guidance and insulin titration guidance during the hospital stay (12). Currently available commercial electronic glucose management systems may facilitate implementation of insulin protocols in the hospital (13,14).

Diabetes Care Teams in the Hospital

Recommendation

16.3 When caring for hospitalized people with diabetes (with an existing

or new diagnosis) or stress hyperglycemia, consult with a specialized diabetes or glucose management team when available. **B**

Care provided by appropriately trained specialists or specialty teams may reduce the length of stay and improve glycemic and other clinical outcomes (15–17). In addition, the increased risk of 30-day readmission following hospitalization that has been attributed to diabetes can be reduced, and costs saved, when inpatient care is provided by a diabetes management team (15,18). In a cross-sectional study comparing usual care to care provided by a virtual glucose management service based on the daily chart review and making recommendations through the electronic health record (EHR), rates of both hyperglycemia and hypoglycemia were reduced by 30–40% (19). In addition, providing diabetes self-management education and developing a diabetes discharge plan that includes continued access to diabetes medications and supplies and ongoing education and support are key strategies to improve long-term outcomes (20,21). Hospital diabetes care teams may include and be led by physicians or other health care professionals trained in diabetes care and education such as nurse practitioners or physician assistants/associates, nurses, registered dietitian nutritionists, or pharmacists (22). Details of diabetes care team composition and other resources are available from the Joint Commission accreditation program for the hospital care of diabetes, the Society of Hospital Medicine workbook, The Leapfrog Group, and the Joint British Diabetes Societies (JBDS) for Inpatient Care Group (23–26).

GLYCEMIC GOALS IN HOSPITALIZED ADULTS

Recommendations

16.4a Insulin should be initiated or intensified for treatment of persistent hyperglycemia starting at a threshold of ≥ 180 mg/dL (≥ 10.0 mmol/L) (confirmed on two occasions within 24 h) for the majority of critically ill individuals (those in the intensive care unit [ICU]). **A**

16.4b Insulin and/or other glucose lowering therapies should be initiated or intensified for treatment of persistent

hyperglycemia starting at a threshold of ≥ 180 mg/dL (≥ 10.0 mmol/L) (confirmed on two occasions within 24 h) for the majority of noncritically ill individuals (those not in the ICU). **B**

16.5a Once therapy is initiated, a glycemic goal of 140–180 mg/dL (7.8–10.0 mmol/L) is recommended for most critically ill individuals (those in the ICU) with hyperglycemia. **A** More stringent individualized glycemic goals may be appropriate for selected critically ill individuals if they can be achieved without significant hypoglycemia. **B**

16.5b For noncritically ill individuals (those not in the ICU), a glycemic goal of 100–180 mg/dL (5.6–10.0 mmol/L) is recommended if it can be achieved without significant hypoglycemia. **B**

Standard Definitions of Glucose Abnormalities

Hyperglycemia in hospitalized individuals is defined as any blood glucose level > 140 mg/dL (> 7.8 mmol/L) based on the threshold for an abnormal glucose level (27). An admission A1C value $\geq 6.5\%$ (≥ 48 mmol/mol) suggests that the onset of diabetes preceded hospitalization (see section 2, “Diagnosis and Classification of Diabetes”). Hypoglycemia is defined as blood glucose < 70 mg/dL (< 3.9 mmol/L) and is further stratified into three categories: level 1 (glucose concentration of 54–69 mg/dL [3.0 – 3.8 mmol/L]), level 2 (glucose concentration < 54 mg/dL [< 3.0 mmol/L], which is typically the threshold for neuroglycopenic symptoms), and level 3 (a clinical event characterized by altered mental and/or physical functioning that requires assistance from another person for recovery) (Table 6.4). Levels 2 and 3 hypoglycemia require immediate intervention and correction of low blood glucose. Prompt treatment of level 1 hypoglycemia is recommended for prevention of progression to more significant level 2 and level 3 hypoglycemia.

Glycemic Goals

In a landmark clinical trial conducted in a surgical intensive care unit (ICU), Van den Berghe et al. (28) demonstrated that an intensive intravenous insulin protocol with a glycemic goal of 80–110 mg/dL (4.4–6.1 mmol/L) reduced mortality by 40% compared with a standard approach

of a glycemic goal of 180–215 mg/dL (10–12 mmol/L) in critically ill hospitalized individuals with diabetes and/or stress hyperglycemia and recent surgery. However, several multicenter studies, including the Normoglycemia in Intensive Care Evaluation and Survival Using Glucose Algorithm Regulation (NICE-SUGAR) trial, in critically ill hospitalized individuals in medical and surgical ICUs (29–31) failed to replicate these data. In the NICE-SUGAR trial, critically ill individuals randomized to intensive glycemic management (80–110 mg/dL [4.4–6.1 mmol/L]) derived no significant treatment advantage compared with a group with more moderate glycemic goals (140–180 mg/dL [7.8–10.0 mmol/L]) and had slightly but significantly higher mortality (27.5% vs. 25%). The intensively treated group had 10- to 15-fold greater rates of hypoglycemia. The findings from the NICE-SUGAR trial, supported by several meta-analyses showed higher rates of hypoglycemia and an increase in mortality with more aggressive glycemic management goals compared with moderate glycemic goals (29,32,33). More recently, a multicenter randomized controlled trial comparing tight and liberal glucose management in critically ill individuals not receiving early parenteral nutrition showed no benefit of tight glycemic management despite effective glucose separation between the groups and remarkably low rates of hypoglycemia in both groups (1.0% in tight group vs. 0.7% in liberal group) (30). Based on these clinical trials and results of other observational studies, insulin and/or other therapies should be initiated for the treatment of persistent hyperglycemia ≥ 180 mg/dL (≥ 10.0 mmol/L). Once therapy is initiated, a glycemic goal of 140–180 mg/dL (7.8–10.0 mmol/L) is recommended for most critically ill individuals. More stringent glycemic goals, such as 110–140 mg/dL (6.1–7.8 mmol/L), may be appropriate for selected individuals (e.g., critically ill individuals undergoing cardiac surgery) if they can be achieved without significant hypoglycemia (34,35). For hospitalized individuals without critical illness, a glycemic goal of 100–180 mg/dL (5.6–10.0 mmol/L) is recommended, whether it is hyperglycemia due to newly diagnosed diabetes or stress hyperglycemia or hyperglycemia related to diabetes prior to admission (36,37). It has been found that fasting glucose levels <100 mg/dL (<5.6 mmol/L) are predictors of hypoglycemia within the next 24 h (38) and therefore

necessitate basal insulin dose adjustments. Higher glycemic levels (up to 250 mg/dL [13.9 mmol/L]) may be acceptable in selected populations (terminally ill individuals with short life expectancy, advanced kidney failure [and/or on dialysis], high risk for hypoglycemia, and/or labile glycemic excursions). In these individuals, less aggressive treatment goals that would help avoid symptomatic hypoglycemia and/or hyperglycemia are often appropriate. Clinical judgment combined with ongoing assessment of clinical status, including changes in the trajectory of glucose measures, illness severity, nutritional status, or concomitant medications that might affect glucose levels (e.g., glucocorticoids), should be incorporated into the day-to-day decisions regarding treatment goals.

GLUCOSE MONITORING

In hospitalized individuals with diabetes who are eating, point-of-care (POC) blood glucose monitoring should be performed before meals; in those not eating, glucose monitoring is advised every 4–6 h (36). More frequent POC blood glucose monitoring typically ranging from every 30 min to every 2 h is recommended for safe use of intravenous insulin therapy.

Hospital blood glucose monitoring should be performed with U.S. Food and Drug Administration (FDA)-approved POC hospital-calibrated glucose monitoring systems (39) (Table 7.1). POC blood glucose monitors provide the advantage of immediate bedside results, and studies suggest that while POC measurements are less accurate and less precise than those from laboratory glucose analyzers, they provide adequate information for usual practice except in rare instances where care has been compromised (40,41). Particular attention should be given to factors that may cause errors in POC measurement such as perfusion abnormalities, edema, anemia or erythrocytosis, and several medications commonly used in the hospital (39). The FDA has established standards for capillary (finger-stick) POC glucose monitoring in the hospital (39). The balance between analytic requirements (e.g., accuracy, precision, and interference) and clinical requirements (e.g., rapidity, simplicity, and POC) has not been uniformly resolved (39–42), and most hospitals have arrived at their own policies to balance these parameters. It is critically important that devices selected for in-hospital use,

and the workflow through which they are applied, undergo careful analysis of performance and reliability and ongoing quality assessments (42). Best practice dictates that any POC glucose result that does not correlate with the individual's clinical status should be confirmed by repeating the test first and measuring a sample in the clinical laboratory if the second result is similar, particularly for asymptomatic hypoglycemic events.

Continuous Glucose Monitoring

Recommendations

16.6 In people with diabetes using a personal continuous glucose monitoring (CGM) device, the use of CGM should be continued during hospitalization if clinically appropriate, with confirmatory point-of-care (POC) blood glucose measurements for insulin dosing decisions and hypoglycemia assessment, if resources and training are available, and according to an institutional protocol. **B**

While supporting individuals who wish to continue use of personal continuous glucose monitoring (CGM) devices is encouraged, currently it is recommended that confirmatory POC be used for insulin dosing. However, a recent retrospective study demonstrated the feasibility of implementation of a hospital-wide personal CGM policy that included EHR integration and CGM validation for insulin dosing; the policy resulted in favorable hospitalized individual and nurse satisfaction (43). Validation criteria to ensure adequate accuracy of CGM have been based on a modified version of FDA criteria for integrated CGM devices. Known as the 20/20 criterion, it requires a CGM reading to be within $\pm 20\%$ of the POC measurement when blood glucose is ≥ 70 mg/dL or within ± 20 mg/dL of the POC measurement when blood glucose is < 70 mg/dL. Several other studies have demonstrated that inpatient use of hospital-owned CGM devices is feasible and has advantages over POC glucose monitoring in improving glycemic management, detecting hypoglycemia (particularly nocturnal, prolonged and/or asymptomatic hypoglycemia [44,45]), and reducing recurrent hypoglycemia (43,46–48). However, at this time, none of the CGM devices have been approved by the FDA for inpatient use. During the coronavirus disease 2019

(COVID-19) pandemic, many institutions used CGM in ICU and non-ICU settings, with the aim of minimizing exposure time and saving personal protective equipment, under an FDA policy of enforcement discretion (49,50). Data on the safety and efficacy of real-time CGM use in the hospital, particularly with implementation of remote monitoring (e.g., a glucose telemetry system), has grown (47,50–52). However, a recent multicenter randomized clinical trial did not show a benefit of using CGM over POC monitoring for insulin adjustment in individuals with type 2 diabetes hospitalized for noncritical illness (53). Both groups achieved similar mean blood glucose levels (170 ± 32 vs. 175 ± 33 [$P = 0.25$]) with similarly low levels of hypoglycemia. The discrepancies in the results of clinical trials may be related to treatment algorithms rather than the method of glucose monitoring. Before the COVID-19 pandemic, the use of hospital CGM was mostly restricted to remote monitoring and facilitation of insulin adjustment based on daily CGM data, rather than as a replacement for POC. However, hospital CGM was successfully used in conjunction with periodic POC monitoring in hybrid protocols used for intravenous insulin titrations, decreasing the burden of hourly POC testing (54–56).

Due to an ongoing interest in use of hospital CGM systems, a recent consensus on good practice points for use of CGM devices in hospital settings has been published (57). For more general information on CGM, see section 7, “Diabetes Technology.”

Insulin Pump Use in the Hospital

Recommendation

16.7 Continue use of insulin pump including automated insulin delivery in people with diabetes who are hospitalized when clinically appropriate. This is contingent upon availability of necessary supplies, resources, training, ongoing competency assessments, and implementation of institutional diabetes technology protocols. **C**

Data on inpatient use of hybrid closed-loop systems (currently commercially available automated insulin delivery [AID] devices) are limited to feasibility trials (58). In a randomized controlled trial, people with type 2 diabetes receiving noncritical care had significantly better glycemia with the

use of an automated, fully closed-loop insulin delivery system than with conventional subcutaneous insulin therapy, without a higher risk of hypoglycemia (59). Continuation of insulin pump or AID system use should be supported during hospitalization when clinically appropriate in individuals who are willing and able to self-manage their devices, with proper staff training and supervision. An observational study in children demonstrated improvement in individual satisfaction and improved detection of glycemic excursions with continued use of personal devices (60). Consultation with the endocrinology/diabetes care team or diabetes care and education specialists, if available, is recommended, especially if the reason for admission is suspected to be related to device malfunction or lack of adequate education, training, or use. Best practices ensuring safe use of AID systems in the hospital setting are evolving. Many institutions still require POC blood glucose monitoring with variable frequency (1–6 times daily) for individuals continuing insulin pump or AID system use. Since AID systems cannot function without using CGM data, it is important to ensure and document CGM accuracy by cross-checking CGM readings with POC or blood glucose readings periodically (at least once daily) or when clinically appropriate. To consider CGM readings valid, current criteria require a CGM reading to be within $\pm 20\%$ of POC or laboratory blood glucose measurement or within ± 20 mg/dL when POC or laboratory blood glucose is ≤ 70 mg/dL (43). In addition, CGM and AID data should be reviewed and documented daily (e.g., before meals and at bedtime) and pump settings should be adjusted as needed to ensure that the individual is meeting treatment goals. Hospitals are encouraged to develop institutional policies and have available trained personnel with knowledge of diabetes technology. In a recent survey, less than half the hospitals had these policies in place (61).

For more general information on AID, see section 7, “Diabetes Technology.”

GLUCOSE-LOWERING TREATMENT IN HOSPITALIZED INDIVIDUALS

An individualized approach for glycemic management is encouraged throughout the hospital stay and should take into consideration several predictive factors for achieving glycemic goals, such as prior home

use and doses of insulin or noninsulin therapy, expected level of insulin resistance, prior A1C, current glucose levels, nutritional intake, duration of diabetes, glucose altering medications, and the goal of treatment for primary disease.

Insulin Therapy

Recommendations

16.8a Continuous intravenous insulin infusion is recommended for achieving glycemic goals and avoiding hypoglycemia in critically ill individuals. **A**

16.8b Basal insulin or a basal plus correction insulin plan is the preferred treatment for noncritically ill hospitalized individuals with poor or no oral intake. **A**

16.9 An insulin plan with basal, prandial, and correction components is the preferred treatment for most noncritically ill hospitalized individuals with adequate nutritional intake. **A**

16.10 For most individuals, sole use of a correction or supplemental insulin without basal insulin (formerly referred to as a sliding scale) in the inpatient setting is discouraged. **A**

Critical Care Setting

Continuous intravenous insulin infusion is the most effective method for achieving specific glycemic goals and avoiding hypoglycemia in the critical care setting. Intravenous insulin infusions should be administered using validated written or computerized protocols that allow for predefined adjustments in the insulin infusion rate based on glycemic fluctuations and immediate past and current insulin infusion rates (62). For individuals who are eating but continue to need intravenous insulin infusion, prandial coverage may be provided as rapid-acting insulin administered subcutaneously, as this would prevent large fluctuations in intravenous insulin requirement and subsequent hypoglycemia risk (63).

Transitioning From Intravenous to Subcutaneous Insulin

When discontinuing intravenous insulin, a transition protocol should be used. Subcutaneous basal insulin should be given 2 h before intravenous infusion is discontinued, with the aim of minimizing rebound hyperglycemia while the subcutaneous insulin achieves its effect (63).

Emerging data from studies in people with hyperglycemia with and without diabetic

ketoacidosis (DKA) show that the administration of a low dose (0.15–0.3 units/kg) of basal insulin analog in addition to intravenous insulin infusion may reduce the duration of insulin infusion and length of hospital stay and prevent rebound hyperglycemia without increased risk of hypoglycemia (64–67). This may be particularly beneficial for people with type 1 diabetes to minimize the risk for DKA should insulin infusion be stopped for a prolonged period of time.

For transitioning, the total daily dose of subcutaneous insulin may be calculated using a weight-based approach, based on prior home insulin dose or based on the insulin infusion rate during the prior 6–8 h when stable glycemic goals were achieved (12). It is important to ensure correct dosing either by using an insulin pen or meticulous pharmacy and nursing supervision of the dose drawn from a vial.

Noncritical Care Setting

In most instances, insulin is the preferred treatment for hyperglycemia in hospitalized individuals. In certain circumstances, it may be appropriate to continue home oral glucose-lowering medications or initiate use of agents such as dipeptidyl peptidase 4 inhibitors (DPP-4i) for mild hyperglycemia.

Scheduled subcutaneous insulin orders are recommended for the management of hyperglycemia in people with diabetes and hyperglycemia. Use of insulin analogs or human insulin results in similar glycemic outcomes in the hospital setting, but human insulin may increase the risk of hypoglycemic events (68). The use of subcutaneous rapid- or short-acting correctional insulin before meals, or every 4–6 h if no meals are given or if the individual is receiving continuous enteral or parenteral nutrition, is indicated to correct or prevent hyperglycemia. Basal insulin, or a basal plus bolus correction schedule, is the preferred treatment for noncritically ill hospitalized individuals with inadequate or restricted oral intake. An insulin schedule with basal, prandial, and correction components is the preferred treatment for most noncritically ill hospitalized people with diabetes with adequate nutritional intake.

Typically, total daily insulin dose is calculated based on body weight and sensitivity to insulin, with 0.3–0.6 units/kg/day as the usual starting dose (69). Initial total daily insulin dose may also be estimated from the last 6–8 h of insulin infusion

rate or the insulin dose received in previous hospitalization or calculated as 80% of the home insulin dose, as the situation applies. If calculating from the insulin infusion rate, about 60% of the calculated total daily dose should be used to account for glucotoxicity. Half of the estimated total daily insulin should be given as basal insulin and half as nutritional insulin. Correctional insulin scales should be proportional to the total daily dose of insulin e.g., low scale for insulin dose <40 units/day, medium for 40–80 units/day, and high for >80 units/day. Correctional insulin dosing should typically start at 140 or 150 mg/dL (7.8 or 8.3 mmol/L) for adequate glycemic management. Several reports indicate that inpatient use of insulin pens is safe and may improve nurse satisfaction when safety protocols, including nursing education and bar code scanning procedures, are in place to guarantee single-person use (70–73).

The decision to restart a home insulin plan upon hospitalization should take into account the individual's adoption of their insulin plan while at home as well as the change in their clinical status, including nutrition and kidney function.

A randomized controlled trial has shown that basal plus bolus insulin plan improved glycemic outcomes and reduced hospital complications compared with a correction or supplemental insulin without basal insulin (formerly known as sliding scale) for people with type 2 diabetes admitted for general surgery (74). Prolonged use of correction or supplemental insulin without basal insulin is strongly discouraged in the inpatient setting, with the exception of people with type 2 diabetes in noncritical care with mild hyperglycemia or stress hyperglycemia who maintain blood glucose <180 mg/dL (75,76).

A prospective randomized inpatient study of 70/30 intermediate-acting (NPH)/regular insulin mixture versus basal-bolus therapy showed comparable glycemic outcomes but significantly increased hypoglycemia in the group receiving the insulin mixture (77). Therefore, insulin mixtures such as 75/25, 70/30, or 50/50 insulins are not routinely recommended for in-hospital use.

Data on the use of concentrated insulins such as glargine U-300, degludec U-200, and U-500 regular insulin in the inpatient and perioperative settings are limited and have shown variable results (78–81). Hypoglycemia and dosing errors are a particular concern for individuals using

U-500 insulin whose inpatient insulin needs are reduced up to 75% compared with home dosing regardless of preadmission glycemia (82). If concentrated insulin must be used in a specific situation, the risk of dosing errors can be reduced by using a pen device or having the dose drawn by a pharmacist. Consultation with a diabetes care team should be considered in this situation.

Type 1 Diabetes

For people with type 1 diabetes, correctional insulin alone is contraindicated because insulin dosing based solely on premeal glucose levels does not account for basal insulin requirements or caloric intake and increases the risk of both hypoglycemia and hyperglycemia (83). An insulin schedule with basal and correction components is necessary for all hospitalized individuals with type 1 diabetes, even for those taking nothing by mouth, with the addition of prandial insulin when individuals are eating. Policies and practice alerts in the EHR should be put in place to ensure that basal insulin (given subcutaneously, via insulin pump or by insulin infusion) is not held for people with type 1 diabetes, especially during care transitions, and that ongoing prescriber and nursing education is provided (71).

Noninsulin Therapies

Recommendation

16.11 It is recommended that use of a sodium–glucose cotransporter 2 inhibitor be initiated or continued during hospitalization if indicated for heart failure, providing there are no contraindications. **A**

While sodium–glucose cotransporter 2 (SGLT2) inhibitors are not recommended for glycemic management in the hospital setting, they may be initiated or continued for people with type 2 diabetes hospitalized with heart failure if there are no contraindications and after recovery from the acute illness (84–89). SGLT2 inhibitors should be avoided in cases of severe illness, in people with ketonemia or ketonuria, and during prolonged fasting and surgical procedures (90). Proactive adjustment of insulin and diuretic dosing is recommended during hospitalization and/or discharge, especially in collaboration with a cardiology/heart failure consultation team. It is recommended that

SGLT2 inhibitors be stopped 3 days before scheduled surgeries (4 days for ertugliflozin) (90).

A few randomized trials demonstrated the safety and efficacy of DPP-4i in specific groups of hospitalized people with diabetes (91–93). The use of DPP-4i with or without basal insulin may be a safer and simpler plan for people with mild to moderate hyperglycemia on admission (e.g., admission glucose <180–200 mg/dL), with reduced risk of hypoglycemia (91,92). However, the FDA states that health care professionals should consider discontinuing saxagliptin and alogliptin in people who develop heart failure (94). It is worth noting that in the case of linagliptin, no renal dose adjustment is required. Data on the inpatient use of glucagon-like peptide 1 receptor agonists (GLP-1 RAs) are still mostly limited to research studies and select populations that are medically stable (95,96). Therefore, GLP-1 RA drugs should be held for acutely ill individuals in the hospital setting.

HYPOGLYCEMIA

Recommendations

16.12 A hypoglycemia management protocol should be adopted by all health systems. A plan for identifying, treating, and preventing hypoglycemia should be established for each individual. Episodes of hypoglycemia in the hospital should be documented in the health record and tracked to inform quality improvements. **C**

16.13 Treatment plans should be reviewed and changed as necessary to prevent hypoglycemia and recurrent hypoglycemia when a blood glucose value of <70 mg/dL (<3.9 mmol/L) is documented. **C**

People with or without diabetes may experience hypoglycemia in the hospital setting. While hypoglycemia is associated with increased mortality (97,98), in many cases, it is a marker of an underlying disease rather than the cause of fatality. However, hypoglycemia is a severe consequence of dysregulated metabolism and/or diabetes treatment, and it is imperative that it be minimized during hospitalization. Many episodes of inpatient hypoglycemia are preventable. A hypoglycemia prevention and management protocol should be adopted and

implemented by each hospital or hospital system. A standardized hospital-wide, nurse-initiated hypoglycemia treatment protocol should be in place to immediately address blood glucose levels <70 mg/dL (<3.9 mmol/L) (99,100). In addition, individualized plans for preventing and treating hypoglycemia for each person should also be developed. The treatment plan should be reviewed any time a blood glucose value of <70 mg/dL (<3.9 mmol/L) occurs, as this level often predicts subsequent level 3 hypoglycemia. Episodes of hypoglycemia in the hospital should be documented in the EHR and tracked (101). A key strategy is embedding hypoglycemia treatment into all insulin and insulin infusion orders.

Inpatient Hypoglycemia: Risk Factors, Treatment, and Prevention

Insulin is one of the most common medications that causes adverse events in hospitalized individuals. Errors in insulin dosing, missed doses, and/or administration errors including incorrect insulin type and/or timing of dose occur relatively frequently (102–104) and include prescriber (ordering), pharmacy (dispensing), and nursing (administration) errors. Common preventable sources of iatrogenic hypoglycemia are improper prescribing of other glucose-lowering medications and inappropriate management and follow-up of the first episode of hypoglycemia. Kidney failure is an important risk factor for hypoglycemia in the hospital (105), possibly as a result of decreased insulin clearance. Other related factors for hypoglycemia include advanced age, comorbidities including heart and liver failure, sepsis, and malnutrition, among others (106). Studies of “bundled” preventive therapies, including proactive surveillance of glycemic outliers and an interprofessional data-driven approach to glycemic management, showed that hypoglycemic episodes in the hospital could be reduced or prevented (107,108). Compared with baseline, studies found that hypoglycemic events decreased by 56–80% (100,107,108). The Joint Commission, a quality improvement and patient safety in health care organization, recommends that all hypoglycemic episodes be evaluated for a root cause and the episodes be aggregated and reviewed to address systemic issues and possible solutions (26).

In addition to errors with insulin treatment, iatrogenic hypoglycemia may occur

after a sudden reduction of corticosteroid dose, reduced oral intake, emesis, inappropriate timing of short- or rapid-acting insulin doses in relation to meals, reduced infusion rate of intravenous dextrose, unexpected interruption of enteral or parenteral feedings, prolonged procedures or surgery, delayed or missed blood glucose checks, and altered ability of the individual to report symptoms.

Studies show promise for CGM to alert the wearer or care staff of impending hypoglycemia, offering an opportunity to mitigate it before it happens (46,48). The use of personal CGM and AID devices may also help avoid hypoglycemia. Thus, the use of diabetes technology may help reduce the risk of hypoglycemia in future.

Treatment of hypoglycemia includes administering 15 g of fast-acting carbohydrate (to those who can swallow and do not have NPO status) or administering intravenous glucose or glucagon. Blood glucose should be monitored every 15 min and treatment hypoglycemia repeated until it is stabilized above 70 mg/dL (3.9 mmol/L).

Predicting and Preventing Severe Hypoglycemia

In people with diabetes, it is well established that an episode of severe hypoglycemia increases the risk for a subsequent event, partly because of impaired counterregulation (109). In a study of hospitalized individuals, 84% of people who had an episode of severe hypoglycemia (defined as <40 mg/dL [<2.2 mmol/L]) had a preceding episode of hypoglycemia (<70 mg/dL [<3.9 mmol/L]) during the same admission (110). In another study of hypoglycemic episodes (defined as <50 mg/dL [<2.8 mmol/L]), 78% of individuals were taking basal insulin, with the incidence of hypoglycemia peaking between midnight and 6:00 A.M. (111). Despite recognition of hypoglycemia, 75% of individuals did not have their dose of basal insulin changed before the next basal insulin administration (111). Several groups have developed algorithms to predict episodes of hypoglycemia in the inpatient setting (112,113). Models such as these are potentially important and, once validated for general use, could provide a valuable tool to reduce rates of hypoglycemia in the hospital. In one retrospective cohort study, a fasting blood glucose of <100 mg/dL was shown to be a predictor of next-day hypoglycemia (38).

MEDICAL NUTRITION THERAPY IN THE HOSPITAL

The goals of medical nutrition therapy in the hospital are to provide adequate calories to meet metabolic demands, optimize glycemic outcomes, address personal food preferences, and facilitate the creation of a discharge plan. The ADA does not endorse any single meal plan or specified percentages of macronutrients. Current nutrition recommendations advise individualization based on treatment goals, physiological parameters, and medication use. Controlled carbohydrate meal plans, where the amount of carbohydrate on each meal tray is calculated, are preferred by many hospitals, as they facilitate matching the prandial insulin dose to the amount of carbohydrate given (114). Orders should also indicate that the glucose check, meal delivery, and nutritional insulin coverage should be coordinated—a concept also known as a “meal triad”—as their variability often creates the possibility of hyperglycemic and hypoglycemic events (20). Some hospitals offer “meals on demand,” where individuals may order meals from the menu at any time during the day. This option improves patient satisfaction with hospital but complicates glucose monitoring–insulin–meal coordination and can lead to insulin stacking if meals are too close together (115). Finally, if the hospital food service supports carbohydrate counting, this option should be made available to people with diabetes counting carbohydrates at home, especially people wearing insulin pumps (115,116).

SELF-MANAGEMENT IN THE HOSPITAL

Diabetes self-management in the hospital may be appropriate for select individuals who wish to continue to perform self-care while acutely ill (117–119). Candidates include children with parental supervision, adolescents, and adults who successfully perform diabetes self-management at home and whose cognitive and physical skills needed to successfully self-administer insulin and perform glucose monitoring are not compromised by acute illness or delirium (7). In addition, they should have adequate oral intake and have stable insulin requirements. If self-management is supported, a policy should include a requirement that people with diabetes and the care team agree on a

daily basis during hospitalization that self-management is appropriate. Hospital personal medication policies may include guidance for people with diabetes who wish to take their own or hospital-dispensed insulin and noninsulin medications during their hospital stay. A hospital policy for personal medication may include a pharmacy exception on a case-by-case basis as determined in consultation with the care team. Pharmacy must verify any home medication and require a prescriber order for the individual to self-administer home or hospital-dispensed medication under the supervision of the registered nurse. If an insulin pump or CGM device is worn, hospital policy and procedures delineating guidelines for wearing an insulin pump and/or CGM device should be developed according to consensus guidelines, including the changing of insulin infusion sites and CGM glucose sensors (120).

STANDARDS FOR SPECIAL SITUATIONS

Enteral and Parenteral Feedings

For individuals receiving enteral or parenteral nutrition who require insulin, the insulin orders should include coverage of basal, prandial, and correctional needs (115). It is essential that people with type 1 diabetes continue to receive basal insulin even if feedings are discontinued.

Commercially available enteral nutrition preparations contain variable amounts of carbohydrates and may be infused at different rates (116) that may affect nutritional insulin needs. Most adults receiving basal insulin should continue with their basal dose, while the insulin dose for the total daily nutritional component may be calculated as 1 unit of insulin for every 10–15 g of carbohydrate in the enteral and parenteral formulations. To avoid hypoglycemia, it is important not to cover all insulin needs using basal insulin only. Rapid-acting insulin every 4 h, regular insulin every 6 h, or NPH insulin every 8–12 h are options for coverage of nutritional needs during continuous administration of enteral tube feeds. However, a regular insulin-based plan has been associated with better glycemic management with fewer daily injections in individuals receiving continuous tube feeds (121). An automated self-adjusting insulin algorithm was shown to be safe and effective in controlling hyperglycemia in

hospitalized individuals receiving enteral nutrition or total parenteral nutrition (122). Correctional insulin should also be administered subcutaneously every 6 h with regular human insulin or rapid-acting insulin every 4 h. If enteral nutrition is interrupted, intravenous dextrose may be given for duration of active insulin time.

For adults receiving enteral bolus feedings, approximately 1 unit of rapid-acting insulin per every 10–15 g of carbohydrate should be given subcutaneously before each feeding. To mitigate any hyperglycemia, correctional insulin should be added as needed before each feeding.

In individuals receiving nocturnal tube feeding, NPH insulin administered along with the initiation of the feeding to cover this nutritional load is a reasonable approach.

For individuals receiving continuous peripheral or central parenteral nutrition, human regular insulin may be added to the total parenteral nutrition solution, particularly if >20 units of correctional insulin have been required in the past 24 h. A starting dose of 1 unit of regular human insulin for every 10 g of dextrose has been recommended (115) and should be adjusted daily in the solution. Adding insulin to the parenteral nutrition bag is the safest way to prevent hypoglycemia if the parenteral nutrition is stopped or interrupted, though subcutaneous insulin glargine has been shown to achieve equivalent management of glycemia (123). Correctional insulin should be administered subcutaneously to address any hyperglycemia.

Because continuous enteral or parenteral nutrition results in a continuous postprandial state, efforts to bring blood glucose levels to below 140 mg/dL (7.8 mmol/L) substantially increase the risk of hypoglycemia in these individuals.

Glucocorticoid Therapy

The prevalence of consistent use of glucocorticoid therapy in hospitalized individuals can approach 10–15%, and these medications can induce hyperglycemia in 56–86% of these individuals with and without preexisting diabetes (124–126). Glucocorticoid type and duration of action must be considered in determining appropriate insulin treatments. Daily-ingested intermediate-acting glucocorticoids such as prednisone reach peak plasma levels in 4–6 h but have pharmacologic actions that can last throughout the day. When

monitored by CGM, the typical glycemic pattern for individuals treated with daily prednisone or prednisolone, administered in the morning, is characterized by normal or mild fasting hyperglycemia, with trends of increasing hyperglycemia during the afternoon, and peaking in the evening. These hyperglycemic excursions are more pronounced in individuals with type 2 diabetes than in those without diabetes (127).

For individuals treated with once- or twice-daily steroids, administering NPH insulin with prednisone or prednisolone dosing is a frequently used approach, aimed at matching the NPH actions with the steroid-induced hyperglycemic response. NPH may be administered in addition to daily basal-bolus insulin or in addition to oral glucose-lowering medications, depending on the type of diabetes and recent diabetes medication prior to starting steroids (128). Because NPH action peaks about 4–6 h after administration, it is recommended that it be administered concomitantly with intermediate-acting steroids (129). For long-acting glucocorticoids such as dexamethasone and multi-dose or continuous glucocorticoid use, long-acting basal insulin may be required to manage fasting blood glucose levels. For higher doses of glucocorticoids, increasing doses of prandial (if eating) and correction insulin, sometimes as much as 40–60% or more, are often needed in addition to basal insulin (130,131). A retrospective study found that increasing the ratio of insulin to steroids was positively associated with improved time in range (70–180 mg/dL [3.9–10.0 mmol/L]); however, there was an increase in hypoglycemia (125). If insulin orders are initiated, daily adjustments based on levels of glycemia and anticipated changes in type, dosages, and duration of glucocorticoids, along with POC blood glucose monitoring, are critical to reducing hypoglycemia and hyperglycemia.

Perioperative Care

Recommendations

16.14 To improve postoperative outcomes after elective surgery, a preoperative A1C goal <8% (<64 mmol/mol) is recommended within 3 months, with individualized risk-to-benefit ratio assessment. **C** The 14-day glucose management indicator goal <8% and/or time in range >50% can also be used. **E**

16.15 Blood glucose before, during, and after surgery should be monitored and maintained between 100 and 180 mg/dL (5.6 and 10.0 mmol/L). Goals may differ depending on the surgery, risk for hypoglycemia, and glucose-lowering therapy. **E**

It is estimated that up to 20% of individuals undergoing major general surgery have diabetes, and 23–60% have prediabetes or undiagnosed diabetes. Surgical stress and counterregulatory hormone release increase the risk of hyperglycemia as well as mortality, infection, and length of stay (131,132). Perioperative hyperglycemia is a risk factor for postoperative infections and other complications (133,134). A meta-analysis showed that preoperative and perioperative hyperglycemia were associated with surgical site infections (135). The glycemic threshold for an increase in complications is estimated to be somewhere between 100 and 180 mg/dL (5.5 and 10 mmol/L) in most of these studies (135–138). Overall evidence supports preadmission treatment of hyperglycemia in people scheduled for elective surgery as an effective means of reducing adverse outcomes (139,140). Current data also suggest an optimal A1C goal between 7% and 8% preoperatively, as it is associated with better glycemic management in the perioperative period and decreased length of hospital stay (139,141–144). If available, 14-day CGM data with a glucose management indicator <8% or time in range >50% before elective surgery may be used in lieu of A1C as evidence of adequate preoperative glycemic management. However, due to lack of interventional data, postponing surgery based on A1C or glucose management indicator alone is not recommended, as it may lead to unnecessary delay or denying of required surgery. Some institutions have developed optimization programs to lower A1C prior to elective surgery. These programs have been shown to result in improved perioperative glycemic management and decreased length of hospital stay after surgery (139). In individuals undergoing noncardiac general surgery, basal insulin plus premeal short- or rapid-acting insulin (basal-bolus) coverage has been associated with improved glycemic outcomes and lower rates of perioperative complications compared with the reactive, correction-only short- or

rapid-acting insulin coverage alone with no basal insulin dosing (74,145). In addition to glycemic goals, the following points need attention:

1. Stricter perioperative glycemic goals are not advised because they may not improve outcomes and are associated with increased hypoglycemia (146).
2. Blood glucose should be monitored at least every 2–4 h while the individual takes nothing by mouth, and insulin should be administered as needed. Insulin is the only recommended glucose-lowering medication in the perioperative period.
3. CGM should not be used alone for glucose monitoring during surgery (147).
4. Metformin and other oral glucose-lowering agents should be held on the day of surgery or procedure. See below for SGLT2 inhibitor and GLP-1 RA use in the perioperative period.
5. Individuals using an insulin pump may continue pump use during surgery if this is consistent with institutional policies and surgical procedures (148). This would require an interprofessional approach and adequate support systems in the hospital. If an insulin pump cannot be used during surgery, an alternative plan (insulin infusion or basal plus correctional insulin) should be initiated before surgery. Compared with usual dosing, a reduction of 25% of basal insulin dose given the evening before surgery is more likely to achieve perioperative blood glucose goals with a lower risk for hypoglycemia (149). Insulin dose reductions also include NPH insulin to one-half of the dose or long-acting basal insulin analogs to 75–80% of the dose or adjustment of insulin pump (if not in automated mode) basal rates based on the type of diabetes and clinical judgment. However, the decision needs to be individualized, as the dose reduction may not be appropriate for some people with type 1 diabetes.

SGLT2 Inhibitors in the Perioperative Period

SGLT2 inhibitors should be held for 3–4 days before elective surgery. Individuals using SGLT2 inhibitors who undergo nonelective surgeries should be closely

monitored for DKA after surgery; the possibility of euglycemic DKA should be considered.

The FDA advises considering temporary discontinuation of SGLT2 inhibitors at least 3 days prior to surgery and ensuring risk factors for ketoacidosis are resolved prior to reinitiating therapy. In a retrospective study of individuals with type 2 diabetes using SGLT2 inhibitors and requiring emergency surgery, the incidence of DKA was 4.9% for individuals using SGLT2 inhibitors and 3.5% for individuals not using SGLT2 inhibitors (150). After adjustment for covariates, the differences between the two groups were not statistically significant. However, because the diagnosis of DKA was based on an ICD-10 code, it is possible that some cases of DKA were missed in the SGLT2 inhibitor group, especially cases of euglycemic DKA. Other studies have shown a higher risk of DKA or anion gap acidosis associated with SGLT2 inhibitor use in the perioperative period (151–153). Therefore, until further prospective studies are conducted, as an abundance of caution, SGLT2 inhibitors should be held for 3–4 days before surgery. The medication may be restarted in the hospital setting for heart failure indication when nutritional intake is resumed, as explained above.

GLP-1 or Dual GIP and GLP-1 RAs and the Perioperative Period

With increasing use of GLP-1–based medications, there are concerns about the safety of these medications in the perioperative period. These medications may be associated with nausea, vomiting, and delayed gastric emptying, and there have been case reports of pulmonary aspiration during general anesthesia and deep sedation (154). Individuals taking a GLP-1 RA medication have higher chances of increased residual gastric content despite fasting for the procedure as needed (155). Based on these reports, FDA added a warning to the label of all GLP-1 RA or dual glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 RA medications about the possibility of pulmonary aspiration during surgeries or procedures requiring general anesthesia or deep sedation (156). However, there is insufficient information on how to mitigate the risk of pulmonary aspiration in this situation. Even if the medication is held, the duration required to withhold the medication is unknown because 1 week of holding a once-weekly

medication is likely insufficient to mitigate the risk (157). In a retrospective study, withholding semaglutide up to 30 days (with an average of 10 days) was still associated with increased residual gastric content (158).

The risk of aspiration pneumonia with increased gastric content in this setting is still unknown. In some retrospective studies, no increase in risk of aspiration pneumonia was found in association with GLP-1 RAs (159,160). The American Society of Anesthesiologists initially recommended holding GLP-1 RAs on the day of the procedure or surgery for daily dose agents and for at least 7 days prior to the procedure or surgery for once-weekly dose agents (161). However, more recently, multiple societies and expert groups have advised a more personalized approach, allowing individuals at low risk for delayed stomach emptying who undergo elective surgery to continue taking their GLP-1 RA medications and suggesting a liquid nutrition protocol for 24 h before the procedure or other measures for those at higher risk for significant gastrointestinal side effects (162–164).

A personalized approach for perioperative management of individuals taking a GLP-1 RA or a dual GIP and GLP-1 RA is recommended. Factors such as the primary indication of these medications (e.g., diabetes or obesity treatment); current glycemic management; dose, duration, and characteristics of the drug; gastrointestinal symptoms; type of surgery or procedure and its urgency; and type of anesthesia should be considered. In addition, a preoperative gastric ultrasound may be considered to quantify gastric contents. In individuals with symptoms suggesting delayed gastric emptying (nausea, vomiting, dyspepsia, or abdominal distension), implementation of full stomach precautions may be considered. A liquid nutrition protocol for 24 h before the procedure may be helpful. If a decision is made to hold the drug and worsening of glycemia is anticipated, an alternative strategy for perioperative glycemic management (e.g., insulin) should be implemented.

Diabetic Ketoacidosis and Hyperglycemic Hyperosmolar State

Recommendations

16.16 Manage diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar state (HHS) by administering intravenous fluids, insulin, and electrolytes

(Fig. 16.1) and by closely monitoring during treatment, ensuring timely and bridged transition to maintenance subcutaneous insulin administration, and identifying and treating the precipitating cause. **A**

16.17 The discharge planning process should include education on the recognition, prevention, and management of DKA and/or HHS for all individuals affected by or at high risk for these events to prevent recurrence and readmission. **B**

DKA and the hyperglycemic hyperosmolar state (HHS) are serious, acute, and life-threatening hyperglycemic emergencies in individuals with diabetes (165) that incur substantial morbidity, mortality, and costs (166). Approximately 1% of all hospitalizations in people with diabetes are for hyperglycemic crises. The diagnostic criteria for DKA and HHS are summarized in **Table 16.1**; all criteria must be met to establish these diagnoses. Importantly, approximately 10% of people experiencing DKA present with euglycemic DKA (plasma glucose <200 mg/dL [<11.1 mmol/L]); therefore, DKA diagnosis requires either the presence of hyperglycemia or prior history of diabetes (165). Euglycemic DKA develops in the presence of low insulin levels and can be associated with a variety of factors including reduced food intake, pregnancy, alcohol use, liver failure, and/or SGLT2 inhibitor therapy (167). Additionally, DKA and HHS often present concurrently (168), though few studies have examined mixed DKA-HHS events.

There has been a concerning rise in the rate of hyperglycemic crises in people with both type 1 diabetes and type 2 diabetes over the past decade (169–171). Recent data suggest hyperglycemic crisis rates of up to 44.5–82.6 per 1,000 person-years among people with type 1 diabetes (169,172) and up to 3.2 per 1,000 person-years among people with type 2 diabetes (169). While DKA mortality decreased in the first decade of the 21st century (166), these improvements have plateaued in the past decade (170,172,173). Most recently available data for inpatient mortality during hospital admission for DKA ranges from 0.2% in type 1 diabetes (174) to 1.0% in type 2 diabetes (166,175). Inpatient mortality among people with type 2 diabetes hospitalized for HHS decreased from

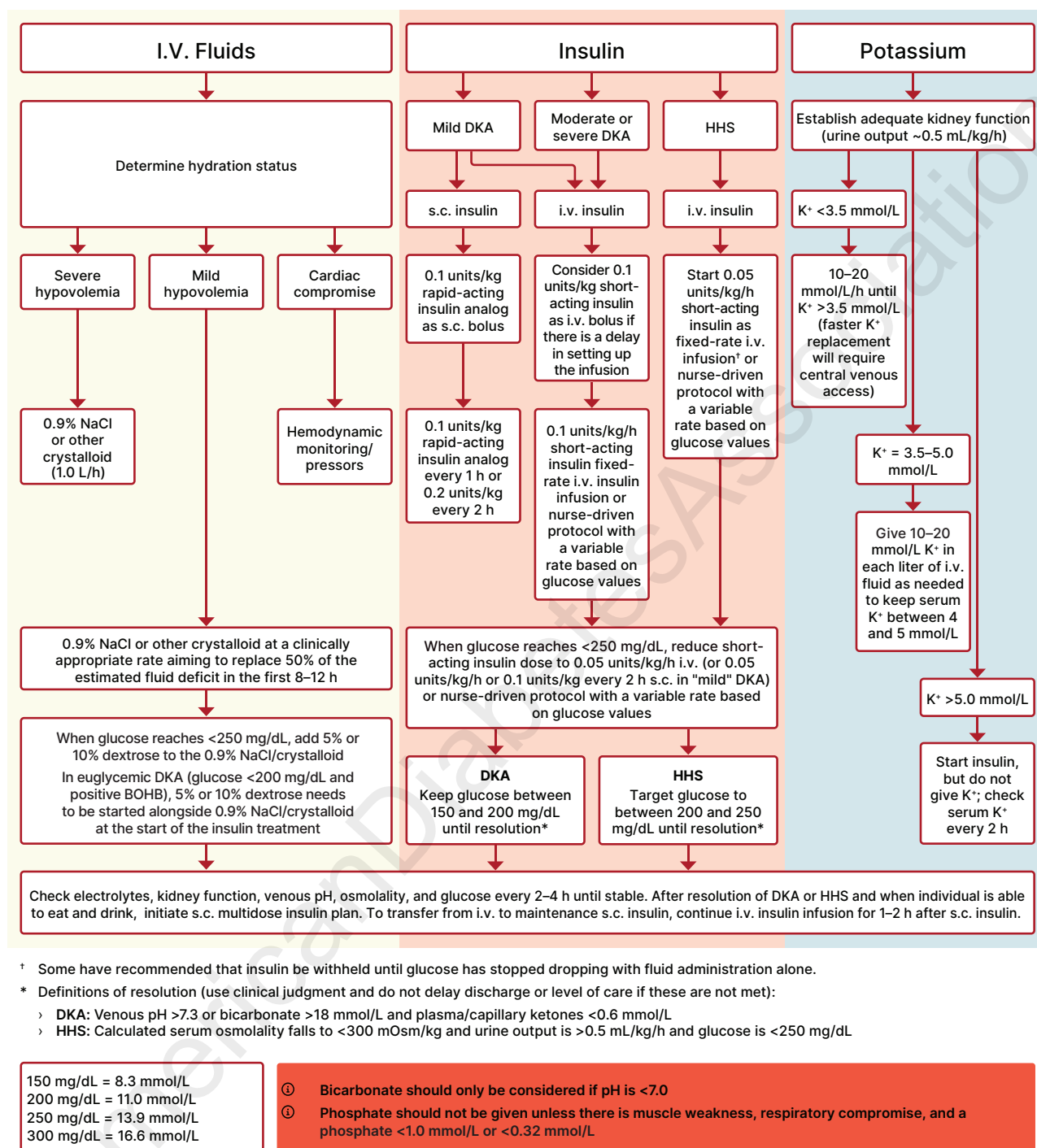


Figure 16.1—Treatment pathways for diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar state (HHS). BOHB, β -hydroxybutyrate. Adapted from Umpierrez et al. (165).

1.44% in 2008 to 0.77% in 2018 (176). The only study to have examined inpatient mortality for mixed DKA-HHS found it to be higher than mortality for HHS or DKA alone (168). Mortality rates reported in low- and middle-income countries are much higher than those in developed countries, potentially because of delayed diagnosis and treatment (165). People

discharged after an episode of DKA have a 1-year age-corrected mortality rate that is 13 times higher than the general population (177).

There is considerable variability in the presentation of DKA and HHS, including euglycemic DKA (defined as plasma glucose levels <200 mg/dL [<11.1 mmol/L]) in the presence of ketosis and metabolic

acidosis), mild to moderate hyperglycemia and acidosis, or severe hyperglycemia, dehydration, and coma; therefore, individualization of treatment based on a careful clinical and laboratory assessment is needed (165). Differences in the clinical presentation of DKS and HHS are shown in **Table 16.2**, though there is a considerable overlap.

Table 16.1—Diagnostic criteria for DKA and HHS

DKA	
Diabetes/hyperglycemia	Glucose ≥ 200 mg/dL (11.1 mmol/L) or prior history of diabetes
Ketosis	β -Hydroxybutyrate concentration ≥ 3.0 mmol/L or urine ketone strip 2+ or greater
Metabolic acidosis	pH < 7.3 and/or bicarbonate concentration < 18 mmol/L
HHS	
Hyperglycemia	Plasma glucose ≥ 600 mg/dL (33.3 mmol/L)
Hyperosmolality	Calculated effective serum osmolality > 300 mOsm/kg (calculated as $[2 \times \text{Na}^+ \text{ (mmol/L)} + \text{glucose (mmol/L)}]$) or total serum osmolality > 320 mOsm/kg $[2 \times \text{Na}^+ \text{ (mmol/L)} + \text{glucose (mmol/L)} + \text{urea (mmol/L)}]$
Absence of significant ketonemia	β -Hydroxybutyrate concentration < 3.0 mmol/L OR urine ketone strip less than 2+
Absence of acidosis	pH ≥ 7.3 and bicarbonate concentration ≥ 15 mmol/L
Adapted from Umpierrez et al. (165).	

Management goals include restoration of circulatory volume and tissue perfusion, resolution of ketoacidosis, and correction of electrolyte imbalance and acidosis. It is also essential to treat and manage any underlying cause of DKA, such as sepsis, myocardial infarction, or stroke. For severe DKA and HHS management, continuous intravenous insulin infusion should be given for correction of hyperglycemia, hyperketonemia, and acid-base disorder following a fixed-rate intravenous insulin infusion (165) or nurse-driven protocol with a variable rate based on glucose values (178). If a nurse-driven insulin infusion protocol is used, the infusion rate should be no less than 1 unit/h to allow for acidosis resolution. Successful transition from intravenous to subcutaneous insulin requires administration of basal insulin 2–4 h before the intravenous insulin is stopped to prevent recurrence of ketoacidosis and rebound hyperglycemia while the subcutaneous insulin action rises (63,179). Studies have reported that

the administration of a low dose of basal insulin analog in addition to intravenous insulin infusion early in the course of treatment may prevent rebound hyperglycemia without increased risk of hypoglycemia (64–66,179). Individuals with mild and uncomplicated DKA can be managed with subcutaneous rapid-acting insulin doses given every 1–2 h (180), and this treatment may be administered in the emergency department or step-down units (181). This approach may be safer and more cost-effective than treatment with intravenous insulin. There is no significant difference in outcomes for intravenous human regular insulin versus subcutaneous rapid-acting analogs when combined with aggressive fluid management for treating mild or moderate DKA (182). Therefore, if subcutaneous insulin administration is used, it is important to provide an adequate fluid replacement, frequent POC blood glucose monitoring, treatment of any concurrent infections, and appropriate follow-up to avoid recurrent DKA.

Several studies have shown that the use of bicarbonate in people with DKA made no difference in the resolution of acidosis or time to discharge, and its use is generally not recommended. For further treatment information and in-depth review, refer to the ADA consensus report “Hyperglycemic Crises in Adults With Diabetes” (165).

TRANSITION FROM THE HOSPITAL TO THE AMBULATORY SETTING

Recommendation

16.18 A structured discharge plan should be tailored to the individual with diabetes. **B** For those not being discharged to home, consider the capabilities of the facility for diabetes management. **E**

A structured discharge plan tailored to the individual may reduce the length of hospital stay and readmission rates and increase satisfaction with the hospital experience (183). Multiple strategies are key, including diabetes self-management education prior to discharge, diabetes medication reconciliation with attention to access, affordability, and scheduled virtual and/or face-to-face follow-up visits after discharge. Discharge planning should begin at admission and be updated as individual needs change (184,185). Individualization and shared decision-making is key when creating a safe and effective discharge plan.

The transition from the acute care setting presents risks for all people with diabetes. Individuals may be discharged to varied settings, including home (with or without visiting nurse services), assisted living, rehabilitation, or skilled nursing facilities. For individuals discharged to home or assisted living, the optimal discharge plan will need to consider diabetes type and severity, effects of the

Table 16.2—Clinical presentation in people with diabetes with DKA and HHS

DKA	HHS
Develops over hours to days	Develops over days to a week
Usually alert	Change in cognitive state common
Polyuria, polydipsia, weight loss, and dehydration	
Nausea, vomiting, and abdominal pain	Often copresenting with other acute illness
Kussmaul respiration	
One-third of hyperglycemic emergencies have a hybrid DKA-HHS presentation	

Adapted from Umpierrez et al. (165).

illness on blood glucose levels, and the individual's circumstances, capabilities, and preferences as well as the facility-related capabilities to manage diabetes (21,186–188). See section 13, "Older Adults," for more information.

An outpatient follow-up visit with primary care, endocrinology, or a diabetes care and education specialist within 1 month of discharge is advised for all individuals experiencing hyperglycemia and/or hypoglycemia in the hospital. If glycemic management medications are changed or glucose management is not optimal at discharge, an earlier appointment (in 1–2 weeks) is preferred, and frequent contact to consider therapy adjustments may be needed to avoid hyperglycemia and hypoglycemia. A discharge algorithm for glycemic medication adjustment, based on admission A1C, diabetes medications before admission, and insulin usage during hospitalization was found useful to guide treatment decisions and significantly improved A1C after discharge (4).

Clear communication with outpatient health care professionals directly or via hospital discharge summaries facilitates safe transitions to outpatient care. Providing information regarding the root cause of hyperglycemia (or the plan for determining the cause), related complications and comorbidities, and recommended treatments can assist outpatient health care professionals as they assume ongoing care.

The Agency for Healthcare Research and Quality recommends that, at a minimum, discharge plans include medication reconciliation, structured discharge communication, and education for the individual with diabetes (189).

Medication Reconciliation

- Home and hospital medications must be cross-checked to ensure the safety of new and old prescriptions, that no chronic medications are stopped, and that there is no duplication of medications under different brand names.
- Prescriptions for new or changed medications should be filled and reviewed with the individual and care partners at or before discharge whenever possible.

Structured Discharge Communication

- Information on medication changes, pending tests and studies, and follow-up needs must be accurately and

promptly communicated to outpatient health care professionals.

- Discharge summaries should be transmitted to the primary care health care professional as soon as possible after discharge.
- Scheduling follow-up appointments prior to discharge with people with diabetes agreeing to the time and place increases the likelihood that they will attend.

Education for the Person With Diabetes

- Identify the health care professionals who will provide follow-up and diabetes care after discharge.
- Assess the level of understanding related to diabetes diagnosis, glucose monitoring, home glucose goals, and when to call a health care professional.
- Provide information on choosing healthy food at home and referral to an outpatient registered dietitian nutritionist or diabetes care and education specialist to guide individualization of the meal plan, if needed.
- Review when and how to take blood glucose-lowering medications, including insulin administration and noninsulin injectables.
- Review sick-day management (21,187).
- Review proper use and disposal of diabetes supplies, e.g., insulin pens, pen needles, syringes, glucose meters, and lancets.

People with diabetes must be provided with appropriate durable medical equipment, medications, supplies (e.g., blood glucose test strips or CGM sensors), prescriptions, and appropriate education at the time of discharge to avoid a potentially dangerous hiatus in care.

PREVENTING ADMISSIONS AND READMISSIONS

For people with diabetes, the hospital readmission rate is between 14% and 20%, which is nearly twice that for people without diabetes (184,190). This may result in increased diabetes distress and has significant financial implications. Of people with diabetes who are hospitalized, 30% have two or more days of hospital stays, and these admissions account for over 50% of hospital costs for diabetes (191). Factors contributing to readmission include male sex, longer duration of prior

hospitalization, number of previous hospitalizations, number and severity of comorbidities, and lower socioeconomic and/or educational status; factors that may reduce readmission rates include scheduled home health visits and timely ambulatory follow-up care (184,190). While there is no standardized protocol to prevent readmissions, several successful strategies have been reported that identify high-risk individuals and offer some possible solutions (184). To prevent readmissions, monitor insulin adjustments for individuals admitted with A1C >9% (>75 mmol/mol) (192) or DKA (193,194) and follow a transitional care model (195). For individuals hospitalized with severe hypoglycemia, impaired awareness of hypoglycemia, or high risk for hypoglycemia (kidney failure, intensive insulin management, frailty, inadequate support system, etc.), consider prescribing glucagon to treat any future severe hypoglycemia events (196). For people with diabetes and chronic kidney disease, collaborative person-centered medical homes may decrease risk-adjusted readmission rates (197). Since recent studies have shown that use of CGM may prevent emergency department visits and hospital admission in people with type 1 and type 2 diabetes, it may be beneficial to initiate CGM just prior to discharge to facilitate follow-up and possibly prevent acute diabetes-related complications and readmission (198).

Age is also an important risk factor in hospitalization and readmission among people with diabetes (refer to section 13, "Older Adults," for detailed information). Successful proactive care transitions from inpatient to outpatient settings are key strategies for preventing readmission and emergency department visits.

THE FUTURE

Inpatient diabetes management is challenging for hospitals, health care professionals, and people with diabetes, as acute illness increases the risk of both hypoglycemia and hyperglycemia. The use of decision support tools and practice advisories in the EHR has facilitated health care professionals following the recommendations in this standard of care. In addition, personal and hospital-owned diabetes devices and dosing algorithms are changing the way we provide care. Future enhancements will likely continue to improve the quality of care

we deliver in hospitals and in transitions from inpatient to outpatient.

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17. Diabetes Advocacy: Standards of Care in Diabetes—2026

American Diabetes Association
Professional Practice Committee for
Diabetes*

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The American Diabetes Association (ADA) “Standards of Care in Diabetes” includes the ADA’s current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. Members of the ADA Professional Practice Committee for Diabetes, an interprofessional expert committee, are responsible for updating the Standards of Care annually, or more frequently as warranted. For a detailed description of ADA standards, statements, and reports, as well as the evidence-grading system for ADA’s clinical practice recommendations and a full list of Professional Practice Committee members, please refer to Introduction and Methodology. Readers who wish to comment on the Standards of Care are invited to do so at professional.diabetes.org/SOC.

Managing the daily health demands of diabetes can be challenging. People living with diabetes should not have to face discrimination due to diabetes. By advocating for the rights of those with diabetes at all levels, the American Diabetes Association (ADA) can help to ensure that they live a healthy and productive life. A strategic goal of the ADA is for more children, adolescents, and adults with diabetes to live free from the burden of discrimination. The ADA is also focused on making sure cost is not a barrier to successful diabetes management.

One tactic for achieving these goals has been to implement the ADA “Standards of Care in Diabetes” through advocacy-oriented statements. The ADA publishes evidence-based, peer-reviewed statements on topics such as diabetes and employment, diabetes and driving, insulin access and affordability, and diabetes management in certain settings such as schools, childcare programs, and detention facilities. In addition to the ADA’s clinical documents, these advocacy statements are important tools in educating schools, employers, licensing agencies, policymakers, and others about the intersection of diabetes management and the law and for providing scientifically supported policy recommendations.

ADVOCACY STATEMENTS

The following is a partial list of advocacy statements ordered by publication date, with the most recent statement appearing first. A comprehensive list of advocacy statements is available at professional.diabetes.org/content/key-statements-and-reports.

Diabetes Care in the School Setting

A sizable portion of a child’s day is spent in school, so close communication with and training and cooperation of school personnel are essential to optimize diabetes management, safety, and access to all school-sponsored opportunities. Additionally, the statement further details optimal use of technologies, management of diabetes, behavioral health considerations, and guidance for diabetes care in special situations (e.g., emergency situations or clinical trial participation). Refer to the published ADA

*A complete list of members of the American Diabetes Association Professional Practice Committee for Diabetes can be found at <https://doi.org/10.2337/dc26-SINT>.

Duality of interest information for each contributor is available at <https://doi.org/10.2337/dc26-SDIS>.

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statement for diabetes management information for students with diabetes in elementary and secondary school settings (1).

Diabetes and Driving

People with diabetes who wish to operate on-road motor vehicles are subject to various licensing requirements applied by both state and federal jurisdictions. For an overview of existing licensing rules for people with diabetes, factors that impact driving for this population, diabetes technology use, and general guidelines for assessing driver fitness and determining appropriate licensing restrictions, refer to the published ADA statement (2).

Diabetes Management in Detention Facilities

People with diabetes who are in detention facilities deserve equitable care that meets national standards. As many facilities differ and have unique challenges, written policies and procedures are essential to create a solid foundation and infrastructure for diabetes management and the training of medical and security staff. Policies should address considerations such as security needs, transfers, access to medical personnel, needed supplies and equipment, and empowering diabetes self-management. For a comprehensive

discussion on these considerations, refer to the published ADA statement (3).

Care of Young Children With Diabetes in the Childcare and Community Setting

Very young children (aged <5 years) with diabetes have legal protections and can be safely cared for by childcare professionals with appropriate training, access to resources, and a communication system with parents or guardians and the child's diabetes health care professional. Refer to the published ADA advocacy statement for information on young children aged <5 years in settings such as childcare centers, preschools, camps, and other programs (4).

Insulin Access and Affordability

The ADA's Insulin Access and Affordability Working Group compiled public information and convened a series of meetings with stakeholders throughout the insulin supply chain to learn how each entity affects the cost of insulin for the consumer. Their conclusions and recommendations are published in an ADA statement (5).

Diabetes and Employment

Any person with diabetes, whether insulin treated or noninsulin treated, should be eligible for any employment for which they are otherwise qualified. Employment decisions should never

be based on generalizations or stereotypes regarding the effects of diabetes. For a general set of guidelines for evaluating individuals with diabetes for employment, including how an assessment should be performed and what changes (accommodations) in the workplace may be needed for an individual with diabetes, refer to the published ADA statement (6).

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Disclosures: Standards of Care in Diabetes—2026

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Committee members disclosed the following financial or other dualities of interest covering the period 12 months before December 2025

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