Prostatic Urethral Lift (UroLift™ System) Clinical Coverage Criteria

Description

Prostatic urethral lift is a procedure for the treatment of lower urinary tract symptoms attributed to benign prostatic hyperplasia (LUTS/BPH). The prostatic urethral lift procedure involves the insertion of one or more permanent implants into the prostate with the goal of retracting enlarged prostatic tissue, widening the urethra and enhancing urinary flow.

Policy

This Policy applies to the following Fallon Health products:

☒ Medicare Advantage (Fallon Medicare Plus, Fallon Medicare Plus Central)

☒ MassHealth ACO

☒ NaviCare HMO SNP, NaviCare SCO

☒ PACE (Summit Eldercare PACE, Fallon Health Weinberg PACE)

☒ Community Care

Prostatic urethral lift (PUL) requires prior authorization.

Medicare Advantage (Fallon Medicare Plus, Fallon Medicare Plus Central)
Fallon Health complies with CMS's national coverage determinations (NCDs), local coverage determinations (LCDs) of Medicare Contractors with jurisdiction for claims in the Plan's service area, and applicable Medicare statutes and regulations when making medical necessity determinations for Medicare Advantage members. When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, Fallon Health may create internal coverage criteria under specific circumstances described at § 422.101(b)(6)(i) and (ii).

Medicare statutes and regulations do not have coverage criteria for prostatic urethral lift. Medicare does not have an NCD for prostatic urethral lift. National Government Services, Inc. is the Part A/B Medicare Administrative Contractor (MAC) with jurisdiction over Part A and B services in Fallon Health's service area. National Government Services, Inc. does not have an *active* LCD for prostatic urethral lift. National Government Services, Inc. has a *retired* LCD for Prostatic Urethral Lift (PUL) (L36601). This LCD was retired on 02/28/2018. Per LCD L36601, *"All local policy rules, requirements, and limitations within this LCD will no longer be applied on a prepayment basis, but as with any billed service, claims may be subject to post-payment review* (MCD search 10/22/2024)."

Coverage criteria for prostatic urethral lift are not fully established by Medicare, therefore, the Plan's clinical coverage criteria are applicable.

MassHealth ACO
Fallon Health follows Medical Necessity Guidelines published by MassHealth when making medical necessity determinations for MassHealth members. In the absence of Medical Necessity Guidelines published by MassHealth, Fallon Health may create clinical coverage criteria in accordance with the definition of Medical Necessity in 130 CMR 450.204.

MassHealth does not have Guidelines for Medical Necessity Determination for prostatic urethral lift (MassHealth website search 10/22/2024). Fallon Health's Clinical Coverage Criteria will be used to determine medical necessity for prostatic urethral lift for MassHealth ACO members.

NaviCare HMO SNP, NaviCare SCO
For plan members enrolled in NaviCare, Fallon Health first follow's CMS's national coverage determinations (NCDs), local coverage determinations (LCDs) of Medicare Contractors with jurisdiction for claims in the Plan's service area, and applicable Medicare statutes and regulations when making medical necessity determinations.

When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, or if the NaviCare member does not meet coverage criteria in applicable Medicare statutes, regulations, NCDs or LCDs, Fallon Health then follows Medical Necessity Guidelines published by MassHealth when making necessity determinations for NaviCare members.

PACE (Summit Eldercare PACE, Fallon Health Weinberg PACE)
Each PACE plan member is assigned to an Interdisciplinary Team. PACE provides participants with all the care and services covered by Medicare and Medicaid, as authorized by the interdisciplinary team, as well as additional medically necessary care and services not covered by Medicare and Medicaid. With the exception of emergency care and out-of-area urgently needed care, all care and services provided to PACE plan members must be authorized by the interdisciplinary team.

Fallon Health Clinical Coverage Criteria

These Fallon Health Clinical Coverage Criteria apply to all products.

Prostatic urethral lift (UroLift™ System) is considered medically necessary as an alternative to TURP for the treatment of LUTS attributed to BPH when all of the following coverage criteria are met:

1. AUA symptom index (AUA-SI)/International Prostate Symptom Score (IPSS) ≥ 13; and
2. Maximum urinary flow rate (Qmax) ≤ 15 ml/sec for a voided volume greater than 125 cc; and
3. Prostate volume is ≥ 30 cc and ≤ 80 cc, as determined by ultrasonography, CT or MRI performed within the past 12 months; and
4. Prostate anatomy is without obstructive median lobe as determined by ultrasonography, CT or MRI performed within the past 12 months; and
5. Prostate-specific antigen < 10 ng/l, unless prostate biopsy is negative for cancer, and
6. LUTS attributed to BPH are refractory to medical therapy (defined as a trial of at least 4 weeks with an alpha blocker or PDE5 and/or at least a 6-month trial with a 5-ARI), or the plan member has significant side effects or contraindications to medical therapy, and
7. None of the following apply:
    a. Active urinary tract infection at time of treatment, or
    b. History of prostatitis requiring antibiotic treatment in the past 12 months, or
    c. History of cystolithiasis in the past 3 months, or
    d. Allergy to nickel.

UroLift™System implants are MRI-conditional but can be safely scanned at field strengths of up to 3 Tesla, even immediately after the procedure.

The number of implants will vary by patient due to the unique characteristics of the prostate and prostatic urethra; clinical data supports an average of 4-6 implants per patient.

Exclusions

- Any use of prostatic urethral lift (UroLift™ System) that does not meet Fallon Health Clinical Coverage Criteria is considered experimental/investigational and not medically necessary.

Summary of Evidence

Background

Benign prostatic hyperplasia (BPH) is nearly ubiquitous in the aging male with increases in prevalence starting at age 40-45 years, reaching 60% by age 60, and 80% by age 80 (Lerner et al., 2021a). While BPH, or histological hyperplasia, in and of itself does not require treatment and is not the target of therapeutic intervention, it can lead to an enlargement of the prostate called benign prostatic enlargement (BPE). The onset of the enlargement is highly variable as is the growth rate, and not all men with BPH will develop any evidence of BPE. The prostate gland may eventually cause obstruction at the level of the bladder neck, which in turn is termed benign prostatic obstruction (BPO), assuming a non-cancerous anatomy. It is important to realize that not all men with BPE will develop obstruction or BPO, just as not all men with BPH will have BPE (AUA, 2021).

In assessing the burden of disease, the Urologic Diseases in America BPH Project examined the prevalence of moderate-to-severe LUTS reported in U.S. population-based studies that used the definition of an AUA Symptom Index (AUA-SI) score of ≥ 7. Results from the Olmsted County Study (OCS) showed a progressive increase in the prevalence of moderate-to-severe LUTS, rising to nearly 50% by the eighth decade of life. The odds of developing moderate-to-severe symptoms increased progressively after age 50 years and were 3.5- and 2.4-fold greater in men with a prostate volume >50 mL and in those with a flow rate of <10 mL/sec, respectively (Lerner et al., 2021a).

BPH is not a life-threatening condition, however, the impact of BPH on quality of life (QoL) can be significant and should not be underestimated. When the effect of BPH-associated LUTS on QoL was studied in a number of community-based populations, the most important motivations for seeking treatment were the severity and the degree of bother associated with the symptoms (AUA, 2021). The primary goal of treatment is to alleviate bothersome LUTS attributed to BPH (LUTS/BPH). In the initial evaluation of patients presenting with bothersome LUTS possibly attributed to BPH, clinicians should obtain a medical history, conduct a physical examination, administer the International Prostate Symptom Score (IPSS), and perform a urinalysis (Lerner 2021a).

The most prevalent and generally first line approach is behavioral and lifestyle modifications (e.g., fluid restriction, avoidance of substances with diuretic properties) followed by medical therapy, including alpha-adrenergic antagonists (alpha blockers), 5-alpha reductase inhibitors (5-ARIs), phosphodiesterase 5 selective inhibitors (PDE5Is), anticholinergics, and beta-3 agonists - which may be utilized alone, or in combination to take advantage of their different mechanisms of action (Lerner et al., 2021a). Although effective treatments for LUTS/BPH are available, this condition often occurs in the context of common, age-related comorbidities such as cardiovascular disease, hypertension, and erectile dysfunction. When selecting an appropriate course of therapy, these side effects and any impact they may have on existing comorbid conditions must be considered.

An initial trial of medical management over 4 weeks with an alpha blocker or PDE5, and over 6-12 months with a 5-ARI is reasonable in men with bothersome LUTS (AUA, 2021). Patients with bothersome LUTS/BPH who elect initial medical management and do not have symptom improvement and/or experience intolerable side effects should undergo further evaluation and consideration of change in medical management or surgical intervention (AUA, 2021).

Despite the prevalent use of medical therapy for the treatment of LUTS/BPH, there exist clinical scenarios in which conservative management, including behavioral and lifestyle changes, or medical therapy are either inadequate or inappropriate. Indications for surgical procedures in these scenarios include a desire by the patient to avoid taking a daily medication, failure of medical therapy to sufficiently ameliorate bothersome LUTS, intolerable pharmaceutical side effects, and/or the following conditions resulting from BPH and for which medical therapy is insufficient: chronic renal insufficiency (defined as GFR < 60 for at least 3 months) secondary to

BPH, refractory urinary retention secondary to BPH, recurrent urinary tract infections (UTIs), recurrent bladder stones or gross hematuria due to BPH (Lerner et al., 2021b).

Prior to surgical intervention for LUTS/BPH, clinicians should consider assessment of prostate size and shape by transrectal or abdominal ultrasonography, or by cross-sectional imaging (i.e., MRI or CT) if such studies are available prior to intervention. Many patients may have had such imaging as part of the workup for PSA elevation and/or prostate biopsy, or non-urologic conditions that include evaluation of pelvic anatomy; therefore, any such imaging obtained in the recent past preceding the planned surgical intervention may be utilized for size and shape assessment to verify suitability for the therapeutic alternatives under consideration. Imaging obtained within 12 months is preferred; however, given that prostate growth rates are 1.6% per year on average, older imaging can likely give a reasonably accurate estimate of current size if that is all that is available (AUA, 2021).

Surgical treatment of LUTS/BPH has three general types: 1. Transurethral resection; 2. Simple prostatectomy; and 3. Minimally invasive procedures.

Transurethral resection of the prostate or TURP is a procedure where the prostate is resected from an endoscopic approach. TURP was the first successful, minimally invasive surgical procedure of the modern era. To this day, TURP remains the criterion standard therapy for obstructive prostatic hypertrophy and is both the surgical treatment of choice and the standard of care when other methods fail. TURP is performed using two techniques: monopolar TURP (M-TURP) and bipolar TURP (B-TURP).

In patients for whom the physical size of the prostate cannot be addressed via a safe or efficacious transurethral approach, simple prostatectomy may be considered using an open, laparoscopic or robotic-assisted approach.

Minimally invasive procedures have been developed with the goal of providing a safe and effective alternative to TURP. These include but are not limited to:

- Transurethral waterjet ablation, (also referred to as robotic waterjet ablation or Aquablation)
- Prostatic Urethral Lift (PUL)
- Water Vapor Thermal Therapy (Rezum System)
- Holmium laser enucleation of the prostate (HoLEP)

Prostatic Urethral Lift (PUL)
UroLift™UroLift™UroLift™At this time, only one implantable transprostatic tissue retractor system (Product Code PEW) has received FDA 510(K) clearance (UroLift™ System, NeoTract, Inc., Pleasanton, CA). Subsequent clearances have been made based on substantial equivalence to the original device, including UroLift™ 2 System, UroLift™ Advanced Tissue Control (ATC) System, and the UroLift™ 2 Advanced Tissue Control (ATC) System.

The UroLift™ System (Model UL400) (NeoTract, Inc., Pleasanton, CA), received FDA 510(k) clearance on September 13, 2013 (K130551). The UroLift™ System was originally approved for the treatment of symptoms due to urinary outflow obstruction secondary to BPH in men 50 years of age or older. Contraindications to the use of this PUL device included prostate volumes > 80 cc and obstructive or protruding medial lobe of the prostate.

The UroLift™ 2 System (Model UL500) received 510(k) clearance on March 15, 2016 (K153584). The UroLift™ 2 System is substantially similar to the predicate device, UrolLift System UL400. Both generations (UL400 and UL500) use the same UroLift™ Implant. The only differences are in the delivery device. The UroLift™ delivery device is designed to access the prostatic urethra and deliver the UroLift™ Implant through a lateral lobe of the prostate.

On December 28, 2017 (K173087), the FDA expanded the indications for the UroLift™ System (UL400) and the UroLift™ 2 System (UL500) to include the treatment of symptoms due to urinary outflow obstruction secondary to BPH, including lateral and median lobe hyperplasia, in men 45 years of age or older.

NCT02625545:
Median lobe clinical study: NeoTract conducted a prospective, multicenter, non-blinded, single arm study to demonstrate the safety and effectiveness of the UroLift™ System for subjects with symptomatic benign prostatic hyperplasia with an enlarged median lobe.

Study Title: Median Lobe Prostatic UroLift™ System Procedure (MedLift)
Study Objectives: Evaluate the safety and effectiveness of the UroLift™® System when used in symptomatic benign prostatic hyperplasia (BPH) subjects with an enlarged median lobe.
Study Design: Prospective, multicenter, non-blinded, single arm (non-randomized) study.
Sample Size: 45 subjects were enrolled. Subject Population: Males 50 years or older diagnosed with symptomatic benign prostatic hyperplasia (BPH).
Follow-up: 1, 3, 6, and 12 months. For this submission, the report primarily presents results through 6 months of follow-up. A partial subset of subjects who have returned for the 12 month follow-up are included where noted (18 of 45 at time of submission).
Effectiveness Endpoint: At 6 months, the 95% lower confidence limit of the mean percent improvement in subject's International Prostatic Symptom Score (IPSS) over baseline for the UroLift™ System must be ≥ 25%. Results: At 6 months, the 95% lower confidence limit of the mean percent improvement in subject's International Prostatic Symptom Score (IPSS) over baseline for the UroLift™ System was 50.8% (substantially above the goal of ≥ 25%). The mean percent change at 6 months was 57.7%.

Safety Endpoint: The composite observed rate of post-procedure device related serious complications ≤15% at 3 months. Composite device related serious complications for this endpoint are 1) de Novo (new) severe urinary retention lasting more than 21 consecutive days post procedure, 2) device related formation of fistula between the rectum and urethra, 3) perforation of the rectum or GI tract, 4) damage to ureter or ureteral orifices, 5) damage to the trigone requiring surgical repair or 6) de novo, sustained erectile dysfunction. A Clinical Events Committee (CEC) will adjudicate adverse events and relevant subject questionnaires to evaluate against safety endpoint. Results: The CEC adjudicated the adverse events and relevant subject questionnaires to evaluate against the safety endpoint. The safety endpoint was achieved with 0% (5.7% CI upper limit) meeting criteria within the composite. In addition, from 3 to 6 months, there were no reported events that would meet the endpoint criteria.

The clinical study data demonstrates that treatment of the enlarged median lobe with the UroLift™ System is as safe and effective as treatment of the lateral lobe.

Reduction of Age in Indication:
The FDA Guidance for Industry and Food and Drug Administration Staff entitled "Guidance for the Non-Clinical and Clinical Investigation of Devices Used for the Treatment of Benign Prostatic Hyperplasia (BPH)" was issued on August 17, 2010 and recommended that the patient selection protocol criteria for enrollment include men over 50 "because BPH is generally K173087 Page 3 of 5 NeoTract, Inc. 29 September 2017 Traditional 510(k) UroLift™ System Confidential Page 9 of 52 confined to older men." Approximately one month later in September 2010, the AUA released the 2010 update to the AUA Guideline on the Management of Benign Prostatic Hyperplasia. In this guideline, the index patient was updated to be a male > 45 years of age who is consulting a qualified healthcare provider for his lower urinary tract symptoms (LUTS). The AUA panel lowered the age for inclusion in this Guideline from age 50 to age 45, as this lower age group can commonly present with LUTS. Literature data demonstrates that the prevalence of BPH in ages 40-49 are not dramatically different compared to ages 50-59. The estimated difference in prevalence of histopathologic BPH is < 10% between age 45 and 50. In addition, the estimated difference in volume is < 2 g for prostates in men age 45 and 50. Literature data also

demonstrates similar incidences of lower urinary tract symptoms for men aged 40-49 compared to those aged 50-59 (8.6% and 9.5%, respectively). Based on multiple studies, the difference between the population of men age 45 and age 50 in terms of histopathology, volume, and symptomatology appears minimal for BPH. Treatment of BPH earlier at age 45 is not expected to create new or unexpected risks for the patient. As such, the reduction in age from 50 to 45 years old is substantially equivalent to the predicate devices (K133281 and K172359) based on the literature data.

On December 20, 2019, the FDA approved a modification to the contraindications for the UroLift™ System (K193269). The modification is to change one contraindication from "The UroLift™ System is contraindicated for men with Prostate volume of >80 cc" to "The UroLift™ System is contraindicated for men with Prostate volume of >100 cc." This is based on a clinical literature review. The indications for use and remaining contraindications do not change as a result of this submission.

The UroLift™ System is indicated for the treatment of symptoms due to urinary outflow obstruction secondary to benign prostatic hyperplasia (BPH), including lateral and median lobe hyperplasia, in men 45 years of age or older.

Contraindications
The UroLift™ System should not be used if the patient has:

- Prostate volume of >100 cc
- A urinary tract infection
- Urethra conditions that may prevent insertion of delivery system into bladder
- Urinary incontinence due to incompetent sphincter
- Current gross hematuria

On July 31, 2020, the FDA approved a modification to the contraindications for to increase the prostate size limitation from 80cc to 100cc. for the UroLift™ 2 System (K201837).

The UroLift™ 2 System is indicated for the treatment of symptoms due to urinary outflow obstruction secondary to benign prostatic hyperplasia (BPH), including lateral and median lobe hyperplasia, in men 45 years of age or older.

Contraindications
The UroLift™ 2 System should not be used if the patient has:

- Prostate volume of >100 cc
- A urinary tract infection
- Urethra conditions that may prevent insertion of delivery system into bladder
- Urinary incontinence due to incompetent sphincter
- Current gross hematuria

On June 5, 2020, the UroLift™ Advanced Tissue Control (ATC) System received FDA-clearance (K200441). This device is a modification of the UroLift™ UL400 System (last cleared in K193269). The primary difference is the addition of a wing component on the distal tip of the UL400 which provides a larger footprint. This design feature is intended to provide better mobilization of tissue when performing the UroLift™ System procedure. The indications and contraindications are the same as the UroLift™ System (UL400).

The UroLift™ System is indicated for the treatment of symptoms due to urinary outflow obstruction secondary to benign prostatic hyperplasia (BPH), including lateral and median lobe hyperplasia, in men 45 years of age or older.

CONTRAINDICATIONS
The UroLift™ System should not be used if the patient has:

- Prostate volume of >100 cc
- A urinary tract infection
- Urethra conditions that may prevent insertion of delivery system into bladder
- Urinary incontinence due to incompetent sphincter
- Current gross hematuria

On September 22, 2023, the UroLift™ 2 ATC Advanced Tissue Control System received FDA-clearance (K232558). This device is a modification of the UroLift™ UL500 System (last cleared in K201837). The primary difference is the addition of a wing component on the distal tip of the UL500 which provides a larger footprint. This design feature is intended to provide better mobilization of tissue when performing the UroLift™ System procedure. The indications and contraindications are the same as the UroLift™ System (UL500).

The UroLift™ 2 ATC Advanced Tissue Control System is indicated for the treatment of symptoms due to urinary outflow obstruction secondary to benign prostatic hyperplasia (BPH), including lateral and median lobe hyperplasia, in men 45 years of age or older. 03.7

CONTRAINDICATIONS
The UroLift™ 2 ATC Advanced Tissue Control System should not be used if the patient has:
- Prostate volume of >100 cc
- A urinary tract infection
- Urethra conditions that may prevent insertion of delivery system into bladder • Urinary incontinence due to incompetent sphincter
- Current gross hematuria

Randomized controlled trials
PUL versus sham
Prostatic urethral lift was compared to sham in a multicenter randomized controlled trial (*The Safety and Effectiveness of UroLift™: LIFT Pivotal Study (LIFT)*, Clinicaltrials.gov NCT01294150). Subjects and questionnaire administrators were blinded through the 3-month primary efficacy endpoint. One-year results were reported by Roehrborn et al., 2013. Eligible subjects were at least 50 years old, had no prior surgical treatment for BPH, and were required to undergo washouts of 2 weeks for alpha-blocker, 3 months for 5 alpha-reductase inhibitor and 3 days for anticoagulants. *Admission to the study required AUASI 13 or greater, Qmax 12 ml per second or less with a 125 ml voided volume and a 30 to 80 cc prostate. Subjects were excluded for median lobe obstruction, retention, PVR greater than 250 ml, active infection, prostate specific antigen greater than 10 ng/ml (unless negative biopsy), cystolithiasis within 3 months and bacterial prostatitis within 1 year.* The two hundred and six (206) subjects were randomized 2:1 to active treatment with the PUL device (n=140) or a sham procedure (n=66). *Mean age was 67 ± 8.6 years in the PUL group. Mean prostate volume (cc) in the PUL group was 44.5 ± 12.4.* During the PUL procedure, UroLift™ implants are permanently implanted to retract obstructing lateral lobes and expand the urethral lumen. An average of 4.9 implants (range 2-11) was delivered with 4 implants being the most common number (42%) and 85% receiving 6 implants or less. Thirty-two percent of PUL subjects required catheterization for failed voiding trial resulting in mean catheter duration of 0.9 days for the total cohort. The rigid cystoscopy control (sham) procedure was performed in a manner that simulated active PUL treatment. The primary efficacy end point was to demonstrate, on an intent-to-treat (ITT) basis, that the reduction in IPSS at 3 months after the PUL procedure was at least 25% greater than that of sham. All subjects in the PUL group were followed through one year to evaluate durability of effect. Secondary efficacy endpoints included Qmax, QoL, BPH Impact Index (BPHII), and assessments of sexual function (International Index of Erectile Function, IIEF, and Male Sexual Health Questionnaire for Ejaculatory Dysfunction, MSHQ-EjD). The protocol calls for follow-up visits on an annual basis to 5 years. All subjects were unblinded after the 3-month end point and control patients were offered the PUL or other intervention if symptoms persisted.

For the ITT primary endpoint, Roehrborn et al., 2013, reported an 88% greater reduction in IPSS after PUL compared to sham at 3 months (IPSS improvement: PUL 11.1 ± 7.7, sham 5.9 ± 7.7. p=0.003). Improvements in QoL and Qmax were also significantly greater for PUL compared to sham in the 3-month ITT analysis (Qmax improvement: PUL 4.28 ± 5.16, sham 1.98 ± 4.88, p = 0.005); QOL improvement: PUL 2.2 ± 1.8, sham 1.0 ± 1.5, p < 0.001). The results of this study in conjunction with comparative data from other published studies (McNicholas et al, 2013, Chin et al, 2012, Sønksen et al., 2015) indicate a reproducible therapeutic response after PUL. One hundred twenty-three (123) patients were included in the per protocol analysis at 12 months. Qmax increased significantly from 8.1 to 12.4 mL/s compared to baseline at three months and this result was confirmed at twelve months. Qmax improvement (4 ml per second) was both clinically and statistically significant (p<0.0001). A relevant benefit with regard to PVR was not demonstrated compared to baseline or sham. The authors commented on the "*formidable sham effect observed in this study*," suggesting it is likely due to a combination of placebo, dilation and regression.

Two serious adverse events were adjudicated as related to the procedure. The first entailed an overnight stay for clot retention coincident with reinitiating warfarin therapy, and the second was a subject who required removal of a bladder stone at 12 months that had formed from confirmed bladder gravel at baseline and was not associated with an implant. One subject died of unrelated causes as adjudicated by clinical events committee and data monitoring committee. Less serious adverse events (postoperative dysuria, hematuria, pain/discomfort and urgency) were typically mild to moderate and resolved within 2 weeks. There was no incidence of de novo sustained ejaculatory or erectile dysfunction.

Outcome Measure	**PUL n=140 mean (SD)**	**Control n=66 mean (SD)**	**P value**
AUASI Score at baseline	22.2 (5.4)	24.4 (5.8)	
AUASI at 3 months	11.2 (7.65)	18.5 (8.59)	
Change	-11.1 (7.67)	-5.9 (7.66)	p=0.003
Qmax baseline	8.02 (2.43)	7.93 (2.41)	
Qmax at 3 months	12.29 (5.40)	9.91 (4.29)	
Change	4.28 (5.16)	1.98 (4.88)	p=0.005
QOL Score at baseline	4.6 (1.1)	4.7 (1.1)	
QOL at 3 months	2.4 (1.7)	3.6 (1.6)	
Change	-2.2 (1.8)	-1.0 (1.5)	p<0.001
BPHII Score at baseline	6.9 (2.8)	7.0 (3.0)	
BPHII at 3 months	3.0 (3.1)	4.9 (3.2)	
Change	-3.9 (3.2)	-2.1 (3.3)	p<0.001

Adapted from Roehrborn et al., 2013

Additional publications of the LIFT study reported 3-year and 5-year results (Roehrborn et al., 2015 and Roehrborn et al., 2017, respectively).

Roehrborn et al., 2015, reported the 3-year results of the LIFT Study (Clinicaltrials.gov: NCT01294150). LUTS severity (IPSS), quality of life, Qmax, sexual function, and adverse events were assessed throughout follow-up. Over 3 years follow-up of 140 PUL subjects, 129 (92.1%) were available and 11 subjects were lost to follow-up. Of the 129 available subjects, 93 were

included in the effectiveness analysis. Of the 36 subjects who were not included in the 3 year analysis, 3 had missing data, 3 were censored for protocol deviations, 13 were censored for alpha-blocker or 5-ARI use at time of follow-up, and two were censored for unrelated prostate procedures. The remaining 15 subjects (10.7% of the originally enrolled 140) underwent surgical retreatment for LUTS (6 received additional PUL implants and 9 underwent TURP or laser vaporization. Average improvements from baseline (% change) through 3 years were significant for total IPSS (41.1% ± 34.5%, p <0.0001), quality of life (48.8% ± 37.4%, p<0.0001), BPHII (53.2% ± 3.3%, p < 0.0001), Qmax (53.1% ± 85.1, p<0.0001), and individual IPSS symptoms. IPSS subgroup analysis showed that both voiding and storage function improved significantly by 4 weeks after PUL and remain so to 3 years (p,0.0001). Symptomatic improvement was independent of prostate size. There were no de novo, sustained ejaculatory or erectile dysfunction events and all sexual function assessments showed average stability or improvement after PUL. Sexual function was preserved with no reported adverse events for PUL participants of de novo sustained erectile or ejaculatory dysfunction. Participants who underwent PUL procedure had average erectile function as measured by SHIM score above baseline at all follow-up time points. In addition, ejaculatory function as measured by average MSHQ-EjD was improved through follow-up (p=0.129 at 3 years). Bother associated with ejaculatory function was also improved significantly at every follow-up interval (p=<=0.0002). The cumulative rate of surgical reintervention for failure to cure by 3 years after PUL was 10.7%. This rate is similar to rates reported after TURP (2.3%-4.3% at 1 year, 5.8%-9.7% at 5 years) and laser vaporization (1.7%-5.3% at 1 year, 6.7% at 2 years, 6.8%-34% at 5 years). Other minimally invasive therapies such as TUMT and TUNA are known to have significantly higher retreatment rates than TURP.

Roehrborn et al., 2017 reported the 5-year results of the LIFT study (Clinicaltrials.gov: NCT01294150). Participants who deviated from the study protocol, underwent additional surgical treatment or were taking BPH medication were excluded from the per protocol analysis. Thirty-six (36) subjects were not available (18 lost to follow-up, 9 died of unrelated causes, 5 exited for treatment of an unrelated cancer and 4 exited after undergoing TURP). The rate of surgical reintervention for failure to cure was 13.6% after 5 years with 6 (4.3%) receiving additional PUL implants and 13 (9.3%) undergoing TURP or laser ablation (including 4 exited subjects). Of the 19 retreated subjects, 18 had severe baseline LUTS (IPSS ≥ 20) and one subject's baseline IPSS was 19. At 5 years, 15 (10.7%) subjects were taking an alpha blocker or 5-alpha reductase inhibitor. The authors reported efficacy results using both per protocol analysis and ITT analysis, to show that loss to follow-up did not affect study data. For the ITT analysis, the last observation carried forward (LOCF) method was used. Of the 140 subjects originally randomized, data were available for 72 (51.4%). No statistical difference in results was seen at 5 years between per protocol and ITT analyses. For the ITT analysis, IPSS score at 5 years compared to baseline was -7.85 (-35%, p<0.0001). QOL, Qmax and BPHII also improved significantly: -2.08 (-44.4%), 3.21 (49.9%), and -3.41 (-46.8%), respectively. For the per protocol analysis, five-year data demonstrated a decrease in mean IPSS scores over time; however, IPSS remained significantly improved from baseline (mean improvement in IPSS per protocol at 3, 12, 24, 36, 60 months compared to baseline: -11.14 (-49.7%), -10.61 (-47.4%), -9.13 (-41.4%), -8.83 (-41.1%), -7.56 (-35.9%), respectively). QOL, Qmax and BPHII also improved significantly: -2.32 (-50.3%), 3.48 (49.3%), and -3.48 (-51.8%), respectively. Adverse events were mild to moderate and transient. Sexual function was stable over 5 years with no subjects reporting an adverse event of de novo sustained ejaculatory or erectile dysfunction. In addition to sustained efficacy, durability can be assessed by the rate of surgical reintervention for recurrent BPH symptoms. The cumulative surgical reintervention rate for PUL subjects in the LIFT study was 10.7% after 3 years and 13.6% after 5 years. By way of comparison the surgical reintervention rate for TURP at 5 years is 5.8% - 7.0%. Use of BPH medication after PUL was 3.6% at 1 year and 10.7% at 5 years post procedure.

	At 5 years Intent-to-treat (n=140) Change from baseline, percent change from baseline, p value	**At 5 years Per Protocol (n=72) Change from baseline, percent change from baseline, p value**
IPSS	-7.85, -35.0% p<0.0001	-7.56, -35.9 % p<0.0001

QOL	-2.08, -44.4% p<0.0001	-2.32, -50.3% p<0.0001
Qmax	3.21, 49.9% p<0.0001	3.48, 44.3% p<0.0001
BPHII	-3.41, -46.8% p<0.0001	-3.48, -51.8% p<0.0001

Adapted from Roehrborn et al., 2017

PUL versus TURP

Prostatic urethral lift was compared to TURP in a randomized nonblinded controlled trial at ten European centers [Comparison of the UroLift™ System to TURP for Benign Prostatic Hyperplasia (BPH6), ClinicalTrials.gov NCT01533038]. One-year results were reported by Sønksen et al., 2015. Eligible participants were at least 50 years, candidates for TURP, and enrolled by investigators if they met the study inclusion criteria (IPSS > 12, Qmax ≤ 15 ml/s for 125 ml voided volume, post void residual volume < 350 ml, prostate volume ≤ 60 cm^3 on ultrasound). Exclusion criteria included active urinary tract infection at time of treatment, bacterial prostatitis within 1 year of index procedure, cystolithiasis within 3 months of the index procedure, obstructive medial lobe as assessed by ultrasound and cystoscopy, current urinary retention. Eighty patients were enrolled (PUL = 45, TURP = 35). One patient in the PUL group was excluded for protocol deviation. Mean age in the PUL group was 63 ± 6.8 years and mean prostate volume was 38 ± 12 cm^3. The primary outcome measure was to show that PUL is not inferior to TURP in terms of the BPH6 composite endpoint at 12 months. The BPH6 composite endpoint[1] is made up of the following six elements. A subject is a responder if all six elements are met:

- LUTS Relief Reduction ≥ 30% reduction in International Prostate Symptom Score (IPSS) compared to baseline
- Recovery Experience: Return to pre-operative activity levels measured by quality of recovery (QoR) visual analog scale (VAS)
- Erectile function: Less than 6-point reduction in Sexual Health Inventory for Men (SHIM) compared to baseline
- Ejaculatory function: Response on MSHQ-EjD that indicates emission of semen. This excludes the response "Could not ejaculate"
- Continence: Incontinence Severity Index (ISI) score of 4 points or less at all follow-up time points
- Safety: No procedure-related adverse event greater than Grade I on the Clavien-Dindo classification system modified for TURP at any time during procedure or follow up

Two modifications were made to the original element definitions to increase the quality and relevance of the analysis. In the original endpoint definition, the sexual function elements were assessed at a single time point, 12 months. Because sexual activity can vary from month to month, both elements were modified to instead assess sustained effects during 12 months. In addition, the majority of patients reported a return to preoperative activity by 1 month on a separate questionnaire, yet scored >70 rather than >80 on the quality of recovery (QoR) visual analog scale (VAS). The threshold for quality of recovery was thus lowered from 80 to 70 to address this correlation.

The proportion of participants who met the original BPH6 composite endpoint was 34.9% for the PUL group and 8.6% for the TURP group (noninferiority p = 0.0002). Although designed to detect noninferiority, the study demonstrated superiority of PUL over TURP in terms of the BPH6 responder endpoint (superiority p = 0.006). The refined BPH6 primary endpoint was also met by 52.3% of PUL and 20.0% of TURP patients (noninferiority p < 0.0001; superiority p = 0.005). At each follow-up interval, the responder rate was significantly higher for PUL than for TURP patients (p = 0.0002–0.006).

Analysis of the BPH6 element endpoints demonstrated that TURP was superior to PUL in reducing IPSS (91% vs 73%, p = 0.05The proportion of patients achieving the refined BPH6

[1] The BPH6 composite endpoint is as yet not validated, although it is composed of individually validated instruments.

recovery endpoint (QoR VAS ≥ 70 by 1 month) was 82% in the PUL group, which was significantly better than the 53% in the TURP group (p = 0.008). With the original threshold, 57% PUL compared to 32% TURP patients achieved the recovery endpoint. Furthermore, 74% of the TURP group had a catheter for more than 24 hours, compared to just 45% of the PUL group (p = 0.01). The average number of days to discharge was significantly lower (1.0 vs 1.9 days) and the return to preoperative activity levels was significantly faster (11 vs 17 days) for PUL than for TURP patients.

No significant differences were observed for erectile function, continence, or grade II+ adverse events; this may be a result of insufficient study power for detection of differences in these elements of BPH6. Both study procedures effectively mitigated LUTS. At 12 months, PUL yielded a mean improvement of 11.4 ± 8.4 in IPSS and the IPSS improvement after TURP was 15.4 ± 6.8 (p = 0.02).

Although the results for the BPH6 safety element were better for the PUL than for the TURP group (93% vs 79%), the difference was not significant (p = 0.1). Reintervention for failure to cure occurred in 6.8% (3/44) of PUL and 5.7% (2/35) of TURP patients. No subject in either study arm started taking an alpha blocker or 5 alpha reductase inhibitor.

Secondary endpoints included comparison of treatment groups with respect to International Prostate Symptom Score (IPSS), IPSS QoL, BPH impact index (BPH II), peak flow rate (Qmax), Male Sexual Health Questionnaire for Ejaculatory Dysfunction (MSHQ-EjD), and post-void residual volume (PVR). The authors noted that while the study size was sufficiently powered to address the primary endpoint, it was not powered to ensure that the sample size was sufficient to detect meaningful differences in secondary endpoints.

Gratzke et al., 2017 reported 2-year results for the BPH6 study secondary endpoints (IPSS, IPSS QoL, BPHII, peak flow rate (Qmax), MSHQ-EjD, and post-void residual volume (PVR)) and added some additional QoL indicators to provide a more complete characterization after LUTS treatment for BPH.

Significant improvements in IPSS, IPSS QoL, BPH Impact Index (BPHII) and Qmax were observed in both arms through 2-year follow-up. IPSS change with TURP was superior to that with PUL at 1 and 2 years (p=0.013 and p = 0.004, respectively) and TURP was superior with regard to Qmax at all time points. QoL and BPHII improvements were not statistically different between study arms at any timepoint. Erectile function was preserved in both arms as assessed by SHIM at all time points. Ejaculatory function was superior for PUL compared with TURP (p < 0.001), with patients in the TURP arm experiencing a significant decline (p < 0.001) in MSHQ-EjD function score from 1 month after the procedure and onwards. This difference was further demonstrated in the BPH6 ejaculatory function category, as 100% of patients in the PUL arm had preserved function, while 34% of patients in the TURP group reported they ‘could not ejaculate’ at 2 years. Durability of effect is another important characteristic of treatment options. Over the 2-year follow up, six patients in the PUL arm (13.3%) and two in the TURP arm (5.7%) underwent retreatment for return of LUTS. Secondary treatments included an additional PUL, intradetrusor botox, laser treatment or TURP procedure. One patient in the PUL arm underwent removal of an implant that had been deployed too proximally, such that part of the implant was exposed to the bladder and caused intermittent hematuria.

TURP has long been considered the gold standard surgical treatment for maximum relief of LUTS/BPH; however, TURP is associated with long-term complications that include ejaculatory dysfunction. Gratzke et al. concluded “*It has long been established that TURP offers maximum improvement in IPSS and Qmax, but the BPH6 study results indicate that an exclusive focus on these two goals may not result in the greatest improvement in quality of life for patients who value other important health outcomes. If on one hand, a man is likely to be satisfied with the 43% mean IPSS improvement that PUL offers at 2 years and highly values avoiding sexual dysfunction or episodic incontinence, PUL is perhaps the better choice. If, on the other hand,*

sexual function and high quality, rapid recovery are not important concerns, TURP may be the better choice to maximize impact on LUTS."

Cohort studies
In the LIFT study, 66 patients underwent a sham procedure and were assessed at baseline through to 3 months via IPSS, Qmax, IPSS quality of life (QoL) question, BPH Impact Index (BPHII), PVR, and sexual function questionnaires by an assessor blinded to the enrollment arm. After 3 months, patients in the sham group were offered PUL or another intervention if symptoms persisted. Those patients who elected PUL treatment were assessed before crossover to PUL, and at 0.5, 1, 3, 6, 12, and 24 months after PUL. Of the 66 sham patients, 53 (80%) elected to undergo PUL treatment, entering the crossover study, (Rukstalis et al., 2016). Two patients were later excluded for protocol deviations associated with data collection methods, leaving 51 patients in the crossover cohort for analysis. Mean age was 64 ± 7.8 years; mean prostate volume was 40.53 ± 9.92 ml. During the 24- month follow-up period, four patients (8%) progressed to TURP and one (2%) required additional PUL implants. No patients were taking an a-blocker or 5a-reductase inhibitor for LUTS at the time of the 24-month follow-up. Three patients withdrew from the study, and one missed the 24- month follow-up visit, leaving 42 subjects available for per protocol evaluation at 24 months. After crossover PUL treatment, IPSS improved significantly within 2 weeks and achieved peak improvement at 3 months (13.12 ± 7.34 (52.7%), $p < 0.001$)), and although improvement was still significant through 24 months (9.60 ± 8.48 (35.5%), $p < 0.001$), IPSS trended downward at each timepoint after 3 months. Qmax improved significantly at 3 months (4.00 ± 6.53 (76.0%), $p < 0.001$) and this improvement was stable through 24 months (4.18 ± 6.50 (77.2%), $p < 0.001$). BPHII and QoL were significantly improved at 1-month post-PUL compared to baseline and significant improvement was maintained through 24 months. The SHIM scores were not significantly different however MSHQ-EjD function and bother scores both showed significant improvement beginning at 1-month post-PUL and significant improvement was maintained through the 24-month follow-up. Adverse events were in general mild to moderate and typically resolved by 2 weeks post-PUL. Ten devices (4%) were later found to have been inadvertently deployed such that part of the implant was exposed to urine within the bladder and developed surface encrustation. Over the 24-month follow-up period, three patents had their encrusted devices removed, and one additional patient underwent removal of a non-encrusted device prophylactically. In each case LUTS either remained stable or improved after removal.

Obstructive Median or Middle Lobe
The approach of retracting enlarged prostatic lobes using UroLift™ implants has been studied in men with lateral lobe (LL) enlargement. There are only limited data on treating patients with a prostatic median lobe enlargement due to BPH. In the LIFT study, 5.3% of those subjects assessed for randomization were excluded for an obstructive median or middle lobe (OML) (Roehrborn et al. 2017). MedLift is a U.S. Food and Drug Administration-approved Investigational Device Exemption (IDE) extension of the LIFT study to determine the safety and efficacy of PUL for the treatment of OML (Study of Median Lobe Prostatic UroLift™ Procedure, Clinicaltrials.gov NCT02625545). Results of Medlift are published by Rukstalis et al., 2019. Inclusion criteria were for this non-randomized cohort were identical to the LIFT randomized controlled trial, except requiring an OML. Enrollment criteria included age ≥ 50 years, IPSS ≥ 13, peak flow rate (Qmax) ≤ 12 mL/s with a 125 mL voided volume and 30–80 cc intraurethral prostatic volume as measured by transrectal ultrasound, and in the opinion of the investigator, the middle or median lobe appeared obstructive and would have contraindicated a purely LL PUL. The primary objective was to determine the effectiveness and safety of PUL for treating subjects with OML. The primary endpoint was to demonstrate at 6 months that the mean percent improvement in IPSS over baseline for PUL was > 30%. Of the 71 screened subjects, 45 were enrolled. The study was powered to have 95% probability of establishing the true percent improvement in IPSS score from baseline to 6 months was greater than 25%, with 95% confidence. All (45 of 45; 100%) procedures initiated were successfully completed. An average of 6.3 implants were used per subject, of which 1.3 implants on average were needed to treat the middle lobe. Average length of stay after procedure was 2.4 hours (median 1.8, SD 2.7) with only one subject staying overnight (18.5 hours stay). A catheter was placed post-operatively without a voiding trial in 29/45

subjects (64.4%). An additional 7 subjects (15.6%) failed a voiding trial and required a catheter prior to discharge. Mean catheter duration was 1.2 days averaged over the total cohort. Peri-operative adverse events were typically mild to moderate and transient, with the most frequent being hematuria and dysuria. Over the one-year course of the study, few related adverse events occurred after the first month.

The primary effectiveness endpoint was met. The mean improvement in IPSS at 6 months was 57.7%, with mean IPSS improvement maintained through 12 months at 55.1%. The observed rate of post-procedure device related serious complications was 0%, thereby achieving the primary safety composite endpoint. There was no significant difference in any efficacy measure between PP and ITT analyses. Mean IPSS improvement at 1, 3, 6, and 12 months was at least 13.5 points and significantly better than baseline at every time point ($p < 0.0001$). QoL and BPHII were similarly improved (>60% and >70%, respectively at 3, 6, and 12 months). Mean Qmax improvement ranged from 90–130% throughout follow up. At 1 month, 65% subjects reported >80 on the Quality of Recovery scale, 95% reported feeling 'better' with 80% feeling 'much' or 'very much better,' and 89% would recommend the procedure. By 3 months, 93% would recommend the procedure. Sexual function was preserved with no PUL subjects reporting de novo sustained ejaculatory or erectile dysfunction. There was no significant degradation in mean erectile function (IIEF-5) or ejaculatory function (MSHQ-EjD Function) over the course of follow up. Bother due to ejaculatory function improved rapidly and remained modestly improved at 1 year, $p = 0.001$.

At one-year follow up, no subject had been lost to follow up or exited the study. No subject required BPH LUTS medications for return of symptoms. Surgical retreatment for failure to cure occurred in 1 subject (2%) who received additional PUL implants at 9 months with no adverse effect from the presence of implants. No implant was observed to have developed encrustation or stone formation throughout the study and no implants were removed. No subject required a surgical intervention for a related adverse event.

The MedLift study demonstrated that outcomes from PUL treatment of OML are not dissimilar to PUL treatment of lateral lobe.

Prostates ≥ 80 cc

Eure et al., 2019 published results of a protocol-driven retrospective chart review and analysis of 1,413 consecutive patients who received PUL across 14 sites in North America and Australia. A total of 1,248 spontaneously voiding subjects (Group A) and 165 urinary retention subjects (Group B) constituted this real-world retrospective (RWR) study. Baseline demographics and symptom outcomes for the total study population were compared with those reported in the randomized controlled LIFT study. Group A subjects provided baseline symptom and flow data, whereas Group B subjects were in urinary retention at baseline. Mean differences in International Prostate Symptom Score (IPSS), quality of life (QoL), and maximum urinary flow rate (Qmax) were evaluated at 1, 3, 6, 12, and 24 months post-procedure for all subjects in Group A and Group B. Subgroup analyses were conducted for moderate to severe symptoms (IPSS ≥ 13, [n = 1047), age (<50 years, n = 17), prostate volume (<30 cc, n = 165; 30 to <60 cc, n = 353; 60 to <80 n = 105, and ≥ 80 cc, n = 38), site of service (clinic office, n = 392), prior prostate cancer treatment (n = 73) and diabetes (n = 243). Absolute symptom scores after PUL were statistically compared between Groups A and B. Adverse events, surgical retreatments, and catheterization rates were independently calculated for Groups A and B. Compared with the LIFT study, RWR subjects were older (70 vs 67 years, $p < 0.001$), had lower baseline IPSS (19.2 vs 22.3, $p < 0.0001$), lower QoL (4.0 vs 4.6, $p < 0.0001$), and higher Qmax (12.6 vs 7.9 mL/second, $p < 0.0001$). Seventeen subjects < 50 years received PUL and experienced Seventeen subjects <50 years received PUL and experienced.

After PUL, IPSS values for Group A improved significantly from baseline at all timepoints by at least 8.1 points ($p < 0.0001$). Mean QoL improved at 24 months by 41%. For subjects with baseline IPSS ≥ 13, IPSS improvement and percentage change per timepoint were not significantly different compared with subjects from the LIFT study at 1, 3, 6, 12, and 24 months.

Most perioperative adverse events were mild to moderate and resolved by 4 weeks. Over the course of the study, 72 subjects underwent either a PUL retreatment (n = 39) or an alternative surgical intervention (17 laser procedures and 16 TURPs), 11 of which included removal of implants. Only one additional subject required a procedure specifically to remove a UroLift™ System implant.

Median and mean prostate size (determined predominantly by transrectal ultrasonography) for the RWR total study population was 41 and 45 cc, 95% CI (43.7–46.7), respectively. Subjects received an average of 4.6 implants (–1.3, range 2–10). No significant differences in symptom response emerged based on prostate volume. Group A subjects with prostate volumes < 30 cc (n = 165) had significant improvements from baseline at all timepoints and effectiveness in this group was comparable to the subjects with prostate volumes ≥ 30 cc (n = 496). Although small patient numbers beyond 6 months limited analysis, 38 subjects with prostates ≥ 80 cc experienced similar absolute symptom scores throughout follow-up compared to subjects with smaller prostates (< 80 cc, n = 623; IPSS baseline: 19.4 vs 17.6, p = 0.1; 1 month: 10.6 vs 9.0, p = 0.3; 6 months: 10.0 vs 9.6, p = 0.8). There were also no significant differences in overall adverse event rate (p = 0.5) and catheter-free rates (p = 0.1) after PUL.

The authors noted, "*Unlike 5-ARI treatment and some thermal therapies that are not indicated for the treatment of prostates <30 cc, PUL has no lower bound on prostate volume in its indication. Far fewer BPH patients have prostates >80 cc, but it is encouraging to see that PUL was similarly effective in this group as well. The modestly attenuated symptom improvement in this study compared with L.I.F.T. is expected due to the known effect of baseline symptom score on subsequent symptom improvement. When analyzing RWR subjects matched to LIFT baseline criteria (IPSS ≥ 13), differences in symptom improvement disappear. Rates of adverse events for RWR subjects are also comparable with previous controlled studies. In the LIFT study, 10.7% (15/140) of subjects required a procedure to remove implants to rectify placement issues. As a result, deployment accuracy became a central issue in technique training. It is encouraging that considerably fewer subjects in this real-world retrospective study required implant removal*. *Upon FDA approval in 2013, PUL was indicated for the treatment of prostates <80 g in men < 50 years. The robust symptom improvements seen within RWR subjects <50 years and prostate sizes <30 and >80 provides evidence that PUL can significantly benefit these patients*."

Systematic reviews and meta-analyses
Several systematic reviews and meta-analyses have been published that combined data from randomized controlled trials (RCTs) with non-RCTs (Jing et al., 2020, Xiang et al., 2020, Perera et al., 2015). Systematic reviews and meta-analyses that combine results derived solely from high quality RCTs are considered Level I evidence (CEBM Levels of Evidence).

Jing et al. conducted a systematic review and meta-analyses to evaluate the effectiveness of PUL through 24 months follow-up. A total of 11 studies with 1,443 patients met inclusion criteria. The cutoff date for inclusion was publication prior to December 1, 2019. Change from baseline was compared for IPSS, QoL, Qmax, PVR, and SHIM, and then compared to TURP. Trend graphs of the changes in each indicator were created to attempt to clarify the effectiveness of PUL. Data for each follow-up time point (1, 3, 6, 12, and 24 months) were analyzed in terms of baseline characteristics and functional and sexual health outcomes. At 24 months, the changes of three indicators were statistically significant (IPSS 9.40 points, p < 0.001; Qmax 3.39 ml/s, p < 0.001; QoL 1.99 points, p < 0.001) but were not as effective as TURP. The trend plots show that the effect of PUL on IPSS, Qmax and QoL peaks at 3 or 6 months and then weakens over time. By only looking at the outcomes at 24 months compared to baseline, this trend would not be noticed. PUL showed no influence on SHIM, indicating that PUL has no effect on patients' sexual function. PUL showed no effect on PVR.

Jung et al., 2019 conducted a Cochrane review of prostatic urethral lift for treatment of LUTS in men with BPH. Two randomized controlled trials were included (Roehrborn et al., 2013, PUL vs sham and Gratzke et al., 2017, PUL vs TURP). While Roehrborn and colleagues published five-

year follow-up data for PUL vs sham as an extended open-label study, only the three-month follow-up data for which there was a concurrent comparison group (PUL and sham) was used in accordance with the published protocol. The follow-up duration of PUL vs TURP was 24 months. The mean age was 65.6 years, mean IPSS was 22.7, mean Qmax was 8.9 mL/second, and mean prostate volume was 42.2 mL. Both studies included participants with IPSS > 12 and prostate volume < 80 mL. One study used Qmax ≤ 12 ml/second and one study used Qmax ≤ 15 ml/second. Major exclusion criteria included active urinary tract infection, urinary retention, raised PSA level suspicious of prostate cancer, history of prior prostate-related surgery such as TURP or laser procedure, and other medical conditions or medical comorbidities that represented relative or absolute contraindications for TURP or PUL. Jung et al. concluded that PUL may improve urological symptom scores and quality of life similarly as sham surgery short term. Compared to TURP, PUL is less effective in improving urological symptom scores both short and long term but may offer advantages with regards to the preservation of ejaculatory function. There is considerable uncertainty or lack of evidence (or both) with regards to the risk of major adverse events and retreatment rates over time. The certainly of evidence was consistently downgraded for study limitations, including attrition bias due to high rates of participants not included in the analysis.
Jung et al. see the following as research priorities:

- Further studies of greater methodological rigor comparing PUL to TURP as well as other treatment modalities. Studies should be of sufficient duration (24 months or longer) and transparently report on treatment-related adverse events and retreatment rates.
- Data to help inform which men may be most suitable for PUL based on characteristics such as age, prostate volume, and symptom scores. Given the large numbers of alternative treatment modalities to treat men with LUTS secondary to BPH, this represents important information that should be shared with men considering surgical treatment.

Guidelines
The American Urological Association (AUA) Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia: AUA Guideline (Published 2021; Amended 2023)

- PUL should be considered as a treatment option for patients with LUTS/BPH provided prostate volume 30-80cc and verified absence of an obstructive middle lobe. (Moderate Recommendation; Evidence Level: Grade C)
- PUL may be offered as a treatment option to eligible patients who desire preservation of erectile and ejaculatory function. (Conditional Recommendation; Evidence Level: Grade C)

The Panel limited this guideline statement to include patients with a prostate lacking an obstructive middle lobe, consistent with the LIFT study criteria. The Panel identified an observational cohort study (n=45 patients) observing improvements in urinary and sexual health outcomes from baseline in patients with an obstructive middle lobe following PUL. This study was excluded from formal efficacy analysis because it was a nonrandomized cohort study utilizing historic controls rather than an RCT (Lerner 2021b).

A 2023 AUA Guideline Amendment was published by Sandhu et al., 2024. In 2023, an update review assessing abstracts from new studies published since the initial release of the 2019 Guideline was completed utilizing the same search strategies employed in the original guideline with search dates updated through October 2022. Relevant literature was graded and incorporated into existing text to produce the 2023 amendment. The Amendment resulted in changes to statements/supporting text on combination therapy, photoselective vaporization of the prostate (PVP), water vapor thermal therapy (WVTT), laser enucleation, and prostate artery embolization (PAE). A new statement on temporary implanted prostatic devices (TIPD) was added. In addition, statements on transurethral needle ablation (TUNA) and transurethral microwave thermotherapy (TUMT) were removed and information regarding these legacy technologies was added to the background section. References and the accompanying treatment algorithms were updated to align with the updated text. The Amendment did not result in changes to the previous recommendation for robotic waterjet treatment (RWT).

Similarly, the 2022 European Association of Urology (EAU) Guidelines recommend offering prostatic urethral lift (UroLift™) to men with LUTS interested in preserving ejaculatory function, with prostates < 70 mL and no middle lobe obstruction (Gravas et al., 2023).

Analysis of Evidence (Rationale for Determination)

Two randomized controlled trials (RCTs) and one crossover cohort study provide evidence that PUL significantly improves IPSS, Qmax and QoL; however, these improvements are inferior to TURP at 24 months. TURP has long been considered the gold standard surgical treatment for maximum relief of LUTS/BPH; however, TURP is associated with long-term complications that include ejaculatory dysfunction. PUL preserved ejaculatory function when compared to TURP through 24 months ($p < 0.001$).

Based on this review of the current evidence, Fallon Health considers PUL medically necessary as an alternative to TURP for the treatment of LUTS attributed to BPH when coverage criteria are met. The coverage criteria are derived from inclusion criteria in the RCTs, and are consistent with AUA Guideline recommendations.

The efficacy of PUL in large prostates of 80 cc or larger has not been shown. The RCTs enrolled men with prostates within specific size ranges. Fallon Health's coverage criteria reflect the prostate volume included in the RCTs and AUA Guideline recommendations (i.e., ≥ 30 cc and ≤ 80 cc). Fallon Health recognizes that the PUL procedure does not necessarily lack efficacy in prostates larger than 80 cc, however RCT evidence of efficacy is lacking.

There are only limited data on treating patients with an obstructive median lobe. It appears that patients with an obstructive median lobe can be effectively treated with a variation in the standard technique, but RCTs are needed. The AUA panel identified the MedLift study but excluded it from formal efficacy analysis because it was a nonrandomized cohort study using historical controls rather than a randomized controlled trial (AUA, 2021).

The AUA panel recognizes that many devices do not necessarily lack efficacy in prostates below or above 30-80 cc, however, there is insufficient evidence to make formal recommendations beyond those sizes identified (AUA, 2021).

Longer-term studies are needed to evaluate the duration of the effect. Meta-analysis shows that the effect of PUL on IPSS, Qmax and QoL peak at 3 or 6 months and then weaken over time. By only looking at the outcomes at 24 months compared to baseline, this trend would not be noticed (Jing et al., 2020).

Studies comparing PUL to other surgical techniques are needed, this represents important information that should be shared with patients considering surgical treatment.

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Coding

The following codes are included below for informational purposes only; inclusion of a code does not constitute or imply coverage or reimbursement.

The number of implants will vary by patient due to the unique characteristics of the prostate and prostatic urethra; clinical data supports an average of 4-6 implants per patient.

Physicians reimbursed under the Medicare Physician Fee Schedule should report insertion of transprostatic implants with CPT code 52441 or 52442. CPT code 52441 is used to report the initial implant and add-on CPT code 52442 used for reporting each additional implant. The Medically Unlikely Edit (MUE) assigned to CPT code 52442 is 6. Because CPT code 52442 must always be billed with CPT code 52441, the maximum number of payable units (implants) per procedure on initial claim submission is 7.

Outpatient hospitals and ambulatory surgical centers (ASCs) reimbursed under the Medicare Outpatient Prospective Payment System (OPPS) or Medicare Ambulatory Surgery Center (ASC) Payment System must bill either C9739 or C9740 for the insertion of transprostatic implants. Because of the structure of these codes, C9739 used for cases using 1 to 3 implants and C9740 used for cases using 4 or more implants. The MUE assigned to C9739 and C9740 is 1. Outpatient hospitals and ASCs reimbursed under Medicare payment methodologies must not bill for transprostatic implants using CPT 52441 or 52442.

Fallon Health follows Subchapter 6 of the MassHealth Provider Manual for MassHealth ACO members. Payable codes and modifiers for surgical services are listed in Subchapter 6 of the Physician Manual, Acute Outpatent Hospital Manual and Freestanding Ambulatory Surgery Center Manual. For MassHealth ACO members, physicians and outpatient hospitals must bill CPT 52441 and 52442 for insertion of transprostatic implants.

Code	Description
52441	Cystourethroscopy, with insertion of permanent adjustable transprostatic implant; single implant
52442	Cystourethroscopy, with insertion of permanent adjustable transprostatic implant; each additional permanent adjustable transprostatic implant (list separately in addition to code for primary procedure)

Outpatient Hospitals and Ambulatory Surgical Centers Reimbursed under the Medicare Outpatient Prospective Payment System (OPPS) or Medicare Ambulatory Surgery Center (ASC) Payment System

CMS created HCPCS codes C9739 and C9740 for outpatient hospital and ambulatory surgical center (ASC) billing for the insertion of transprostatic implants effective April 1, 2014. The AMA's CPT Editorial Panel created CPT codes 52441 and 52442 for the insertion of transprostatic implants effective January 1, 2015. As discussed in the CY 2015 OPPS/ASC Final Rule with Comment Period (79 FR 66853 through 66854), CMS did not adopt CPT codes 52441 and 52442 for outpatient hospital or ASC billing because the code descriptors do not accurately capture the number of implants typically provided in a hospital outpatient or ASC setting.

In the OPPS and ASC Payment System, HCPCS C9739 and C9740 are assigned to a device-intensive APC which requires reporting the appropriate device code and associated cost (but does not result in additional reimbursement). Effective January 1, 2017, CMS created HCPCS code C1889 to be used to report devices implanted or inserted during a device-intensive procedure that are not described by a specific Level II HCPCS Category C-code.

Code	Description
C9739	Cystourethroscopy, with insertion of transprostatic implant; 1 to 3 implants
C9740	Cystourethroscopy, with insertion of transprostatic implant; 4 or more implants
C1889	Implantable/insertable device for device intensive procedure, not otherwise classified

ICD-10-CM Diagnosis Code

Code	Description
40.1	Benign prostatic hyperplasia with lower urinary tract symptoms

Policy history

Origination date: 12/01/2023
Review date(s)l: Technology Assessment Committee: 04/25/2023, 09/26/2023 (policy origination), 10/29/2024 (annual review; updated Summary of Evidence; updated References; updated Coding section).
UM Committee: 11/19/2024 (annual review).

Not all services mentioned in this policy are covered for all products or employer groups. Coverage is based upon the terms of a member's particular benefit plan which may contain its own specific provisions for coverage and exclusions regardless of medical necessity. Please consult the product's Evidence of Coverage for exclusions or other benefit limitations applicable to this service or supply. If there is any discrepancy between this policy and a member's benefit plan, the provisions of the benefit plan will govern. However, applicable state mandates take precedence with respect to fully insured plans and self-funded non-ERISA (e.g., government, school boards, church) plans. Unless otherwise specifically excluded, federal mandates will apply to all plans.