

Lower Urinary Tract Symptoms in Men

A Review




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IMPORTANCE Up to 40% of men older than 50 years have lower urinary tract symptoms, including urinary urgency, nocturia, and weak urinary stream, due to disorders of the bladder and prostate. These symptoms negatively affect quality of life and may be associated with urinary retention, which can cause kidney insufficiency, bladder calculi, hematuria, and urinary tract infections.

OBSERVATIONS In men, lower urinary tract symptoms can be caused by bladder outlet obstruction secondary to benign prostatic hyperplasia (BPH), an overactive bladder detrusor (a syndrome of urinary urgency and frequency), or both. Behavioral therapy, including pelvic floor physical therapy, timed voiding (voiding at specific intervals), and fluid restriction, can improve symptoms. Medications including α -blockers (such as tamsulosin), 5 α -reductase inhibitors (such as finasteride), and phosphodiesterase 5 inhibitors (such as tadalafil) improve lower urinary tract symptoms (mean improvement, 3-10 points on the International Prostate Symptom Score [IPSS], which ranges from 0-35, with higher scores indicating greater severity) and can prevent symptom worsening measured by increased IPSS greater than or equal to 4 points or development of secondary sequelae, such as urinary retention. Combination therapies are more effective than monotherapy. For example, α -blockade (eg, tamsulosin) combined with 5 α -reductase inhibition (eg, finasteride) lowers progression risk to less than 10% compared with 10% to 15% with monotherapy. Treatment for overactive bladder detrusor, including anticholinergics (eg, trospium) and β_3 agonists (eg, mirabegron), reduces voiding frequency by 2 to 4 times per day and reduces episodes of urinary incontinence by 10 to 20 times per week. Surgery (eg, transurethral resection of the prostate, holmium laser enucleation of the prostate) and minimally invasive surgery are highly effective for refractory or complicated cases of BPH, defined as persistent symptoms despite behavioral and pharmacologic therapy, and these therapies can improve IPSS by 10 to 15 points. Minimally invasive procedures, such as water vapor therapy (endoscopic injection of steam into BPH tissue) and prostatic urethral lift (endoscopic insertion of nonabsorbable suture implants that mechanically open the urethra), have lower complication rates of incontinence (0%-8%), erectile dysfunction (0%-3%), and retrograde ejaculation (0%-3%) but are associated with increased need for surgical retreatment (3.4%-21%) compared with transurethral resection of the prostate (5%) and holmium laser enucleation of the prostate (3.3%).

CONCLUSIONS AND RELEVANCE Lower urinary tract symptoms, defined as urinary urgency, nocturia, or weak stream, are common among men and are usually caused by BPH, overactive bladder detrusor, or both. First-line therapy consists of behavioral intervention, such as pelvic floor physical therapy and timed voiding, as well as pharmacologic therapy, including α -adrenergic blockers (tamsulosin), 5 α -reductase inhibitors (finasteride), phosphodiesterase inhibitors (tadalafil), anticholinergics (trospium), and β_3 agonists (mirabegron).

JAMA. doi:10.1001/jama.2025.7045
Published online July 14, 2025.

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Lower urinary tract symptoms (LUTS) affect approximately 2.3 billion people worldwide,¹ of whom approximately half are men.^{2,3} In the United States, population-based data from Olmstead County reported that 13% of men aged 40 to 49 years and 28% of men older than 70 years had benign prostatic hyperplasia (BPH) or LUTS.⁴ In primary care settings, where most men receive initial evaluation and treatment, up to 40% of men older than 50 years may have BPH or LUTS.⁵ In a large retrospective claims data study, nearly 63% of men aged 65 years and older had filled a prescription indicated for BPH within 5 years of diagnosis of BPH or LUTS.⁶ Lower urinary tract symptoms in men may also arise from an overactive bladder detrusor (OAB, a syndrome of urinary urgency and frequency). This Narrative Review summarizes current evidence on the epidemiology, pathophysiology, diagnosis, and management of LUTS in men (Box).

Methods

An initial PubMed search was performed between January 1, 2019, and February 4, 2024, and updated through January 31, 2025, for English-language articles containing *BPH*, *LUTS*, *OAB*, or all 3 in the title. Included article types were randomized clinical trials (RCTs), systematic reviews, meta-analyses, and practice guidelines (European Association of Urology⁷ and American Urological Association clinical practice guidelines⁸⁻¹⁰). Of 499 identified articles, 86 were included, consisting of 28 RCTs, 26 systematic reviews, 10 prospective longitudinal cohort studies, 8 cross-sectional studies, 7 guidelines, and 7 meta-analyses.

Discussion

Pathophysiology of LUTS

During normal voiding physiology, bladder filling is characterized by increased sympathetic detrusor muscle tone and somatic external urethral sphincter tone to maintain continence. When the bladder is adequately filled, afferent stimulation of sensory nerves in the detrusor alerts the brain of the need to void; when appropriate, the brain coordinates voiding by activating the brainstem pontine micturition center to decrease detrusor sympathetic tone, increase detrusor parasympathetic tone, and decrease somatic sphincter tone. Abnormalities in the anatomy or physiology of any of these processes can lead to LUTS.

Men presenting with LUTS often receive a diagnosis of BPH, a pathologic diagnosis of prostate gland enlargement that can be asymptomatic or symptomatic. When BPH causes physiologic obstruction of the prostatic urethra, it is referred to as bladder outlet obstruction, which causes obstructive symptoms by increasing urinary outflow resistance and impeding urinary flow. Chronic bladder outlet obstruction can lead to collagen deposition in the bladder wall, causing diffuse bladder wall thickening, decreased detrusor contractility, and decreased bladder compliance (ability of the bladder to increase volume without significant increase in intravesical pressures) and may cause bladder diverticula.¹¹ These sequelae can further exacerbate obstructive LUTS or cause irritative symptoms, such as urgency, frequency, and incontinence (ie, overactive bladder).¹² Chronic urinary retention secondary to bladder outlet obstruction or decom-

Box. Commonly Asked Questions and Answers About Male Lower Urinary Tract Symptoms

1. What Are Typical Lower Urinary Tract Symptoms?

Lower urinary tract symptoms (LUTS) are categorized into obstructive and irritative symptoms. Obstructive symptoms include urinary hesitancy, intermittent urinary stream, slow/weak stream, straining to void, and a sensation of incomplete emptying; irritative symptoms include urinary frequency, urgency, urge incontinence, nocturia, bladder pain, and dysuria.

2. Should Clinicians Identify the Specific Cause of LUTS?

It is not necessary to identify the specific cause of LUTS before initiation of behavioral or pharmacologic therapy because most men with LUTS will have some degree of bladder outlet obstruction due to benign prostatic hyperplasia, an overactive bladder, or both. Invasive testing, such as cystoscopy, may be necessary if patients do not respond to 1 or more pharmacotherapies or if they have hematuria.

3. What Are the First-Line Medications for LUTS?

For patients with primarily obstructive symptoms, α_1 antagonists, such as tamsulosin and silodosin; 5 α -reductase inhibitors, such as finasteride and dutasteride; and phosphodiesterase 5 inhibitors, such as tadalafil, are first-line therapy. For patients with a significant component of irritative symptoms, such as frequency and urge incontinence, which often coexist with obstructive symptoms, β_3 antagonists (eg, mirabegron, vibegron) and anticholinergic therapies (eg, oxybutynin, trospium) prescribed alone or in combination are recommended.

pensated detrusor can lead to hydronephrosis, kidney insufficiency, bladder calculi, hematuria, and recurrent urinary tract infections.

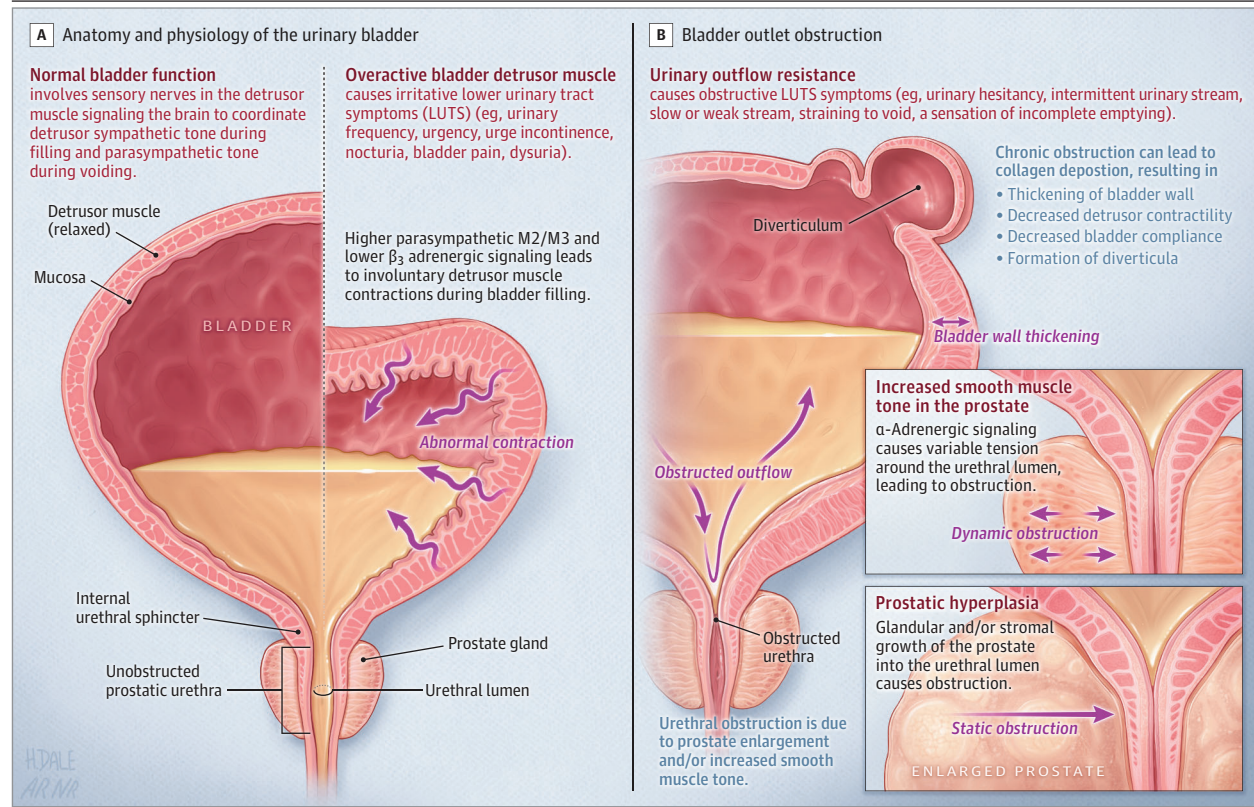
Male voiding symptoms caused by bladder outlet obstruction are due to 2 mechanisms (Figure 1).¹³ First, androgen-dependent hyperplasia of both glandular and stromal prostate elements grows into the lumen of the prostatic urethra, leading to static obstruction (ie, fixed mechanical blockage to urine flow).¹⁴ This hyperplasia is due to lifelong exposure to testosterone, which is converted in the prostate to the more active dihydrotestosterone by 5 α -reductase. Second, activation of the α_{1A} receptor of prostatic smooth muscle increases muscle tone around the urethral lumen, causing dynamic obstruction (ie, variable, as opposed to fixed, blockage to urine flow).¹¹ However, the severity of patient self-reported LUTS does not necessarily correlate with prostate size or degree of bladder outlet obstruction.¹⁴

The major pathologic contributor to irritative symptoms is thought to be detrusor overactivity, characterized by uninhibited, involuntary detrusor contractions during bladder filling.¹⁵ Detrusor overactivity is caused by parasympathetic muscarinic M2/M3 and β_3 -adrenergic signaling that decreases bladder compliance and causes sensations of urgency and frequency (Figure 1).¹⁵ It has been postulated that dysfunctional neurologic control of the bladder in efferent parasympathetic signals from the brain to the bladder or sensory afferent pathways from the bladder to the brain may contribute to detrusor overactivity. Additionally, inappropriate release of adenosine triphosphate by urothelial cells during bladder filling may contribute to detrusor overactivity.¹⁶

Epidemiology of LUTS

Benign prostatic hyperplasia has an estimated global incidence of 280 per 100 000 and prevalence of 2480 per 100 000 based on

Figure 1. Pathophysiology of Male Lower Urinary Tract Symptoms



the 2019 Global Burden of Disease study.^{17,18} Benign prostatic hyperplasia is found during autopsy in approximately 50% of men aged 51 to 60 years and up to 90% of men aged 80 years or older.¹² Up to 50% of men aged 75 years with BPH report symptoms.¹¹ The prevalence of BPH based on claims data (*International Classification of Diseases* coding) is lower than that identified in autopsy studies. In studies of claims data, 5% to 6% of men aged 40 to 64 years and 29% to 33% of men older than 65 years had BPH, likely because not all men with BPH develop symptoms or seek treatment.¹⁹ In the EPIC study, a cross-sectional questionnaire of 19 165 individuals in Canada, Germany, Italy, Sweden, and the United Kingdom, 26% of men reported obstructive LUTS indicative of BPH, whereas 51% reported irritative LUTS.²⁰

Overactive bladder detrusor affects approximately 16% of men in the United States.^{20,21} In the Epidemiology of Lower Urinary Tract Symptoms cross-sectional study, in which 9416 men in the United States, United Kingdom, and Sweden completed a questionnaire, 27% of men reported LUTS consistent with OAB (defined as the presence of urinary urgency or urge incontinence in the past 4 weeks) at least sometimes, and 16% reported that frequency of LUTS was often.²²

Risk Factors for Male LUTS

Lower urinary tract symptoms in men are associated with older age, and the prevalence of LUTS is approximately 29% to 33% in men after age 65 years.^{19,23} Additional risk factors for BPH and LUTS include family history²⁴ and metabolic syndrome (obesity, dyslipidemia, hypertension, and insulin resistance).^{25,26} One prospective observational study of 5667 men reported a 10% higher incidence of

BPH at 7-year follow-up for every increase of 0.05 in baseline waist-to-hip ratio.²⁶ Both older age and bladder outlet obstruction are risk factors for developing OAB.^{20,27}

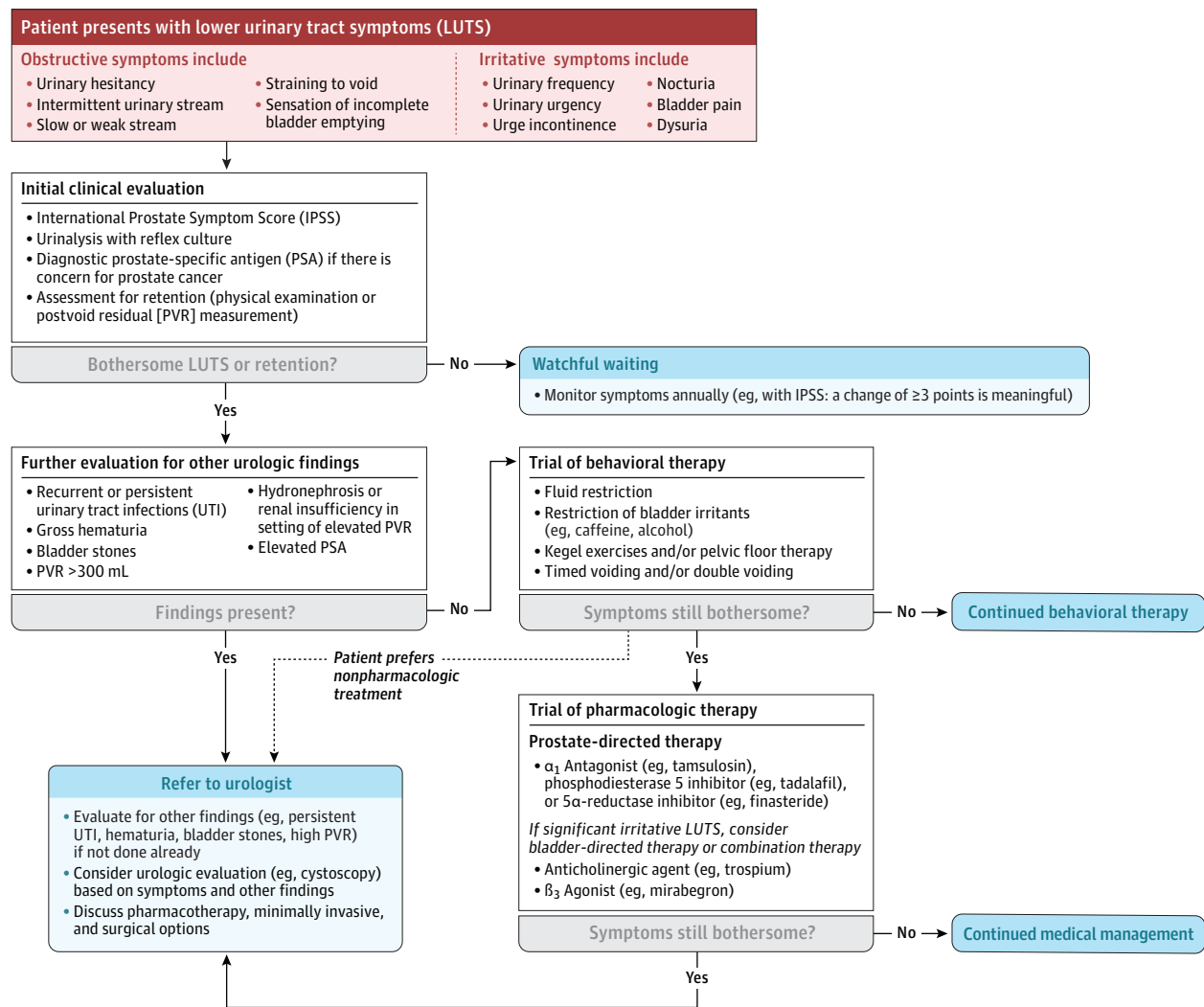
Clinical Presentation

Male LUTS are grouped into 2 categories: obstructive and irritative symptoms.²⁸ Obstructive symptoms, consisting of urinary hesitancy, intermittent urinary stream, slow or weak stream, straining to void, and a sensation of incomplete emptying, are commonly due to BPH or bladder outlet obstruction, urethral strictures, or a decompensated detrusor. Irritative symptoms, consisting of urinary frequency, urgency, urge incontinence, nocturia, bladder pain, and dysuria, may be due to OAB or bladder irritants, such as urinary tract infections and bladder stones.²⁹ Men may also present with a distended bladder or overflow incontinence due to urinary retention. Less common causes of LUTS include prostate or bladder malignancy and neurologic disease, such as multiple sclerosis, Parkinson disease, stroke, and spinal cord injuries, which may lead to overactive or underactive bladder (impaired detrusor contractility that presents with obstructive-like symptoms). Poorly controlled diabetes may cause urinary frequency secondary to osmotic diuresis or diabetic neurogenic bladder.

Evaluation of Symptoms

Quantification of LUTS severity and how LUTS interfere with quality of life is recommended by guidelines and can guide therapy (Figure 2).^{7,9} The International Prostate Symptom Score (IPSS) is a self-administered, validated questionnaire that assesses symptoms during

Figure 2. Male Lower Urinary Tract Symptoms Evaluation and Management



Adapted from Sandhu et al.¹⁰ This algorithm has not been validated.

the past month and contains 7 symptom severity items using a 5-point Likert scale and an eighth item scored on a 7-point Likert scale. The score ranges from 0 to 35. Scores from 0 to 7 are considered mild LUTS, 8 to 19 moderate LUTS, and greater than 20 severe LUTS (eFigure in Supplement 1).³⁰ A decrease of at least 3 points in IPSS is considered a meaningful response to treatment. Lower urinary tract symptoms may also be quantified using other validated questionnaires, such as the Lower Urinary Tract Dysfunction Research Network Symptom Index-10,³¹ which assesses symptoms during the past week and includes additional questions regarding urge incontinence, stress incontinence, and bladder pain. Use of this questionnaire or IPSS is recommended for quantification of LUTS at baseline and after implementing treatment.

Diagnosis

Evaluation also includes a voiding diary, urinalysis, urine culture, bladder ultrasonography, and serum prostate-specific antigen level if there is concern for prostate cancer. A voiding diary, which documents fluid intake and voided volumes on a 24-hour worksheet,

can assess whether LUTS are secondary to diuretic use, excessive fluid intake, or caffeine consumption. Urinalysis is helpful to rule out urinary tract infection. Patients with irritative symptoms and microscopic hematuria on urinalysis should be referred to a urologist for further evaluation and possible cystoscopy. Physical examination, including palpation of the lower abdomen for bladder distention or bladder scan ultrasonography to measure a postvoid residual volume, helps identify urinary retention (postvoid residual volume > 300 mL).³² Digital rectal examination has limited value because digital prostate size assessment correlates poorly with actual prostate size.

First-Line Management

Treatment options can be categorized into 4 groups, from least to most invasive, as follows: (1) behavioral modification; (2) pharmacologic therapy, including medications that treat bladder outlet obstruction (such as α -blockers) and medications that treat OAB (such as anticholinergics); (3) minimally invasive surgical therapy; and (4) surgery. Treatment should be selected according to severity of symptoms and shared

decision-making. Men with a high IPSS who are not bothered by their symptoms may not require intervention, whereas individuals with mild or moderate bothersome symptoms may select treatment.

Behavioral Modifications

Some men drink large quantities of fluids (>2 L/d), resulting in urinary urgency and frequency,³³ whereas others drink fluids before bed, exacerbating nocturia. Eliminating excess fluid intake and restricting fluid several hours before sleep are the major components of behavioral modification.³⁴ Other behavioral therapy includes Kegel exercises and pelvic floor physical therapy for urgency and timed voiding (voiding at specific intervals [eg, every 90 minutes while awake] even without feeling an urge) and double voiding (voiding again 30 seconds after the first void) to address incomplete bladder emptying.^{8,35,36}

A systematic review reported that behavioral approaches including education and reassurance; restriction of fluid, caffeine, and alcohol; and bladder training were more effective than watchful waiting (mean difference IPSS improvement of 7.4 between groups; 95% CI, 6.1-8.8) and were comparable to pharmacologic management (difference in mean IPSS improvement of 0 between groups).^{37,38} Initiating treatment with a structured behavioral program (education, restriction of fluid, and bladder training) decreased IPSS by 1.8 (95% CI, -2.66 to -0.95) compared with standard of care.³⁹ Among men with OAB, RCTs have demonstrated comparable efficacy between behavioral and pharmacologic therapy.^{36,40} An equivalence RCT of 143 men comparing 8 weeks of behavioral therapy (pelvic floor exercises; urge suppression techniques, such as attempting to diminish urge sensation by using pelvic floor contractions; and delayed voiding) vs oxybutynin (5-30 mg) found that the 2 treatments were equivalent in reducing voiding frequency and patient satisfaction with voiding symptoms. Daily voids were reduced by 2.2 in the behavioral group vs 2.0 in the oxybutynin group, which were equivalent on statistical testing ($P < .01$); 56.5% of men were completely satisfied with improvement in the behavioral group vs 42.4% in the oxybutynin group (nonsignificant difference, $P = .16$).⁴⁰ Another RCT of 204 participants reported significantly fewer daily voids after behavioral therapy (8.8 voids [SD, 2.1]) compared with after pharmacotherapy with tolterodine plus tamsulosin (10.3 voids [SD, 2.7]; $P < .001$) and a nonsignificant difference between behavioral therapy alone compared with combined behavioral therapy plus pharmacotherapy (8.2 voids [SD, 2.3]; $P = .19$).³⁶

Caffeine can exacerbate frequency and irritative symptoms through diuresis and detrusor excitatory effects mediated via central micturition centers.⁴¹ For some men, elimination or substantial reduction in caffeine intake sufficiently improves their symptoms. A 2020 systematic review concluded that caffeine reduction was associated with improvement in symptoms of urinary urgency and nocturnal enuresis.⁴² However, the studies included in the systematic review had small sample sizes (194 participants from 3 RCTs and 48 participants from 2 interrupted time series studies) and the study populations were heterogeneous. Thus, the systematic review had significant limitations.

Pharmacologic Therapy

Pharmacologic therapies to improve bladder outlet obstruction in people with LUTS include α -blockers (eg, tamsulosin), 5 α -reductase inhibitors (5-ARIs; eg, finasteride), and phosphodiester-

ase 5 inhibitors (eg, tadalafil); these medications improve IPSS by a mean of 3 to 10 points. Pharmacologic therapies to improve OAB in people with LUTS include anticholinergic drugs (eg, trospium) and β_3 agonists (eg, mirabegron). These drugs may be used as monotherapy or combined with medications in another category to achieve an additive effect. Understanding mechanisms of action and potential adverse effects can facilitate more effective therapy combinations. Efficacy is similar among medications within a given drug class. Therefore, medications should not be interchanged within a class due to lack of response, but they may be switched due to adverse effects.⁸ Meta-analyses of 23 studies including 1044 participants that measured urodynamic testing before and after treatment showed that α -blockers and 5-ARIs were associated with reduced bladder outlet obstruction index and increased maximum urinary flow rate.^{43,44} After the minimal time for onset of treatment effect has passed (Table 1), symptoms should be reevaluated for response and therapy may be discontinued or adjusted appropriately.

α -Adrenergic Receptor Blocker Medications

α -Adrenergic receptor activation in the prostate gland stroma and bladder neck can cause dynamic obstruction of urine flow, and therefore medications that block α -adrenergic receptors may improve symptoms of LUTS.⁴⁵ Commonly used α -adrenergic blocking medications (Table 1) typically have onset of action within 3 to 7 days and meaningfully reduce LUTS (mean IPSS improvement, 5-10 points). For patients not achieving a significant response (≥ 3 -point IPSS improvement) after a minimum trial period listed for each drug in Table 1, treatment may be discontinued.⁴⁶ Common adverse effects of α -blockers include retrograde ejaculation, erectile dysfunction, dizziness, and fatigue (1%-20%). Floppy iris syndrome, in which the iris dilator muscle is unusually lax due to α_1 antagonism, is an adverse effect occurring in 15% to 86% of patients taking α antagonists and increases the complexity of cataract surgery. Most ophthalmologists are familiar with this phenomenon, and use of appropriate retractors during cataract surgery minimizes complications. Prescribing alternatives to α -blocker medications may be useful for patients who have cataracts, but individuals already taking α -blockers may continue them because discontinuation does not reduce floppy iris risk.⁴⁷

5-ARIs

Inhibiting 5 α -reductase, which converts testosterone to dihydrotestosterone,¹⁴ inhibits prostate cellular growth and leads to prostate cell atrophy. 5 α -Reductase medications (finasteride, dutasteride) reduce prostate size by approximately 20% and are associated with a 25% to 75% reduction in serum prostate-specific antigen and a 3- to 4-point IPSS improvement.^{10,48} However, 3 to 6 months are typically required for patients to experience clinical improvement. Because 5-ARIs are most effective in larger prostate glands, guidelines recommend the drugs for men with a large prostate, defined by prostate-specific antigen level greater than 1.5 ng/mL or prostate volume greater than 30 g on imaging.^{8,10} Potential adverse effects include erectile dysfunction, decreased ejaculation and libido, and gynecomastia (1%-8%) (Table 1). In 2011, the Food and Drug Administration added information to the warnings and precautions section of 5-ARI labels about possible increased risk of high-grade prostate cancer, although recent evidence suggested that this association may not exist.^{49,50}

Table 1. Drug Therapies for Lower Urinary Tract Symptoms

| Class | Mechanism of action | Medication | Dose options | Minimum time to effect | Adverse effects and other considerations ^a | Degree of efficacy ^{a,b} |
|---------------------------------------|---|--------------|--|------------------------|---|-----------------------------------|
| Prostate-directed agents | | | | | | |
| α-Blockers, α _{1A} selective | Reduces adrenergic tone of prostate stroma to relieve dynamic urethral obstruction | Tamsulosin | 0.4-0.8 mg Daily | 3-7 d | Retrograde ejaculation (8%-28%), headache (2%-19%), dizziness (3%-15%), fatigue (3%-4%), nasal congestion (2%-13%), orthostatic hypotension (0.2%-4%); terazosin and IR doxazosin have highest rate of dizziness; silodosin and tamsulosin have highest rate of retrograde ejaculation; risk of intraoperative floppy iris syndrome highest with tamsulosin; small increase in risk of heart failure for patients with risk factors | -9.6 (IPSS) |
| | | Silodosin | 8 mg Daily | | | -6.5 (IPSS) |
| α-Blockers, nonselective | | Doxazosin | 1-8 mg Daily, IR; 4-8 mg daily, ER | 2-4 wk | | -6.1 (IPSS) |
| | | Terazosin | 1-10 mg Daily | | | -5.3 (IPSS) |
| | | Alfuzosin | 10 mg Daily | | | -6.9 (IPSS) |
| 5α-Reductase inhibitors | Inhibits conversion of testosterone to dihydrotestosterone to arrest prostate cell growth | Finasteride | 5 mg Daily | 3-6 mo | Erectile dysfunction (1%-8%), low libido (0.3%-6%), low ejaculate volume (2%-4%), gynecomastia (0.5%-2%); can decrease PSA (by mean of 50%), leading to later detection and higher-grade prostate cancer | -3.3 (IPSS) |
| | | Dutasteride | 0.5 mg Daily | | | -3.8 (IPSS) |
| PDE5 inhibitors | Promotes smooth muscle relaxation around urethra | Tadalafil | 5 mg Daily | 4 wk | Headache (11%-5%), flushing (2%-3%); contraindicated for patients taking nitrates and guanylate cyclase stimulators; hypotension may be increased when taken with α-blockers | -5.6 (IPSS) |
| Bladder-directed agents | | | | | | |
| Anticholinergics | Inhibits parasympathetic tone to decrease activation and contraction of the detrusor muscle, thereby enhancing compliance | Oxybutynin | 2.5-5 mg Twice per day/3 times per day, IR 5-30 mg daily, ER; transdermal patch twice weekly | 4-6 wk | Dry mouth (20%-70%), constipation (9%-15%), headache (4%), dry eyes (1%-3%); oxybutynin has highest risk of CNS adverse effects (somnolence, dizziness, delirium, memory impairment); urinary retention possible (1%-3%) | -19.4 (UI); -3.5 (frequency) |
| | | Tolterodine | 1-2 mg Twice per day; 2-4 mg daily, ER | | | -10.6 (UI); -1.7 (frequency) |
| | | Trospium | 20 mg Twice per day; 60 mg daily, ER | | | -15.4 (UI); -2.4 (frequency) |
| | | Darifenacin | 7.5-15 mg Daily | | | -11.4 (UI); -1.9 (frequency) |
| | | Solifenacin | 5-10 mg Daily | | | -14.0 (UI); -3.0 (frequency) |
| | | Fesoterodine | 4-8 mg Daily | | | -16.9 (UI); -1.9 (frequency) |
| β ₃ Agonists | Increases detrusor sympathetic tone to block detrusor contraction, thereby enhancing compliance | Mirabegron | 25-50 mg Daily | 4-6 wk | Increased BP (8%-11%), urinary tract infection (3%-4%), nasopharyngitis (3%-4%), headache (2%-3%); mirabegron contraindicated in severe uncontrolled HTN; monitor BP | -11.0 (UI); -1.9 (frequency) |
| | | Vibegron | 75 mg Daily | | | -14.0 (UI); -1.8 (frequency) |

Abbreviations: BP, blood pressure; CNS, central nervous system; ER, extended release; HTN, hypertension; IPSS, International Prostate Symptom Score; IR, immediate release; PDE5, phosphodiesterase 5; PSA, prostate-specific antigen; UI, urge incontinence episodes per week.

^a Adverse effect and efficacy rates were obtained from US Food and Drug Administration prescribing information labels.

^b Efficacy measures: for prostate-directed agents, efficacy is reported as mean change in IPSS from baseline; for bladder-directed agents, efficacy is reported as mean change in number of UI and mean change in number of micturitions per 24 hours (frequency). See Evaluation of Symptoms section for details on IPSS. A meaningful improvement in the IPSS is considered a decrease of greater than or equal to 3 points.

Phosphodiesterase 5 Inhibitors

Phosphodiesterase 5 inhibitors (tadalafil), commonly used for erectile dysfunction, increase the bioavailability of cyclic guanosine mono-

phosphate and promote vasodilation in smooth muscle of the bladder, prostate, and urethra, in addition to erectile tissues of the penis.⁵¹ Tadalafil is a phosphodiesterase 5 inhibitor with a half-life of 17 to

20 hours that improved BPH and LUTS (mean 5.6-point IPSS improvement compared with placebo) in several large RCTs.^{52,53} Tadalafil may be used instead of or in combination with α -blocking medications, even for men without erectile dysfunction.^{54,55} Although headache and flushing are common with phosphodiesterase 5 inhibitors (2%-11%), few patients with LUTS discontinue tadalafil alone or in combination with α -blockers due to adverse effects.⁵⁶ Use of tadalafil is contraindicated for patients taking nitrate medications (eg, nitroglycerin, isosorbide mononitrate). Tadalafil may reduce postvoid urine dribbling and provide an alternative to α -blockade when it causes adverse effects, such as dizziness or fatigue.⁵⁷

Anticholinergic Medications

Anticholinergic medications (eg, trospium) inhibit parasympathetic muscarinic signaling, relaxing the bladder detrusor and increasing bladder compliance (Table 1).^{15,28,29} All anticholinergic medications for LUTS have similar efficacy (reduction in frequency by 2-4 voids per day and reduction in incontinence episodes by 10-20 per week) and are associated with dry mouth, dry eyes, and mild constipation (up to 70%).²⁹ Recently, risk for dementia has been associated with long-term use of anticholinergics (>365 days) (odds ratio, 1.50; 95% CI, 1.22-1.85).⁵⁸ Specifically among patients with OAB, 7 observational studies that included 4542 to 71 668 participants reported that anticholinergics were associated with increased risk for dementia by 10% to 65%.⁵⁹⁻⁶² For example, a case-control study including 25 642 patients taking anticholinergics for OAB reported an odds ratio of 1.65 (95% CI, 1.56-1.75), with bladder anticholinergics having been prescribed to 11.7% of patients with dementia and 8.3% of controls.⁶¹ However, a retrospective propensity-matched cohort study with 782 matched pairs showed no association of anticholinergic medication use with cognitive decline. Thus, the risk of dementia associated with anticholinergic medications remains controversial, and further study of this association is warranted.⁶³ The risk of urinary retention with anticholinergic medications is low (\approx 1%), but these medications should be used with caution for patients with incomplete bladder emptying (postvoid residual volume >150 mL).⁶⁴ Anticholinergic therapy may exacerbate narrow-angle glaucoma and should be avoided for patients with this condition.

β_3 Agonists

β_3 -Adrenergic agonism in the detrusor promotes bladder relaxation, improves nocturia, and increases functional bladder capacity (volume at the end of bladder filling, typically 300-400 mL in healthy adults).⁶⁵⁻⁶⁷ The efficacy of β_3 agonists mirabegron and vibegron is similar to that of anticholinergics, reducing frequency by approximately 2 voids per day. Adverse effects include mild increases in systolic blood pressure by 3 to 10 mm Hg for doses 50 to 200 mg, urinary tract infection, headache, and nasopharyngitis (2%-11%) (Table 1). β_3 Agonists are an alternative therapy for OAB when anticholinergics are contraindicated or not tolerated. If OAB symptoms do not respond adequately to anticholinergic and β_3 agonist medications, neuromodulation therapies, such as posterior tibial nerve stimulation of the sacral nerve plexus, can be effective.⁶⁸

Combination Pharmacologic Therapy

Combination medication therapy can improve IPSS by an additional 1 to 3 points compared with monotherapy, but combination

therapy is associated with greater costs and potential for increased adverse effects. Combining an α -blocker (tamsulosin) with 5-ARIs (finasteride),^{69,70} tadalafil,^{71,72} anticholinergics (trospium), and β_3 agonists (mirabegron)⁷³ is safe and effective (eTable in Supplement 1). Combining tadalafil with a β_3 agonist (mirabegron) can reduce LUTS.^{74,75} Men with erectile dysfunction may benefit from combinations that include a phosphodiesterase 5 inhibitor; those with irritative symptoms may benefit from addition of an anticholinergic or β_3 agonist. If adding a second or third agent does not meaningfully improve symptoms or results in intolerable adverse effects, they may be discontinued. When a 5-ARI and α -blocker are taken in combination for at least 3 to 6 months, symptoms continue to be controlled in approximately 70% of patients even if the α -blocker is discontinued, and patients can continue taking the 5-ARI alone.⁷⁶ In older men (>65 years) who are taking medications for multiple chronic conditions, risks associated with polypharmacy should be considered when adding a second or third medication for LUTS.

Referral to Urology for Surgical Management

Surgery for LUTS is reserved for men who have bothersome symptoms despite medical therapy, urinary retention, recurrent urinary tract infections related to incomplete bladder emptying, bladder stones, or kidney deterioration, defined as glomerular filtration rate less than 60 for at least 3 months.⁷⁹ Using claims data, the Urologic Diseases in America Compendium documented that 1.7% of men aged 40 to 64 years and 2.4% of men older than 65 years underwent a BPH- and LUTS-related procedure between 2012 and 2021.¹⁹ Although these procedures are performed by urologists, familiarity with these treatments helps primary care clinicians to counsel patients about potentially appropriate procedures.

Surgeries for BPH are performed under regional or general anesthesia in the operating room and require a short hospitalization and catheter duration of less than 24 hours. Surgical therapies include transurethral resection of the prostate, holmium laser enucleation of the prostate (transurethral endoscopic removal of BPH tissue using laser), laser photovaporization (transurethral endoscopic resection of BPH tissue using laser), robotic water-jet ablation therapy (robotically guided, endoscopic application of high-pressure water jet to resect BPH tissue), and simple prostatectomy (Table 2).⁷⁷⁻¹⁰⁰ Surgery for LUTS improves symptoms more than behavioral and pharmacologic therapy (mean IPSS improvement, 12-15 points) (Table 2). However, surgery is associated with a higher risk of adverse effects, including incontinence (0%-20%), erectile dysfunction (0%-20%), and retrograde ejaculation (7%-92%) (Table 2).

Minimally invasive surgical therapies, commonly performed in an ambulatory surgical center or office setting with local analgesia and mild sedation, include prostatic urethral lift, water vapor thermotherapy, temporary implantable nitinol device, and prostatic artery embolization. Minimally invasive surgical therapies have efficacy comparable to surgery (mean IPSS improvement, 9-14 points) but have less effect on urinary flow improvement as measured by peak flow rate (3.7-8.4 mL/s for minimally invasive surgical therapy vs 6.3-22 mL/s for surgery) (Table 2) and are associated with higher rates of needing retreatment with a different procedure.^{77,101} However, compared with surgery, minimally invasive surgical therapies have fewer adverse effects (urinary incontinence, 0%-8%; erectile dysfunction, 0%-3%; and retrograde ejaculation, 0%-3%) (Table 2;

Table 2. Surgical Therapy and Minimally Invasive Surgical Therapy

| Procedure | Description | Prostate size appropriate for the procedure ^a | Efficacy | | | Adverse effects, % | | |
|---|---|--|--------------------------------------|--|--|------------------------|------------------------------------|---|
| | | | Reported change in IPSS ^b | Change in maximum urinary flow rate (mL/s) | Proportion requiring surgical retreatment, % ⁷⁷ | Incontinence at 0-3 mo | Erectile dysfunction ⁷⁸ | Retrograde ejaculation ^{78,79} |
| Surgery | | | | | | | | |
| Transurethral resection of the prostate ⁸⁰ | Endoscopic resection of BPH tissue using electrocautery | <80 g | −15.1 at 12 mo, −13.2 at 60 mo | +10.6 at 12 mo, +6.3 at 60 mo | 5 at 24 mo, 7.7 at 60 mo | 0-5 | 14 | 60-75 |
| Holmium laser enucleation of the prostate ⁸¹⁻⁸³ | Endoscopic removal of BPH tissue using laser | Any size | −12.0 at 12 mo, −14.4 at 60 mo | +14.0 at 12 mo, +15.7 at 60 mo | 3.3 at 24 mo, 6.6 at 60 mo | 0-3 | 5-10 | 78-92 |
| Simple prostatectomy ⁸⁴⁻⁸⁷ | Open or robotic transabdominal removal of BPH tissue | Large or very large, typically considered >80 g | −14 to −22 at 8-40 mo | +12 to +22 at 8-40 mo | 1.3 at 12 mo, 4.4 at 60 mo | 0-20 | 3-5 | 80-90 |
| Robotic water-jet ablation therapy (aquablation) ^{88,89} | Robotically guided, endoscopic application of high-pressure water jet to resect BPH tissue | 30-80 g | −15.1 at 12 mo, −15.1 at 60 mo | +10.3 at 12 mo, +8.7 at 60 mo | 3.1 at 24 mo, 4.1 at 60 mo | 0 | 0 | 7-10 |
| Transurethral incision of the prostate ^{90,91} | Endoscopic incision of the bladder neck | ≤30 g | −12.7 at 48 mo | +8.2 at 48 mo | 13 at 60 mo | 0-2 | 8 | 22 |
| Laser photovaporization of the prostate ⁹² | Endoscopic resection of BPH tissue using laser | Any size (<100 g in some studies) | −14.3 at 24 mo | +12.1 at 24 mo | 7.1 at 60 mo | 10 | 0-20 | 20-50 |
| Minimally invasive surgical therapy | | | | | | | | |
| Water vapor therapy ^{93,94} | Endoscopic injection of steam into BPH tissue | 30-80 g | −11.3 at 3 mo, −11.1 at 60 mo | +5.6 at 12 mo, +4.1 at 60 mo | 1-3.4 at 12 mo, 4.4-7.5 at 60 mo | 0-4 | 0-3 | 0-3 |
| Prostatic urethral lift ⁹⁵ | Endoscopic insertion of nonabsorbable suture implants that mechanically open the urethra | <80-100 g | −11.0 at 1 mo, −9.7 at 24 mo | +4.3 at 1 mo, +3.7 at 24 mo | 4-19 at 24 mo | 0-8 | 0 | 0 |
| Temporary implantable nitinol device ⁹⁶⁻⁹⁸ | Endoscopically placed, temporary metallic wire device that passively reshapes prostatic urethra | <75 g | −10.5 at 1 mo, −12.0 at 24 mo | +3.9 at 1 mo, +8.4 at 24 mo | 10 at 24 mo | 0-3 | 0 | 0 |
| Prostatic artery embolization ^{99,100} | Embolization of prostatic blood supply performed by interventional radiology | Any size | −11.6 at 1 mo, −14.5 at 12-36 mo | +6.1 at 1 mo, +4.1 at 12-36 mo | 13-21 at 24 mo | 0 | 0 | 0-1 |

Abbreviations: BPH, benign prostatic hyperplasia; IPSS, International Prostate Symptom Score.

^b See Evaluation of Symptoms section for details on IPSS.

^a Normal or physiologic prostate size is less than or equal to 30 g.

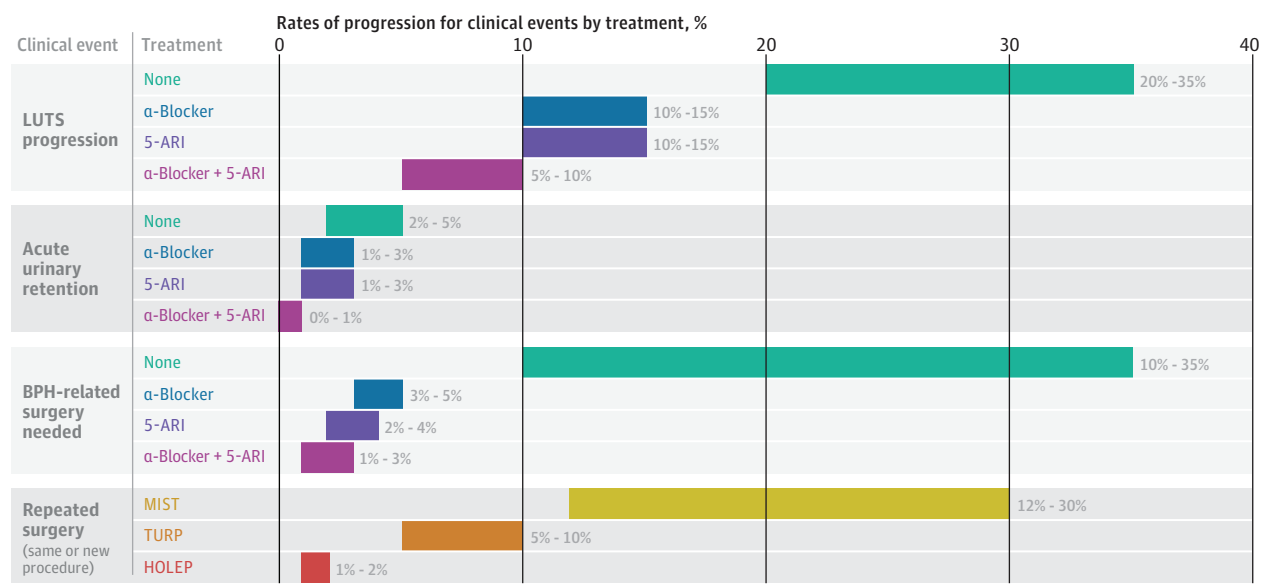
eAppendix in [Supplement 1](#)).¹⁰² Surgery and minimally invasive surgical therapies primarily alleviate bladder outlet obstruction; patients with persistent irritative symptoms may still require treatment of OAB after surgery.²⁹

Prognosis

Several large studies have documented the natural history of untreated BPH and LUTS.¹⁰³⁻¹⁰⁶ Overall clinical progression has been defined as an increase in IPSS by at least 4 points or progression into the severe range (IPSS >20), recurrent urinary tract infections, bladder stones, new incontinence, kidney insufficiency, or acute urinary retention. Untreated, 20% to 35% of men with BPH or LUTS

experience clinical progression during 4 years ([Figure 3](#)). Risk factors associated with progression are older age, severe LUTS at presentation, low maximum urinary flow rate, high postvoid residual volume, large prostate volume, and high prostate-specific antigen level.^{107,108} In a prospective questionnaire study that included 25 879 men with IPSS 0 to 7, 36% progressed to moderate or worsening LUTS, 10% initiated pharmacotherapy, and 15% underwent surgery during 6 years of follow-up.¹⁰⁴ In a study that randomized 556 male veterans with moderate BPH symptoms to transurethral resection of the prostate vs watchful waiting, 36% in the untreated cohort underwent transurethral resection of the prostate during 5 years of follow-up.¹⁰⁵

Figure 3. Prognosis of Untreated and Treated Male Lower Urinary Tract Symptoms



ARI indicates α -reductase inhibitor; BPH, benign prostatic hyperplasia; HOLEP, holmium laser enucleation of the prostate; LUTS, lower urinary tract symptoms; MIST, minimally invasive surgical therapy; and TURP, transurethral resection of the prostate.

Several large studies have demonstrated that α -blockers and 5-ARIs decreased the rate of clinical progression, risk of acute urinary retention, and need for surgery compared with watchful waiting.^{107,109-113} Combining an α -blocker and 5-ARI decreased each of these outcomes more than either monotherapy alone (Figure 3).^{107,113} In a trial of 3047 men aged 50 years or older with IPSS 8 to 30 and without prior therapy for LUTS, doxazosin reduced clinical progression by 39% (progression rate, 4.5-2.7 per 100 person-years), finasteride by 34% (progression rate, 4.5-2.9 per 100 person-years), and the combination by 66% (progression rate, 4.5-1.5 per 100 person-years) compared with placebo during a mean follow-up of 4.5 years. Compared with placebo, finasteride and the combination of doxazosin-finasteride reduced acute urinary retention by 68% (0.6-0.2 per 100 person-years) and 81% (0.6-0.1 per 100 person-years), respectively, during a mean follow-up of 4.5 years.¹⁰⁹ A trial of 1522 men aged 55 years or older with IPSS at least 13 reported that, compared with placebo, alfuzosin decreased symptom deterioration (11.7% vs 16.8%), overall clinical progression (16.3% vs 22.1%), and surgery (5.1% vs 6.5%) at 2-year follow-up and had no effect on acute urinary retention.¹¹⁰ A study of 4844 men aged 50 years or older with IPSS at least 12 showed that dutasteride plus tamsulosin compared with tamsulosin alone reduced the relative risk of acute urinary retention by 67.6% (6.8% vs 2.2%) and surgery by 70.6% (7.8% vs 2.4%); and compared with dutasteride alone, by 18.3% (2.7% vs 2.2%) and 31.1% (3.5% vs 2.4%) at 4-year follow-up.¹¹² On average, α -blockade combined with 5 α -reductase inhibition lowers progression risk to less than 10% compared with 10% to 15% with monotherapy. The proportion of patients requiring reoperation is approximately 3.4% to 21% after minimally invasive surgical therapy, 5% after transurethral resection of the prostate, and 3.3% after holmium laser enucleation of the prostate at 4 to 10 years of follow-up (Figure 3).¹¹⁴⁻¹¹⁶

Practical Considerations and Application of Evidence

For BPH and LUTS, α -blockers (tamsulosin) are often prescribed first because of their rapid onset of symptom improvement of 3 to 7 days. However, patients may not improve or may develop adverse effects, such as hypotension and dizziness, retrograde ejaculation, and erectile dysfunction. Relative to other α -blocking medications, silodosin has fewer cardiovascular adverse effects, such as dizziness, whereas alfuzosin has lower risk for retrograde ejaculation. Therapeutic properties of tadalafil, a phosphodiesterase 5 inhibitor, can treat both LUTS and erectile dysfunction. For men with prominent irritative OAB symptoms, such as frequency and urge incontinence, starting with an OAB agent (anticholinergic or β_3 agonist) may be preferred. For patients with preexisting constipation or concerns about cognitive decline, anticholinergics should be avoided and β_3 agonist medications should be selected when OAB therapy is needed because β_3 agonists are associated with a lower risk of cognitive decline than anticholinergic medications.¹¹⁷

Limitations

This review has several limitations. First, it did not evaluate the quality of the included literature. Second, not all aspects of LUTS management were discussed. Third, some relevant articles may have been missed. Fourth, this narrative focused on men and did not review the topic of LUTS among women.

Conclusions

Lower urinary tract symptoms, defined as urinary urgency, nocturia, or weak stream, are common symptoms among men and are usually caused by BPH or OAB. First-line therapy consists of behavioral intervention, such as pelvic floor physical therapy and timed voiding,

as well as pharmacologic therapy, including α -adrenergic blockers (eg, tamsulosin), 5-ARIs (eg, finasteride), phosphodiesterase inhibitors (eg, tadalafil), anticholinergics (eg, trospium), and β_3 agonists (eg, mirabegron).

ARTICLE INFORMATION

Accepted for Publication: April 21, 2025.

Published Online: July 14, 2025.
doi:10.1001/jama.2025.7045

Conflict of Interest Disclosures: Dr Daw reported consulting fees from Boston Scientific, Cook, Ethicon, and Storz; and grants from Blue Cross Blue Shield of Michigan and the Patient-Centered Outcomes Research Institute outside the submitted work. No other disclosures were reported.

Submissions: We encourage authors to submit papers for consideration as a Review. Please contact Kristin Walter, MD, at kristin.walter@jamanetwork.org.

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