

A practical approach to the management of lower urinary tract symptoms among men

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Lower urinary tract symptoms (LUTS) are common among Australian men, with prevalence of one or more symptoms increasing from less than 20% among men aged under 45 years to 48% of men aged 65–79 years¹ and 70% of men aged 80 years and over.² Not all men with LUTS have benign prostatic hyperplasia (BPH), and not all men with BPH have LUTS.³ Additionally, symptoms caused by BPH can be difficult to distinguish from those resulting from an overactive bladder (OAB).

There are no up-to-date peer-reviewed guidelines that address this issue in the Australian context. This clinical update was produced by collaboration between five Australian clinicians, with general practitioner and urologist representation. It aims to provide primary care practitioners with a practical, evidence-based approach to the diagnosis and management of these two common conditions.

A practical approach to diagnosis

Most men with LUTS will have either BPH or OAB, or both.⁴ As BPH can be difficult to distinguish from OAB, it may be more practical to determine whether (a) either BPH or OAB is likely or (b) neither are probable, as patients with BPH and OAB can often be managed in the primary care setting, whereas those with uncertain or other diagnoses may require referral to a urologist.

OAB is characterised by urinary frequency, urgency and nocturia,⁵ whereas patients with BPH may present with any combination of voiding, storage (usually most bothersome) or post-micturition symptoms (Box 1).⁶

Symptom severity

The International Prostate Symptom Score (IPSS) (Box 2) is a validated tool that is used to help determine need for therapy and monitor treatment response. The IPSS ranks symptoms as mild (IPSS 0–7), moderate (8–18) or severe (19–35), and impact on quality of life is rated from 0 (best) to 6 (worst). Although symptom scoring systems are underused in general practice,⁷ use of the IPSS is encouraged. The IPSS is not a reliable diagnostic tool for LUTS, but serves as a measure of LUTS after the diagnosis is established.

Other contributing factors

Some medical conditions (eg, diabetes mellitus and heart failure) and medications (eg, diuretics, phenothiazines, antidepressants and β -agonists) may exacerbate or cause LUTS, as can alcohol and caffeine use. Management of medical comorbidity should be optimised and alcohol and caffeine consumption minimised. Patients with bothersome LUTS and a history of urogenital surgery or trauma should be referred to a urologist.

Digital rectal examination

All men with LUTS should undergo digital rectal examination (DRE) during their initial examination to assess prostate size and examine for abnormalities that may suggest prostate cancer.

ABSTRACT

- Lower urinary tract symptoms (LUTS) are common among Australian men over the age of 45 years; most men with LUTS will have benign prostatic hyperplasia (BPH), overactive bladder (OAB), or both.
- The cause of LUTS should be diagnosed by assessing symptom severity and excluding of medical or pharmaceutical causes. All men with LUTS should undergo digital rectal examination; other diagnostic tools include urine and blood testing, voiding charts and imaging.
- Depending on disease severity, impact on quality of life, patient preference, presence of complications and fitness for surgery, BPH is managed with watchful waiting, pharmacotherapy (α -blockers or 5- α -reductase inhibitors), minimally invasive surgical therapies or surgery.
- OAB is initially treated with behavioural therapy; if this is ineffective, pharmacotherapy (usually antimuscarinics) can be used.
- Patients with LUTS with a provisional diagnosis other than BPH or OAB, or with complications or poor response to pharmacotherapy, should be referred to a urologist.

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1 Symptoms suggestive of benign prostatic hyperplasia or overactive bladder⁶

Voiding symptoms

- Weak stream
- Hesitancy
- Intermittency
- Abdominal straining
- Incomplete bladder emptying

Storage symptoms

- Frequency (by day and night)
- Nocturia
- Urgency
- Urinary incontinence

Postmicturition symptoms

- Sensation of incomplete bladder emptying ◆

Abnormalities of the urethral meatus should be excluded. DRE should be repeated if symptoms significantly change or complications develop.

Clinical investigations

Box 3 summarises the investigations recommended for men who present with LUTS. Prostate-specific antigen (PSA) testing should only be considered to support differential diagnosis (to exclude advanced prostate cancer among older men with symptoms of bladder overflow

2 The International Prostate Symptom Score (IPSS)

	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always	Score
Incomplete emptying: over the past month, how often have you had a sensation of not emptying your bladder completely after you finish urinating?	0	1	2	3	4	5	
Frequency: over the past month, how often have you had to urinate again less than two hours after you finished urinating?	0	1	2	3	4	5	
Intermittency: over the past month, how often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
Urgency: over the last month, how difficult have you found it to postpone urination?	0	1	2	3	4	5	
Weak stream: over the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5	
Straining: over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5	
Nocturia	None	Once	Twice	Three times	Four times	≥ 5 times	Score
Over the past month, how many times did you most typically get up to urinate from the time you went to bed until the time you got up in the morning?	0	1	2	3	4	5	
Total IPSS							
Quality of life (QOL) due to urinary symptoms				Mixed: about equally satisfied and dissatisfied			
	Delighted	Pleased	Mostly satisfied		Mostly dissatisfied	Unhappy	Terrible
If you were to spend the rest of your life with your urinary condition the way it is now, how would you feel about that?	0	1	2	3	4	5	6
Total IPSS (including QOL score)							
(0–7, mildly symptomatic; 8–19, moderately symptomatic; 20–35 severely symptomatic)							

obstruction), treatment decisions and monitoring (when managed with watchful waiting or 5- α -reductase inhibitors [5ARIs]).

Disease progression

Although most patients with LUTS due to BPH remain clinically stable in the short-to-medium term,⁸ BPH is a progressive condition and, over time, patients are at increasing risk of symptom deterioration, acute urinary retention and the need for surgical intervention.⁹ Risk factors for symptom progression should be considered, as they influence treatment choice (Box 4).

Urologist referral

The initial approach to a man presenting with LUTS should be to determine whether BPH, OAB or neither is likely (Box 5). Patients with provisional diagnoses other than BPH or OAB should be considered for referral, as should those with disease complications. Patients with a provisional diagnosis of BPH can be treated initially for BPH; if symptoms do not improve, a trial of OAB therapy should be considered. A corresponding approach is applied to patients with a provisional diagnosis of OAB. We recommend that patients whose conditions fail to respond to both BPH and OAB therapy are referred to a urologist. Other indications for referral are summarised in Box 6.

A practical approach to treatment of benign prostatic hyperplasia

There are four types of treatment available for BPH — watchful waiting, pharmacotherapy, minimally invasive surgical therapies (MISTs) and surgery. Selection depends on disease severity, impact on quality of life, patient preference, presence of complications and fitness for surgery.¹¹

Watchful waiting

Watchful waiting is the monitoring of a patient without medical or surgical intervention; it generally entails education, reassurance, periodic review and lifestyle advice.⁸ Its rationale is that BPH, left untreated, does not clinically progress in most men with LUTS (about 85% have stable disease 4 years after diagnosis) and few develop urinary retention or other complications.⁹ Watchful waiting is generally recommended for men with mild-to-moderate symptoms whose quality of life is not impaired and who have no disease complications.

Patients should be reviewed annually. They should be warned of the small risk of developing urinary tract infection, urinary retention, haematuria, bladder calculi and bladder and upper urinary tract dysfunction, and advised to re-present if haematuria occurs or their symptoms worsen.

Pharmacotherapy

There are two classes of medications for BPH — α -blockers and 5ARIs.¹¹ α -Blockers can provide prompt symptom relief but do not prevent disease progression, whereas 5ARIs slow disease progression but may take up to 6 months to alleviate symptoms. Treatment choice depends primarily on prostate size (as estimated

by DRE and/or PSA level), impact on quality of life, likelihood of progression and affordability (Box 7).

α -Blockers

α -Blockers are the main pharmacological treatment for LUTS due to BPH. They act by blocking α_1 -adrenoceptors in the prostate, with consequent reduction of smooth muscle tone.¹³ There are three known subtypes of α_1 -receptors — α_{1A} is predominately expressed in the prostate, α_{1B} in vascular tissue and α_{1D} in the bladder.¹³ Of the four available α_1 -blockers, tamsulosin demonstrates selective affinity for α_{1A} and α_{1D} receptors; alfuzosin, prazosin and terazosin show equal affinity for all α_1 -receptor subtypes.¹³ Alfuzosin has selective tissue distribution to the prostate. Prazosin has a less favourable side-effect profile than the other medications and requires multiple daily dosing; it is consequently not recommended by overseas BPH guidelines.^{8,14-16}

A comprehensive review of studies comparing α_1 -blockers concluded that alfuzosin, tamsulosin and terazosin have comparable efficacy with regard to mean improvement in symptom score (30%–45%) and maximal urinary flow rate (15%–30%).¹³ Alfuzosin and tamsulosin are considered to be better tolerated than terazosin, with fewer cardiovascular adverse effects (dizziness and orthostatic hypotension) and lower rates of treatment discontinuation.¹³ Other common adverse effects of α -blockers include headaches, asthenia, drowsiness and nasal congestion, although prevalence is similar to placebo.⁸

With regard to sexual function, abnormal ejaculation is mainly associated with tamsulosin use (incidence, 4%–5%)¹³ but not with alfuzosin.

3 Investigations recommended for men presenting with lower urinary tract symptoms

Urinalysis and urine microscopy

- To exclude urinary tract infection and haematuria

Blood tests

- Blood glucose level to screen for diabetes mellitus
- Creatinine level to exclude renal impairment
- Prostate-specific antigen level to support differential diagnosis (ie, to exclude advanced prostate cancer among older men with bladder overflow obstruction) and treatment decisions, and to monitor response to therapy (watchful waiting or 5- α -reductase inhibitor use)

Voiding chart

- Involves the recording of date, time of day and night, volume voided and fluid intake over at least 3 days
- Helps exclude polyuria, which may be misinterpreted as increased frequency, and conditions associated with nocturnal diuresis (eg, heart failure)

Imaging

- Postvoid residual (PVR) ultrasound
- PVR volume > 50 mL has been associated with a higher risk of disease progression in controlled clinical trials; however, PVR may be influenced by voided volume and test conditions. For practical purposes, urology referral should be considered for patients with PVR > 250 mL

Optional

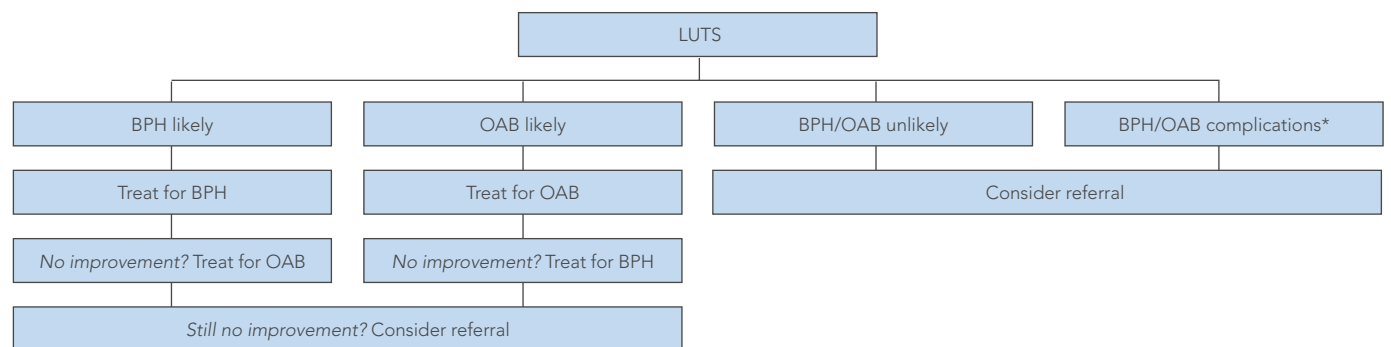
- Urinary tract ultrasound*
- Uroflowmetry*
- Pressure flow urodynamic study
- Cystoscopy

*Urinary tract ultrasound and uroflowmetry are non-invasive and easily repeated; they are generally preferred over pressure flow urodynamic study and cystoscopy, which are usually arranged after urology review. ◆

4 Risk factors for progression of benign prostatic hyperplasia

- Age > 70 years¹⁰
- Increased prostate-specific antigen level (≥ 1.5 ng/mL)¹⁰
- Enlarged prostate (> 30 mL)⁹
- Severity of lower urinary tract symptoms or worsening of symptoms over time⁹
- Poor urinary flow rate⁹
- Postvoid residual volume > 50 mL
- Failure to respond to medical therapy
- Previous episode of acute urinary retention ◆

5 Management of LUTS in men



LUTS = lower urinary tract symptoms. BPH = benign prostatic hyperplasia. OAB = overactive bladder. *BPH and OAB complications include urinary retention, benign prostatic bleeding and urinary tract infection. A history of haematuria always warrants investigation and referral, regardless of the number of episodes and whether it has resolved. ◆

Patients taking α -blockers should be reviewed 1 month and 6 months after initiation of therapy. Prazosin and terazosin require dose titration, whereas alfuzosin and tamsulosin are commenced at full therapeutic dose.¹⁷ Postural blood pressure changes should be monitored upon initiation and dose titration, with caution exercised in patients using concurrent hypotensive therapy. For the one-third of men who do not experience significant symptom reduction with α_1 -blockers, treatment should be ceased after 1 month.⁸

5- α -reductase inhibitors

5ARIs are recommended for use by men with large prostates (> 30 mL)¹⁸ or PSA levels \geq 1.4 ng/mL.¹⁹ By preventing conversion of testosterone to dihydrotestosterone, they reduce prostatic volume by 18% to 30% and result in decreased risk of clinical progression, acute urinary retention and surgical intervention.¹⁹ 5ARIs are less effective than α_1 -blockers at improving IPSS score (15% v 30%–45%, respectively) and urinary flow rate. Sympto-

matic benefit can take over 3–6 months of treatment. Accordingly, patients with large prostates and bothersome symptoms requiring prompt relief may benefit from combined therapy.

Dutasteride and finasteride are available in Australia.²⁰ Both are similarly efficacious in terms of symptom score and urinary flow rate improvement, with comparable tolerability. Adverse events associated with finasteride include decreased libido (6.4%), impotence (8.1%), decreased ejaculate (3.7%) and uncommonly (< 1%) rash, breast enlargement and breast tenderness.⁸ Long-term treatment with finasteride reduces PSA; PSA should be multiplied by 2.0 after 1–2 years of treatment, by 2.3 after 2–7 years of treatment and by 2.5 thereafter to allow correct interpretation.²¹ Patients taking 5ARIs are commonly reviewed 3 and 6 months after initiation.

Combined therapy

A double-blind, randomised, parallel-group trial of 4844 men with moderate-to-severe symptoms of BPH demonstrated that the combined use of an α_1 -blocker (tamsulosin) and a 5ARI (dutasteride) conferred significant improvement in symptom score and quality of life than either drug alone ($P < 0.001$).²⁰ Significant improvements observed from 3 months were maintained for the 4-year follow-up. Recently, fixed-dose combination pills containing tamsulosin 0.4 mg and dutasteride 0.5 mg have become available at a lower cost than the combined cost of the two single agents.

These results are consistent with those of another trial that showed combination therapy conferred greater clinical benefit than single drug treatment ($P < 0.001$).⁹ Accordingly, men with enlarged prostates should be offered combination therapy after balancing costs and side-effect risks.

Herbal remedies

Saw palmetto, African plum, South African star grass, stinging nettle, and rye pollen are popular herbal remedies for LUTS in Australia. Saw palmetto is the most extensively studied; however, a

6 Indications for referral to a urologist

- Conditions other than benign prostatic hyperplasia and overactive bladder, including:
 - Suspected prostate cancer
 - Meatal stenosis
 - Potential neurological cause
- Complications of benign prostatic hyperplasia:
 - Urinary retention
 - Urinary tract infection
 - Haematuria or benign prostatic bleeding
- Uncertain diagnosis
- Symptoms impair quality of life
- Poor response to pharmacotherapy
- Prior genitourinary surgery or trauma
- Postvoid residual urine volume > 250 mL

7 Pharmacotherapy for benign prostatic hyperplasia

	α -Blockers	5- α -reductase inhibitors	Combined therapy
Ideal patient characteristics			
Prostate size	Any size	Enlarged (> 30 g)	Enlarged
Prostate-specific antigen	\leq 1.5 ng/mL	> 1.5 ng/mL	> 1.5 ng/mL
Impact on quality of life	Bothersome symptoms requiring prompt relief	Symptoms not bothersome	Bothersome symptoms requiring prompt relief
Likelihood of progression	Low	High	High
Approximate cost/month*	Prazosin, \$5.60; Others: \$50 (\$5.60 for concession card holders and those entitled to the RPBS*)	\$35–\$70 (\$5.60 if entitled to the RPBS;* \$34.20 on PBS authority — requires use in conjunction with α -blocker and initiation by urologist)	\$60–\$130 (\$11.20 if entitled to the RPBS*)
Efficacy			
IPSS improvement	30%–45%	15%	30%–45%
Effect on disease progression	Nil	Decrease risk of urinary retention and surgery and reduce prostate size by 20%–30%	Reduces clinical progression more than either drug used alone

RPBS = Repatriation Pharmaceutical Benefits Scheme. PBS = Pharmaceutical Benefits Scheme. IPSS = International Prostate Symptom Score. 5ARI = 5- α -reductase inhibitor.

* Some medications are subsidised by the Australian Government's PBS. Only one α -blocker (prazosin) is PBS listed. Only one 5ARI (dutasteride) is PBS listed but on authority restriction, but both 5ARIs and α -blockers are subsidised for war veterans under the RPBS, but only "where surgery is inappropriate, or where other drug treatment has failed or is contraindicated".¹² Accordingly, pharmacotherapy for BPH can be costly for patients and can influence treatment choice.

8 Prescribing antimuscarinic agents

Common adverse effects

- Dry mouth
- Constipation
- Sedation
- Impaired cognitive function
- Blurred vision.

Contraindications

- Narrow-angle glaucoma
- Urinary retention
- Gastric retention
- Renal impairment (use solifenacin and tolterodine with caution)
- Moderate hepatic impairment (use darifenacin, solifenacin and tolterodine with caution)
- Severe hepatic impairment (avoid use of darifenacin).

Practice points

- Darifenacin and solifenacin should be swallowed whole.

Recommended review schedule

- Four to 6 weeks

Cochrane review concluded that it confers “little or no efficacy” in the treatment of BPH symptoms.²²

There is no convincing evidence to support that herbal remedies are better than placebo for the management of LUTS.

Surgery

Surgical intervention is appropriate for patients who decline or whose conditions do not respond to pharmacotherapy and for those with BPH-related complications. Transurethral resection of the prostate (TURP) is the most common intervention and has proven efficacy and durability. Other common surgical interventions include transurethral incision of the prostate (TUIP), laser and open prostatectomy, as well as MISTs such as transurethral microwave thermotherapy, transurethral needle ablation and prostatic stenting.

As morbidity from TURP is common, laser surgery is gaining significant popularity. MISTs generally have lower morbidity, but are less effective and are characterised by a higher reoperation rate than more invasive procedures.²³ TUIP has symptomatic improvement equivalent to TURP in smaller prostates (≤ 30 mL), but higher rates of subsequent surgery.⁸ Open prostatectomy is principally considered for very large prostates. Prostatic stents are advocated only in high-risk patients due to common associated morbidity.²³

Patients should be advised that these procedures all commonly result in transient storage LUTS. Common early complications following TURP include postoperative bleeding and urinary tract infection. Early urgency incontinence is common (20%–30%) but is unlikely to persist ($<0.5\%$), and permanent ejaculatory dysfunction occurs in 53%–75% of patients.²⁴

A practical approach to treatment of overactive bladder

Patients with a postvoid residual volume >250 mL and/or poor urinary flow should be referred to a urologist; other patients can be managed in the primary care setting. Behavioural therapy as an initial approach should be discussed with all patients, with pharmacotherapy reserved for patients with bothersome symp-

9 Resources for doctors and patients

- Andrology Australia (<http://www.andrologyaustralia.org>) provides information on prostate health, including LUTS, PSA testing, BPH and prostate cancer.
- The Continence Foundation of Australia (<http://www.continence.org.au>) provides information and courses about prostate disorders and urinary incontinence, and distributes maps of public toilet locations.
- FingerTip Urology (<http://www.bjui.org/FingertipUrology.aspx>) provides illustrated slides on “Lower urinary tract symptoms in middle-aged and elderly men”. ◆

oms. Patients who fail to respond should be considered for a trial of BPH therapy and urologist referral if this is unsatisfactory.

Behavioural therapy

All patients with suspected OAB should be educated regarding bladder training.²⁵ A common approach is as follows:

- Gradually increase the time between toilet stops, aiming to reduce the number of voids per day to normal (4–6 voids/day and 1–2 voids at night).
- Upon feeling the urge to urinate, delay urination for 1 minute. Gradually increase the delay to 5 minutes. If the urge passes, don't urinate until the urge returns.
- Refrain from pre-emptive voids.

Pharmacotherapy

The abnormal and involuntary contractions of the bladder's detrusor muscle result from stimulation of muscarinic receptors; muscarinic receptor antagonists are accordingly the mainstay of pharmacotherapy. Tricyclic antidepressants (particularly imipramine) and α -blockers can be considered for patients with contraindications to antimuscarinic agents.⁵

Antimuscarinics

Five antimuscarinics are approved for OAB treatment in Australia: oxybutynin, tolterodine, propantheline (rarely prescribed), solifenacin and darifenacin.¹⁷ Oxybutynin is a relatively non-selective antimuscarinic with many years of clinical use; tolterodine is a newer agent and has a similar efficacy and adverse-effect profile. Solifenacin (a competitive, selective M_1 - and M_3 -receptor antagonist) and darifenacin (a selective M_3 -receptor antagonist) are being increasingly used due to their superior adverse effect profiles. The adverse effects of and contraindications to antimuscarinic agents are summarised in Box 8.

Conclusions

The approach to management of LUTS among men has changed significantly over the past decade. Much of this has been on the basis of improved understanding of the natural history of LUTS and clinical trials of newer therapeutic options. This process continues to evolve, and it is anticipated that further understanding of individualised risk for BPH progression will see a more tailored approach with the greater use of different combinations of drug therapy in the future. There are currently several newer pharmacological and MIST options at advanced stages of clinical trials, and it is anticipated that a significant additional number of treatment options will become available

over the next 5 to 10 years. Resources for doctors and patients are shown in Box 9.

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Competing interests

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