

THE CANADIAN JOURNAL OF  
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**The practical update  
for family physicians  
in the diagnosis  
and management  
of overactive bladder  
and lower urinary  
tract symptoms**

**Indexed in  
*Index Medicus/  
MEDLINE  
and  
Current Contents/  
Clinical Medicine***

**Volume 24  
Supplement 1  
October 2017**

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*This supplement has been graciously supported  
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## Program Title

Family Physicians in Urology OAB/LUTS Program (ID-188370).

## Program Format

Online Self-Learning.

## Learning Objectives

Upon completion of the online self-learning program, participants should be able to:

1. Recognize the quality of life impact of OAB/LUTS.
2. Review the practical diagnostic approach.
3. Differentiate and discuss pharmacological approaches to OAB/LUTS.
4. Evaluate the initial and alternative treatment options for OAB.
5. Differentiate the beneficial (efficacy) and adverse effects (safety) of antimuscarinic, beta-3 agonist in men and women as well as risks and benefits of male-LUTS therapies.
6. Review a practical OAB/LUTS algorithm with reference to the latest CUA guidelines.

## Target Audience

This online self-learning program was developed to assess and enhance the knowledge of family physicians in Canada.

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# *The practical update for family physicians in the diagnosis and management of overactive bladder and lower urinary tract symptoms*

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BARKIN J, HABERT J, WONG A, LEE LYT. The practical update for family physicians in the diagnosis and management of overactive bladder and lower urinary tract symptoms. *Can J Urol* 2017;24(Suppl 1):1-11.

**Objective:** To provide family physicians with an up-to-date, practical overview of the diagnosis and management of overactive bladder (OAB) alone or with bladder outlet obstruction.

**Main message:** OAB is urinary urgency with or without incontinence, often accompanied by frequency and nocturia, in the absence of urinary tract infection and can affect both men and women. Men often have co-existing OAB

associated with bladder outlet obstruction, and benign prostatic hyperplasia. OAB can interfere with sleep, social activities, and sexual encounters, and it increases the risk of falls.

**Conclusion:** Many patients with OAB seek initial evaluation and treatment from their family physicians. Optimal management of OAB by family physicians will improve patients' quality of life. More severe cases or "red flags" uncovered while making the diagnosis, might warrant referral to a urologist.

**Key Words:** overactive bladder, lower urinary tract symptoms, diagnosis, management

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## **Overactive bladder alone**

### **Introduction**

Overactive bladder (OAB) is urinary urgency with or without incontinence, often accompanied by frequency and nocturia, in the absence of urinary tract infection or other obvious pathology.<sup>1</sup> OAB can have significant impact on activities of daily living, recreational activities, and psychological and sexual well-being.<sup>2</sup> In the EPIC study<sup>3</sup> in which 19,000 individuals in five countries including Canada were asked about OAB in a phone survey, the overall prevalence was 11.8% (10.8% in men and 12.8% in women), and the prevalence increased with increasing age.<sup>4</sup>

The underlying mechanism of OAB is detrusor muscle overactivity. About two-thirds of patients have "dry" OAB, defined as urgency and frequency with or without nocturia, without urinary urgency incontinence, and the remaining third of patients have "wet" OAB, defined as urgency and frequency with or without nocturia, with urgency urinary incontinence.<sup>5</sup> There are two types of incontinence. Stress urinary incontinence (SUI), also referred to as stress incontinence, is defined as the loss of urine associated with laughing, coughing, lifting, straining, jumping, or other physical activity. Urgency urinary incontinence (UUI) is defined as the sudden desire to void, which cannot be consciously suppressed and results in the loss of a small amount of urine. If a patient has both SUI and UUI, he or she is termed to have "mixed urinary incontinence."

Men often have co-existing bladder outlet obstruction due to benign prostatic hyperplasia (BPH), and OAB.<sup>2</sup> Up to 50% of men with bladder outlet obstruction have

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This article has been peer reviewed

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concurrent OAB.<sup>6</sup> According to the National Overactive Bladder Evaluation (NOBLE) study,<sup>7</sup> UUI may be less prevalent in men. However, the overall prevalence of OAB symptoms is similar in men and women.

OAB can have a significant negative impact on quality of life, by interfering with sleep, social activities, and sexual function, increasing the risks of falls, and financial burden for diapers, laundry and pads. However, a recent study reported that only about half of family physicians (54%) regularly initiated a discussion about urgency incontinence in patients with suspected OAB; 30% discussed OAB with some patients; and 15% of the physicians only discussed urgency incontinence if a patient asked about it.<sup>8</sup>

## Diagnosis and work up

OAB is diagnosed with a pertinent patient history and physical examination.

### Urological history

The family physician should ask the patient about the following topics.

#### 1. *The presence or absence of OAB and lower urinary tract symptoms (LUTS)*

Guidelines recommend using validated questionnaires such as the Overactive Bladder Questionnaire (OAB-q), the Overactive Bladder Satisfaction Questionnaire (OAB-S), and the Urogenital Distress Inventory (UDI).

The AUA–International Prostate Symptom Score may be helpful in assessing concurrent BPH/bladder outlet obstruction symptoms in men.

Table 1 presents some simpler questions that the clinician may use to determine the presence or absence of OAB/LUTS.<sup>9</sup>

#### 2. *The presence or absence of dysuria and hematuria*

The presence of dysuria or hematuria may signal a urinary tract infection (UTI), bladder stone, upper tract urolithiasis, or malignancy. A UTI may exhibit overlapping symptoms with OAB. Frequency, urgency and pain along with negative urine culture may indicate interstitial cystitis. When the patient has gross hematuria or significant microscopic hematuria (> 3 RBC/HPF)<sup>10</sup> but no UTI, the family physician should request a urine cytological examination and consider urinary tract imaging with ultrasound or CT scan. He or she should refer a patient who has a positive finding on a cytological exam or imaging or in the setting of persistent hematuria to a urologist for further assessment. Patients who are also elderly and have risk factors such as a history of smoking should also undergo cystoscopy.

#### 3. *Fluid intake, type of fluids*

This may be determined by having the patient fill out a voiding diary. Fluid intake can affect bladder function. Inadequate or excessive fluid intake can worsen urinary symptoms. Caffeinated, acidic or alcoholic beverages may worsen urinary urgency or frequency symptoms.<sup>11</sup>

TABLE 1. Questions to diagnose overactive bladder (OAB)<sup>9</sup>

Question	Diagnosis if reply is positive
Do you get sudden urges to go to the bathroom that are so strong you cannot ignore them?	OAB
How often do you go to the bathroom? Is it more than 8 times in a 24 hour period?	OAB
Do you have uncontrollable urges to urinate, which sometimes lead to wetting accidents?	Urge incontinence
Do you leak urine on the way to the bathroom?	Urge incontinence
Do you get up two or more times during the night to go to the bathroom, and void small volumes?	OAB
Do you avoid places or activities if you cannot be sure that there is a bathroom nearby?	OAB
When in an unfamiliar place, do you automatically look for the nearest bathroom?	OAB
Do you leak urine when you laugh, sneeze, or lift something?	Stress incontinence
Do you use absorbent pads to keep from wetting your clothes?	Stress or urge incontinence
Do you have slow stream, hesitancy, dribbling, or (for men) spraying?	Bladder outlet obstruction

#### 4. Consumption of spicy foods and smoking

Both of which are irritants to the bladder.

#### 5. Neurologic disease, psychiatric disorders

Neurological disease such as stroke, Parkinson disease, multiple sclerosis, and spinal cord injury may produce or worsen symptoms of OAB. Psychiatric disorders along with psychotropic drugs can impact voiding.<sup>12</sup>

#### 6. Obstetric and gynecological history in women

Women with previous obstetric or gynecological surgery or pelvic radiotherapy may have bowel symptoms, constipation, or OAB. Pelvic floor prolapse can cause symptoms that are similar to those due to OAB.

#### 7. Medication use

Medications that can affect bladder function include angiotensin-converting enzyme (ACE) inhibitors (which can cause coughing and stress incontinence), alpha blockers or stimulants, antihistamines, antidepressants, antipsychotics, anticholinergics, beta antagonists (such as metoprolol), diuretics, opioids, and sedatives.

#### 8. Other medical issues

Previous surgery and radiation can induce symptoms of OAB. Narrow-angle glaucoma, uncontrolled hypertension, and cognitive impairment can limit OAB treatment options.

#### 9. Comorbidities

Obesity, type 2 diabetes, and chronic UTIs can increase urinary frequency and urgency.

### Physical examination

#### *In women*

A physical examination of a woman with suspected OAB should include an abdominal examination to look for bladder distension and a pelvic examination to look for vaginal prolapse, urethral irritation, or atrophic vaginitis. Women with vaginal atrophy who receive oral or topical hormone replacement therapy may or may not have reduced frequency of urge incontinence and recurrent UTIs.<sup>13</sup>

#### *In men*

A physical examination of a man with suspected OAB should include an abdominal examination to rule out a distended bladder, an examination of the urethral meatus and foreskin tightness to ensure there is no obstruction, and a digital rectal examination (DRE) to rule out a grossly enlarged benign prostate or possible prostate cancer.

### Interventions

#### *Voiding diary*

This may be helpful to assess fluid intake and voiding volumes, and it may also be useful to assess response to treatment. This daily diary tracks what the patient drinks including volume, and any activity that might cause leakage.

#### *Urinalysis and culture*

A urinalysis is recommended for all patients who have symptoms of OAB, and it can reveal bacteria, hematuria, pyuria, proteinuria, or glycosuria. A urine culture, if indicated from the urinalysis, will identify the type of bacteria in a UTI. Patients with OAB and a UTI should be treated with an antibiotic. Elderly patients or those with a chronic catheter may have asymptomatic bacteriuria, which usually does not require treatment. Pregnant women or patients who are about to have urologic surgery should be treated with antibiotics. If a patient has significant microscopic hematuria, he or she should have a urine cytology test, to look for cancer cells.

#### *Ultrasound and post-void residual volume*

If the clinician is not sure if a patient is retaining urine, then a non-volume loaded pre-and post-void ultrasound is appropriate. In the typical protocol for a pelvic ultrasound, the patient is instructed to drink a large amount of fluid, that overly stretches the bladder such that the post-void residual volume (PVR) volume is often falsely elevated. This can be avoided by doing a pre-void ultrasound without instructing the patient to drink copious amounts of water before the bladder volume measurement and then doing a post-void bladder ultrasound.

If a patient has PVR > 150 cc, then he or she should be referred to a urologist. In a Dutch study of 50 to 75-year-old men, 83% had PVR < 50 cc, 9% had PVR between 50 cc and 100 cc, and only 8% had a PVR > 100 cc.<sup>14</sup>

#### *Abdominal and pelvic (kidney, ureter, and bladder) ultrasound*

If a patient has significant microscopic or gross hematuria, a family physician should refer the patient to a urologist and can request an ultrasound at the same time.

#### *Cystoscopy and urodynamic assessment*

This would only be done by a urologist, if a patient has not responded to treatment suggested by the family physician.

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## Treatments

### Behavioral therapies

Behavioral therapies are recommended as the initial treatment for OAB. These therapies are noninvasive and reversible, but require time and effort by the patient.

The 2017 Canadian Urological Association (CUA) guideline on adult on overactive bladder<sup>2</sup> classifies the therapies as having Grade A, B, or C level of evidence, based on the Oxford Grading system.<sup>15</sup> The guideline lists the following types of behavioral therapies for OAB:

- *Bladder training.* Timed voiding and delayed voiding are used to change the patient's voiding pattern and increase voiding intervals. (Grade A)
- *Pelvic floor muscle training.* This includes biofeedback, urge control strategies, and urge suppression. (Grade B)
- *Weight loss.* This can decrease urgency incontinence by 42% compared to 26% in a control group. (Grade A)
- *Decrease fluid intake by 25%.* (Grade B)
- *Treat constipation. Increase fiber intake.* (Grade B)
- *Stop smoking.* (Grade C)
- *Reduce or stop consuming caffeine and alcohol.* (Grade B)

Table 2 also summarizes behavioral therapies for OAB.

Family physicians need to counsel patients about behavioral changes to improve OAB symptoms.<sup>16</sup> If patients can successfully make these changes, OAB can be significantly improved, and many patients will not require pharmacotherapy. This is especially important for elderly patients, since they might have comorbidities and/or be taking multiple drugs making them more susceptible to the side effects from medical therapies for OAB.

#### Fluid intake

Most patients do not know that the optimal amount of total daily fluid intake is about 1500 cc. Some patients report that they need to “flush out their kidneys” with multiple liters of fluid daily. Others may not realize that fruits and vegetables contain a lot of water or that that

drinking a lot of fluid at night after supper increases the likelihood of nocturia. These common misconceptions can be addressed with the proper questions and the use of voiding diaries.<sup>17</sup>

Patients who have an irritable bladder may have nocturia with small volumes of fluid, whereas patients with OAB will have nocturia with a large amount of fluid, due to absorption of excess fluid from surrounding tissues into the bladder, when the patient is lying flat in bed.

### Pharmacotherapies

OAB is a result of abnormal afferent nerve signaling to the bladder, which leads to contraction as opposed to relaxation of the bladder wall muscles. Two classes of medications are available to treat OAB: antimuscarinic (anticholinergic) agents and a beta-3 adrenoceptor agonist. The available pharmacotherapies for OAB are summarized in Table 3.

#### Antimuscarinic agents

Antimuscarinic agents that are approved in Canada to treat OAB include oxybutynin (transdermal patch, immediate release, and extended release), tolterodine (Detrol), darifenacin (Enablex), trospium (Trosec), solifenacin (Vesicare), propiverine (Mictoryl) and fesoterodine (Toviaz).

These medications decrease afferent signals to the bladder and block the M2 and M3 receptors in the bladder, which decreases detrusor overactivity. However, they also affect other muscarinic receptors throughout the body and may cause side effects of dry mouth, pruritus, dry eyes, gastrointestinal side effects (constipation), and neurologic (cognition) effects.<sup>18</sup> Antimuscarinic agents are contraindicated in patients with narrow-angle glaucoma, since they may precipitate acute angle-closure.

Earlier anticholinergic agents such as oxybutynin immediate release (IR) can be associated with significant side effects and require 3 or 4 times a day dosing.

TABLE 2. Behavioral therapies for overactive bladder (OAB)

Technique	Frequency	Urgency	UII	MUI
Fluid intake, ↓ caffeine/alcohol, bowel habits	X	X	X	X
Bladder training	X	X	X	X
Scheduled voiding		X	X	X
PFM training			X	X
Urge control techniques	X	X	X	X

MUI = mixed urinary incontinence; PFM = pelvic floor muscle; UII = urge urinary incontinence

TABLE 3. Drugs for overactive bladder (OAB) and their recommended dosages\*

Name	Available dosage forms	Typical daily dose
Darifenacin ER	7.5 mg, 15 mg tablets	7.5-15 mg daily
Fesoterodine ER	4 mg, 8 mg tablets	4-8 mg daily
Mirabegron	25 mg, 50 mg tablets	25-50 mg daily
Oxybutynin IR	2.5 mg, 5 mg tablets, 1 mg/mL syrup	5 mg bid - qid
Oxybutynin ER	5 mg, 10 mg tablets	15-30 mg daily
Oxybutynin (transdermal patch)	1 patch (36 mg)	1 patch every 3-4 days
Oxybutynin (transdermal gel)	1 sachet (10% oxybutynin)	1 sachet daily
Propiverine MR	30 mg, 45 mg capsules	30-45 mg daily
Solifenacin	5 mg, 10 mg tablets	5-10 mg daily
Tolterodine	1 mg, 2 mg tablets	1-2 mg bid
Tolterodine ER	2 mg, 4 mg capsules	2-4 mg daily
Trospium	20 mg tablets	20 mg daily - bid

\*see product monograph if adjustments are necessary in the elderly or renal impaired  
ER = extended release; IR = immediate release; MR = modified release

However, most newer anticholinergic/antimuscarinic agents are taken once a day and are more selective for the M3 receptor in the bladder as opposed to the M2 or M1 receptors in other areas of the body.<sup>19</sup>

Propiverine (Mictoryl), the newest antimuscarinic agent approved in Canada, is reported to inhibit the efferent stimulus of the pelvic nerve and be calcium modulating causing musculotrophic spasmolysis.<sup>20</sup>

Apart from oxybutynin IR, propiverine IR is the only anticholinergic agent that is approved in Canada for OAB in children. The recommended total daily dosage for children under 35 kg is 0.8 mg/kg in two divided doses (refer to product monograph for dosing schedule). It is also approved to treat OAB in adults at a dose of 30 mg MR or 45 mg MR capsules per day. It has a similar side-effect profile as other daily-dosed antimuscarinics.<sup>21</sup> Leng reported in a recent non-inferiority trial comparing propiverine 30 mg MR to tolterodine 4 mg a significantly greater reduction in "voids/24 hours" and UUI episodes in the propiverine group over the tolterodine group. There were no differences in the incidence of adverse drug reactions.<sup>22</sup>

In a review of these seven antimuscarinic agents for the treatment of OAB, treatment with any of these agents led to similar reductions frequency, urgency, and incontinence episodes compared to placebo, and the agents had similar safety profiles.<sup>23</sup>

### *Beta-3 adrenoreceptor agonist*

Mirabegron (Myrbetriq) is the only beta-3 adrenoreceptor agonist available in Canada. It acts on the beta-3 receptors, leading to bladder relaxation, improved

urine storage, and thus reduced urinary frequency and incontinence.<sup>24</sup> The most common side effects are hypertension, (mainly in young women, and infrequently), nasopharyngitis, and UTI.

In a 52-week trial<sup>25</sup> that compared mirabegron to tolterodine for the treatment of OAB in patients older than 65, there were no significant differences in the rates of treatment-emergent adverse events of hypertension (10.4% and 12.9% for mirabegron and tolterodine, respectively), UTI (8.0% and 8.3%), dry mouth (3.1% and 10.2%), dizziness (4.8% and 3.6%), constipation (4.2% and 3.3%), and changes in cognition changes (0% in both).

In another study,<sup>26</sup> patients with incontinence were initially treated with solifenacin and those who were still incontinent after 4 weeks were treated with solifenacin and mirabegron, and more patients became continent on dual therapy versus solifenacin alone.

The beta-3 receptor agonist had similar efficacy as antimuscarinic agents in studies that have compared the two drug classes head-to-head.<sup>25</sup> Mirabegron was less likely than antimuscarinics to cause dry mouth and constipation.<sup>27</sup>

In the 52-week study of mirabegron, there were no reported changes in cognition in the younger or elderly patients. There is also no concern of the use of a beta-3 agonist in patients with glaucoma, since it has no effect on this condition.<sup>28</sup>

This agent may also be a slightly safer choice in an elderly patient who already has a high anticholinergic burden because of other medications. The addition of another anticholinergic agent to treat OAB, may increase the incidence of typical antimuscarinic side effects.

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### *Pharmacotherapy for OAB in elderly patients*

Physicians should use caution when prescribing any medication to frail elderly patients. Such patients are more susceptible to adverse drug events, related to polypharmacy, medical comorbidities and drug interactions. There is also concern about cognitive impairment and anticholinergic load. Cognitive effects are difficult to detect due to their subtlety and are often attributed to aging. However, in one 10-year study, patients with the highest exposure to oxybutynin were significantly more likely to have cognitive impairment.<sup>29</sup> If lifestyle changes are not successful to manage OAB in frail, elderly patients, initial lower doses of pharmacotherapies may be considered.

In 2015, a group of international experts published results from a systematic review of drugs to treat lower urinary tract symptoms (LUTS) that are regularly used by older patients (age 65 and older); they classified drugs for appropriateness in older patients, based on efficacy, safety and tolerability, by using the Fit fOR The Aged (FORTA) classification system.<sup>30</sup>

The experts identified 16 drugs with 896 publications; of those, only 25 clinical trials had data specifying results in older people. No drug was classed as FORTA-A (indispensable). Three drugs were classed as FORTA-B (beneficial): dutasteride, fesoterodine and finasteride. All of the other drugs were either classified as Forta-C (questionable) or Forta-D (avoid).<sup>30</sup> The design of the FORTA study has raised much concern by clinicians because it only included the peer reviewed published trials specifically in the elderly (25/896). Most drugs were given an unfavorable rating simply because there were no qualifying studies.

Subsequent to the publication of the FORTA review, there have been some additional published reports on the safety of some of these agents in elderly patients.<sup>25</sup>

A trial by Wagg et al published in 2013 looked at 12 weeks of treatment with fesoterodine versus placebo in patients who were 65 to 75 years old and older than 75 years old. There were no worsening of Mini-Mental State Examination (MMSE) scores or increased adverse event rates with this pharmacotherapy in the older patients, and the medication discontinuation rates were similar in both age groups.<sup>31</sup> In a placebo based-propiverine trial in elderly (> 60 years old) OAB patients with an average of 21 concomitant drugs and 18 concomitant disease, there were no new cardiac events (including Q-T interval changes) in the propiverine arm.<sup>32</sup> The effect of propiverine on cognition in the elderly with mild to moderate deficits based on MMSE<sup>33</sup> or Alzheimers Disease (AD) has been reported.<sup>34</sup> These studies have shown OAB treatment benefits with no changes in cognition or worsening of AD symptoms.<sup>2</sup>

### *Other therapies for patients who are referred to a urologist*

Patients with refractory OAB may be referred to a urologist who might employ different therapies. The patients might be given combination therapy with an antimuscarinic agent plus a beta-3 receptor agonist.<sup>26,35,36</sup>

Or, the patient might be given an intradetrusor injection of onabotulinumtoxin A (BOTOX), typically 100 units. In a recent study, 60% of patients who received a BOTOX injection versus 29.2% who received placebo reported symptom improvements, which lasted for 7 months.<sup>37</sup> The main side effects were urinary retention, need for catheterization, gross hematuria, and UTI.

A urologist might consider giving the patient posterior tibial nerve stimulation (PTNS) or sacral nerve stimulation.<sup>2</sup>

## Summary

For patients with OAB, the most recent CUA guidelines recommend first-line treatment with behavioral therapy, and if needed, second-line therapy with either an antimuscarinic agent or the beta-3 receptor agonist. Both classes of drugs are equally effective. However, importantly, both classes of drugs are contraindicated in patients with uncontrolled hypertension. If a patient does not respond or does not tolerate an anticholinergic/antimuscarinic drug, they may be switched to another agent in that class or to the beta-3 receptor agonist. Or a patient may be switched from the beta-3 receptor agonist to an anticholinergic/antimuscarinic agent. If the patient still has refractory OAB, he or she may be referred to a urologist, who might treat the patient with other treatment options.

## **OAB secondary to benign prostatic obstruction**

### Introduction

Benign prostatic hyperplasia (BPH) is formally diagnosed by histological examination although the term is often used to describe prostate related symptoms BPH may result in benign prostatic obstruction caused by enlargement of the prostate, which cause voiding symptoms. Benign prostatic obstruction (BPO) is one of the most common causes of LUTS in a man over the age of 50. The greatest risk factor for the symptoms associated with enlarged benign prostate is age. It is estimated that a least 50% of the men over the age of 60 and up to 80% of the men over the age of 80 will have symptoms related to an enlarged prostate.<sup>38</sup> Usually, when a man presents to the family physician describing symptoms of frequency and urgency plus a slow urine

stream, the most likely diagnosis is LUTS secondary to BPO. Two articles recently published in *The Canadian Journal of Urology* Supplements summarizes how family physicians can manage male patients who have LUTS secondary to an enlarged prostate.<sup>9,39</sup>

## Diagnosis and work up

The diagnosis and work up for a man with LUTS secondary to BPO is the same as for a patient with OAB alone. The critical difference is that men with LUTS secondary to BPO will usually have both voiding symptoms as well as urine storage symptoms. That is, if a man's major symptoms are frequency, urgency, and nocturia, with or without urgency urinary incontinence, (storage symptoms) then his diagnosis is OAB alone.

However, if a man describes symptoms of slow urine stream, hesitancy, straining, terminal dribbling, and a feeling of incomplete emptying, (voiding symptoms) these symptoms are likely secondary to an enlarged prostate and obstruction.

The clinical examination of a man with suspected LUTS secondary to BPO is the same as for a patient with OAB alone, with the addition of digital rectal examination (DRE) of the prostate. Where appropriate consideration of prostate-specific antigen (PSA) testing for prostate cancer may be considered. This helps make the diagnosis and to recommend the initial therapeutic approach. The size of the prostate helps determine whether monotherapy with an alpha blocker or combination therapy with an alpha blocker and a 5-alpha reductase inhibitor (5-ARI) is appropriate. Guidelines suggest that if the prostate volume is greater than 30 mL to 35 mL, starting a patient on combination therapy may provide the best treatment response.<sup>40</sup>

## BPO management

### *Alpha blockers and 5-ARIs*

Two classes of medication are very effective to manage LUTS secondary to BPO: alpha blockers and 5-ARIs. Alpha blockers block alpha receptors in the bladder neck, which opens the bladder neck to allow a greater urinary stream and more efficient bladder emptying, which results in decreased frequency. Alpha blockers provide a very quick onset of action. Usually, symptom response is experienced within 5-14 days.

5-ARIs are often used to manage an enlarged prostate. These medications prevent the conversion of testosterone to dihydrotestosterone in the prostate. Dihydrotestosterone causes prostate growth, and by blocking the conversion of testosterone to dihydrotestosterone, the prostate is expected to shrink

by about 30%. Response has a slow onset and can take up to 6 months. PSA levels in men treated with a 5-ARI are expected to drop by approximately 50% by 6 months after therapy initiation.

The question of reduction of combination therapy has been raised. In a double-blinded study of men who had been on combination therapy with an alpha blocker and a 5-ARI for 6 months, in a blinded manner, some of the men had their alpha blocker removed. Three months later, 75% of the men who unknowingly had only been on 5-ARI mono-therapy, still "felt the same or better" than 3 months earlier. This response suggested that the alpha blocker could be safely withdrawn in a proportion of men after 6 months of combination therapy. In most cases, men who stayed on the 5-ARI treatment alone did not have progression of BPO or LUTS symptoms.<sup>41</sup>

Another long term study showed that men who continue with combination therapy do better than those who receive monotherapy. The recommendation was that if there is no compelling reason to stop combination therapy, then do not do it.<sup>42</sup> The most common side effects associated with alpha blocker therapy are retrograde ejaculation or decreased ejaculation, and the most common side effect associated with 5-ARI therapy is erectile dysfunction.<sup>42</sup>

Another trial showed that if a man stops the alpha blocker therapy because of erectile dysfunction or retrograde ejaculation, but still has urinary frequency and urgency, he can be prescribed daily tadalafil (Cialis), which has been approved for the management of LUTS and erectile dysfunction. Tadalafil plus a 5-ARI improves erectile dysfunction and treats the symptoms of urinary frequency while mitigating the side effect of retrograde ejaculation.<sup>43</sup>

If a young man presents with symptoms of urgency frequency, and nocturia, the next step should be to examine the prostate. If there are no symptoms of obstruction and the prostate feels that it is less than 30 mL in volume, then the physician can prescribe an oral OAB medication. However, if the physician is not sure about the volume of the prostate, he can order a transrectal ultrasound to determine its true volume.

If the patient's symptoms are not only related to problems with urine storage, then the patient can be offered an alpha blocker and followed within 2 to 4 weeks. The patient will respond to alpha blocker therapy, if it is the appropriate therapy, very quickly.<sup>44</sup> At the follow up visit, if the patient has had some improvement in the obstructive symptoms but still has significant urinary urgency and frequency, then the addition of an OAB medication is appropriate.<sup>45</sup> It is very important to encourage any patients with OAB to take the medication

The practical update for family physicians in the diagnosis and management of overactive bladder and lower urinary tract symptoms

for at least 30 days, since it takes up to 30 days to see the maximum therapeutic effect of the OAB medication.

*Other treatments*

If a man does not respond to medical therapy for LUTS or cannot tolerate the medications, then other interventional approaches can be used to manage the BPO.<sup>39</sup> These interventions traditionally include laser-assisted or electro-coagulative resection, vaporization, or enucleation of the prostate. All are done under general anesthesia and require being admitted to hospital for 1 or more days.<sup>46</sup> Virtually all of these procedures will also cause retrograde ejaculation and possibly erectile dysfunction. Those expected side effects encouraged the development of UroLift. UroLift involves the delivery of a number of transurethral stitches that literally pull the prostate open from the inside. This can be done through a rigid cystoscope under local anesthetic or with some intravenous sedation. The stitches are placed starting distal to the bladder neck, which prevents the development of retrograde ejaculation.<sup>47</sup>

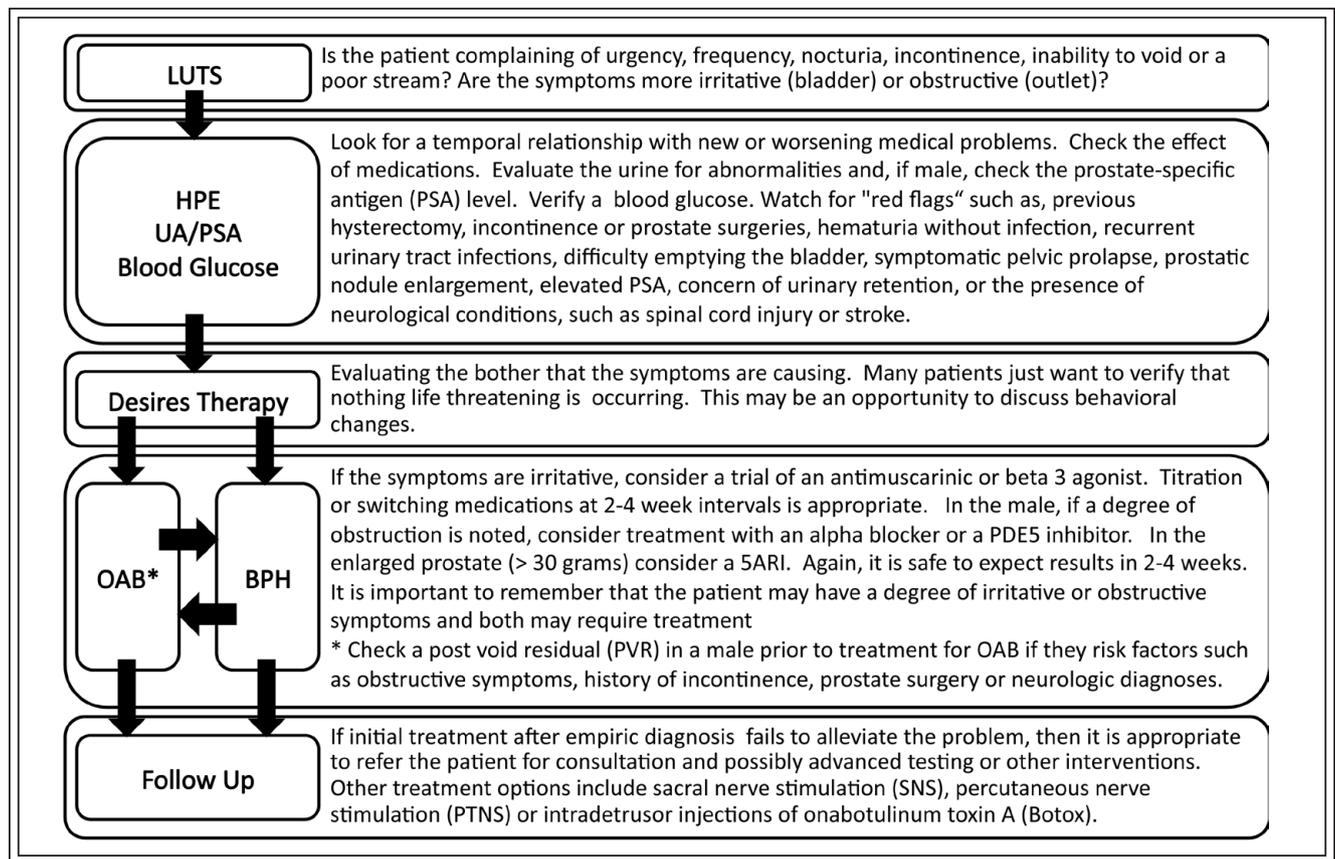
Recently published 5-year data from the LIFT study demonstrated long term efficacy with low retreatment rates. There was no incidence of ejaculatory dysfunction

and a trend towards improvement in erectile dysfunction in the patients. All of the procedures were done on an outpatient basis.<sup>48</sup>

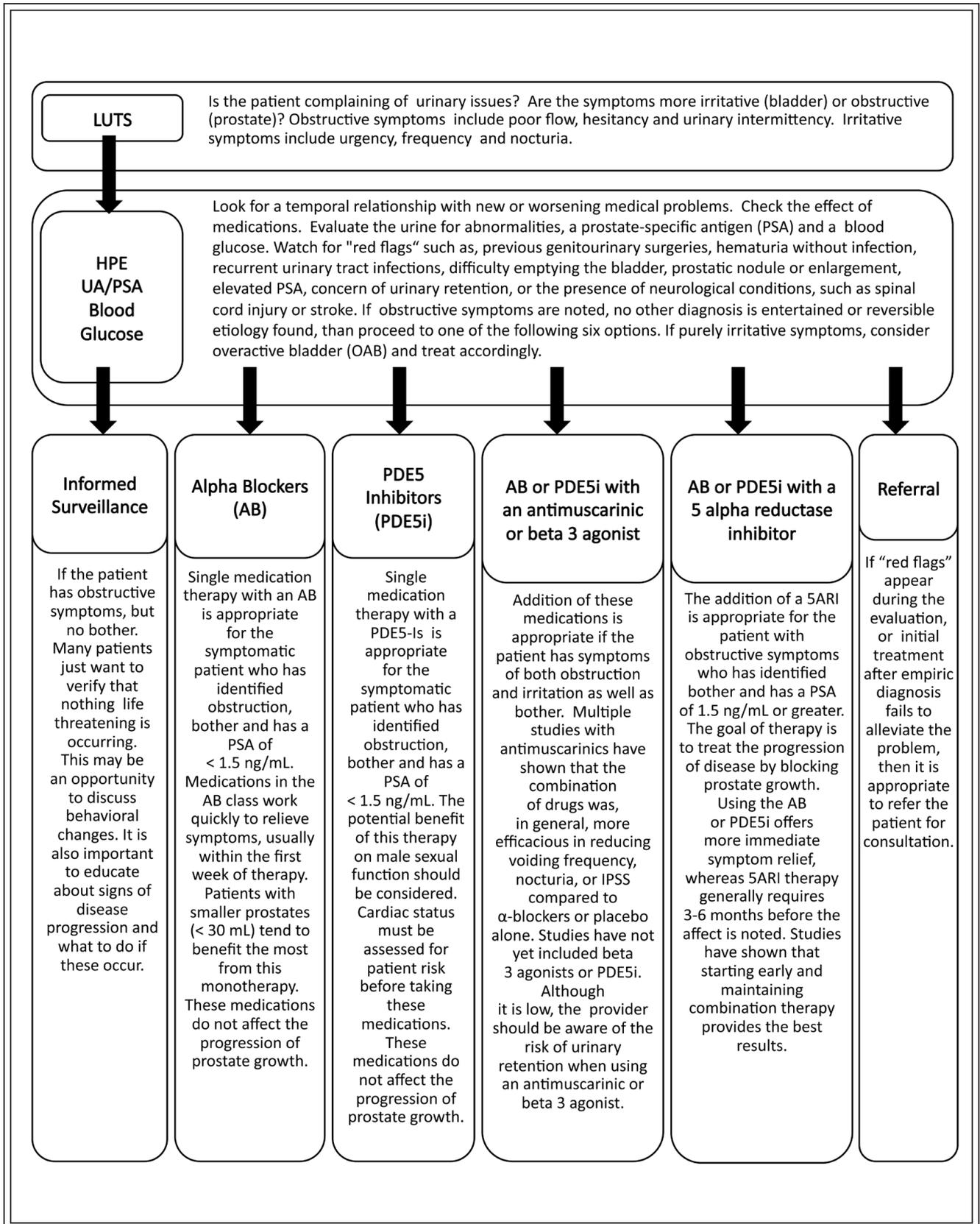
**Summary**

OAB is very common in men and women. Diagnosis and treatment for patients presenting with symptoms suggesting OAB alone or with BPO are summarized in two algorithms, Figures 1 and 2,<sup>9,39</sup> designed to provide an evidence based, effective approach for the family physician.

Certain clinical or lab findings are red flags suggesting that the patient may have a serious condition or is failing treatment, and should be referred to a urologist.<sup>19,49,50</sup> These red flags include a patient history of having recurrent, difficult to manage UTIs or severe symptoms from bladder outlet obstruction or bladder-related pain or neurologic symptoms. Red flags from patient assessment include bladder or pelvic pain; gross or microscopic hematuria; elevated post-residual volume (PVR > 200 mL); elevated PSA and abnormal prostate on DRE; recurrent positive urine culture; or abnormal imaging findings. Other red flags include being a smoker and having hematuria.



**Figure 1.** Practical approach in evaluating the patient with symptoms consistent with OAB.<sup>9</sup>



**Figure 2.** Algorithm describing a family physician approach to a patient with BPH-LUTS.<sup>39</sup>

## Disclosures

Dr. Jack Barkin is a speaker, investigator and on the advisory boards for Astellas, Pfizer, Allergan, NeoTract, Duchesnay and GlaxoSmithKline. Dr. Jeffrey Habert is a speaker and on the advisory boards for Amgen, Allergan, Bristol Myers Squibb, Boehringer Ingelheim, AstraZeneca, Pfizer, Eli-Lilly, Lundbeck, Purdue, Bayer, Novo-Nordisk, Janssen and Servier. Dr. Amy Wong and Dr. Livia YT Lee have no disclosures. □

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## CASE I. Overactive bladder in an elderly woman

### Case

- Evelyn is a 72-year-old widow who came under your care after her former family physician retired 6 months ago.
- She is a retired teacher and lives alone, and her only daughter is married and lives in Australia.
- She came to see you for prescription refills and reported to have been urinating more frequently, often with an urgent need to rush to the bathroom, and intermittent urine leakage accidents.
- She bought incontinence pads, but the urine leakage is causing her embarrassment and the fear of having an accident in a social setting.
- Evelyn smoked 30 pack years but quit two decades ago, and she is a social drinker.
- She is obese (body mass index [BMI] of 32) and has a history of hypertension, hypothyroidism, gastroesophageal reflux disease (GERD) and chronic insomnia.
- She had a complete hysterectomy for fibroids when she was 48 years old.
- She is taking amlodipine (5 mg/day), hydrochlorothiazide (25 mg/day) for blood pressure control, levothyroxine (0.125 mg/day), pantoprazole (40 mg/day) for reflux symptoms, and lorazepam (0.5 mg at bedtime) for insomnia.
- She is eager to obtain a solution from you for her urinary symptoms.

### Questions

There may be more than one correct answer. Please choose one answer only.

1. What is the most significant information in Evelyn's history that prompts you to consider a diagnosis of OAB?
  1. An urge to void
  2. Incident of urinary incontinence
  3. Urinary frequency
  4. All of the above
  5. None of the above
  
2. What other information do you need to make a differential diagnosis?
  1. Symptoms of dysuria, positive urinalysis or hematuria.
  2. Polydipsia and malaise
  3. Urinary incontinence on coughing or sneezing
  4. Symptom of vaginal prolapse on straining
  5. Ease of starting a urinary stream and strength of the urinary flow
  6. Voiding diary
  7. All of the above

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**3. If you found significant microscopic hematuria, which of the following investigations would you order next?**

1. Urine for cytology
2. Renal and bladder ultrasound
3. Cystoscopy
4. Pelvic ultrasound
5. Kidney ureter bladder ultrasound

**The history and investigations confirmed a diagnosis of OAB**

**4. Now, what could be the options in your management of her symptoms?**

1. Reducing caffeine and carbonated beverages, fluid management
2. Weight loss
3. Manage constipation
4. Scheduled voiding regimen
5. Pelvic floor muscle therapy exercises
6. Biofeedback
7. All of the above

**On her follow-up visit one month later, Evelyn reports that her daily activities are still interrupted by the urinary symptoms even after she completed the recommended behavioral therapy.**

**5. What is the first line of treatment you would now consider?**

1. Antimuscarinics
2. Tricyclic antidepressants
3. Topical estrogen agents
4. Alpha 1 blockers
5. Beta-3 Agonist

**6. What are the most commonly reported side effects of antimuscarinics used to treat OAB?**

1. Constipation
2. Dry mouth
3. Dizziness
4. Dry eyes
5. All of the above

**7. Which muscarinic receptor antagonist would you avoid if Evelyn has a history of cognitive deficit?**

1. Trospium
2. Darifenacin
3. Tolterodine
4. Oxybutynin
5. Mirabegron

**8. What medical condition would be a contraindication for you to start her on an antimuscarinics agent in the treatment of OAB?**

1. Frequent urinary tract infections
2. Narrow angle glaucoma
3. Wolff-Parkinson-White syndrome
4. Parkinsonism

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9. What other medications should be identified when one is considering an antimuscarinics agent in the treatment of OAB?
1. Antihistamines
  2. Antispasmodics
  3. Antipsychotics
  4. Antidepressants
  5. Cholinesterase inhibitors
  6. Anticonvulsants
  7. All of the above
10. For which medications on her current list would you consider a replacement to avoid additional adverse reactions or drug interaction, if you are considering medical treatment of her OAB symptoms?
1. Amlodipine
  2. Hydrochlorothiazide
  3. Levothyroxine
  4. Pantoprazole
  5. Lorazepam

### CASE II. Overactive bladder and benign prostatic obstruction

#### Case

- Bill is a 45-year-old man who is married and works as a public transit driver.
- He smokes, and he drinks 1 to 2 beers and 3 to 4 cups of coffee a day.
- He has hypertension and hyperlipidemia.
- You saw him 3 months ago for increasingly bothersome nocturia (3-4- small volumes), urgency frequency, and a slower urinary stream.
- His prostate was smooth and about 25 ccs.
- His PSA was 1.20 ng/mL.
- You diagnosed him with LUTS, secondary to benign prostatic obstruction, and started him on the alpha blocker silodosin (8 mg/day at bedtime).
- He is also taking perindopril (8 mg/day) and atorvastatin (20 mg/day at bedtime).
- He reports that after taking the silodosin, his nocturia decreased from 3 to 4 small volumes/night to 1 to 2 small volumes/night, and his urinary stream improved.
- However, he has some retrograde ejaculation, but this does not bother him.
- He came in today because he still has daytime frequency (~6-8x) which is really difficult with his job as bus driver; he also has significant urgency (“almost peed my pants a few times”), which is very upsetting.

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# POST-TEST FOR CPD

## Questions

There may be more than one correct answer. Please choose one answer only.

1. **What are the typical symptoms of OAB?**
  1. Frequency and nocturia
  2. Slow stream, nocturia, and hesitancy
  3. Urgency and frequency, with or without urge incontinence
  4. Frequency, dysuria, and hematuria
  
2. **Which of the following are urine voiding symptoms as opposed to urine storage symptoms?**
  1. Slow stream
  2. Hesitancy
  3. Frequency
  4. Post void dribbling
  5. Urgency/urge incontinence
  
3. **What investigations would you now perform on Bill?**
  1. Refer him to urologist
  2. Transrectal prostate ultrasound
  3. Repeat his PSA
  4. Urinalysis and culture
  5. Pre- and post-void bladder ultrasound (non-volume loaded)
  
4. **Which of the following are NOT red flags warranting a referral to a urologist?**
  1. Frequency
  2. Hematuria
  3. Urinary retention
  4. Renal impairment
  5. Abnormal PSA and/or abnormal prostate exam
  6. No drop in PSA after 6 months of 5-ARI therapy
  
5. **What treatment options could you offer Bill?**
  1. Behavioral therapy only
  2. An antimuscarinic medication
  3. A beta-3 receptor agonist medication
  4. A 5-alpha reductase inhibitor
  5. Phosphodiesterase-type 5 (PDE-5) daily
  
6. **You decide to start Bill on an OAB oral medication. What else should you do?**
  1. Stop his silodosin
  2. Do a transrectal ultrasound and bladder ultrasound prior
  3. Add the OAB med to silodosin
  4. Start 5-ARI, and see him in 4 months





