

## 2010 Update: Guidelines for the management of benign prostatic hyperplasia

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### Introduction

Within the past decade, a number of significant advancements have occurred in our knowledge of benign prostatic hyperplasia (BPH) resulting in new approaches to both the diagnosis and treatment of this common and potentially progressive condition of aging men. The current document attempts to summarize the state-of-the-art knowledge regarding BPH and to highlight the essential diagnostic and therapeutic information in a Canadian context. The information included in this document was obtained from a MEDLINE search of the English language literature. Although references of historical importance are included, management recommendations are based on literature published between 2000 and 2009.

These guidelines are directed toward the typical male patient over 50 years of age, presenting with lower urinary tract symptoms (LUTS) believed to be associated with benign prostatic obstruction (BPO). Men with LUTS associated with non-BPO causes will require more extensive diagnostic workup, different treatment considerations and their management will not be covered in this document.

In this document we will address both diagnostic and treatment issues. **Diagnostic guidelines** are described in the following terms as: mandatory, recommended, optional or not recommended. **Guidelines for treatment** are described using the terminology: standard of care (evidence-based, whenever possible), optional (insufficient evidence or patient preference) or not recommended (based on the best available evidence). Whenever possible, levels of evidence and grades of recommendation will be provided to support guideline statements.

### Diagnostic guidelines

**Mandatory:** In the initial evaluation of a man presenting with LUTS, the evaluation of symptom severity and bother is essential. Medical history should include relevant prior

and current illnesses as well as prior surgery and trauma. Current medication, including over-the-counter drugs and phytotherapeutic agents, must be reviewed. A focused physical examination, including a digital rectal exam (DRE), is also mandatory. Urinalysis is required to rule out diagnoses other than BPH that may cause LUTS and may require additional diagnostic tests.<sup>1-9</sup>

- History
- Physical examination including DRE
- Urinalysis (routine and microscopic, culture and sensitivity)

**Recommended:** A formal symptom inventory (e.g., International Prostate Symptom Score (IPSS) or AUA Symptom Score) is recommended for an objective assessment of symptoms at initial contact, for follow-up of symptom evolution for those on watchful waiting and for evaluation of response to treatment.<sup>10-17</sup> (**Level 2 Evidence, Grade C Recommendation**).

Testing of prostate-specific antigen (PSA) should be offered to patients who have at least a 10-year life expectancy and for whom knowledge of the presence of prostate cancer would change management, as well as those for whom PSA measurement may change the management of their voiding symptoms (estimate for prostate volume). Among patients without prostate cancer, serum PSA may also be a useful surrogate marker of prostate size and may also predict risk of BPH progression.<sup>18</sup>

- Symptom inventory (should include bother assessment)
- PSA (selected patients)

**Optional:** In cases where the physician feels it is indicated, it is reasonable to proceed with one or more of the following:

- Serum creatinine
- Urine cytology (if irritative symptoms are significant component of LUTS)<sup>3</sup>
- Uroflow
- Voiding diary
- Post-void residual
- Sexual function questionnaire

**Not Recommended:** The following diagnostic modalities are not recommended in the routine initial evaluation of a typical patient with BPH-associated LUTS.

These investigations may be required in patients with a definite indication, such as hematuria, uncertain diagnosis, DRE abnormalities, poor response to medical therapy or for surgical planning.<sup>5</sup>

- Cystoscopy
- Cytology
- Urodynamics
- Radiological evaluation of upper urinary tract
- Prostate ultrasound
- Prostate biopsy

An algorithm summarizing the appropriate diagnostic steps in the workup of a man with LUTS is shown in Figure 1.

## Treatment guidelines

### Principles of treatment

Therapeutic decision-making should be guided by the severity of the symptoms, the degree of bother and patient preference. Information on the risks and benefits of BPH treatment options should be explained to all patients who are bothered enough to consider therapy. Patients should be invited to participate as much as possible in the treatment selection.

**Standard of Care:** Patients with mild symptoms (e.g., IPSS <7) should be counselled about a combination of lifestyle modification and watchful waiting. Patients with mild symp-

toms and severe bother should undergo further assessment.

**Optional:** Treatment options for patients with bothersome moderate (e.g., IPSS 8 – 18) and severe (e.g., IPSS 19 – 35) symptoms of BPH include watchful waiting/lifestyle modification, as well as medical, minimally invasive or surgical therapies.

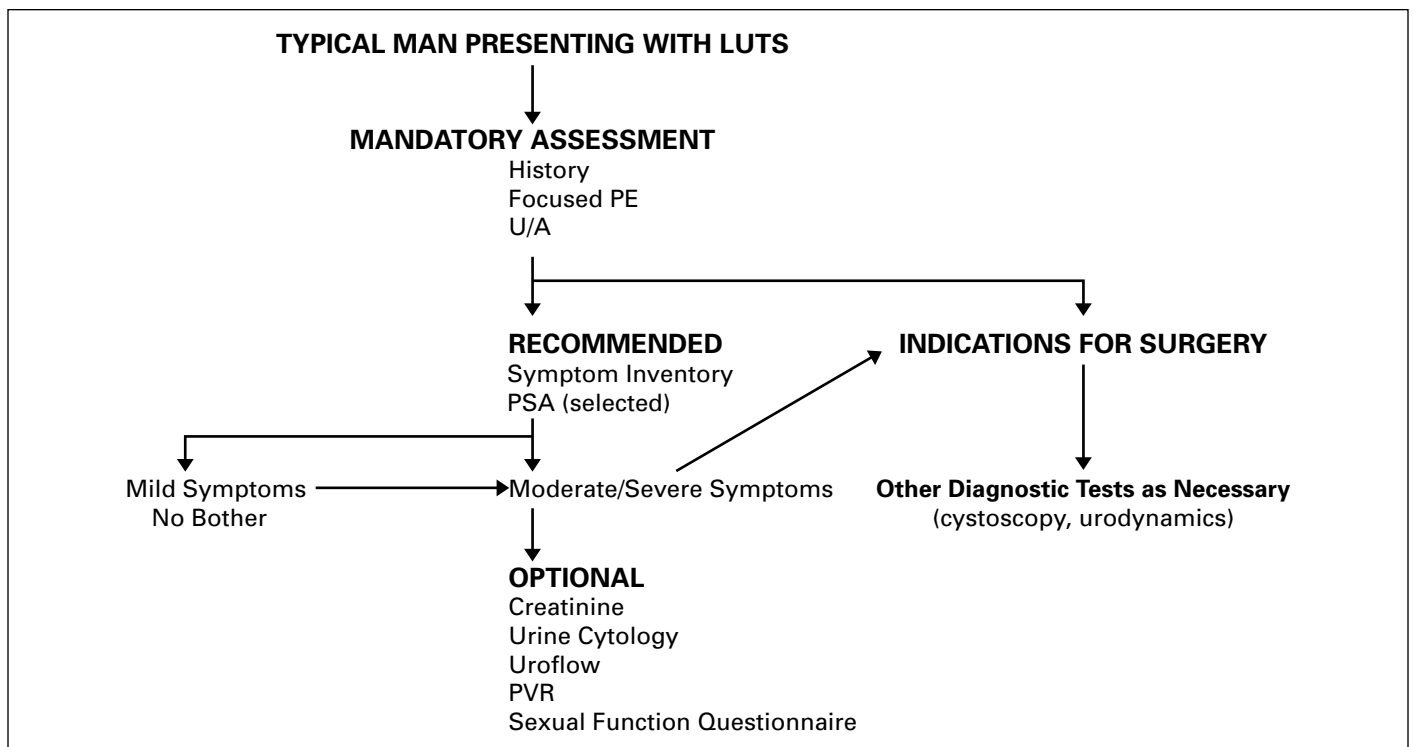
### Lifestyle modifications with watchful waiting

**Standard of Care:** Patients on watchful waiting should have periodic physician-monitored visits.

**Optional:** Physicians can use baseline age, LUTS severity, prostate volume and/or serum PSA to advise patients of their individual risk of symptom progression, acute urinary retention or future need for BPH-related surgery (these risk factors identify patients at risk for progression).

**Optional:** A variety of lifestyle changes may be suggested for patients with nonbothersome symptoms. These can include the following:

- Fluid restriction particularly prior to bedtime
- Avoidance of caffeinated beverages, spicy foods
- Avoidance/monitoring of some drugs (e.g., diuretics, decongestants, antihistamines, antidepressants)
- Timed or organized voiding (bladder retraining)
- Pelvic floor exercises
- Avoidance or treatment of constipation



**Fig. 1.** Diagnostic algorithm. LUTS = lower urinary tract symptoms; PE = physical examination; U/A = urinalysis; PSA = prostate-specific antigen; PVR = post-void residual.

## Medical treatment

### Alpha-blockers

**Optional:** Alpha-blockers are an excellent first-line therapeutic option for men with symptomatic bother who desire treatment.<sup>19-27</sup> (**Level 1 Evidence, Grade A Recommendation**).

Alfuzosin, doxazosin, tamsulosin and terazosin are appropriate treatment options for LUTS secondary to BPH. They do not alter the natural progression of the disease.

**Recommendation:** Although there are differences in the adverse-event profiles of these agents, we believe that all 4 agents have equal clinical effectiveness. The choice of agent should depend on the patient's comorbidities, side effect profiles and tolerance.

### 5 alpha-reductase inhibitors

**Optional:** The 5 alpha-reductase inhibitors (dutasteride and finasteride) are appropriate and effective treatments for patients with LUTS associated with demonstrable prostatic enlargement.<sup>28</sup> Several studies have demonstrated that in addition to improving symptoms, the natural history of BPH can be altered through a reduction in the risk of acute urinary retention (AUR) and the need for surgical intervention.<sup>28-31</sup> (**Level 1 Evidence, Grade A Recommendation**).

Prognostic factors suggesting the potential for BPH risk progression<sup>32-34</sup> include:

- Serum PSA >1.4 ng/mL
- Age >50
- Gland volume >30 cc

### Combination therapy (alpha-blocker and 5 alpha-reductase inhibitor)

**Optional:** The combination of an alpha-adrenergic receptor blocker and a 5 alpha-reductase inhibitor is an appropriate and effective treatment strategy for patients with LUTS associated with prostatic enlargement. Clinical trial results have shown that combination therapy significantly improves in symptom score and peak urinary flow compared with either of the monotherapy options. Combination medical therapy can effectively delay symptomatic disease progression, while combination therapy and/or 5 alpha-reductase monotherapy is associated with decreased risk of urinary retention and/or prostate surgery.<sup>29-30,35</sup> (**Level 1 Evidence, Grade A Recommendation**).

Patients successfully treated with combination therapy may be given the option of discontinuing the alpha-blocker after 6 to 9 months of therapy.<sup>36,37</sup> If symptoms recur, the alpha-blocker should be restarted.

### Role of anticholinergics medications

Level 1 Evidence would suggest that for selected patients with bladder outlet obstruction due to BPH and concomitant detrusor overactivity, combination therapy with an alpha-receptor antagonist and anticholinergic can be helpful.<sup>38</sup> (**Level 1 Evidence, Grade A Recommendation**) Caution is recommended, however, when considering these agents in men with an elevated residual urine volume or a history of spontaneous urinary retention.

### Role of phosphodiesterase inhibitors

The phosphodiesterase (PDE) isoenzymes 4 and 5 are present in the prostate and regulate smooth muscle tone. Subsequent isoenzyme inhibition with medications, such as sildenafil and tadalafil, have shown improvement in symptoms and quality-of-life in men with LUTS.<sup>39</sup> At the present time, however, these agents are not recommended for men with symptomatic BPH-related LUTS.

### Phytotherapies

**Optional:** If patients are interested in complementary approaches (phytotherapeutic or other supplements) for LUTS secondary to BPH, they may be counselled that some plant extracts, such as *Serenoa repens* (saw palmetto berry extract) and *Pygeum africanum* (African Plum), have shown some efficacy in several small clinical series. (**Level 3 Evidence, Grade B Recommendation**).

Saw palmetto has been studied most rigorously, including a published randomized controlled double-blind trial which failed to show any significant difference over placebo in symptom score, maximum flow rate, prostate size, residual urine volume, PSA levels or quality of life over a 1-year period.<sup>40,41</sup> (**Level 2 Evidence, Grade B Recommendation**)

**Not Recommended:** Phytotherapeutic agents and other dietary supplements cannot be recommended as the standard treatment of BPH at this time.

## Surgery

### Transurethral resection of the prostate (TURP)

**Standard of Care:** Monopolar TURP remains the gold standard treatment for patients with bothersome moderate or severe LUTS who request active treatment or who either fail or do not want medical therapy.<sup>42-51</sup> (**Level 2 Evidence Grade B Recommendation**).

Patients should be informed that the procedure may be associated with short- and long-term complications. Recent data suggest that contemporary TURP-related morbidity

includes a risk of blood transfusion and TUR syndrome ranging from 2.0% to 4.8% and 0 to 1.1% of cases, respectively,<sup>52</sup> while the need for retreatment can be as high as 14.7% during an 8-year follow-up.<sup>53</sup>

**Optional:** Bipolar TURP has evolved as an equivalent alternative to the monopolar technique, (**Level 2 Evidence, Grade B Recommendation**). Recent reports suggest bipolar resection is associated with a reduction in the risk of dilutional hyponatremia (TUR syndrome), improvements in intraoperative visibility and may result in shorter catheterization times.<sup>54-57</sup>

### Laser prostatectomy

**Optional:** Several laser wavelengths (Potassium titanyl phosphate [KTP], Holmium:Yttrium aluminium garnet [Ho:YAG], Thulium) and delivery systems (end-firing; side-firing; interstitial) are available for prostatic tissue coagulation or vaporization/ablation and each has particular characteristics and potential advantages.

Holmium laser enucleation (HoLEP) can be used effectively in larger glands and in patients on anticoagulation with reported reduced hospitalization, bleeding and duration of catheterization. Results both early and long-term are similar to TURP, confirming this modality is a suitable first-line surgical option among urologists skilled with the technique.<sup>58</sup> Randomized trials comparing HoLEP to TURP and to open prostatectomy have demonstrated favourable outcomes especially among men with larger prostates.<sup>59,60</sup> (**Level 1-2 Evidence, Grade B Recommendation**).

Greenlight laser or photoselective vaporization prostatectomy (PVP) is a suitable treatment option for most men considering surgical alternatives, particularly for those on anticoagulation.<sup>61,62</sup> (**Level 2 Evidence, Grade B Recommendation**).

**Standard of Care:** Absolute indications to recommend TURP include: urinary retention (intractable) and renal insufficiency (caused by BPO). Relative indications to recommend TURP include: failure of medical therapy, recurrent cystitis, bladder calculi and persistent prostatic bleeding.

### Transurethral incision of the prostate (TUIP)

**Optional:** TUIP is appropriate surgical therapy for men with prostate gland volumes less than 30 grams. These patients should experience symptom improvements similar to TURP with a lower incidence of retrograde ejaculation.<sup>63</sup>

### Open prostatectomy

**Optional:** Open prostatectomy remains indicated for men whose prostates, in the view of the treating urologist, are too large for TURP for fear of incomplete resection, significant

bleeding or the risk of dilutional hyponatremia (TUR syndrome).

## Minimally invasive surgical therapies (MIST)

### Transurethral microwave therapy (TUMT)

**Optional:** TUMT is a reasonable treatment consideration for the patient who has moderate symptoms, small to moderate gland size and a desire to avoid more invasive therapy for potentially less effective results.<sup>64</sup> TUMT may be associated with a higher re-treatment rate over a 5-year follow-up interval than for men receiving TURP.<sup>64,65</sup> TUMT is not an insurable service anywhere in Canada at this time; patients are required to pay for this procedure.

### Transurethral needle ablation (TUNA)

**Optional:** TUNA may be a therapeutic option for the relief of symptoms in the younger, active individual in whom sexual function remains an important quality of life issue (less risk of retrograde ejaculation), however limited data is available on long-term outcomes.<sup>66-68</sup> TUNA is not an insurable service anywhere in Canada at this time; patients are required to pay for this procedure.

### Stents

**Optional:** Temporary and permanent stents may be considered in patients with severe urinary obstruction secondary to BPH who are medically unfit for surgery (or waiting to become medically fit for surgery or MIST).<sup>69</sup> Stents are not recommended as standard therapy for LUTS associated with BPH.

### Other MIST therapies

**Not Recommended:** Although clinical trials have been or are being conducted to assess a number of other novel interventions, the following evolving MIST therapies are not recommended as standard therapy at this time.

- Absolute ethanol injection
- High intensity focused ultrasound
- Water-induced thermotherapy
- Intraprostatic botulinum toxin injection

The therapeutic options available to the patient with bothersome LUTS stratified by symptom severity and prostate gland size are displayed in Fig. 2.

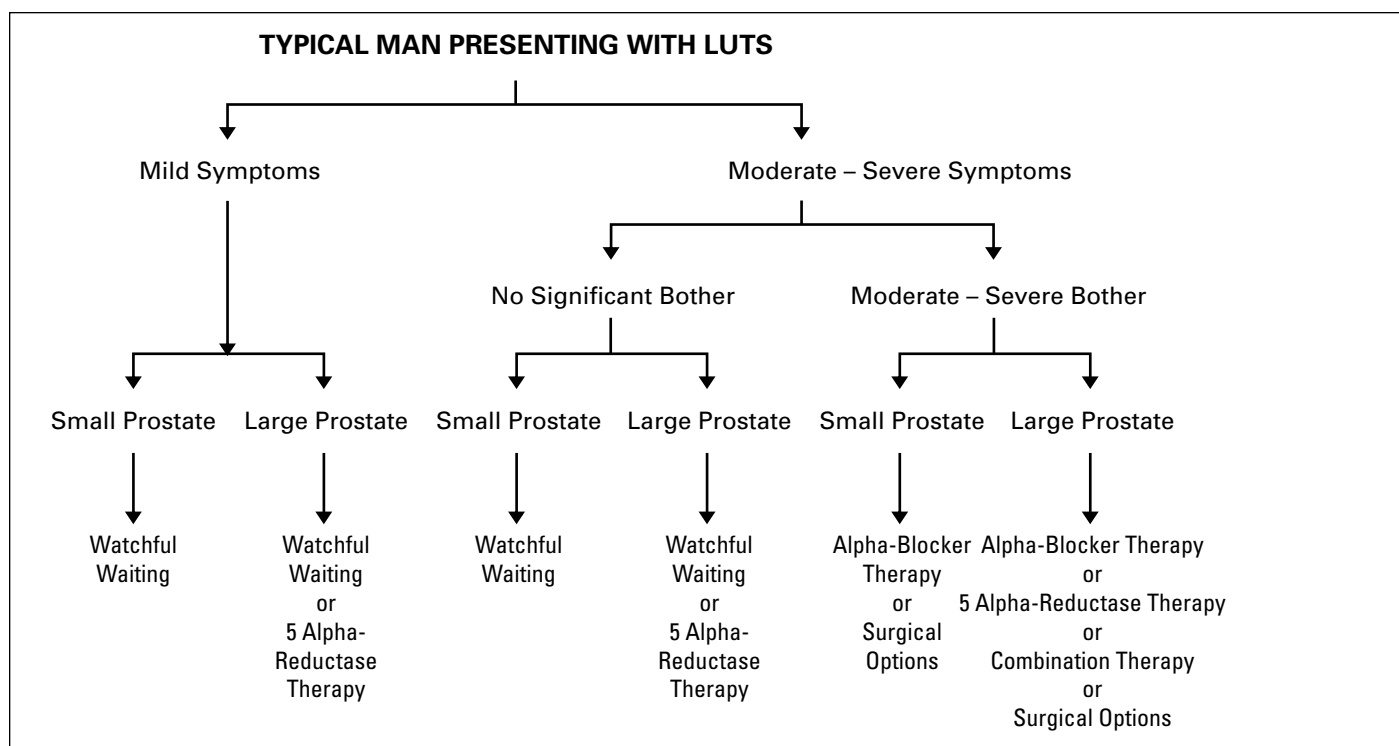


Fig. 2. Therapeutic algorithm. LUTS = lower urinary tract symptoms.

## Special situations

### Symptomatic prostatic enlargement but without bothersome symptoms

**Optional:** Patients with symptomatic prostatic enlargement in the absence of significant bother may be offered a 5 alpha-reductase inhibitor to prevent progression of the disease. The disadvantages and the need for long-term daily therapy should be discussed with the patient in relation to his risk of progression.

### Acute urinary retention

**Standard of Care:** Men with AUR due to BPH should be offered a trial of voiding 2 to 7 days after catheterization while receiving an alpha-blocker. Recent data suggest that in patients with AUR, the use alpha-blockers (specifically tamsulosin and alfuzosin) during the period of catheterization will increase the chances of successful voiding after catheter removal and may decrease the risk of future prostate surgery.<sup>70,71</sup> (**Level 1 Evidence, Grade A Recommendation**).

If the trial of voiding fails, the patient should be considered for surgical intervention.

### BPH-related bleeding

**Standard of Care:** A complete assessment, including history and physical examination, urinalysis (routine microscopy, culture & sensitivity, cytology), upper tract radiologic assessment and cystoscopy, is necessary to exclude other sources of bleeding.

**Optional:** In men with BPH-related hematuria, a trial with a 5 alpha-reductase inhibitor is appropriate. If the bleeding persists, TURP is recommended. (**Level 3 Evidence, Grade B Recommendation**).

### BPH patients with prostate cancer concern

**Optional:** The BPH patient with an elevated serum PSA and negative prostate biopsy may be counselled on the proven benefits of using finasteride, a Type 2 selective 5 alpha-reductase inhibitor or dutasteride, a dual Type 1 and 2, 5 alpha-reductase inhibitor for prostate cancer risk reduction.<sup>72,73</sup> (**Level 1 Evidence, Grade A Recommendation**).

While both finasteride and dutasteride uses were associated with similar reductions in the overall rate of prostate cancer, there was one observed difference between the trials.<sup>72,73</sup> In the PCPT (Prostate Cancer Prevention Trial) study, a slight increase in the risk of high grade (Gleason 8 or greater) prostate cancer was observed among the finasteride cohort compared to the placebo group.<sup>72</sup> Most experts

believe this phenomenon was due to an artifact of prostate glandular cyto-reduction, induced by the 5 alpha-reductase inhibitor, although some controversy exists.<sup>74</sup> In the REDUCE (Reduction by Dutasteride of Prostate Cancer Events) trial, the number of patients found to have Gleason 7 or greater prostate cancer was not significantly different between the dutasteride and placebo groups.<sup>73</sup>

Patients who experience a rising PSA after 6 to 12 months of 5 alpha-reductase inhibitor therapy should be assessed for the possibility of high-grade prostate cancer.<sup>75</sup>

## Summary

BPH is one of the most common age-related disorders afflicting men. As the aging of the Canadian population continues, more men will be seeking advice and looking for guidance from their health care providers on the management of their symptoms. It is hoped the information offered in this guideline document will aid Canadian urologists, as they strive to provide state-of-the-art care to their patients.

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