

GUIDELINES AT-A-GLANCE

For Primary Care Providers

A Quick Reference for Primary Care Providers

Current Guidelines on:

- Benign Prostatic Hyperplasia
- Erectile Dysfunction
- Interstitial Cystitis/
Bladder Pain Syndrome
- Premature Ejaculation
- Prostate Cancer

Current Best Practice Statements on:

- Male Infertility

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DEAR READER,

The *Guidelines-At-A-Glance for Primary Care Physicians* pocket guide, targeted to primary care providers, contains essential summarized information from a number of American Urological Association's (AUA) guidelines and best practice statements. The evidence-based documents from which the summaries are derived were developed by multidisciplinary panels of leading physicians and other health experts, and underwent extensive peer review prior to publication. The development of the summaries was coordinated by Matt T. Rosenberg, MD, while the individual documents were edited by Dr. Rosenberg and Mikel Gray, PhD, CUNP, CCCN, FAANP, FAAN, and reviewed by the original panel chairs. This ready reference tool will provide up-to-date, evidence-based statements, expert clinical opinion, and pertinent information to help practicing primary care clinicians provide optimal patient care.

Sincerely,
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This document provides guidance only and does not establish a fixed set of rules or define the legal standard of care. As medical knowledge expands and technology advances, the guidelines and best practice statements may change. Today they represent not an absolute mandate but rather current proposals or recommendations for treatment under the specific conditions described. For all of these reasons, the AUA Guideline and Best Practice Statements do not preempt physician judgment in individual cases. Also, treating physicians must take into account variations in resources, and in patient tolerances, needs and preferences. Conformance with the recommendations reflected in this document cannot guarantee a successful outcome. Each topic in this pocket guide was developed as a summary of the full AUA Guideline for that particular subject. The full AUA guideline on each topic should be consulted as the final authority.

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An appreciation of the prevalence of the diseases and problems listed in this pocket guide leave no doubt as to the underdiagnosis and undertreatment of many urological conditions. Just as compelling is the knowledge that earlier diagnosis and treatment of urologic conditions generally results in more favorable outcomes. It is also no surprise to the Primary Care Provider (PCP) that they are the first caregiver to interact with the patient regarding their symptoms. However, it is a striking fact that average PCP may only receive the most basic of education in urologic diseases. In addition, in practice, although the PCP may appreciate the seriousness of the potential pathology or the impact of a condition on quality of life, they may not have an adequate amount of time or the material resources to perform a complete or complex evaluation. Therefore, the reality is that urologic care is becoming a continuum that starts in the office of the PCP and may or should end in the office of the urological specialist.

Dr. Gray and I have reviewed these guidelines with the intent of demonstrating to the PCP what can be done in their office to effectively diagnose and treat the patient with urologic issues, while at the same time efficiently refer the patient when further evaluation or treatment is necessary. We have aimed to keep recommendations in line with the concept of 'simplicity, effectiveness and safety'; is the evaluation simple enough to be accomplished in the office of the PCP?, are the treatments effective and readily available?, what is safe for office-based primary care and what are the indications for referral to the urological specialist?

It is a tremendous honor to be involved in this effort to bring urological education to my colleagues in primary care. I would like to thank Dr. Gray and the panel chairs for their tireless efforts. However, we should applaud the leadership of the AUA for recognizing the important role of the PCP in the urological continuum of care. It is our hope that not only will these guidelines assist the practice of the PCP but they will also stimulate further conversation between urologists and PCPs as we strive to improve patient outcomes.

Sincerely,
Matt T. Rosenberg, MD
AUA Primary Care Education Initiatives Coordinator

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Text appearing in *italics* identifies modifications to the individual guidelines specifically for primary care as provided by the panel for this publication and may not be derived from the original AUA guidelines panel's evidence-based review process.

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MANAGEMENT OF BENIGN PROSTATIC HYPERPLASIA

Guideline (2010)

The FDA has stated that 5-ARIs are not indicated for the chemoprevention of prostate cancer as there may be an increased risk of high grade prostate cancer (GLEASON GRADES 8, 9, 10) with their use for this purpose. Regardless of 5-ARI use for chemoprevention, the FDA continues to support 5-ARI use in men with LUTS secondary to prostate enlargement/BPH/BNO because of this class has a proven benefit in improving LUTS and reducing the risk of AUR and need for surgery.

Benign prostatic hyperplasia (BPH) can be associated with bothersome lower urinary tract symptoms (LUTS) that affect quality of life by interfering with normal daily activities and sleep patterns. Since the impact of LUTS on a patient's quality of life is highly variable and is not directly related to any measurable physiologic factors, the patient's perception of the severity of the condition, and the degree to which it interferes with his lifestyle and causes embarrassment, should be primary considerations in management.

A framework for diagnosis and treatment of BPH/LUTS in an index patient of greater than 45 years of age without significant risk of non-BPH causes is presented (Figure 1). This Guideline addresses LUTS secondary to BPH (LUTS/BPH); that is, the patient does not have a history suggesting non-BPH causes of LUTS and

the LUTS may or may not be associated with an enlarged prostate gland*, bladder outlet obstruction (BOO), or histological BPH. Two treatment algorithms, one on the basic management of LUTS in men and one on the detailed management for persistent bothersome LUTS were adapted for this Guideline from the 2005 International Consultation of Urologic Diseases and reiterated in a 2009 in an article by Abrams et al (2009).

**Prostatic enlargement was defined as a size of 30 grams or more or a PSA of 1.5 or greater by a majority of the literature reviewed in the development of this Guideline.*

All statements contained within this Guideline are based on outcomes data and are tempered by the Panel's expert opinion. Guidelines statements are graded using three evidence-based levels and two consensus-based levels with respect to the degree of flexibility in their application. Please refer to the full Guideline for the grades of individual statements.

Evaluation of Benign Prostatic Hyperplasia

The goal of evaluating patients presenting with LUTS is to establish that the symptoms are due to BPH, with treatment focusing not only on alleviating symptoms, but also on altering disease progression and preventing complications.

Initial Evaluation

- The initial evaluation should include:
 - ◆ A medical history to identify other causes of voiding dysfunction or comorbidities that may complicate treatment;
 - ◆ a physical examination, including both digital rectal and

focused neurological examinations;

- ◆ a urinalysis performed by dipstick testing or microscopic examination of the sediment to screen for hematuria, glucose and urinary tract infection (UTI);

** If concerned about diabetes, consider testing serum glucose or hemoglobin A1c.*

- ◆ and measurement of the serum prostate-specific antigen (PSA) offered to patients 1) with at least a 10-year life expectancy and for whom knowledge of the presence of prostate cancer would change management, or 2) for whom the PSA measurement may change the management of the patient's voiding symptoms.

Frequency volume charts should be used when nocturia is the dominant symptom, and also in other settings. Urine cytology is an optional test in men with a predominance of irritative symptoms, especially with a history of smoking or other risk factors, to aid in the diagnosis of bladder carcinoma in situ and bladder cancer. The routine measurement of serum creatinine levels is **not** recommended.

Symptom Assessment

Symptom quantification is important to determine disease severity, document therapeutic response to therapy and detect symptom progression in men managed by watchful waiting.

- Administer the AUA Symptom Index (identical to the seven symptom questions of the International Prostate Symptom Score [IPSS]).
- *Primary Care Providers are encouraged to administer the*

complete AUA Symptom Index; if the complete index is unavailable, at the very least a conversation regarding urgency of urination (BPH SI Q.4) should be initiated.

- Administer other validated assessment instruments, including the BPH Impact Index, if warranted.

Other Diagnostic Tests

- Additional diagnostic tests (pressure-flow urodynamics studies, urethroscopy and ultrasound [transabdominal or transrectal]) are not recommended in the initial evaluation of LUTS but are optional in the following settings when choosing invasive therapies, particularly if the outcome of the pressure-flow study may impact choice of intervention, or if prostate size and anatomical configuration are important considerations for a given treatment modality.
- Urinary flow rate recording and measurement of post-void residual urine usually are not necessary prior to the institution of watchful waiting or medical therapy. However, they may be helpful in patients with a complex medical history, those with persistent or bothersome LUTS after basic management and in those desiring invasive therapy. *These diagnostics tests may be beyond the realm of many primary care providers, in which case a urologic referral is recommended.*
- Filling cystometography and upper urinary tract imaging by ultrasonography or excretory urography are not recommended in the typical patient unless the patient has hematuria, UTI, renal insufficiency or a history of urolithiasis or urinary tract surgery. *It is not recommended that Primary*

Care Providers order these diagnostic tests, Patients with hematuria, UTI, renal sufficiency or a history of urolithiasis or urinary tract surgery should be referred to a urologist.

Initial Management and Preliminary Discussion of Treatment Options with the Patient

Patients with Mild Symptoms

- Watchful waiting is the treatment of choice in patients with mild symptoms of BPH (AUA Symptom Score <8) and patients with moderate or severe symptoms who are not bothered by their symptoms (i.e., do not interfere with the daily activities of living).
- A urologist should be consulted (if not done already) if a patient has persistent, bothersome LUTS after basic management.

Patients with Moderate to Severe Symptoms

- Treatment options for patients with bothersome moderate to severe symptoms of BPH (AUA Symptom Score ≥8) include watchful waiting and the medical, minimally invasive or surgical therapies defined in Table 1.
- Explain the benefits and harms of the BPH treatment options (including watchful waiting) using the information provided in the full text document (on www.AUAnet.org), to patients with moderate to severe symptoms (AUA Symptom Score ≥8) who are bothered enough to consider therapy.

Treatment Recommendations

Watchful Waiting

- Watchful waiting is indicated for patients with mild or non-bothersome symptoms whose overall health is not compromised by bladder outlet obstruction.

Medical Treatment

Alpha-adrenergic Blockers

- Alfuzosin, doxazosin, tamsulosin and terazosin are appropriate treatment options for patients with LUTS secondary to BPH and are believed to have equal clinical effectiveness. These drugs should be the first treatment of choice when BOO symptoms predominate.

**Evaluation of silodosin was not included in this Guideline due to the timing and cutoff date of the literature search.*

- The older, less costly generic alpha blockers remain reasonable choices. These require dose titration and blood pressure monitoring.
- Physicians and patients should be aware that a surgical condition termed Intraoperative Floppy Iris Syndrome (IFIS) has been observed during cataract surgery in some patients treated with alpha-1 blockers. Most reports were in patients taking the alpha-1 blocker when IFIS occurred, but in some cases, the alpha-1 blocker had been stopped prior to surgery. The benefit of stopping alpha-1 blocker therapy prior to cataract surgery has not been established. Men with planned cataract surgery should avoid the initiation of alpha blockers until their cataract surgery is completed.
- Prazosin or phenoxybenzamine should not be used in this setting.

5 Alpha-reductase Inhibitors

Finasteride and dutasteride are:

- Appropriate and effective treatments in patients with LUTS associated with demonstrable prostatic enlargement.
- Indicated for patients with symptomatic prostatic enlargement but no bother, to prevent disease progression. [Present the disadvantages of this approach (side effects and the need for long-term daily therapy) to the patient with an estimate of his baseline risk of progression to aid in informed decision making.]
- **Not** appropriate for men with LUTS without evidence of prostatic enlargement.
- **Finasteride is an appropriate and effective treatment alternative in men with refractory hematuria presumably due to prostatic bleeding (i.e., after exclusion of any other causes of hematuria). A similar level of evidence concerning dutasteride was not reviewed; it is the expert opinion of the Panel that dutasteride likely functions in a similar fashion.**
- **Overall, there is insufficient evidence to recommend using 5-ARIs preoperatively in the setting of a scheduled TURP to reduce intraoperative bleeding or reduce the need for blood transfusions.**

Anticholinergic Agents

- Are appropriate and effective in men with predominately irritative symptoms and without an elevated post-void residual (PVR).

- Baseline PVR should be assessed prior to starting anticholinergic therapy. **Anticholinergics should be used with caution in patients with a post-void residual greater than 250 to 300 mL.**

Combination Therapy

- Concomitant use of an alpha-adrenergic receptor blocker and a 5 alpha-reductase inhibitor - or an alpha-adrenergic receptor blocker and an anticholinergic - is an appropriate and effective treatment for patients with LUTS associated with demonstrable prostatic enlargement.

Complementary and Alternative Medicines (CAM)

- No dietary supplement, combination phytotherapeutic agent or other nonconventional therapy is recommended for the management of LUTS secondary to BPH.
- Available data do not suggest that saw palmetto has a clinically meaningful effect on LUTS secondary to BPH. Further clinical trials are in progress and the results of these studies will elucidate the potential value of saw palmetto extracts in the management of patients with BPH.
- The paucity of published high quality, single extract clinical trials of *Urtica dioica* do not provide a sufficient evidence base with which to recommend for or against its use for the treatment of LUTS secondary to BPH.

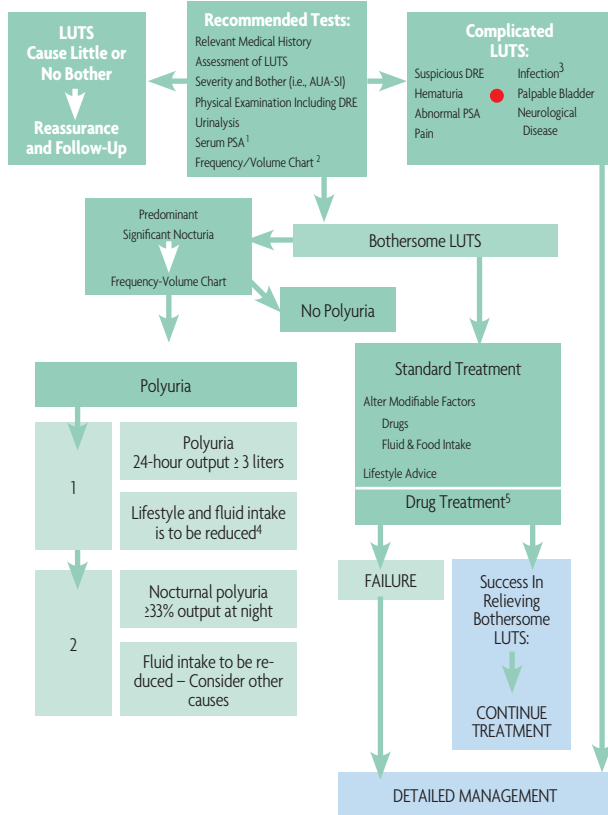
Surgical Procedures

- *All such patients should be referred to urology for further assessment and treatment.*

- *Surgery should be considered for patients for whom conservative measures have been exhausted.*
- *Surgery is recommended for patients with these uncommon or serious complications of BPH :*
 - ◆ Refractory retention who have failed at least one attempt at catheter removal. In patients who are not surgical candidates, treatment with intermittent catheterization, an indwelling catheter or stent is recommended.
 - ◆ Renal insufficiency clearly due to BPH.
 - ◆ Recurrent UTIs, recurrent gross hematuria or bladder stones clearly due to BPH and refractory to other therapies.
 - ◆ A bladder diverticulum is not an absolute indication for surgery, unless it is associated with recurrent UTI or progressive bladder dysfunction.
- Concomitant administration of an alpha blocker is an option prior to attempted catheter removal in patients with urinary retention.

FIGURE 1.

Basic Management of LUTS in Men



1 When life expectancy is > 10 years and if the diagnosis of prostate cancer can modify the management. For the AUA PSA Best Practice Statement: 2009 Update, see: www.auanet.org.

2 When significant nocturia is a predominant symptom.

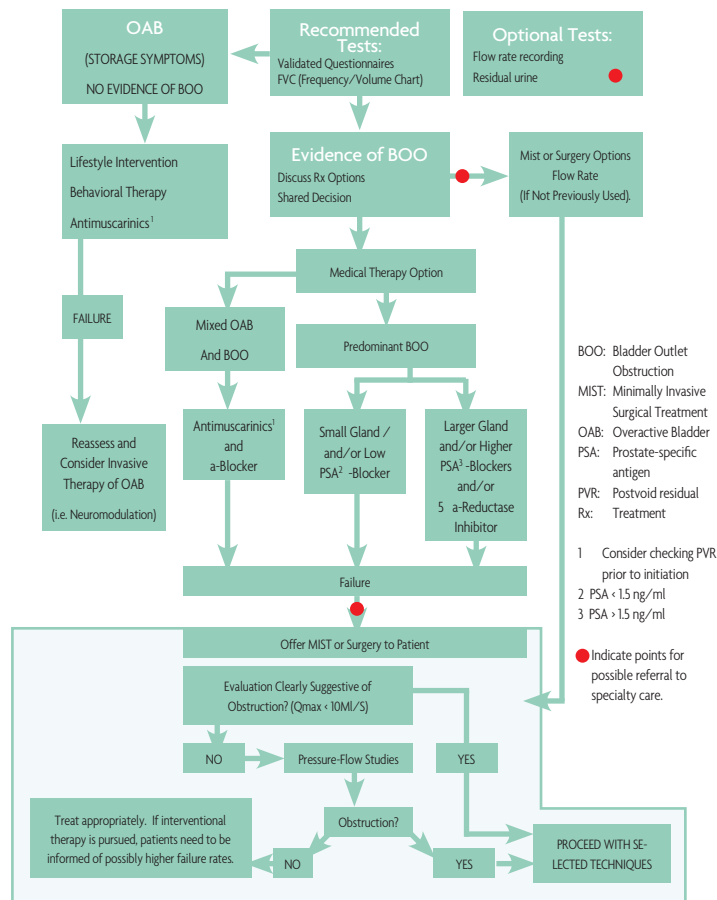
3 Assess and start treatment before referral.

4 In practice, advise patients with symptoms to aim for a urine output of about 1 liter/24 hours

5 See Figure 2

FIGURE 2.

Detailed Management for Persistent Bothersome LUTS after Basic Management



BOO: Bladder Outlet Obstruction
MIST: Minimally Invasive Surgical Treatment
OAB: Overactive Bladder
PSA: Prostate-specific antigen
PVR: Postvoid residual Rx: Treatment

1 Consider checking PVR prior to initiation

2 PSA < 1.5 ng/ml

3 PSA > 1.5 ng/ml

● Indicate points for possible referral to specialty care.

TABLE 1.1

The American Urological Association (AUA) Symptom Index for Benign Prostatic Hyperplasia (BPH) and the Disease Specific Quality of Life Question

Patient Name: _____ DOB: _____ ID: _____ Date of assessment: _____

Initial Assessment () Monitor during: _____ Therapy () after: _____ Therapy/surgery () _____

AUA BPH Symptom Score

	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
1. Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?	0	1	2	3	4	5
2. 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
3. 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
4. Over the past month, how often have you found it difficult to postpone urination?	0	1	2	3	4	5
5. Over the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5
6. Over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5
	None	1 time	2 times	3 times	4 times	5 or more times
7. Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?	0	1	2	3	4	5
Total Symptom Score						

The Disease Specific Quality of Life Question

The International Prostate Symptom Score uses the same 7 questions as the AUA Symptom Index (presented above) with the addition of the following Disease Specific Quality of Life Question (bother score) scored on a scale from 0 to 6 points (delighted to terrible):

“If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?”

FREQUENCY AND VOLUME CHART

This chart is a very important part of the preparation you need for your appointment with the urologist. It will help provide your urologist with information that may relate to your symptoms and will be useful in making a diagnosis and providing treatment. It is essential that you complete the chart and bring it with you to your appointment.

Please continue your normal schedule of eating/drinking and activity so we have a record of how much you normally drink (fluid intake), how much urine you make, and how often you empty your bladder on a daily basis.

Keep the diary with you and fill it out, as completely as possible, for three days before your Urology appointment. These do not have to be three consecutive days, but should each encompass a 24-hour period of time. To measure your urine, you can purchase an inexpensive measuring cup (i.e. 2 cup). You want something that will be easy to carry with you. This is a record of your urine output & fluid intake.

- Choose 3 days (entire 24 hrs) to complete this chart – they DO NOT have to be 3 days in a row.
- Pick days which will be convenient for you to measure and record everything that pertains to you on the chart.
- A plastic measuring cup, small bowl or urinal can be used to measure your urine volume each time you empty your bladder.

INSTRUCTIONS:

1. Record separate times for voids, catheterizations, leaks and fluid intake.
2. If you use a catheter to empty your bladder, note the urine volumes obtained.
3. Measure urine volumes and fluid intake volumes in either ounces or / cc’s (1cc = 1ml).
4. When recording a leak – please record the amount you leaked, whether you had to change your pad, your activity during the leak and your degree of urgency using the scale on the chart.
5. If you experience bladder or pelvic pain – please indicate the severity of pain that you have with each event noted using the scale on the chart.

- increased latency time associated with age
- psychosexual relationship problems
- ✦ contraindications for drug therapy
- ✦ additional risk factors (e.g., smoking, pelvic, perineal or penile trauma or surgery, neurologic disease, endocrinopathy, obesity, pelvic radiation therapy, Peyronie's disease, prescription or recreational drug use)
- ✦ other critical elements
 - alterations of sexual desire, ejaculation and orgasm
 - presence of genital pain
 - presence of genital deformity
 - lifestyle factors (e.g., sexual orientation, presence of spouse or partner and quality of the relationship with the partner)
 - history of partner's sexual function
- Perform a physical evaluation except in established patients with a new complaint of ED. Include:
 - ✦ a focused examination of the abdomen, penis, testicles, secondary sexual characteristics and lower extremity pulses
 - ✦ a digital rectal examination and a serum PSA measurement in men >50 years of age with an estimated life expectancy of more than 10 years and
 - ✦ additional assessments in select patients including
 - testosterone levels (*total and bioavailable*)
 - vascular and/or neurological,
 - nocturnal erections.

In established patients with a new complaint of ED, this assessment should be individualized.

Initial Management and Discussion of Treatment Options with the Patient

Begin management by identifying organic comorbidities and psychosexual dysfunctions, and appropriately treating them or triaging care. Consider non-surgical or surgical therapies (Table 1).

- Inform patient (and partner) of risks and benefits of available treatments.
- Consider comorbid conditions. Patients at intermediate and high risk for cardiovascular disease should be referred to a cardiologist.
- Choose treatment jointly with the patient and the partner, taking into consideration patient preferences and expectations.
- Initiate treatment in a step-wise fashion, with increasing invasiveness and risk balanced against the likelihood of efficacy.

Treatment Recommendations

Non-surgical Therapies

- Oral phosphodiesterase type 5 (PDE5) inhibitors (e.g., sildenafil, tadalafil, vardenafil) are first-line therapies unless contraindicated.
 - ✦ Monitor patients for efficacy, side effects and change in health status or medication.
 - ✦ If a patient fails to respond, determine adequacy of PDE5 inhibition before proceeding to other therapies. Recommend a different PDE5 inhibitor, or proceed with more invasive therapies.
 - ✦ Use caution if the patient is taking alpha blockers.

- ♦ PDE5 inhibitors are contraindicated in patients taking organic nitrates or in whom sexual activity is unsafe.
- *Consider referral to a urologist for alprostadil intra-urethral suppositories for a patient who has failed therapy with or is not a candidate for PDE5 inhibitors*
 - ♦ *The urologist will supervise initial dose due to risk of syncope*
 - ♦ *Consider referral to a urologist for Intracavernous vasoactive drug injection therapy for a patient who has failed therapy or, not a candidate for a PDE5 inhibitor*
- *The urologist will supervise initial injection to determine dose, monitor for prolonged erection, and instruct patient on proper technique*
 - ♦ *The urologist will schedule periodic follow-ups to check for corporal fibrosis, review injection technique, and adjust therapy as necessary*
 - ♦ *The urologist will choose either monotherapy with alprostadil or combination therapy with other vasoactive drugs (bimix and trimix) which can increase efficacy or reduce side effects (Note: bimix and trimix are available only in pharmacies offering compounding services)*
- Alprostadil intra-urethral suppositories
 - ♦ Consider using for a patient who has failed therapy with or is not a candidate for PDE5 inhibitors.
 - ♦ Supervise initial dose due to risk of syncope.
 - ♦ Can be used in combination with other treatment modalities, such as penile constriction devices or oral PDE5 inhibitors.
- Intracavernous vasoactive drug injection therapy

- ♦ Supervise initial injection to determine dose, monitor for prolonged erection and instruct patient on proper technique.
- ♦ Schedule periodic follow-ups to check for corporal fibrosis, review injection technique, and adjust therapy as necessary.
- ♦ Choose either monotherapy with alprostadil and papaverine or combination therapy with other vasoactive drugs (e.g., bimix and trimix) which can increase efficacy or reduce side effects (Note: bimix and trimix are available only in pharmacies offering compounding services).
- ♦ Inform the patient of potential for prolonged erection (lasting four hours), have a plan for the urgent treatment and inform the patient of the plan.
- Vacuum constriction devices
 - ♦ Recommend only those devices that contain a vacuum limiter.
- Other treatment modalities
 - ♦ Trazodone, yohimbine and herbal therapies are not recommended.
 - ♦ Testosterone is not indicated for treatment of ED in patients with a normal serum testosterone level.
 - ♦ Topical therapies do not appear to have significant efficacy beyond intra-urethral administration of alprostadil.

Surgical Therapies

- *Consider referral to a urologist for evaluation of a penile prosthesis implantation for the patient who does not respond to more conservative therapies*
- *Consider referral to a urologist for evaluation for vascular surgery for the patient who does not respond to more conservative therapies*

TABLE 1.

Treatment Options for Patients with Erectile Dysfunction

Non-surgical Therapies
Oral drug therapy (alphabetical order)* PDE5 inhibitors: Sildenafil Tadalafil Vardenafil
Intra-urethral drug therapy Alprostadil suppositories
Intracavernous vasoactive drug injection Alprostadil therapy Papaverine Papaverine-phenolamine Papaverine-alprostadil Papaverine-phenolamine-alprostadil
Vacuum constriction devices
Psychosexual therapy
Surgical Therapies Penile prosthesis implantation Malleable (noninflatable) rods Inflatable prostheses
Vascular surgery

* *Avanafil* was approved for treatment of ED after publication and latest verification in 2009.

INTERSTITIAL CYSTITIS/ BLADDER PAIN SYNDROME (IC/BPS)

Guideline (2011)

Interstitial Cystitis/Bladder Pain Syndrome is an unpleasant sensation (pain, pressure, discomfort) perceived to be related to the urinary bladder, and associated with lower urinary tract symptoms of more than six weeks duration, in the absence of infection or other identifiable causes. The effects of IC/BPS on psychosocial function and health-related quality of life are pervasive and insidious, impairing work life, psychosocial well-being, personal relationships and general health. This Guideline aims to provide direction on recognition of IC/BPS, appropriate diagnosis, treatment and indications for referral to a urologist. IC/BPS patients experience lower urinary tract symptoms including pain, urgency, and voiding frequency. It is important that treatment approaches reduce these symptoms and increase patient quality of life without increasing adverse events and patient burden. Referral to a urologist or gynecologist experienced in the care of patients with IC/BPS should be considered when the diagnosis is in doubt or if the primary provider lacks experience or expertise managing the many problems associated with this condition, or in patients who will need more complex therapeutic interventions as noted in the text.

This Guideline provides a useful synthesis of the evidence along with guidance from a panel of clinical experts. The panel has emphasized that treatment of IC/BPS must be individualized; the most effective approach for a particular patient is best deter-

mined by the individual clinician and patient. To guide clinicians, the panel has developed a treatment algorithm that includes elements for a basic assessment, as well as available first-line through sixth-line treatments.

All statements contained within this Guideline are based on outcomes data and are tempered by the Panel's expert opinion. Guidelines statements are graded using three evidence-based levels and two consensus-based levels with respect to the degree of flexibility in their application. Each statement is linked to the body of evidence strength and the Panel's judgment regarding the balance between benefits and risks/burdens. Please refer to the full Guideline for the grades of individual statements.

Evaluation and Diagnosis of IC/BPS

- The basic assessment should include a careful history, physical examination, and laboratory examination to rule in symptoms that characterize IC/BPS and rule out other confusable disorders (see text for details). [such as an acute urinary tract infection].
- Baseline voiding symptoms and pain levels should be obtained in order to measure subsequent treatment effects.
- Cystoscopy and/or urodynamics should be considered as an aid to diagnosis only for complex presentations; these tests are not necessary for making the diagnosis in uncomplicated presentations.

Strategies for the Treatment of IC/BPS

- Treatment strategies should proceed using more con-

servative therapies first, with less conservative therapies employed if symptom control is inadequate for acceptable quality of life; because of their irreversibility, surgical treatments (other than fulguration of Hunner's lesions) are appropriate only after other treatment alternatives have been exhausted, or at any time in the rare instance when an end-stage small, fibrotic bladder has been confirmed and the patient's quality of life suggests a positive risk-benefit ratio for major surgery. (i.e., end-stage, small, fibrotic bladder that comprises upper urinary tract function).

- Initial treatment type and level should depend on symptom severity, clinician judgment, and patient preferences; appropriate entry points into the treatment portion of the algorithm depend on these factors.
- Multiple, simultaneous treatments may be considered if it is in the best interests of the patient; baseline symptom assessment and regular symptom level re-assessment are essential to document efficacy of single and combined treatments.
- Ineffective treatments should be stopped once a clinically meaningful interval has elapsed.
- Pain management should be continually assessed for effectiveness because of its importance to quality of life. If pain management is inadequate, then consideration should be given to a multidisciplinary approach and the patient referred appropriately.
- The IC/BPS diagnosis should be reconsidered if no improvement occurs after multiple treatment approaches.

Treatments that may be offered

Treatments that may be offered are divided into first-, second-, third-, fourth-, fifth-, and sixth-line groups based on the balance between potential benefits to the patient, potential severity of adverse events and the reversibility of the treatment. See full Guideline for protocols, study details, and rationales.

First-Line Treatments (Should be performed on all patients)

- Patients should be educated about normal bladder function, what is known and not known about IC/BPS, the benefits vs. risks/burdens of the available treatment alternatives, the fact that no single treatment has been found effective for the majority of patients, and the fact that acceptable symptom control may require trials of multiple therapeutic options (including combination therapy) before it is achieved.
- *Note: Normal bladder function may include voiding frequency (≤ 8 voids per day), nocturia (less than 3 episodes per night), and absence of urgency (a strong and sudden desire to urinate that is difficult to defer) or pain (pressure, pain or discomfort localized to the bladder or urethra).*
- Self-care practices and behavioral modifications that can improve symptoms should be discussed and implemented as feasible.
- Patients should be encouraged to implement stress management practices to improve coping techniques and manage stress-induced symptom exacerbations.

Note: Behavioral modification strategies may include: altering the concentration and/or volume of urine, either by fluid restriction or additional hydration; application of local heat or cold over

the bladder or perineum; avoidance of certain foods known to be common bladder irritants for IC/BPS patients such as coffee or citrus products; use of an elimination diet to determine which foods or fluids may contribute to symptoms; over-the-counter products (e.g., neutraceuticals, calcium glycerophosphates, pyridium); techniques applied to trigger points and areas of hypersensitivity (e.g., application of heat or cold); strategies to manage IC/BPS flare-ups (e.g. meditation, imagery⁹¹; pelvic floor muscle relaxation; and bladder training with urge suppression⁹²⁻⁹⁴). Other controllable behaviors or conditions that in some patients may worsen symptoms include certain types of exercise (e.g., pelvic floor muscle exercises – see below under Physical Therapy), sexual intercourse, wearing of tight-fitting clothing and the presence of constipation.

Second-line treatments

- Appropriate manual physical therapy techniques (e.g., maneuvers that resolve pelvic, abdominal and/or hip muscular trigger points, lengthen muscle contractures, and release painful scars and other connective tissue restrictions), if appropriately-trained clinicians are available, should be offered. Pelvic floor strengthening exercises (e.g., Kegel exercises) should be avoided.
- Multimodal pain management approaches (e.g., pharmacological, stress management, manual therapy if available) should be initiated.
- Amitriptyline, cimetidine, hydroxyzine, or pentosan polysulfate may be administered as second-line oral medications (listed in alphabetical order; no hierarchy is implied).

- DMSO, heparin, or lidocaine may be administered as second-line intravesical treatments (listed in alphabetical order; no hierarchy is implied).
- *Third-, fourth-, fifth- and sixth-line treatments usually occur following a referral to a urologist with expertise in the management of IC/PBS.*

Third-line treatments

- Cystoscopy under anesthesia with short-duration, low-pressure hydrodistension may be undertaken if first- and second-line treatments have not provided acceptable symptom control and quality of life or if the patient's presenting symptoms suggest a more-invasive approach is appropriate.
- If Hunner's lesions are present, then fulguration (with laser or electrocautery) and/or injection of triamcinolone should be performed.

Fourth-line treatment

- A trial of neurostimulation may be performed and, if successful, implantation of permanent neurostimulation devices may be undertaken if other treatments have not provided adequate symptom control and quality of life or if the clinician and patient agree that symptoms require this approach.

Fifth-line treatments

- Cyclosporine A may be administered as an oral medication if other treatments have not provided adequate symptom control and quality of life or if the clinician and patient agree that symptoms require this approach.

- Intradetrusor botulinum toxin A (BTX-A) may be administered if other treatments have not provided adequate symptom control and quality of life or if the clinician and patient agree that symptoms require this approach. Patients must be willing to accept the possibility that post-treatment intermittent self-catheterization may be necessary.

Sixth-line treatment

- Major surgery (e.g., substitution cystoplasty, urinary diversion with or without cystectomy) may be undertaken in carefully selected patients for whom all other therapies have failed to provide adequate symptom control and quality of life.

Treatments that should not be offered

The treatments below appear to lack efficacy and/or appear to be accompanied by unacceptable adverse event profiles. See body of Guideline for study details and rationales.

- Long-term oral antibiotic administration should not be offered. Intravesical instillation of bacillus Calmette-Guerin (BCG) should not be offered outside of investigational study settings.
- Intravesical instillation of resiniferatoxin should not be offered.
- High-pressure, long-duration hydrodistension should not be offered.
- Systemic (oral) long-term glucocorticoid administration should not be offered.

Initial screening includes:

- A reproductive history (coital frequency and timing, duration of infertility, and prior fertility, childhood illnesses and developmental history, systemic medical illnesses, prior surgeries, sexual history including sexually transmitted infections, gonadotoxin exposure including heat exposure), and
- two semen analyses (Table 1).

* *Additional risks may include: exposure to chemicals and heat, hot baths, steam baths, radiation, cigarettes, alcohol, illicit drugs and anabolic steroids*

■ Perform *full evaluation* of male infertility if:

- ✦ the initial screening evaluation is abnormal,
- ✦ couples have unexplained infertility, and
- ✦ infertility persists following treatment of a female factor.

Full evaluation includes:

- A medical history consisting of
 - a reproductive history (see above),
 - a complete medical and surgical history,
 - a review of medications (prescription and nonprescription) and allergies, lifestyle exposures and systems, family reproductive history, and past infections such as sexually transmitted diseases and respiratory infections.
- A focused physical examination (including penis, testes, vasa, epididymes, varicocele, secondary sex characteristics, and digital rectal examination),
- at least two semen analyses,
- other procedures and tests as needed to narrow differential diagnosis or help with prognosis.

■ Other procedures and tests for assessing male fertility

Endocrine Evaluation (Table 2)

- ✦ Perform if:
 - sperm count is <10 million/mL,
 - sexual function is impaired,
 - clinical findings suggest a specific endocrinopathy.
- ✦ The *initial* endocrine evaluation includes:
 - serum follicle-stimulating-hormone (FSH),
 - serum testosterone level; if low, repeat measurement of total and free (or bioavailable) testosterone and obtain serum luteinizing hormone (LH) and prolactin level.

■ *Post-Ejaculatory Urinalysis* (UA)

- ✦ Perform to diagnose possible retrograde ejaculation in patients with ejaculate volumes < 1.0 mL, except in patients with bilateral vasal agenesis or clinical signs of hypogonadism.

■ *Transrectal Ultrasonography* (TRUS)

- ✦ Perform in:
 - azoospermic patients with palpable vasa and low ejaculate volumes to identify ejaculatory duct obstruction.

■ *Scrotal Ultrasonography*

- ✦ Perform if physical examination of the scrotum is difficult or inadequate or if a testicular mass is suspected.

■ *Specialized Tests*

- ✦ *Sperm morphology* by rigid (strict) criteria is not consistently predictive of fecundity; do not use in isolation to make prognostic or therapeutic decisions.
- ✦ *DNA integrity testing* (evaluation of degree of sperm DNA fragmentation): evidence to support routine use is

insufficient.

- ◆ *Reactive oxygen species* (ROS) testing is not predictive of pregnancy independent of routine semen parameters nor are any therapies proven to correct an abnormal test result; data are insufficient to support the routine use of ROS testing.
- ◆ Specialized tests on semen (including leukocyte quantification, antisperm antibody testing, sperm viability, examination of sperm-cervical mucus interaction, zona-free hamster oocyte test/sperm penetration assay, human zona pellucid binding tests) are not required for routine diagnosis. May use individual tests in certain patients for identifying the etiology of specific semen parameter abnormalities or in cases of unexplained infertility or for selecting therapy.

■ Genetic Screening

- ◆ Most common genetic factors related to male infertility:
 - Cystic fibrosis gene mutations associated with congenital bilateral absence of the vas deferens (CBAVD).
 - Sex chromosomal abnormalities (aneuploidy) resulting in impaired sperm production and often with impaired testosterone production.
 - Y-chromosome microdeletions associated with isolated spermatogenic impairment.
- ◆ Inform patients with:
 - Nonobstructive azoospermia or severe oligospermia that they might have chromosomal abnormalities or Y-chromosome microdeletions.
 - Azoospermia due to CBAVD that they probably have an abnormality of the cystic fibrosis transmembrane conductance regulator (CFTR) gene.

◆ Offer:

- Genetic counseling and CFTR mutations testing for a patient with CBAVD and to the female partner before proceeding with treatments that utilize the sperm of a man with CBAVD.
- Include at minimum a panel of common point mutations and the 5T allele; currently there is no consensus on the minimum number of mutations that should be tested.
- ◆ Imaging for renal abnormalities to men with unilateral vassal agenesis or CBAVD and no evidence of CFTR abnormalities.
- ◆ Gene sequencing may be considered in couples where the wife is a carrier and the husband with CBAVD tests negative on a routine panel of CFTR mutations.
- ◆ Karyotyping and genetic counseling to patients with non-obstructive azoospermia and severe oligospermia (<5 million sperm/mL).
- ◆ Y-chromosome microdeletion analysis to men with non-obstructive azoospermia or severe oligospermia.
 - There are insufficient data to recommend a minimal number of sequence tagged sites to test for in patients undergoing Y chromosome microdeletion analysis.
 - Although the prognosis for sperm retrieval is poor in patients having large deletions involving AZF region a or b, the results of Y chromosome deletion analysis cannot absolutely predict the absence of sperm.

EVALUATION OF AZOOSPERMIC MALE

Best Practice Statement (2010)

- Absence of the vasa deferentia (vasal agenesis)
 - ✦ Consider TRUS in patients with unilateral vasal agenesis for evaluation of the ampullary portion of the existing vas deferens and the seminal vesicles since these patients may have segmental atresia of the vas deferens causing obstructive azoospermia.
 - ✦ Offer genetic counseling and testing for CFTR mutations to male and also to female partner before proceeding with treatments that use sperm of a man with CBAVD.
 - ✦ Imaging of the kidneys for abnormalities should be offered to men with unilateral vasal agenesis or to men with CBAVD and no evidence of CFTR abnormalities.
- Bilateral testicular atrophy
 - ✦ Offer genetic testing (chromosomal abnormalities and Y-chromosome microdeletions) to patients with primary testicular failure (FSH levels elevated with normal or low serum testosterone).
 - ✦ Evaluate patients with acquired hypogonadotropic hypogonadism (low FSH, bilaterally small testes and low serum testosterone levels) for functioning and nonfunctioning pituitary tumors by serum prolactin measurement and pituitary gland imaging.
- * *Low gonadotropin levels leading to low sperm production occurring in a patient who had developed this condition following puberty.*
- Ductal obstruction

In patients with normal ejaculate volume (> 1.0 mL), normal testicular size, at least one palpable vas deferens, and normal FSH levels:

- ✦ Perform diagnostic testicular biopsy to distinguish between obstructive and nonobstructive causes.
- ✦ Vasography should not be performed at the time of biopsy unless reconstructive surgery is undertaken at the same time.

In patients with low ejaculate volume (< 1.0 mL) not caused by hypogonadism or CBAVD and palpable vasa perform:

- ✦ a testicular biopsy to confirm obstruction,
- ✦ TRUS with or without seminal vesicle aspiration and seminal vesiculography to identify obstruction in the distal male reproductive tract,
- ✦ alternatively, vasography to identify the site of reproductive tract obstruction but not unless reconstructive surgery is undertaken at the same surgical procedure.

MANAGEMENT OF OBSTRUCTIVE AZOOSPERMIA

Best Practice Statement (2010)

- Treatment options include:
 - ✦ Surgery
 - microsurgical reconstruction of the reproductive tract
 - transurethral resection of the ejaculatory ducts (TURED)
 - ✦ Sperm retrieval techniques and in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI) (Table 3)
 - There is no evidence that either fertilization or pregnancy rates are different using either fresh or thawed cryopreserved sperm. Base the timing of sperm

retrieval in relation to oocyte retrieval on local preference and expertise.

- There is no evidence that the site or method of sperm retrieval affects outcome of IVF with ICSI for patients with obstructive azoospermia. Base the choice of sperm retrieval by either percutaneous or open surgery from either the testis or epididymis on local preferences and expertise.
- Open surgical testicular sperm retrieval with or without microscopic magnification is recommended for patients with nonobstructive azoospermia.
- The patient should be apprised of the associated risks of IVF/ICSI.

■ Microsurgical reconstruction is preferable to sperm retrieval with IVF/ICSI in men with prior vasectomy if the obstructive interval is less than 15 years and no female fertility risk factors are present.

- ◆ If epididymal obstruction is present, the decision to use either microsurgical reconstruction or sperm retrieval with IVF/ICSI should be individualized.
- ◆ Vasoepididymostomy should be performed by an expert in reproductive microsurgery.

* Often when performing a vasectomy reversal an obstruction in the epididymis is identified. In these instances, the vas must be connected to the epididymis instead of to the other end of the vas. Expertise in microsurgery is thus emphasized here, as performing a vasoepididymostomy may require greater expertise/specialization than performing a vasovasostomy.

- Sperm retrieval/ICSI is preferred to surgical treatment in cases
 - ◆ of advanced female age,
 - ◆ of female factors requiring IVF,
 - ◆ if the chance for success with sperm retrieval/ICSI exceeds the chance for success with surgical treatment, or
 - ◆ if sperm retrieval/ICSI is preferred by the couple for financial reasons.

TABLE 1.

Semen Analysis: Reference Values

On at least two occasions (≥ 1 month apart, if possible):	
Ejaculate volume	1.5-5.0 ml
pH	> 7.2
Sperm concentration	>20 million/ml
Total sperm number	>40 million/ejaculate
Percent motility	>50%
Forward progression	>2 (scale 0-4)
Normal morphology	>50% normal*
	>30% normal**
	>14% normal***
And:	
Sperm agglutination	< 2 (Scale 0-3)
Viscosity	<3 (Scale 0-4)

*World Health Organization, 1987 **World Health Organization, 1992 ***Kruuger (Tygerberg) Strict Criteria, World Health Organization, 1999

TABLE 2.

Endocrine Evaluation: The Relationship of Testosterone, LH, FSH and Prolactin with Clinical Condition

Clinical Condition	FSH	LH	Testosterone	Prolactin
Normal spermatogenesis	Normal	Normal	Normal	Normal
Hypogonadotropic hypogonadism	Low	Low	Low	Normal
Abnormal spermatogenesis*	High/Normal	Normal	Normal	Normal
Complete testicular failure/	High	High	Low	Normal
Prolactin-secreting pituitary tumor	Normal/Low	Normal/Low	Low	High

* Many men with abnormal spermatogenesis have a normal serum FSH, but a marked elevation of serum FSH is clearly indicative of an abnormality in spermatogenesis.

TABLE 3.

Obstructive Azoospermia: Sperm Retrieval Techniques

	Advantages	Disadvantages
Microsurgical epididymal sperm aspiration (MESA)	Large quantity of sperm obtained suitable for several IVF/ICSI cycles in one procedure	Requires microsurgical skills Incision with post-op discomfort Higher cost compared to percutaneous procedures
Percutaneous epididymal sperm aspiration (PESA)	No microsurgical skills required Fast Minimum post-op discomfort	Fewer sperm retrieved Risk of epididymal damage
Testicular sperm extraction (TESE) and microTESE	No microsurgical skills required except when micro TESE performed	Risk of testicular damage with multiple biopsies Incision with post-op discomfort Higher cost compared to percutaneous procedures
Percutaneous testicular sperm aspiration (TESA)	No microsurgical skills required Fast and easy post-op discomfort Minimally invasive	Fewer sperm retrieved

PHARMACOLOGIC MANAGEMENT OF PREMATURE EJACULATION

Guideline (2004)

Premature ejaculation (PE) is one of the most common male sexual disorders. Because a universally accepted definition of PE has yet to be established, for the purposes of this Guideline, the panel defined PE as the following: ejaculation that occurs sooner than desired, either before or shortly after penetration, causing distress to either one or both partners. Although the exact etiology of PE is unknown, treatments have encompassed psychological, behavioral and pharmacologic interventions. The present recommendations address pharmacologic therapies only.

Patient Evaluation

The diagnosis of PE is based on sexual history alone.

Obtain a detailed sexual history from all patients with ejaculatory complaints.

- Components of the historical evaluation:
 - ◆ frequency and duration of PE
 - ◆ relationship to specific partners
 - ◆ occurrence with all or some attempts
 - ◆ degree of stimulus resulting in PE
 - ◆ nature and frequency of sexual activity
 - ◆ impact of PE on sexual activity
 - ◆ types and quality of personal relationships and quality of life
 - ◆ aggravating or alleviating factors

- ◆ relationship to drug use or abuse

The review should, at a minimum, include the following questions:

- Does ejaculation occur sooner than you or your partner would like?
- Do you have any difficulty obtaining or maintaining erections?
- Determine whether erectile dysfunction (ED) is a concurrent problem. In patients with concomitant PE and ED, treat ED first.
- Laboratory or physiological testing is not required unless the history and physical examination reveal indications beyond uncomplicated PE. *Physical examination should include examination of the external genitalia.*

Patient Management

Patient and partner satisfaction is the primary target outcome for treatment.

- Reassure the patient and, if possible, his partner that PE is common and treatable. *While treatment does not cure this condition, it can often improve symptoms, albeit with potential side effects.*
- Inform the patient of the treatment options and their risk and benefits prior to any intervention:
The selective serotonin reuptake inhibitors (fluoxetine, paroxetine, and sertraline), a tricyclic antidepressant (clomipramine) and topical anesthetic agents (lidocaine/prilocaine

cream) (Table 1) can be used to effectively treat PE.

- Base treatment choice on both physician judgment and patient preference.

Medical Treatment

Serotonin Reuptake Inhibitors (SRIs) – Selective and Nonselective

- Whether continuous or situational dosing is more effective is unclear. Choice of regimen is based on frequency of sexual activity. The optimal interval for situational dosing before intercourse has not been established.
- Therapy most likely will be needed on a continuing basis. PE usually returns upon discontinuing therapy.
- Although the adverse effects of the SRIs have been well-described in the management of clinical depression, consider the following facts when prescribing these agents for PE:
 - ◆ Evidence to date suggests that adverse event profiles for SRIs in the treatment of PE are similar to those reported in patients with depression (nausea, dry mouth, drowsiness and reduced libido).
 - ◆ Doses effective in the treatment of PE are usually lower than those recommended in the treatment of depression.
 - ◆ Adverse event profiles may differ among patients depending on the dosing regimen prescribed (continuous daily dosing or situational dosing). Despite lower doses in medication compared to treatment of depression, practitioners should be aware that the possibility of psychiatric side effects (such as mania in bipolar or hypomanic patients) of SRIs exists.

- Pharmacodynamic drug interactions resulting in a “serotonergic syndrome” have been reported rarely with the concomitant use of monoamine oxidase inhibitors, lithium, sumatriptan and tryptophan. Pharmacokinetic interactions resulting in alterations of drug blood levels may occur with the anticonvulsants, benzodiazepines, cimetidine, tricyclic antidepressants, antipsychotic agents, tolbutamide, antiarrhythmics and warfarin, especially in elderly patients.
- None of the SRIs have been approved by the U.S. Food and Drug Administration for the treatment of PE.

Topical Anesthetic Agents

- Should be applied to the penis prior to intercourse and used with or without a condom. The condom may be removed and penis washed clean prior to intercourse.
- Prolonged application (30 to 45 minutes) may result in loss of erection due to numbness. Diffusion of residual topical anesthetic into the vaginal wall may produce numbness of the partner.
- *Practitioners should verify and document that patients have informed their partners on their chosen form of therapy.*

TABLE 1.

Medical Therapy Options for the Treatment of Premature Ejaculation*

Oral Therapies	Trade Names [†]	Recommended Dose ^{‡§}
Nonselective Serotonin Reuptake Inhibitor		
Clomipramine	Anafranil®	25 to 50 mg/day or 25 mg 4 to 24 h pre-intercourse
Selective Serotonin Reuptake Inhibitors		
Fluoxetine	Prozac®, Sarafem®	5 to 20 mg/day
Paroxetine	Paxil®	10, 20, 40 mg/day or 20 mg 3 to 4 h pre-intercourse
Sertraline	Zoloft®	25 to 200 mg/day or 50 mg 4 to 8 h pre-intercourse
Topical Therapies		
Lidocaine/ prilocaine cream	EMLA® Cream	Lidocaine 2.5%/prilocaine 2.5% 20 to 30 minutes pre-intercourse

* This list does not reflect order of choice or efficacy.

† Trade names listed may not be all-inclusive.

‡ Peak plasma concentrations occur 2 to 8 hours (h) postdose and half-lives range from 1 to 3 days.

§ Titrate doses from low to high based on response.

Medical therapies currently employed in the management of PE have not been approved by the U.S. Food and Drug Administration for this indication. Treatment with oral antidepressants should be started at the lowest possible dose that is compatible with success.

MANAGEMENT OF CLINICALLY LOCALIZED PROSTATE CANCER

Guideline (2007)

This Guideline provides recommendations for the management of the contemporary man whose tumor is clinically localized stage T1 (normal digital rectal examination [DRE]) or T2 (abnormal DRE but no evidence of disease beyond the confines of the prostate) with no evidence of spread to regional lymph nodes (N0 or NX) or evidence of metastatic spread (M0).

Initial Evaluation

- Assess the following prior to treatment decisions:
 - ◆ Patient's life expectancy
 - With relatively long life expectancy, localized prostate cancer can be a cause of morbidity and mortality.
 - At an advanced age or with a relative short life expectancy, the chance of disease progression or death from prostate cancer is reduced.
 - ◆ Patient's overall health status
 - Overall health status influences life expectancy and may affect patient response to adverse events resulting from a particular intervention.
 - Urinary, sexual and bowel functions are important treatment determinants.
 - ◆ Patient's tumor characteristics
 - PSA level, velocity and doubling time, Gleason score and tumor stage are predictive of cancer outcomes.

Treatment Recommendations

- Inform patients about and discuss the estimates for the benefits and harms of commonly accepted initial interventions, including, at a minimum, active surveillance, external beam and interstitial radiotherapy, and radical prostatectomy.

Patients should be referred to a urologist with expertise in the management of prostate cancer for treatments listed below.

Treatment of the Low-risk Patient, defined as PSA ≤ 10 ng/mL, Gleason score ≤ 6 and clinical stage T1c or T2a

- Active surveillance, interstitial prostate brachytherapy, external beam radiotherapy and radical prostatectomy are appropriate treatment options. Study outcomes data do not provide clear-cut evidence for the superiority of any one treatment.
- Consider patient preferences and functional status related to urinary, sexual and bowel function in decision making. Particular treatments have the potential to improve, to worsen, or to have no effect on health conditions making no one treatment preferable for all patients.
- Consider the following when counseling patients regarding treatment options:
 - ◆ Two randomized controlled clinical trials show that higher dose radiation may decrease the risk of PSA recurrence; and
 - ◆ Based on outcomes of one randomized controlled clinical

trial, when watchful waiting and radical prostatectomy are compared, radical prostatectomy may be associated with a lower risk of cancer recurrence, cancer-related death and improved survival.

- Inform patients who are considering specific treatment options of the findings of recent high-quality clinical trials, including that:
 - ◆ For those considering external beam radiotherapy, higher dose radiation may decrease the risk of PSA recurrence.
 - ◆ When compared with watchful waiting, radical prostatectomy may lower the risk of cancer recurrence and improve survival.
- Determine the aim of second-line therapy (curative or palliative) for patients choosing active surveillance and tailor follow-up accordingly.

Treatment of the Intermediate-risk Patient, defined as PSA >10 to 20 ng/mL or a Gleason score of 7 or clinical stage T2b but not qualifying for high risk

- Active surveillance, interstitial prostate brachytherapy, external beam radiotherapy and radical prostatectomy are appropriate treatment options. Study outcomes data do not provide clear-cut evidence for the superiority of any one treatment.
 - ◆ Consider patient preferences and functional status related to urinary, sexual and bowel function in decision making.
- Consider the following when counseling patients regarding treatment options:

- ◆ Based on outcomes of one randomized controlled clinical trial, the use of neoadjuvant and concurrent hormonal therapy for a total of six months may prolong survival in the patient who has opted for conventional external beam radiotherapy;
- ◆ based on outcomes of one randomized controlled clinical trial, when watchful waiting and radical prostatectomy are compared, radical prostatectomy may be associated with a lower risk of cancer recurrence, cancer-related death and improved survival; and
- ◆ based on outcomes of two randomized controlled clinical trials, higher dose radiation may decrease the risk of PSA recurrence.
- Inform patients who are considering specific treatment options of the findings of recent high-quality clinical trials, including that:
 - ◆ For those considering external beam radiotherapy, the use of hormonal therapy combined with conventional dose radiotherapy may prolong survival.
 - ◆ When compared with watchful waiting, radical prostatectomy may lower the risk of cancer recurrence and improve survival.
 - ◆ For those considering external beam radiotherapy, higher dose radiation may decrease the risk of PSA recurrence.
- Determine the aim of second-line therapy (curative or palliative) for patients choosing active surveillance and tailor follow-up accordingly.

Treatment of the High-risk Patient, defined as PSA >20 ng/mL or a Gleason score of 8 to 10 or clinical stage T2c

- Although active surveillance, interstitial prostate brachytherapy, external beam radiotherapy and radical prostatectomy are treatment options, recurrence rates are high. Study outcomes data do not provide clear-cut evidence for the superiority of any one treatment.
- Consider the following when counseling patients regarding treatment options:
 - ◆ based on outcomes of one randomized controlled clinical trial, when watchful waiting and radical prostatectomy are compared, radical prostatectomy may be associated with a lower risk of cancer recurrence, cancer-related death and improved survival; and
 - ◆ based on results of two randomized controlled clinical trials, the use of adjuvant and concurrent hormonal therapy may prolong survival in the patient who has opted for radiotherapy.
- Inform high-risk patients who are considering specific treatment options of the findings of recent high-quality clinical trials, including that:
 - ◆ When compared with watchful waiting, radical prostatectomy may lower the risk of cancer recurrence and improve survival.
 - ◆ For those considering external beam radiotherapy, use of hormonal therapy combined with conventional radiotherapy may prolong survival.
- Active treatment may be a preferred option because of a high risk of disease progression and death from disease.

- All treatments chosen for high-risk patients (non-nerve-sparing prostatectomy, higher dose radiation or radiation combined with hormonal therapy) are associated with a high risk of erectile dysfunction.

Additional Treatment Guidelines

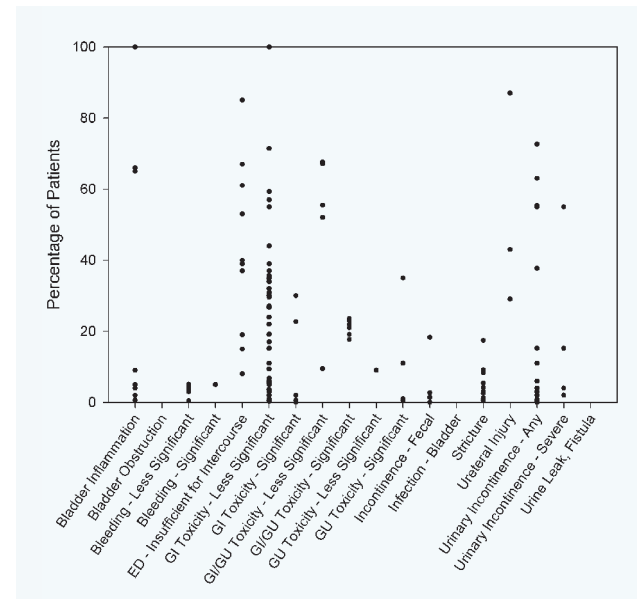
- Offer patients the opportunity to enroll in clinical trials examining new forms of therapy, including combination therapies, with the goal of improved outcomes.
- First-line hormone therapy is seldom indicated in patients with localized prostate cancer. An exception may be for/in:
 - ♦ palliation of symptomatic patients with more extensive or poorly differentiated tumors whose life expectancies are too short to benefit from treatment with curative intent. The morbidities of androgen deprivation therapy (ADT) should be considered in the context of the existing comorbidities of the patient when choosing palliative ADT.

Treatment Complications

Figures 1, 2 and 3 show the variability of complication rates for external beam radiotherapy, interstitial prostate brachytherapy and radical prostatectomy. Each circle on a graph represents one series reporting the complication. The graphs simply show the highest rate reported, disregarding the timing and neither the size of each series nor the confidence interval for the indicated percentage is indicated.

FIGURE 1.

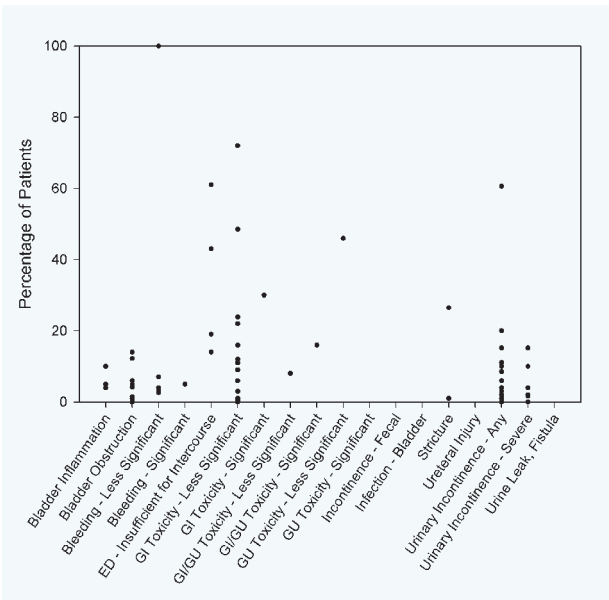
Rate of Complications Reported with External Beam Radiotherapy*



* For some complications, no data were available. ED, erectile dysfunction; GI, gastrointestinal; GU, genitourinary.

FIGURE 2.

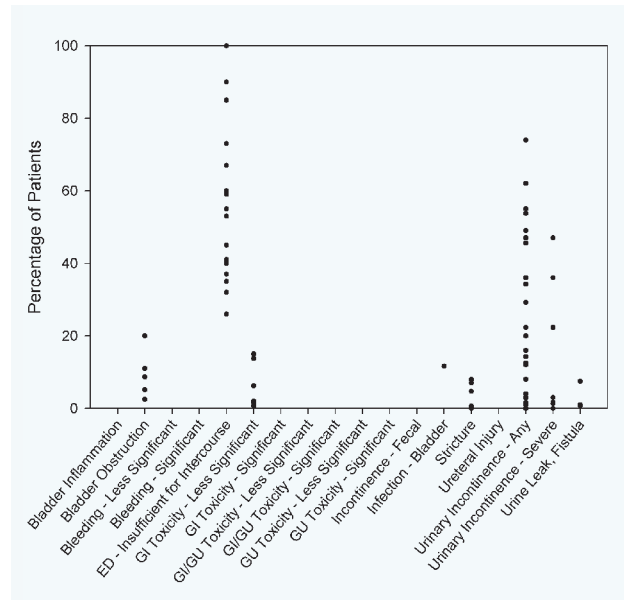
Rate of Complications Reported With Interstitial Prostate Brachytherapy*



* For some complications, no data were available. ED, erectile dysfunction; GI, gastrointestinal; GU, genitourinary.

FIGURE 3.

Rate of Complications Reported With Radical Prostatectomy*



* For some complications, no data were available. ED, erectile dysfunction; GI, gastrointestinal; GU, genitourinary.

