

URINARY INCONTINENCE IN THE OLDER ADULT

BY KRISTEN COOK, PHARM.D., BCPS; AND
LINDA M. SOBESKI, PHARM.D., BCPS

Reviewed by Gregory J. Hughes, Pharm.D., BCPS, CGP; and Helen M. LoSasso, Pharm.D., BCPS



LEARNING OBJECTIVES

1. Evaluate symptoms to accurately classify a patient with urinary incontinence (UI).
2. Apply an understanding of the pathophysiology and risk factors for UI to patient care.
3. Evaluate the most recent clinical evidence for pharmacologic and nonpharmacologic treatment of UI.
4. Design a patient-specific treatment plan to achieve optimal outcomes in an elderly patient with UI.
5. Assess for reversible causes in the patient with UI.
6. Analyze the risks and benefits of using UI medications in patients with dementia.

INTRODUCTION

The [International Continence Society](#) defines urinary incontinence (UI) as the involuntary loss of urine. In both men and women, age is a consistently reported risk factor for UI; however, it is not considered a normal consequence of aging. Overall, UI affects up to 30% of community-dwelling older adults and more than 50% of nursing home residents. It is about 2–3 times more common in women

than in men until 80 years of age, after which UI rates are similar. Despite its high prevalence, up to one-half of cases may not be reported because individuals with UI may not seek medical intervention. Embarrassment and the perception that UI is an expected consequence of aging are common factors in lack of treatment.

Urinary incontinence is categorized according to pathophysiology and clinical presentation. The four main categories are (1) stress urinary incontinence (SUI), (2) urge urinary incontinence (UUI), (3) overflow incontinence, and (4) functional incontinence. Mixed types of incontinence are common and may complicate diagnosis and treatment because of overlapping symptoms.

Studies have found that UI significantly affects psychological well-being and health care-related quality of life. Urinary incontinence may impair sexual function, restrict activities, interfere with interpersonal relationships, decrease self-esteem, increase caregiver burden, increase financial burden, and cause anxiety or depression. It is a common precipitant of institutionalization in older adults. Because of current demographic trends, UI is an increasingly common medical and socioeconomic problem.

BASELINE KNOWLEDGE STATEMENTS

Readers of this chapter are presumed to be familiar with the following:

- Urinary tract anatomy and physiology
- Mechanism of action and basic pharmacology of drugs used to treat UI
- Effect of UI on quality of life
- Basic pathophysiology of the different types of UI
- Treatment of benign prostatic hyperplasia

ADDITIONAL READINGS

The following free resources are available for readers wishing additional background information on this topic.

- Lucas MG, Bedretdinova D, Bosch JLHR, et al.; for the European Association of Urology. [Guidelines on Urinary Incontinence](#), 2013.
- Lucas MG, Bosch RJL, Burkhard FC, et al.; for the European Association of Urology. [EAU Guidelines on Assessment and Nonsurgical Management of Urinary Incontinence](#), 2012.

ABBREVIATIONS IN THIS CHAPTER

BPB	Benign prostatic hyperplasia
CVA	Cerebrovascular accident
LUTS	Lower urinary tract symptoms
OAB	Overactive bladder
PMR	Pelvic muscle rehabilitation
PVR	Post void residual
RCT	Randomized controlled trial
SNS	Sacral nerve stimulation
SUI	Stress urinary incontinence
UI	Urinary incontinence
UTI	Urinary tract infection
UUID	Urge urinary incontinence

Pathophysiology

Continence requires both an appropriately functioning lower urinary tract and the physical and cognitive ability to use a toilet. Function of the lower urinary tract is complicated and not completely understood. In individuals with normal physiology, activation of the sympathetic nervous system aids in closing the bladder neck; the bladder

fills without leakage while the parasympathetic nervous system is inhibited. As the bladder fills and pressure rises, increased parasympathetic tone causes the detrusor muscle to contract and the bladder to empty. The primary neurotransmitter involved in bladder contraction is acetylcholine, which acts at muscarinic receptors. Muscarinic 2 receptors are usually found in the lower urinary tract; however, most UI drug therapy targets the muscarinic 3 receptors, which are thought to have a larger role in bladder emptying. α -Adrenergic receptors are involved in urethral smooth muscle control.

Several classifications of incontinence are based on the underlying problem in the lower urinary tract. Although the terms *overactive bladder* (OAB) and *urge incontinence* are used interchangeably, they describe two different conditions. Overactive bladder is a symptom syndrome that includes frequency, urgency, and nocturia. These can all occur with or without urge incontinence. Although the definitions are distinct, these two conditions are treated in the same manner. Table 1-1 outlines the main classifications of UI.

Age-related changes within the urinary tract contribute to the increased prevalence of UI in the older population. These changes include decreases in bladder compliance,

Table 1-1. Types of Urinary Incontinence

Type	Definition	Common Causes
Stress	Involuntary loss of urine (small amounts) with increasing intraabdominal pressure (e.g., coughing, laughing, exercise)	Weak pelvic floor muscles (childbirth, pregnancy, menopause) Bladder outlet or urethral sphincter weakness Post-urologic surgery
Urge	Leakage of urine (can be large volumes) because of inability to delay voiding after sensation of bladder fullness is perceived	Detrusor overactivity, either isolated or associated with one or more of the following: Local genitourinary conditions (e.g., tumors, stones, diverticula, outflow obstruction) CNS disorder (e.g., stroke, parkinsonism, dementia, spinal cord injury)
Overflow	Leakage of urine (small amounts) caused by either mechanical forces on an overdistended bladder (resulting in stress leakage) or other effects of urinary retention on bladder and sphincter function (contributing to urge leakage)	Anatomic obstruction by prostate, stricture, cystocele Acontractile bladder associated with diabetes or spinal cord injury Neurogenic associated with multiple sclerosis or other spinal cord lesions Medication effect (see Table 1-2)
Functional	Urinary accidents associated with the inability to toilet because of impairment of cognitive and/or physical functioning, psychological unwillingness, or environmental barriers	Severe dementia or other neurologic disorder Psychological factors such as depression and hostility

CNS = central nervous system.

Adapted with permission from Halter JB, Ouslander JG, Tinetti ME, et al. Hazzard's Geriatric Medicine and Gerontology, 6th ed. New York: McGraw-Hill, 2009:720.

bladder capacity, urethral closing pressure, and ability to postpone voiding; increases in involuntary detrusor contractions, post void residual (PVR), and frequency of voiding; and weakened pelvic floor musculature (in women) and prostatic enlargement (in men). In addition to age-associated factors, chronic disease burden can contribute to UI.

Epidemiology/Functional Impact

Prevalence estimates of UI vary significantly by type of incontinence, definition of UI, and target populations, as well as with variations in study design. Urinary incontinence is reported to affect 30%–60% of women who are middle-aged and older. The NOBLE (National Overactive Bladder Evaluation) Program estimated that one-third of women older than 65 suffer from OAB, with about two-thirds of these cases associated with incontinence. Stress urinary incontinence affects about 13% of women 19–44 years of age and 22% of women 45–64 years of age. In older women, mixed incontinence is most common and accounts for about 50% of all cases.

Risk factors for UI in women include age, race/ethnicity, childbirth, hysterectomy, oral hormone therapy, obesity, cognitive impairment, mobility impairment, and diabetes. Control of the lower urinary tract system in women is directly affected by loss of pelvic organ support and loss of estrogen at menopause. Up to 70% of women with UI relate the onset of symptoms with menopause. Both qualitative and quantitative changes in the connective tissue of the urogenital tract are believed to contribute to SUI. Recent investigations suggest a higher prevalence of SUI in postmenopausal women who possess a collagen type I $\alpha 1$ *Sp1* polymorphism (Sioutis 2011). Type 1 collagen is the main structural protein in connective tissue. Polymorphism may be associated with alterations in the quality and quantity of pelvic floor collagen.

Because UI is more common in women, there are fewer studies evaluating the prevalence and epidemiology of UI in men. In men, UI has a later and more sudden onset than in women. The National Health and Nutrition Examination Study reported an overall UI prevalence in men of 4.5%; this prevalence increased to 16% in men 75 years or older. Factors associated with UI in men of this study were age, major depression, benign prostatic hyperplasia (BPH), and hypertension (Markland 2010). In other studies, associated risk factors included lower urinary tract symptoms (LUTS), impaired mobility, and urethral surgery or irradiation. Despite surgical advances, UI remains a common complication for 12%–16% of men after surgery for prostate cancer.

Several comorbid conditions are associated with UI in both men and women. Urinary incontinence is common after a cerebrovascular accident (CVA), with 40%–60% of patients experiencing UI during hospitalization immediately after a CVA. The incidence significantly declines over several months; however, up to one-third of

patients continue to have UI at 12 months after a CVA. A case-control analysis noted a higher incidence of UI in community-dwelling individuals with CVA (28%) than in those without stroke (20%) (Divani 2011). Risk factors for UI after stroke include hemiparesis, depression, impaired cognition, age older than 75 years, dysphagia, visual field defect, and motor weakness.

Other conditions resulting in impaired mobility and/or cognition (e.g., Parkinson disease, osteoarthritis, dementia) are also associated with UI. Urinary frequency and nocturia associated with congestive heart failure or peripheral venous insufficiency can contribute to UI. Diabetes is an independent risk factor for developing UI because of polyneuropathy, changes in fluid intake, and diabetes-related functional impairment.

Urinary incontinence has a significant socioeconomic impact. Individuals with UI may suffer medical and quality-of-life consequences that compromise overall well-being. Urinary incontinence has been associated with an increased risk of urinary tract infections (UTIs), pressure ulcers, falls, fractures, and sleep disturbance, all of which may lead to functional impairment and decline in overall health status. Urinary incontinence is a well-recognized risk factor for nursing home placement. Incontinence after a stroke adversely affects 2-year survival, disability, and functional outcome; it is also associated with a 4-fold increased risk of institutionalization at 1 year (Kolominsky-Rabas 2003). Psychological and social complications of UI include isolation, depression, anxiety, impaired sexual function, decreased work productivity, increased functional dependency, and increased caregiver burden.

According to the [National Institutes of Health](#), the annual direct cost of UI in the United States was about \$19.5 billion in 2000. Up to 70% of the cost is attributed to routine care such as incontinence pads and diapers, protective items, laundry, odor control, and skin care products. A major contributor to this figure is the cost of institutional care.

CLINICAL EVALUATION AND DIAGNOSIS

In a large Medicare study, only 56% of patients who self-reported UI symptoms had them discussed at their most recent health care visit (Mardon 2006). Screening is necessary to identify patients because many patients do not report symptoms. Screening questions such as “Do you ever leak urine when you do not want to?” and “Do you ever leak urine when you cough, sneeze, or laugh?” are now part of health care quality assessments through Medicare.

Women in the Medicare population reported incontinence symptoms at a rate of 43.6% and men at a rate of 27.9% (Mardon 2006). The reporting of bothersome symptoms increased with age for both men and women.

The Agency for Healthcare Research and Quality recommends a basic diagnostic evaluation for UI. A thorough history should focus on specific symptoms, as well as quality of life and impact on the patient and caregivers. A bladder diary can be used to identify patterns and measure treatment efficacy. Bladder diaries keep track of things such as liquid intake, number of trips to the bathroom, activities during leakage, strength of urge to void, and accidental leaks. A freely accessible [bladder diary](#) can be found online courtesy of the National Institutes of Health. An abdominal, rectal, and genital physical examination should be performed, and a urinalysis should be used to rule out infection or glucosuria. There is no need to treat asymptomatic bacteriuria in the institutionalized patient; treatment has not been shown to decrease UI (Lucas 2012; Johnson 2009). In noninstitutionalized patients, this is less clear. Treatment may be attempted first to see whether incontinence improves (Johnson 2009). Some groups recommend that PVRs be measured for all patients; however, this is controversial. The American Urological Association recommends a PVR if, after a history and urinalysis, the diagnosis of OAB is unclear. The European Association of Urology cites a lack of evidence for routine PVR measurement. Post void residuals help determine the amount of urinary retention and should be performed in patients at high risk of urinary

retention, including those who have diabetes, are taking anticholinergic drugs, have a neurologic disorder, or have symptoms of voiding difficulty or retention. A PVR of less than 100 mL is normal; greater than 200 mL is considered abnormal. Between those two values, the PVR must be interpreted with other information about the patient. Specialty testing (e.g., urodynamics) is not necessary during initial evaluation and treatment.

Another important part of the initial evaluation of UI is to identify any reversible causes or contributors. Several chronic diseases and conditions can contribute to UI. These include UTIs, atrophic vaginitis, urinary tract surgeries (prostatectomy), constipation, uncontrolled diabetes, chronic venous insufficiency, delirium, and mobility restraint. Appropriate treatment for each of these conditions should be implemented and incontinence reassessed. Several drugs can also cause or exacerbate UI (Table 1-2).

MANAGEMENT OF UI

Nonpharmacologic Treatment

Nonpharmacologic and behavioral strategies are important in the comprehensive management of UI. Noninvasive lifestyle and behavioral interventions are the first-line treatment of choice in the elderly population.

Table 1-2. Drugs That Can Affect Continence

Drug	Effects on Continence
Alcohol	Increased frequency, urgency, sedation, immobility
α-Adrenergic agonists	Outlet obstruction (men)
α-Adrenergic blockers	Stress leakage (women)
ACE inhibitors	Cough worsens stress incontinence
Anticholinergics	Impaired emptying, retention, delirium, sedation, constipation, fecal impaction
Antipsychotics	Anticholinergic effects plus rigidity and immobility
Calcium channel blockers	Impaired detrusor contractility and retention; dihydropyridine agents can cause pedal edema, leading to nocturnal polyuria
Cholinesterase inhibitors	Urinary incontinence, interactions with antimuscarinics
Estrogen	Worsens stress and mixed leakage in women
GABAergic agents (gabapentin and pregabalin)	Edema causing nocturia and nighttime incontinence
Loop diuretics	Polyuria, frequency, urgency
Narcotic analgesics	Urinary retention, fecal impaction, sedation, delirium
NSAIDs	Pedal edema causing nocturnal polyuria
Sedative hypnotics	Sedation, delirium, immobility
Thiazolidinediones	Pedal edema causing nocturnal polyuria

ACE = angiotensin-converting enzyme; GABA = γ -aminobutyric acid; NSAID = nonsteroidal anti-inflammatory drug; TCA = tricyclic antidepressant. Adapted with permission from: Reuben DB, Herr KA, Pacala JT, et al. Geriatrics at Your Fingertips, 14th ed. New York: American Geriatrics Society, 2012.

Advantages of behavioral interventions include low cost, absence of adverse effects, and ease of implementation. These interventions should be individually tailored; their effectiveness largely depends on patient motivation, functional capacity, and cognitive function.

Lifestyle Modification

Lifestyle modifications for UI include smoking cessation, caffeine and alcohol reduction, weight loss, and modified fluid intake. The relationship between caffeine intake and OAB appears to be dose-dependent. Patients consuming greater than 400 mg/day of caffeine are 2.4 times more likely to experience detrusor instability. Reductions in caffeine intake should be undertaken gradually to avoid withdrawal symptoms. Data exist to suggest obesity and type 2 diabetes mellitus as independent risk factors for UI in women. In the Action for Health in Diabetes (Look AHEAD) trial, moderate weight loss was reported to reduce the incidence but not improve the resolution rate of UI among overweight women with type 2 diabetes mellitus (Phelan 2012). Another recent study of UI in overweight women reported that weight loss decreased the cost of incontinence management by 81% and was independently associated with decreased frequency of incontinence (Subak 2012). Modified fluid intake encourages reductions in fluid intake during the evening hours. Many patients will restrict fluid on their own in an attempt to manage incontinence. Patient education regarding the timing of fluid intake is critical; overall, fluid restriction is not recommended because it may lead to dehydration and increased risk of UTIs.

Additional supportive measures include education about bladder health, use of absorbent products, and appropriate skin care. Environmental interventions such as toilet proximity, safe path to bathroom, raised toilet seats, grab bars, and toilet substitutes (e.g., urinals, commodes) are particularly useful for patients with functional incontinence.

Behavioral Therapy

The goal of behavioral interventions is to achieve a satisfactory voiding pattern. Patient-dependent behavioral therapies require functional capacity, learning ability, and patient motivation. Patients with functional disability or cognitive impairment require systematic toileting assistance, and they are often dependent on caregivers for successful implementation of behavioral interventions.

Bladder training is an urge suppression technique that is effective in patients with intact cognition, adequate functional ability to toilet, and motivation to cooperate. The patient gradually increases toileting intervals by resisting or inhibiting the sensation of urgency. Patients learn to urinate according to a scheduled timetable, rather than with the symptoms of urge. Distraction and relaxation techniques are employed to help delay voiding and allow the development of increased bladder capacity. The

goal interval is initially based on the patient's individual voiding habits. Intervals are increased by 15- to 30-minute increments per week until a voiding interval of 3–4 hours is achieved. Bladder diaries can be a useful adjunct to bladder training. The efficacy of bladder training has been shown in several studies, with a reduction in incontinence episodes and a decrease in volume of urine lost (Subak 2002; Fantl 1991). Regular voiding at timed intervals to avoid a full bladder or prevent involuntary bladder contractions is a useful behavioral strategy for all types of incontinence.

Pelvic muscle rehabilitation (PMR), also referred to as Kegel exercises, is commonly used as a treatment strategy for SUI and UUI. Repetitive contraction and relaxation of the pelvic floor muscles is used to improve the reflex inhibition of involuntary detrusor contractions and enhance the ability to voluntarily contract the external sphincter. In randomized clinical trials, PMR reduced episodes of UI by 54%–75% compared with reductions of 6%–16% without treatment (Goode 2010). A systematic review of PMR for UI in men after prostatectomy found that PMR, with or without biofeedback, improved continence compared to no PMR (MacDonald 2007). Some patients have difficulty identifying and isolating pelvic floor muscles. Biofeedback and vaginal weights are tools that are sometimes used to help patients correctly perform the exercises. Studies have failed to show a benefit of PMR combined with biofeedback or vaginal weights over PMR alone. Referral to a nurse specialist or physical therapist may be of benefit for the patient who is cognitively intact but who has difficulty effectively performing the exercises. In summary, PMR is a safe but labor-intensive approach that requires a motivated and cooperative patient.

Devices

Sacral nerve stimulation (SNS) has U.S. Food and Drug Administration (FDA) approval for use in the treatment of patients with severe refractory UUI when behavioral management and medications fail or are not tolerated. In SNS, a generator device is inserted subcutaneously in the lower back or buttocks. A lead is attached to the S3 sacral nerve, and electrical stimulation results in decreased contraction of the detrusor muscle. Studies of SNS have shown significant decreases in the number of incontinence episodes as well as incontinence pads used in patients with OAB. Efficacy data from randomized controlled trials (RCTs) show that complete continence or significant improvement was achieved in about 80% of patients who received SNS compared with 3% in control groups (Brazzelli 2006). Patients with a higher number of daily incontinence episodes (greater than 10) are most likely to benefit. Surgical revision rates range from 3% to 33% and are attributed to lack of efficacy or infection.

The extracorporeal magnetic innervation chair has FDA approval for use in the treatment of uncomplicated mild SUI. A low-intensity magnetic field is used to strengthen

pelvic floor muscles. Treatments are generally given for 20 minutes twice weekly for 8 weeks total.

Women with good manual dexterity are candidates for intravaginal support devices or urethral occlusion inserts. These devices offer the option of temporary or occasional use and are suitable for patients with exercise-induced SUI. Pessaries are often employed in older women who have not responded to behavioral therapies. Insertion is performed by a health care provider, and the pessary can be removed for cleaning and reinserted every 4–6 weeks. Pessaries are suitable for temporary or long-term use. Monitoring for vaginal infection and ulceration is critical to the safe use of these devices. A study conducted in patients with SUI compared pessaries alone, behavioral treatment alone, or a combination of pessary and behavioral treatment. The reported patient satisfaction rate was greater than 50% for all treatment groups at 12 months (Richter 2010).

Urinary catheters are reserved for patients with chronic bladder-emptying difficulty and elevated PVR. Catheters may also be useful as a temporary measure in patients with open skin wounds that must be protected from urine. Severely or terminally ill patients with chronic UI who are bedbound may also be appropriate candidates for a urinary catheter.

Invasive Treatments

Surgical management of SUI is common in the United States, with more than 200,000 procedures performed annually. Surgery is considered the most effective treatment when SUI is accompanied by uterine prolapse. The Burch colposuspension procedure involves supporting the anterior vaginal wall to the Cooper ligament through a laparoscopic incision. In recent years, the midurethral mesh sling has replaced the Burch procedure as the new gold standard. The midurethral sling procedure employs transvaginal placement of a synthetic mesh below the midurethral area. The Burch procedure and the midurethral sling have comparable rates for cure and complications; however, the midurethral sling procedure offers the advantage of a less-invasive approach, shorter operative times, technical ease, and ability to be performed in the outpatient setting. Reported cure rates are 77%–96%. Recent data suggest that the overall reoperation rate after SUI surgery is higher for the midurethral sling (13.0%) than for the Burch procedure (10.8%) (Jonsson Funk 2012).

Periurethral injection of bulking agents (e.g., collagen) improves urethral closure in SUI and may be beneficial in mild cases of postprostatectomy SUI. High short-term cure rates are achieved; however, effectiveness is lost over time, and repeated interventions are often necessary. Reinjection may be associated with inflammatory reactions and scarring, which makes further treatment difficult. The use of bulking agents may be appropriate for patients with refractory SUI who have shown sphincter incompetence based on urodynamic studies.

Although not a first-line therapy, artificial urinary sphincters are the most effective treatment for intractable postprostatectomy SUI in men. Subjective satisfaction rates reach 85%–95%; however, the risk of infection is high (1.8%–10%). Other potential complications include tissue atrophy resulting in worsening incontinence, urethral erosion, and device defects. These complications often necessitate reoperation or removal of the system, with device defects accounting for about one-half of all revision procedures.

Pharmacologic Treatment

Nonpharmacologic or behavioral therapy should always be implemented for patients with UI, but pharmacotherapy is often added to help alleviate symptoms. Pharmacotherapy does not cure UI. Drugs should not be implemented without the failure or addition of behavioral therapies because of potential adverse effects. Currently, data are limited to support the combination of drugs and behavioral therapy over each separately (Burgio 2010; Burgio 2008). Figure 1-1 describes the management of the patient with UI.

Antimuscarinics

The most commonly prescribed UI drug class is muscarinic receptor blockers. These drugs are primarily used for UUI. During the past 10 years, there have been several additions to this class, with the hope that these new drugs would be more selective for muscarinic receptors in the bladder. This specificity was aimed at reducing the common anticholinergic adverse effects of these medications.

Comparative Efficacy and Tolerability

Oxybutynin remains the gold standard by which other agents are measured. It was the first approved antimuscarinic agent for UI. The immediate-release formulation has significant anticholinergic effects, however, and it is thought that the longer-acting formulations, as well as the topical and transdermal formulations, have fewer adverse effects. The oxybutynin extended-release formulation may reduce first-pass metabolism, decreasing the active metabolite *N*-desethyloxybutynin. This metabolite is thought to cause many of the anticholinergic adverse effects. The oxybutynin transdermal patch and gel also bypass first-pass metabolism.

The oxybutynin transdermal patch must be applied every 3 or 4 days, whereas the gel must be applied daily. In a comparison of anticholinergic adverse effects, the rates of xerostomia with oxybutynin were 71% with immediate release, 29%–61% with extended release, 4%–10% with the transdermal patch, and 2%–12% with gel. The reported adverse event rates for other anticholinergic effects in the package inserts are listed in Table 1-3.

In general, dry mouth occurs less often with extended-release formulations, and many of the anticholinergic adverse effects appear to be dose related. The risk

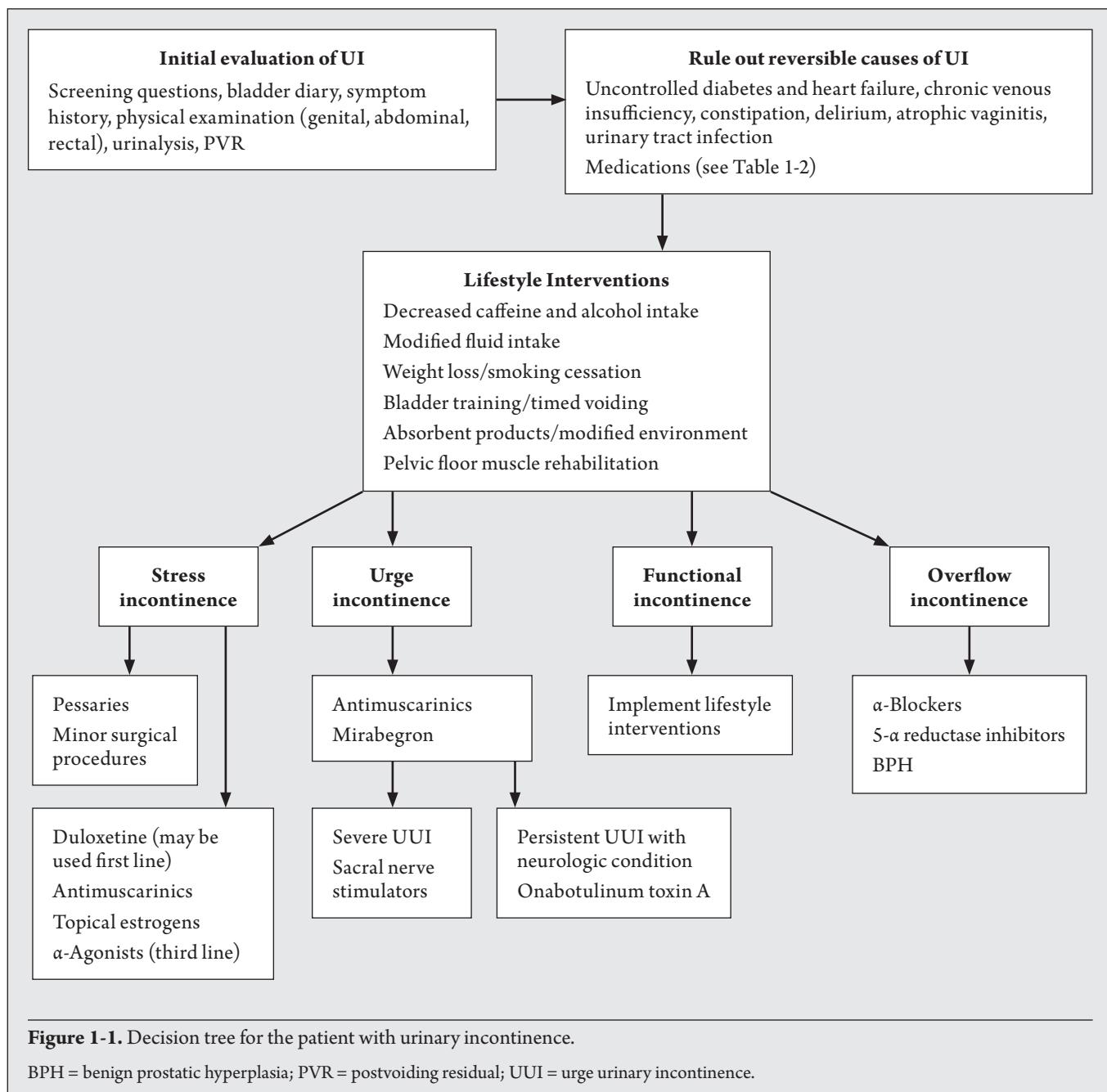


Figure 1-1. Decision tree for the patient with urinary incontinence.

BPH = benign prostatic hyperplasia; PVR = postvoiding residual; UUI = urge urinary incontinence.

of constipation appears to be slightly greater in the higher-dosage forms of some of the newer agents (i.e., solifenacina and darifenacina). There is no evidence that QT prolongation is a major adverse effect of the antimuscarinics when used at usual dosages. Some evidence exists that these agents prolong QT intervals in higher dosages or overdose (Hesch 2007). Clinically, it is important to note whether a patient is taking other QT-prolonging agents when initiating antimuscarinics because there may be a small additive effect (Hesch 2007).

Evidence is insufficient to support other agents (e.g., tolterodine, fesoterodine, trospium) over oxybutynin

with respect to better efficacy or tolerability. This is mainly because of the lack of head-to-head trials. Solifenacina and darifenacina were believed to be uroselective agents when they were developed. However, the available data do not show that these agents are any better with respect to anticholinergic adverse effects, and they should not be chosen on the basis of being uroselective.

A recent systematic review evaluated the efficacy and tolerability of several antimuscarinic agents for UUI in women. This review included literature from 1966 to 2011, and only RCTs were eligible. In the 94 trials analyzed, antimuscarinics had only a small benefit over

Table 1-3. Adverse Effect Profiles of Antimuscarinic Agents Used for UI

Adverse Effect	Dry Mouth (%)	Constipation (%)	Nausea (%)	Headache (%)	Somnolence (%)	Dizziness (%)	Confusion (%)	Tachycardia (%)	Urinary Retention (%)	Dry Eyes (%)	Blurred/ Abnormal Vision (%)
Oxybutynin IR	71.4	15.1	11.6	7.5	14.6	16.6	2–5	2–5	6.0		9.6
Oxybutynin ER	29.0	7.0	2.0	6.0	2.0	4.0				3.0	1.0
Oxybutynin transdermal	9.6	3.3	1–2		1–2						2.5
Tolterodine IR	35.0	7.0		7.0	3.0	5.0				3.0	2.0
Tolterodine ER	23.0	6.0		6.0	3.0				1.2	3.0	1.0
Trospium IR	20.1	9.6		4.2							1.2
Trospium XR	10.7	8.5	1.4								1.6
Solifenac 5 mg	10.9	5.4	1.7		1.9	1.8			0	0.3	3.8
Solifenac 10 mg	27.6	13.4	3.3		1.8	1.9			1.4	1.6	4.8
Darifenac 7.5 mg	20.2	14.8	2.7		0.9						1.5
Darifenac 15 mg	35.3	21.3	1.5		2.1						2.1
Fesoterodine 4 mg	18.8	4.0	0.7				< 1		0.2	1.4	< 1
Fesoterodine 8 mg	34.6	6.0	1.9						1.1	3.7	

ER = extended release; IR = immediate release; UI = urinary incontinence; XR = extended release.

Information from manufacturers' package inserts.

placebo in achieving continence and improving UI symptoms. When all drugs were analyzed together, the absolute risk difference in continence was less than 20% (Shamliyan 2012). The drug class also had a significantly higher discontinuation rate than placebo because of adverse effects. The lowest rates of discontinuation were with solifenac 5 mg daily. More than 50% of patients had discontinued treatment with their antimuscarinic at 1 year (Shamliyan 2012). Dry mouth was the most common adverse event reported in the analysis. The review also evaluated the trials that compared antimuscarinics with each other. Fesoterodine was more effective than tolterodine, producing greater rates of continence, but it also had a higher discontinuation rate because of adverse effects. There was no difference in UI improvement between oxybutynin and tolterodine, although treatment discontinuation rates for oxybutynin were greater.

Overall, a small benefit in UI symptoms was seen with antimuscarinic drugs compared with placebo. None of the agents showed superiority on the basis of current evidence. Solifenac 5 mg had the lowest discontinuation rate because of adverse effects and could be an option if other urge incontinence treatments have failed the patient. One of the main limitations of this analysis is that more than 80% of the patients included were women, reducing the generalizability of the conclusions to men (Shamliyan 2012).

Because efficacy is similar across the antimuscarinic class, the choice of a first-line agent is often influenced by cost, drug interactions, patient comorbidities, adverse effects, and route of administration. Oxybutynin

immediate release costs significantly less than most of the other agents. Solifenac and the extended-release and transdermal formulations of other agents may have fewer anticholinergic adverse effects. These alternatives may be preferred when the patient has comorbidities that make these adverse effects particularly problematic.

Discontinuation rates do not typically differ with these formulations. Skin reactions may limit the use of transdermal products because rates of pruritus and rash can be as high as 15% (Dmochowski 2002). The 2012 [American Geriatrics Society Beers Criteria](#) lists the oral antimuscarinics as a class that exacerbates constipation and that should be avoided unless no alternative is available (AGS 2012).

Drug interactions may also influence the choice of antimuscarinic. Tolterodine is metabolized by cytochrome P450 (CYP) 2D6 in most patients. Some patients have a genetic polymorphism that hampers metabolism through the 2D6 pathway. These poor metabolizers rely more on the CYP3A4 pathway for metabolism. In patients who are taking potent CYP 2D6 or 3A4 inhibitors, the dosage of tolterodine should be reduced by 50%. Darifenac is metabolized by CYP 2D6 and 3A4, but no formal dosage reductions are recommended for this drug. Fesoterodine and solifenac are metabolized by CYP3A4, and their maximal daily dosages with potent CYP3A4 inhibitors are 4 mg and 5 mg, respectively.

Antimuscarinics should exert their effect within the first month a patient takes them. Follow-up should then be done to assess adverse effects and efficacy.

Over-the-counter Oxybutynin Transdermal

In January 2013, the FDA approved the switch of oxybutynin transdermal from prescription-only status to over the counter (OTC) (FDA Briefing Document 2012). This was despite the Nonprescription Drugs Advisory Committee vote in November 2012 against the switch to OTC status. Oxytrol (oxybutynin transdermal) is currently projected to come to the OTC market in September 2013. Three types of studies were done to present evidence to the FDA to approve this switch: a label comprehension study, which was aimed at assessing whether patients could understand the directions/labeling; a self-selection study, which was aimed at assessing whether the appropriate patients chose to use the product; and an actual use study, which determined whether patients who were using the product discontinued use appropriately and followed labeling instructions. In these studies, 90% of men appropriately did not select the product for themselves, and 92% of pregnant patients appropriately did not select the product. In the actual use study, 3.4% of patients continued using the oxybutynin transdermal product when they should have discontinued. All cases were reviewed by physicians to determine whether patients should have discontinued. Originally, 14.4% should have discontinued according to labeling, but that number was reduced to 3.4% after physician reviews. In those with UTIs, 98% discontinued appropriately.

The OTC oxybutynin transdermal product will be marketed only to women older than 18 years. This is because men were not as able to effectively differentiate urinary symptoms caused by OAB from other causes of UI such as BPH. The packaging will have a pink box and will state in large letters that this product is for women so that men are discouraged from using it. The labeling for the new OTC product will state that the product is to be used only for symptoms that have been present for at least 3 months. This will help women who have UTIs or are in early pregnancy avoid use of the product. The labeling also is meant to prominently show symptoms that are cause for discontinuation. The OTC oxybutynin transdermal labeling states the medication should also result in improvement in 2 weeks. If symptoms persist or worsen during or after this period, the patient should seek medical advice.

Use with Cholinesterase Inhibitors and in Patients with Dementia

Urinary incontinence is often seen in elderly patients with dementia. The antimuscarinic agents used to treat UUI directly oppose many drugs that treat dementia by increasing cholinergic transmission. Whether antimuscarinics should be prescribed with cholinesterase inhibitors is controversial, as is whether they should be prescribed in general to patients with baseline cognitive impairment.

One overlooked issue is that cholinesterase inhibitors have the ability to increase or possibly even precipitate UI episodes. Only minimal rates of UI are cited in the package

inserts for donepezil (1%–3%), rivastigmine (not listed), and galantamine (less than 1%–2%); however, clinically, this is an important issue to consider. One retrospective study looked at the possible cascade of being prescribed an antimuscarinic agent in response to an adverse effect from a cholinesterase inhibitor. The study looked at 44,884 older adults, of whom 20,491 were prescribed a cholinesterase inhibitor (95% donepezil). The results showed that 4.5% of those prescribed a cholinesterase inhibitor were also prescribed an antimuscarinic agent. Another 3.1% of those not taking a cholinesterase inhibitor were prescribed one by the study's conclusion (Gill 2005). This increase was statistically significant. An important consideration in patients taking both a cholinesterase inhibitor and an antimuscarinic agent is taking a detailed history of when UI symptoms started or worsened in relation to the addition of these drugs. A dose reduction or risk-benefit analysis of the cholinesterase inhibitor may be needed to improve UI.

Dementia itself can worsen UI; this places an even larger burden on caregivers. Up to one-third of patients with dementia are taking both cholinesterase inhibitors and antimuscarinics. There is conflicting evidence on the extent to which antimuscarinics affect cognition or potentially reduce the efficacy of cholinesterase inhibitors. A prospective cohort study of 3536 nursing home patients who were taking a cholinesterase inhibitor found that 10.6% were prescribed oxybutynin or tolterodine in the 2-year study period. The authors found that using these two agents together created an additional 0.54 decrease in ADL (activities of daily living) points (0–28 scale) ($p=0.01$). The MDS-COGS (Minimum Data Set Cognition Scale) score was used to assess cognitive decline, which did not differ between groups (Sink 2008). Similarly, another RCT of 50 female nursing home patients found no change in cognition when oxybutynin extended release was administered for 4 weeks (Lackner 2008). These two trials cannot be generalized to the community-dwelling elderly adult because they were performed in the nursing home population. The smaller changes may have a greater effect on the highly functional community-dwelling elderly adult. Several case reports also show cognitive decline with antimuscarinics (Donnellan 1997).

There is no definitive evidence of whether antimuscarinics should be used in patients with cognitive impairment or in patients taking a cholinesterase inhibitor. Clinicians should consider the possible interactions carefully. If an antimuscarinic is believed necessary in these patients, cognitive function should be monitored when initiating the drug and on a regular basis thereafter.

Use with α -Blockers

Men are underrepresented in trials of UI drugs, constituting only 10%–25% of study subjects. Drugs used for UI are thought to have similar efficacy and tolerability in the male population. Although the LUTS of UUI and bladder outlet obstruction or BPH are similar, a distinction must be made because the use of antimuscarinic agents in BPH

can cause significant urinary retention. Using α -blockers concomitantly with antimuscarinics has become a subject of interest. In a few trials, this combination has shown improvement in LUTS (Chapple 2010). For a detailed discussion on using α -blockers concomitantly with antimuscarinics, see the chapter on BPH in this book.

Duloxetine

Although duloxetine is approved in Europe for use in SUI, this remains an off-label use in the United States. The [2012 European Association of Urology Guidelines](#) suggest offering duloxetine to both men and women who would like symptom relief from SUI, giving this recommendation a grade A evidence level. Trials in the United States for this indication are ongoing. Several trials have looked at duloxetine versus placebo, usually at a dose of 40 mg twice daily. These studies have evaluated UI frequency episodes and found significant median decreases in these episodes with duloxetine to be 50%–54% versus placebo at 27%–40% (Millard 2004; Van Kerrebroeck 2004; Dmochowski 2003).

A 2009 Cochrane review of studies comparing duloxetine with placebo included 10 RCTs with 3944 adults having SUI. Trial duration was only 3–12 weeks, but the frequency of incontinence episodes was reduced by up to 50% with duloxetine compared with placebo (Mariappan 2005). It was not known whether this benefit could be sustained, but the available evidence suggested it was a good option for the treatment of SUI.

Duloxetine has shown improvement in quality of life in several trials, with some patients seeing benefit within 2 weeks of initiation. The typical dose is 40 mg twice daily, and the most common adverse effect reported in most trials was nausea (4%–24%), possibly related to rapid dose escalation (Millard 2004; Van Kerrebroeck 2004; Dmochowski 2003). Duloxetine is metabolized by CYP 2D6 and 1A2, and caution must be used with inhibitors of these two enzymes. In the 2012 American Geriatrics Society Beers Criteria, duloxetine is listed with other serotonin-norepinephrine reuptake inhibitors for use with caution in elderly patients because of the risk of syndrome of inappropriate antidiuretic hormone or hyponatremia (AGS 2012). Duloxetine is not recommended when the CrCl is less than 30 mL/minute.

α -Agonists

The use of α -agonists for SUI is not as common now that duloxetine is considered a first-line agent. Some guidelines do not even list α -agonists as an option for treatment anymore. Contraindications to the use of these agents (i.e., hypertension, arrhythmia, coronary artery disease, myocardial infarction, hyperthyroidism, kidney failure, and narrow angle glaucoma) make them difficult to use. The adverse effects of hypertension, headache, anxiety, and insomnia make these agents even less attractive.

Estrogens

Oral and topical estrogen therapy was thought to improve the symptoms of SUI by increasing α -receptors and local circulation. Both the Heart and Estrogen/Progestin Replacement Study (HERS) and the Women's Health Initiative study showed increased UI with the use of oral estrogens. In the HERS study, 39% of patients had worsening of incontinence, whereas only 27% in the placebo group had similar outcomes (Grady 2001). Oral estrogen also carries a risk of cardiovascular adverse events, possible worsening cognition, and increased breast cancer risk. Oral estrogen should not be routinely used for SUI. Topical estrogens can be used, and doses for vaginal atrophy are recommended in this case. The 2012 European Association of Urology guidelines also endorse topical estrogen as an option for SUI, with a grade A level recommendation. The 2012 Beers Criteria recommend against the use of oral or transdermal patch estrogen in women.

Botulinum Toxin

In 2011, the FDA approved the labeling of Onabotulinum toxin A for use in patients with detrusor overactivity associated with a neurologic condition (e.g., spinal cord injury, multiple sclerosis) and inadequate response to anticholinergic therapy. The injections are intradetrusor by cystoscopy. According to the package insert, in preapproval studies, the frequency of incontinence episodes at week 12 was decreased by 19.6% in the Onabotulinum toxin A group compared with 8.9% in the placebo group. One of the primary risks of using Onabotulinum toxin A is acute urinary retention. Patients must be willing to undergo catheterization as part of this therapy. In the preapproval trials, catheterization at any time was required by 30.6% of patients in the treatment group versus 6.7% in the placebo group. Prophylactic antibiotics should be given 1–3 days before the injection, again on the day of the injection, and 1–3 days after the injection. Aminoglycosides cannot be used because of their interference with neuromuscular transmission, which can potentiate the effects of Onabotulinum toxin A. Antiplatelet drugs also must be discontinued 3 days before injection. The per-treatment dose is 200 units, and treatments should not be repeated any sooner than 12 weeks. According to the package insert, the mean effect of the injection in the initial trials lasted 42–48 weeks.

In early 2013, Onabotulinum toxin A was also approved for use in OAB in those who cannot use or do not respond adequately to antimuscarinic medications. The injections are administered as described previously with cystoscopy. The dosing for this indication is 100 units. This is administered by giving 20 injections of 5 units each about 1 cm apart in the detrusor muscle. The dose can be repeated if the effect wears off, but it must have been at least 12 weeks since the previous dose. The median time to requiring a second dose was 24 weeks in approval studies.

In the clinical trials for this indication, 1105 patients were followed for 12 weeks (median time to repeat 24 weeks) after injection with Onabotulinum toxin A or placebo. The episodes of incontinence were 1.6–1.8 times less likely to occur in the treatment group. The main adverse urologic events in the studies were UTIs (19% vs. 6%), urinary retention (6% vs. 0%), and dysuria (9% vs. 7%). Providing prophylactic antibiotic therapy and withholding antiplatelets is the same as previously recommended for Onabotulinum toxin A. It should not be used in patients with a PVR greater than 200 mL unless they are performing self-catheterization. This information and more extensive administration information can be found in the manufacturer's package insert.

Mirabegron

Mirabegron, a new β_3 -adrenergic receptor agonist, was approved in mid-2012 for the treatment of OAB with urgency symptoms. Stimulation of the β_3 -receptor causes bladder relaxation during filling. At very high doses (i.e., 200 mg), there was some stimulation of the β_1 -adrenergic receptors, but overall, mirabegron has low intrinsic activity for β_1 - or β_2 -receptors. The starting daily dose is 25 mg; if there is inadequate response at 8 weeks, it can be titrated up to 50 mg. Patients with a CrCl of 15–29 mL/minute/ $1.73m^2$ or moderate liver disease should receive only the 25-mg dose.

According to the package insert, in preapproval trials, mirabegron at 25 mg and 50 mg daily significantly decreased the number of incontinence episodes in 24 hours and the number of micturations in 24 hours over placebo. Decreases were only in the 1–2 micturition range but were statistically significant. Mirabegron should be used with caution in patients taking antimuscarinic therapy or in those who have bladder outlet obstruction because it can cause urinary retention. The most common adverse effect in initial trials was hypertension; healthy volunteers had a mean increase in blood pressure of 3.5 mm Hg systolic and 1.5 mm Hg diastolic. Patients with uncontrolled hypertension (i.e., greater than 180 mm Hg systolic or 110 mm Hg diastolic) should not take mirabegron. Adverse event rates for the 25-mg daily dose were as follows: hypertension (11.3%), nasopharyngitis (3.5%), UTIs (4.2%), and headache (2.1%).

Mirabegron inhibits CYP2D6 metabolism, and caution should be used with other drugs that are 2D6 substrates or inhibitors. Mirabegron increases the area under the curve of digoxin by 27% when these are coadministered. The lowest dose of digoxin should be used, and monitoring should be continued regularly. When used concurrently, mirabegron increases warfarin concentrations as much as 9%, and warfarin dose adjustments may be needed.

Mirabegron's place in therapy is yet to be determined. Patients with significant cardiovascular issues may not be good candidates for this agent. Cost is also to

be determined but will likely significantly exceed that of other antimuscarinic agents. Those with cognitive impairment may be a target patient population for this agent if it is not cost-prohibitive.

CONCLUSION

Urinary incontinence has a large economic and functional impact and will become an even larger issue in the health care system as the population continues to age. Pharmacists can have a large effect on reducing this burden by reviewing the medication profiles of all patients with UI to identify potential reversible causes as well as evaluate for concurrent anticholinergic drugs. Pharmacists are in a prime position to help guide the choice of antimuscarinic with respect to cost, adverse effect profile, patient comorbidities, and administration. Discontinuation rates of antimuscarinics are high because of intolerable adverse effects. It is important for the pharmacist to counsel patients on what to expect from these agents and when they should see results. For patients seeing benefit, adjunctive treatment can be recommended to help with adverse effects such as constipation and dry mouth.

Practice Points

- There is no single antimuscarinic agent with significant data to show that it is the first-line choice for urinary incontinence. Cost and comorbidities should be determining factors when selecting a drug.
- Oxybutynin immediate release is sometimes cited as the medication to try first line because no overwhelming evidence exists that it is tolerated any worse than other drugs, and it is known to be as efficacious as other agents.
- Topical preparations of antimuscarinic drugs have not been shown superior to other agents and therefore cannot be recommended as first-line treatment.
- The use of antimuscarinic agents in those with cognitive impairment is not contraindicated; however, these drugs must be used at the lowest dose possible and for the fewest daily doses. Patients and caregivers must be counseled on watching for worsening cognition. Urinary incontinence is a leading cause of institutionalization, and use of these drugs in patients with cognitive impairment may delay this. These two factors must be weighed in each individual patient.

REFERENCES

- The American Geriatrics Society 2012 Beers Criteria Update Expert Panel. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc* 2012;60:616-31.
[PubMed Link](#)
- Brazzelli M, Murray A, Fraser C. Efficacy and safety of sacral nerve stimulation for urinary urge incontinence: a systematic review. *J Urol* 2006;175:835-41.
[PubMed Link](#)
- Burgio KL, Goode PS, Richter HE, et al. Combined behavioral and individualized drug therapy versus individualized drug therapy alone for urge incontinence in women. *J Urol* 2010;184:598-603.
[PubMed Link](#)
- Burgio KL, Kraus SR, Menefee S, et al. Behavioral therapy to enable women with urge incontinence to discontinue drug treatment: a randomized trial. *Ann Intern Med* 2008;149:161-9.
[PubMed Link](#)
- Chapple C. Antimuscarinics in men with lower urinary tract symptoms suggestive of bladder outlet obstruction due to benign prostatic hyperplasia. *Curr Opin Urol* 2010;20:43-8.
[PubMed Link](#)
- Divani AA, Majidi S, Barrett S, et al. Consequences of stroke in community-dwelling elderly: the health and retirement study, 1998 to 2008. *Stroke* 2011;42:1821-5.
[PubMed Link](#)
- Dmochowski RR, Davila GW, Zinner NR, et al. Efficacy and safety of transdermal oxybutynin in patients with urge and mixed urinary incontinence. *J Urol* 2002;168:580.
[PubMed Link](#)
- Dmochowski RR, Miklos JR, Norton PA, et al. Duloxetine versus placebo for the treatment of North American women with stress urinary incontinence. *J Urol* 2003;170(4 pt 1):1259-63.
[PubMed Link](#)
- Donnellan CA, Fook L, McDonald P, et al. Lesson of the week: oxybutynin and cognitive dysfunction. *BMJ* 1997;315:1363.
[PubMed Link](#)
- Fantl JA, Wyman JF, McClish DK, et al. Efficacy of bladder training in older women with urinary incontinence. *JAMA* 1991;265:609-13.
- Gill SS, Mamdani M, Nagile G, et al. A prescribing cascade involving cholinesterase inhibitors and anticholinergic drugs. *Arch Intern Med* 2005;165:808-13.
[PubMed Link](#)
- Goode PS, Burgio KL, Richter HE, et al. Incontinence in older women. *JAMA* 2010;303:2172-81.
[PubMed Link](#)
- Grady D, Brown JS, Vittinghoff E, et al. Postmenopausal hormones and incontinence: the Heart and Estrogen/Progestin Replacement Study. *Obstet Gynecol* 2001;97:116-20.
[PubMed Link](#)
- Hesch K. Agents for treatment of overactive bladder: a therapeutic class review. *Proc (Bayl Univ Med Cent)* 2007;20:307-14.
[PubMed Link](#)
- Johnson TM II, Ouslander JG. Incontinence. In: Halter JB, Ouslander JG, Tinetti ME, et al., eds. *Hazzard's Geriatric Medicine and Gerontology*, 6th ed. New York: McGraw-Hill, 2009.
- Jonsson Funk M, Siddiqui NY, Kawasaki A, et al. Long-term outcomes after stress urinary incontinence surgery. *Obstet Gynecol* 2012;120:83-90.
[PubMed Link](#)
- Kolominsky-Rabas PL, Hilz MJ, Neundoerfer B, et al. Impact of urinary incontinence after stroke: results from a prospective population-based stroke register. *Neurourol Urodyn* 2003;22:322-7.
[PubMed Link](#)
- Lackner TE, Wyman JF, McCarthy TC, et al. Randomized, placebo-controlled trial of the cognitive effect, safety, and tolerability of oral extended-release oxybutynin in cognitively impaired nursing home residents with urge urinary incontinence. *J Am Geriatr Soc* 2008;56:862-70.
[PubMed Link](#)
- Lucas MG, Bosch RJ, Burkhard FC, et al. EAU guidelines on assessment and nonsurgical management of urinary incontinence. *Eur Urol* 2012;62:1130-42.
[PubMed Link](#)
- Mardon RE, Halim S, Pawlson LG, et al. Management of urinary incontinence in Medicare-managed beneficiaries: results from the 2004 Medicare Health Outcomes Survey. *Arch Intern Med* 2006;166:1128-33.
[PubMed Link](#)
- Markland AD, Goode PS, Redden DT, et al. Prevalence of urinary incontinence in men: results from the National Health and Nutrition Examination Survey. *J Urol* 2010;184:1022-7.
[PubMed Link](#)
- Mariappan P, Ballantyne Z, N'Dow JM, et al. Serotonin and noradrenaline reuptake inhibitors (SNRI) for stress urinary incontinence in adults. *Cochrane Database Syst Rev* 2005;3:CD004742.
[PubMed Link](#)
- MacDonald R, Fink HA, Huckabay C, et al. Pelvic floor muscle training to improve urinary incontinence after radical prostatectomy: a systematic review of effectiveness. *Br J Urol* 2007;100:76-81.
[PubMed Link](#)

Millard RJ, Moore K, Rencken R, et al. Duloxetine vs placebo in the treatment of stress urinary incontinence: a four continent randomized clinical trial. *BJU Int* 2004;93:311-8.

[PubMed Link](#)

Partial Rx to OTC Switch for Oxybutynin Transdermal System. FDA Briefing Document for Nonprescription Drugs Advisory Committee Briefing Document. NDA 202-211, Nov. 9, 2012. Accessed March 21, 2013.

[Internet Link](#)

Phelan S, Kanaya AM, Subak LL, et al. Weight loss prevents urinary incontinence in women with type 2 diabetes: results from the Look AHEAD trial. *J Urol* 2012;187:939-44.

[PubMed Link](#)

Richter HE, Burgio KL, Brubaker L, et al. Continence pessary compared with behavioral therapy or combined therapy for stress incontinence: a randomized controlled trial. *Obstet Gynecol* 2010;115:609-17.

[PubMed Link](#)

Shamliyan T, Wyman JF, Ramakrishnan R, et al. Benefits and harms of pharmacologic treatment for urinary incontinence in women: a systematic review. *Ann Intern Med* 2012;156:861-74.

[PubMed Link](#)

Sink KM, Thomas J II, Xu H, et al. Dual use of bladder anticholinergics and cholinesterase inhibitors: long term functional and cognitive outcomes. *J Am Geriatr Soc* 2008;56:847-53.

[PubMed Link](#)

Sioutis D, Economus E, Lambrinoudaki I, et al. Sp1 collagen I A1 polymorphism in women with stress urinary incontinence. *Int Urogynecol J* 2011;22:835-9.

[PubMed Link](#)

Subak LL, Marinilli Pinto A, Wing R, et al. Decrease in urinary incontinence management costs in women enrolled in a clinical trial of weight loss to treat urinary incontinence. *Obstet Gynecol* 2012;120:227-83.

[PubMed Link](#)

Subak LL, Quesenberry CP, Posner SF, et al. The effect of behavioral therapy on urinary incontinence: a randomized controlled trial. *Obstet Gynecol* 2002;100:72-8.

[PubMed Link](#)

Van Kerrebroeck P, Abrams P, Lange R, et al. Duloxetine versus placebo in the treatment of European and Canadian women with stress urinary incontinence. *BJOG* 2004;111:249-57.

[PubMed Link](#)

SELF-ASSESSMENT QUESTIONS

Questions 1 and 2 pertain to the following case.

R.Z. is a 70-year-old woman who presents with increased urinary frequency and a few episodes of urinary incontinence (UI) during the past few weeks. These episodes do not occur during periods of coughing, sneezing, or laughing. R.Z. recently lost her job and has no prescription drug coverage. She was seen 4 weeks ago as a new patient in your family medicine clinic, and the following drugs were initiated: amlodipine 5 mg, calcium carbonate 500 mg/vitamin D 200 international units daily, alendronate 70 mg weekly, metformin 500 mg twice daily, and citalopram 10 mg daily. The only drug she was taking 4 weeks ago was hydrochlorothiazide 25 mg daily, which she has taken for the past 3 years. Her medical history is significant for osteoporosis, diastolic heart failure, hypertension, type 2 diabetes mellitus, and depression. Laboratory test results from 4 weeks ago include hemoglobin A1C (A1C) 7.3%, SCr 1.1 mg/dL, and potassium 4.0 mEq/L.

1. Which one of the following is the best intervention for R.Z.?
 - A. Initiate duloxetine 40 mg twice daily.
 - B. Initiate furosemide 20 mg daily.
 - C. Discontinue amlodipine 5 mg daily.
 - D. Discontinue hydrochlorothiazide 25 mg daily.
2. Four weeks later, R.Z. returns, and her UI symptoms have not resolved. The symptoms have been particularly bothersome when she has been out searching for a job. This has also worsened her depression. Which one of the following would be best to initiate in R.Z.?
 - A. Oxybutynin immediate release 2.5 mg twice daily.
 - B. Solifenacin 5 mg daily.
 - C. Vaginal estrogen.
 - D. Duloxetine 40 mg twice daily
3. A 62-year-old woman with urge urinary incontinence (UI) comes to your clinic. She is taking mirtazapine 30 mg for depression, but her depression is not improving. Her primary care physician wants to switch her to fluoxetine 10 mg daily. Which one of the following would be the best choice for this patient's UUI to avoid drug interactions?
 - A. Tolterodine.
 - B. Oxybutynin.
 - C. Trospium.
 - D. Darifenacin.

4. In which one of the following patients would a post void residual (PVR) be most important as part of an initial evaluation for lower urinary tract symptoms and UI?
 - A. A 36-year-old woman who has urine leakage with coughing.
 - B. A 51-year-old man with type 2 diabetes mellitus who has urine dribbling and increased frequency.
 - C. A 50-year-old woman with epilepsy who has UI with seizures.
 - D. A 45-year-old woman with burning on urination and increased frequency.

Questions 5 and 6 pertain to the following case.

T.R. is a 67-year-old woman who has been initiated on mirabegron 25 mg daily for UUI. She has tried nothing else in the past for UI. Her medical history includes heart failure, deep venous thrombosis (three episodes), hypertension, hyperlipidemia, and generalized anxiety disorder. Her current home drugs are as follows: carvedilol 6.25 mg twice daily, lisinopril 10 mg daily, warfarin 3 mg daily, digoxin 0.125 mg daily, pravastatin 40 mg daily, and escitalopram 10 mg daily. T.R.'s calculated CrCl is 60 mL/minute/1.73m². Her sitting blood pressure today is 132/80 mm Hg, and her heart rate is 76 beats/minute.

5. Which one of the following option groups would be best to counsel T.R. to monitor for upon initiation of mirabegron?
 - A. Cough, shortness of breath.
 - B. Nausea, vomiting, and diarrhea.
 - C. Swelling, warmth, redness in legs.
 - D. Significant muscle weakness.
6. T.R. does well on mirabegron. Two months later, she has been titrated to 50 mg daily and returns to the clinic for follow-up. She reports a significant decrease in incontinence symptoms. There have been no changes in her medications or medical history. T.R.'s CrCl today is 45 mL/minute/1.73m². Blood pressure and heart rate today are 182/88 mm Hg and 86 beats/minute. Which one of the following is best to recommend regarding T.R.'s mirabegron dosage?
 - A. Continue at 50 mg daily.
 - B. Reduce to 25 mg daily.
 - C. Change to solifenacin 5 mg daily.
 - D. Change to duloxetine 40 mg twice daily.

7. An 80-year-old community-dwelling woman describes increased frequency and urgency with urination for the past 2 months. She denies pain with urination and does not have a fever today. Her medical history includes hypertension and constipation with two episodes of bowel obstruction. Her home drugs include sennosides 8.6 mg three times daily, docusate 100 mg twice daily, lisinopril 5 mg daily, and aspirin 81 mg daily. She gets a rash with sulfa drugs. Her urinalysis is positive for bacteriuria. Which one of the following is best to initiate in this patient?
- Ciprofloxacin 500 mg twice daily for 7 days.
 - Oxybutynin extended release 5 mg daily.
 - Sulfamethoxazole 800 mg/trimethoprim 160 mg twice daily for 10 days.
 - Darifenacin 7.5 mg daily.
- Questions 8 and 9 pertain to the following case.**
- P.Q. is a 62-year-old woman (height 60 inches, weight 56 kg) who has been using vaginal estrogen for 1 year for symptoms of stress urinary incontinence (SUI). This was effective until a couple of months ago, when her symptoms began to return. Her medical history includes coronary artery bypass graft (times 1), hypertension, hyperlipidemia, osteoporosis, peripheral neuropathy, osteoarthritis, and depression. Her other medications include aspirin 81 mg daily, metoprolol 25 mg twice daily, lisinopril 10 mg daily, rosuvastatin 10 mg daily, alendronate 70 mg weekly, calcium carbonate 500 mg/vitamin D 200 units twice daily, gabapentin 300 mg twice daily, zolpidem 10 mg daily, ibuprofen 200 mg twice daily, and bupropion SR 150 mg twice daily. Blood pressure is 158/76 mm Hg, heart rate 72 beats/minute, and SCr 1.1 mg/dL. P.Q. would like to try other drug therapy for her UI because she and her husband travel a lot, and it is bothersome on these trips. Her symptoms occur throughout the day, usually with coughing or sneezing.
- Which one of the following would be best to recommend for P.Q.?
 - Duloxetine 20 mg twice daily.
 - Oral conjugated estrogens 0.3 mg/medroxyprogesterone 1.5 mg daily.
 - Pseudoephedrine 30 mg three times daily.
 - Solifenacin 5 mg daily.
 - Which one of the following drugs is most likely exacerbating P.Q.'s incontinence?
 - Gabapentin.
 - Ibuprofen.
 - Lisinopril.
 - Zolpidem.
 - An 83-year-old man with Alzheimer disease is being cared for at home. During the past 2 months, his wife has noticed that it is increasingly difficult for him to make it to the restroom in time to urinate. He has stopped telling her when he needs to use the restroom, and she is unable to direct him to the restroom in the house quick enough. This is causing significant caregiver stress. His wife believes his cognition has begun to worsen during the past 6 months, and she is considering placing him in a nursing home. His home drugs include terazosin 2 mg at bedtime, aspirin 81 mg daily, donepezil 10 mg at bedtime, lisinopril 5 mg daily, and venlafaxine extended release 75 mg daily. His Mini-Mental State Examination score is 15/30, and his Geriatric Depression Scale is 3/15. Standing blood pressure is 110/70 mm Hg. Which one of the following is best to recommend for this patient?
 - Change terazosin to tamsulosin 0.4 mg daily.
 - Start finasteride 5 mg daily.
 - Change venlafaxine to duloxetine 20 mg twice daily.
 - Discontinue donepezil 10 mg daily.
 - Three weeks ago, a 69-year-old man began taking oxybutynin immediate release 5 mg three times daily for UUI. His medical history is significant for severe psoriasis, bipolar disorder, and osteoarthritis. He noticed about 2 weeks ago that he is having significant dry mouth. The patient has tried several nonpharmacologic options recommended by his local pharmacist, but none has worked. Oxybutynin has been effective, and he is happy with the results on his UUI symptoms. Before taking it, he was using the bathroom 20 times during the day; he feels this number has been cut in half. However, he does not feel he will be able to take this medication much longer because of the dry mouth. Which one of the following is best to recommend for this patient?
 - Oxybutynin extended release.
 - Oxybutynin transdermal patch.
 - Oxybutynin 10% gel.
 - Oxybutynin immediate release 5 mg at bedtime.
 - A 45-year-old man with multiple sclerosis has problems with increased urinary frequency and urgency on a daily basis. He is currently taking no drugs for this problem. In the past, he has tried oxybutynin transdermal patch 3.9 mg/day and tolterodine immediate release 2 mg twice daily; neither resulted in significant improvement. The patient's PVR is 50 cc. Which one of the following is best to recommend for this patient?
 - Darifenacin 7.5 mg daily.

- B. Onabotulinum toxin A 200 units of intradetrusor injection.
- C. Mirabegron 25 mg daily.
- D. Duloxetine 20 mg twice daily.
13. An 86-year-old man presents to the geriatrics clinic with new-onset dribbling and urinary urgency. His medical history includes osteoporosis, insomnia, depression, and type 2 diabetes mellitus. His home drugs include glipizide 5 mg twice daily, citalopram 20 mg daily, diphenhydramine 50 mg at bedtime, alendronate 70 mg weekly, cholecalciferol 1000 units daily, simvastatin 10 mg daily, aspirin 81 mg daily, and loratadine 10 mg daily. His PVR in the clinic today is 310 cc. Recent laboratory test results include A1C 7.5% and SCr 1.2 mg/dL. Which one of the following is best to recommend for this patient?
- A. Start tamsulosin 0.4 mg daily.
- B. Start tolterodine extended release 2 mg daily.
- C. Increase glipizide to 10 mg twice daily.
- D. Discontinue diphenhydramine 50 mg daily.
14. A 69-year-old woman experiences urine loss when she coughs, sneezes, or lifts something heavy. She uses an incontinence pad for protection. She was started on estrogen 0.625 mg daily at menopause, but this was discontinued 5 years ago. Her medical history is significant for six vaginal deliveries, osteoarthritis, hypertension, and severe Alzheimer dementia. Her home drugs include acetaminophen 1000 mg twice daily and lisinopril 10 mg daily. Which one of the following is best to recommend for this patient's UI?
- A. Pelvic muscle rehabilitation.
- B. Periurethral injection of a bulking agent.
- C. Duloxetine 40 mg twice daily.
- D. Conjugated estrogen 0.625 mg daily.
- Questions 15 and 16 pertain to the following case.**
- B.K. is a 57-year-old woman (height 65 inches, weight 64 kg) who has progressive difficulty with bladder control during the daytime. When she feels like she needs to use the toilet, she is sometimes unable to get to the bathroom on time. She has experienced a few "accidents" and is deeply embarrassed. When she exercises or coughs, she loses small amounts of urine. Her home drugs include alendronate 70 mg weekly for osteoporosis, loratadine 10 mg daily for allergies, calcium carbonate 600 mg twice daily, vitamin D 1000 units daily, and ibuprofen 200 mg once daily for osteoarthritis. She is a lifelong smoker and does not drink alcohol. She consumes 1 cup of regular coffee with each meal. She complains of some osteoarthritis pain and her pain scale rating is 2/10.
15. Which one of the following best explains B.K.'s symptoms of UI?
- A. Pedal edema caused by ibuprofen.
- B. Functional disability because of osteoarthritis.
- C. Decreased parasympathetic tone because of the aging process.
- D. Weakening of the pelvic floor musculature caused by loss of estrogen.
16. Which one of the following is the best intervention to recommend for B.K.?
- A. Absorbent pads.
- B. Decaffeinated coffee.
- C. Weight loss.
- D. Fluid restriction.
17. A 72-year-old woman (height 66 inches, weight 54 kg) receives a diagnosis of UUI. She lives with her spouse, who is retired. She is mildly cognitively impaired and has mild limitations in performing activities of daily living. Her home drugs include donepezil 10 mg at bedtime and memantine 10 mg twice daily for moderate Alzheimer disease, pravastatin 40 mg in the evening for hyperlipidemia, levothyroxine 75 mcg daily for hypothyroidism, sertraline 50 mg daily for depression, and metoprolol 25 mg twice daily for hypertension. She does not smoke or drink alcohol. She drinks only decaffeinated coffee. Which one of the following is best to recommend for this patient's UUI?
- A. Discontinue donepezil 10 mg daily.
- B. Begin trospium 20 mg daily.
- C. Begin pelvic floor rehabilitation.
- D. Begin prompted toileting on a regular schedule.
18. A 76-year-old woman (height 62 inches, weight 59 kg) with a diagnosis of SUI continues to have frequent episodes, despite attempts at pelvic floor rehabilitation with Kegel exercises. A pelvic examination reveals normal genitourinary anatomy. Her medical history is significant for hypertension, hyperlipidemia, insomnia, and chronic kidney insufficiency. Her home drugs include atorvastatin 40 mg daily, amlo-dipine 10 mg daily, enteric-coated aspirin 81 mg daily, and calcium 600 mg/vitamin D 400 international units twice daily. Her blood pressure is 152/88 mm Hg, and her heart rate is 68 beats/minute. Her most recent laboratory results are as follows: TC 182 mg/dL, LDL cholesterol 111 mg/dL, sodium 135 mEq/L, chloride 101 mEq/L, potassium 3.8 mEq/L, serum glucose 88 mg/dL, and SCr 1.5 mg/dL. Which one of the following is best to recommend for this patient?
- A. Duloxetine 40 mg twice daily.
- B. Pessary placement.
- C. Sacral nerve stimulation.
- D. Midurethral sling.

19. Two months ago, a 67-year-old man presented to the clinic with symptoms of urinary urgency, nocturia, and incontinence. His incontinence episodes are characterized by the loss of large amounts of urine. His PVR was 45 mL, and his prostate examination was normal. He was initiated on oxybutynin 5 mg three times daily. Today, he returns to the clinic for follow-up. He now reports that the symptoms of urgency are improved, but he continues to be incontinent of small amounts of urine both day and night. His PVR today is 315 mL. His medical history is significant for diabetes and congestive heart failure. His other current drugs include glipizide extended release 10 mg daily, furosemide 20 mg every morning, potassium chloride 20 mEq daily, lisinopril 40 mg daily, metoprolol extended release 50 mg daily, and enteric-coated aspirin 81 mg daily. His laboratory results are as follows: A1C 7.6%, sodium 140 mEq/L, potassium 4.1 mEq/L, and SCr 0.9 mg/dL. Which one of the following best explains this patient's current symptoms?

- A. Increased urine volume secondary to furosemide.
- B. Increased intraabdominal pressure secondary to angiotensin-converting enzyme inhibitor cough.
- C. Detrusor underactivity secondary to oxybutynin.
- D. Urethral relaxation secondary to β -blocker.

20. A 70-year-old man has difficulty with bladder control since undergoing radical prostatectomy for prostatic carcinoma 6 months ago. He reports excessive dribbling and must wear a pad to prevent soiling his clothing. He loses small amounts of urine during physical exertion. Cystoscopy shows normal sphincter morphology. His medical history is significant for hypertension, constipation, glaucoma, gastroesophageal reflux disease, and insomnia. His current drugs include losartan 100 mg daily, senna 8.6 mg daily, timolol 0.5% one drop in both eyes twice daily, and pantoprazole 40 mg daily. His blood pressure is 153/82 mm Hg, and his SCr is 1.1 mg/dL. Which one of the following is the best initial treatment for this patient?

- A. Duloxetine 40 mg twice daily.
- B. Pseudoephedrine 30 mg twice daily.
- C. Pelvic floor rehabilitation.
- D. Artificial urethral sphincter.

LEARNER CHAPTER EVALUATION: URINARY INCONTINENCE IN THE OLDER ADULT.

As you take the posttest for this chapter, also evaluate the material's quality and usefulness, as well as the achievement of learning objectives. Rate each item using this 5-point scale:

- Strongly agree
- Agree
- Neutral
- Disagree
- Strongly disagree

1. The content of the chapter met my educational needs.
2. The content of the chapter satisfied my expectations.
3. The author presented the chapter content effectively.
4. The content of the chapter was relevant to my practice and presented at the appropriate depth and scope.
5. The content of the chapter was objective and balanced.
6. The content of the chapter is free of bias, promotion, or advertisement of commercial products.
7. The content of the chapter was useful to me.
8. The teaching and learning methods used in the chapter were effective.
9. The active learning methods used in the chapter were effective.
10. The learning assessment activities used in the chapter were effective.
11. The chapter was effective overall.

Use the 5-point scale to indicate whether this chapter prepared you to accomplish the following learning objectives:

12. Evaluate symptoms to accurately classify a patient with urinary incontinence.
13. Apply an understanding of the pathophysiology and risk factors for urinary incontinence to patient care.
14. Evaluate the most recent clinical evidence for pharmacologic and nonpharmacologic treatment of urinary incontinence.
15. Design a patient-specific treatment plan to achieve optimal outcomes in an elderly patient with urinary incontinence.
16. Assess for reversible causes in the patient with urinary incontinence.
17. Analyze the risks and benefits of using urinary incontinence medications in patients with dementia.
18. Please provide any specific comments relating to any perceptions of bias, promotion, or advertisement of commercial products.
19. Please expand on any of your above responses, and/or provide any additional comments regarding this chapter: