JAMA | Review

Urinary Incontinence in Women
A Review

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IMPORTANCE Urinary incontinence, the involuntary loss of urine, is a common health condition that may decrease quality of life. Ten to twenty percent of women and up to 77% of women residing in nursing homes have urinary incontinence, yet only 25% seek or receive treatment.

OBSERVATIONS This review summarizes the evaluation and therapeutic options for women affected by urinary incontinence. The initial assessment should focus on understanding the effect of incontinence on quality of life, the patient's goals and preferences for treatment, the results of previous treatments, and the presence of concomitant conditions, such as advanced pelvic organ prolapse, that may require referral. Infection and hematuria need to be ruled out. In the absence of urinary infection or serious underlying pathology (such as cancer or serious neurologic disease) associated with urinary incontinence, the clinician should initiate unsupervised pelvic muscle exercises and lifestyle modifications appropriate to the patient to reduce her symptoms. These recommendations can include weight loss, adequate hydration, avoidance of excessive fluids, and regular voiding intervals that reduce urgency incontinence episodes. Urgency incontinence medications, with timely reassessment of symptoms, can be started without extensive evaluation. Specialist treatments for urgency incontinence include onabotulinumtoxinA and percutaneous or implanted neuromodulators. Stress incontinence surgery, the midurethral sling, is associated with symptom improvement in 48% to 90% of women and has low rates of mesh complications (<5%).

CONCLUSIONS AND RELEVANCE Urinary incontinence is common in women, although few seek care despite many effective treatment options. Clinicians should prioritize urinary incontinence detection, identify and treat modifiable factors, incorporate patient preference into evaluation and treatment, initiate conservative and medical therapy, and refer to specialists when underlying pathology is identified or conservative measures are ineffective.

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Nearly 50% of adult women may experience urinary incontinence, the involuntary loss of urine.[1] This condition increases with age, affecting 10% to 20% of all women and up to 77% of elderly women residing in nursing homes.[2-7] Variability in case definition affects prevalence rates.[8] The most current epidemiologic data suggest an overall prevalence of 17% in women older than 20 years and 38% in women older than 60 years.[5,7] Recent reports indicate that 37.5% of young women (30-50 years) in a primary care setting report stress incontinence.[9] According to the 2009-2010 National Ambulatory and Hospital Medical Care Survey, an estimated 6.8 million women had a primary diagnosis or chief complaint of urinary incontinence; 15.3% were treated in a primary care setting.[10] Despite this high prevalence, incontinence remains underdiagnosed and undertreated. Only 25% of affected women seek care, and of those, less than half receive treatment.[11] Untreated incontinence is associated with falls and fractures, sleep disturbances, depression, and urinary tract infections.[12-14] Older women with lower urinary tract symptoms, including urinary incontinence, are 1.5 to 2.3 times more likely to experience falls, leading to increased overall morbidity, mortality, and health care costs.[14]

This review article provides clinicians with a stepwise approach to evaluation and evidence-based treatments for most women with urinary incontinence, including indications for referral to an incontinence specialist. All clinicians who treat adult women should be knowledgeable about current evidence for evaluation and treatment of urinary incontinence.

Methods

This search identified articles using PubMed, EMBASE Ovid, and the Cochrane Library to identify high-quality, multicenter randomized controlled trials; systematic reviews; meta-analyses; and practice guidelines from January 2000 to July 2017 that assessed urinary incontinence evaluation and treatment. The authors selected several landmark, multicenter, randomized, comparative efficacy trials

that have important implications for current clinical practice and constructed summary tables of that evidence for stress and urgency incontinence. The prospectively followed cohorts of these trials also provide the highest levels of evidence on the moderate-term safety and efficacy of the most common incontinence therapies for women. Because of the limited comparative efficacy trials across all available incontinence medications, we calculated the average reduction in urinary frequency, urgency incontinence episodes, and common adverse effects, using the trial evidence used for Food and Drug Administration (FDA) registration of the most commonly prescribed medications.

Detection and Evaluation of Incontinence

History

Many women do not volunteer incontinence symptoms to their primary care provider because of embarrassment, lack of knowledge, or misconception about treatment.[15,16] Once incontinence is detected, the clinician should determine symptom severity and desire for treatment as early as possible. A general principle of care is the need to balance diagnostic certainty with the risk or invasiveness of therapy. In all women, the clinician should identify and treat reversible causes such as urinary tract infection, excessive fluid intake (>2 L/day), use or timing of medications that may worsen incontinence (ie, diuretics), and comorbid conditions contributing to incontinence (obesity, constipation, sleep apnea, tobacco use, dementia, and depression). The **Box** outlines signs or symptoms suggesting serious underlying pathology, such as cancer or serious neurologic disease, that should prompt immediate referral to an incontinence specialist.

Most women do not require an extensive preliminary evaluation of urinary incontinence because initial noninvasive treatments may be begun without clear differentiation between the 2 most common urinary incontinence subtypes, stress and urgency incontinence. The history should focus on the onset, duration, severity, frequency and effect on quality of life. **Figure 1** displays 3 simple items in a validated questionnaire to help clinicians discern the common incontinence subtypes. Briefly, the questionnaire describes various life situations and asks participants whether they experienced urinary incontinence during the past 3 months (even a small amount), whether they experienced involuntary urinary leaking, and when they experienced it most often.[17]

Stress incontinence is characterized by involuntary loss of urine with increases in abdominal pressure such as exercise or coughing. The main etiology is a poorly functioning urethral closure mechanism and is associated with loss of anatomic support or trauma from vaginal childbirth, obesity, and situations that repetitively increase intra-abdominal pressure, such as chronic constipation, heavy lifting, and high-impact exercise.[18-23] Urgency incontinence is characterized by a sudden compelling desire to pass urine that is difficult to defer.[24] Affected women experience little warning before incontinence episodes and an increase in urinary frequency both day and night. In most women, urgency incontinence is idiopathic. However, it is common in a subset of women with systemic neurologic conditions (eg, Parkinson disease, multiple sclerosis, pelvic or spinal nerve injury). Overflow incontinence symptoms are similar to those of stress and urgency incontinence, but this type of incontinence is associated with incomplete emptying of the bladder. It is more common in women with underlying systemic neurologic disease or anatomic abnormalities such as urethral obstruction. Many women with incontinence experience coexisting stress and urgency symptoms, usually called mixed urinary incontinence.

Box. Indications for Incontinence Specialist Referral

- Symptoms or physical examination concerning for neurologic disease
- Lifelong history of incontinence (present since childhood)
- Recurrent symptomatic urinary tract infections
- Pelvic organ prolapse beyond the hymen
- Elevated postvoid residual (expert opinion suggests >1/3 total volume or 100 mL in adults, > 150 mL in older patients)
- Long-term catheterization
- Difficulty passing a urethral catheter
- Diagnostic uncertainty or poor improvement with treatment
- Dominant symptom of pain
- Sterile hematuria (gross or microscopic)

Recent urinary microbiome research shows that the diversity of the urinary microbiota in women with urgency incontinence may differ from the lactobacillus-predominant resident flora of continent adult women.[25-28] Given the uncertain etiology and likely multifactorial nature of urgency incontinence, individualized treatment strategies are not yet available. Future research in this area may help characterize populations of women who may benefit most from specific therapies.

Examination

Guidelines from international and specialty organizations are largely consistent in their recommendations for the initial incontinence evaluation, which includes history, physical examination, urinary tract infection testing, urinary stress testing, and assessment of postvoid residual.[29-34] Urinalysis should be used to identify urinary tract infection and detect hematuria, pyuria, or glycosuria because these may represent comorbid conditions associated with incontinence. When history taking and urinalysis do not provide a clear etiology of incontinence symptoms, a written voiding diary recording quantity and timing of fluid intake and urine output during 1 to 3 days can provide information about potential modifiable factors associated with incontinence episodes. **Figure 2** displays diaries of common abnormal voiding patterns. Improved fluid intake patterns can reduce urgency and frequency symptoms in women who infrequently drink large volumes of liquids. More frequent, regular voiding can reduce symptoms in women who have infrequent, large-volume voids.

Pelvic examination is recommended when findings, such as detection of a pelvic mass, would alter the planned intervention or influence treatment selection. In postmenopausal women, clinicians should look for vaginal atrophy, which can effectively be treated with vaginal estrogen. Pelvic examination may identify conditions requiring prompt referral (Box). In addition, clinicians should look for pelvic organ prolapse beyond the vagina because it is associated with a higher risk of urinary retention. For these patients, referral to a specialist for treatment addressing both prolapse and incontinence may be warranted. Clinicians can assess pelvic floor muscle integrity and

Figure 1. The 3 Incontinence Questions Questionnaire

1. During the last 3 months, have you leaked urine (even a small amount)? ☐ Yes ☐ No (questionnaire completed)
2. During the last 3 months, did you leak urine (check all that apply):
   - ☐ a. When you were performing some physical activity, such as coughing, sneezing, lifting, or exercise?
   - ☐ b. When you had the urge or the feeling that you needed to empty your bladder, but you could not get to the toilet fast enough?
   - ☐ c. Without physical activity and without a sense of urgency?
3. During the last 3 months, did you leak urine most often (check only one):
   - ☐ a. When you were performing some physical activity, such as coughing, sneezing, lifting, or exercise?
   - ☐ b. When you had the urge or the feeling that you needed to empty your bladder, but you could not get to the toilet fast enough?
   - ☐ c. Without physical activity and without a sense of urgency?
   - ☐ d. About equally as often with physical activity as with a sense of urgency?

Definitions of type of urinary incontinence based on response to question 3

Response	Type of incontinence
a. Most often with physical activity	Stress only or stress predominant
b. Most often with the urge to empty the bladder	Urge only or urge predominant
c. Without physical activity or sense of urgency	Other cause only or other cause predominant
d. About equally with physical activity and sense of urgency	Mixed

Response to the third question enables classification of incontinence subtype.
Reproduced with permission from the *Annals of Internal Medicine*.[17]

function during the bimanual pelvic examination by asking the patient to contract her pelvic floor muscles (**Figure 3**). Women who are unable to isolate pelvic floor muscles or who are unable to properly perform pelvic floor muscle contraction often benefit from supervised pelvic floor physical therapy instead of simple verbal instructions or handouts on pelvic exercises.

Additional Assessments

When the diagnosis is unclear or the initial treatment is unsuccessful, consultation with an incontinence specialist can determine whether additional diagnostic studies are needed. Current clinical guidelines offer different recommendations about the utility of these diagnostic tests.[29-34] All clinicians can conduct the simple urinary stress test. While in the lithotomic or standing position, the patient strains or coughs with a comfortably full bladder while the clinician directly observes the urethra meatus for urine leakage. Leakage during these maneuvers is highly suggestive of stress incontinence (positive predictive value of 78% to 97%).[35] Urodynamic studies are not necessary in the evaluation of uncomplicated urinary incontinence or before every stress incontinence surgery. This conclusion is based on results of a multicenter randomized clinical trial of 630 women with stress urinary incontinence symptoms. In women with demonstrable stress incontinence, defined as a positive cough stress test result in the trial, a preoperative office evaluation provided a noninferior 12-month treatment outcome in women who underwent stress incontinence surgery.[36] Urodynamic testing is still used when specialists seek specific information about bladder and urethral physiology or to characterize urinary incontinence subtypes.

Within 10 minutes after a measured void, a postvoid residual should be obtained by either catheterization or ultrasonography. There is no established normative value for postvoid residual. Experts consider less than 100 mL for voided volumes of greater than 200 mL or one-third of total voided volume as normal. Postvoid residual measurement is recommended when patients report incomplete voiding, have pelvic organ prolapse beyond the hymen, or will undergo stress urinary incontinence surgery. Assessment of the postvoid residual is not required before medication is prescribed for urgency incontinence. However, because these medications can cause urinary retention, clinicians should stop the medication and proceed with additional assessment if new or worsening bladder symptoms develop.

Evidence-Based Incontinence Treatment

Selection of treatment is based on the nature of the predominant symptom (stress vs urgency incontinence), a woman's goals and expectations for improvement or cure, her level of commitment to therapy, her tolerance of risk or adverse effects, and her financial situation. Some women prefer to attempt all conservative options before more invasive ones. Others may prioritize expediency or efficacy, accepting risks of surgery or more invasive approaches. Individual patient counseling should include information about expected symptom reduction, estimated time commitment, complications, and adverse effects, as well as expected out-of-pocket expense.

Behavior and Lifestyle Modification

Nearly all initial incontinence therapy should start with noninvasive measures because the benefits are associated with low risk and limited expense. Clinicians can offer these lifestyle modifications, including smoking cessation, regardless of the incontinence subtype. Management of constipation and avoidance of excessive fluids, with reduction in consumption of caffeine, carbonated beverages, diet beverages, and alcohol, should be discussed.[37] Fluid-management strategies promote frequent intake of small amounts of fluid (ie, 4-5 oz/hour) up to 2 L a day of predominantly water in lieu of large, episodic fluid intakes (ie, 36 oz in one drink). Timed voiding measures, or voiding at intervals that are tailored to each patient (typically every 2 to 3 hours) during the day, can reduce urgency incontinence episodes. Although systematic reviews do not

Figure 2. Diaries of Common Abnormal Voiding Patterns

A Sample voiding diary with abnormal intake pattern

Time	Voided amount, mL	Intake amount and type	Leakage (sm, med, lg)	Urgency present?	Activity
7:00 AM	350				
7:30 AM		Coffee, 3 cups			
8:00 AM			Small	yes	washing dishes
8:30 AM			medium	yes	Preparing for work
11:00 AM	550				
12:00 PM		36 ounces iced tea			
12:15 PM	250		Small	yes	At desk
12:20 PM			medium	yes	At desk
5:00 PM	300				
5:15 PM		36 ounces iced tea			
5:20 PM	250		Small	yes	Preparing meal
6:15 PM			medium	yes	Watching TV

B Sample voiding diary with abnormal voiding pattern

Time	Voided amount, mL	Intake amount and type	Leakage (sm, med, lg)	Urgency present?	Activity
7:00 AM	550	Coffee 1 cup, ½ cup orange juice			
10:30 AM		8oz Lemonade	med	yes	Shopping
11:00 AM	650				
11:30 AM		Large milkshake			
2:30PM			Lg	yes	Driving home
3:00PM	625				
4:00 PM		1 cup herbal tea			
5:30 PM			med	yes	at desk
6:30 PM	575				
7:15PM		1 cup water, 1 glass wine			Preparing meal
9:45 PM			med	yes	Watching TV

A, Abnormal intake patterns, such as infrequent, large volumes can trigger urgency and frequency symptoms that can be reduced with improved intake patterns. B, Abnormal voiding patterns, such as very infrequent voiding of large volumes, may be associated with urgency and urgency incontinence. These symptoms can be reduced with more frequent voiding.

provide strong evidence to support these strategies, in the authors' clinical experience, timed voiding and avoidance of excessive fluids are effective strategies, especially for patients with urgency incontinence.[38-40] **Table 1** summarizes results of important, landmark, randomized trials about urgency incontinence. A multicenter randomized controlled trial evaluated the efficacy of supervised behavioral modification (including pelvic floor muscle exercise instruction, strategies to suppress urge, timed voiding, and fluid management) in addition to drug therapy (tolterodine) for urgency incontinence. Compared with drug therapy alone, combined therapy was more successful, defined by a greater than 70% reduction in incontinence episodes (58% for drug therapy vs 69% for combined therapy). The rates of continued drug use were not different (41%) at 8 months.[41]

Strong evidence supports the recommendation for weight loss in overweight women with incontinence. A randomized clinical trial of a 6-month structured weight loss program vs education alone in 338 overweight and obese women reported a 47% reduction in mean incontinence episodes compared with a 28% reduction in the control group ($P = .01$).[44] The treatment group had a mean 7.8-kg reduction in weight (8%) vs a mean 1.5-kg reduction (1.6%) in the control group, and these patients were more likely than controls to have a clinically meaningful reduction in all incontinence episodes (47% vs 28%; $P < .01$). Women in the treatment group experienced a decrease in weekly incontinence episodes, from a baseline mean (SD) of 24 (18) episodes to 13 (15) episodes. The effect was more pronounced for stress incontinence, with a reduction from 9 (11) to 4 (7) episodes (58% vs 33%; $P = .02$).[44]

Pelvic Floor Muscle Exercise

Systematic reviews consistently report efficacy for pelvic floor muscle exercises for women with urinary incontinence.[45-50] Although there are no significant risks or expenses for unsupervised exercises, they require personal engagement and time commitment. Clinicians can

Figure 3. Assessment of Pelvic Muscle Tone and Contraction During Pelvic Examination

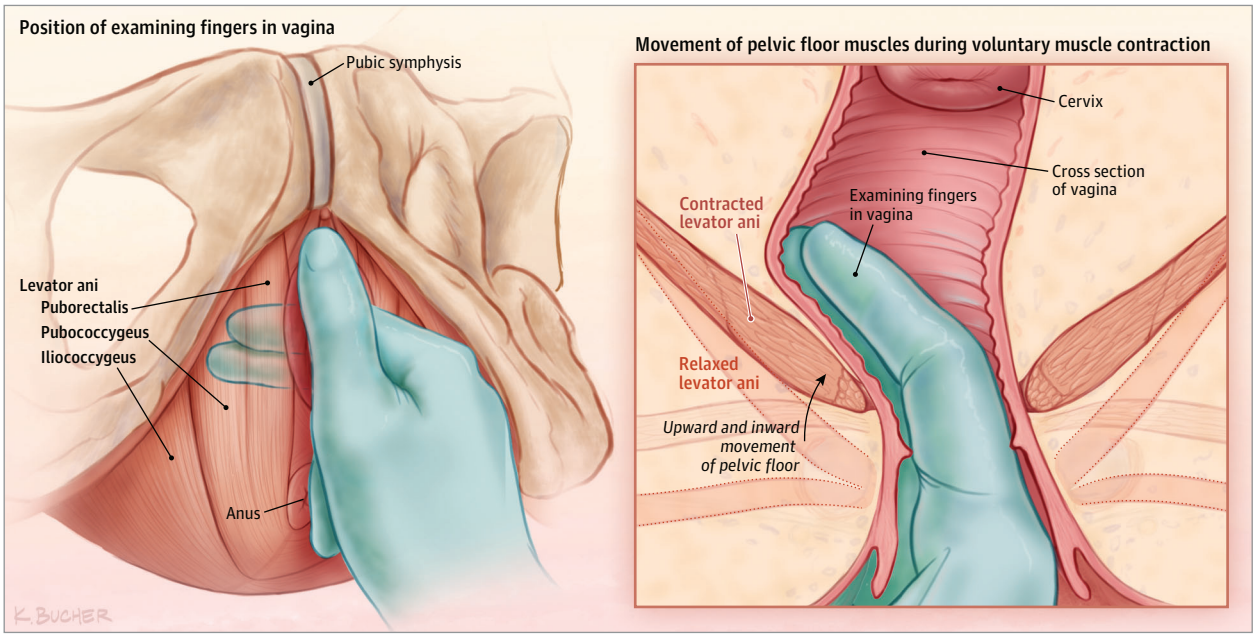

Table 1. Landmark Clinical Trials in Urgency Urinary Incontinence (UUI) Treatment

	BE-DRI[41]	ABC[42]	ROSETTA[43]
Study design	Open label, 2-stage RCT, superiority Stage 1, treatment Stage 2, withdrawal of treatment	Double-blind, double-placebo-controlled RCT, superiority	Open label RCT, superiority
Comparison groups	Anticholinergic vs anticholinergic and behavioral therapy	Anticholinergic vs 100 U of onabotulinumtoxinA injection	Sacral nerve stimulation vs 200 U of onabotulinumtoxinA injection
No. of participants enrolled	307	249	381
No. of sites	9	10	9
No. of participants assessed	Stage 1, 269 Stage 2, 237	241	364
Outcome point, mo	8	6	6
Age, mean (SD), y	57 (13.8)	58 (11.4)	63 (11.6)
Concomitant stress incontinence symptoms, %	97	Yes (percentage not reported)	Not reported

(continued)

provide simple exercise instructions for the patient if she is able to contract her pelvic floor muscle. Thirty contractions per day (3 sets of 10 contractions held for 10 seconds each) is typically recommended; patients should not be instructed to interrupt their urine stream while performing their daily exercises. There are numerous modalities to assist with pelvic floor muscle exercises, but there is insufficient evidence to suggest that any specific exercise program is superior to another.[50] A systematic review of clinical trials focusing on 12-month outcomes for supervised pelvic floor muscle training reported stress urinary incontinence cure rates of 58.8% at 12 months. Patients considered cured reported being completely continent or had no evidence of stress urinary incontinence on physical testing, with a significant reduction in their incontinence episodes.[51] The addition of vaginal weighted cones, biofeedback, or other feedback may improve these cure rates over exercise alone.[48,49] Women should be encouraged to pursue a modality that facilitates compliance.

There is some evidence that bladder control pessaries are effective and may be preferable for women who have stress urinary incontinence during specific situations; for example, only during exercise.[52] **Table 2** highlights important, high-impact, stress incontinence treatment trials. In a multicenter randomized trial of pessary vs behavioral therapy with pelvic floor exercises vs combination therapy, 33% of women treated with a pessary reported no bothersome incontinence compared with 49% in the behavioral therapy group ($P = .006$). Although overall satisfaction at 3 months was higher with the behavioral therapy group (75% vs 63%; $P = .02$), there were no differences after 12 months, with 50% overall satisfaction.[53] Over-the-counter vaginal insert devices, such as Impressa, may provide an alternative noninvasive treatment, although comparative data are lacking. The addition of vaginal devices to pelvic floor exercises is not more effective than either modality alone.[50,53] A recent randomized trial from China reported the efficacy of acupuncture for stress incontinence.[60] Future studies will be needed to determine the role

Table 1. Landmark Clinical Trials in Urgency Urinary Incontinence (UUI) Treatment (continued)

	BE-DRI[41]	ABC[42]	ROSETTA[43]
Results			
Primary outcome (success definition)	No drug treatment and 7-d diary: >70% reduction of UI episodes/wk	3-d diary: change in mean daily urgency urinary incontinence episodes/d	3-d diary: change in mean daily urgency urinary incontinence episodes/d
Secondary outcome definition	UDI and OABq at 10 wk (before withdrawal of medication) Patient-reported satisfaction	OABq-SF, PFDI, PFIQ Proportion of participants with complete resolution of urgency urinary incontinence	OABq-SF, OAB-SAT-q Proportion of participants with complete resolution of urgency urinary incontinence
Primary outcome	Successful discontinuation of therapy Life table estimate: Combination therapy, 41% Medication, 41% 0% difference (95% CI, -12% to 12%) Completed cases estimate: Combination therapy, 36% Medication, 34% 2% difference (95% CI, -10% to 14%)	Mean urgency urinary incontinence episodes/d: Anticholinergic, 3.4 BTA, 3.3 (*P* = .81)	Mean urgency urinary incontinence episodes/d: BTA, -3.9 SNS, -3.3 Mean difference, 0.63 (95% CI, 0.13 to 1.14) (*P* = .01)
Secondary incontinence outcomes	70% reduction in UI episodes/wk: Combination therapy, 69% Medication, 58% 11% difference (95% CI, −0.3% to 22%)	Complete resolution: Anticholinergic, 16 (13%) BTA, 30 (27%) (*P* = .003)	Complete resolution: BTA, 20% SNS, 4% Treatment difference, −16% (95% CI, −26% to −5%) (*P* < .001)
Satisfaction	Combination therapy, 53% Medication, 40% 13% difference (95% CI, 1% to 25%)	Not reported	OAB-SAT-q mean score: BTA, 67.7 SNS, 59.8 Mean difference, 7.8 (95% CI, 1.6 to 14.1) (*P* = .01)
Quality of life and symptom bother	UDI mean change in score from baseline: Combination therapy, 70 Medication, 60 (*P* < .001) OABq mean change in score from baseline: Combination therapy, 37 Medication, 30 (*P* < .001)	OABq-SF mean change from baseline: Symptom severity Anticholinergic, -44.55 BTA, -44.08 (*P* = .87) Quality of life Anticholinergic, 37.05 BTA, 37.13 (*P* = .98) No differences between groups for change from baseline in total scores of PFDI-SF and PFIQ-SF	OABq-SF mean change from baseline: Symptom severity BTA, -46.7 SNS, -38.6 point reduction Mean difference, 8.1 (95% CI, 3.0 to 13.3) (*P* = .002) Quality of life BTA, 41.6 SNS, 38.1 Mean difference, -3.6 (95% CI, -8.7 to 1.5) (*P* = .17)
Complications			
Dry mouth	Not reported	Anticholinergic, 58 (46%) BTA, 37 (31%) (*P* = .02)	Not reported
Constipation	Not reported	Anticholinergic, 36 (28%) BTA, 25 (21%) (*P*= .06)	Not reported
Catheter use at 1 mo 6 mo	Not reported	Anticholinergic, 0 BTA, 3 (3%) (*P* = .11) Anticholinergic, 0 BTA, 1 (1%) (*P* = .49)	BTA, 16 (8%) SNS, 0 BTA, 4 (2%) SNS, 0 (*P* values not reported)
Urinary tract infection	Not reported	Anticholinergic, 16 (13%) BTA, 40 (33%) (*P* < .001)	BTA, 66 (35%) SNS, 20 (11%); Risk difference, 23% (95% CI, -33% to -13%) (*P* < .001)
Device revision/surgery	Not applicable	Not applicable	BTA, 0 SNS, 6 (3%) (*P* value not reported)

Abbreviations: ABC, anticholinergic vs botulinum toxin comparison; BE-DRI, Behavior Enhances Drug Reduction of Incontinence; BTA, onabotulinumtoxinA; OABq, Overactive Bladder Questionnaire; OAB-SAT-q, Overactive Bladder Satisfaction of Treatment Questionnaire (range, 0-100; higher scores indicate better satisfaction); OABq-SF, Overactive Bladder Questionnaire–Short Form (range, 0-100; higher scores indicate a better quality of life, and higher scores on symptom severity indicate greater symptom severity); PFDI, Pelvic Floor Distress Inventory; PFDI-SF, Pelvic Floor Distress Inventory–Short Form (range, 0 to 300, with higher values indicating greater distress); PFIQ, Pelvic Floor Impact Questionnaire; PFIQ-SF, Pelvic Floor Impact Questionnaire–Short Form (range, 0 to 300, with higher values indicating greater negative effect on daily life); RCT, randomized clinical trial; ROSETTA, Refractory Overactive Bladder: Sacral Neuromodulation vs Botulinum Toxin Assessment; SNS; sacral nerve stimulation; UDI, Urogenital Distress Inventory (range, 0-100; higher scores indicate greater distress).

Table 2. Important Clinical Trials in Stress Incontinence Treatment

Study and Design	ATLAS[53] RCT, Superiority	Ward et al[54] RCT, Superiority	Ward et al[55] Observational	SISTER[56] RCT, Superiority	SISTER[57] Observational	TOMUS[58] RCT, Noninferiority	TOMUS[59] Observational
Comparison groups	3 Groups: pessary, behavioral therapy, combination	RMUS vs Burch colposuspension		Burch vs rectus fascia PVS		Retropubic midurethral sling (RMUS) vs transobturator midurethral sling (TMUS)	
No. enrolled	446	344	344	655	482	597	597
No. of sites	9	14	11	8	8	8	8
Results, No. assessed	366	279	121	520	357	565	516
Outcome point	3 mo	6 mo	5 y	2 y	5 y	1 y	2 y
Patient age, mean (SD), y	49 (11.9)	50 (8)	50 (8)	52 (10.5)	53 (10.5)	53 (11)	53 (11)
Concomitant prolapse surgery, No. (%)	No	No	No	380 (58)	380 (58)	77 (26)	77 (26)
Primary Outcome: Success Definition							
	"Much better" or "very much better" with PGI-I and no bothersome stress incontinence symptoms on UDI	Urodynamic studies with no stress incontinence and negative pad test result (<1 g of urine loss into pad in 1 h)	Negative pad test result (<1 g of urine loss into pad in 1 h)	Overall: No incontinence by self-report or diary Negative stress test result No further stress incontinence treatment Stress incontinence specific: No incontinence by self-report Negative stress test result No further stress incontinence treatment	Composite: No stress incontinence by self-report No incontinence on diary No further stress incontinence treatment	Objective: Negative stress test result Negative pad result (<15 g of urine loss into pad in 24 h) No re-treatment for stress incontinence Subjective: No stress incontinence by self-report No stress incontinence on 3-d diary No re-treatment for stress incontinence	Objective: Negative stress test result Negative pad result (<15 g of urine loss into pad in 24 h) No further stress incontinence treatment Subjective: No stress incontinence by self-report No stress incontinence on 3-d diary No re-treatment for stress incontinence
Primary Outcome							
	PGI-I: Pessary 59 (40%), behavioral 72 (49%), combination 80 (53%) Pessary vs behavioral (P = .49) UDI: Pessary 49 (33%), behavioral 71 (49%), combination 66 (44%) Pessary vs behavioral (P = .006) Pessary vs combination (P = .05) Behavioral vs combination (P = .42)	RMUS 115 (66%) Burch 97 (57%) (P = .099) 9% difference (95% CI, −4.7% to 21.3%)	RMUS 58 (81%) Burch 44 (90%) (P = .21)	Overall: PVS 153 (47%) Burch 125 (38%) (P = .01) Stress incontinence specific: PVS 215 (66%) Burch 161 (49%) (P < .001)	PVS 100 (30.8%) Burch 79 (24.1%) (P = .05)	Objective: RMUS 235 (80.8%) TMUS 232 (77.7%) 3.0% difference, met equivalence (95% CI, −3.6% to 9.6%) Subjective: RMUS 181 (62.2%) TMUS 163 (55.8%) 6.4% difference, did not meet equivalence (95% CI, −1.6% to 14.3%)	Objective: RMUS 196 (77.3%) TMUS 190 (72.3%) 5.1% difference, did not meet equivalence (95% CI, −2.0% to 12.1%) Subjective: RMUS 141 (55.7%) TMUS 127 (48.3%) 7.4% difference, did not meet equivalence (95% CI, −0.7% to 15.5%)

(continued)

Table 2. Important Clinical Trials in Stress Incontinence Treatment (continued)

Study and Design	ATLAS[53] RCT, Superiority	Ward et al[54] RCT, Superiority	Ward et al[55] Observational	SISTER[56] RCT, Superiority	SISTER[57] Observational	TOMUS[58] RCT, Noninferiority	TOMUS[59] Observational
Secondary Outcomes							
Secondary incontinence outcomes	>75% reduction in stress incontinence episodes: Pessary 69 (46%) behavioral 68 (47%) combination 80 (53%) (*P* > .05)	Stress incontinence reported: RMUS 54 (34%) Burch 37 (29%) (*P* = .95) Urgency reported: RMUS 51 (32%) Burch 42 (33%) (*P* = .54)	Stress incontinence reported: RMUS 51 (29%) Burch 46 (24%) (*P* = .54) Urgency reported: RMUS 86 (40%) Burch 77 (37%) (*P* = .40)	Urge incontinence treatment: Burch 65 (20%) PVS 87 (27%) (*P* = .04)	Not reported	Mean (SD) change UDI total: RMUS 107 (48) TMUS 110 (51) (*P* = .41) Mean (SD) change UDI stress: RMUS 61 (28) TMUS 62 (28) (*P* = .82) Mean (SD) change IIQ total: RMUS 127 (95) TMUS 133 (98)	Change from baseline in UDI total: RMUS −100 TMUS −107 (*P* = .13) Not reported Change from baseline in total IIQ: RMUS −125 TMUS −124 (*P* = .89)
Satisfaction	Pessary 94 (63%) Behavioral 110 (75%) Combination 118 (79%) Pessary vs behavioral (*P* = .03) Pessary vs combination (*P* = .003)	Not reported	Not reported	PVS 280 (86%) Burch 257 (78%) (*P* = .02)	PVS 271 (83%) Burch 240 (73%) (*P* = .04)	RMUS 250 (85.9%) TMUS 262 (90%) (*P* = .14)	RMUS 257 (86.3%) TMUS 263 (88.1%) (*P* = .58)
Repeated incontinence surgery	Not applicable	Not reported	RMUS 4 (2.3%) Burch 5 (3.4%) (*P* = .74)	Burch 11 (3%) PVS 2 (0.6%) (*P* < .001)	PVS 7 (2%) Burch 39 (12%) (*P* < .001)	Not reported	Not reported
Complications							
Serious adverse events	None	Not reported	Not reported	PVS 43 (13%) Burch 32 (10%) (*P* = .20)	None reported	RMUS 41 (13.8%) TMUS 19 (6.4%) (*P* = .003)	RMUS 45 (15.1%) TMUS 25 (8.4%) (*P* = .011)
Adverse events	Vaginal discharge: Pessary (16%) Behavioral (6%) Combination (9%)	Total adverse events: RMUS 67 (39% Burch 65 (45%) (*P* = .36)	Not reported	PVS 206 (63%) Burch 156 (47%) (*P* < .001)	PVS 22 (9%) Burch 23 (10%) (*P* value not reported)	RMUS 110 (36.9%) TMUS 89 (29.8%) (*P* = .07)	RMUS 121 (40.6%) TMUS 98 (32.8%) (*P* = .05)
De novo urge incontinence	Not reported	Not reported	RMUS 1 (1%) Burch 3 (4%) (*P* value not reported))	No difference 3% each group	PVS 3 Burch7 (*P* value not reported)	RMUS 0% TMUS 1 (.3%) (*P* = .5)	RMUS 0 TMUS 1 (0.3%) (P > .99)
Surgery or use of catheter to correct voiding dysfunction	Not applicable	Catheterization >8 mo: RMUS 5 (3%) Burch 11 (8%) (*P* = .07)	Surgery: RMUS 4 (2%) Burch 5 (3%) (*P* = .74)	Surgery: PVS 19 (6%) Burch 0 (*P* value not reported) Catheter use <6 wk postoperatively: PVS 181 (57%) Burch 138 (43%) (*P* = .04)	PVS 7 Burch 1	RMUS 8 (2.7%) TMUS 0% (*P* = .004)	RMUS 9 (3.0%) TMUS 0% (*P* = .002)
Urinary tract infection	Not reported	RMUS 38 (22%) Burch 46 (32%) (*P* = .07)	Not reported	PVS 156 (48%) Burch 105 (32%) (*P* = .06)	PVS 21 Burch 21 (*P* value not reported)	RMUS 40 (13.4%) TMUS 24 (8.0%) (*P* = .04)	RMUS 51 (17.1%) TMUS 32 (10.7%) (*P* = .03)
Bladder injury	Not applicable	RMUS 15 (9%) Burch 3 (2%) (*P* = .013)	Not reported	PVS 2 (0.6%) Burch 10 (3%) (*P* value not reported)	Not applicable	RMUS 15 (5%) TMUS 0% (*P* value not reported)	Not applicable

(continued)

Table 2. Important Clinical Trials in Stress Incontinence Treatment (continued)

Study and Design	ATLAS[53] RCT, Superiority	Ward et al[54] RCT, Superiority	Ward et al[55] Observational	SISTER[56] RCT, Superiority	SISTER[57] Observational	TOMUS[58] RCT, Noninferiority	TOMUS[59] Observational
Pain >6 wk	Not reported	Not reported	Not reported	No difference	Not reported	RMUS 7 (2.3%) TMUS 6 (2.0%) (*P* = .79)	RMUS 7 (2.3%) TMUS 6 (2%) (*P* = .79)
Mesh complication	Not applicable	RMUS 1 (1.8%)	RMUS 6 (3%)	Not applicable	Not applicable	RMUS 5 (1.6%) TMUS 13 (4.3%) (*P* value not reported)	RMUS 14 (4.7%) TMUS 9 (2.7%) (*P* value not reported)
Neurologic symptoms >6 wk	Not reported	Not reported	Not reported	Not reported	Burch 1	RMUS 12 (4%) TMUS 28 (9.4%) (*P* = .01)	RMUS 15 (5.4%) TMUS 29 (9.7%) (*P* = .045)

Abbreviations: ATLAS, Ambulatory Treatments for Leakage Associated With Stress Incontinence; IIQ, Incontinence Impact Questionnaire (score, 0-300; higher number indicates greater effect of symptoms); OR, odds ratio; PGI-I, Patient Global Impression of Improvement (assessed from "very much worse" to "very much better"); PVS, pubovaginal sling; RCT, randomized clinical trial; SISTER, Stress Incontinence Surgical Treatment Efficacy Trial; TOMUS, Trial of Midurethral Slings; UDI, Urinary Distress Inventory (score, 0-300; higher number indicates more distress).

of acupuncture for women in the United States, given the limited availability and lack of insurance coverage.

Medications

There are no FDA-approved medications for stress incontinence. There are 6 FDA medications in the primary medication class for urgency incontinence (darifenacin, fesoterodine, oxybutynin, solifenacin, tolterodine, and trospium). These medications are used as second-line treatment.[32] **Table 3** displays the magnitude of improvements reported in FDA regulatory trials of medication for treatment of urgency incontinence. Most efficacy data for these medications are from short-term, industry-supported studies with moderate- to high-level evidence to support efficacy compared with placebo. The medications for treating urgency incontinence have not all been directly compared for efficacy or adverse effects. The magnitude of improvements reported in FDA regulatory trials ranges from 53% to 80% reduction in urinary incontinence episodes and 12% to 32% reduction in urinary frequency, with placebo rates of improvement from 30% to 47% for incontinence episodes and 8% to 15% for urinary frequency. Medication selection is generally made according to formulary availability, patient costs, and specific clinical factors.

Anticholinergic medications block muscarinic receptors in the smooth muscle of the bladder, thus inhibiting detrusor contraction. These medications are associated with moderate improvements in urgency, frequency, and urgency incontinence episodes.[61-65] The proportion of patients reporting symptom control with anticholinergic medications is 49% (interquartile range, 35.6%-58%).[51] Discontinuation because of adverse effects (dry mouth and constipation) is common, with less than 50% of patients continuing prescribed medication beyond 6 months and less than 36% beyond 1 year.[66] Patients may prefer the convenience of daily medication or a lower medication cost associated with multiple daily dosing. Once-daily dosing of medication also may improve adherence to treatment.[67] Specialty guidelines recommend using the extended-release formulation over the immediate-release one to minimize adverse effects.[32]

Contraindications to anticholinergic medications include untreated narrow-angle glaucoma (an uncommon condition). This class of drugs may aggravate existing cardiac arrhythmias. Although 2 drugs in this class, solifenacin and tolterodine, are reported to prolong the QT interval, routine electrocardiogram is not recommended before prescribing this medication. Recent research raises questions regarding the association of long-term anticholinergic exposure with dementia.[68]

β-3 Agonists are also available for treating urgency incontinence. Stimulation of the β-3 pathway promotes smooth muscle relaxation of the bladder to increase urine storage. Mirabegron, the only FDA-approved drug in this class, has efficacy that is better than placebo's and not different from that of anticholinergics, and has reported symptom control rates of 43.5% to 45.8% at 12 months.[51,65,69,70] Mirabegron's adverse effects include the possibility of increasing hypertension. It may provide synergistic effects with anticholinergic medications in women who have insufficient response with monotherapy.[71-73]

Table 3 displays the rates of the most common adverse effects, constipation and dry mouth, as reported in registration studies of FDA-approved medications for urgency incontinence. A systematic

Table 3. Considerations for Food and Drug Administration–Approved Medications for Urgency Incontinence Treatment[a]

Generic Drug Name (Year of FDA Approval)	Dose Options	Efficacy, %[b]		Most Common Adverse Effects, %[c]		Special Considerations	Patients Most Likely to Benefit
		Reduction in Urinary Frequency	Reduction in Incontinence Episodes/d	Constipation	Dry Mouth		
Placebo		8-15	30-47	0-4.8	0-8	Likely effect of behavior modification	
Anticholinergics							
Oxybutynin oral (IR, 1975; ER, 1999)	5 mg IR 5, 10, 15 mg ER	Not reported	80 (ER)	15 (IR) 9 (10 mg ER)	71 (IR) 35 (10 mg ER)	IR is inexpensive, with many adverse effects, concern for cognitive impairment ER formula preferred	Uninsured/underinsured, healthy, low risk of cognitive effects
Oxybutynin transdermal (patch, 2003; gel, 2011)	Patch, 3.9 mg/d Gel, 1 g/d	18 22	62 (patch) 56 (gel)	3 (patch) 1 (gel)	9 (patch) 8 (gel)	Lowest adverse effect profile, but skin reactions common (16%)	Unable to tolerate oral formulations
Tolterodine (IR, 1998; ER, 2000)	2 and 4 mg ER	17	53	6 (4 mg ER)	23 (4 mg)	Generic, available over the counter	Uninsured/underinsured
Solifenacin ER (2004)	5 and 10 mg	23	54	5 (5 mg) 13 (10 mg)	11 (5 mg) 28 (10 mg)	Pills can be cut in half	Covered drug plan/ high co-pay
Darifenacin ER (2004)	7.5 and 15 mg	32	64	15 (7.5 mg) 21 (15 mg)	20 (7.5 mg) 35 (15 mg)	No QT-interval prolongation, low CNS absorption	Elderly/dementia risk, cardiac concerns
Trospium chloride (IR, 2004; ER, 2007)	20 mg IR 60 mg ER	20	59	9 (60 mg ER)	11 (60 mg)	No drug-drug interaction, low CNS absorption	Elderly/dementia risk, polypharmacy
Fesoterodine ER (2008)	4 and 8 mg	16	62	4 (4 mg) 6 (8 mg)	19 (4 mg) 35 (8 mg)	Trials in elderly with comorbidities show safety	Covered drug plan
β-Adrenergic: mirabegron ER (2012)	25 and 50 mg	12	54	2.2 (50 mg)	2.8 (50 mg)	Expensive, only drug in its class (new or worse hypertension 7.5% vs 7.6% placebo)	Intolerant or unable to receive anticholinergic

Abbreviations: CNS, central nervous system; ER, extended-release once-daily dosing; FDA, Food and Drug Administration; IR, immediate release.

[a] See full package inserts (available at http://www.rxlist.com) for prescribing data. Data are based on mean results of regulatory studies used for FDA approval and do not represent true between-drug comparisons.

[b] Reported efficacy from average reductions from baseline across FDA trials reported in package inserts of maximum-dose, extended-release preparations, except where noted.

[c] Common adverse effects for extended-release preparations, except where noted. Discontinuation rates are less than 5% for these adverse effects.

review of 86 trials comparing anticholinergic medications revealed comparisons between different therapies for only 4 drugs: oxybutynin, tolterodine, solifenacin, and fesoterodine. The authors concluded that immediate-release tolterodine may be associated with less dry mouth compared with immediate-release oxybutynin, and extended-release formulations of these drugs should be used in preference to immediate-release ones to minimize dry mouth; solifenacin may have better efficacy than immediate-release tolterodine; and fesoterodine may be more efficacious than extended-release tolterodine, with more adverse effects. There were insufficient data to evaluate other anticholinergics or to compare quality of life, cost, or long-term success.[74] The only studies comparing mirabegron to other drugs have been industry sponsored in the setting of comparing combined therapy (ie, mirabegron plus low-dose solifenacin) vs monotherapy. A recent study demonstrated significant reduction in urgency incontinence episodes with 50 mg mirabegron plus 5 mg solifenacin compared with 5 mg solifenacin alone (71% vs 54%; mean adjusted difference, −0.2; $P = .03$); however, no significant difference was achieved compared with mirabegron 50 mg alone (61% reduction). The study was not designed to compare mirabegron 50 mg vs solifenacin 5 mg alone. The placebo group had a 42% reduction in incontinence episodes, and the 10-mg dose that is typically prescribed for solifenacin was not studied.[73]

Local low-dose vaginal estrogens (creams, tablets, or rings) are FDA approved for the treatment of vaginal atrophy. Although non-industry-sponsored multicenter comparative trials are lacking, systematic reviews suggest modest improvement in urinary incontinence in postmenopausal women compared with placebo.[75-77] There is no evidence for efficacy of systemic estrogen for treatment of any form of urinary incontinence; systemic estrogen may worsen incontinence.[75]

Procedures

Stress Incontinence Surgery

Women whose predominantly stress incontinence symptoms persist despite conservative measures may be candidates for surgery. Table 2 displays important stress incontinence treatment trials. Surgery is highly effective, with median cure rates of 84.4% (interquartile range, 74%-90.1%) at 12 months.[51] Historically, the standard surgery for stress incontinence included a retropubic urethropexy or a pubovaginal sling. A multicenter randomized controlled trial of these 2 procedures in 655 women revealed higher stress-incontinence-specific success rates (66% vs 49%; $P < .001$) but higher morbidity (6.1% vs 0% voiding dysfunction requiring reoperation) for the pubovaginal sling compared with urethropexy.[56,57] A European randomized trial of retropubic Burch colposuspension vs retropubic midurethral sling in 344 women revealed no difference in success rates at 6 months and 5 years.[54,55] Currently, the most commonly performed surgery is the midurethral sling, a 30-minute outpatient procedure in which a synthetic mesh sling is placed through either a retropubic or transobturator approach.[78,79] The midurethral sling is the most extensively studied anti-incontinence operation, with documented short-term efficacy (62% to 98%) and long-term efficacy (>5 years: 43% to 92%).[79,80] Complication rates are

low and synthetic mesh erosion occurs in less than 5% of patients.[79] Mesh erosions may require excision because of discharge, bleeding, and pain in the patient and/or her male sexual partner. The Trial of Midurethral Slings revealed similar objective success rates (77.7%-80.8%) and patient satisfaction (85.9%-90%) at 1 year, with small differences in subjective success at 2 years (55.7% vs 48.3% for retropubic vs obturator, respectively).[58,59]

Women with stress incontinence can undergo urethral bulking injection, typically in an office setting under local anesthesia with a cystoscope. The bulking material is injected under the urethral mucosal layer to increase outflow resistance. High-quality multicenter randomized trials are lacking, but systematic reviews suggest lower success rates compared with that for sling procedures.[81,82] Cure rates for injectable bulking agents have been reported in 24.8% to 36.9% of women at 12-month follow-up.[51]

Urgency Incontinence Procedures

There are 3 FDA-approved procedural treatments for women with persistent urgency incontinence symptoms or intolerance to medication. All of these treatments are based on changes in neural regulation.

Percutaneous tibial nerve stimulation is an office procedure in which electrical stimulation via an acupuncture needle is delivered in twelve 30-minute weekly sessions, followed by monthly maintenance therapy. Industry-supported studies of percutaneous tibial nerve stimulation have reported subjective improvement of 60% (95% CI, 49%-75%), with low rates of transient local adverse events (8.5%) and efficacy similar to that of anticholinergic medications.[83-85]

OnabotulinumtoxinA (100 U) is injected into the bladder through a cystoscope with local anesthetic in an office setting. The drug blocks the presynaptic release of acetylcholine to decrease muscarinic receptor activation involved in detrusor contraction. Treatment is effective in approximately 65% of participants for approximately 6 to 12 months.[42] Treatment risks include urinary retention (8%-10%) and urinary tract infections (35%). A large multicenter clinical trial of oral anticholinergic medication demonstrated reductions in incontinence episodes similar to those with onabotulinumtoxinA (100 U) (68% and 66%, respectively) (Table 2).[86] More participants reported resolution of urge urinary incontinence after treatment with onabotulinumtoxinA (13% vs 27%; $P = .003$).

Sacral neuromodulation is an outpatient surgical procedure in which an implanted electrode is placed along the third sacral nerve root to deliver nerve stimulation. When a short-term test is successful, a permanent external stimulator that lasts approximately 5 years can be implanted. After implantation, approximately 60% to 90% of women report improvement and 30% to 50% report cure.[87] A recent multicenter randomized trial of onabotulinumtoxinA, 200 U, compared with sacral neuromodulation demonstrated a small but statistically significant superiority for onabotulinumtoxinA in the reduction of urgency incontinence episodes at 6 months (−3.9 [72%] vs −3.3 [63%], $P = .01$)](Table 1).[43] Urinary tract infections (35% vs 11%) and need for catheterization (8% vs 0%) were more frequent with onabotulinumtoxinA, whereas device revisions and removals occurred in 3% of patients.

Conclusions

Urinary incontinence is common in women, although few seek care despite many effective treatment options. Clinicians should prioritize urinary incontinence detection, identify and treat modifiable factors, incorporate patient preference into evaluation and treatment, initiate conservative and medical therapy, and refer to specialists when underlying pathology is identified or conservative measures are ineffective.

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