# Urinary incontinence in women: Identification, evaluation, and treatment

Christine M Chu, MD

Department of Obstetrics & Gynecology
Division of Female Pelvic Medicine & Reconstructive Surgery



# Financial Disclosures

None

## Objectives

- Examine the prevalence and impact of urinary incontinence (UI)
- Review the anatomy and physiology behind urination and continence
- Learn to categorize common types of urinary incontinence (UI)
- Diagnose urinary incontinence
- Examine the range of treatments for urinary incontinence (UI) subtypes and when to refer to a specialist

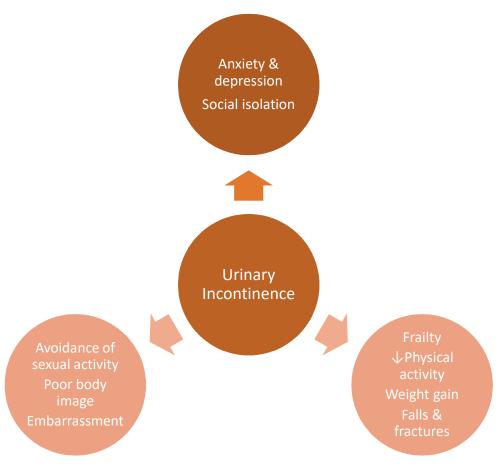
## Urinary incontinence (UI) and women

- 18 million women in the US have urinary incontinence (UI)
  - 10-20% of all women
  - Increases with age
    - Women >20 yo: 17%
    - Women >60 yo: 38%
- UI is more common than diabetes, hypertension, or depression
- In spite of this, only 25% of women seek care
  - Only half of these women see a specialist.

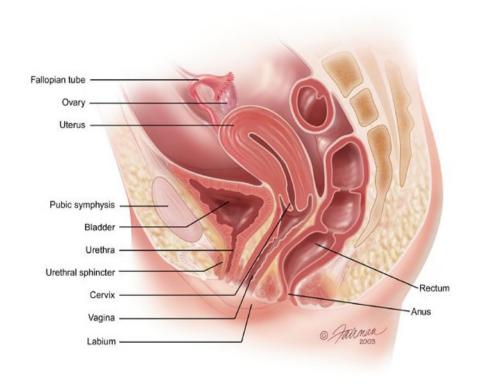


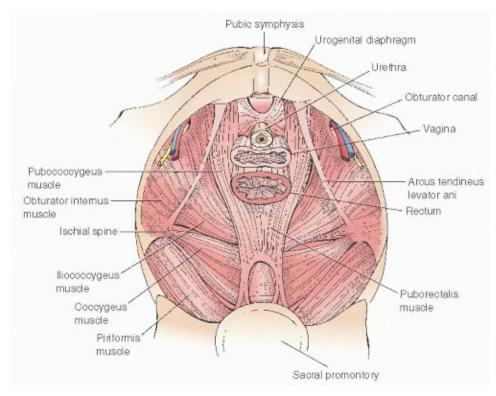
# Misunderstandings about UI

- Urinary incontinence is a normal part of aging or after childbirth
  - UI can significantly impacts health
  - UI can result in dependence on caretakers, admission to long term care facilities
- Bothersome UI will be reported
  - 50% of women with severe UI will not discuss this with their physicians due to embarrassment
- UI is not a serious health condition
  - UI impacts many areas of physical, mental, and sexual health



# Anatomy of the pelvic floor: organs & musculature





## Anatomy of the urethra

- Female urethra
  - 3-5 cm
  - ~6 mm in diameter
  - Supported and embedded in anterior vaginal adventitia
  - Passage
    - Curves slightly through retropubic space
    - Pierces perineal membrane
    - Urethral meatus above vaginal opening
  - Vessels: vesical and internal pudendal arteries
  - Innervation:
    - Distal: pudendal nerve
    - Proximal: pelvic nerve (inferior hypogastric)

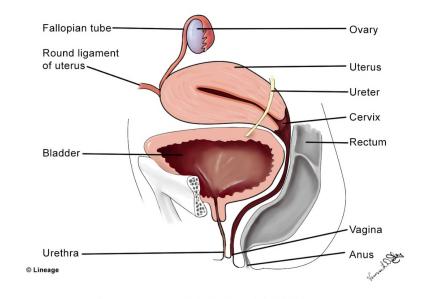
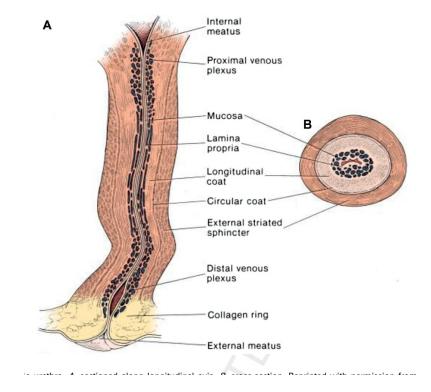


Table 2. Urethral Topography and Urethral and Paraurethral Structures

Location (percentile of urethral length)	Region of the urethra	Structures
0-20	Intramural	Internal urethral meatus
		Detrusor loop
20–60	Midurethra	Striated urethra sphincter muscle
		Smooth muscle
60–80	Urogenital diaphragm	Compressor urethrae muscle
		Urethrovaginal sphincter
		Smooth muscle
80–100	Distal urethra	Bulbocavernosus muscle

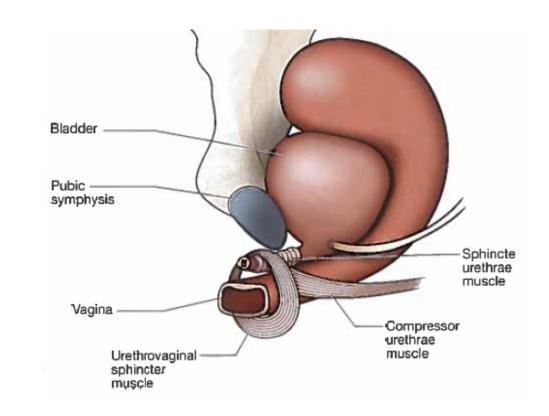
## Anatomy of the urethra

- Epithelium
  - Continuous with vulva and bladder
  - Stratified squamous epithelium → transitional
  - Contains glands
- Lamina propria
  - Loose fibroelastic connective tissue
    - Collagen, fibrocytes, elastic fibers, veins
- Smooth muscle
  - Comprises the internal urethral sphincter
  - Oblique and longitudinal fibers
  - Some circular fibers
  - Alpha-adrenergic and cholinergic control
- Striated muscle
  - Comprises the extrinsic urethral sphincter



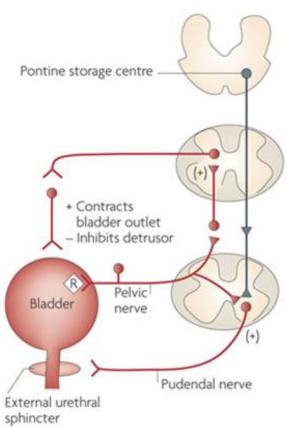
# Anatomy of the urethra

- Extrinsic urethral sphincter
  - Slow twitch muscles
  - Sphincter urethrae
    - Striated band of muscle surrounding proximal 2/3 of urethra
  - Compressor urethrae and urethrovaginal sphincter (deep transverse perineus muscle)
    - Two striated bands of muscle that arch over the ventral, distal 1/3 urethra



# Neurophysiology

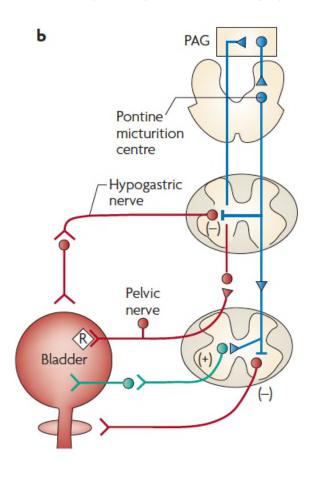
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### Storage

- Distension → low level afferent firing
- Hypogastric nerve outflow (symapathetic)
  - Bladder base and urethra contraction
  - Detrusor relaxation
- Pudendal nerve outflow
  - External urethral sphincter, pelvic floor

# Neurophysiology

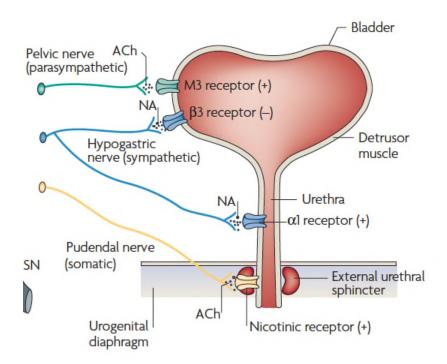


### Voiding

- Increased afferent firing → spinobulbospinal reflex
  - Signaling passes through the pontine micturition center
- Pontine micturition center activation
  - Descending spinal pathway activates parasympathetic outflow
- Sacral parasympathetic outflow (S2-4)
  - Detrusor contraction
  - Urethral/pelvic floor relaxation

# Neurophysiology

Receptors of the bladder



## Types of Incontinence

Stress urinary incontinence

- Urinary leakage with increased intraabdominal pressure
- Leakage with coughing, laughing, sneezing, jumping, lifting

Urgency urinary incontinence
/ Overactive bladder

- Urinary leakage with urgency (strong, inappropriate urge to urinate)
- May be accompanied by frequency, urgency, nocturia

Mixed urinary incontinence

 Urinary leakage with symptoms consistent with both stress and urgency urinary incontinence/ overactive bladder

Continuous incontinence

 Continuous leakage of urine, without provocation, regardless of position

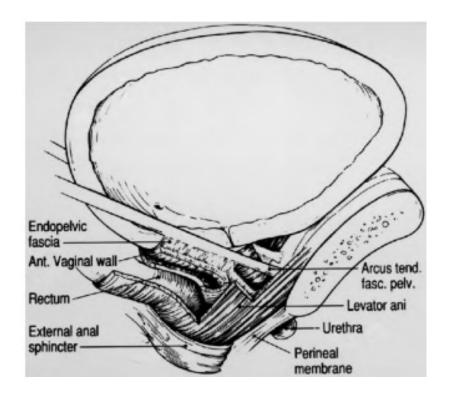
Overflow incontinence

Urinary leakage due to incomplete bladder emptying

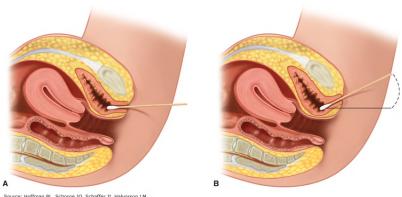
## Stress urinary incontinence

#### Normal

- Urethral closure pressure > bladder pressure
- Transmission of intraabdominal pressure retropubically
- Urethral pressure
  - Endopelvic fascial of anterior vaginal wall, which is connected to the arcus tendineus: compression of bladder neck
  - Levator ani: compression of urethra
  - Contriction of urethral sphincter

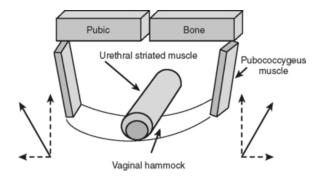


## Stress urinary incontinence



Source: Hoffman BL, Schorge JO, Schaffer JI, Halvorson LM, Bradshaw KD, Cunningham FG: Williams Gynecology, 2nd Edition: www.accessmedicine.com

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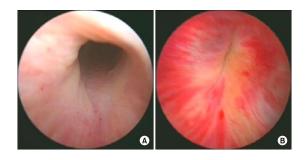


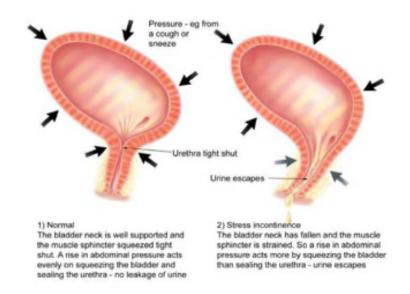
#### Incontinence

- Urethral closure pressure > bladder pressure
- Lack of support
  - Urethral hypermobility
    - Descent of urethra outside of abdominal cavity, decreasing urethral pressure
  - Hammock theory (Delancey)
    - Support of anterior vaginal wall and endopelvic fascia, reinforced by attachment to ATFP and levator ani
  - Integral theory (Petros and Ulmsten)
    - Laxity of anterior vaginal wall and pubourethral ligament in the midurethra resulting in hypermobility

## Stress urinary incontinence

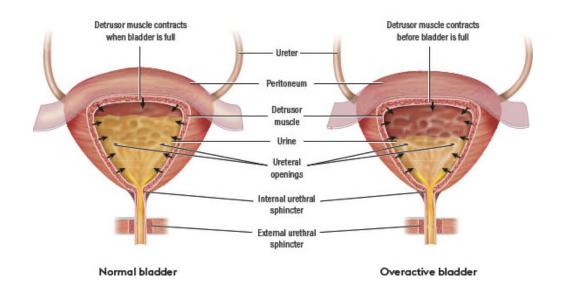
- Intrinsic sphincter deficiency
  - Denervation
  - Surgery
  - Radiation
  - Decrease in strength and striated fibers of sphincter with age
  - Decrease in coaptation of urethra with hypoestrogenic state





# Urgency urinary incontinence/overactive bladder

- Detrusor overactivity
  - Uninhibited detrusor contraction
- Can be associated with neurologic or pathologic disease
- Idiopathic most common
  - No clear etiology



# Urgency urinary incontinence/overactive bladder

- Neurologic impairment
  - Stroke
  - Parkinson disease
  - Brain tumors
  - Spinal cord injuries
  - Multiple sclerosis
- Can result in:
  - Detrusor overactivity
  - Detrusor areflexia
  - Detrusor-sphincter dyssynergia (DSD)

Above brain stem:

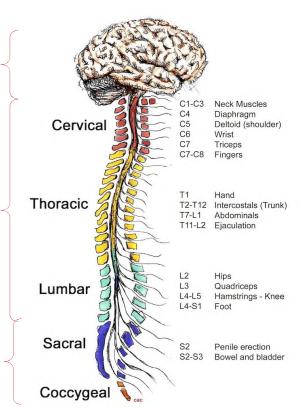
DO

Brain stem to sacral spine:

- DO
- +/- DSD

Sacral spine:

- Detrusor areflexia
- Loss of urethral resistance



# Urgency urinary incontinence/overactive bladder

Fundamental cause of idiopathic UUI/OAB remains unknown

#### Myogenic

- Increased excitability and activity conduction in detrusor myocytes
- Structural and organizational changes of myocytes

#### Neurogenic

- Nerve injury or ischemia
- Hyperexcitability of intramural ganglia
- Increased suburothelial nerve fiber density (abnormal afferent activity)
- Abnormal orbitofrontal cortex activation

#### Inflammation

 Elevated NGF, which triggers changes in afferent or synaptic transmission in CNS

# Urothelial changes

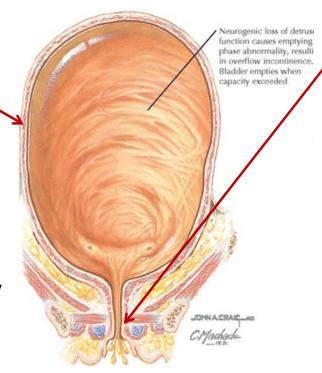
 Abnormalities in receptors function and neurotransmitter release

## Changes in Microbiome

- Increased
   Gardnerella and other bacteria
- Decreased
   Lactobacilli

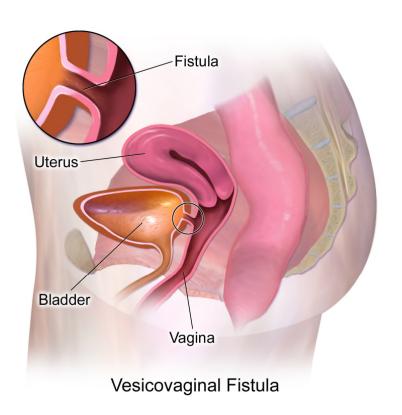
## Overflow incontinence

- Impaired bladder contractility
  - Often neurogenic
    - DM
    - Lumbosacral nerve disease
    - Meningomyelocele
    - MS
    - Herniated disks
    - High spinal cord injuries
  - Often also accompanied by sensory neuropathy



- Bladder outlet obstruction
  - Obstruction due to surgery, radiation
  - Rarely fibroids
  - Occasionally vaginal prolapse

## Continuous incontinence



- Constant leakage without any other symptoms
  - Often representative of urogenital fistula
    - Gynecologic or urinary tract surgery
    - Pelvic radiation
    - Malignancy
  - Rarely due to severely nonfunctioning urethra
    - Prior surgery or radiation with significant scarring
    - Urethral resection
    - Lower motor neuron disease

## Risk factors for incontinence

## Pregnancy/childbirth

• 10.1% vs 15.9% Csection vs 21% SVD

#### Vaginal delivery

 Higher rates of UI compared in SVD vs Csection (HR 2.9)

#### BMI

 Threefold increase of UI vs normal weight women

#### Age

 Prevalence and severity increases with age

#### Genetics

 Increased UI risk in daughters (RR 1.3) and sisters (RR 1.6) of women with UI

#### Oral estrogen

 WHI showed increased risk of UI at least 1/wk with oral HRT (HR 1.49-1.61) vs placebo

#### Physical function

 Physical inability to use the toilet in a timely fashion

#### Diabetes

 Particularly when associated with obesity

#### Hysterectomy

• May be slightly increased, especially in older women (OR 1.6)

#### Cognitive function

• 10-38% in women with cognitive impairment/dementia

## Chronic cough/smoking

#### **Smoking**

Urgency and frequency more common

Vaginal prolapse

#### Caffeine intake

 Greater than 450 mg (vs <150 mg) increased risk of UUI

UTIS

#### Depression

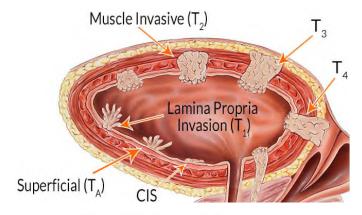
 OR of 2.48 in a population based study Prior pelvic radiation

Prior pelvic surgery

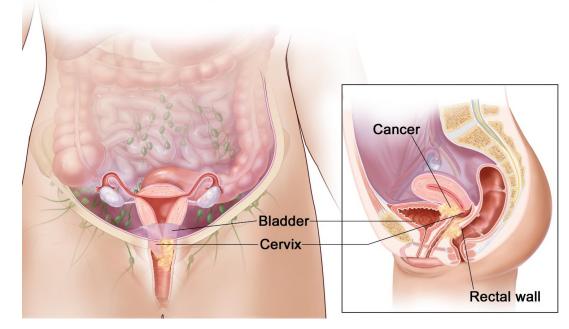
#### High impact activities

 Jumping, running, weight lifting

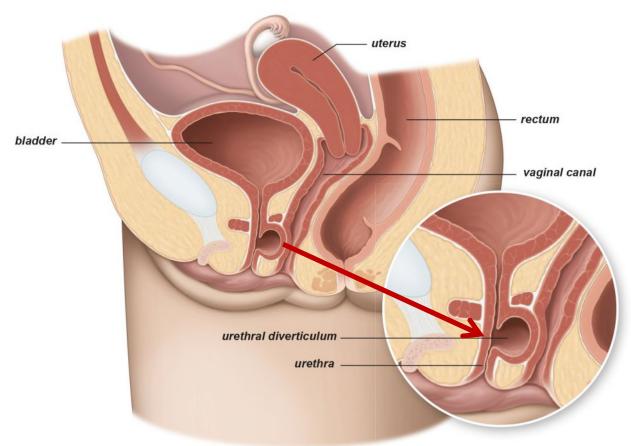
- Neurologic disorders
- UTI
- Malignancies
  - Bladder cancer
  - Cervical cancer



**Stage IVA Cervical Cancer** 

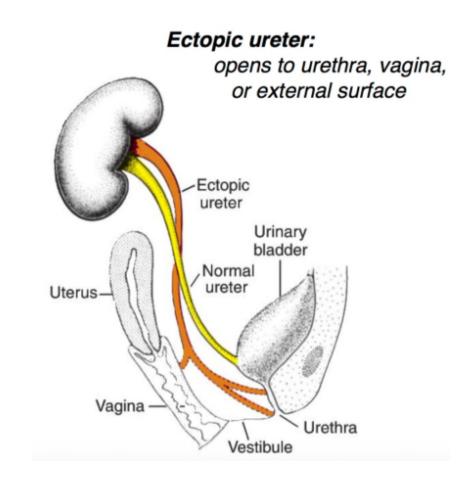


- Neurologic disorders
- UTI
- Malignancies
  - Bladder cancer
  - Cervical cancer
- Urethral diverticula

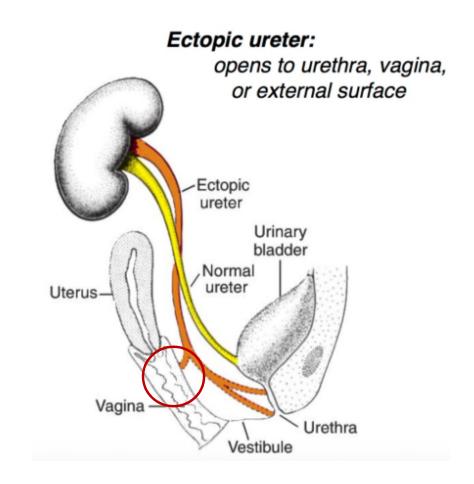


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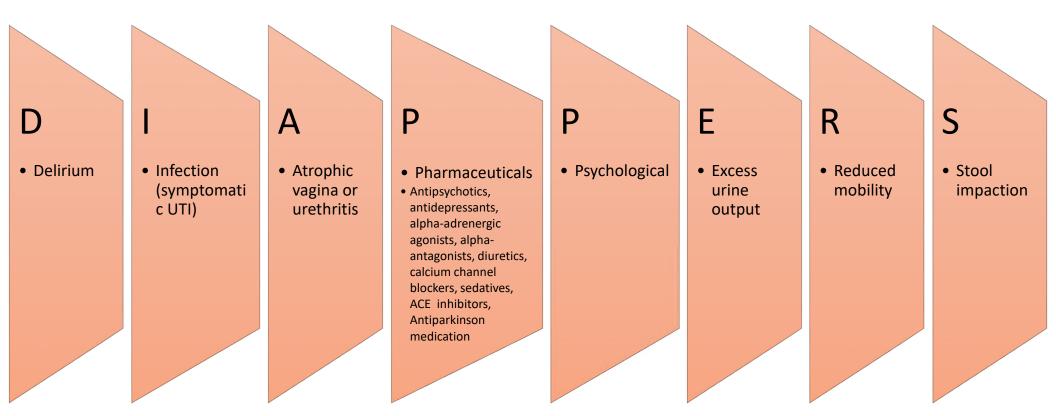
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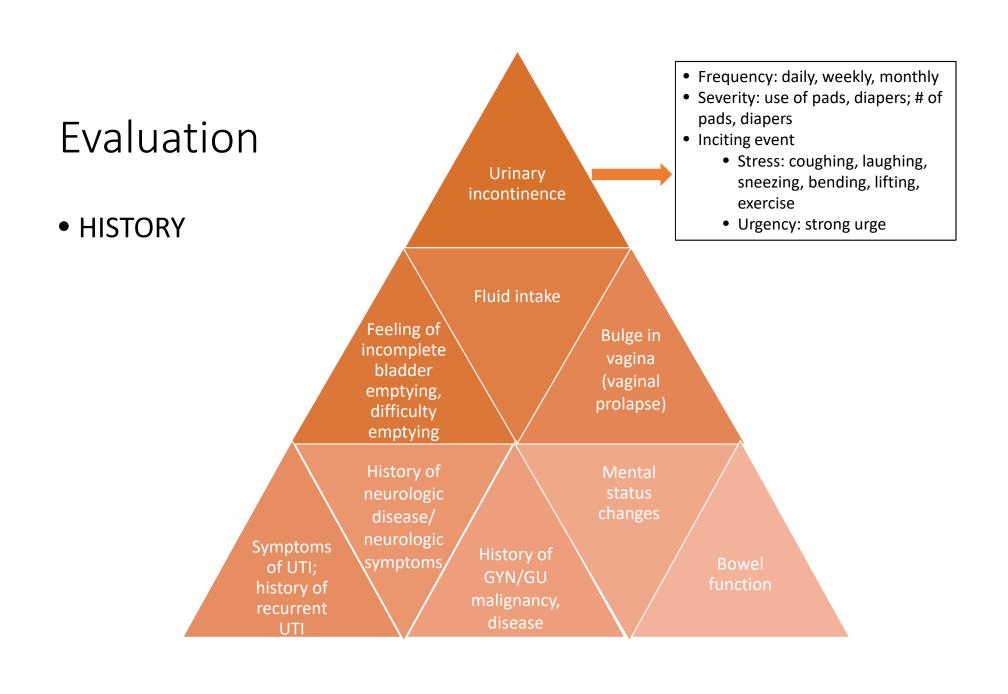


- Elderly and hospitalized patients
  - Keep in mind reversible causes of incontinence



- ASK!
  - Consider screening women with:
    - Women with comorbid conditions
      - Prolapse
      - Bowel symptoms
      - Diabetes
      - Obesity
      - Neurologic disease
    - Postpartum women
    - Women over 65 years old





### QUESTIONNAIRES & DIARIES

#### **QUESTIONNAIRES FOR UI**

#### **Urogenital distress inventory (UDI-6)**

- Part of the Pelvic Floor Distress Inventory-Short From (PFDI-20)
- Symptom severity

#### **Incontinence impact questionnaire (IIQ-7)**

- Part of the Pelvic floor impact questionnaire (PFIQ-7)
- Symptom impact on quality of life

International consultation on incontinence questionnaire (ICIQ)

Bristol female lower urinary tract symptoms questionnaire (BFLUTS)

Incontinence quality of life questionnaire (I-QOL)

Stress and urge incontinence and quality of life questionnaire (SUIQQ)

Urinary incontinence severity score (UISS)

Stress-related leak, emptying ability, anatomy, protection, inhibition, quality of life, mobility and mental status quality of life index (SEAPI-QMM)

Incontinence severity index (ISI)

King's health questionnaire (KHQ)

#### **UROGENITAL DISTRESS INVENTORY (UDI 6)**

Do you experience? If so how much are you bothered by:

	Not at all	A little bit	Moderately	Greatly
1. Frequent urination?	0	1	2	3
2. Urine leakage related to the feeling of urgency?	0	1	2	3
3. Urine leakage related to physical activity, coughing or sneezing?	0	1	2	3
4. Small amounts of urine leakage (that is drops)?	0	1	2	3
5. Difficulty emptying your bladder?	0	1	2	3
6. Pain or discomfort in the lower abdominal or genital area?	0	1	2	3

#### <u>Incontinence Impact Questionnaire – Short Form IIQ-7 (Pre and Post Surgery</u> Questionnaire)

Some people find that accidental urine loss may affect their activities, relationships, and feelings. The questions below refer to areas in your life that may have been influenced or changed by your problem. For each question, circle the response that best describes how much your activities, relationships, and feelings are being affected by urine leakage.

Has urine leakage affected your...

Not at All	Slightly	Moderately	Greatly
0	1	2	3
0	1	2	3
0	1	2	3
0	1	2	3
0	1	2	3
0	1	2	3
0	1	2	3
	0 0 0 0	0 1 0 1 0 1 0 1 0 1 0 1	0 1 2 0 1 2 0 1 2 0 1 2 0 1 2 0 1 2

Items 1 and 2 = physical activity Item 5 = social/relationships Items 3 and 4 = travel
Items 6 and 7 = emotional health

<u>Scoring.</u> Item responses are assigned values of 0 for "not at all," 1 for "slightly," 2 for "moderately," and 3 for "greatly." The average score of items responded to is calculated. The average, which ranges from 0 to 3, is multiplied by 33 1/3 to put scores on a scale of 0 to 100.

### Bladder diary



Patient Name:				

#### Intake and Voiding Diary

This chart is a record of your fluid intake, voiding and urine leakage. Please bring this diary to your next visit.

#### Instructions:

- 1. Choose 4 days (entire 24 hours) to complete this record they do not have to be in a row. Pick days that will be convenient for you to measure every void.
- 2. Begin recording when you wake up in the morning-continue for a full 24 hours.
- 3. Make a separate record for each time you void, leak, or have anything to drink.
- 4. Measure voids (using cc measurements).
- 5. Measure fluid intake in ounces.
- When recording a leak please indicate the volume using a scale of 1-3 \*(1=drops/damp, 2=wet-soaked, 3=bladder emptied), your activity during the leak, and if you had an urge ("yes" or "no").

DAY 1	Date:						
	Amount Voided (in ccs)	Leak Volume (scale of 1-3)	Activity during leak	Was there an urge	Fluid intake (Amount in ounces/type)		
Example							
7:15a	325 cc						
7:45a		2	Watching TV	Yes			
8:15a					8 oz coffee, 8 oz orange juice		
10:30a		1	Jogging	No-			

## • Bladder diary

#### A Sample voiding diary with abnormal intake pattern

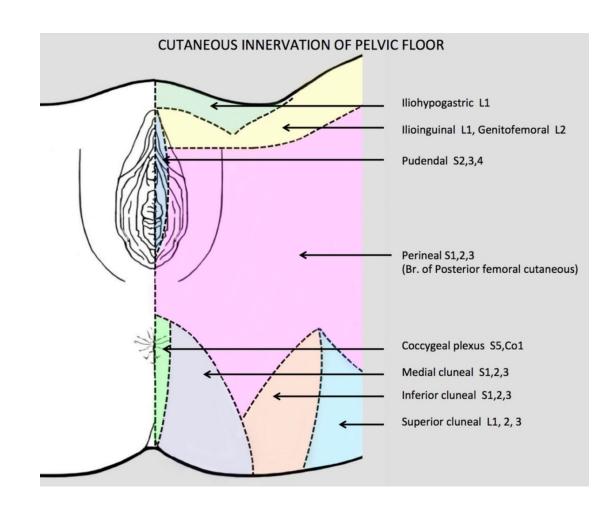
Time	Voided amount, mL	Intake amount and type	Leakage (sm, med, lg)	Urgency present?	Activity
7:00 AM	350				
7:30 AM		Coffee, 3 cups			
8:00 AM			Small	yes	washing dishes
8:30 AM			medium	yes	Preparing for work
00 AM	550				•
2-00 PM		36 ownces joined tea			
2:15 m	250		Small	yes	At desk
2:30 PM			medium	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

## • Bladder diary

#### B Sample voiding diary with abnormal voiding pattern

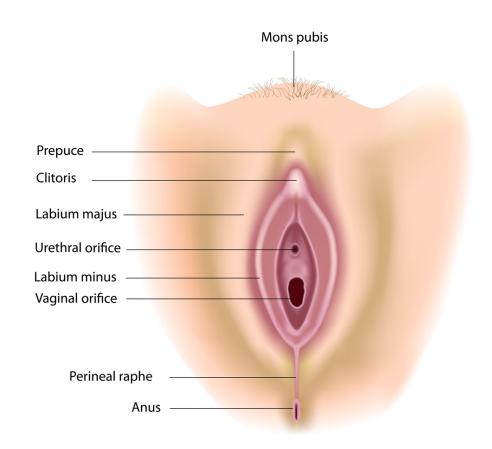
Time	Voided amount, mL	Intake amount and type	Leakage (sm, med, lg)	Urgency present?	Activity
7:00 AM	550	Coffee I cup, 1/2 cup arange juice			
10:30 AM		802 Lemonade	→ med	yes	Shapping
11:00 AF	650				
11:30 AM		Large milkshake			
2/80 PM			► Lg	yes	Driving home
3:00 PM	615				-
4:40 PM		I cup herbal bea			
5:30 PM			→ med	yes	at desk
6:30 Pm	575				
7:15PM		1 cup water, 1 glass wine			Preparing meal Watching TV
9:45 m			med	yes	Watching TV

- PHYSICAL EXAMINATION
  - Obesity
  - Chronic lung conditions/cough
  - Neurologic evaluation
    - Sudden onset of incontinence
    - New onset of neurologic symptoms
    - Longstanding neurologic symptoms



- Pelvic examination
  - Pelvic examination
    - Initiation of conservative management can be started prior to pelvic exam if:
      - Clear categorization of stress or urgency incontinence
      - No suspicion of systemic or pelvic pathology
    - HOWEVER
      - Pelvic floor muscle pain/dysfunction/strength
      - Vaginal atrophy
      - Pelvic or urethral masses
      - Prolapse

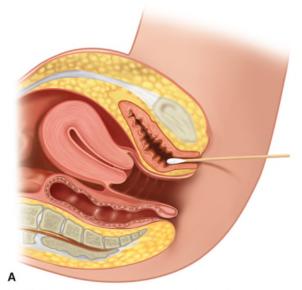
- Pelvic examination
  - Vulvar evaluation



- Pelvic examination
  - Vulvar evaluation
    - Valsalva

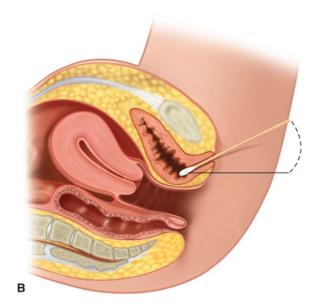


- Pelvic examination
  - Vulvar evaluation
    - Valsalva



Source: Hoffman BL, Schorge JO, Schaffer JI, Halvorson LM, Bradshaw KD, Cunningham FG: Williams Gynecology, 2nd Edition: www.accessmedicine.com

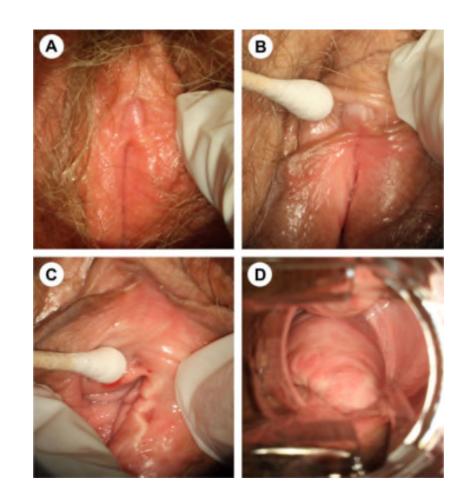
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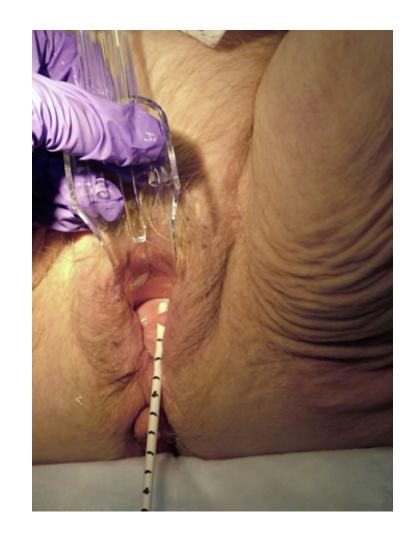
- Pelvic examination
  - Vulvar evaluation
  - Cough stress test
    - Lithotomy OR standing position
    - Comfortably full bladder
      - Spontaneous versus backfilled
    - Evaluate for leakage during Valsalva and cough
    - Positive predictive value of 78-97%



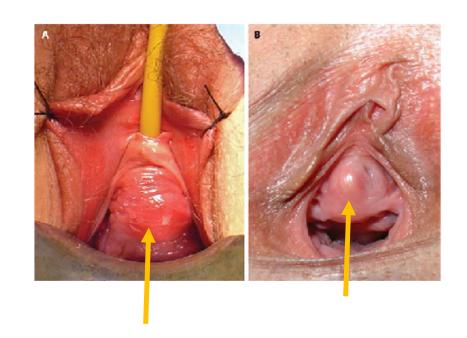
- Pelvic examination
  - Vulvar evaluation
  - Cough stress test
  - Speculum examination
    - Vaginal atrophy
    - Masses
    - Prolapse



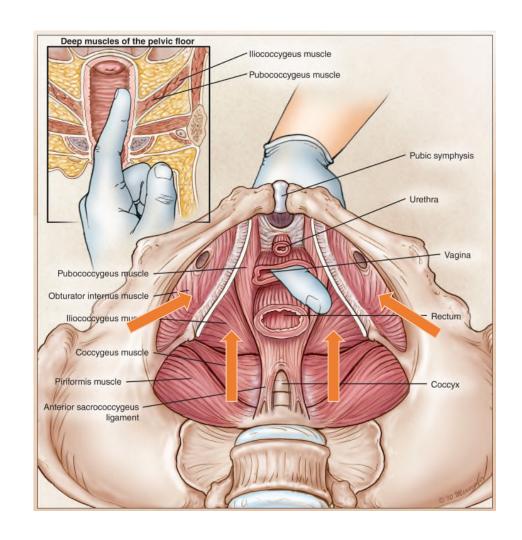
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- Pelvic examination
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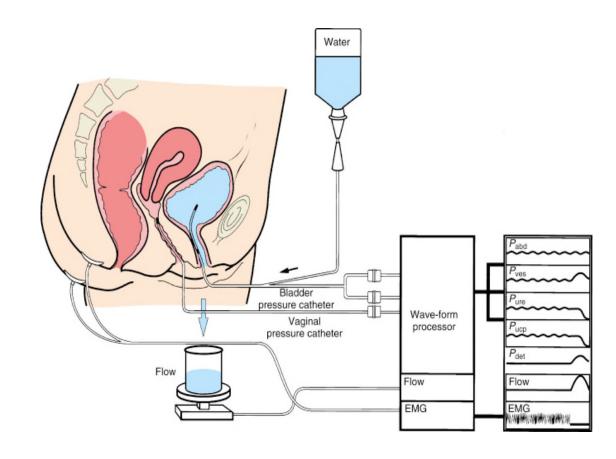
- Pelvic examination
  - Vulvar evaluation
  - Cough stress test
  - Speculum examination
    - Vaginal atrophy
    - Masses
    - Prolapse
  - Bimanual examination
    - Masses
    - Pelvic floor muscle evaluation
      - Strength
      - Pain



- Initial testing
  - Postvoid residual
    - Performed within 10 minutes of voiding
    - <100-150 mL for volumes greater than 200 mL OR <1/3 total voided volume</li>
    - May depend on age
    - Particularly recommended in patients with
      - Neurologic conditions
      - Feeling of incomplete bladder emptying
      - Prolapse beyond the hymen
      - Considering surgery for UI

- Urinalysis
  - UTI
  - Hematuria
  - Pyuria
  - Glycosuria
- Urine culture
  - Test for symptomatic UTI
  - Evaluate hematuria

- Secondary testing
  - Urodynamics testing
    - Is invasive and costly
    - Uncomplicated SUI or UUI does not require urodynamics prior to initiating conservative treatment
    - RCT showed no benefit of urodynamics over simple office evaluation/cough test prior to sling surgery for simple SUI
      - Similar treatment success (76.9% post-urodynamics vs 77.2% office evaluation)



#### Secondary testing

Indications
Neurogenic bladder
Neurologic disease
Abnormal voiding, urinary retention
Prior bladder, prolapse, or incontinence surgery
Prior radiation
Mismatch between signs and symptoms
Severe mixed urinary incontinence, severe urgency
Continuous incontinence with minimal movement
Nocturnal enuresis

#### 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

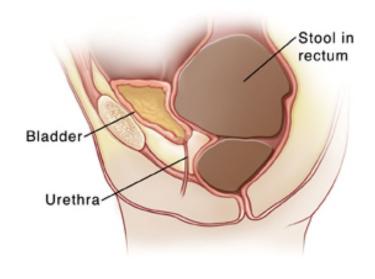
Diagnostic uncertainty or poor improvement with treatment

Dominant symptom of pain

Sterile hematuria (gross or microscopic)

## Treatment: Decision-making

- Should depend on:
  - Predominant symptoms
  - Severity of symptoms
  - Patient's goals
  - Commitment to therapy
  - Risks and adverse effects
- Counseling should involve
  - Guiding expectations (improvement vs cure)
  - Time commitment
  - Complications & adverse effects
  - Expense



- Many can be offered regardless of incontinence type
- Smoking cessation
  - Associated with increased risk of urgency, frequency compared to non-smokers
- Constipation
  - Can impact detrusor overactivity, urinary retention, dysuria, nocturia, and nocturnal enuresis
  - Can worsen pelvic floor muscle dysfunction (straining)

- Timed voiding, bladder training
  - Reducing frequency to every 2-3 hours over time
    - Log initial voiding interval
    - Try to void at increasing set intervals (such as every hour)
    - Increase by 15 minutes to 30 minutes each week
  - Reduction in incontinence episodes, not always reaching significance in studies
    - More successful when frequent follow up with providers





- Fluid management
  - Limit excessive liquids
    - 50-60 oz
    - Decrease or eliminate liquid after dinner or 4 hours before bedtime



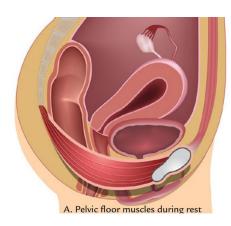


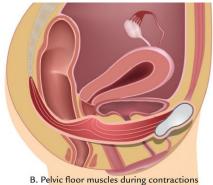
- Fluid management
  - Reduction of alcohol, caffeine, soda, and artificial sweetener consumption
    - Caffeine
      - ≥204 mg/day associated with urinary incontinence
      - Modest increased risk of urinary incontinence in those with >450 mg vs <150 mg daily (RR 1.19) in the NHS</li>
    - Alcohol
      - Some association with urinary incontinence (OR 1.31-3.51)
    - Carbonated beverages
      - Some association with urgency and UUI
      - Some increase in urgency with diet sodas
    - Artificial sweeteners
      - G-protein-coupled receptors for sweet taste can be found in the bladder urothelium





- Weight loss
  - In overweight and obese women
  - Supported by evidence
    - RCT comparing 6 mo weight loss program vs education alone
    - Mean loss of 8% of body weight (vs 1.6% in control) resulted in
      - Meaningful reduction in all UI episodes (47% vs 28%, p<0.01)</li>
      - Weekly UI episode reduction (24→13 vs 18→15)
      - Greater effect on stress UI episodes than other subtypes.





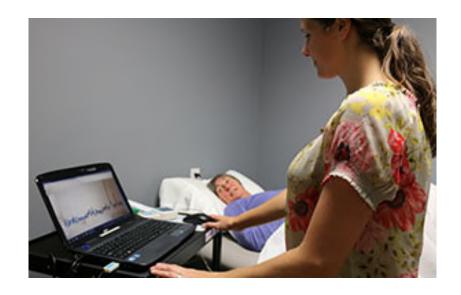
- Pelvic floor muscle training
  - Good efficacy in studies
    - 3-4 sets of 10-15 contractions per day over 10 seconds
    - Pelvic floor muscle training groups more likely than placebo to report cure (RR 5.5), cure & improvement (RR 2.35)
      - Greater effect in those with SUI subtype
        - 8 times more likely to be cured
    - May be more effective when
      - Supervision with therapy (working with trained physical therapists)
      - Combined group and individual sessions
      - Greater frequency of sessions (at least weekly)

Subak LL et al. Weight loss to treat urinary incontinence in overweight and obese women. N Engl J Med. 2009

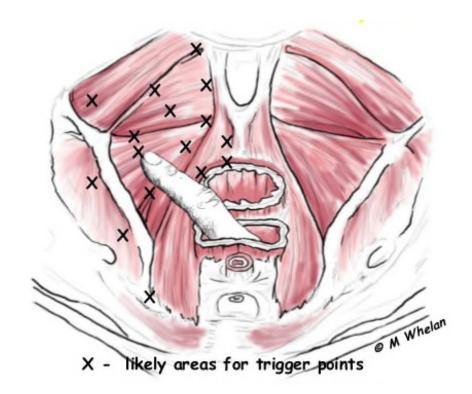
Dumoulin C et al. Pelvic floor muscle training versus no treatment, or inactive control treatments, for urinary incontinence in women. Cochrane Database Syst Rev. 2014

Hay-Smith EJ et al. Comparisons of approaches to pelvic floor muscle training for urinary incontinence in women. Cochrane Database Syst Rev. 2011

- Pelvic floor muscle training
  - Additional modalities
    - Biofeedback +/- electrical stimulation
    - Vaginal weights/cones
  - Similar efficacy of all modalities
  - Likely no to minimal significant difference from pelvic floor muscle training alone
    - Biofeedback may provide additional benefit



- Pelvic floor muscle training
  - Myofascial pain
    - Common in pelvic pain and lower urinary tract symptoms (LUTS)
      - Higher pelvic floor distress and quality of life scores related to prolapse, defecatory dysfunction, and urinary symptoms
    - Kegels or strengthening exercise alone can worsen these symptoms
    - Referral to a knowledgeable specialist or pelvic floor physical therapist can be useful in evaluating for this issue



- Vaginal estrogen
  - Estrogen receptors in the urothelium
  - Low systemic absorption
    - Major systemic risks, such as cardiovascular events or cancer, is not increased
    - Use in patients with breast cancer may be reasonable
  - Some association with improved continence (RR 0.74)
  - May take up to three months to perceive treatment benefit
- Oral estrogen MAY WORSEN incontinence

Vaginal estrogen preparation	Regimen
Vaginal ring (Estring) 7.5 mcg estradiol/day	Inserted into the vagina and replaced every 90 days
Vaginal tablet (Vagifem, Yuvafem) 10 mcg estradiol/tablet	Inserted into the vagina twice weekly
Vaginal estrogen cream 0.625 mg conjugated estrogen/g (Premarin) 100 mcg estradiol/g (Estrace)	0.5 g inserted into the vagina two to three times a week

Cody JD et al. Oestrogen therapy for urinary incontinence in post-menopausal women. Cochrane Database Syst Rev. 2012

- Pessary
  - Fit by a gynecologist or urogynecologist
  - May be particularly useful for
    - Women desiring other non-surgical options
    - Women who desire future childbearing
    - Incontinence with specific activities (exercise, cough)



#### Pessary

- Fit by a gynecologist or urogynecologist
- May be particularly useful for
  - Women desiring other non-surgical options
  - Women who desire future childbearing
  - Incontinence with specific activities (exercise, cough)
- Other devices
  - Impressa





- Pessary
  - ATLAS RCT
    - Pessary vs behavioral therapy (BT) vs combined
    - Satisfaction was >50% at one year
    - Behavioral therapy resulted in greater satisfaction and less bothersome SUI at 3 months, but did not persist at 12 months
    - Combination therapy was better than pessary, but not behavioral therapy.

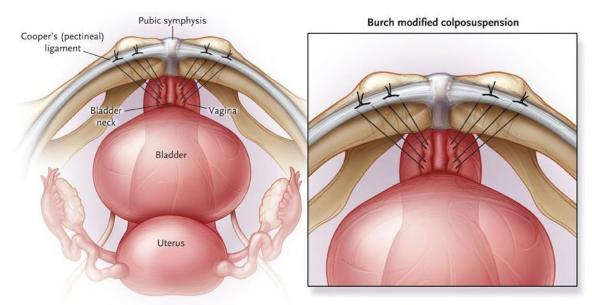
Primary Outcome: Success Definition	Drimany Outcome	Secondary Outcom	Secondary Outcomes	
Timary outcome. Success Definition	Primary Outcome	Secondary Outcom	Secondary Outcomes	
"Much better" or "very much better" with PGI-I and no bothersome stress incontinence symptoms on UDI	PGI-I: Pessary 59 (4 behavioral 72 combination 8 Pessary vs bef (P = .49)	(49%), outcomes 30 (53%)	>75% reduction in stres incontinence episodes: Pessary 69 (46%) behavioral 68 (47%) combination 80 (53%) (P > .05)	
	UDI: Pessary 49 (3 behavioral 71 combination 6 Pessary vs beh	(49%), 56 (44%)		
	(P = .006)  Pessary vs combination (P = .05) Behavioral vs combinat (P = .42)	Satisfaction	Pessary 94 (63%) Behavioral 110 (75%) Combination 118 (79%) Pessary vs behavioral (P = .03) Pessary vs combination (P = .003)	

- Medication
  - No medications are approved for SUI in the United States

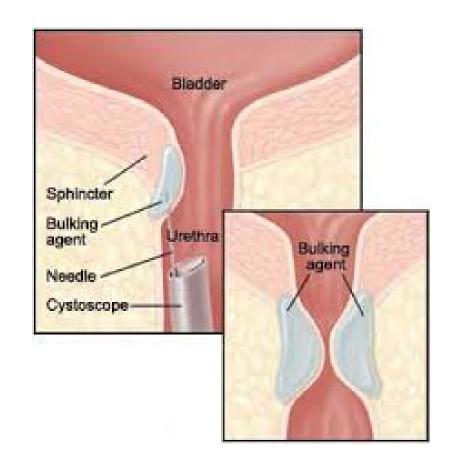
Туре	Examples	Efficacy	Safety issues
α-Adrenoceptor agonists	Ephedrine Phenylpropanolamine (norephedrine) <sup>a</sup> Pseudoephedrine Midodrine Methoxamine Norfenefrine	Stimulated urethral smooth muscle contraction. Efficacy has been demonstrated in both open-label and randomised studies Phenylpropanolamine approved for SUI in Finland; midodrine approved for SUI in Portugal	Elevated blood pressure Sleep disturbances Nausea Dry mouth Headache Tremor Palpitations Exacerbation of abnormal cardiac rhythms
Tricyclic antidepressants	Imipramine	Hypothesised to increase contractility of urethral smooth muscle. Open-label studies show some success in SUI. No controlled studies	Anticholinergic symptoms Orthostatic hypotension Cardiac arrhythmia Weight gain
Serotonin and norepinephrine reuptake inhibitors	pinephrine rhabdosphincter activity. In randomised cl		Nausea Dry mouth Insomnia Constipation Dizziness

- Surgery
  - Efficacy is 84.4% (74-90.1%) at 1 year
  - Procedures include
    - Retropubic urethropexy

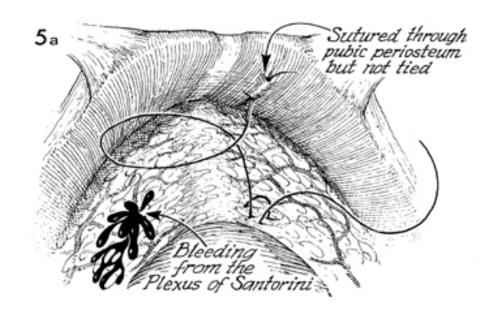
- Surgery
  - Efficacy is 84.4% (74-90.1%) at 1 year
  - Procedures include
    - Retropubic urethropexy
      - Burch colposuspension



- Urethral bulking
  - Injection of various bulking agents into the bladder neck and proximal urethra
  - Success ranges from 48-75%
    - Cure @ 12 mo: 24.8-36.9%
  - Office-based procedure that is an option for
    - Intrinsic sphincter deficiency with fixed urethra
    - Persistent/recurrent SUI after antiincontinence surgery
    - Inability to tolerate surgery or does not want to undergo surgery, but failed conservative management

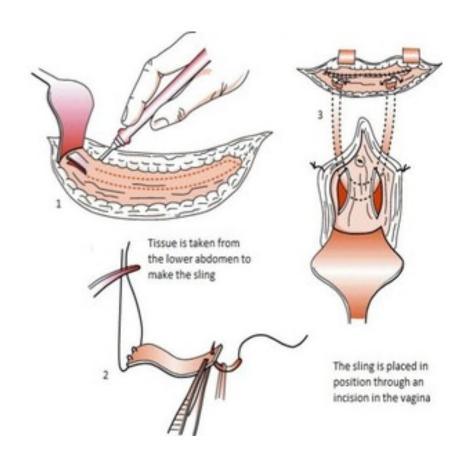


- Surgery
  - Efficacy is 84.4% (74-90.1%) at 1 year
  - Procedures include
    - Retropubic urethropexy
      - Burch colposuspension
      - Marschall-Marchetti-Krantz

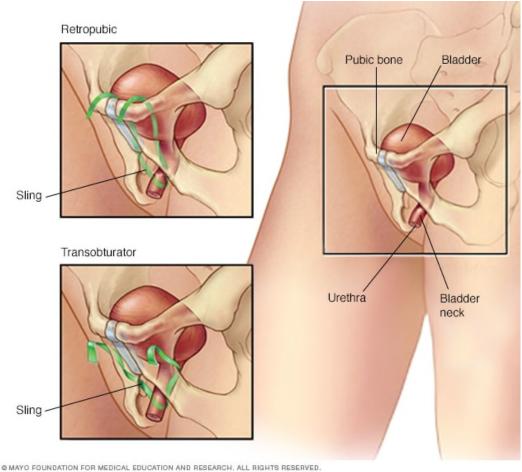


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      - Burch colposuspension
      - Marschall-Marchetti-Krantz
    - Sling procedures

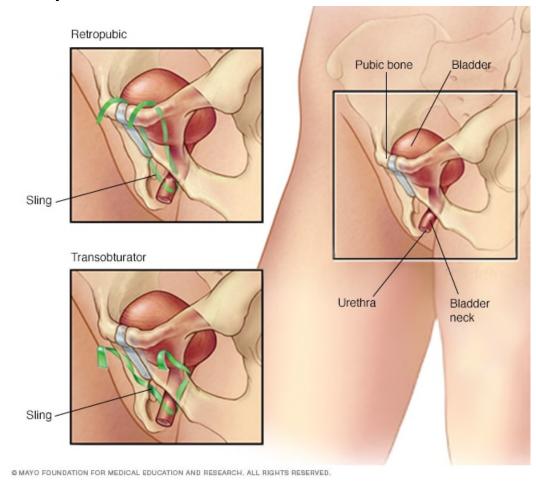
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      - Marschall-Marchetti-Krantz
    - Sling procedures
      - Pubovaginal sling



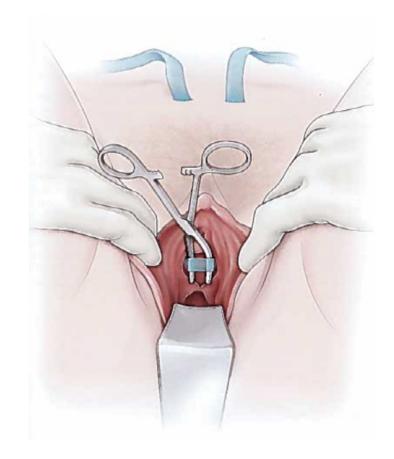
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    - Retropubic urethropexy
      - Burch colposuspension
      - Marschall-Marchetti-Krantz
    - Sling procedures
      - Pubovaginal sling
      - Midurethral sling
        - Retropubic
        - Transobterator



- Surgery
  - Efficacy is 84.4% (74-90.1%) at 1 year
  - Procedures include
    - Retropubic urethropexy
      - Burch colposuspension
      - Marschall-Marchetti-Krantz
    - Sling procedures
      - Pubovaginal sling
      - Midurethral sling
        - Retropubic
        - Transobterator
- Midurethral slings are considered the procedure of choice

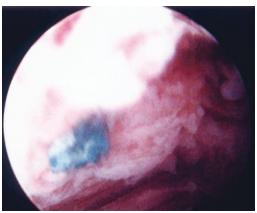


- Midurethral sling
  - Comparable to bladder neck slings, Burch colposuspension
  - Shorter OR time
  - Shorter hospitalization
  - Lower postoperative complications
  - Cost-effective
  - Risks
    - Voiding dysfunction
    - De novo UUI/OAB
    - Mesh complications



- Midurethral sling
  - Mesh complications
    - <5%
      - Exposure
      - Erosion into surrounding structures
        - Urethra
        - Bladder
      - Contraction
  - Should we be concerned?





- Midurethral sling
  - AUGS/SUFU joint statement on mesh for stress incontinence

Polypropylene material is safe and effective as a surgical implant. Polypropylene material has been used in most surgical specialties (including general surgery, cardiovascular surgery, transplant surgery, ophthalmology, otolaryngology, gynecology, and urology) for over five decades, in millions of patients in the US and the world (personal communication with manufacturers of polypropylene suture and mesh). As an isolated thread, polypropylene is a widely used and durable suture material employed in a broad range of sizes and applications. As a knitted material, polypropylene mesh is the consensus graft material for augmenting hernia repairs in a number of areas in the human body and has significantly and favorably impacted the field of hernia surgery. [6,7] As a knitted implant for the surgical treatment of SUI, macroporous, monofilament, light weight polypropylene has demonstrated long term durability, safety, and efficacy up to 17 years. [8]

- Midurethral sling
  - AUGS/SUFU joint statement on mesh for stress incontinence

Polypropylene mesh midurethral slings are a standard of care for the surgical treatment of SUI and represent a great advance in the treatment of this condition for our patients. Since the publication of numerous level one randomized comparative trials, the MUS has become the most common surgical procedure for the treatment of SUI in the US and the developedworld. This procedure has essentially replaced open and transvaginal suspension surgeries for uncomplicated SUI. There have been over 100 surgical procedures developed for the management of SUI and there is now adequate evidence that the MUS is associated with less pain, shorter hospitalization, faster return to usual activities, and reduced costs as compared to historic options that have been used to treat SUI over the past century. Full-length midurethral slings, both retropubic and transobturator, have been extensively studied, are safe and effective relative to other treatment options and remain a leading treatment option and current gold standard for stress incontinence surgery. <sup>[14]</sup> Over 3 million MUS have been placed worldwide and a recent survey indicates that these procedures are used by > 99% of AUGS members. <sup>[15]</sup>

- Midurethral sling
  - AUGS/SUFU joint statement on mesh for stress incontinence

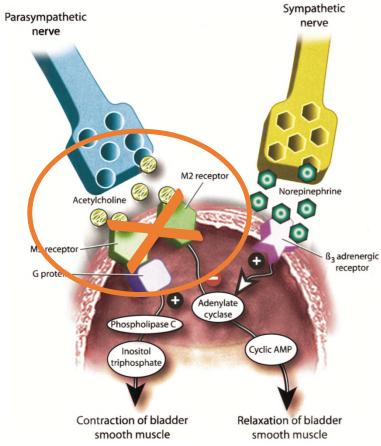
The FDA has clearly stated that the polypropylene MUS is safe and effective in the treatment of SUI. The midurethral sling was not the subject of the 2011 FDA Safety Communication, "Urogynecologic Surgical Mesh: Update on the Safety and Effectiveness of Vaginal Placement for Pelvic Organ Prolapse." In this document, it was explicitly stated: "The FDA continues to evaluate the effects of using surgical mesh for the treatment of SUI and will report about that usage at a later date." In 2013, the FDA website stated clearly that: "The safety and effectiveness of multi-incision slings is well-established in clinical trials that followed patients for up to one-year." [5]

The European Commission enquiry on the safety of surgical meshes supports continuing synthetic sling use for SUI. In 2015 The Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) concluded that synthetic sling SUI surgery is an accepted procedure with proven efficacy and safety in the majority of patients with moderate to severe SUI, when used by an experienced and appropriately trained surgeon. [16]

<ul> <li>Medication</li> </ul>	Table 1. Pharmacologic Therapies Indicated for Overactive Bladder with or without Urgency Incontinence.						
<ul><li>Second</li></ul>	।ffree treatment	Usual Dose					
• Ar <mark>t</mark>	Oxybutynin chloride (Ditropan, Ortho-McNeil-Janssen Pharmaceuticals	5 mg by mouth 3–4 times daily					
• B-3	Pharmaceuticals and available as generic formulation)	5, 10, or 15 mg by mouth once daily					
1	Mirabegron Oxybutyng transdermal patch (Oxytrol, Watson Pharmaceuticals)	One patch applied twice weekly					
L	Oxybutynin gel 10% (Gelnique, Watson Pharmaceuticals)	One sachet applied daily					
5	Tolterodine tartrate (Detrol, Pfizer)	2 mg by mouth twice daily					
1	Tolterodine tartrate long-acting (Detrol LA, Pfizer)	4 mg by mouth once daily					
	Fesoterodine fumarate (Toviaz, Pfizer)*	4 or 8 mg by mouth once daily					
	Solifenacin succinate (Vesicare, Astellas Pharmaceuticals)	5 or 10 mg by mouth once daily					
Ī	Trospium chloride (Sanctura, Allergan)	20 mg by mouth twice daily					
โ	Trospium chloride extended release (Sanctura XR, Allergan)	60 mg by mouth once daily					
	Darifenacin (Enablex, Novartis Pharmaceuticals)	7.5 or 15 mg by mouth once daily					

<sup>\*</sup> Tolterodine is the active metabolite of fesoterodine.

- Anticholinergic medications
  - Block the muscarinic receptors of the detrusor smooth muscle
  - 49% of patients reports symptoms improvement (35.6-58%)
  - High discontinuation rates
    - <50% continue past 6 months
    - <36% continue past 1 year



- Anticholinergic medications
  - Most common side effects are dry eyes, dry mouth, and constipation.
  - Extended release formulations may minimize adverse effects

Table 4  Muscarinic Receptor Types and Effects from Their Blockage				
Salivary glands	M1, M3, M4	Dry mouth		
Cardiac tissue	M2	Tachycardia, palpitations		
Eye (ciliary muscle, iris)	M3, M5	Dry eyes, blurred vision, mydriasis		
Gastrointestinal tract	M1, M2, M3	Slowing of transit time, constipation, effects on sphincter tone and gastric acid secretion		
Central nervous system, brain (cortex and hippocampus)	M1, M2, M3, M4, M5	Effects on memory, cognition and psychomotor speed. Other: confusion, delirium, sedation, hallucinations, sleep disruption		
Bladder (detrusor muscle)	M2, M3	Decreased contraction, urinary retention		

Anticholinergic medications

Table 2: Contradictions to Common OAB Therapies			
Relative	Absolute		
Anticholinergics/Antimuscarinics			
<ul> <li>Urinary retention</li> <li>Controlled acute-angle glaucoma</li> <li>Dementia</li> <li>Ulcerative colitis</li> <li>Congenital or acquired QT prolongation</li> </ul>	<ul> <li>Pregnancy</li> <li>Gastric retention, delayed GI motility disorders</li> <li>Uncontrolled acute-angle glaucoma</li> <li>Myasthenia gravis</li> <li>Known sensitivity to the drug or formulation components</li> </ul>		

- Anticholinergic medications
  - Efficacy between medications is similar
    - Trospium > oxybutynin
    - Solifenacin, fesoterodine > tolterodine
  - Larger doses often increase efficacy as well as adverse effects

		Efficacy, %b		Most Common Adverse Effects, % <sup>c</sup>				
Generic Drug Name (Year of FDA Approval)	Dose Options	Reduction In Urinary Frequency	Incontinence	Constipation	Dry Mouth	Special Considerations	Patients Most Likely to Benefit	
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/underinsure	
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	

Anticholinergic medications and cognition



#### **HHS Public Access**

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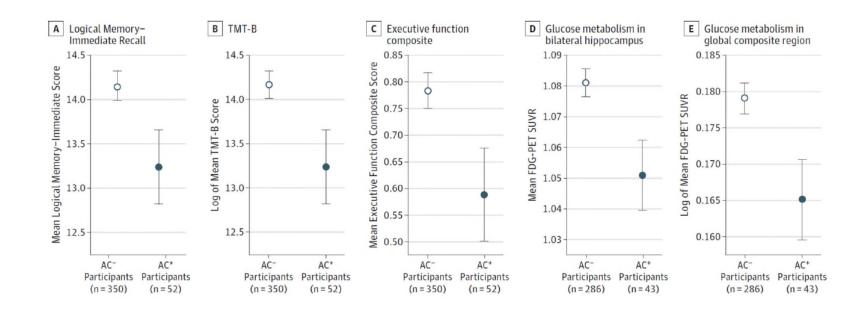
JAMA Neurol, 2016 June 1; 73(6): 721-732. doi:10.1001/jamaneurol.2016.0580.

Association Between Anticholinergic Medication Use and Cognition, Brain Metabolism, and Brain Atrophy in Cognitively Normal Older Adults

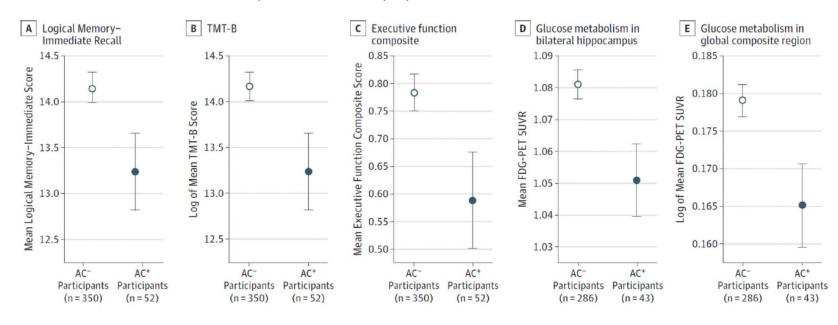
Corresponding Author: Shannon L. Risacher, PhD, Center for Neuroimaging, Department of Radiology and Imaging Sciences, Indiana University School of Medicine, Indiana University Health Neuroscience Center, Ste 4100, 355 W 16th St, Indianapolis, IN 46202 (srisache@iupui.edu).

- Anticholinergic medications and cognition
  - 402 cognitively normal older adults
    - Cohort study of patients involved in the Alzheimer's Disease Neuroimaging Initiative (ADNI) and the Indiana Memory and Aging Study
      - Follow up every 12 months to 18 months
    - Two cohorts
      - AC+
        - N=60
        - Taking at 1+ medication with moderate to high anticholinergic activity
      - AC-:
        - N=391
        - Not taking any medication with anticholinergic activity

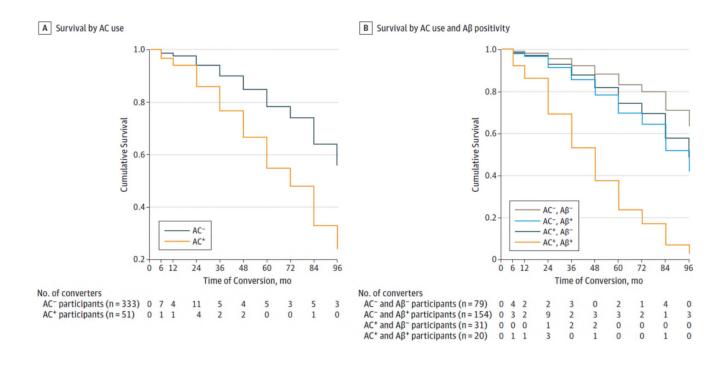
- Anticholinergic medications and cognition
  - AC+ groups had greater association with
    - Poor cognition
    - Reduced glucose metabolism



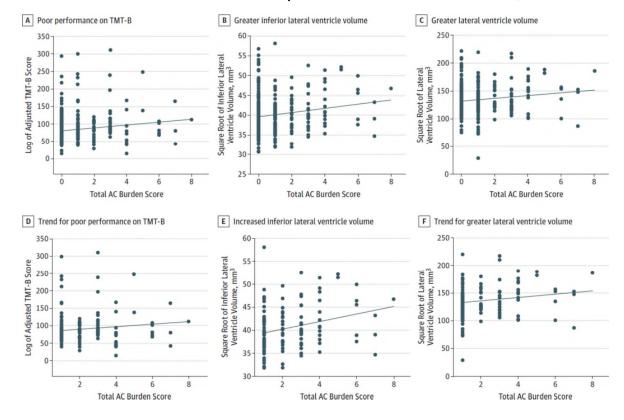
- Anticholinergic medications and cognition
  - AC+ groups had greater association with
    - Poor cognition
    - Reduced glucose metabolism
    - · Whole-brain and temporal lobe atrophy



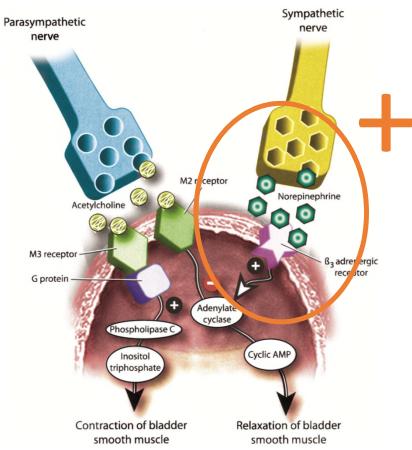
- Anticholinergic medications and cognition
  - AC+ groups had greater association with
    - Clinical decline



- Anticholinergic medications and cognition
  - Greater AC burden was associated with poorer executive function, increased brain atrophy



- β-3 Agonist
  - Mirabegron
    - Promotes relaxation of the detrusor through sympathetic pathway
    - 25 mg daily, 50 mg daily
    - Efficacy 43.5-45.8% at 12 months
      - Comparable to anticholinergics
    - May provide synergistic effect with anticholinergic medications

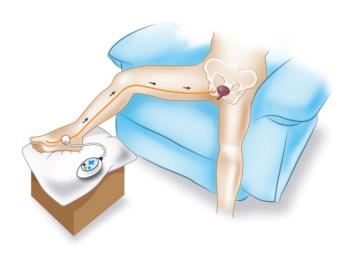


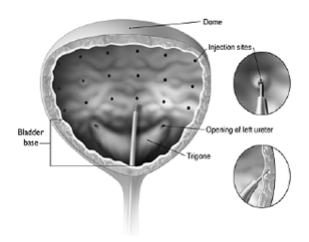
- β-3 Agonist
  - Mirabegron

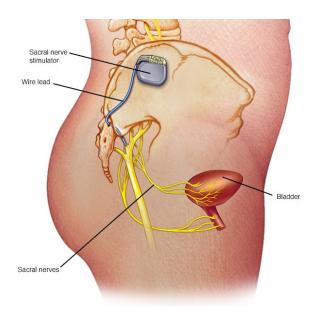
# β<sub>3</sub>-Adrenoreceptor Agonists Requiring dose adjustment (25 mg/day max): Severe renal impairment (creatinine clearance rate 15 to 29 ml/min) Moderate hepatic impairment Use of medications metabolized by CYP2D6 with a narrow therapeutic window (*i.e.*, flecainide, propafenone) Pregnancy Severe uncontrolled hypertension (systolic BP ≥ 180 mmHg, diastolic BP ≥ 110 mmHg) End-stage renal disease Severe hepatic impairment Known sensitivity to the drug or formulation components

- When starting medications
  - Start with lowest dose
  - Extended release formulations tend to have fewer side effects
  - Beware of CNS effects
  - Takes 2-4 weeks to show clinical effect.
    - May take up to 12 weeks for full effect
  - If no improvement, consider:
    - Checking for urinary retention
    - Adherence
    - Adding a medication of a different class
      - ICI-RS Review noted some improvement in OAB symptoms, no additional safety risks with combination therapy

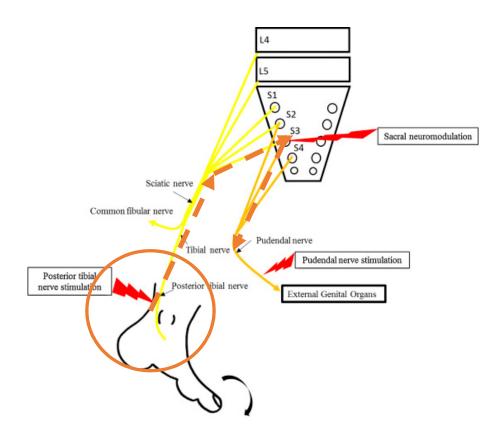
- Third-line treatments
  - Percutaneous tibial nerve stimulation
  - Onabotulinumtoxin A intradetrusor injection
  - Sacral neuromodulation







- Third-line treatments
  - Percutaneous tibial nerve stimulation
    - Neuromodulation through stimulation of the tibial nerve
      - Originates from L4-S3
      - Inhibition of micturition reflex via afferent sacral pathways
    - Temporary placement of a small needle electrode near the medial malleolus
    - Pulse generator connected to the needle
    - Electrical pulses travel from tibial nerve to sacral nerve plexus
  - 30 min stimulation x 1-3 times weekly x 4-12 weeks

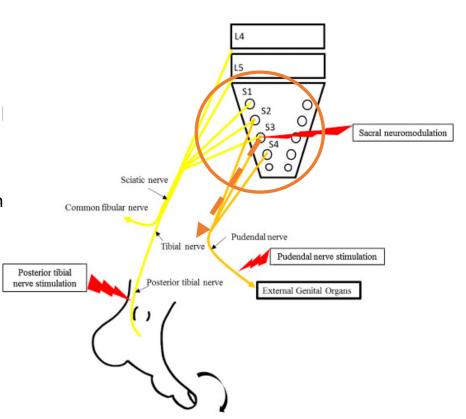


- Third-line treatments
  - Improvement of 60% (49-75%)
  - Improvement in UUI episodes, nocturia, QoL
    - Comparable to anticholinergic medication
    - Better than BT
    - No comparison available to botulinum toxin or sacral neuromodulation

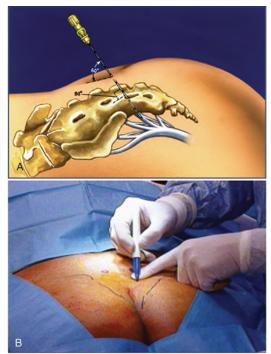
Adverse events	Contraindications
<ul> <li>1-8.5%</li> <li>Bleeding at needle site</li> <li>Bruising at needle site</li> <li>Tingling</li> <li>Mild pain</li> </ul>	<ul> <li>Cardiac pacemaker</li> <li>Other implantable defibrillators</li> <li>Relative contraindications: bleeding disorders, pregnancy, preexisting peripheral nerve damage</li> </ul>

Stewart F et al. Electrical stimulation with non-implanted electrodes for overactive bladder in adults. *Cochrane Database of Systematic Reviews* 2016. Lukacz ES, Santiago-Lastra Y, Albo ME, Brubaker L. Urinary Incontinence in Women: A Review. JAMA. 2017

- Third-line treatments
  - Sacral neuromodulation
    - Implantation of electrodes through the sacra
    - Generally along the S3 sacral nerve
    - Exact mechanism of action is unknown
      - Modification of neural reflexes in S3 and S4 n
      - Direct inhibition to the detrusor muscle
    - May last up to 5-6 years



- Sacral neuromodulation
  - Performed under sedation
  - Performed under fluoroscopic guidance
  - Sent home for 1 week trial
    - Programmed set of stimulation patterns
    - Success: >50% symptomatic improvement
  - If successful, implantation of pulse generator

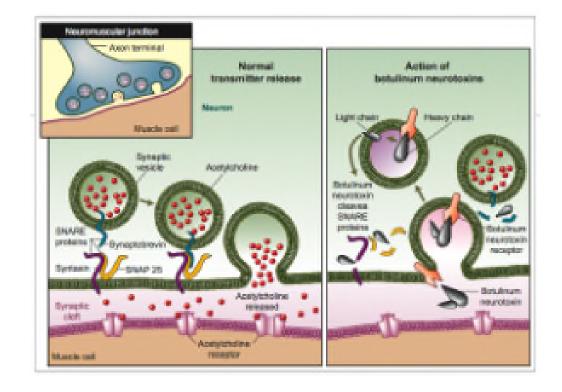


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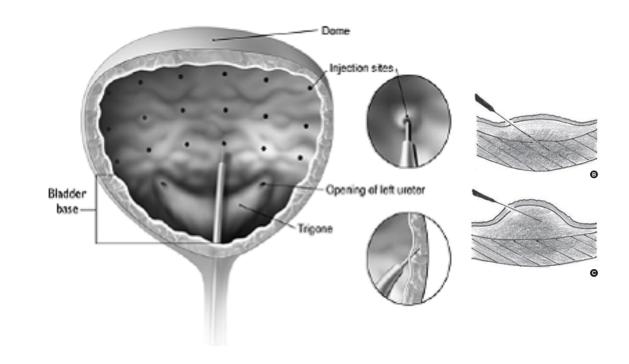
- Sacral neuromodulation
  - 60-90% report improvement
  - 30-50% report cure
  - Surgical revision rate of 3-16%
  - Greater efficacy and improvement in QoL compared with anticholinergic medication

Adverse events	Contraindications
<ul> <li>Device revision or explantation</li> <li>Pain at implantation site</li> <li>Infection at implantation site</li> <li>Erosion at implantation site</li> <li>Transient electric shock</li> </ul>	<ul> <li>Mechanical outlet obstruction</li> <li>Diathermy use</li> <li>Inadequate response to test stimulation</li> <li>Inability to operate the device</li> <li>Relative contraindications: pregnancy, &lt;16 years old, implanted cardiac devices, neurological conditions such as MS, potential need for MRI, bony abnormalities of the sacrum, acute local infections, and coagulation disorders.</li> </ul>

- Third-line treatments
  - Botulinum toxin intradetrusor injection
    - Targets peripheral nerve endings
    - Inhibits release of AcH vesicles at presynaptic neuromuscular junctions



- Botulinum toxin intradetrusor injection
  - Office procedure
  - Injected cystoscopically into the detrusor muscle
    - 10-20 sites
  - Repeat injections are commonly required at 8-12 months
  - Max dose: 360 U within 12 weeks



- Botulinum toxin intradetrusor injection
  - Efficacy 65%
    - Higher doses more effective
    - Doses above 150U results in greater adverse events
  - Greater proportion of complete continence compared to solifenacin

Adverse events	Contraindications
<ul> <li>Transient urinary retention (8-10%)         <ul> <li>Generally occurs within 5-10 days of injection</li> <li>May require self-catheterization until spontaneous resolution</li> </ul> </li> <li>UTI (2-35%)         <ul> <li>Constipation, dry mouth, flu-like symptoms, malaise</li> </ul> </li> </ul>	<ul> <li>Peripheral motor neuropathy (e.g. amyotrophic lateral sclerosis)</li> <li>Neuromuscular junction disorders (e.g. myasthenia gravis)</li> <li>Taking neuromuscular blocking agents</li> <li>Hypersensitivity to botulinum toxin</li> </ul>

- Botulinum toxin intradetrusor injection
  - Versus sacroneuromodulation
  - ROSETTA trial
    - Higher reduction in daily UUI, greater improvement in QoL in botulinum toxin group

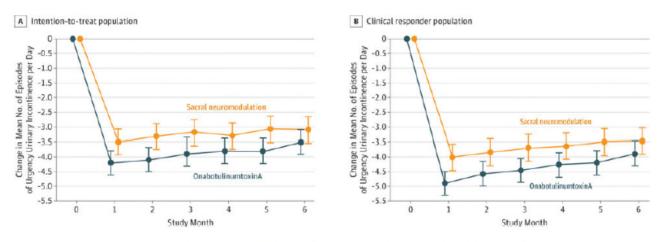


Figure 2. Change From Baseline in Urgency Urinary Incontinence Episodes per Day by Treatment Group by Month

- Botulinum toxin intradetrusor injection
  - Versus sacroneuromodulation
  - ROSETTA trial
    - Greater adverse events in botulinum toxin group
      - 3% SNM (device revision, removal) vs 20% botulinum toxin (CIC)
      - UTI greater in botulinum toxin group (35% vs 11%, p<0.001)</li>

#### Adverse Events

Outcome	OnabotulinumtoxinA (n = 191)	Sacral Neuromodulation (n = 178)	Treatment Group Difference (95% CI)	P Value
Cumulative Urinary Tract Infection, No. (%)				
Through 1 mo	22 (12)	1 (1)	-11 (-21 to -1)	<.001
Through 3 mo	47 (25)	10 (6)	-19 (-29 to -9)	<.001
Through 6 mo	66 (35)	20 (11)	-23 (-33 to -13)	<.001
Adverse surgical events revision or removal sacral neuromodulation through 6 mo		6 (3)		
Intermittent catheterization per-protocol criteria met, No./total (%)				
2 wk	29/191 (16)			
1 mo	16/191 (8)			
3 mo	8/191 (4)			
6 mo	4/191 (2)			
At any visit through 6 mo	38/191 (20)			

- UI is common in women
  - Few women seek care on their own
- Asking is the first step to detection of UI
- Address modifiable risk factors
  - Lifestyle
  - Obesity
  - Diabetes
  - Smoking
  - Diet
  - Fluid intake

- Evaluate UI symptoms and identify the subtype of incontinence
  - Treatment depends on type of incontinence
- Initial evaluation of UI includes:
  - Identification of any conditions and medical problems that could cause UI
  - Urinalysis and urine culture could identify UTI as cause of UI
  - Postvoid residual should be performed in high risk patients
  - Cough stress test is a very specific test for stress incontinence
  - Pelvic exam is not necessary before initiating conservative management unless there is a reason for concern
- Treatment should take into account patient preference and medical decision-making

- Conservative therapy
  - Useful for all UI subtypes
  - Smoking cessation
  - Address constipation
  - Weight loss in overweight and obese women
  - Bladder retraining/timed voiding
  - Fluid management
    - Avoid excessive fluids and bladder irritants
  - Pelvic floor muscle training/physical therapy

- Stress urinary incontinence
  - Pessary/incontinence ring
  - Midurethral sling (gold standard)
  - Periurethral bulking

- Urgency urinary incontinence
  - Medications
    - Anticholinergics
    - B-3 agonist
  - Percutaneous tibial nerve stimulation
  - Sacral neuromodulation
  - Botulinum toxin intradetrusor injection
- Referral to specialist is indicated when conservative measures fail or if underlying pathology, prior surgery, or other concerns are identified