Evaluating and managing urinary incontinence in women – pearls for the front-line provider

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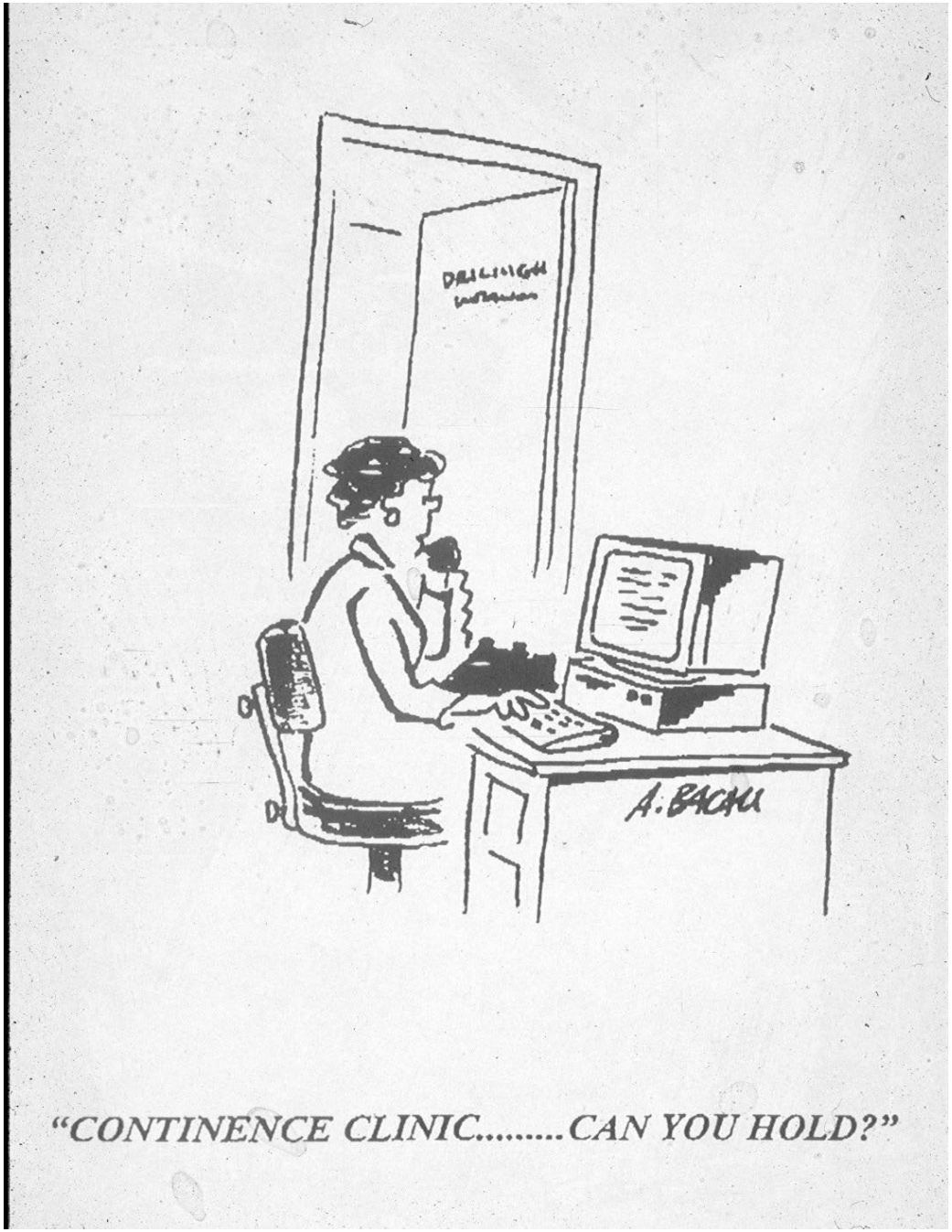
Goals & Objectives

- To recognize prevalence and different forms of urinary incontinence
- To understand basic physiology of continence
- To conduct a basic evaluation of women with incontinence
- To understand how and when to initiate conservative and medical therapy for urinary incontinence
- To identify appropriate patients for referral to a specialist

Overview

- Epidemiology of UI
- Pathophysiology
- Evaluation
  - History
  - Examination
  - Labs
  - When to refer
- 1st & 2nd Line Therapies
  - Behavioral therapy
  - Medical therapy



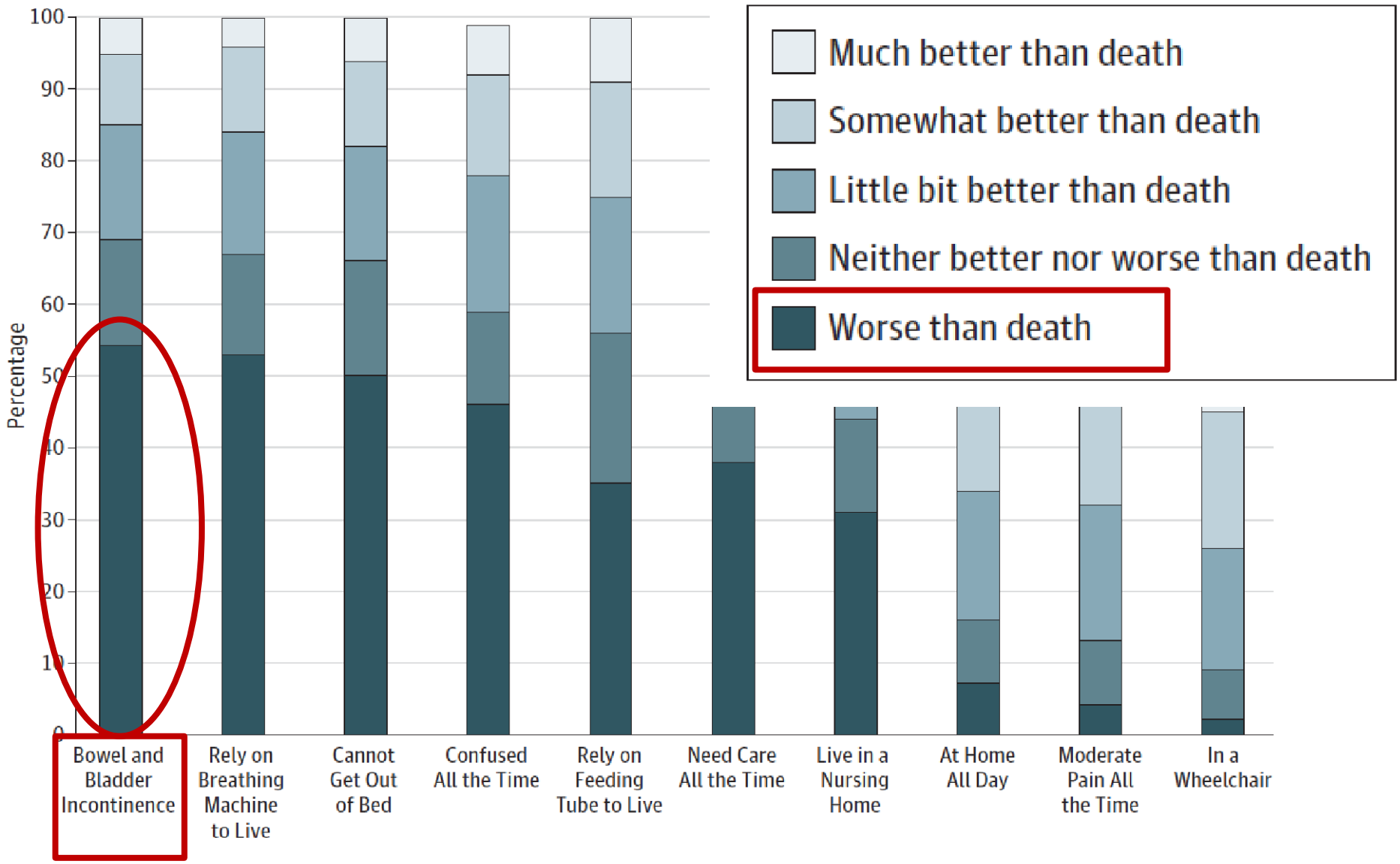
What Is Urinary Incontinence?

The involuntary loss of urine that is sufficient to be perceived as a problem.

The Scope of the Problem

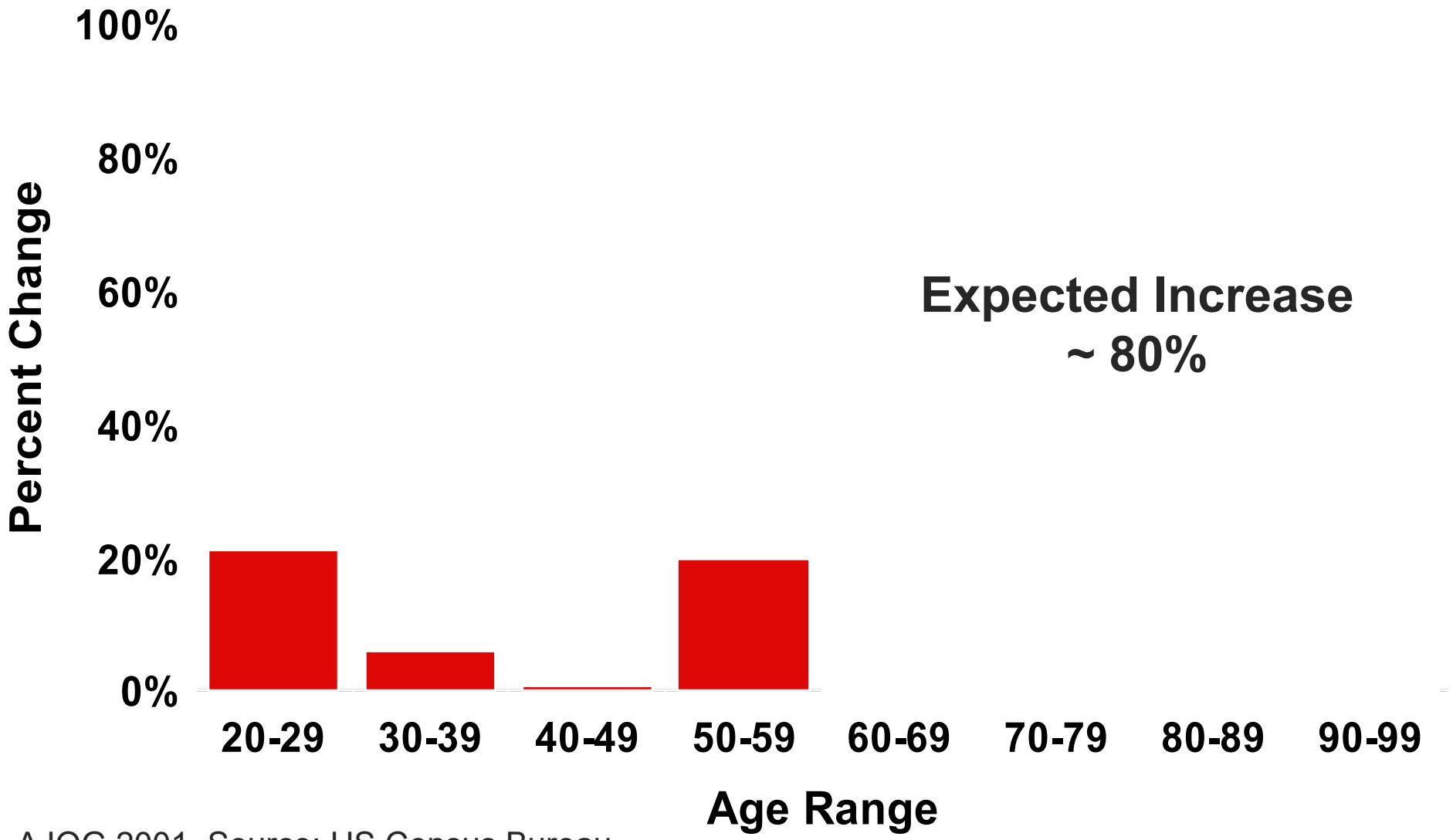
- ~50% of community dwelling women have UI
- 77% of older women in nursing homes have UI
- Huge economic burden in US
  - 2007 National costs of UI = $65.9 Billion
  - **2020 National costs of UI = $82.6 Billion**
- UI is a significant cause of morbidity
- Depression in women with UI is **2x** that of the general population and up to **80%** of women with severe incontinence have depression
- Only 25% of women seek care and fewer 50% actually receive treatment

Impact of Incontinence on QOL



JAMA 2016

Change in Female Population 2000-2030



AJOG 2001. Source: US Census Bureau

Common Myths = Barriers to Care

- Incontinence is a normal part of aging
- Nothing can be done to treat this condition
- Nothing can be done to prevent incontinence
- Surgery or medications are the only treatment options
- Severe incontinence requires a catheter




Facts

- Incontinence is very common
- Pelvic Floor Disorders are NOT a part of normal aging
- There are different types of urinary incontinence
- Various treatments are available and are often very effective




Barriers to Care

Lack of screening by physicians

Post-partum women: 55% given information on UI

Telephone survey: 31% of those with UI had a discussion initiated by their physician

KP Experience

questionnaire study of **130,000** women

40% of respondents experienced UI in the preceding week

5% had physician-documented UI

Recent Changes

Improvement in continence can be achieved in up to 80% of patients

- The National Committee for Quality Assurance (NCQA)
- The NCQA seal is a widely recognized symbol of quality care and service
- The Healthcare Effectiveness Data and Information Set (HEDIS) is used to select the best health plans.
- 184 million people are enrolled in plans that report HEDIS results

Recent Changes

Improvement in continence can be achieved in up to 80% of patients

- HEDIS® includes more than 90 measures across **6 domains** of care:
  - Effectiveness of Care
  - Access/Availability of Care
  - Experience of Care
  - Utilization and Risk Adjusted Utilization
  - Health Plan Descriptive Information
  - Measures Collected Using Electronic Clinical Data Systems
- The Medicare Health Outcomes Survey (MHOS) measures effectiveness of care in HEDIS
- Recent MHOS include questions regarding UI

Healthcare Effectiveness Data and Information Set (HEDIS): Measures of Effective Care for UI

- **Assessment of Presence or Absence of UI in Women**

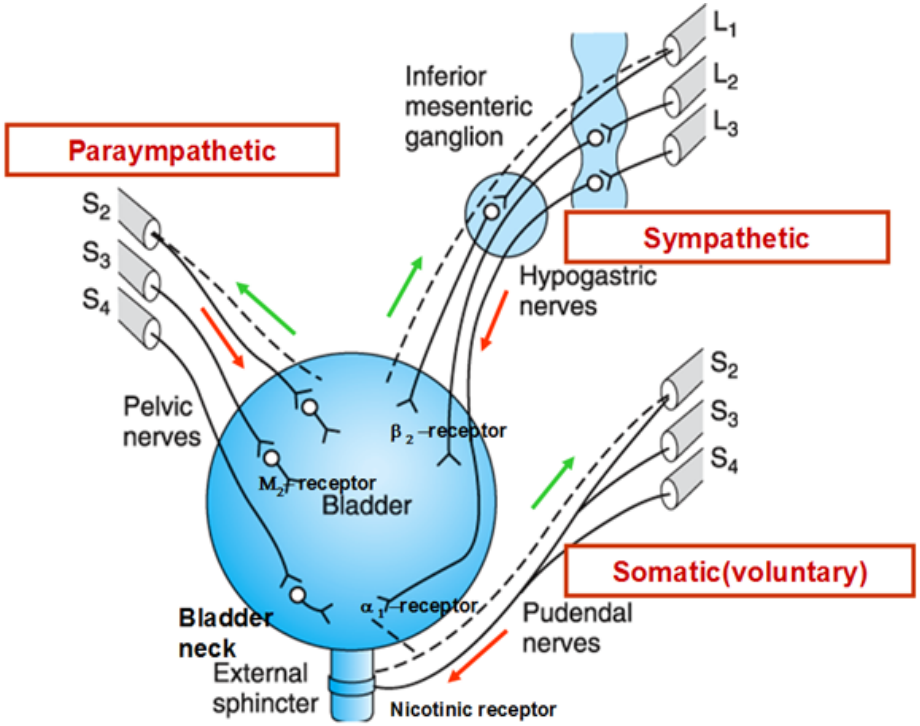
  Percentage of female patients aged 65 years and older assessed for the presence or absence of urinary incontinence within 12 mo

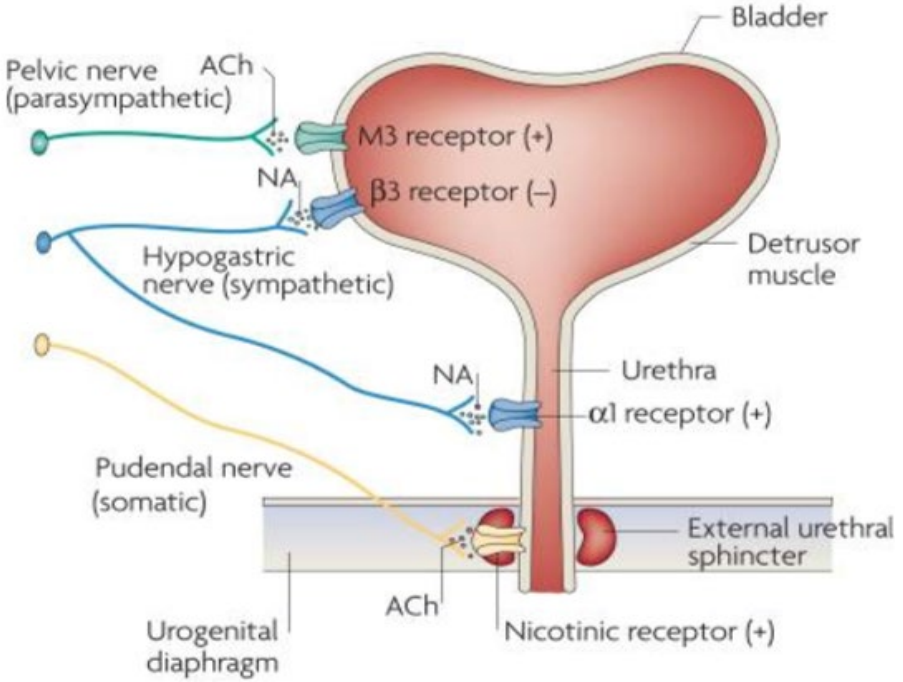
- **Characterization of UI in Women**

  Percentage of female patients aged 65 years and older with a diagnosis of UI whose UI was characterized at least once within 12 mo

- **Plan of Care for UI in Women**

  Percentage of female patients aged 65 years and older with a diagnosis of UI with a documented plan of care for UI at least once within 12 mo





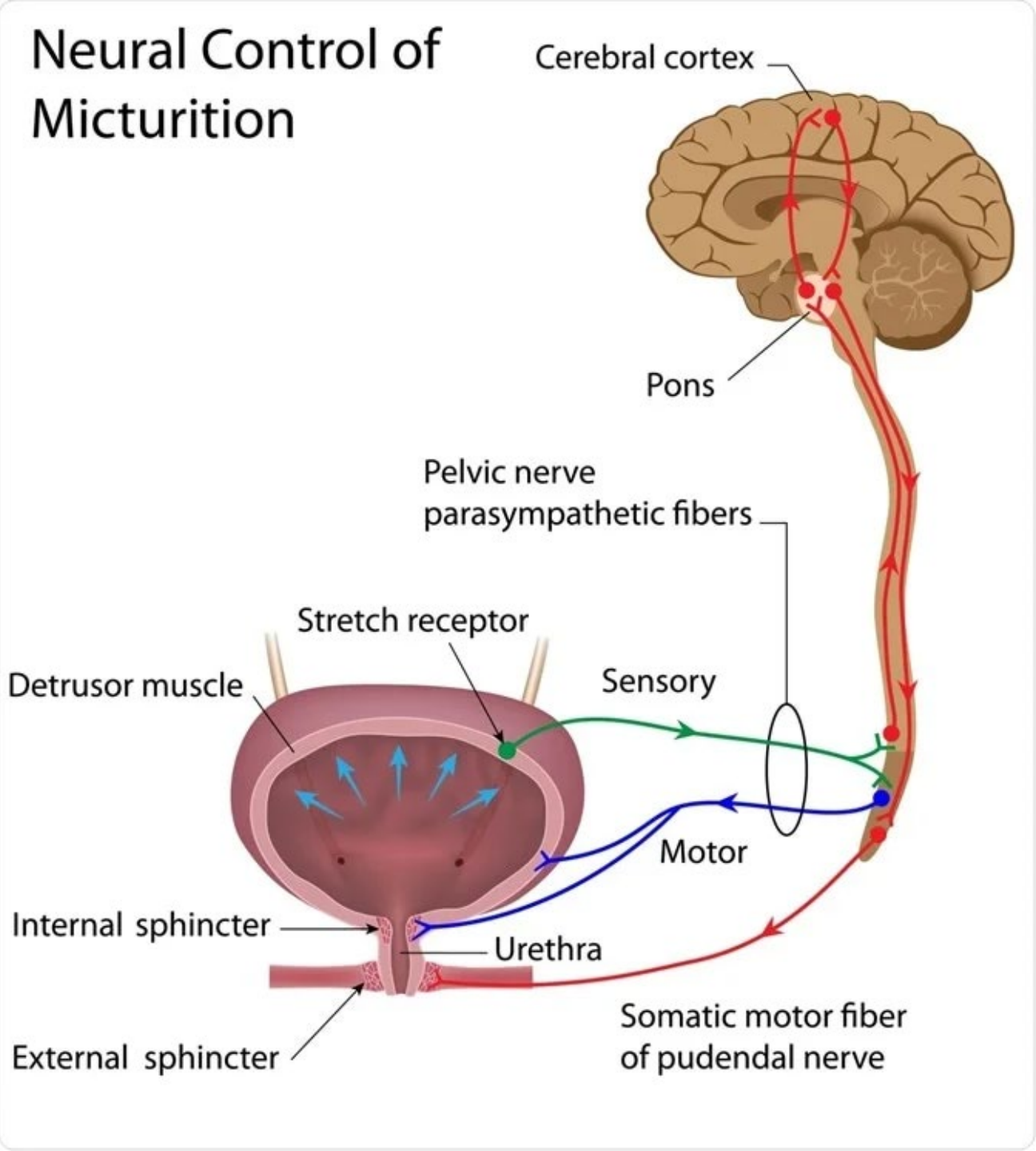
Sympathetic postganglionic neurons release noradrenaline (**NA**)
activates b3 adrenergic receptors -- relaxes bladder smooth muscle
activates a1 adrenergic receptors -- contracts urethral smooth muscle (internal sphincter)

Parasympathetic postganglionic axons in pelvic nerve release acetylcholine (**ACh**)
stimulate M3 muscarinic receptors in the bladder smooth muscle - bladder contraction

Somatic axons in the pudendal nerve release **ACh**
activates nicotinic cholinergic receptors - contract external sphincter striated muscle

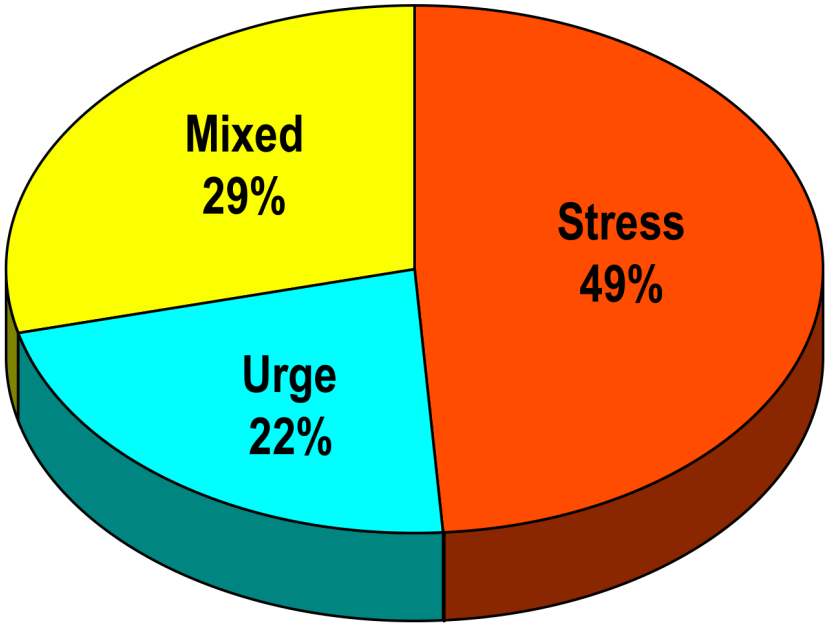
Micturition Reflex

- relaxation of the striated sphincter (somatic innervation)
- relaxation of the smooth muscle sphincter and opening of the bladder neck (sympathetic innervation)
- detrusor contraction (parasympathetic innervation)



Types of Incontinence

- Stress incontinence
- Urge incontinence
- Mixed incontinence
- Overflow incontinence
- Nocturnal enuresis (bedwetting)
- Functional incontinence

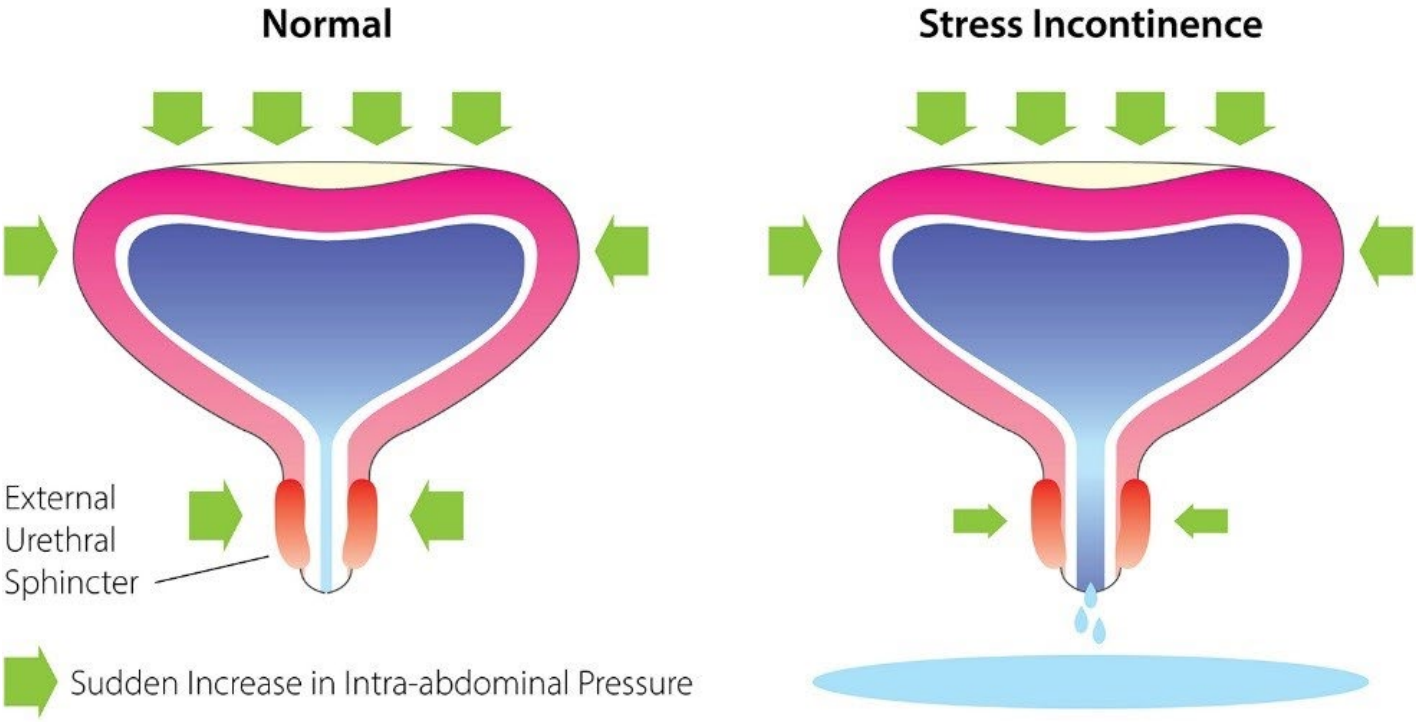


More Definitions

- **Frequency** – complaint by the patient who considers that she voids too often by day
- **Urgency** – complaint of a sudden compelling desire to pass urine, which is difficult to defer
- **Overactive Bladder (OAB)** - an empiric diagnosis
- **Detrusor overactivity** – a *urodynamic observation* characterized by involuntary detrusor contractions during the filling phase
- **Urinary Retention** – a non-painful bladder, which remains palpable or percussable after the patient has passed urine
- **Nocturia**: complaint that one has to wake up ≥ 2 time at night to void

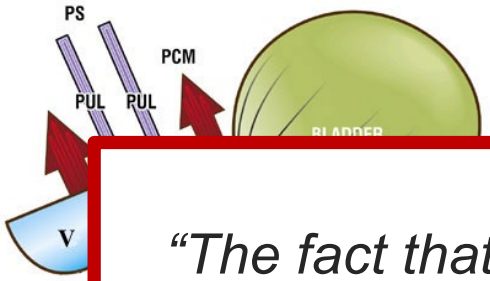
Abrams et al. Am J Obstet Gynecol 2002

Stress Urinary Incontinence (SUI)



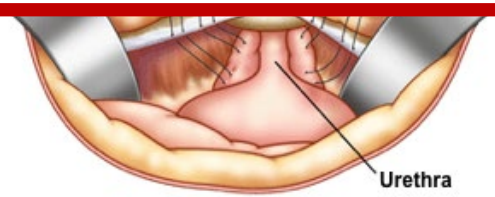
Urinary Continence Mechanisms

Urethral Support



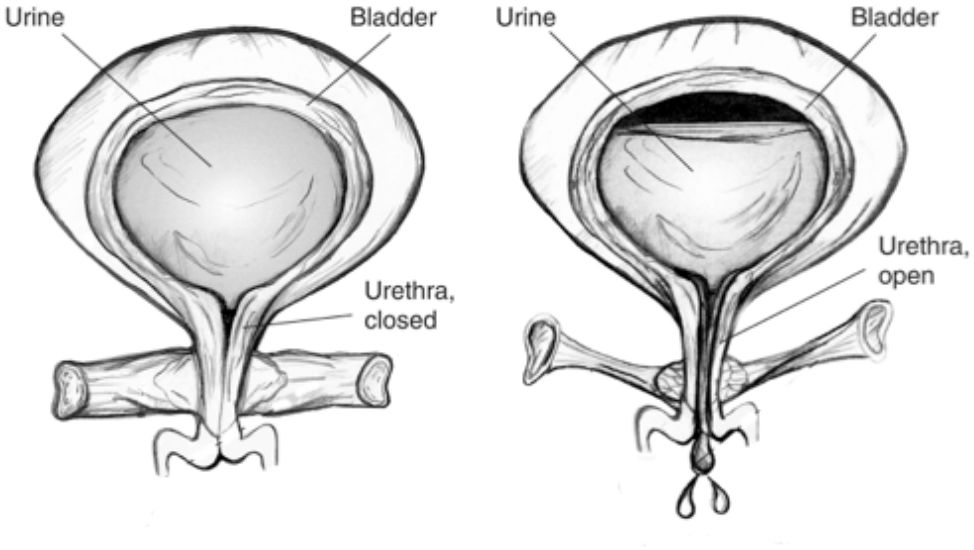
"The fact that these operations are curative says no more about the normal continence mechanism than that success of gastric bypass established the cause of obesity."

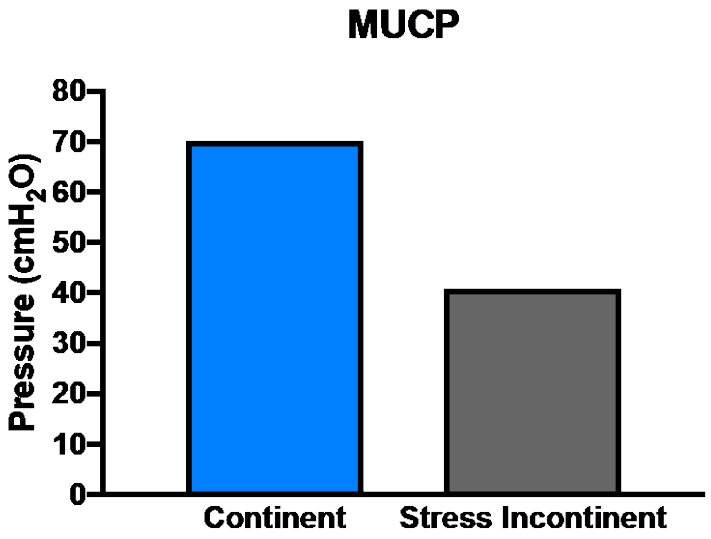
John DeLancey, 1996



Petros, Ulmsten. Acta Obstet Gynecol Scand. 1990.

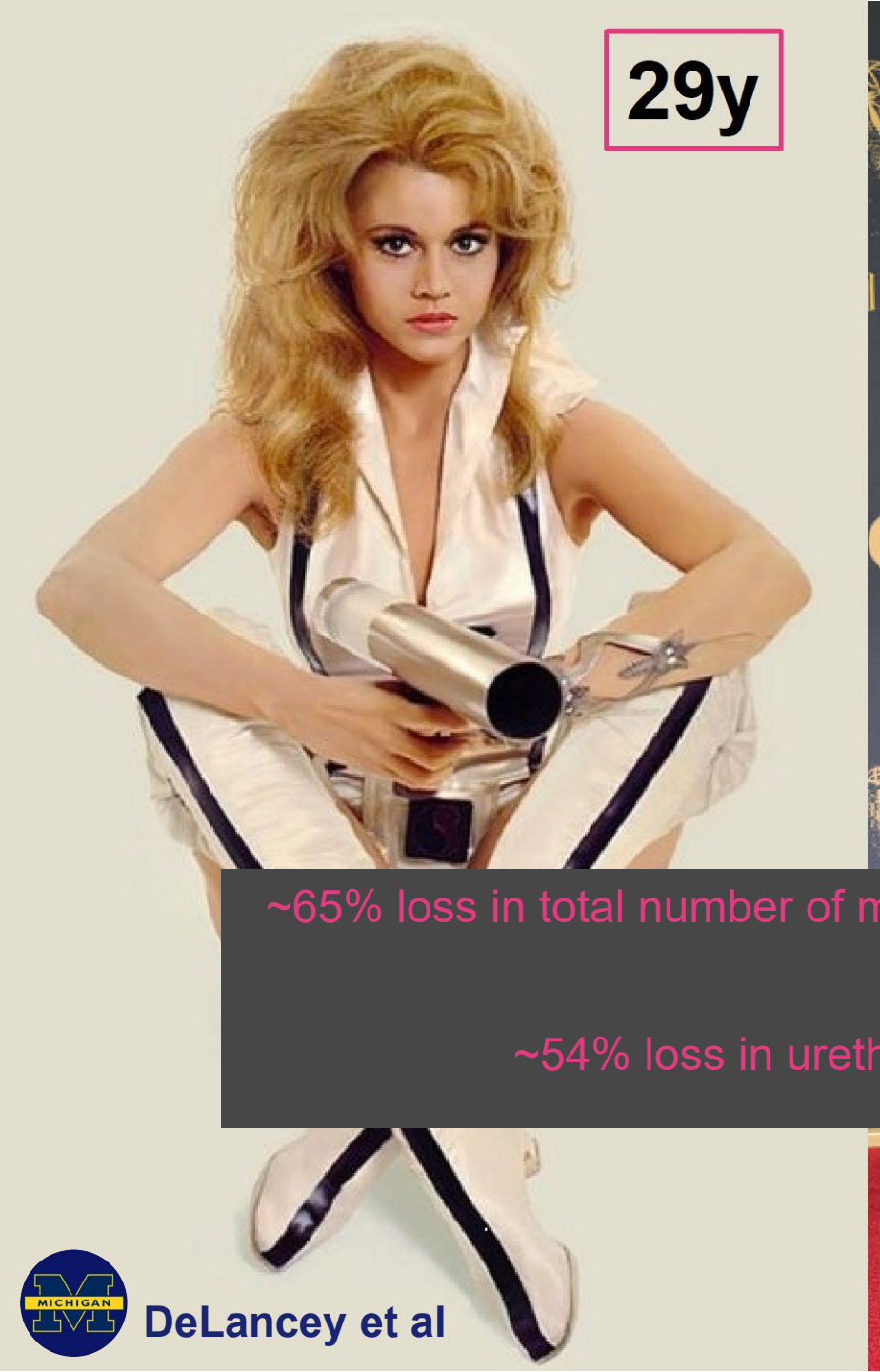
Maximal Urethra Closure Pressure (MUCP) is the strongest predictor of urinary continence





MUCP is a function of the urethral sphincter complex.

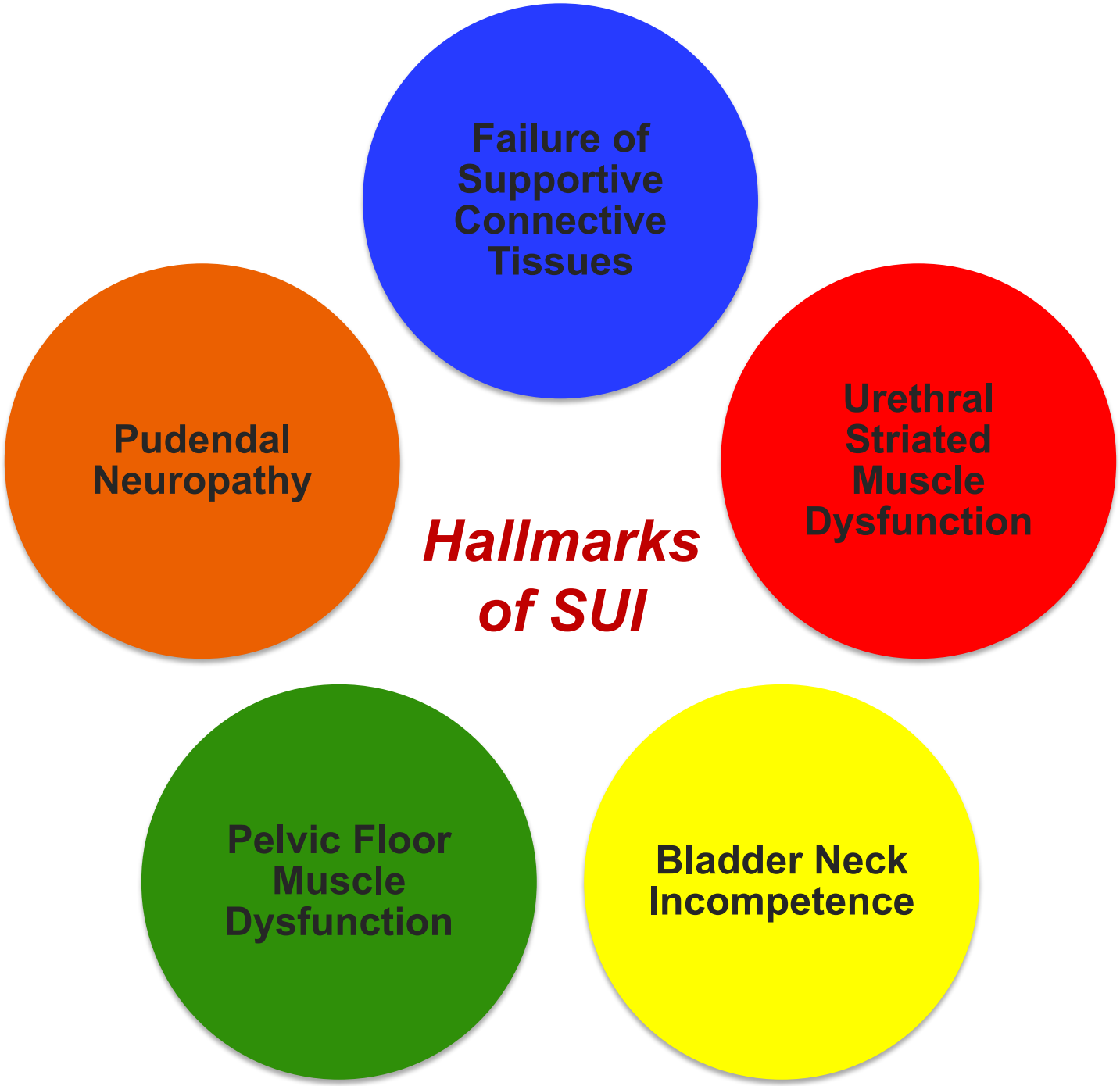
DeLancey, et al. CUAJ. 2012.



~65% loss in total number of muscle fibers in urethral sphincter

~54% loss in urethral closure pressure

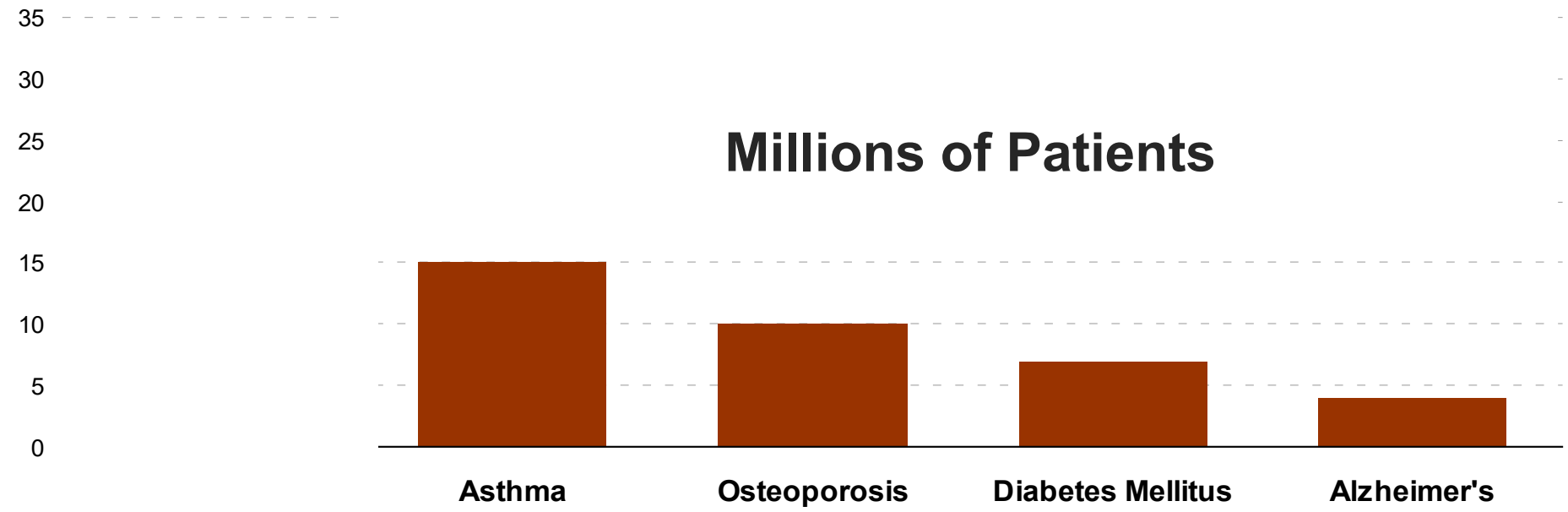
DeLancey et al


Failure of Supportive Connective Tissues
Pudendal Neuropathy
Urethral Striated Muscle Dysfunction
Hallmarks of SUI
Pelvic Floor Muscle Dysfunction
Bladder Neck Incompetence

Urge Urinary Incontinence

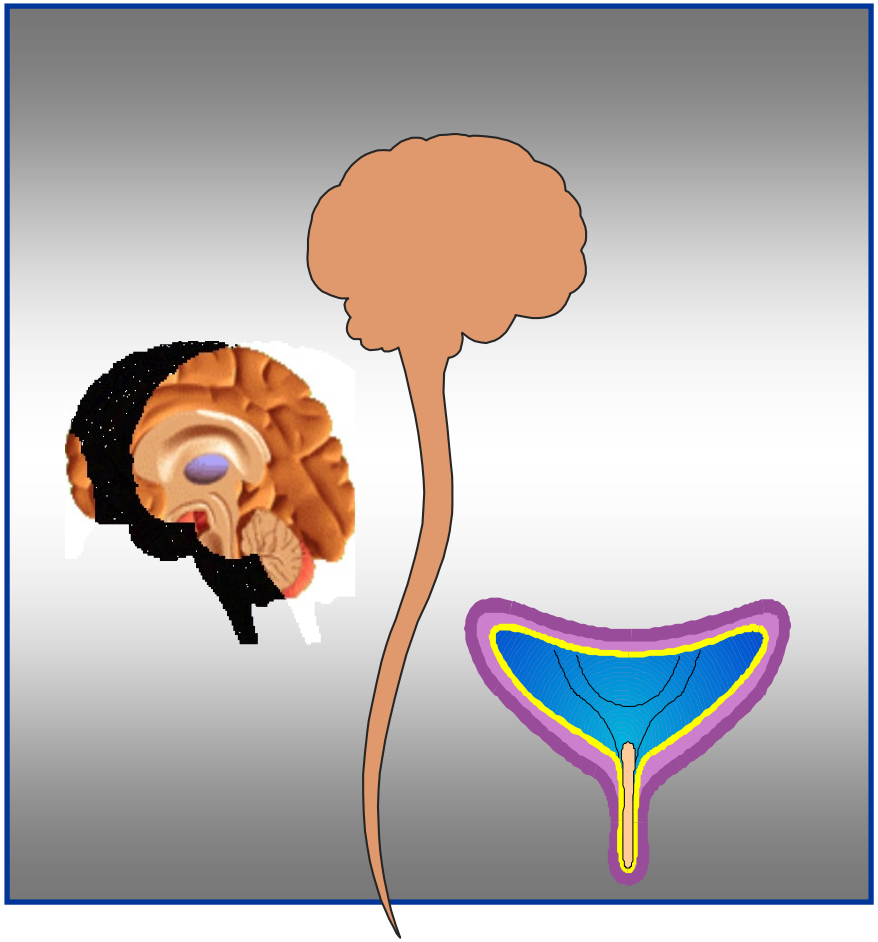
- Strong and unstoppable urges to urinate from bladder contraction
- More than 8 urinations per 24 hours is abnormal
- Often leak at night or on the way to the bathroom
- Surgery does not help and can actually make it worse

Overactive Bladder - OAB



Pathophysiology of Overactive Bladder

- **Neurogenic**
- **Myogenic**
- **Combination**
- **Unknown**



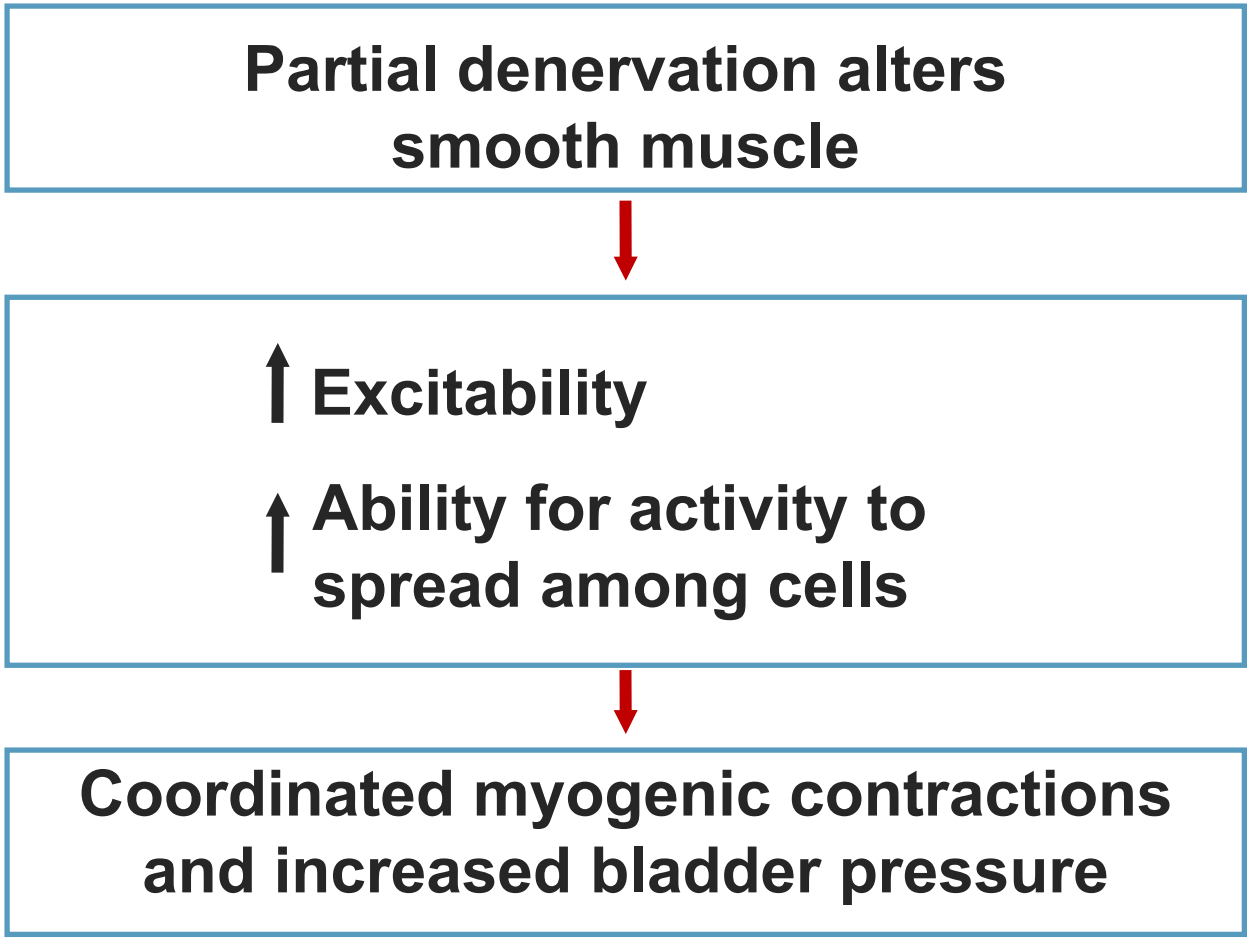
Ouslander J. N Engl J Med 2004

Neurogenic Etiology of Overactive Bladder

- Reduced suprapontine inhibition
- Damaged axonal paths in spinal cord
- Increased LUT afferent input
- Loss of peripheral inhibition
- Enhancement of excitatory neurotransmission in the micturition reflex pathway

de Groat WC. Urology 1997

Myogenic Theory



Turner WH. Pharmacol Ther 1997

Differential Diagnosis:
Reversible and transient causes of UI

D elirium
I nfection
A trophic vaginitis
P harmaceuticals
P sychological
E ndocrine
R estricted mobility
S tool impaction

Fistulas

Congenital malformations

Incontinence Evaluation

- **History**
- **Physical Examination**
- **Laboratory studies**

  Urinalysis +/- Urine Culture
- **Validated Questionnaires**
- **Homework**

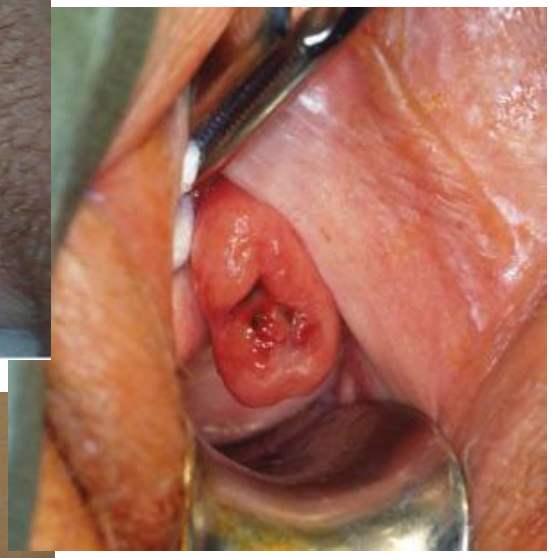
  3-day Voiding Diary
- **Bladder testing**

  Office cystometrics

  Multi-channel Urodynamics
- **Cystoscopy**

Incontinence Evaluation:
Physical Examination

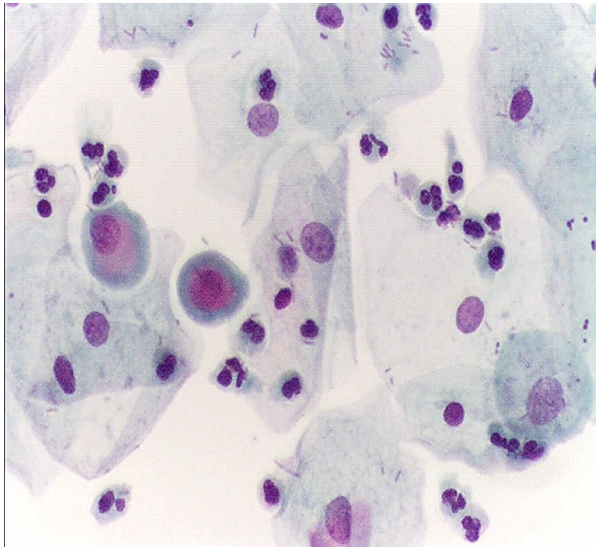
- **External genitalia**
  - Vulva – atrophy, dermatologic conditions
  - Urethra – caruncle, diverticulum
- **Internal genitalia**
  - Atrophy
  - Uterovaginal prolapse (POPQ)
  - Coexisting gynecologic/pelvic pathology
- **Fecal impaction**
- **Neurologic examination**
  - Mental status
  - Lower extremity motor and sensory function
  - Lumbosacral neurologic function



Incontinence Evaluation:
Laboratory Tests

Urine sample

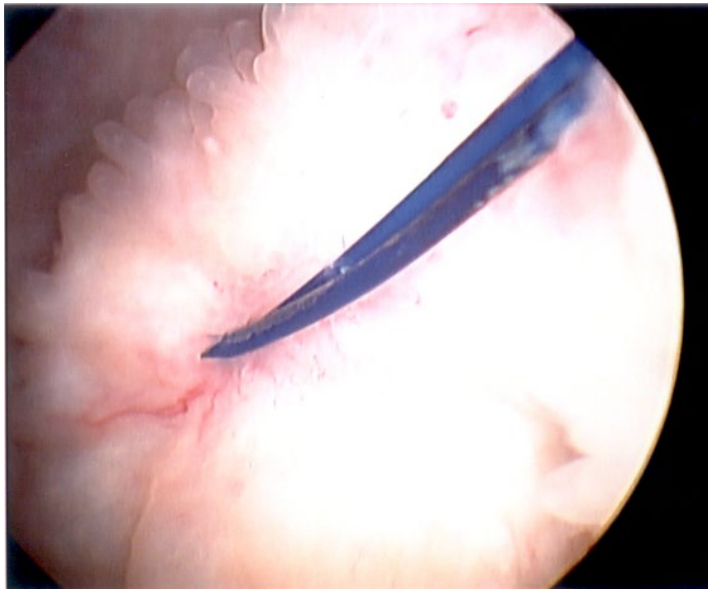
- Clean midstream *OR* catheterized sample
  - Urinalysis
  - Urine culture – *only if indicated*
  - Cytology – *only* if history of microscopic hematuria + risk factors



Simple Cystometrogram

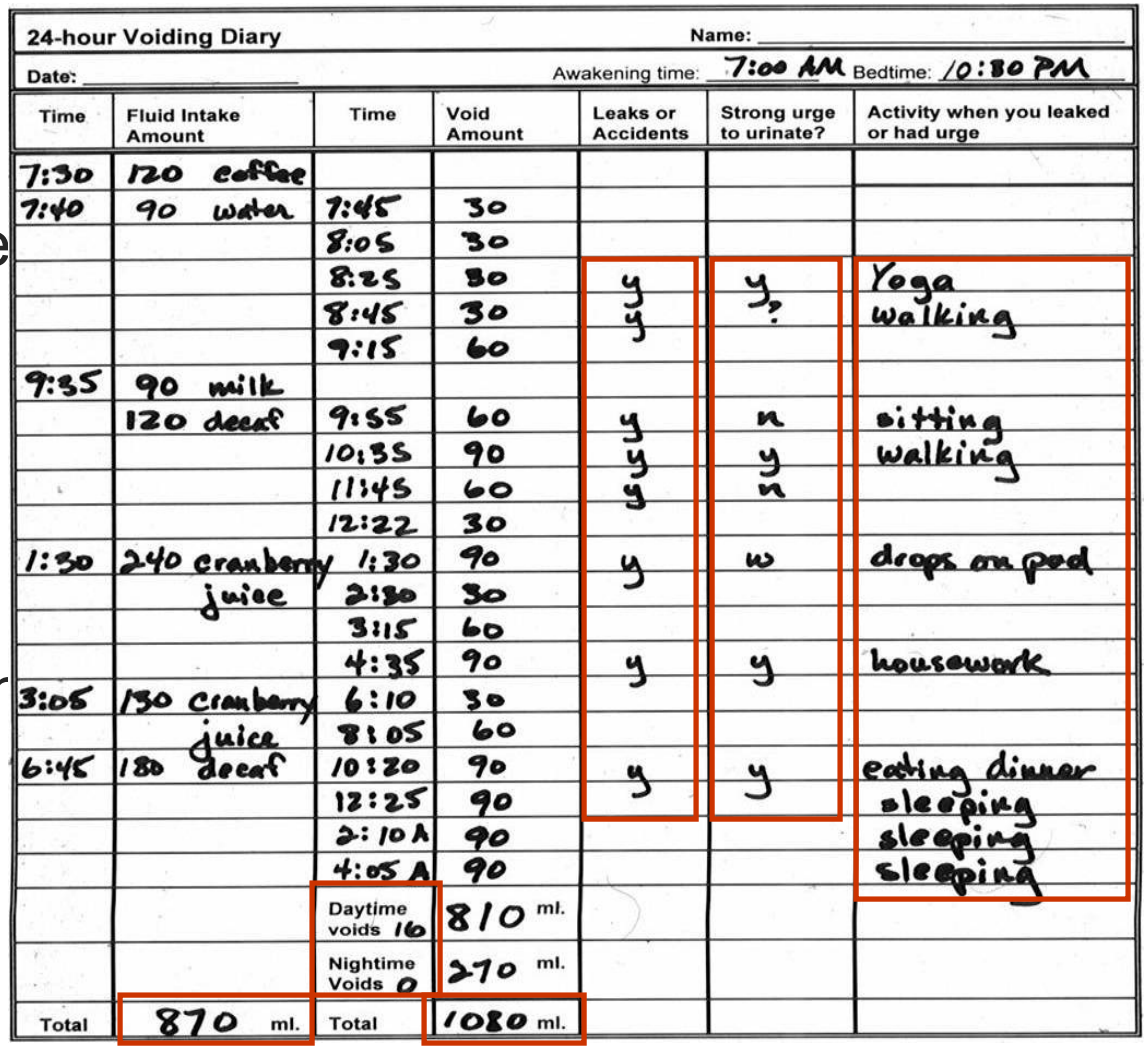
Assesses:

- **Bladder sensation**
- **Bladder capacity**
- **Bladder compliance**
- **Detrusor overactivity**



Homework: 3-day voiding diary

- 24-hour fluid intake
  - Fluid type/volume
- 24-hour voided volume
- Number of voids/day
- Number of urge episodes/day
- Number of leaks/day
  - Activities resulting in leaks



24-hour Voiding Diary — Name:

Date: — Awakening time: 7:00 AM — Bedtime: 10:30 PM

Time	Fluid Intake Amount	Time	Void Amount	Leaks or Accidents	Strong urge to urinate?	Activity when you leaked or had urge
7:30	120 coffee					
7:40	90 water	7:45	30			
		8:05	30			
		8:25	30	y	y	Yoga
		8:45	30	y	?	walking
		9:15	60			
9:35	90 milk					
	120 decaf	9:55	60	y	n	sitting
		10:35	90	y	y	walking
		11:45	60	y	n	
		12:22	30			
1:30	240 cranberry juice	1:30	90	y	w	drops on pad
		2:30	30			
		3:15	60			
		4:35	90	y	y	housework
3:05	130 cranberry juice	6:10	30			
		8:05	60			
6:45	180 decaf	10:20	90	y	y	eating dinner
		12:25	90			sleeping
		2:10 A	90			sleeping
		4:05 A	90			sleeping
		Daytime voids 16	810 ml.			
		Nightime Voids 0	270 ml.			
Total	870 ml.	Total	1080 ml.			

Homework: 3-day voiding diary

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

Homework: 3-day voiding diary

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

1st Line Treatment of Urinary Incontinence

- Requires motivation on both patient and caregiver's part
- Success entirely dependent on intensity of program
- Time intensive for caregiver and patient

1st Line Treatment for UI:
Weight Loss (PRIDE Study)

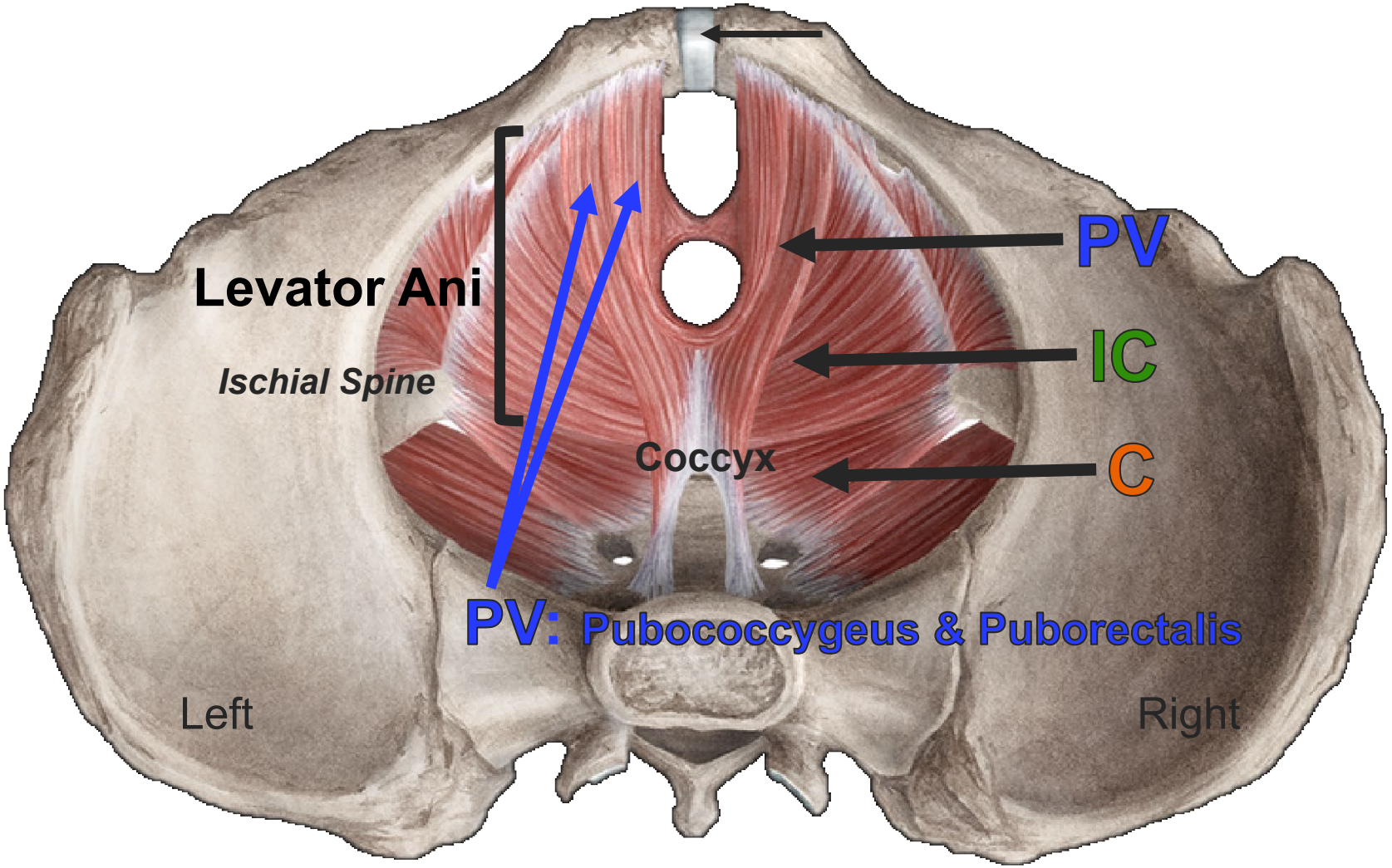
Overweight and obese women with ≥ 10 UI episodes weekly
Behavioral weight loss intervention (226)
Control group (112)
Outcome measures at 12 and 18 months

The percent weight loss:
Intervention group: 8.0%, 7.5% and 5.5% at 6, 12 and 18 mo
Control group 1.5%
} *P* = 0.001

Reduction in SUI episodes at 12 months:
the intervention group: 65%
Controls: 47%
} *P* = 0.001

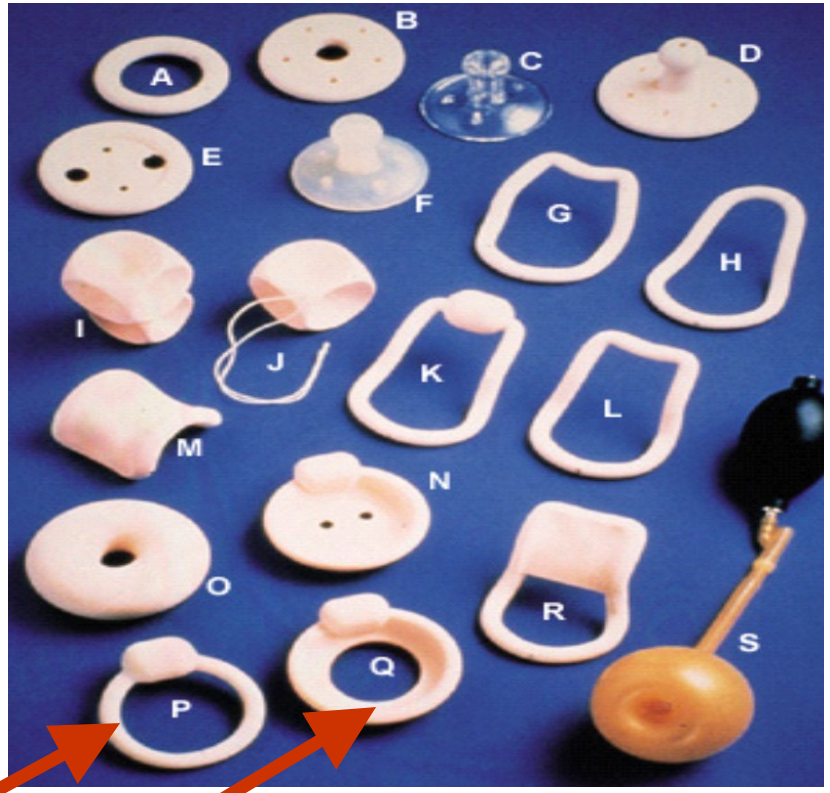
Wing RR et al. J Urol 2010

Treatment for SUI: Pelvic Floor Muscle Exercises



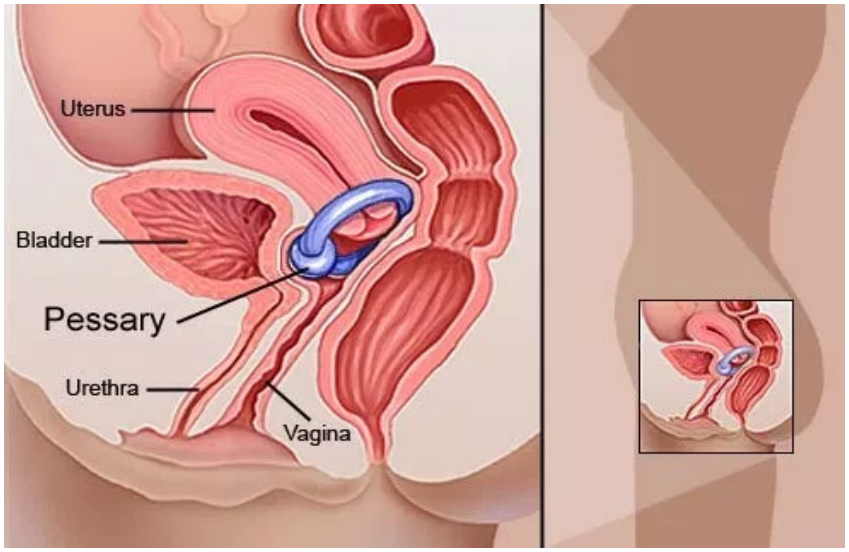
Coccygeus (C) **Iliococcygeus (IC)** **Pubovisceralis (PV)**

Treatments for SUI: pessary

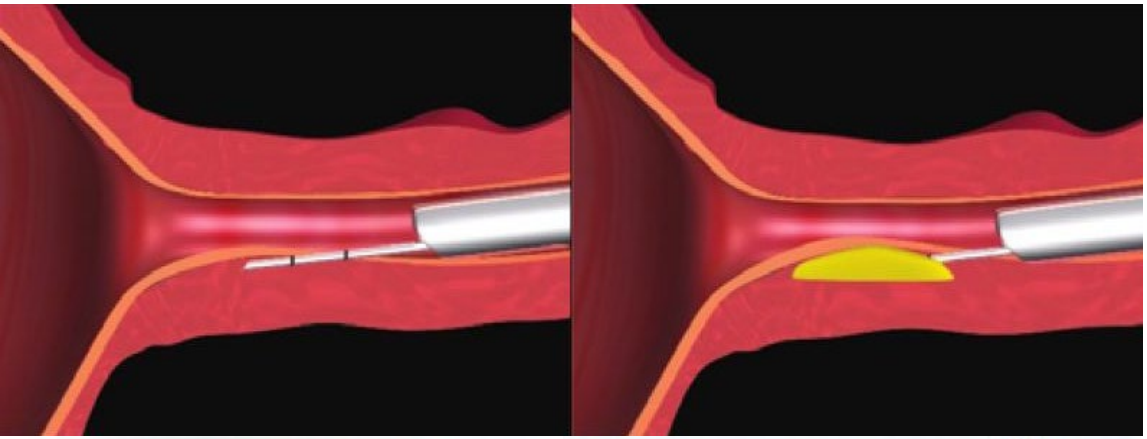


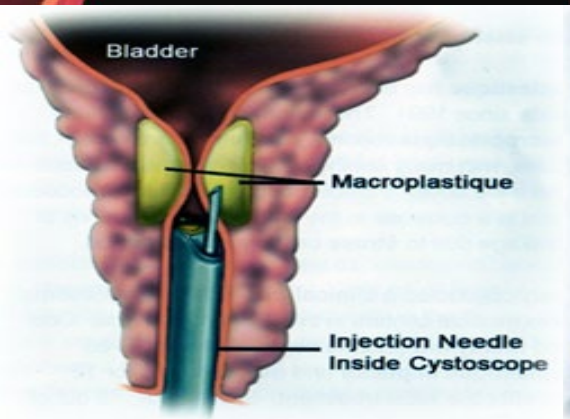
The right fit?

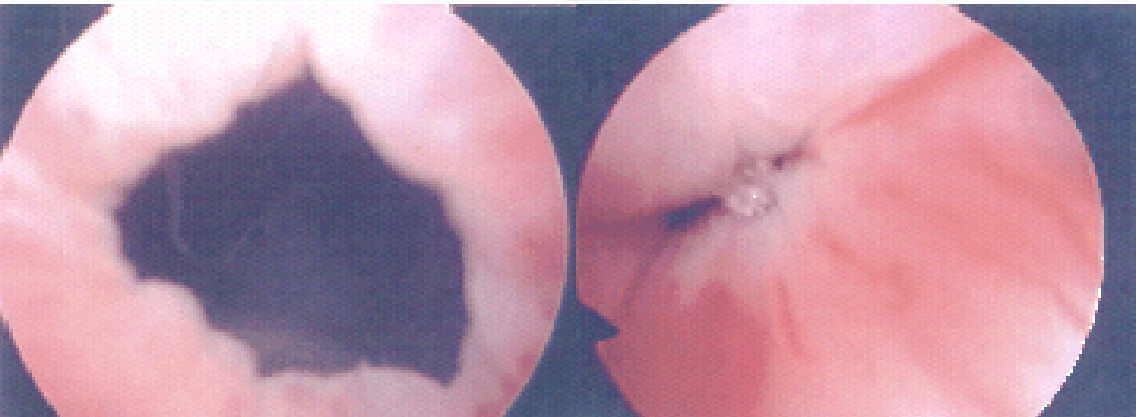
- The pessary should fit snugly behind the pubic symphysis
- The patient is comfortable and unaware of the pessary
- The pessary is not expelled with straining or ambulation
- If expelled: too little
- If causes pain: too big



Surgery for Stress Urinary Incontinence: UBI



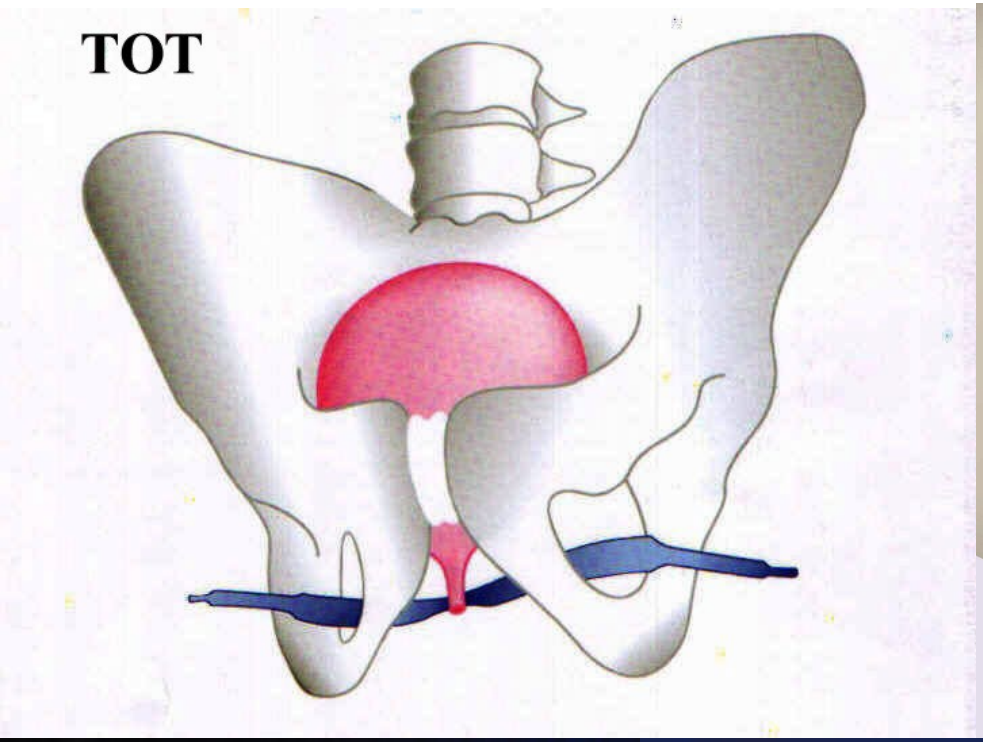


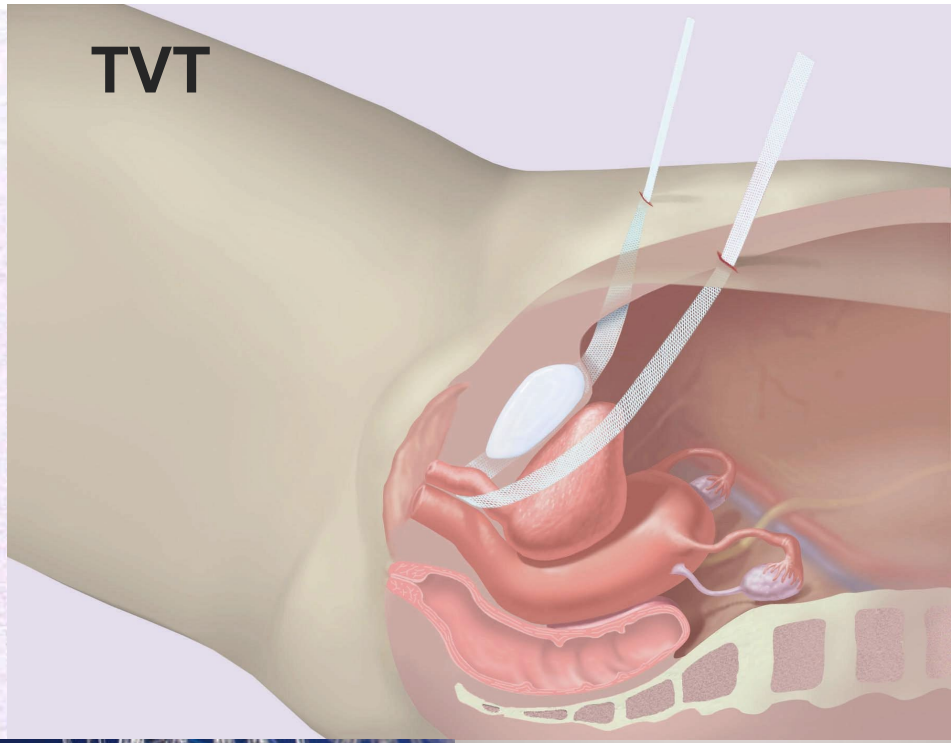


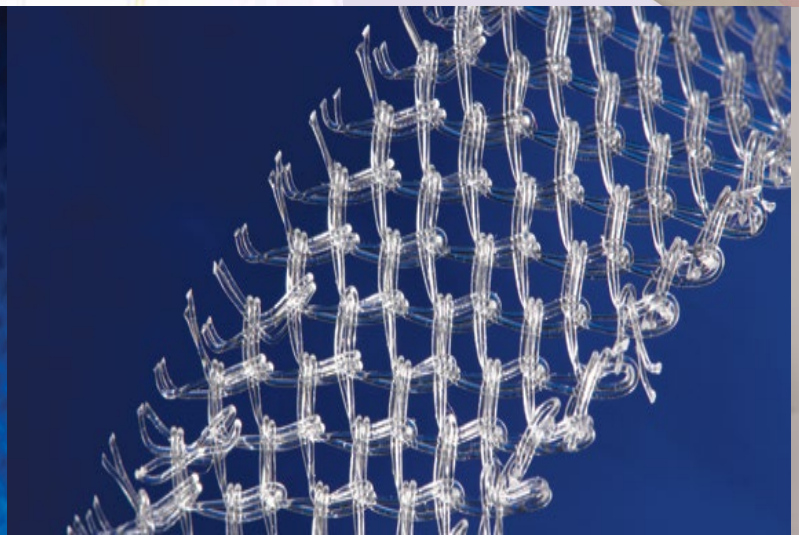
- Minimally invasive
- Local anesthesia
- Can be done in the office
- 12-24 mo: 84% maintained continence
- 67% dry rate at 24 mo

Ghoniem G et al. J Urol 2010

Surgery for Stress Urinary Incontinence: sling







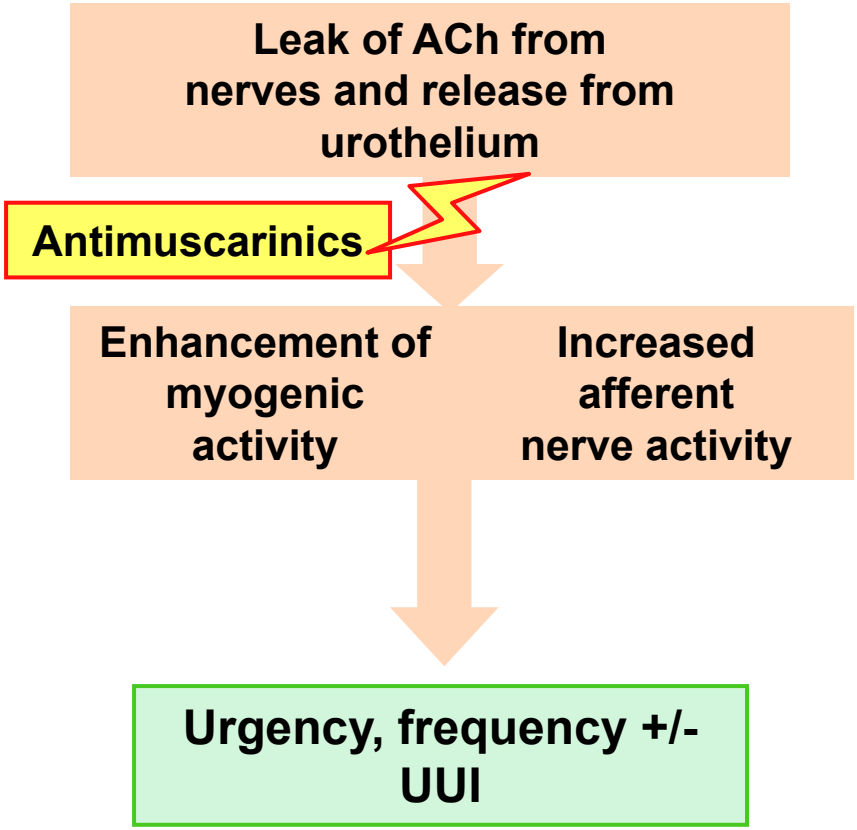
Therapeutic Options for UUI/OAB

- Behavioral modifications
- Weight Loss
- Pelvic floor muscle training +/- Biofeedback
- Pharmacologic agents
- Neuromodulation
- Surgical options

Behavioral Modifications

- Avoid bladder irritants
  - Acidic fluids
  - Caffeine
  - Nicotine
- Avoid excess or unnecessary fluid intake
- Control constipation
- Bladder training
- Timed voids

Effects of Antimuscarinics During Storage



Andersson K-E. Lancet Neurol 2004

Medications

- **Anticholinergics**
  - Darifenacin (Enablex 7.5 & 15 mg)
  - Oxybutynin (Ditropan, Oxytrol patch, Gelnique)
  - Fesoterodine (Toviaz 4 & 8 mg)
  - Solifenacin (Vesicare 5 & 10 mg)
  - Tolterodine (Detrol 2 mg IR, 4 mg ER)
  - **Trospuim chloride** (Sanctura 20 mg IR, 60 mg ER)
- **Beta adrenergics**
  - Mirabegron (Myrbetriq 25 & 50 mg)
  - Vibegron (FDA approval 2021)

  Side effects – hypertension, headache, GI

  Improved outcomes with combined therapy
- **Vaginal estrogen (for GSM/ irritative LUTS)**
  - Ring q 3 mo, tablet 10 mcg or cream 0.5 gm 2x/wk

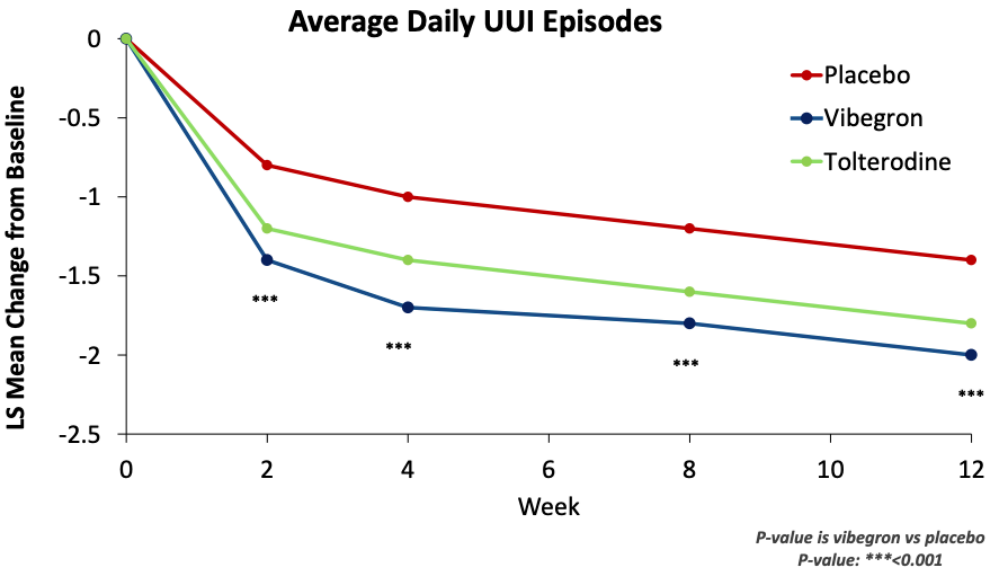
Beta Adrenergic Therapies

- β3 AR: Most highly expressed adrenergic receptor in bladder detrusor muscle
- β3 stimulation leads to relaxation of bladder detrusor muscle, *increasing capacity and reducing symptoms of OAB with no increase in residual volume*
- **Vibegron is a highly selective β3 agonist[1]:**

β-subtype	Vibegron (% Activity)*	Mirabegron (% Activity)*
β_1	0	3.0
β_2	2.0	15.0
β_3	101.0	88.0

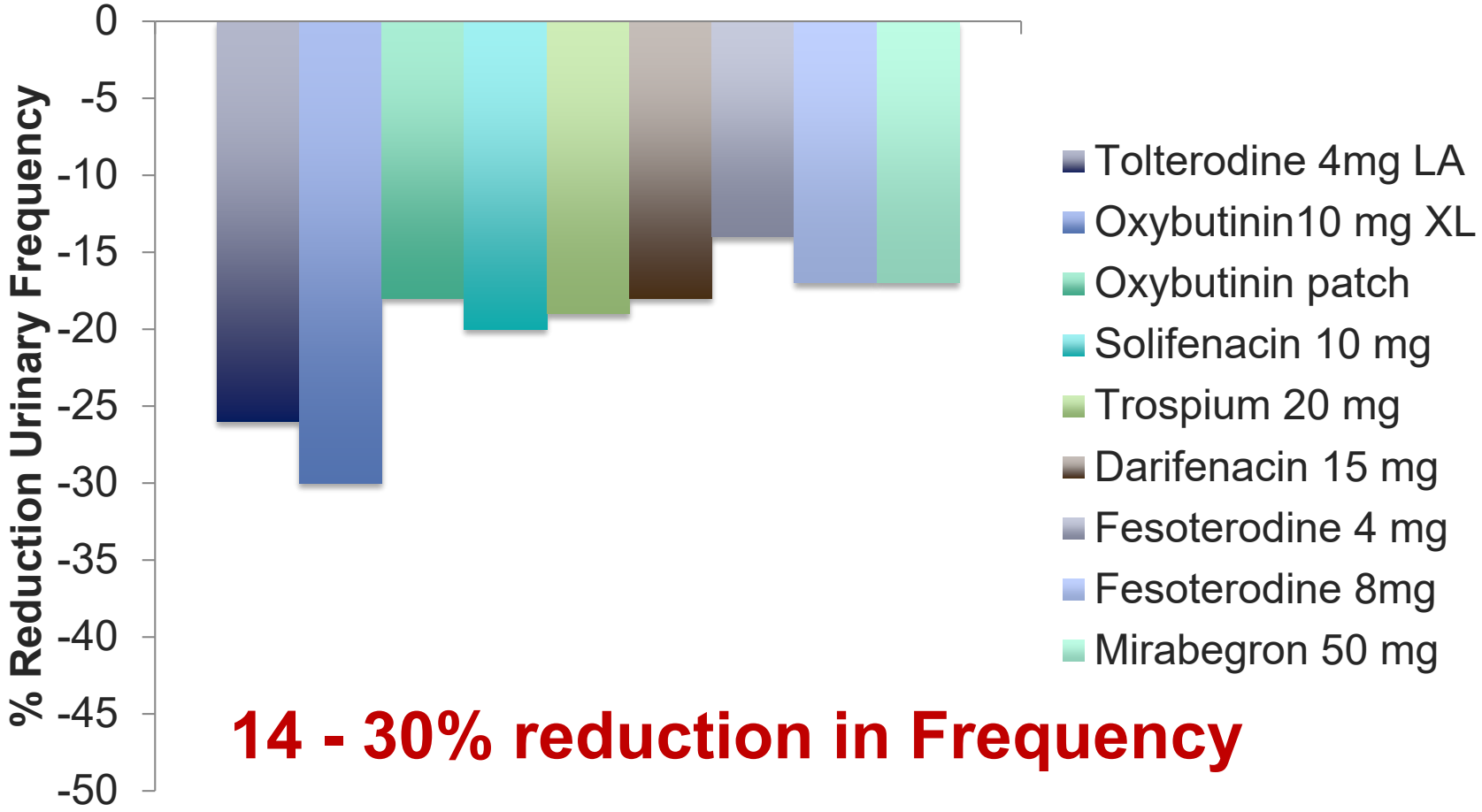
*at 10 μM (exceeds mean human C_{max} values of mirabegron by ~60x and vibegron by ~30x)

- Vibegron does not appear to bind to either β1 or β2 adrenergic receptors in a binding competition assay



ALL FDA Medications:

Reduction in Frequency*

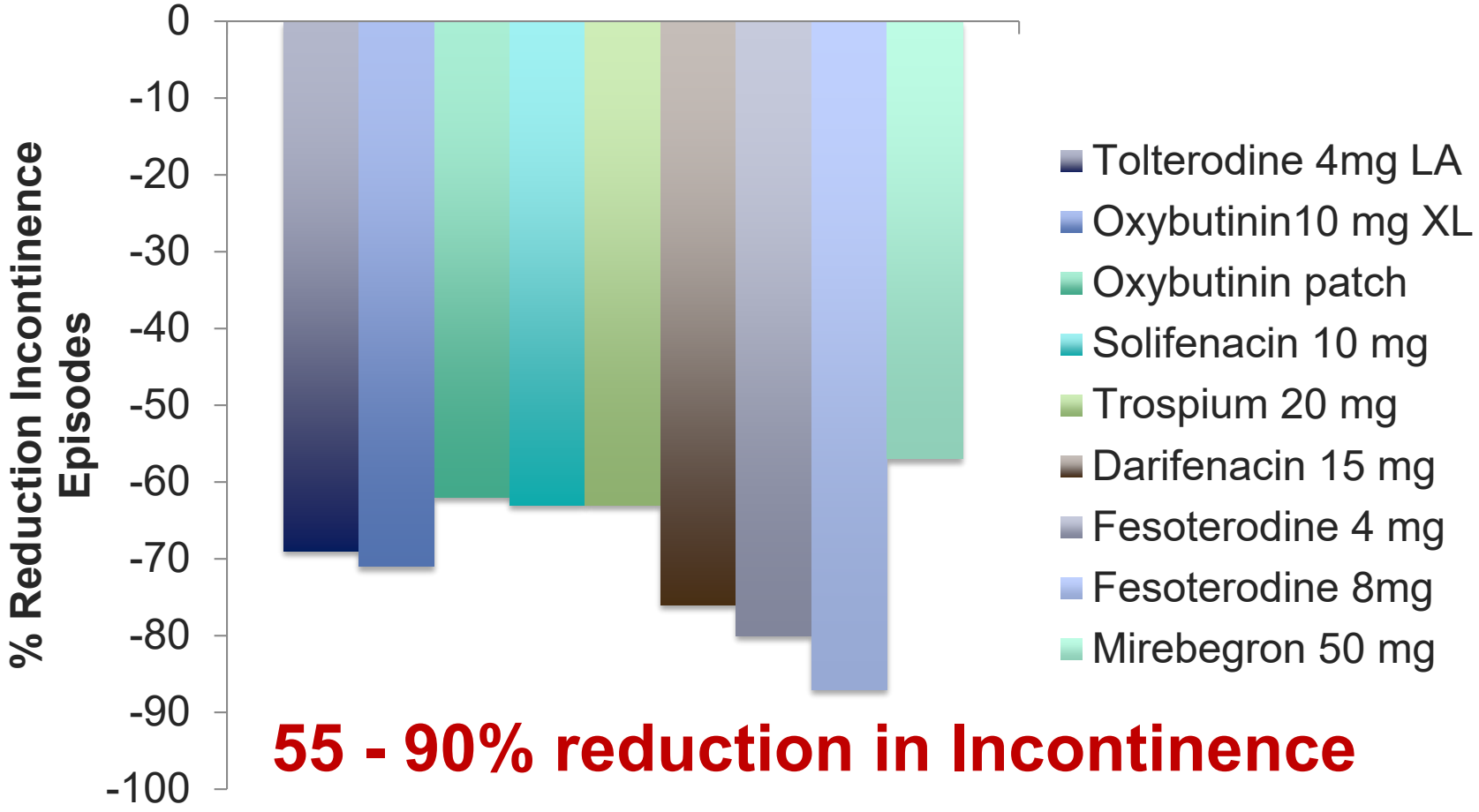


14 - 30% reduction in Frequency

*Not between-drug comparisons.

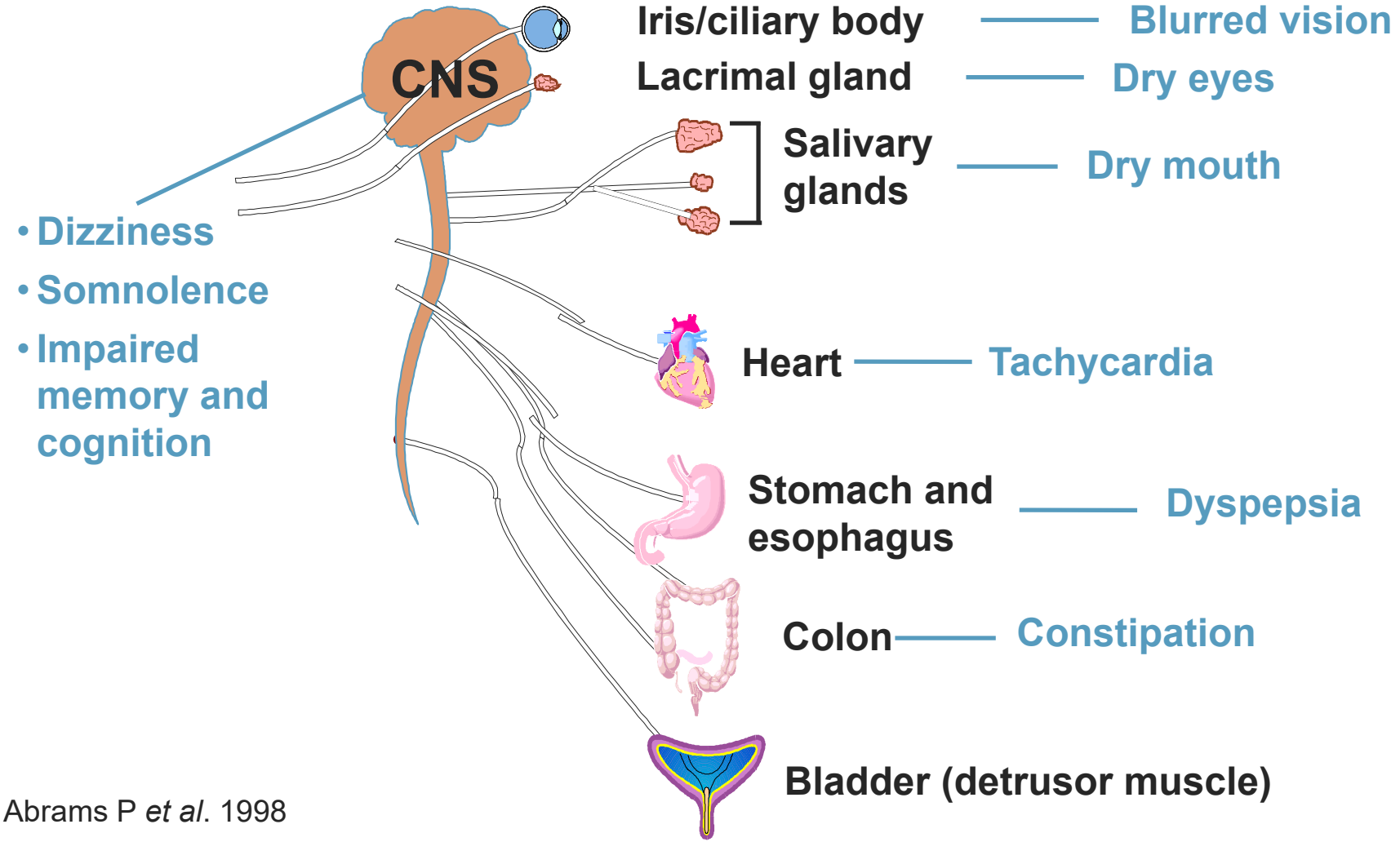
ALL FDA Medications:

Reduction in Urge Incontinence*



55 - 90% reduction in Incontinence

Muscarinic Receptor Distribution & Side Effects



Abrams P *et al*. 1998

2nd Line Therapy for Urgency Urinary Incontinence/OAB

- Efficacy is similar across medications
- Extended release formulations
  - Lower dry mouth
  - Better compliance
- Transdermal lowest dry mouth
- Dose modifications may improve outcomes
- Contraindicated in narrow angle glaucoma, gastroparesis & SVT
- Use with caution
  - Delayed gastric emptying
  - Cholinesterase inhibitors
  - Incomplete bladder emptying
  - Solid KCl preparations – due to delayed gastric emptying

2nd Line Therapy for Urgency Urinary Incontinence/OAB

- Side effect management
- Don't stop drug if effective
  - Fiber, fluid, dose modification or drug change
- Caution with anticholinergic polypharmacy
  - Tricyclic antidepressants
  - Antiemetics (atropine like)
  - Anticholinesterase inhibitors
  - Alzheimer's therapy
  - Parkinson's treatments
- Caution in frail/elderly
  - Dose titrate
  - Some preparations may have less CNS impact

*Anticholinergics Comparisons: Tolerability**

OAB Medication	Constipation (%)	Dry Mouth (%)
Placebo	0 – 4.6%	0 – 8%
Tolterodine ER 4 mg	6%	23%
Oxybutinin ER 10 mg	7%	29%
Oxybutinin TDS 3.9 mg	3.3%	9.6%
Solifenacin 5/10 mg	5.4 / 13.4%	10.9 / 27.6%
Darifenacin 7.5/15 mg	6.2 / 9.6%	19.9 / 35.9%
Trospium 20 mg	9.6%	20.1%

*This slide shows the side effect results of several separate studies and does not represent true between-drug comparisons.

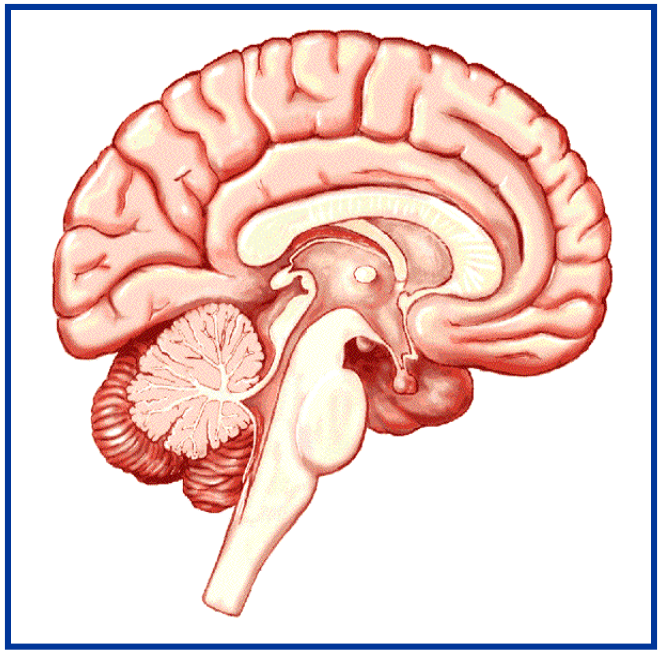
**Discontinuation rates in general are less than 5% for all SEs

2nd Line Therapy for Urgency Urinary Incontinence/OAB

OAB Medication	Special Considerations	My ideal patient
Oxybutinin Oral	IR is cheap, but high side effects. ER improved	Underfunded, healthy, low risk CNS
Oxybutinin transdermal	Lowest side effect profile, but skin reactions common (10%)	Don't like pills
Fesoterodine	Trials in elderly with comorbidities show safety	Covered drug plan
Tolterodine	Was market leader, generic/OTC	Un/under insured
Solifenacin	Pills can be cut in half	Covered drug plan/high copay
Darifenacin	No QT prolongation, low CNS absorption	Elderly/dementia risk, cardiac issues
Trospuim chloride	No drug-drug interaction, low CNS absorption	Elderly/dementia risk, polypharmacy
mirabegron	Expensive, only drug in it's class.	Intolerant or unable to take anticholinergic

Antimuscarinics and the CNS

- ACh is a pivotal mediator of short-term memory and cognition
  - 5 muscarinic receptors
  - M_1 is the best studied; roles of others yet to be elucidated
- Anticholinergic agents that cross the blood-brain barrier (BBB) may disrupt memory and cognition
- Cholinergic system involvement in Alzheimer's disease
  - ACh is decreased



Antimuscarinics and the CNS

Anticholinergic Drug Exposure and the Risk of Dementia

A Nested Case-Control Study**.** Coupland C et al. *JAMA Intern Med.* 2019

Objective: To assess associations between anticholinergic drug treatments and risk of dementia in persons 55 years or older.

Participants: 58, 769 patients with a diagnosis of dementia and 225, 574 matched controls (age, sex) registered in QResearch anonymized database (England). Information on prescriptions for 56 drugs with strong anticholinergic properties was used to calculate measures of cumulative anticholinergic drug exposure

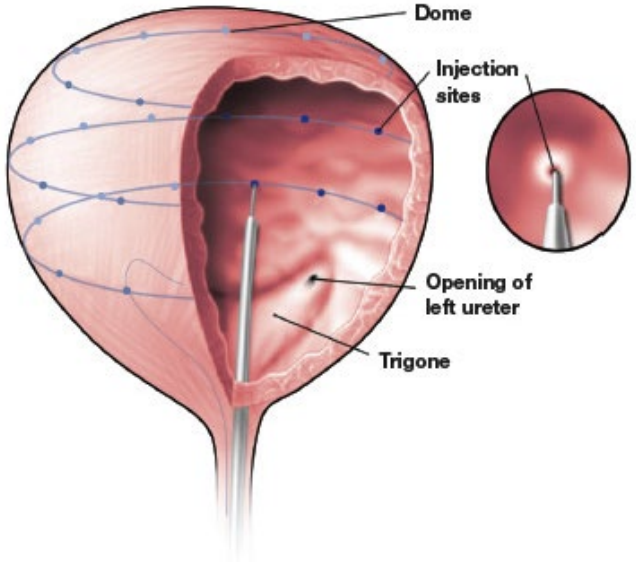
Primary Exposure: the total standardized daily doses (TSDDs) of anticholinergic drugs prescribed in the 1 to 11 years prior to the date of diagnosis of dementia or equivalent date in matched controls (index date).

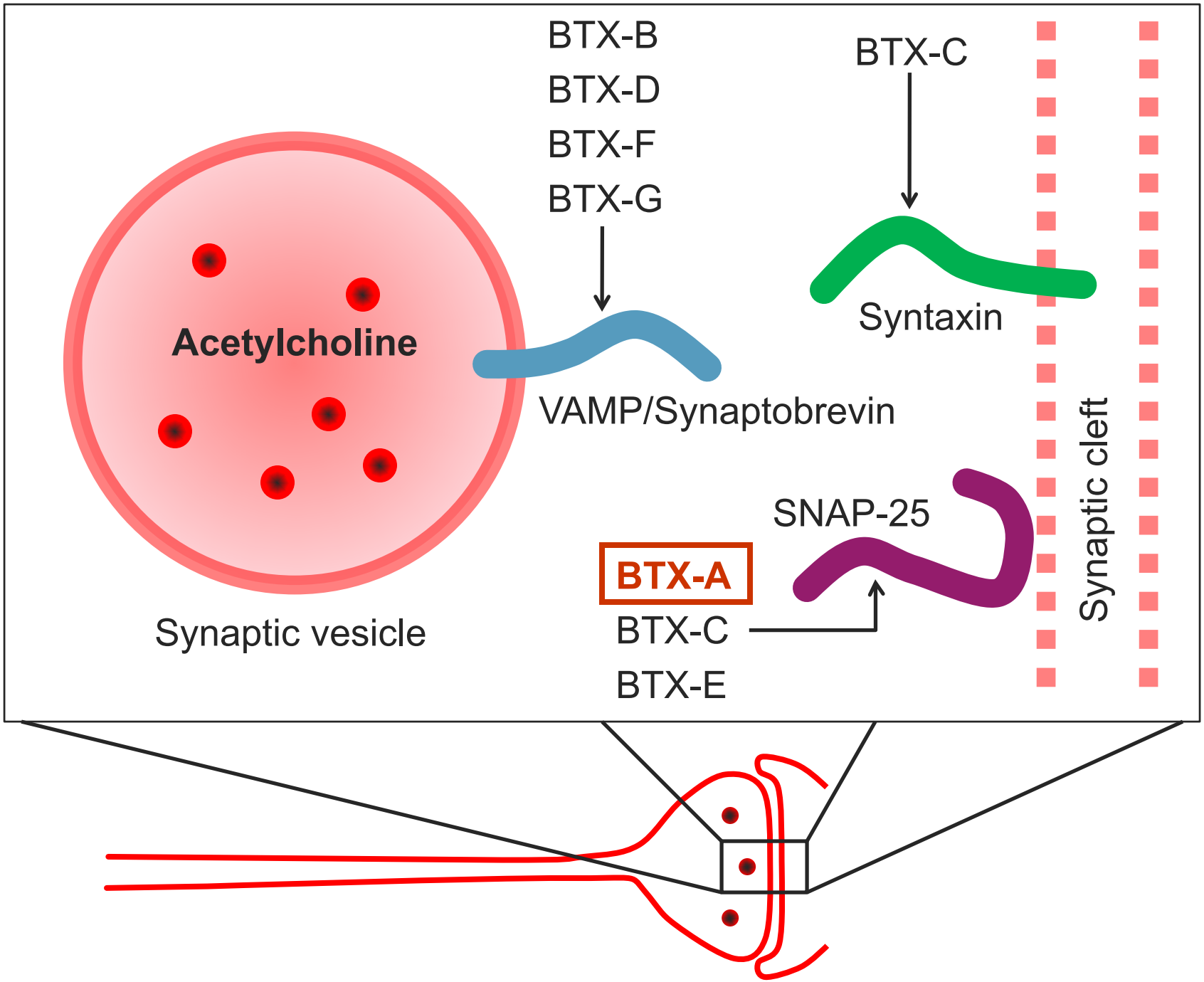
Main Outcomes and Measures Odds ratios (ORs) for dementia associated with cumulative exposure to anticholinergic drugs, adjusted for confounding variables.

Principal Finding: Significant associations of dementia risk with exposure to anticholinergic antidepressants, antiparkinson drugs, antipsychotic drugs, **bladder antimuscarinics** (**AOR1.65; 95%CI 1.56-1.75**), and antiepileptics

Botulinum Toxin

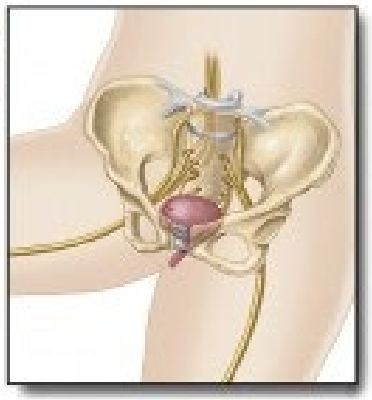
- Neurotoxin protein produced by
- *Clostridium botulinum*
- There are 7 types (A-G)
- BTX-A first approved by FDA for
- medical use in 1989




BTX-B
BTX-D
BTX-F
BTX-G
BTX-C
Acetylcholine
Syntaxin
VAMP/Synaptobrevin
SNAP-25
BTX-A
BTX-C
BTX-E
Synaptic cleft
Synaptic vesicle

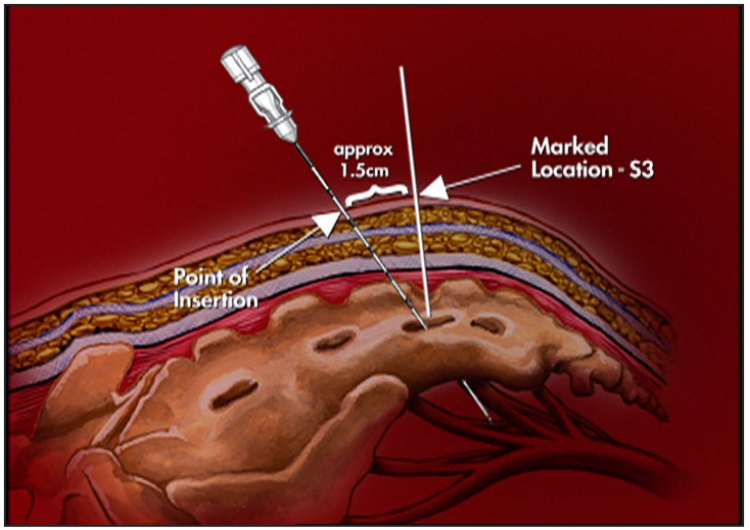
Percutaneous Tibial Nerve Stimulation (PTNS)

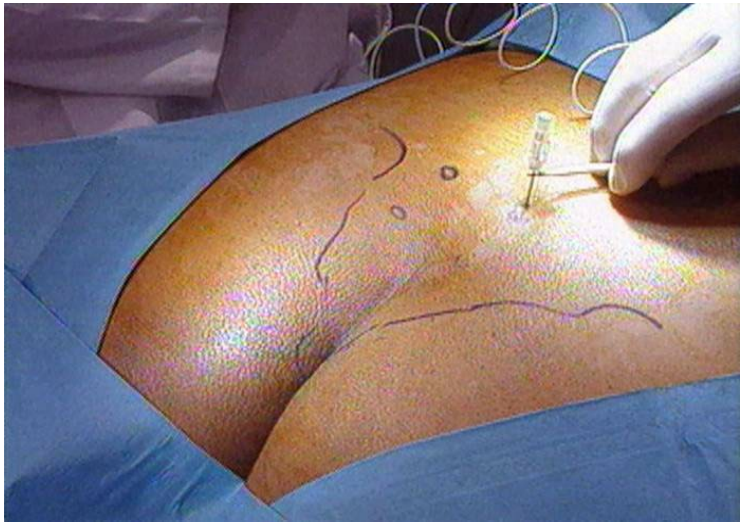
- Sacral nerve plexus: S2-4
- Posterior Tibial Nerve (PTN): L4-5, S1-3
- Common roots
- Depolarization of somatic sacral and lumbar afferent fibers
- 12 weekly sessions
- 30 min each
- By MD/ RNP/ RN/ LVN
- Medication failures
- Patients who do not desire an implantable devise
- Patients with contraindications for an implantable device
- 65-75% satisfaction rates



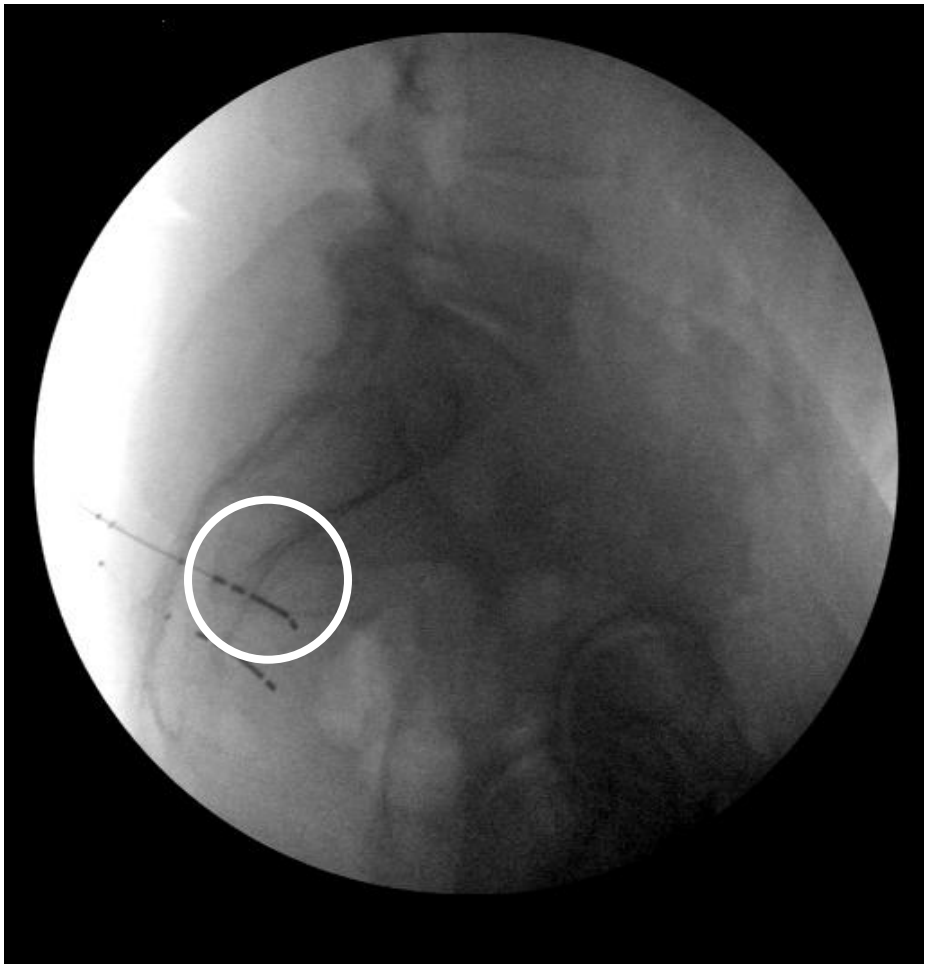
Urgent PC Stimulator, Uroplasty

Sacral Neuromodulation: Interstim and Axonics

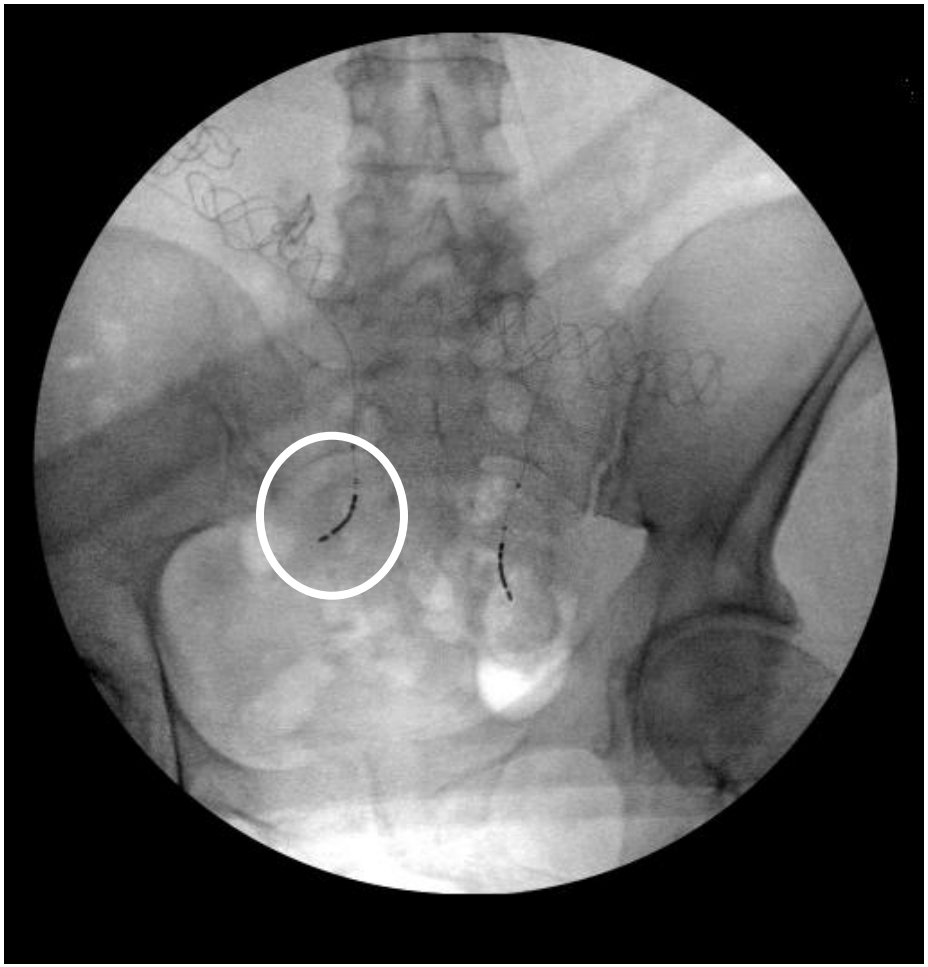




Sacral Neuromodulation: Lead Placement



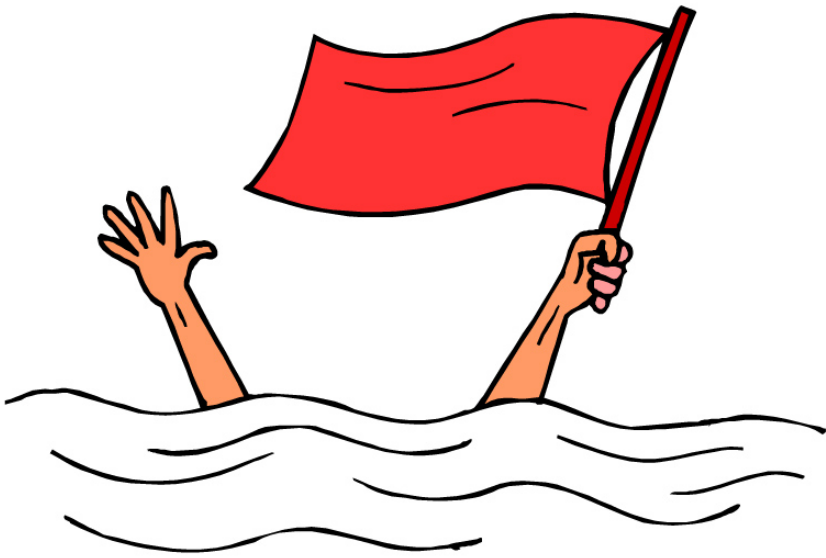
Lateral film



AP film

Red Flags → Need Referral

- Symptoms or physical examination concerning for neurologic disease
- Recurrent symptomatic urinary tract infections
- Pelvic organ prolapse beyond the hymen on pelvic exam, or patient-reported pelvic pressure associated with a visible bulge
- Elevated post void residual (experts suggest > 1/3 total volume or 100 mL adults, > 150 mL older women)
- Long-term catheterization
- Difficulty passing a urethral catheter
- Diagnostic uncertainty
- Poor improvement with treatment
- Dominant symptom of pain
- Sterile hematuria (gross or microscopic)



Summary

- Simple office history and evaluation is sufficient to initiate 1st line therapy
- Behavior modification and pelvic exercises are effective for both SUI & UUI
- OAB Medications have similar efficacy – prescribe based on side effects and coverage
- Refer to specialist for failure of conservative management, bleeding, pain or severe prolapse

...that <u>everything</u> is still
in working order!