Healthy Ageing 101

“Urinary Incontinence in Older Adults”

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Faculty/Presenter Disclosure

Faculty: Dean Elterman, MD, MSc, FRCSC

Relationships with commercial interests:

Grants/Research Support: Boston Scientific, Clarion, Pfizer

Speakers Bureau/Honoraria: Astellas, AbbVie,
Boston Scientific, Laborie

Consulting Fees: Astellas, AbbVie, Boston Scientific, Laborie, Medtronic

Learning Objectives

1) The participant will be able to understand the different forms of urinary incontinence and differentiate them based on history and physical exam

2) The participant will be able to make treatment recommendations for the various forms of urinary incontinence

3) The participant will learn in which situation a referral to a specialist should be made

What Is Overactive Bladder (OAB)?

"**Urgency**, with or without **urgency incontinence**, usually associated with **frequency** and **nocturia**"

—International Continence Society (ICS)

FREQUENCY
The need to frequently urinate (≥8 micturitions/24 hours)

URGENCY
Sudden, compelling desire to void that is difficult to defer

URGENCY INCONTINENCE
Involuntary loss of urine preceded by urgency

NOCTURIA
Waking up ≥2 times at night to void

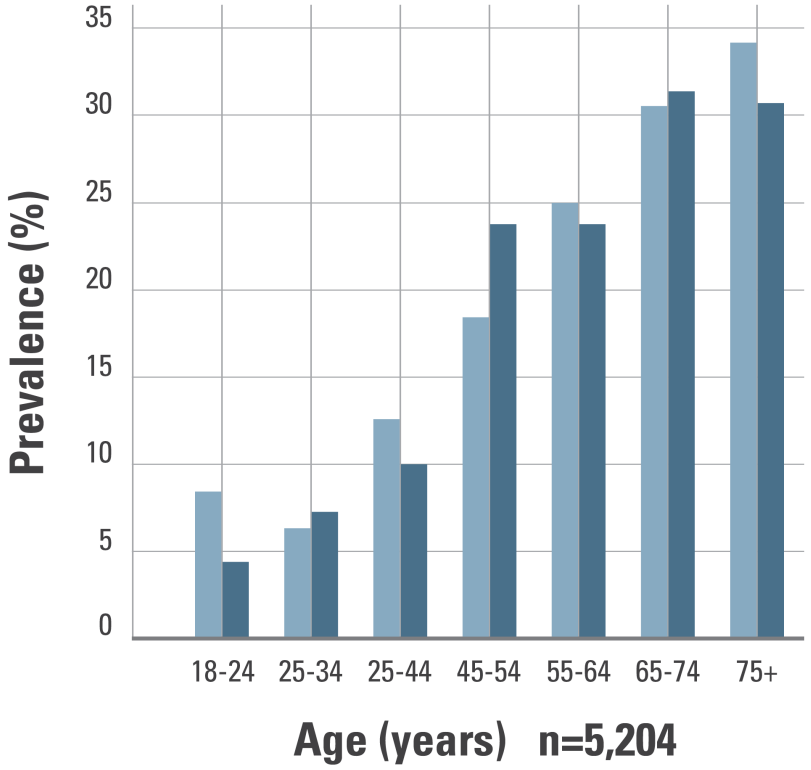
Corcos J et al. *Can J Urol* 2006;13(3):3127-3138; Abrams P et al. *Neurourol* 2002;21:167-178; Wein A et al. *J Urol* 2006;175:S5-S10; Corcos J, Schick E. *Can J Urol* 2004;11(3):2278-2284.

OAB Affects More Than 1 in 10 Canadians

13.9%
of Canadian respondents who reported symptoms

13.1% of men

14.7% of women



Prevalence of OAB is similar in men and women, and increases with age

Men Women
n=1,000

Bettez M et al. *Can Urol Assoc J* 2012;6(5):354-363; Stewart W et al. Prevalence of OAB in the US: results from the NOBLE program. Poster presented at WHO/ICI; July, 2001; Paris, France.

Men With LUTS Often Report More Than One Of The Symptom Subtypes

STORAGE	VOIDING	POST-MICTURITION
		
Frequency **Urgency** **Urge incontinence** **Nocturia**	**Hesitancy** **Intermittency** **Slow stream** **Splitting/spraying** **Straining** **Terminal dribble**	**Sensation of incomplete bladder emptying** **Post-micturition dribble**

48.6% of men possess **both** storage and voiding symptoms.

Aging-related Changes In The Bladder Can Predispose Patients To Chronic Urinary Symptoms

- Atrophic vaginitis & urethritis
- Benign prostatic hyperplasia
- Reduced ability to delay voiding
- Decreased detrusor contractility
- Decreased bladder capacity
- Detrusor overactivity
- Increased postvoid residual (>50 mL)
- Increased urine output later in the day

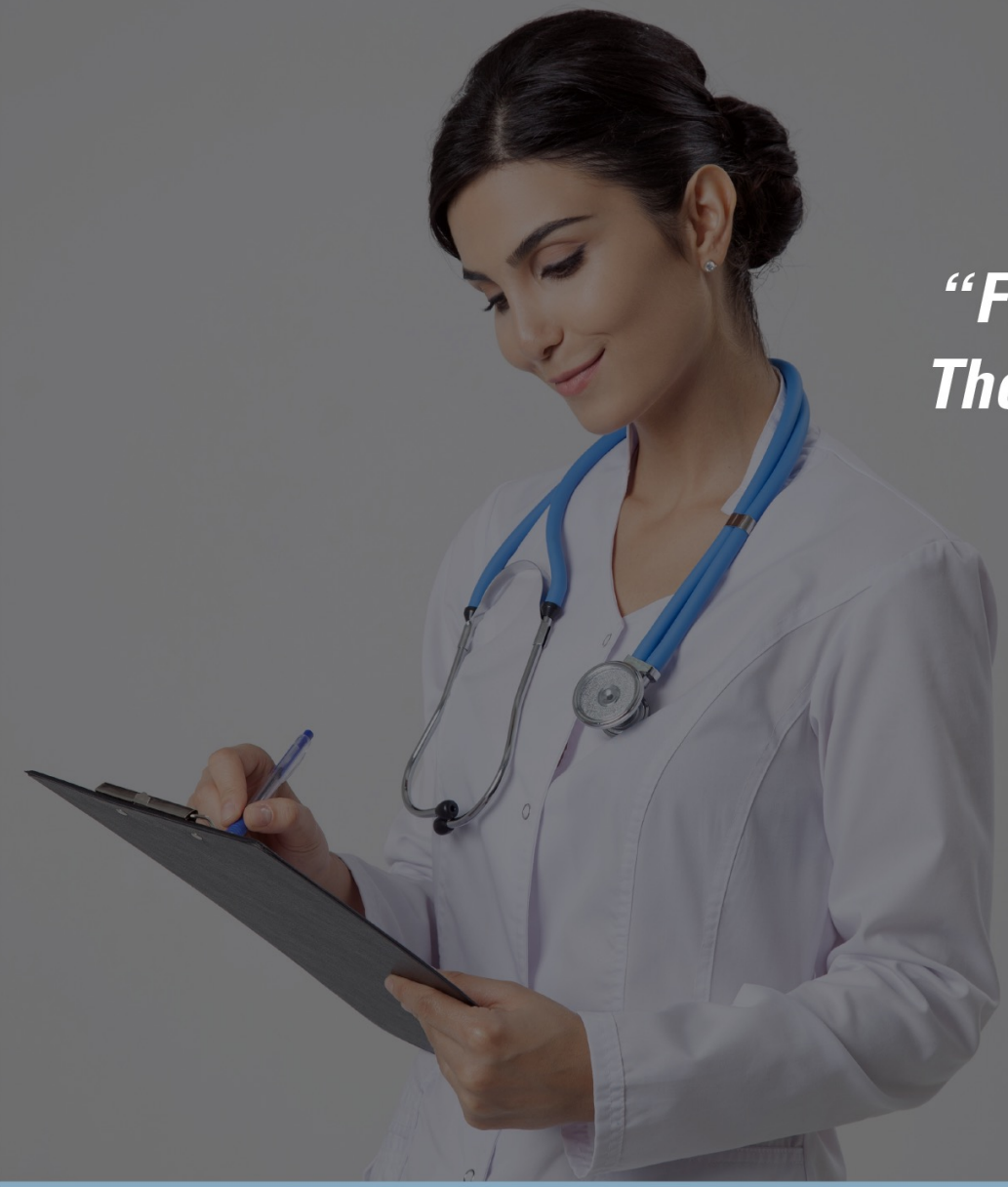
Geriatrics Review Syllabus; 6th Edition. American Geriatrics Society. Pg 186.

OAB in the Elderly

The burden of OAB is even heavier in **older patients**:

- increases with age (>23% over 60 years); increasingly prevalent as the population ages[5,7–11]
- additional health risks: falls and fractures; increased mortality; predictor of institutionalization[7,8,12–16]
- less likely to discuss their OAB symptoms with their physician; more likely to be untreated or under-treated[16–20]
- should not be tolerated as an inevitable part of aging; [7,8]

Screening for Bladder Complaints



“Finish this sentence for me... The thing that bothers me most about my bladder is...”

To successfully store urine…

STORAGE = quiet bladder + closed outlet

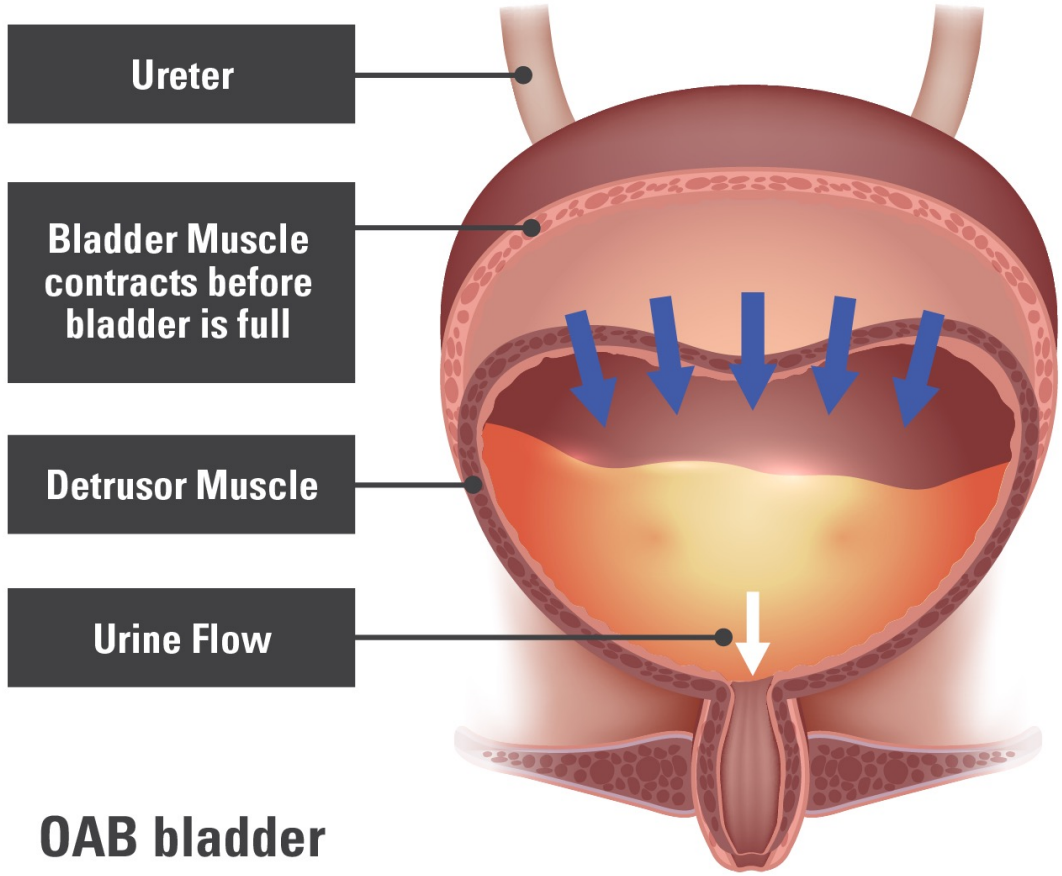
Storage Problems:

OAB

- Bladder not quiet

Stress Incontinence

- Outlet is not closed

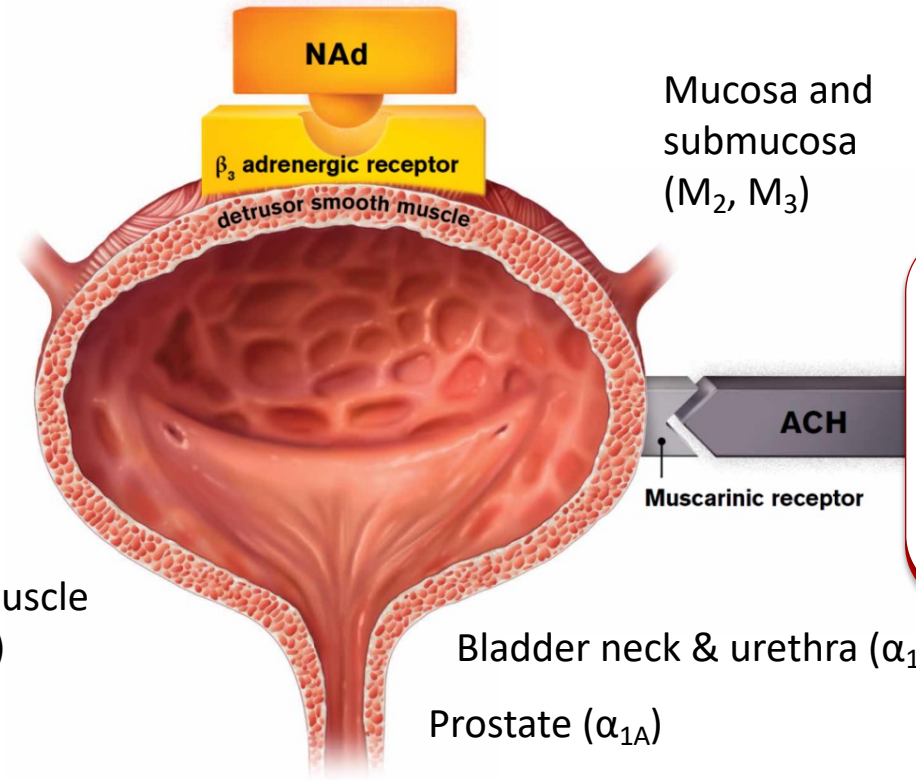


OAB bladder

Bladder Functioning Involves Both The Muscarinic And B-3 Adrenergic Receptors

M = muscarinic
α = α_1 and α_2-adrenergic
β = β_3-adrenergic
NAd = noradrenaline
ACH = acetylcholine

STORAGE PHASE
Sympathetic nerves release NAd, activating **β-adrenoceptors** to **relax** the bladder



Mucosa and submucosa (M_2, M_3)

VOIDING PHASE
Parasympathetic nerves release ACH, activating **M receptors** to **contract** the bladder

Detrusor muscle (M_2, M_3, β_3)

Bladder neck & urethra (α_{1A})

Prostate (α_{1A})

In OAB, the bladder leaves the storage phase by suddenly and involuntarily contracting.

Fowler CJ et al. *Nat Rev Neurosci* 2008;9(6):453-466. François N et al. Chapter 7, In: *Male lower urinary tract symptoms and benign prostatic hyperplasia*, 2014.

What Patients Say

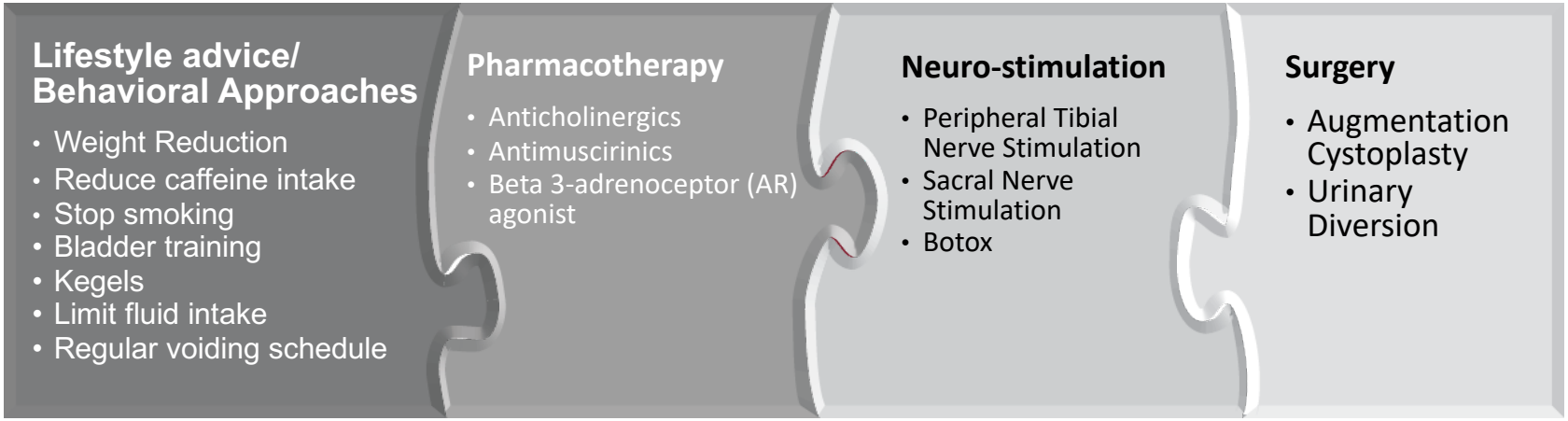
OAB

- *I pee too often compared to my friends*
- *When I'm doing the dishes, I have to suddenly run to the washroom*
- *When I stand from sitting, it just hits me. I can't make it!*
- *I know where every washroom is at the mall*

Stress Incontinence

- *If I laugh or cough, I find myself leaking*
- *I can't jog anymore*
- *Forget about going on a trampoline*

Spectrum of OAB Treatments



Lucas, MG et al. Guidelines on Urinary Incontinence. In: *EAU Guidelines;* edition presented at the 27th EAU Annual Congress, Paris, France; 2012. Online. Accessed 20 Dec 2013. Available at: www.uroweb.org/gls/pdf/19_**Urinary_Incontinence**_LR.pdf

Myrbetriq Product Monograph. Astellas Pharma Canada. March 4, 2013.

Non-pharmacological Treatment

- Limiting fluid consumption to ~ 2-2.5 L/day
- Limiting consumption of caffeine and alcohol
- Bladder training – urgency suppression techniques
- Pelvic floor muscle training*
- Managing constipation
- Smoking cessation
- Consider vaginal estrogen
- Weight reduction if obese

Modified from CUA guidelines
* Effective for SUI and OAB

Functional Aids

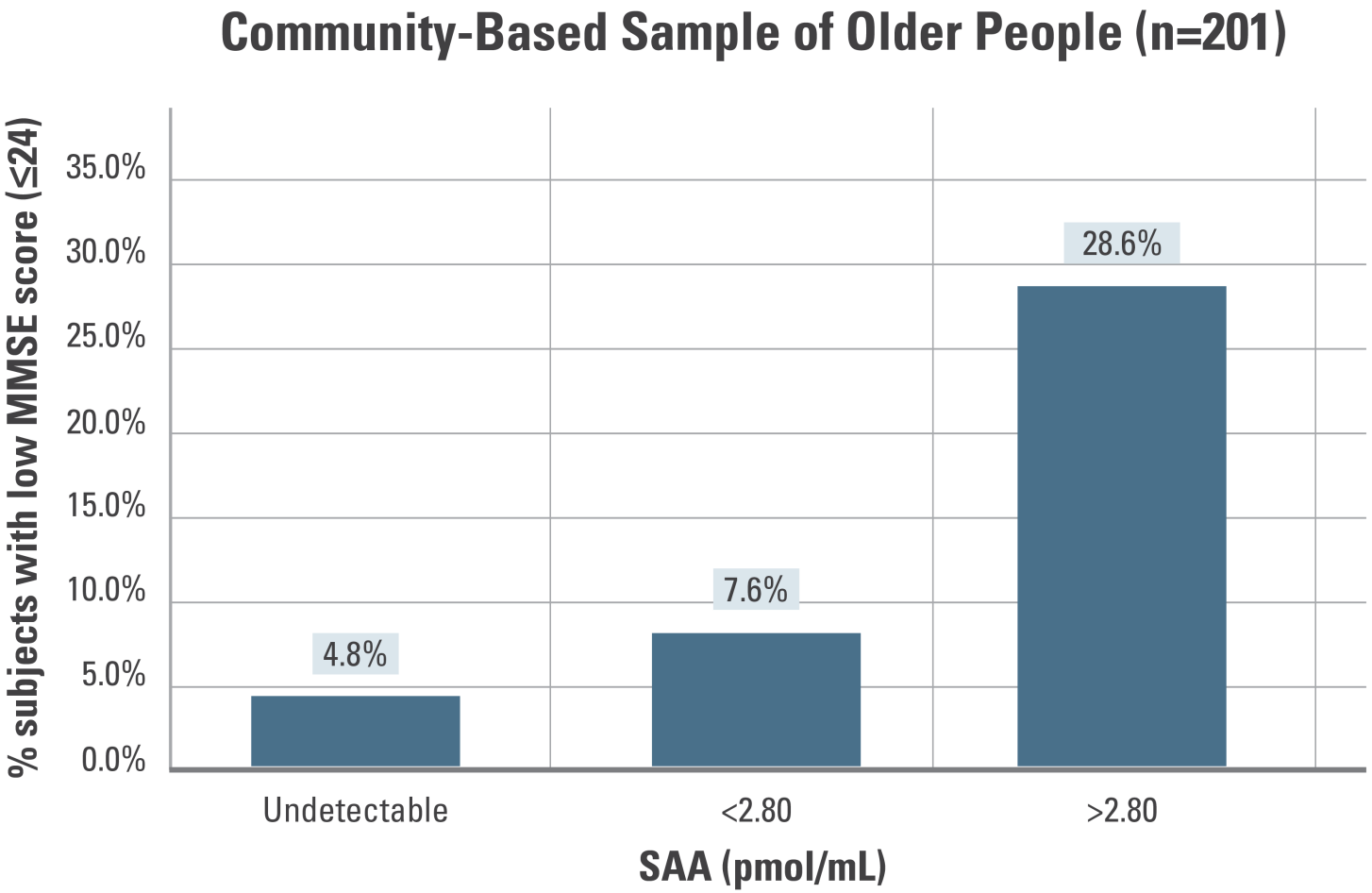
- Bedside commode
- Home care support
  (example – emptying commode in AM)
- Incontinence products
  http://www.continenceproductadvisor.org/

Medication Review

Review medications which might compromise successful toileting and potentially add to anticholinergic load

- **Anticholinergic load (amitriptyline, tiotropium, furosemide)**
- **Impaired emptying (amitriptyline, tiotropium)**
- **Polyuria (dapagliflozin, calcium carbonate, furosemide)**

Anticholinergic Burden and MMSE Scores



MMSE = Mini-mental state examination SAA = serum anticholinergic activity
p<0.05 vs undetectable SAA (logistic regression)

Mulsant BH et al. *Arch Gen Psychiatry* 2003;60: 198–203.

OAB Treatments

Many effective OAB treatments are available to reduce symptoms of OAB

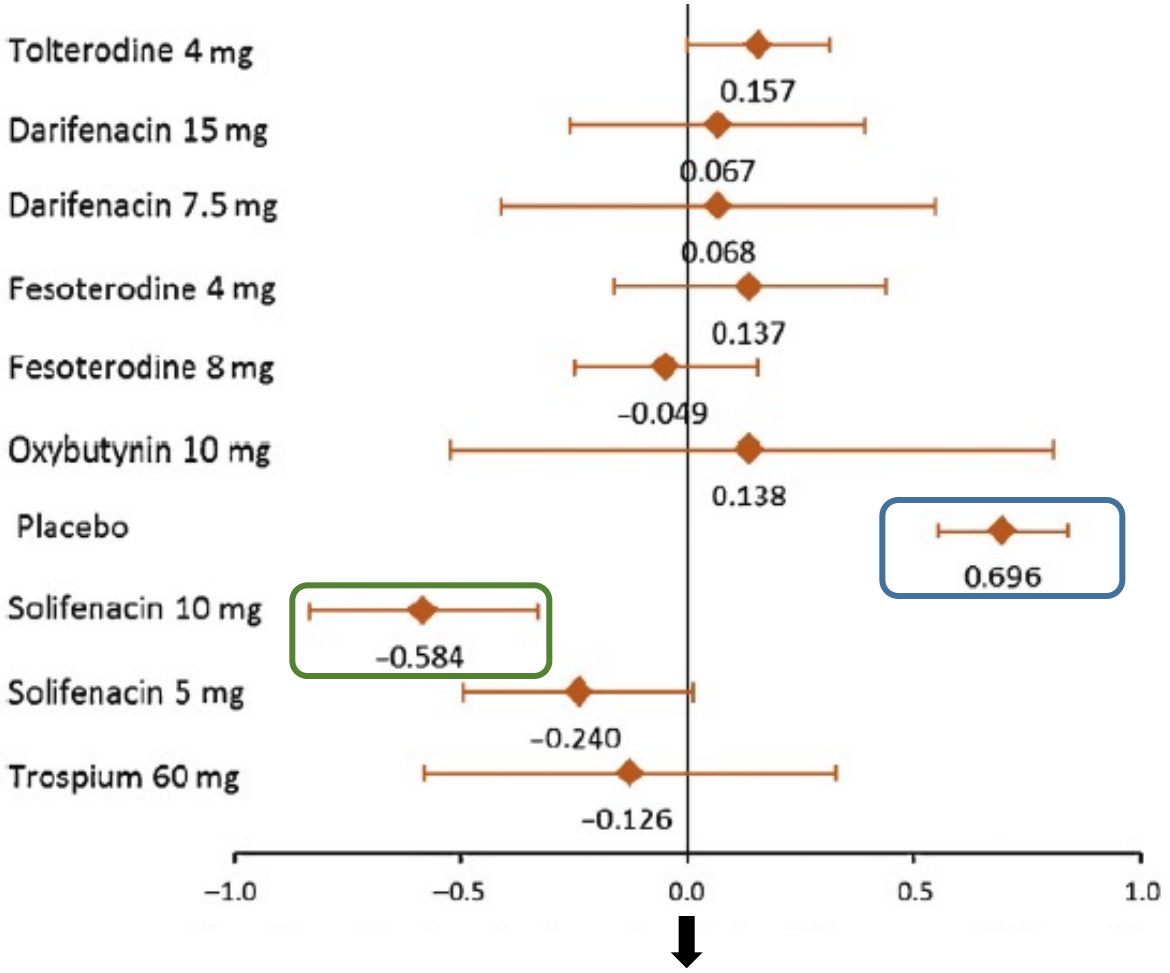
- **Antimuscarinics**
  - Darifenacin
  - Fesoterodine
  - Oxybutynin IR/ER/CR
  - Oxybutynin patch
  - Oxybutynin gel
  - Solifenacin
  - Tolterodine IR/ER
  - Trospium chloride
- **Beta-3 receptor agonists**
  - Mirabegron

Bettez M et al. *Can Urol Assoc J* 2012;6(5):354-363; Gormley EA et al. 2014 guideline available at www.AUAnet.org.

Mixed Treatment Comparison (MTC) Between OAB Treatment Classes: Micturitions

MTC Analysis
Mean change from baseline in number of micturitions

N = 26 RCT
(22,040 patients)



- Less effective than reference
- More effective than reference

All others not significantly different vs. reference

Information includes all available evidence from direct comparisons and indirect comparisons.

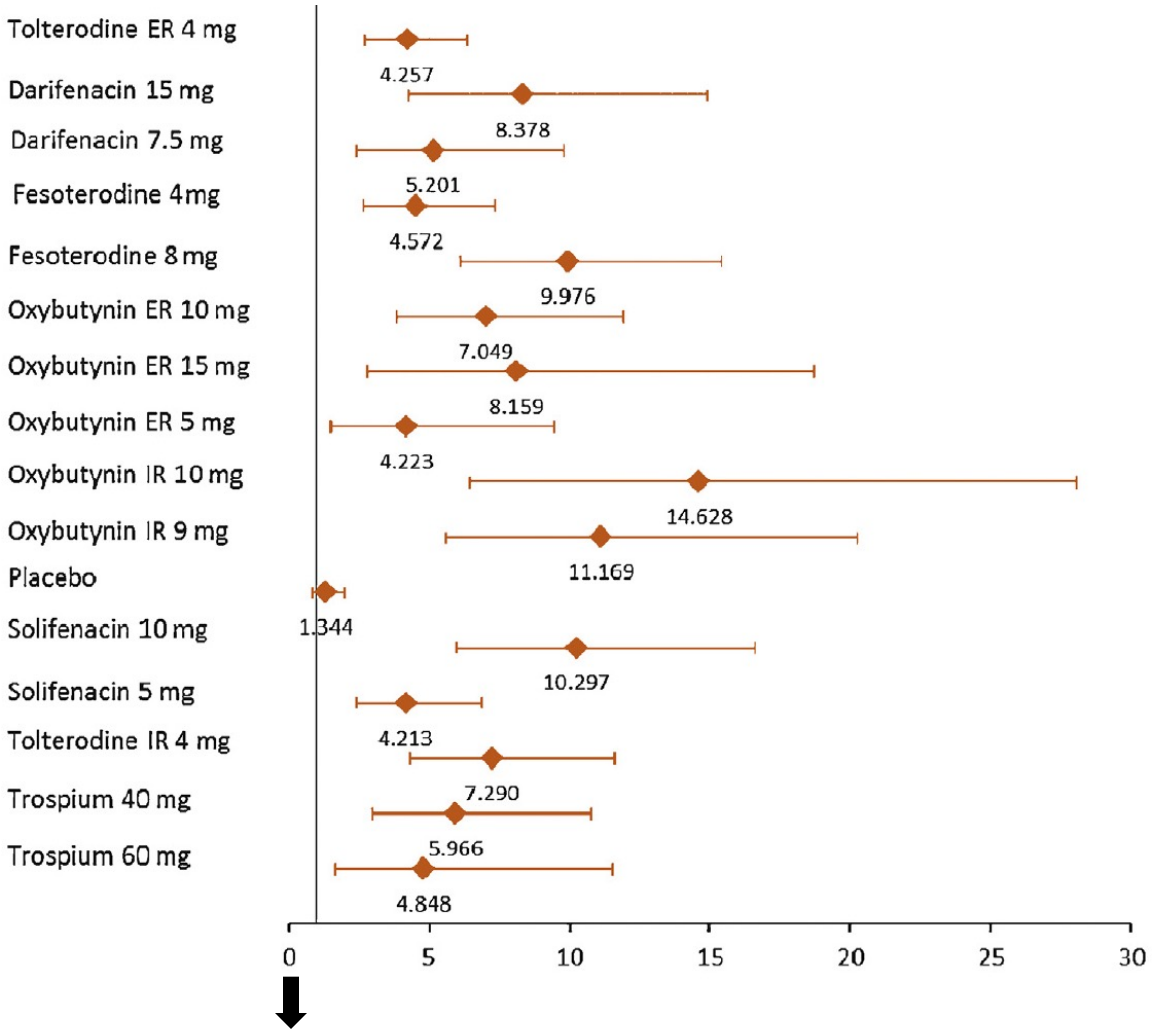
MTC = mixed treatment comp

Maman et al, *Eur. Urol*. 2014;65:755-765

Mixed Treatment Comparison (MTC) Between OAB Treatment Classes: Dry Mouth

MTC Analysis
Odds ratio

N = 44 studies
(27,309 patients)



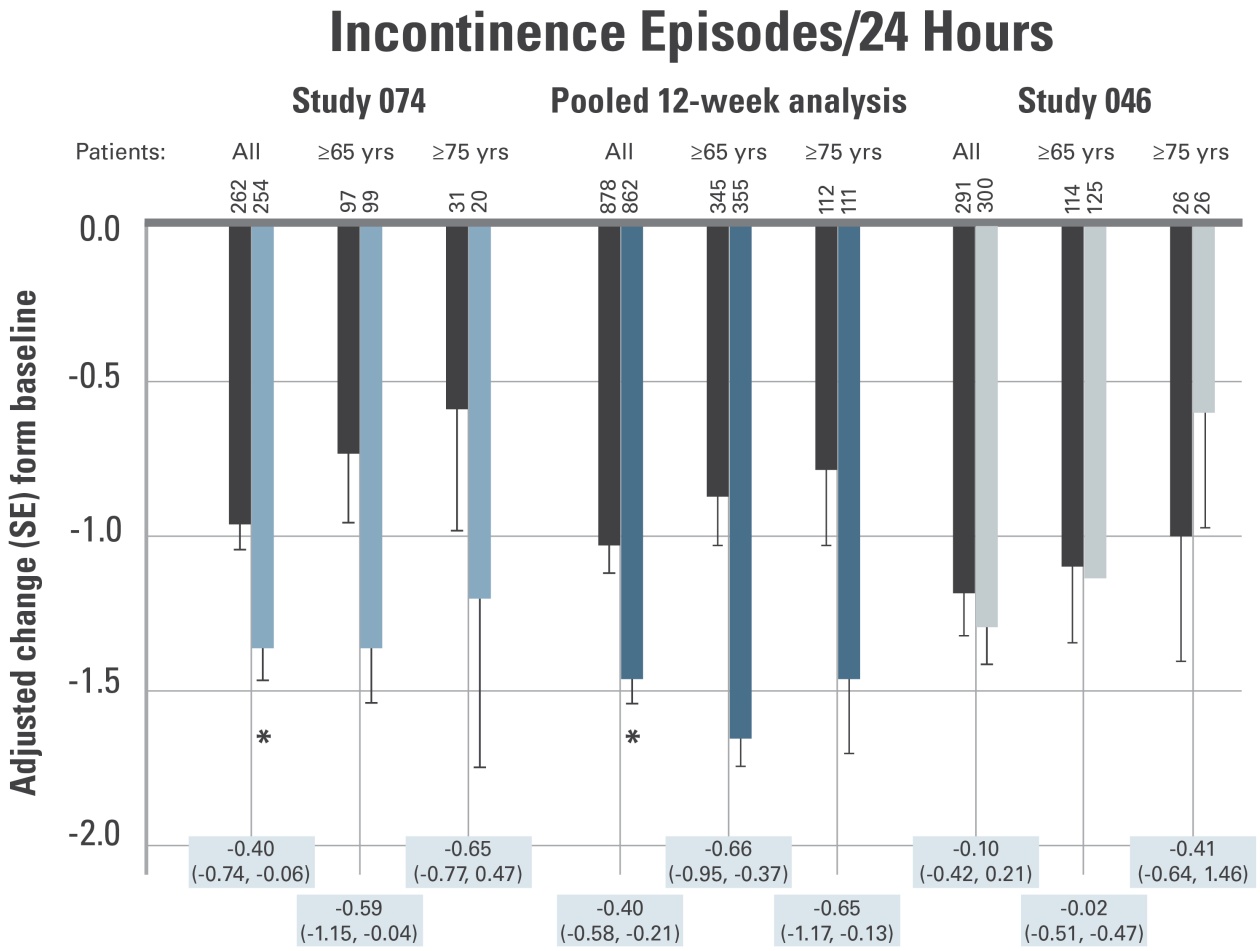
Information includes all available evidence from direct comparisons and indirect comparisons.

MTC = mixed treatment comparison;
RCT = randomized controlled trials.

Maman et al, *Eur. Urol*. 2014;65:755-765.

Mirabegron in Older Persons[1]

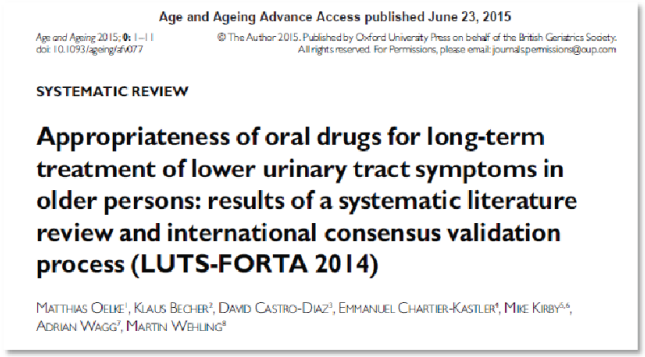
- Beta – 3 agonist
- Active relaxation of bladder in storage phase
- Better adherence than AM[2,3]
- Different AE profile



Statistically significant difference versus placebo at the $p<0.05$ level with multiplicity adjustment

1. Wagg et al, Age and Ageing 2013. 2. Can Urol Assoc J. 2015 Sep-Oct;9(9-10):343-50. doi: 10.5489/cuaj.3098. 3. Int Urogynecol J. 2016 Jan 23. [Epub ahead of print]

Where's the specific evidence for older patients?



Age and Ageing Advance Access published June 23, 2015

Age and Ageing 2015; 0: 1–11
doi: 10.1093/ageing/afv077

SYSTEMATIC REVIEW

Appropriateness of oral drugs for long-term treatment of lower urinary tract symptoms in older persons: results of a systematic literature review and international consensus validation process (LUTS-FORTA 2014)

MATTHIAS OELKE[1], KLAUS BECHER[2], DAVID CASTRO-DIAZ[3], EMMANUEL CHARTIER-KASTLER[4], MIKE KIRBY[5,6], ADRIAN WAGG[7], MARTIN WEHLING[8]

FORTA A (Absolutely) Indispensable drug, clear-cut benefit in terms of efficacy/ safety ratio proven in elderly patients for a given indication	
FORTA B (Beneficial) Drugs with proven or obvious efficacy in the elderly, but limited extent or effect or safety concerns	**Fesoterodine**
FORTA C (Caution) Drugs with questionable efficacy/safety profiles in the elderly, to be avoided or omitted in the presence of too many drugs, lack of benefits or emerging side effects ; review/find alternatives	**Darifenacin** **Mirabegron** **Oxybutynin ER** **Solifenacin** **Tolterodine** **Trospium**
FORTA D (Don't) Avoid in the elderly, omit first, review/find alternatives	**Oxybutynin IR** **Propiverine**

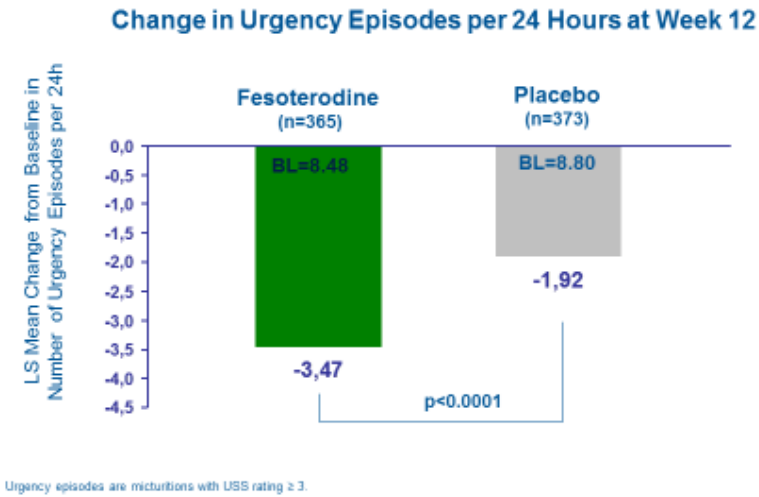
Oelke M et al. Age Aging 2015: 1-11.

SOFIA: Study of Fesoterodine in an Aging Population

A 24-Week, Multi-centre Trial, comprising a 12 Week, Randomised, Double-blind, Placebo-controlled, Parallel-group Phase followed by a 12-Week Open-label Phase, to evaluate the Efficacy and Safety of a Fesoterodine Flexible Dose Regimen in Elderly Patients with Overactive Bladder

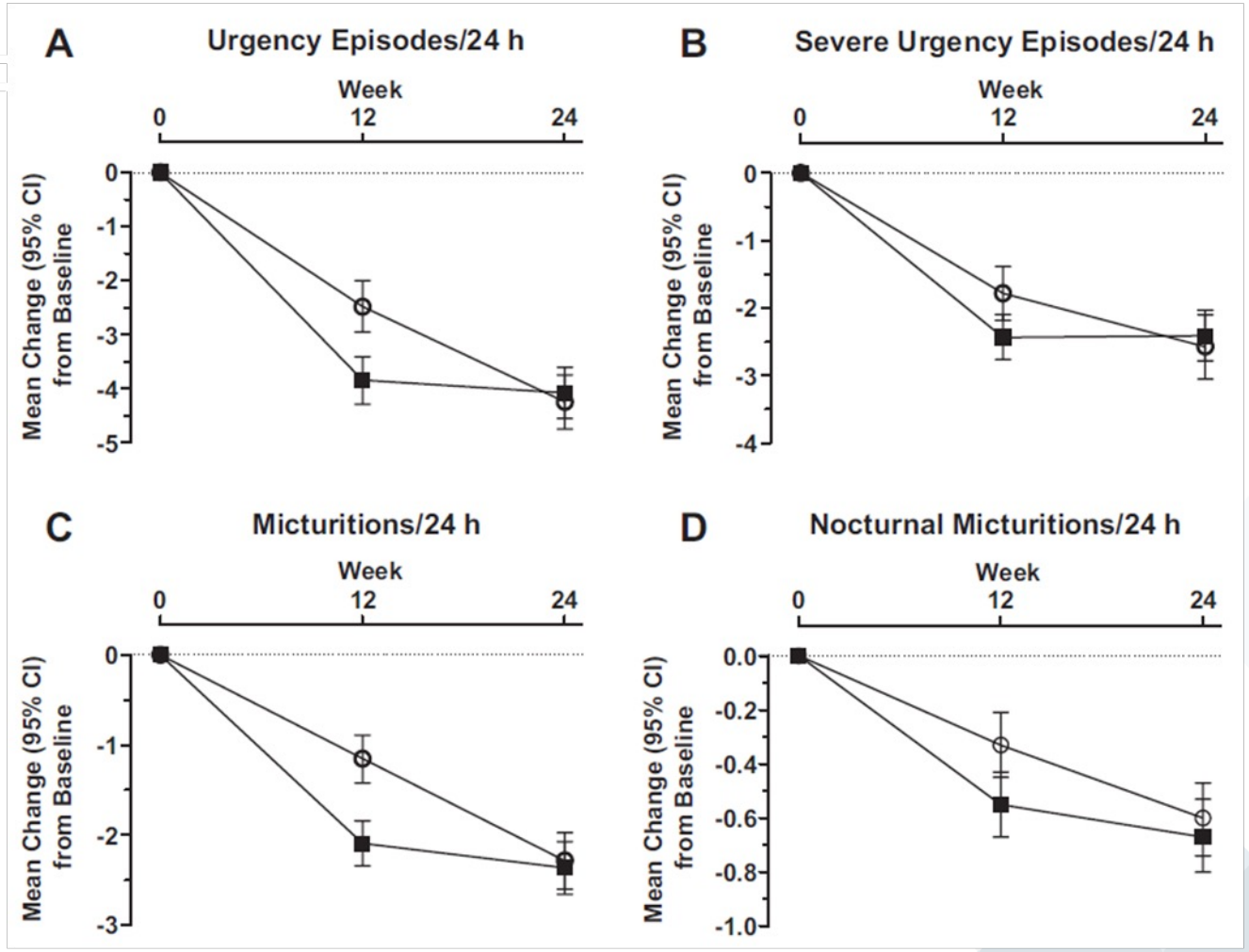
Mean (range)	Fesoterodine (N=392)	Placebo (N=393)
Age (years),	72.6 (65-90)	72.8 (65-89)
≤75 years	265 (68%)	266 (68%)
>75 years	127 (32%)	127 (32%)
Gender Male Female	 179 (46%) 213 (54%)	 188 (48%) 205 (52%)

Fesoterodine Was Superior to Placebo in Reducing Number of Urgency Episodes



J Am Geriatr Soc. 2013 Feb;61(2):185-93.

Remember to give enough time for maximal efficacy



Neurourol Urodyn. 2014 Jan;33(1):106-14.

LU Code 290: physician judgement

Thank you for your follow-up email asking if the Ministry can recover a payment to a pharmacy for mirabegron for a patient with either anticholinergic load issues or pre-existing cognitive impairment if a physician used limited use (LU) reason for use (RFU) code 290.

The decision for use of this drug is entirely up to the clinical judgement of the physician. As long as prescription has LU RFU code 290 written on it (or the pharmacist confirms with the physician that LU RFU code 290 is appropriate), and as long as the pharmacist sees no problem with using LU RFU code 290 for that patient, then the Ministry would not recover a payment to a pharmacy if under the clinical judgement of the physician, and under the professional judgement of the pharmacist, LU RFU code 290 is appropriate for that specific patient.

In other words, if in the clinical judgement of the physician it is not appropriate to try a prior trial on oxybutynin because of either anticholinergic load issues or pre-existing cognitive impairment, etc., and as long as the physician confirms this in writing (by writing the LU RFU code 290 on the prescription – and explains that LU RFU code 290 is being utilized without a trial of oxybutynin for reasons such as anticholinergic load or cognitive impairment) or provides the LU RFU code verbally to the pharmacist who then documents that information on the prescription, then the Ministry would not recover a payment for mirabegron from the pharmacy.

I hope you find this information helpful.

Sincerely,

When to Refer to Urology

- When medications fail (2 AM, 1 Beta-3, Combination)
  - Consideration of 3rd line treatments (Botox, Sacral Neuromodulation)

- Severe symptoms of bladder outlet obstruction
- Bladder-related pain
- Hematuria (gross or microscopic)
- Elevated post void residual (>150mL)
- Elevated PSA/Abnormal DRE**
- Recurrent symptomatic UTI (not bacteriuria of elderly)

Botox Treatment

- Administered via rigid or flexible cystoscope as 20 intradetrusor injections, sparing trigone
  - 0.5 mL per site

    -4% lidocaine left inside for 30 min

- Increase
  - Bladder capacity
  - Volume at first reflex detrusor contractio
  - Compliance
- Decrease detrusor pressures during filling ar voiding
- Improvement in urgency – thought to be afferently mediated

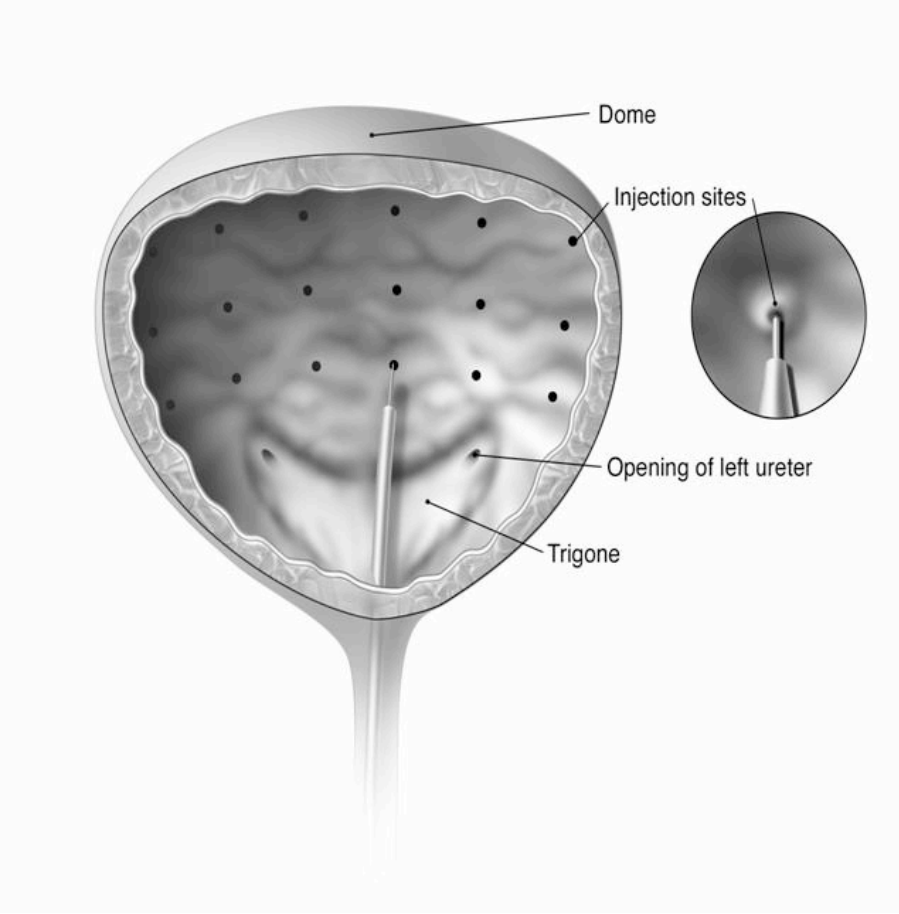
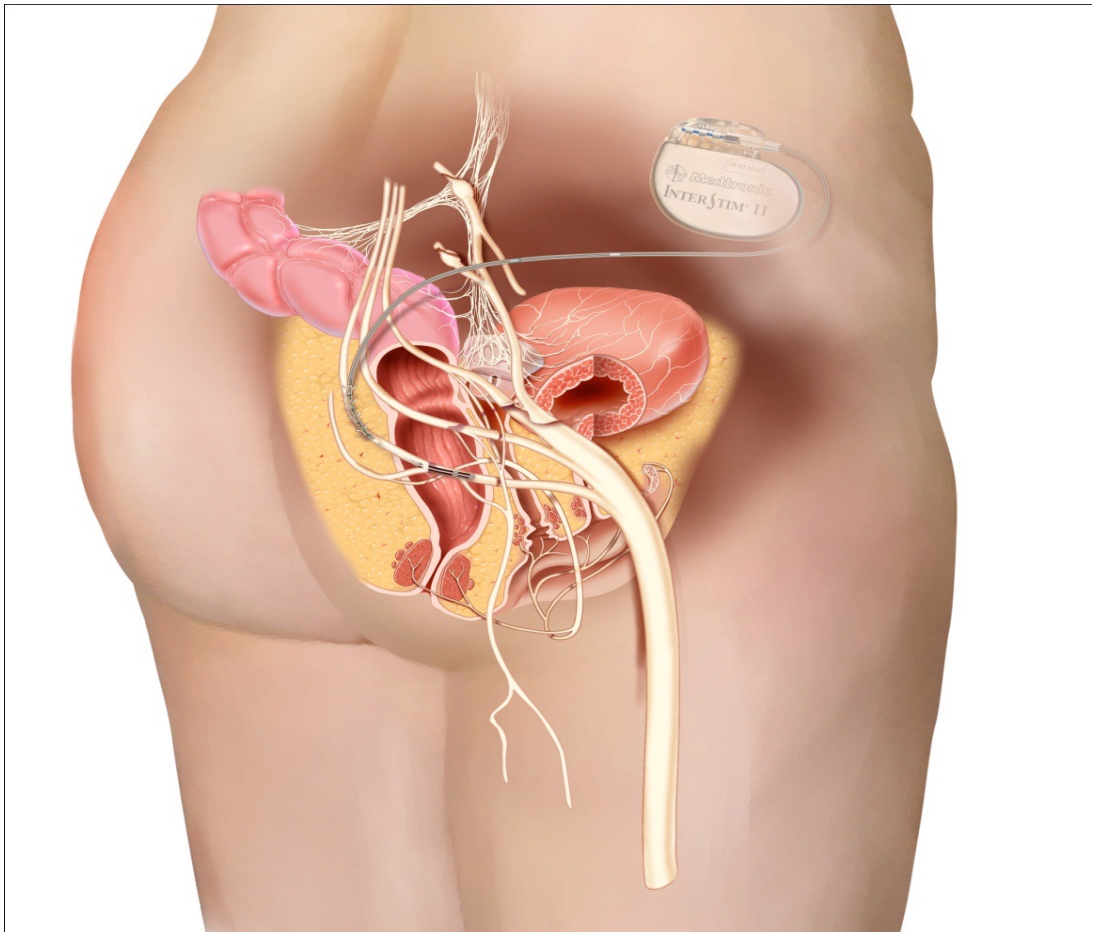
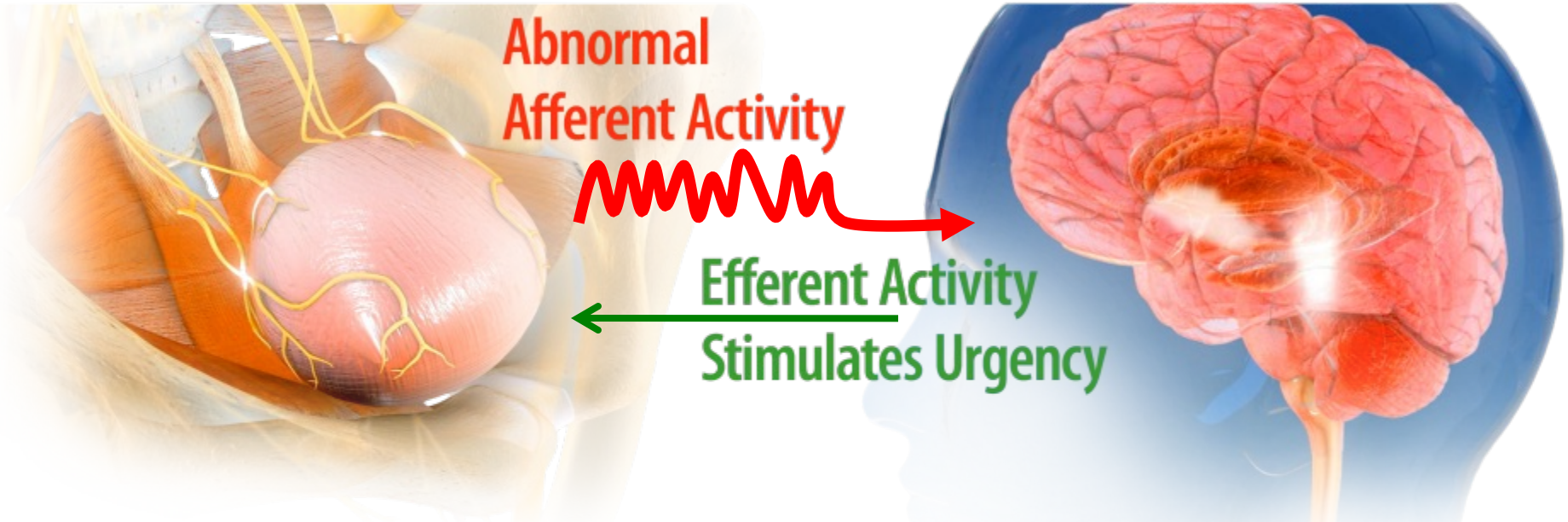


Image obtained from BOTOX® product monograph. Allergan Inc. Markham, ON, 2013.

Sacral Neuromodulation



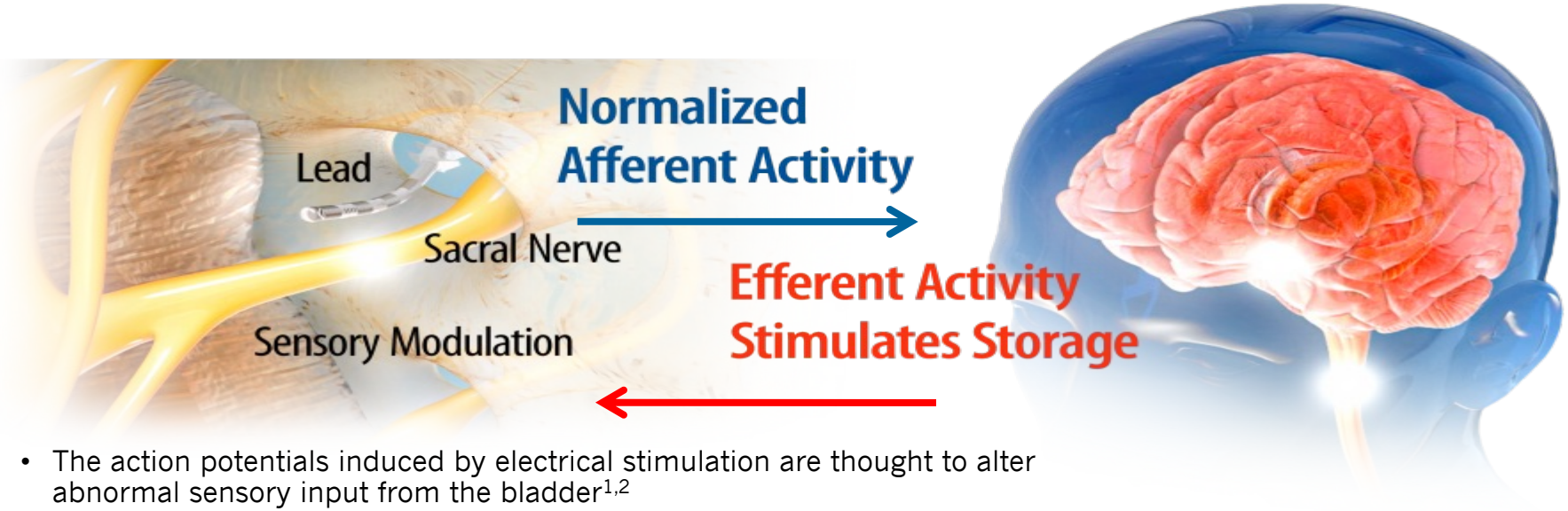
Dysfunction of Afferent Signaling in OAB/FI



- OAB/FI may be a result of increased, abnormal afferent activity, resulting in increased efferent signaling[1]
- Consequently, voluntary control of micturition is compromised[1]

Reference: 1. Leng WW, Morrisroe SN. *Urol Clin N Am.* 2006;33:491-501.

Modulation of Abnormal Afferent Activity within CNS

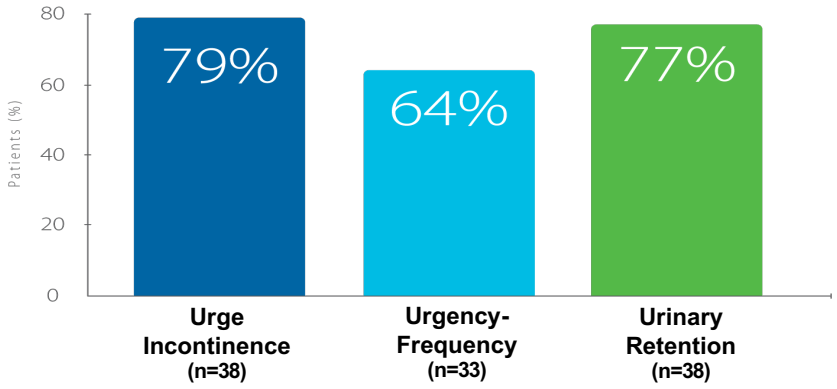


- The action potentials induced by electrical stimulation are thought to alter abnormal sensory input from the bladder[1,2]
- Efferent pathways are uninhibited so as not to suppress voluntary voiding[3]
- Unlike other therapies that target the bladder, bladder regulation occurs without directly influencing the bladder or sphincter muscles[4]

References: 1. Johnson M. *Evidence-Based Practice.* 12th ed. Philadelphia, PA: Elsevier; 2008:259-286. **2.** Chancellor MB, Chartier-Kastler EJ. *Neuromodulation.* 2000;3(1):16-26. **3.** Leng WW, Chancellor MB. *Urol Clin N Am.* 2005;32:11-18. **4.** van der Heesakkers JPFA, Bemelmans BLH. *Curr Opin Urol.* 2006;16:261-267.

Clinical Efficacy of SNM

12-month clinical success for Urinary Control[1]



79% of **urge incontinence** patients achieved clinical success

- 45% remained completely dry
- An additional 34% experienced ≥50% reduction in leaking

64% of **urgency-frequency** patients achieved clinical success

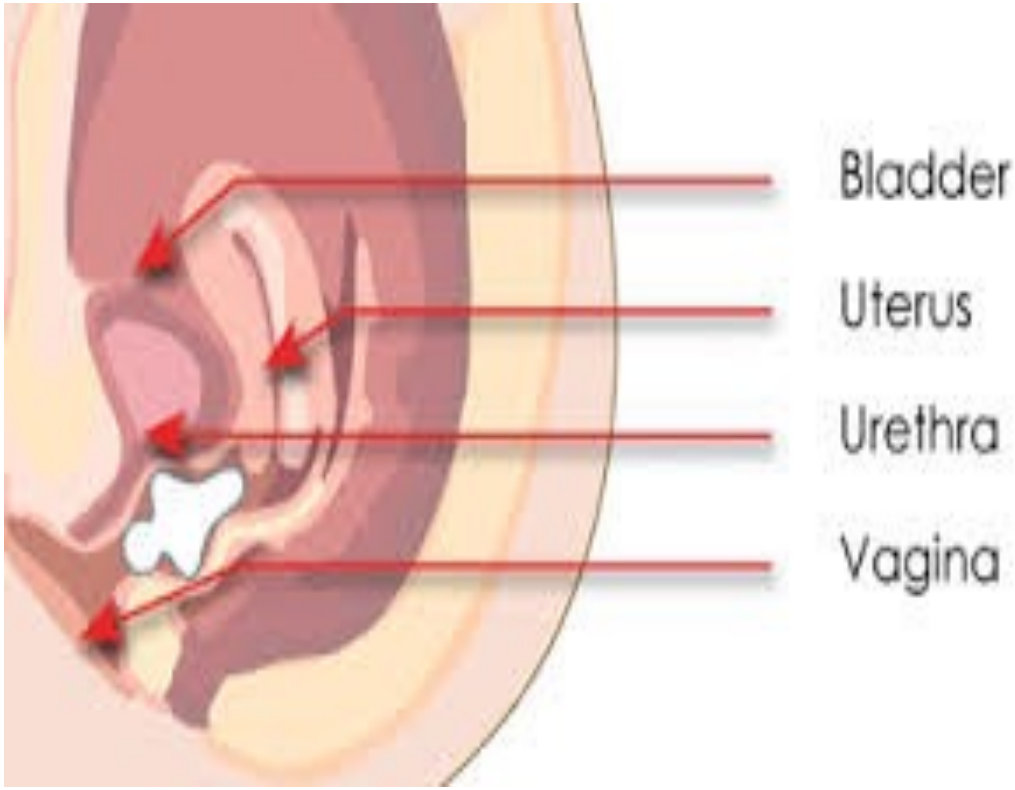
- 31% returned to normal voids (4 to 7 voids/day)
- An additional 33% experienced ≥50% reduction in number of voids

77% of **urinary retention** patients achieved clinical success

- 61% eliminated use of catheters
- An additional 16% experienced ≥50% reduction in catheterized urine volume

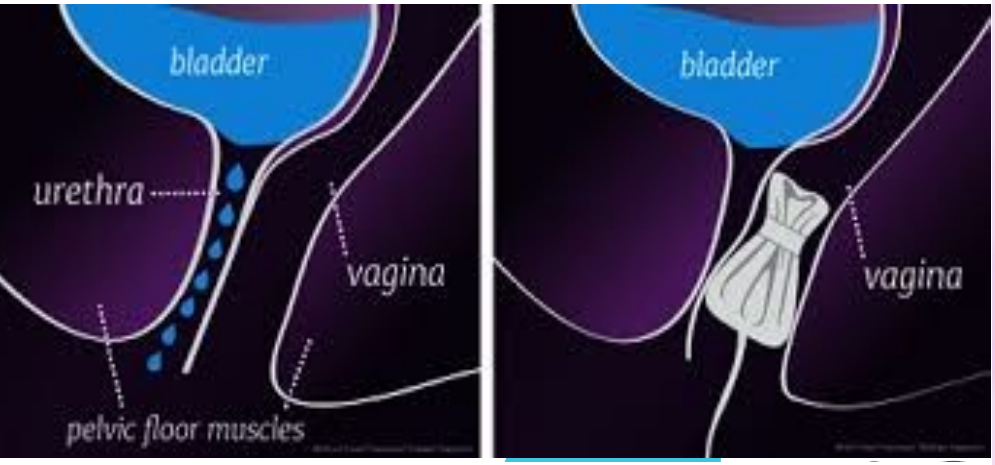
1. Medtronic-sponsored research : InterStim Therapy - Clinical Summary, 2011.

Continence Pessary - Uresta

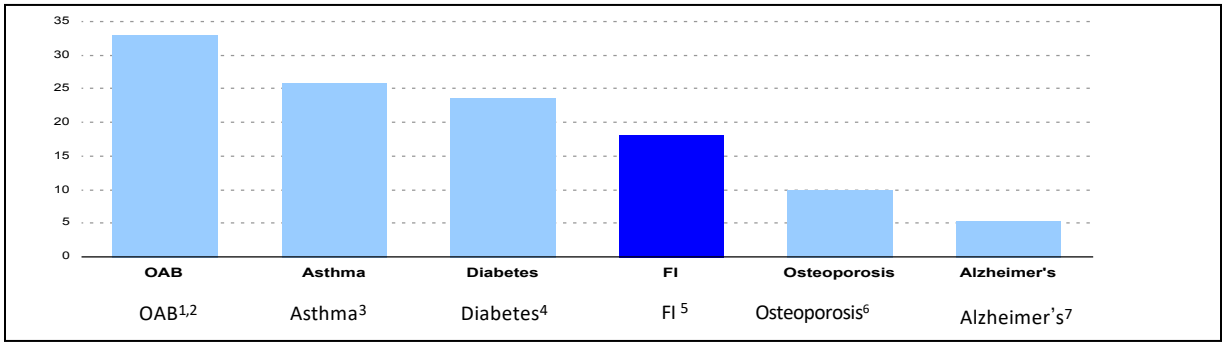


Poise Impressa Bladder Supports

- Novel disposable intravaginal device for SUI
- Silicone arms covered in breathable material
- Worn up to 8 hours per day
- Study showed 85% of women achieved 70% reduction in pad weight gain (p=0.01) (Ziv et al. Am J Obstet Gynecol 2008)



Fecal Incontinence- More Common Than You Might Think



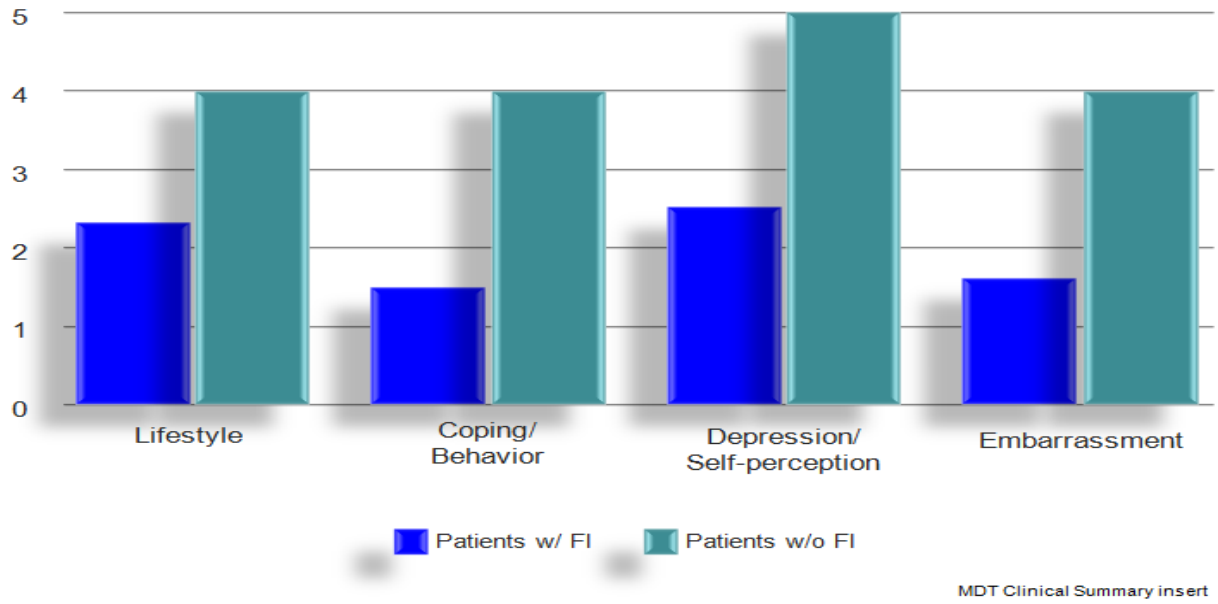
- It is estimated that more than **18 million adults** in the United States
  – 1 in 12 – suffer from fecal incontinence (FI)[5]
- FI is nearly as prevalent as many other chronic diseases and more prevalent than other illnesses well-known to impact many Americans.[1-4,6-7]

1. Stewart, W.F et al. Prevalence and Burden of Overactive Bladder in the United States.*World Jrnl of Urol* 2003:20:327-336
2. Serels S. The wet patient: understanding patients with overactive bladder and incontinence. *Curr Med Res Opin.* 2004;20(6):791-801.
3. Centers for Disease Control and Prevention Website. http://www.cdc.gov/asthma/brfss/03/lifetime/tableL1.htm. Accessed October 18, 2010.
4. National Diabetes Information Clearinghouse Website. http://www.diabetes.niddk.nih.gov/dm/pubs/statistics/#y_people. Accessed October 18, 2010.
5. Whitehead W.E. et al. Fecal Incontinence in US adults: epidemiology and risk factors. *Gastroenterology*. 2009; 137:512-517.
6. National Osteoporosis Foundation Website. http://www.nof.org/node/40. Accessed October 18, 2010.
7. Alzheimer's Association Website. http://www.alz.org/alzheimers_disease_facts_figures.asp. Accessed October 18, 2010.

FI Impacts Quality of Life

Fecal Incontinence Quality of Life Scale (FIQOL) Scores

Note: Higher scores translate to higher quality of life



MDT Clinical Summary insert

FI management: state-of-the-art

Easy, cheap treatments that may or may not work

Unpopular emptying regimens

Treatments few people want

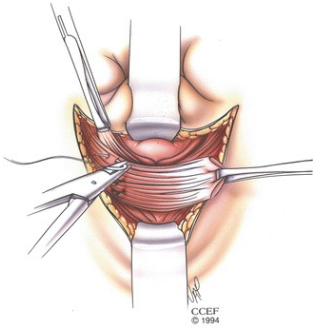
Biofeedback and/or sphincter exercises for the treatment of faecal incontinence in adults (Review)

Norton C, Cody JD

Labour intensive behavioural treatments that may or may not work

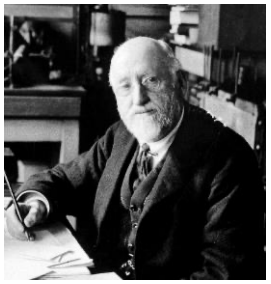
THE COCHRANE COLLABORATION®

A variety of procedures for containment with variable invasiveness and safety

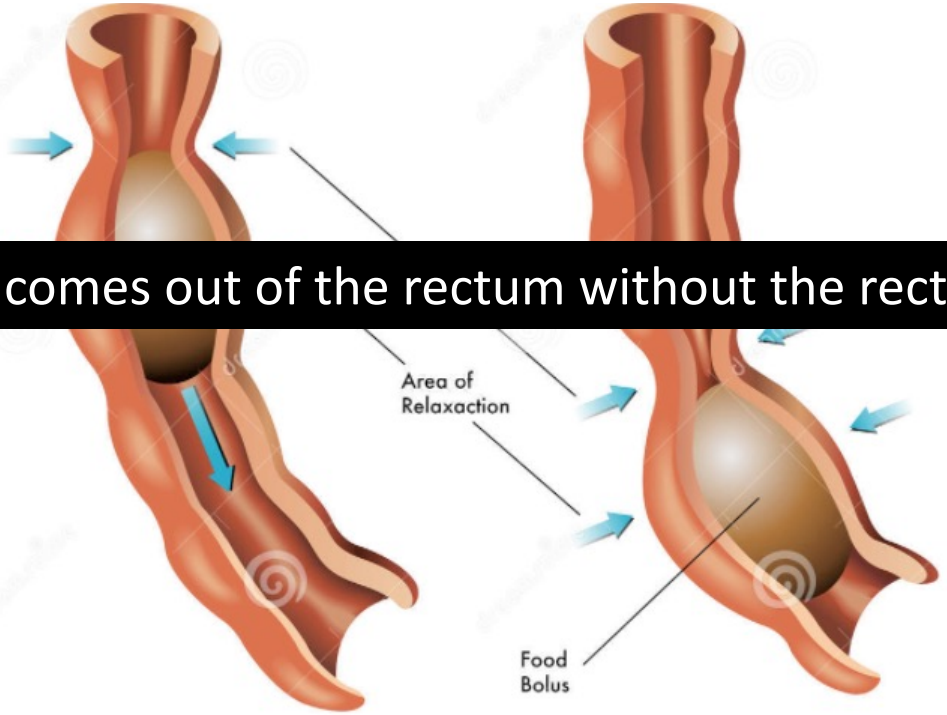


A safe but expensive alternative that we don't fully understand

All GI content is non-Newtonian and does not flow without peristalsis

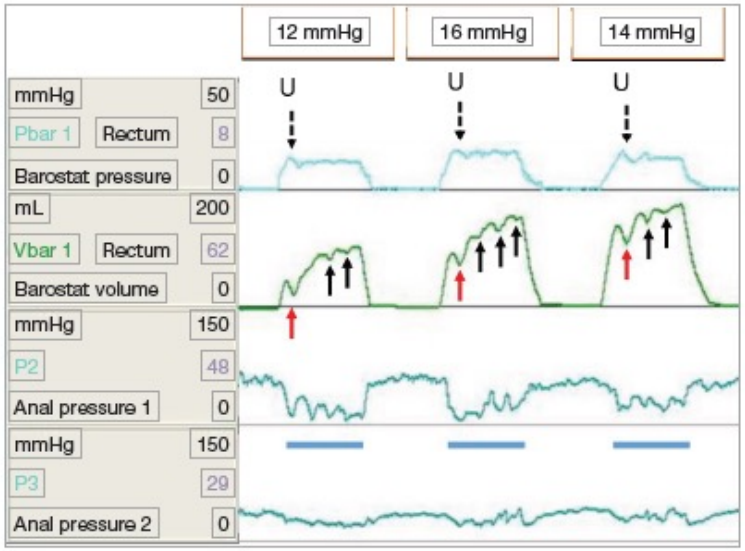


Nothing comes out of the rectum without the rectum pushing it out



(1) Bayliss and Starling: Journ. Physiol., 1899, xxiv, 99.
(2) Bayliss and Starling: Journ. Physiol., 1900, xxvi, 107.
(3) Bayliss and Starling: Journ. Physiol., 1901, xxvi, 125.

Urgency correlates with rectal contractions



Urgency *

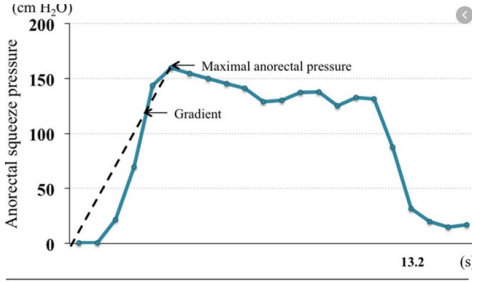
RCR

RAIR

* Corresponds with a rectal contraction

- Read *et al*. Gastroenterology 1986; 90: 53-60.
- Sun WM *et al*. Gut 1990; 31: 1056-61.
- Bannister *et al.,* Br J Surg 1989; 76: 617-621.
- S Vasudevan PhD Thesis (London 2013)

Volitional squeeze of the anal sphincter cannot resist rectal urgency



Parameterers	
Maximal anorectal squeeze pressure (cm H_2O)	159.5
Endurance (s)	13.2
Average (cm H_2O)	94.5
Gradient (cm $H_2O \cdot s^{-1}$)	44.3
Area under the curve (cm $H_2O \cdot s$)	2078.5

Dept. record
~ 30 secs

Review Article

A Joint Mechanism of Action for Sacral Neuromodulation for Bladder and Bowel Dysfunction?

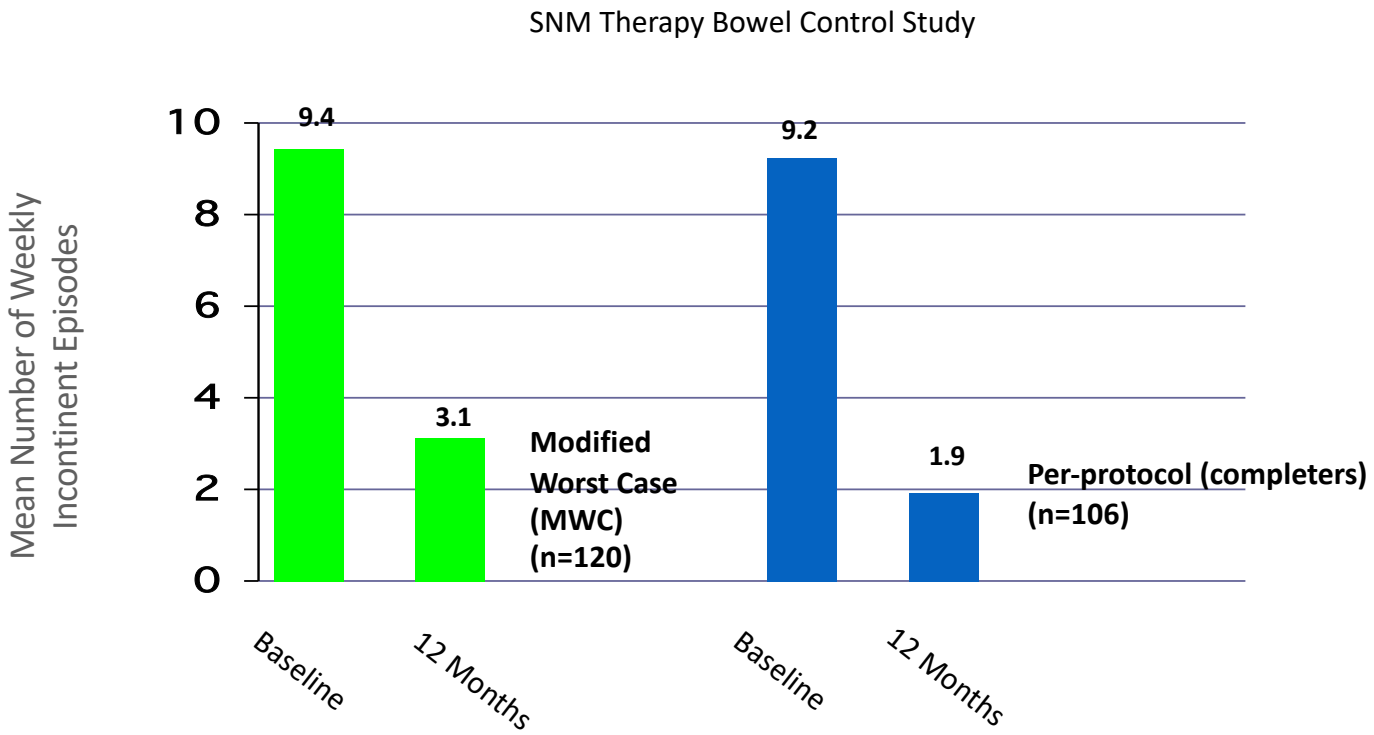
James Jones, Dirk Van de Putte, Dirk De Ridder, Charles Knowles, Ronan O'Connell, Dwight Nelson, An-Sofie Goessaert, and Karel Everaert

Table 3. Effects of SNM on different peripheral and (supra)spinal levels in bowel function: Strength of evidence

Effect of SNM on:	Strength of evidence:	What effect?
Anal		
sensory	C (Human) –	No influence on anal sensation
motor squeeze pressure	D +	Increase—no change (randomized blinded studies all support no change)
motor resting pressure	D (Human) +	Increase—decrease—no change
Rectal		
sensory	D (Human)	Hypersensitivity—Hyposensitivity—No change
	B (Human) +	Normalization of rectal sensation considering baseline sensitivity
motor	B (Human) –	No influence on rectal compliance
Colonic	B (Human) +	Normalization of the colonic motility in incontinence and constipation
Pons and spinal	E	Not known
Brain	A (Animal and humans)	Modulation of brain areas involved in regulation defecation cycle

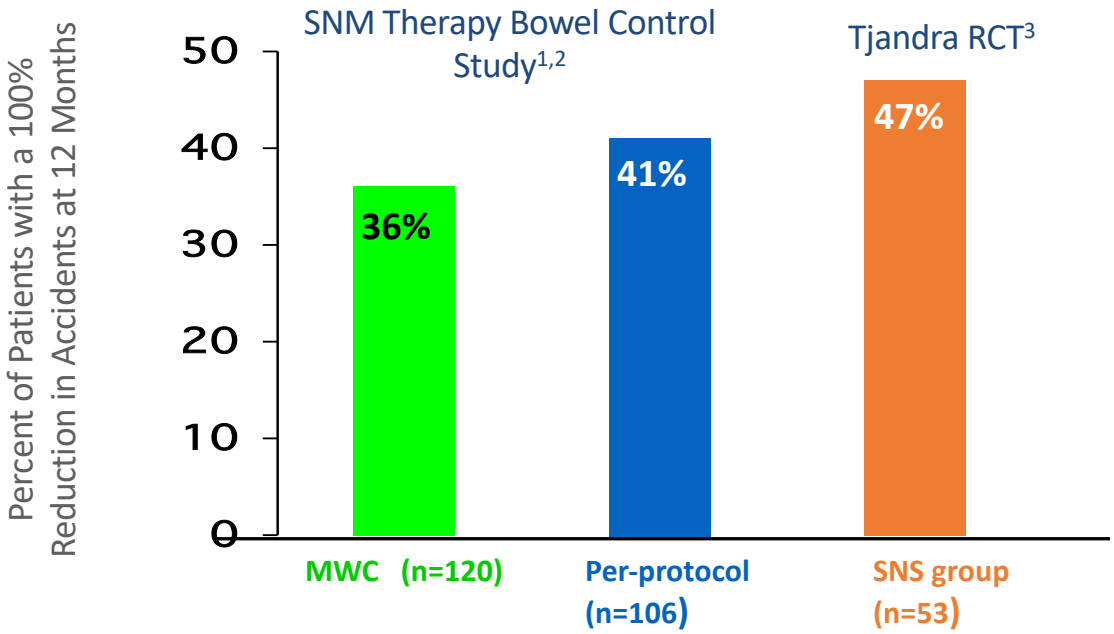
A, strong evidence in multiple species (animal + human); B, strong evidence in 1 species (animal or human); C, weak evidence in at least 1 species; D, contradictory evidence.

Clinical Efficacy: Reduction in Episodes



1. Wexner SD, Coller JA, et al. *Ann Surg*. 2010 Mar;251(3):441-9.
2. Medtronic-sponsored research. InterStim Therapy Clinical Summary - 2011.

Clinical Efficacy: Complete Continence



1. Wexner SD, Coller JA, et al. *Ann Surg*. 2010 Mar;251(3):441-9.

2. Medtronic-sponsored research : InterStim Therapy - Clinical Summary, 2011.

3. Tjandra JJ et al. Sacral nerve stimulation is more effective than optimal medical therapy for severe fecal incontinence: a randomized, controlled study. *Dis Colon Rectum.* May 2008;51(5):494-502.

Key messages

- Management of older persons incontinence needs a broad view and should be treated
- Management of other diseases and medications are as important as managing the bladder condition itself
- Many effective treatments are available, but aged residents in LTC may experience challenges relating to polypharmacy and tolerability
- Avoid oxybutynin, as newer antimuscarinics rarely give cognitive side effects (but consider AC Load)
- Mirabegron is an alternative option with different MOA and side effect profile

Thank you

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