

Urinary Incontinence

Nicholas Rockefeller, MD
2023

NMAFP Winter Refresher

Saturday, February 25,

Urinary Incontinence

- Overflow incontinence
- Functional incontinence
- Insensible incontinence
- **Overactive bladder/urgency urinary incontinence**
- **Stress urinary incontinence**

Urinary Incontinence

- **Delirium**
 - Incontinence may be secondary to delirium and will often stop when acute delirium resolves.
- **Infection**
 - Symptomatic infection may increase urinary tract irritation and resulting incontinence.
- **Atrophy of vaginal tissues**
 - Vaginitis may result in the same symptoms of an infection.
- **Psychological**
 - Depression may be occasionally associated with incontinence.
- **Excessive urine production**
 - Excessive intake, diabetes, hypercalcemia, congestive heart failure and peripheral edema can all lead to polyuria, which can exacerbate incontinence.
- **Restricted mobility**
 - Incontinence may be precipitated or aggravated if the patient is unable to toilet in a timely fashion.
- **Stool impaction**
 - Patients with impacted stool can have urge or overflow urinary incontinence and may also have concomitant fecal incontinence.

Urinary Incontinence

- **Pharmacologic**

- **Sedatives**

- Alcohol and long-acting benzodiazepines
 - confusion and secondary incontinence.

- **Diuretics**

- diuresis may overwhelm the bladder's capacity
 - uninhibited detrusor contractions - urge incontinence

- **Anticholinergics**

- Huge number of meds have anticholinergic properties
 - urinary retention w/frequency and overflow incontinence.

- **Alpha-antagonists**

- Tone in the smooth muscles of the bladder neck and proximal sphincter is decreased with alpha adrenergic antagonists. Women treated with these drugs for hypertension may develop or have an exacerbation of stress incontinence

Urinary Incontinence

- **Overflow incontinence**

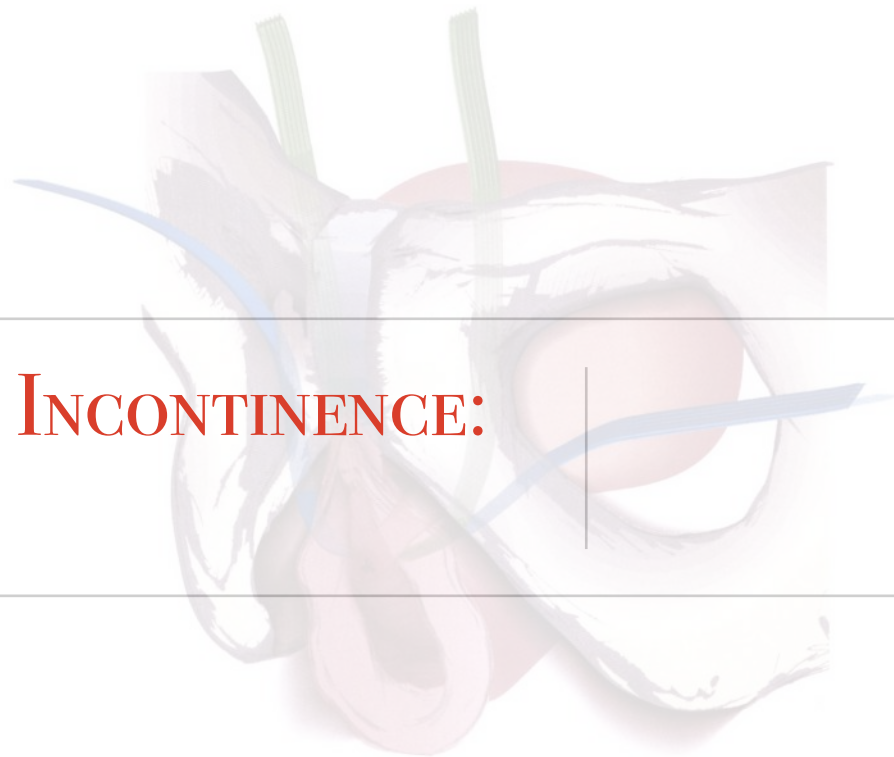
- If post void residual is $>150\text{cc}$, then intermittent self catheterization should be started and titrated frequency until PVR $<150\text{cc}$

- **Functional incontinence**

- Optimization of home factors, bedside commode for geriatric patients with nocturia

- **Insensible incontinence**

- Post void residual, trial of oral medication, urodynamics



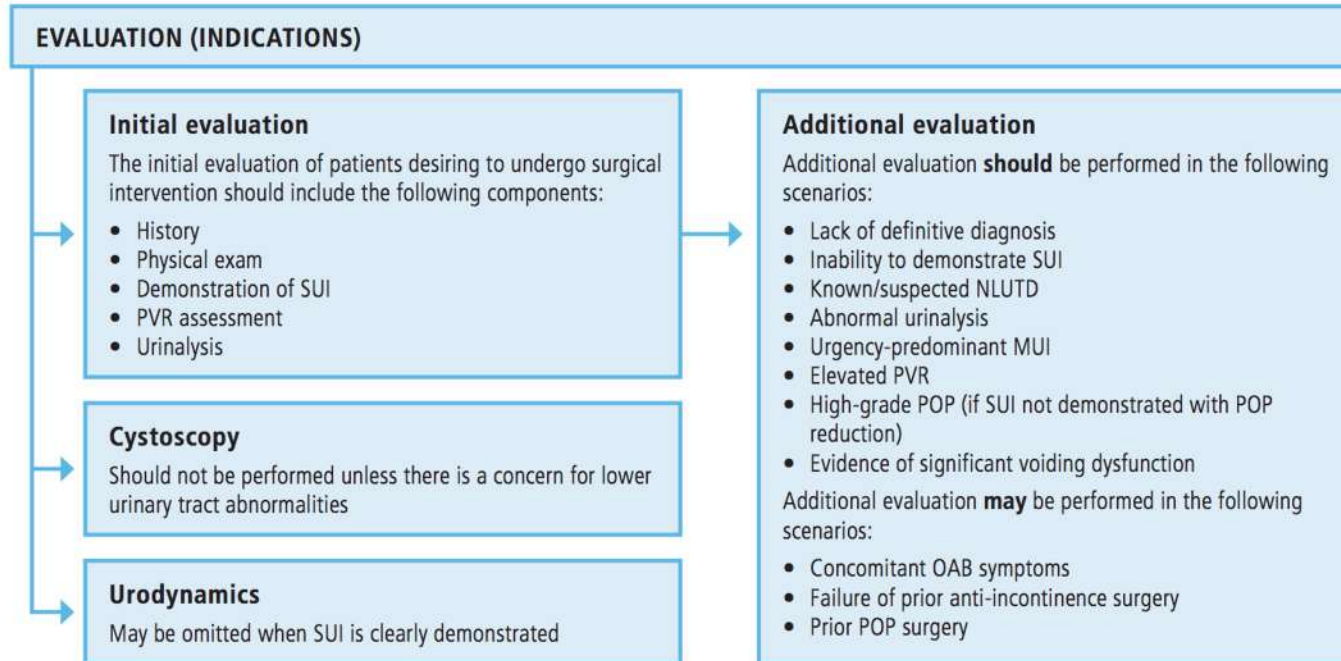
STRESS URINARY INCONTINENCE: TREATMENTS

STRESS URINARY INCONTINENCE (SUI)

- Definitions (AUA):
 - Stress Urinary Incontinence (SUI): the symptom of urinary leakage due to increased abdominal pressure, which can be caused by activities such as sneezing, coughing, exercise, lifting, and position change.
 - Intrinsic sphincter deficiency (ISD): often defined as a leak point pressure of less than 60 cm H₂O or a maximal urethral closure pressure of less than 20 cm H₂O, often in the face of minimal urethral mobility.

STRESS URINARY INCONTINENCE (SUI)

Female Stress Urinary Incontinence: AUA/SUFU Evaluation and Treatment Algorithm



STRESS URINARY INCONTINENCE (SUI)

In patients who wish to undergo treatment, physicians should counsel regarding the availability of observation, pelvic floor muscle training, other non-surgical options, and surgical interventions. Physicians should counsel patients on potential complications specific to the treatment options.

TREATMENT

Non-Surgical

- Continence pessary
- Vaginal inserts
- Pelvic floor muscle exercises

Surgical

- Bulking agents
- Midurethral sling (synthetic)
- Autologous fascia pubovaginal sling
- Burch colposuspension

If a midurethral sling surgery is selected, either the retropubic or transobturator midurethral sling may be offered. A single-incision sling may be offered to index patients if they are informed as to the immaturity of evidence regarding their efficacy and safety. Physicians must discuss the specific risks and benefits of mesh as well as alternatives to a mesh sling.

SPECIAL CASES

1. Fixed immobile urethra

- Pubovaginal sling
- Retropubic midurethral sling
- Urethral bulking agents

2. Concomitant surgery for POP repair and SUI

Any incontinence procedure

3. Concomitant NLUTD

Surgical treatment following appropriate evaluation and counseling

4. Child-bearing, diabetes, obesity, geriatric

Surgical treatment following appropriate evaluation and counseling

Non-Surgical Treatment

Published:
14 May 2014



Cochrane

Trusted evidence.
Informed decisions.
Better health.

Authors:
Dumoulin C, Hay-Smith EC, Mac
Habée-Séguin G

**Pelvic floor muscle training versus no treatment for urinary incontinence
in women**

Primary Review Group:
Incontinence Group

● PFPT

- PFPT should be included in first-line conservative management programs for women with stress and any type of urinary incontinence.
 - SUI treated with PFMT: 8 times more likely than controls to report that they were cured (46/82 (56.1%) versus 5/83 (6.0%), RR 8.38, 95% CI 3.68 to 19.07).
 - 17 times more likely to report cure or improvement (32/58 (55%) versus 2/63 (3.2%), RR 17.33, 95% CI 4.31 to 69.64).

NON-SURGICAL TREATMENT

[Obstet Gynecol.](#) Author manuscript; available in PMC 2010 Aug 3.

Published in final edited form as:

[Obstet Gynecol.](#) 2010 Mar; 115(3): 609–617.

doi: [10.1097/AOG.0b013e3181d055d4](#)

PMCID: PMC2914312

NIHMSID: NIHMS205622

PMID: [20177294](#)

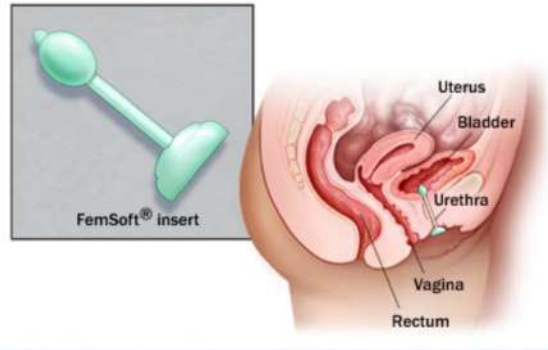
A Trial of Continence Pessary vs. Behavioral Therapy vs. Combined Therapy for Stress Incontinence

[Holly E. Richter](#), PhD, MD,¹ [Kathryn L. Burgio](#), PhD,^{1,2} [Linda Brubaker](#), MD, MS,³ [Ingrid E. Nygaard](#), MD,⁴ [Wen Ye](#), PhD,⁵ [Allison Weidner](#), MD,⁶ [Catherine S. Bradley](#), MD, MS,⁷ [Victoria L. Handa](#), MD, MHS,⁸ [Diane Borello-France](#), PhD,⁹ [Patricia S. Goode](#), MSN, MD,^{1,2} [Halina Zyczynski](#), MD,¹⁰ [Emily S. Lukacz](#), MD,¹¹ [Joseph Schaffer](#), MD,¹² [Matthew Barber](#), MD, MHS,¹³ [Susan Meikle](#), MD, MSPH,¹⁴ and [Cathie Spino](#), DSc⁵, for the Pelvic Floor Disorders Network

- “Ambulatory Treatments for Leakage Associated with Stress Incontinence” (ATLAS)
 - Behavioral therapy resulted in greater patient satisfaction and fewer bothersome incontinence symptoms than pessary at 3 months, but differences did not persist to 12 months.
 - Combination therapy was not superior to single-modality therapy (was superior to Pessary alone but not PFPT alone)

NON-SURGICAL TREATMENT

- Urethral Inserts / Occlusive Devices
 - FemSoft



NON-SURGICAL TREATMENT

- Urethral Inserts / Occlusive Devices
 - Imprensa

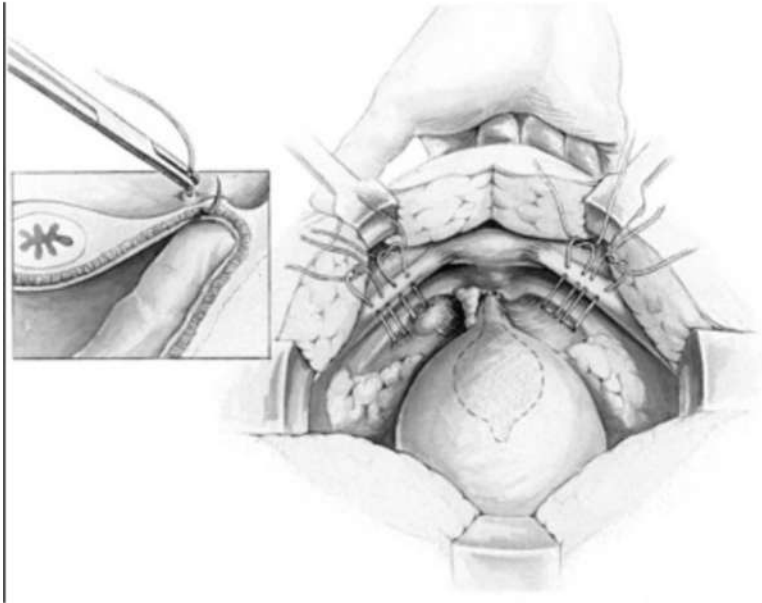
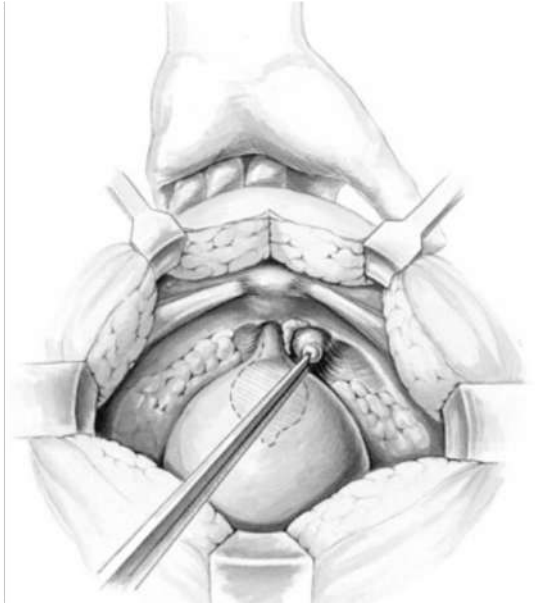


RETROPUBIC OPERATIONS

- Burch Colposuspension (with Tanagho modification)

BURCH PROCEDURES

- Burch Colposuspension (with Tanagho modification)



BURCH PROCEDURES

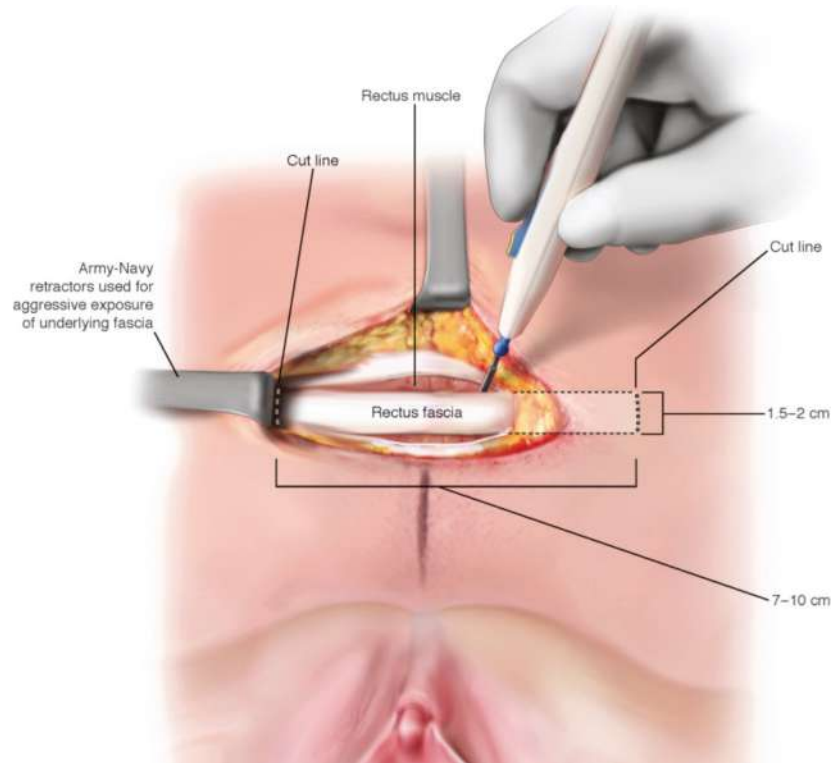
BJOG, 2008 Jan;115(2):219-25; discussion 225.

Randomised trial of laparoscopic Burch colposuspension versus tension-free vaginal tape: long-term follow up.

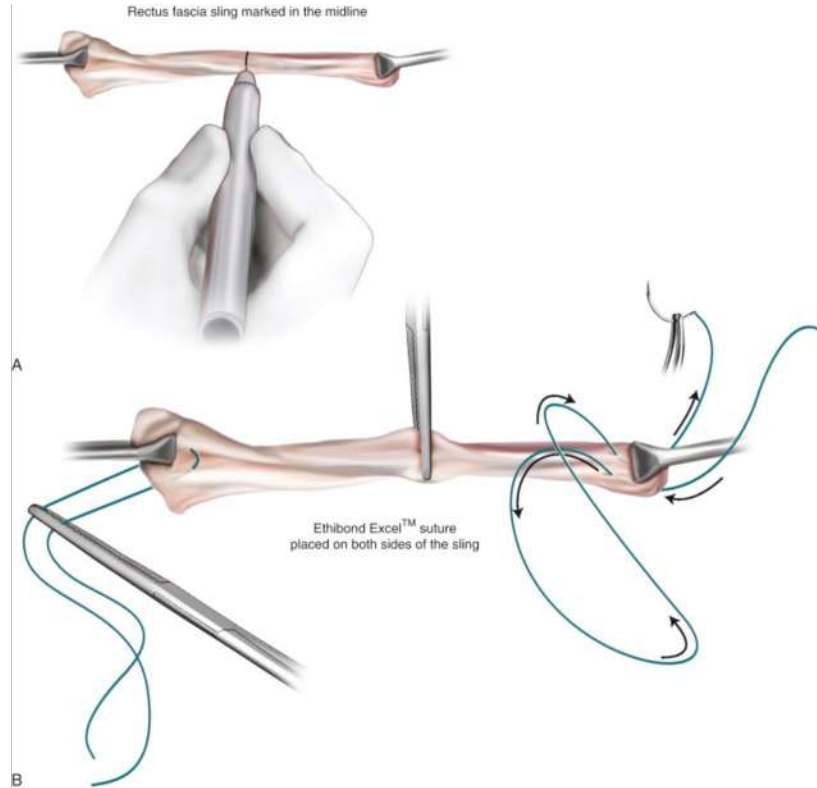
Jelovsek JE¹, Barber MD, Karram MM, Walters MD, Paraiso MF.

- Subjects reporting any urinary incontinence 4-8 yrs after surgery:
 - laparoscopic Burch 58% compared with TVT 48%(Relative Risk (RR):1.19; 95% CI: 0.71-2.0)
- Bothersome SUI symptoms were seen in 11% (LscB) and 8%(TVT), respectively, 4-8 years after surgery ($P = 0.26$).

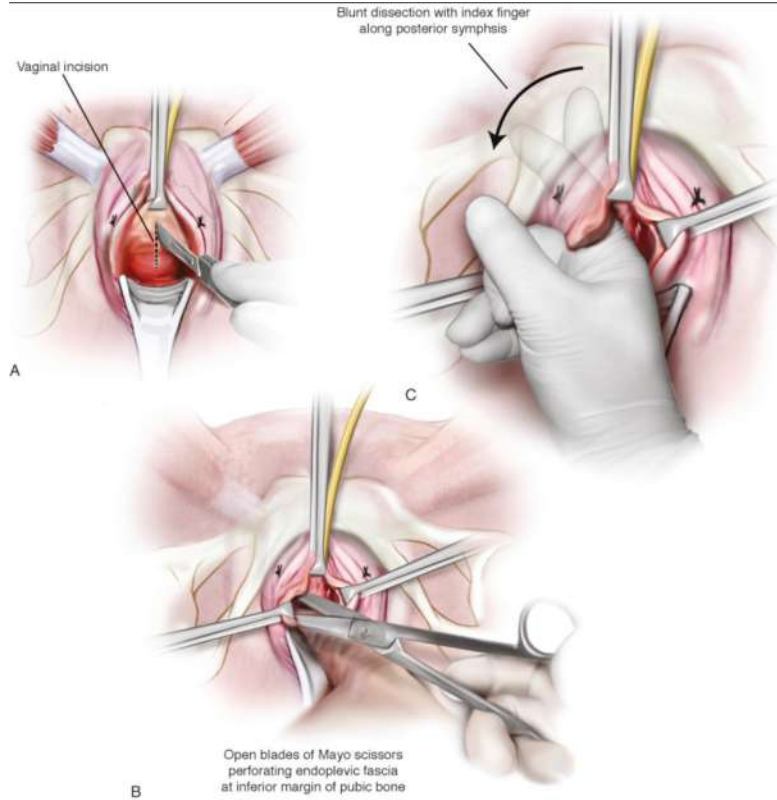
PUBOVAGINAL SLINGS



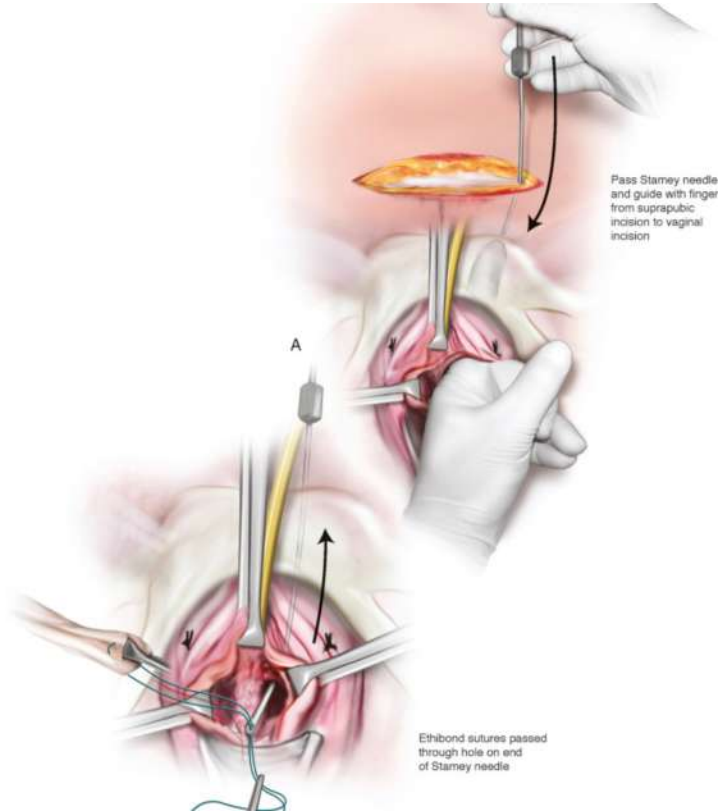
PUBOVAGINAL SLINGS



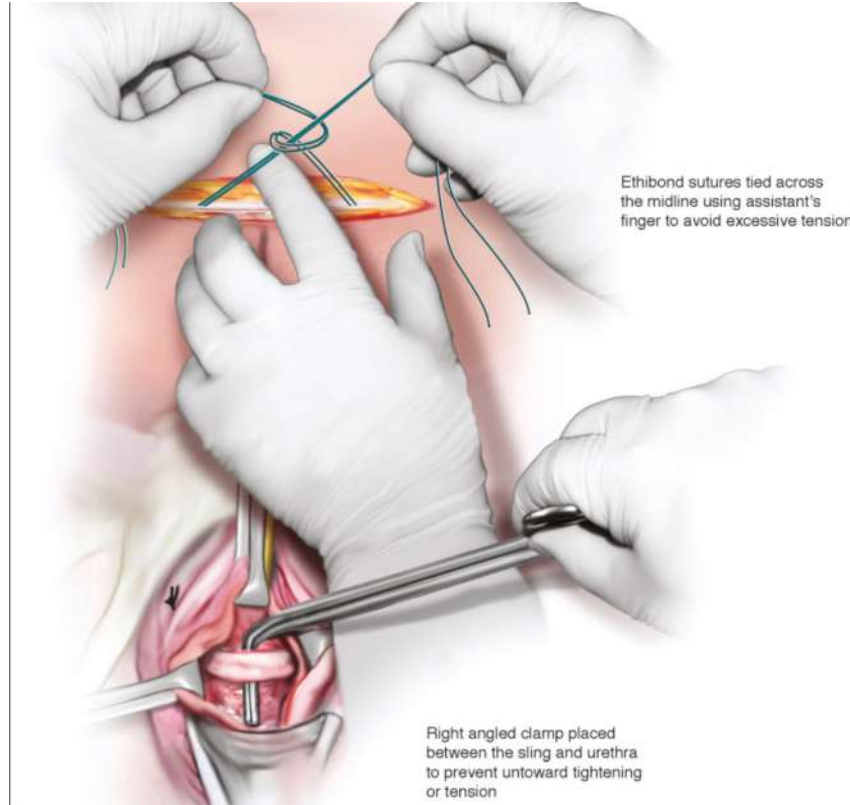
PUBOVAGINAL SLINGS



PUBOVAGINAL SLINGS



PUBOVAGINAL SLINGS



PUBOVAGINAL SLINGS

- SISTER Trial N=655

ORIGINAL ARTICLE

Burch Colposuspension versus Fascial Sling to Reduce Urinary Stress Incontinence

Michael E. Albo, M.D., Holly E. Richter, Ph.D., M.D., Linda Brubaker, M.D., Peggy Norton, M.D., Stephen R. Kraus, M.D., Philippe E. Zimmern, M.D., Toby C. Chai, M.D., Halina Zyczynski, M.D., Ananias C. Diokno, M.D., Sharon Tennstedt, Ph.D., Charles Nager, M.D., L. Keith Lloyd, M.D., et al., for the Urinary Incontinence Treatment Network*

May 24, 2007

N Engl J Med 2007; 356:2143-2155

DOI: 10.1056/NEJMoa070416

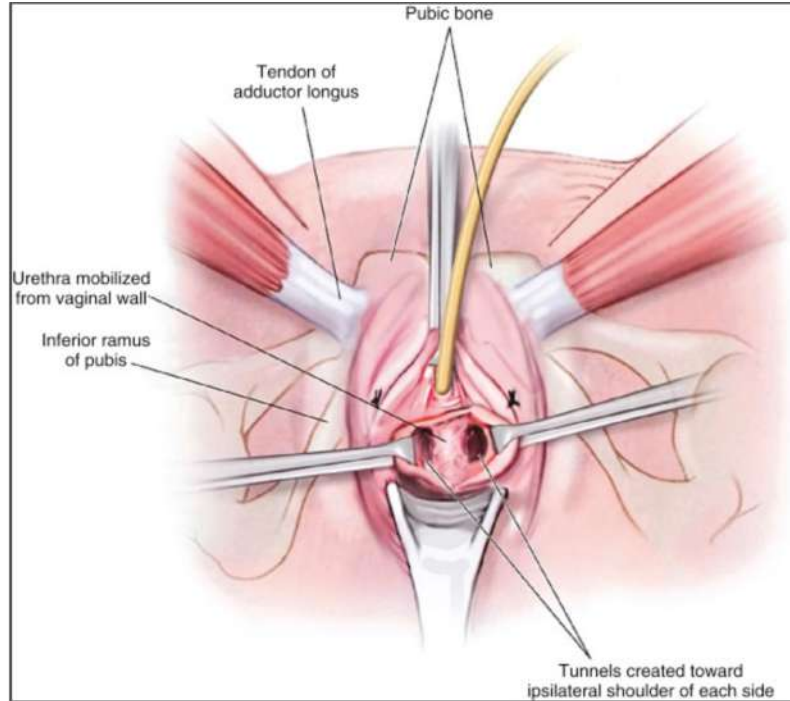
PUBOVAGINAL SLINGS

- N=655 RCT - Pubovaginal sling vs Burch Procedure 520 women (79%) completed the outcome assessment.
- At 24 months, success rates were higher for women who underwent the sling procedure than for those who underwent the Burch procedure,
 - overall success (47% vs. 38%, $P=0.01$)
 - category specific to stress incontinence (66% vs. 49%, $P<0.001$).
- However, more women who underwent the sling procedure had urinary tract infections, difficulty voiding, and postoperative urge incontinence.

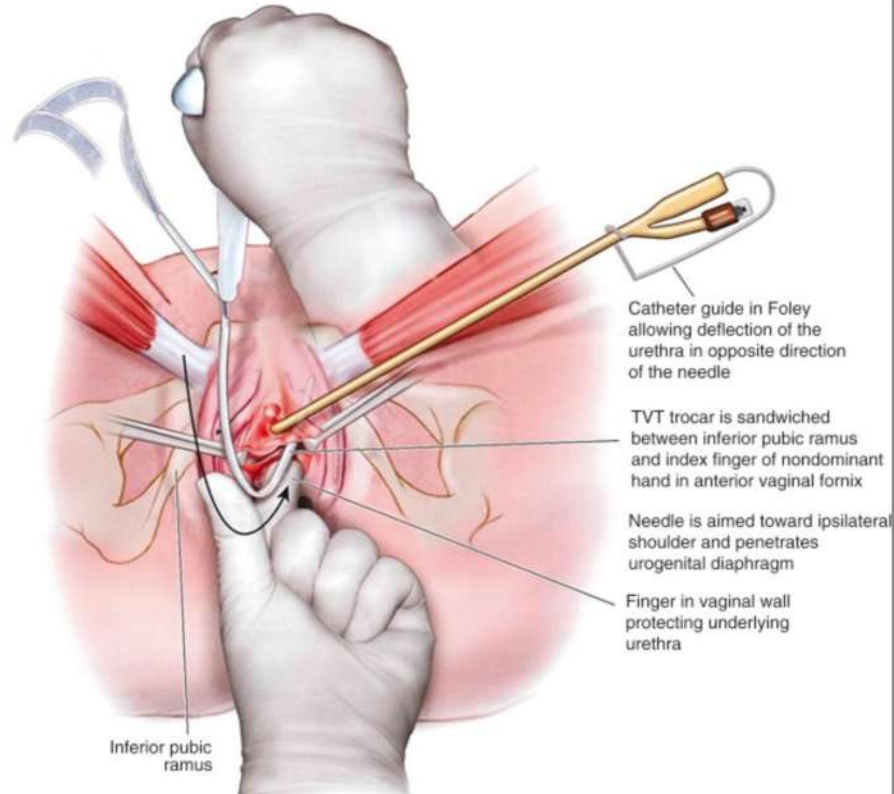
MESH MIDURETHRAL SLING

- Transobturator Tape (TOT)
- Transvaginal Tape (TVT)

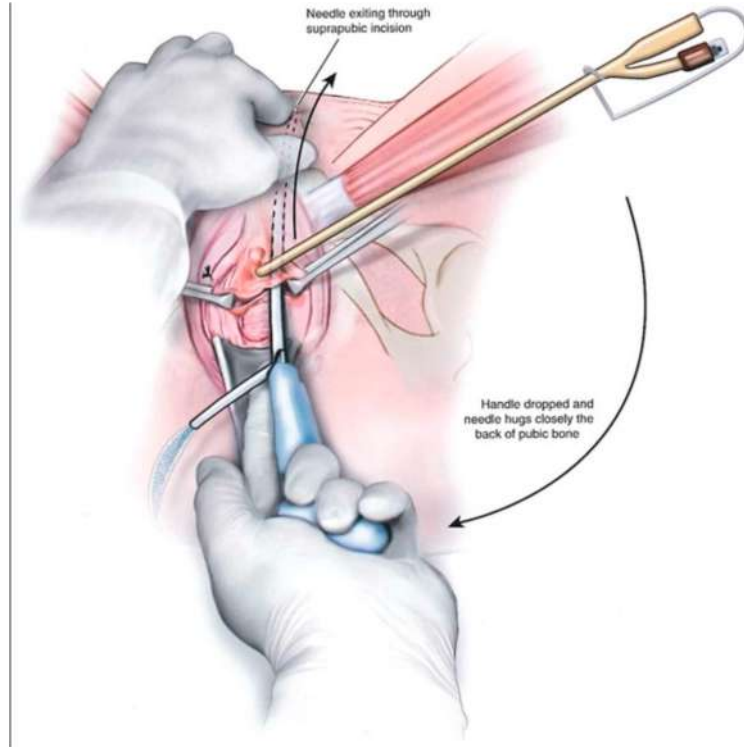
MESH MIDURETHRAL SLING



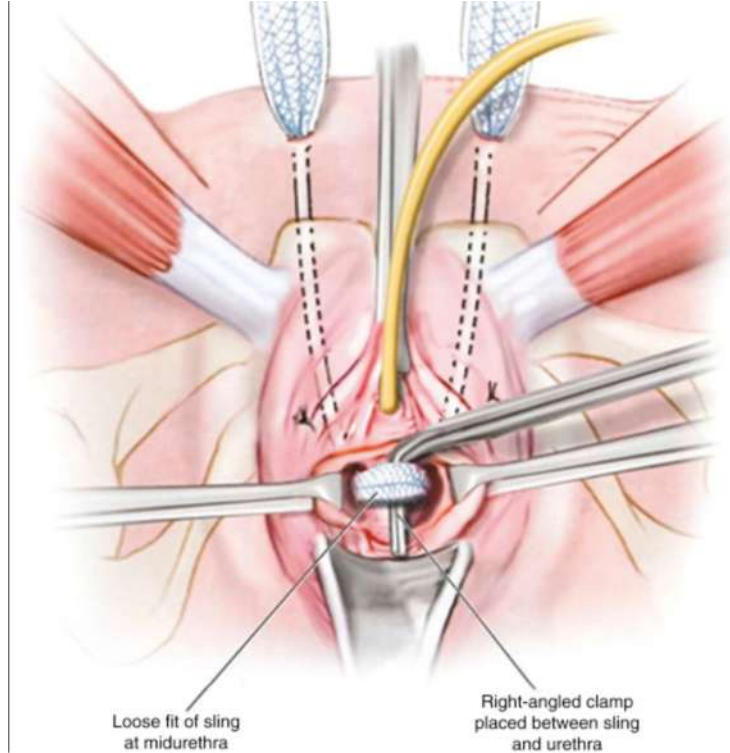
MESH MIDURETHRAL SLING



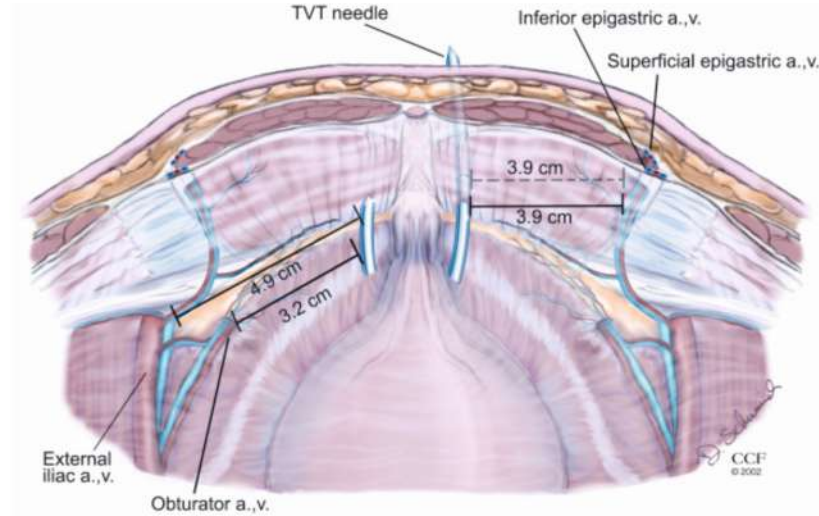
MESH MIDURETHRAL SLING



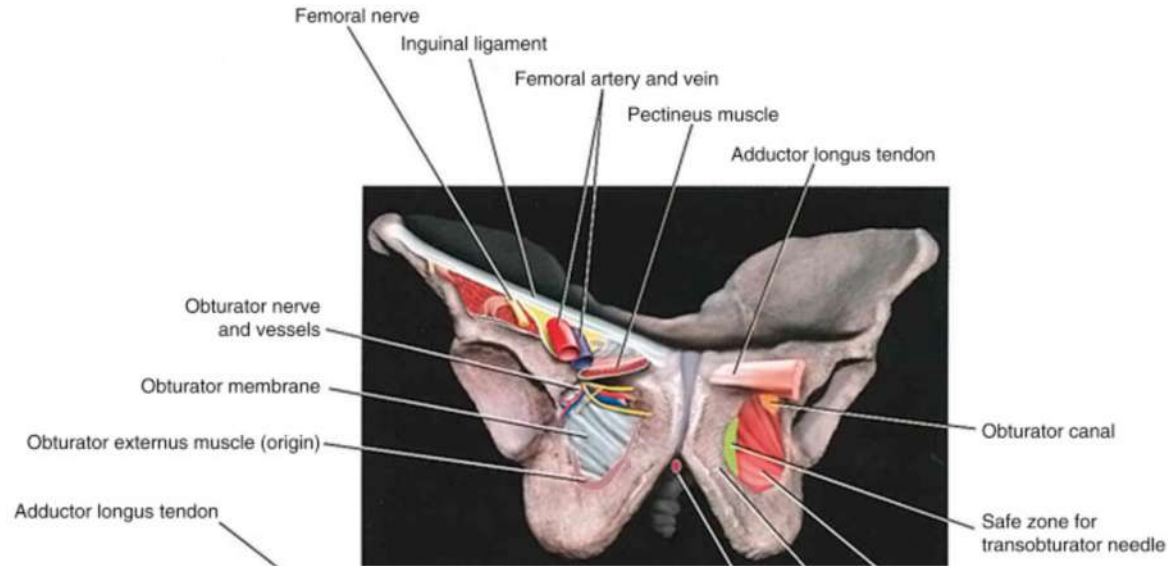
MESH MIDURETHRAL SLING



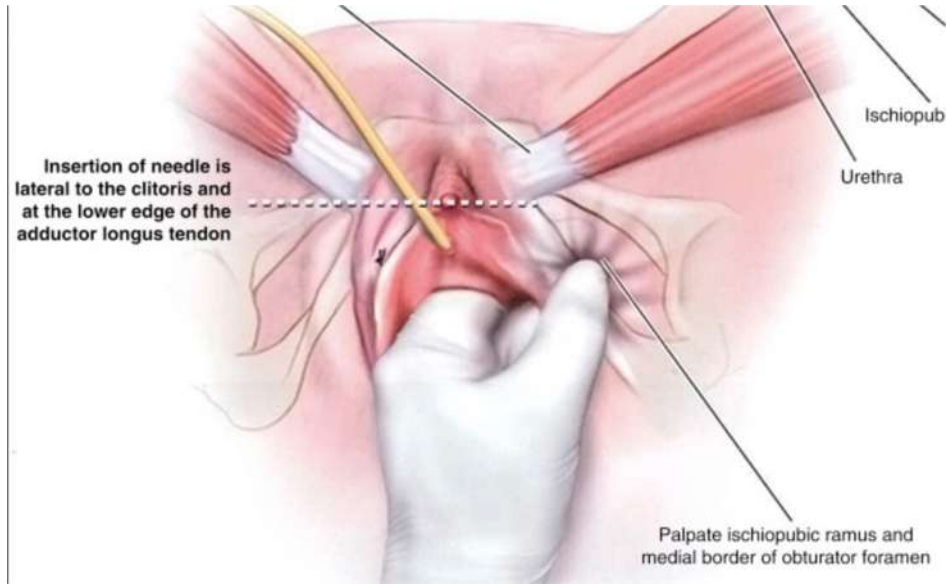
MESH MIDURETHRAL SLING



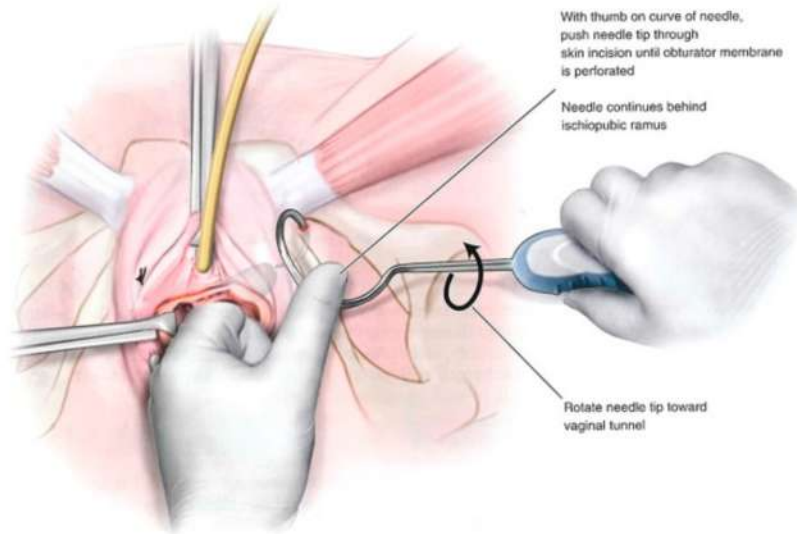
MESH MIDURETHRAL SLING



MESH MIDURETHRAL SLING



MESH MIDURETHRAL SLING



MESH MIDURETHRAL SLING

- Transobturator Tape (TOT)
- Transvaginal Tape (TVT)

MESH MIDURETHRAL SLING

- TOMUS Trial

[N Engl J Med](#). Author manuscript; available in PMC 2010 Dec 3.

Published in final edited form as:

[N Engl J Med. 2010 Jun 3; 362\(22\): 2066–2076.](#)

Published online 2010 May 17. doi: [10.1056/NEJMoa0912658](#)

PMCID: PMC2962585

NIHMSID: NIHMS212424

PMID: [20479459](#)

Retropubic versus Transobturator Midurethral Slings for Stress Incontinence

[Holly E. Richter](#), Ph.D., M.D., [Michael E. Albo](#), M.D., [Halina M. Zyczynski](#), M.D., [Kimberly Kenton](#), M.D., [Peggy A. Norton](#), M.D., [Larry T. Sirls](#), M.D., [Stephen R. Kraus](#), M.D., [Toby C. Chai](#), M.D., [Gary E. Lemack](#), M.D., [Kimberly J. Dandreo](#), M.Sc., [R. Edward Varner](#), M.D., [Shawn Menefee](#), M.D., [Chiara Ghetti](#), M.D., [Linda Brubaker](#), M.D., [Ingrid Nygaard](#), M.D., [Salil Khandwala](#), M.D., [Thomas A. Rozanski](#), M.D., [Harry Johnson](#), M.D., [Joseph Schaffer](#), M.D., [Anne M. Stoddard](#), Sc.D., [Robert L. Holley](#), M.D., [Charles W. Nager](#), M.D., [Pamela Moalli](#), M.D., Ph.D., [Elizabeth Mueller](#), M.D., [Amy M. Arisco](#), M.D., [Marlene Corton](#), M.D., [Sharon Tennstedt](#), Ph.D., [T. Debuene Chang](#), M.D., [E. Ann Gormley](#), M.D., and [Heather J. Litman](#), Ph.D., for the Urinary Incontinence Treatment Network²

MESH MIDURETHRAL SLING

- TOMUS Trial N=597
 - Objective cure rate
 - TVT 80.8%, TOT 77.7%
 - No significant difference, met equivalence
 - Subjective cure rate:
 - 62.2% and 55.8%, respectively, 6.4 percentage-point difference; 95% CI, -1.6 to 14.3)
 - Did not differ significantly but also did not meet the predefined criteria for equivalence

MESH MIDURETHRAL SLING

- TOMUS Trial N=597
 - Objective cure:
 - A provocative stress test standardized to volume and position is performed for direct observation of urine leakage. Observed urine loss from the urethra coincidental with the Valsalva maneuver or cough is a positive test; a negative test indicates no urine loss. Pad testing quantifies the amount of urine involuntarily lost and is used to reflect everyday incontinence; it is negative if loss is <15g/24 hrs.
 - Subjective cure:
 - Absence of self-reported symptoms of stress-type urinary incontinence, as assessed with the use of the Medical, Epidemiological and Social Aspects of Aging (MESA) questionnaire (responded never to all 9 MESA questions), no leakage recorded in a 3-day voiding diary and no retreatment for stress incontinence including behavioral, pharmacologic or surgical treatment.

MESH MIDURETHRAL SLING

- TOMUS Trial
 - Adverse Events:
 - TVT:
 - More bladder perforations from trocar passage (5% vs 0%)
 - More voiding dysfunction requiring surgical intervention (2.7% vs 0%)
 - More postoperative UTI's (15.3% vs 9% - combining culture proven, empirically treated, and recurrent cystitis cases)
 - TOT:
 - Neurologic symptoms (pain, numbness, weakness) (10% vs 5%)
 - Vaginal perforation (4% vs 2.4%)

MESH MIDURETHRAL SLING

- OPUS Trial

[N Engl J Med](#). Author manuscript; available in PMC 2012 Dec 21.

Published in final edited form as:

[N Engl J Med. 2012 Jun 21; 366\(25\): 2358–2367.](#)

doi: [10.1056/NEJMoa1111967](#)

PMCID: PMC3433843

NIHMSID: NIHMS396203

PMID: [22716974](#)

A Midurethral Sling to Reduce Incontinence after Vaginal Prolapse Repair

[John T. Wei](#), M.D., [Ingrid Nygaard](#), M.D., [Holly E. Richter](#), Ph.D., M.D., [Charles W. Nager](#), M.D., [Matthew D. Barber](#), M.D., M.H.S., [Kim Kenton](#), M.D., [Cindy L. Amundsen](#), M.D., [Joseph Schaffer](#), M.D., [Susan F. Meikle](#), M.D., M.S.P.H., and [Cathie Spino](#), D.Sc., for the Pelvic Floor Disorders Network

MESH MIDURETHRAL SLING

- OPUS Trial, N=337
 - At 3 months, the rate of urinary incontinence (or treatment) was 23.6% in the sling group and 49.4% in the sham group ($P < 0.001$).
 - At 12 months, urinary incontinence (allowing for subsequent treatment of incontinence) was present in 27.3% and 43.0% of patients in the sling and sham groups, respectively ($P = 0.002$).
 - NNT (sling to prevent one case of SUI at 12 months) was 6.3.

MESH MIDURETHRAL SLING

- OPUS Trial, N=337
 - Adverse Events greater in sling group ($P \leq 0.05$ for all comparisons).
 - Bladder perforation (6.7% vs. 0%)
 - UTI (31.0% vs. 18.3%)
 - major bleeding complications (3.1% vs. 0%)
 - incomplete bladder emptying 6 weeks after surgery (3.7% vs. 0%)

MESH MIDURETHRAL SLING

Original Investigation

September 17, 2019

Effect of Behavioral and Pelvic Floor Muscle Therapy Combined With Surgery vs Surgery Alone on Incontinence Symptoms Among Women With Mixed Urinary Incontinence The ESTEEM Randomized Clinical Trial

Vivian W. Sung, MD, MPH¹; Diane Borello-France, PT, PhD²; Diane K. Newman, DNP³; [et al](#)

» [Author Affiliations](#)

JAMA. 2019;322(11):1066-1076. doi:10.1001/jama.2019.12467

MESH MIDURETHRAL SLING

- ESTEEM Trial, N=337
 - MUI - sling + PFPT = slight difference in urinary symptoms that is not clinically important

MESH MIDURETHRAL SLING

- ESTEEM Trial, N=337

- **BUT:**

“Previous studies and treatment guidelines have reported that the sling procedure can worsen urgency urinary incontinence,^{5,8} resulting in additional treatment rates to be as high as 25%.^{9,26} Clinical guidelines recommend treating the urgency component prior to consideration of surgery because of this concern.

Both groups in this study reported large reductions in urgency symptoms and had a lower rate (12%) of undergoing additional urinary treatments.

Although the ESTEEM trial did not specifically evaluate whether treating urgency incontinence before surgery is beneficial, this study population was not actively receiving treatment for bothersome urgency incontinence, yet still improved.

It is possible that time spent medically managing the urgency component may unnecessarily delay surgery.

Additionally, overactive bladder medications can have limited efficacy, poor adherence, and adverse effects including potentially irreversible anticholinergic cognitive changes.³⁰ This information may help to guide patient care, referral patterns, and future research.”

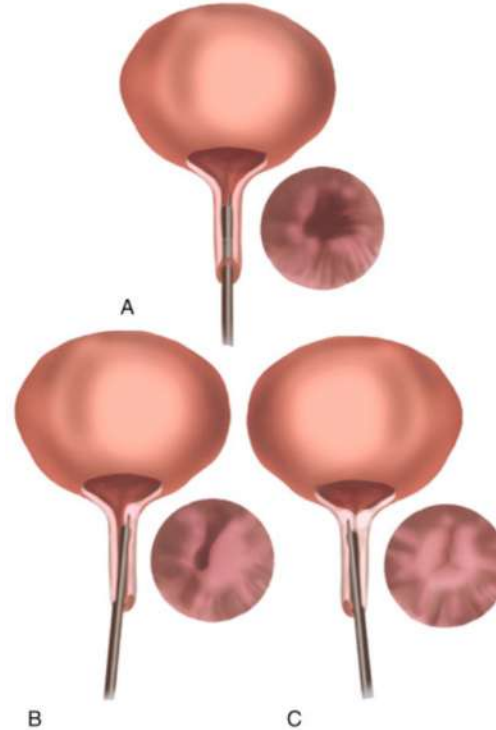
PERIURETHRAL BULKING



Macroplastique® administration device.

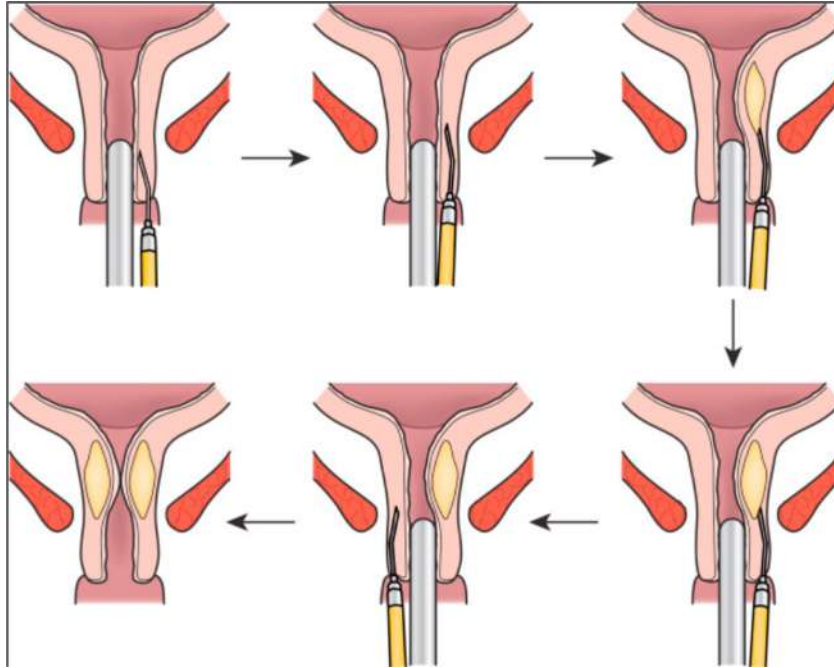


Bulkamid® urethrosopic system.



Transurethral injection method

PERIURETHRAL BULKING



Periurethral injection method

PERIURETHRAL BULKING

Trade Name	Bulking Material	Company	Approval	Carrier Media	Syringe	Needle Gauge/Type	Approaches
Contigen [®]	Bovine dermal collagen cross-linked with gluteraldehyde	Bard, Inc., Covington, GA	1993 (Off market in 2011)	Phosphate-buffered physiological saline	2.5 mL	22- to 23-gauge, rigid or flexible needle	Transurethral or periurethral
Durasphere [®] EXP	Pyrolytic carbon-coated graphite beads	Coloplast Corporation, Minneapolis, MN	1999	Beta glucan and water gel	1.0 and 3.0 mL	18- or 20-gauge, pencil point tip, rigid needle, bent spiral tip needle	Transurethral or periurethral
Coaptite [®]	Calcium hydroxylapatite	Boston Scientific Corporation, Natick, MA	2005	Sodium carboxymethyl cellulose, sterile water, and glycerine	1.0 mL	21-gauge, sidekick rigid needle	Transurethral
Macroplastique [®]	Polydimethyl-siloxane macroparticle	Uroplasty, Geleen, The Netherlands, and Minnetonka, MN	2006	Polyvinylpyrrolidone gel	2.5 mL	18- or 20-gauge, rigid needle	Transurethral

PERIURETHRAL BULKING

- RCT's versus Contigen as active control group

Investigators	Agent	Study Design	Follow-up (months)	Volume of Injections (mL)	Dry/Improved †
Lightner et al. (2001)	Durasphere®	RCT	12	4.8	–/80%
Mayer et al. (2007)	Coaptite®	RCT	12	4	39%/63%
Ghoniem et al. (2009)	Macroplastique®	RCT	12	5	37%/62%

PERIURETHRAL BULKING



Trusted evidence.
Informed decisions.
Better health.

Injections of bulking agents for urinary incontinence in women

Published:

24 July 2017

Authors:

Kirchin V, Page T, Keegan PE,
Atiemo KOM, Cody JD, McClinton
S, Aluko P

PERIURETHRAL BULKING

- Trial N=45 women that compared injection therapy with conservative treatment showed early benefit for the injectable therapy with respect to:
 - continence grade (risk ratio (RR) 0.70, 95% (CI) 0.52 to 0.94)
 - quality of life (mean difference (MD) 0.54, 95% CI 0.16 to 0.92).

PERIURETHRAL BULKING



[Neurourol Urodyn.](#) 2021 Jan; 40(1): 502–508.

Published online 2021 Jan 7. doi: [10.1002/nau.24589](https://doi.org/10.1002/nau.24589)

PMCID: PMC7839440

PMID: [33410544](#)

Seven-year efficacy and safety outcomes of Bulkamid for the treatment of stress urinary incontinence

[Torsten Brosche](#), ¹ [Annette Kuhn](#), ² [Kurt Lobodasch](#), ¹ and [Eric R. Sokol](#) ³

PERIURETHRAL BULKING

- N=1,200
- 67.1% had either cure or substantial improvement after 7 years
- Bother was reduced on validated questionnaires, and QoL was statistically significantly increased

OVERACTIVE
BLADDER:

TREATMENT



DEFINITIONS

ICS Definitions:

- **Overactive Bladder Syndrome**—Urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence, in the absence of urinary tract infection (UTI) or other obvious pathology.
- **Increased daytime urinary frequency**—Complaint that micturition occurs more frequently during waking hours than previously deemed normal by the woman. Seven episodes of micturition per day is felt to be the upper limit of normal, although some variations between populations may exist.
- **Nocturia**—Complaint of interruption of sleep one or more times because of the need to micturate. Each void is preceded and followed by sleep.
- **Urgency**—Complaint of a sudden, compelling desire to pass urine that is difficult to defer.
- **Urgency (urinary) incontinence**—Complaint of involuntary loss of urine associated with urgency.

QUESTION

- **What is the difference between Overactive Bladder and Detrusor Overactivity?**

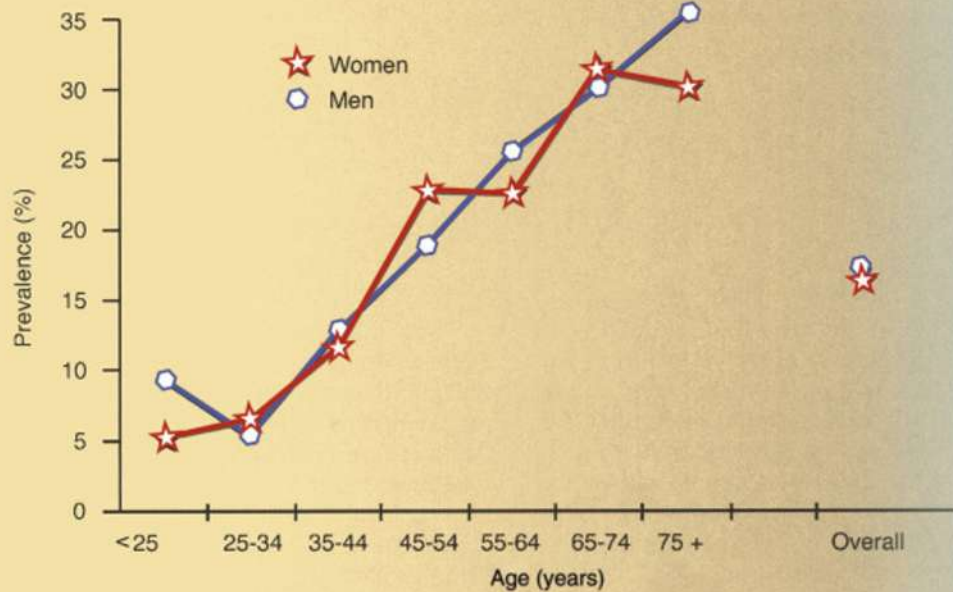
DEFINITIONS

- . The definition of *overactive bladder (OAB)* is based on **symptoms**.
- . In contrast, *detrusor overactivity (DO)* is a **urodynamic observation**.

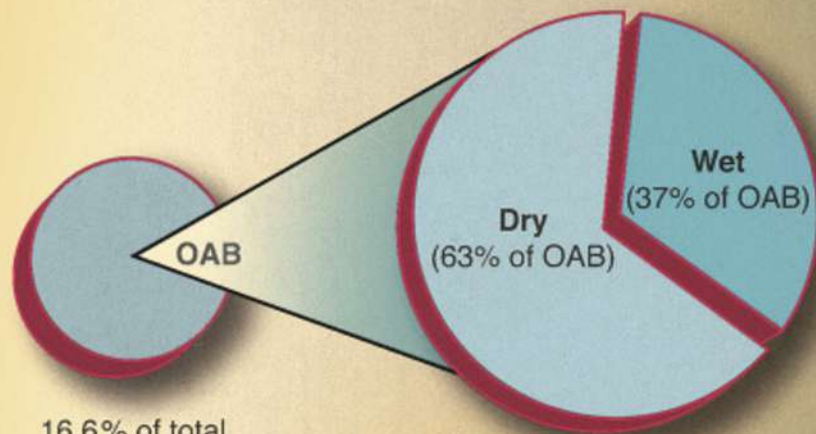
DEFINITIONS

- **What is the difference between Overactive Bladder and Detrusor Overactivity?**
- Detrusor overactivity—is defined as the occurrence of involuntary detrusor contractions during filling cystometry.
 - Contractions may be spontaneous or provoked and produce a wave form on cystometrogram of variable amplitude and duration.
 - No minimum requirement is known for the amplitude of an involuntary detrusor contraction.
 - Detrusor overactivity, with or without urgency and/or urgency incontinence, may be phasic or terminal.
- Detrusor overactivity may be further qualified if the cause is known:
 - neurogenic, when there is a relevant neurologic condition
 - idiopathic, when the cause is unknown

Prevalence of OAB in the US (age and sex specific)

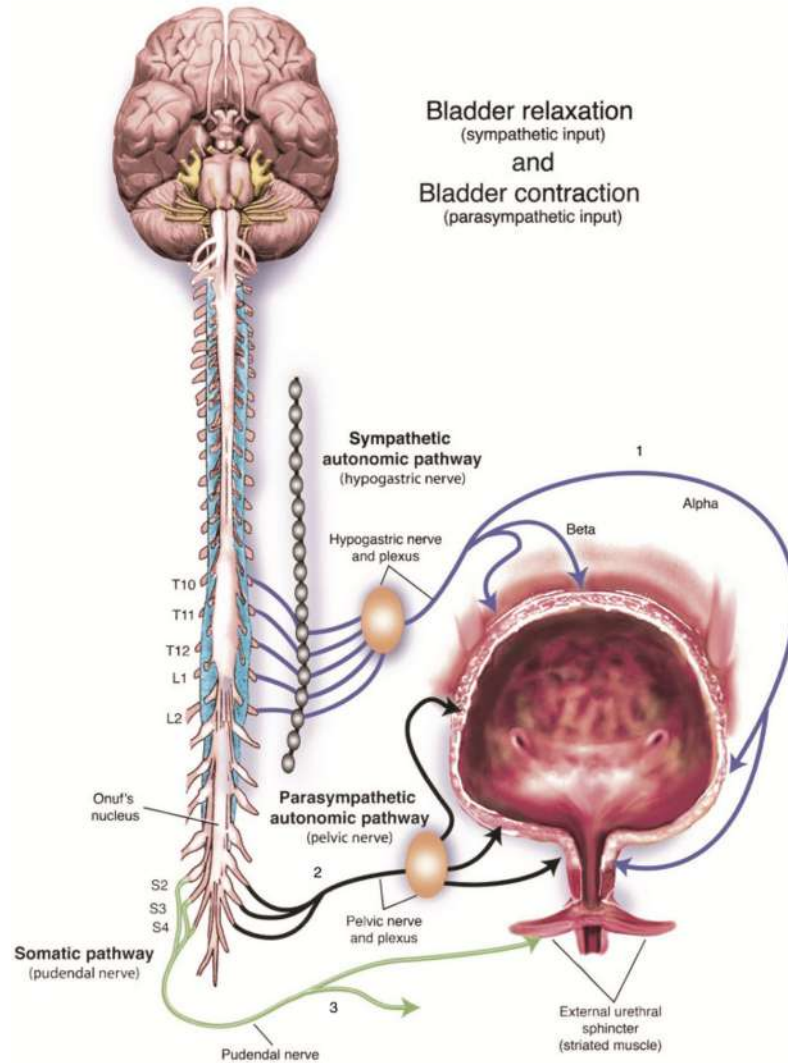


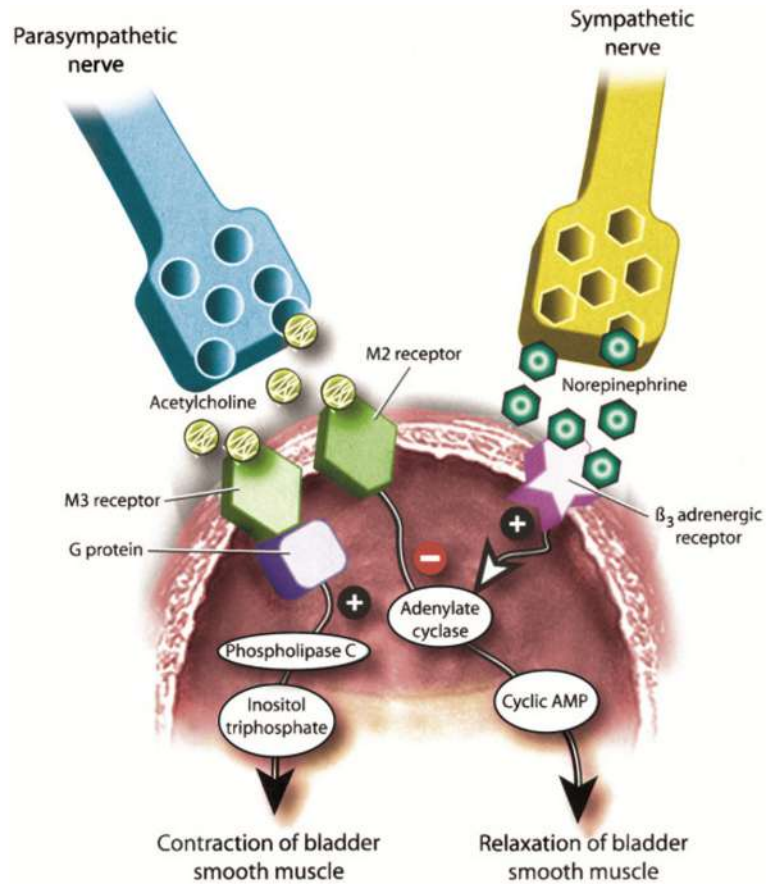
OAB population: wet versus dry

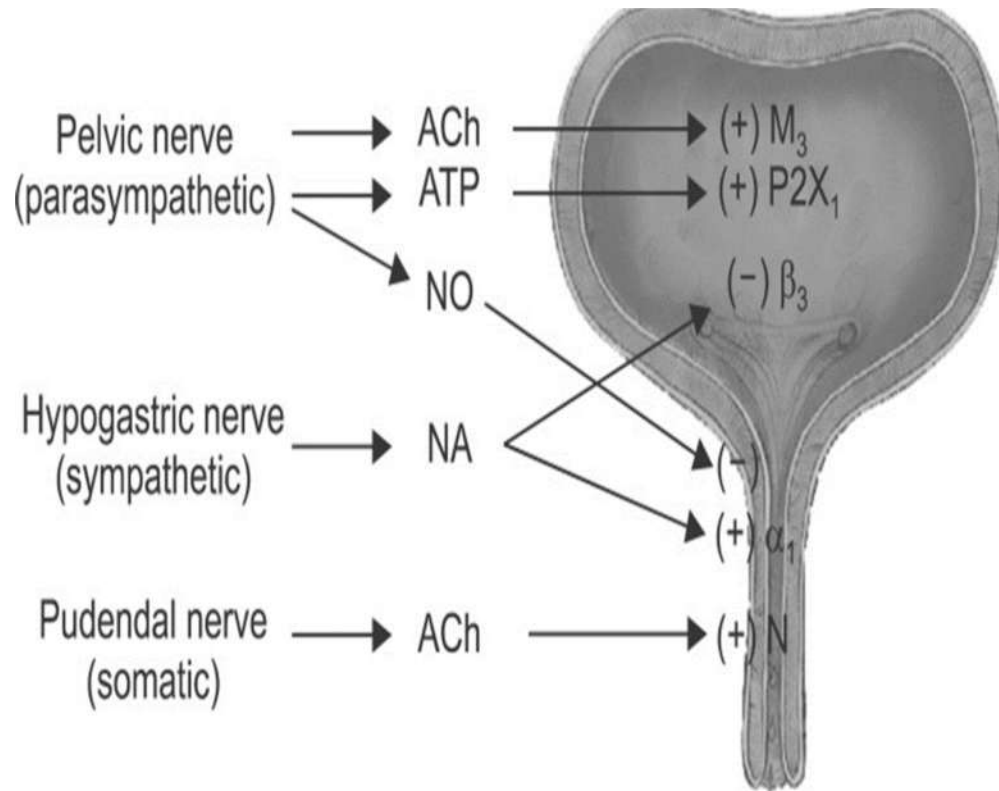


16.6% of total
population

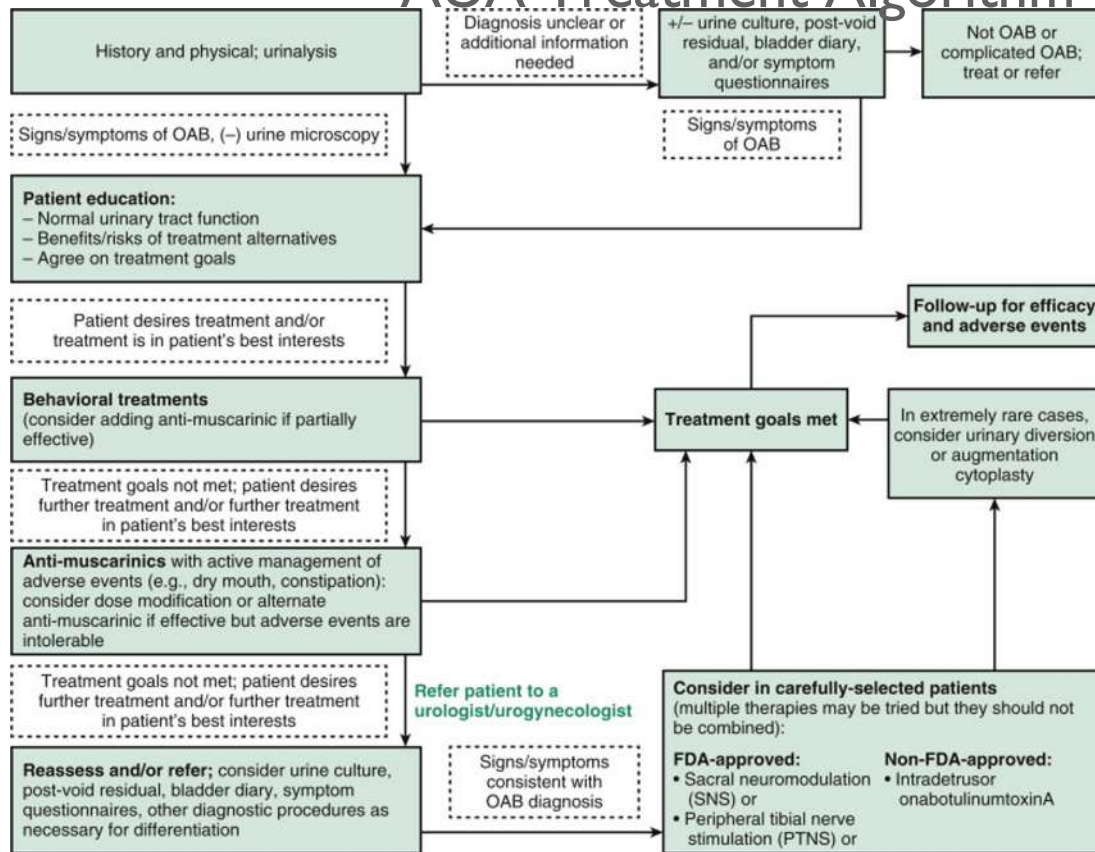
- 10.5% dry (21.2 million)
- 6.1% wet (12.2 million)







AUA Treatment Algorithm



CONSERVATIVE THERAPIES

- **Behavioral treatments (bladder training)**
 - Program of scheduled voiding with progressive increases in the interval between each void
 - Based on assumption that conscious efforts to suppress sensory stimuli will reestablish cortical control over an uninhibited bladder, thus reestablishing normal voiding patterns
 - Enthusiastic patient contact, reassurance, good long-term support, and follow-up are important. Patients must be highly motivated to improve with this therapy.

CONSERVATIVE THERAPIES



American Journal of Obstetrics and Gynecology

Volume 140, Issue 8, 15 August 1981, Pages 885-890



Transactions of the Forty-third Annual Meeting of the South Atlantic Association of Obstetricians and Gynecologists

Detrusor instability syndrome: The use of bladder retraining drills with and without anticholinergics ☆

J. Andrew Fantl M.D., W. Glenn Hurt M.D., Leo J. Dunn M.D.

92 patients with DO on UDS treated by bladder drill, with or without anticholinergic therapy.

Cure rates were the same in both groups: 83% in patients treated with bladder drill and drugs, and 79% in patients treated with bladder drill alone.

CONSERVATIVE THERAPIES

JAGS APRIL 2000-VOL. 48, NO. 4

COMBINED THERAPY FOR INCONTINENCE

Combined Behavioral and Drug Therapy for Urge Incontinence in Older Women

Kathryn L. Burgio, PhD, Julie L. Locher, PhD, and Patricia S. Goode, MD

- . Randomized N=222 women to 3 arms:
 - . biofeedback-assisted behavior training,
 - . behavioral training without biofeedback (verbal feedback based on vaginal palpation), and
 - . self-administered behavioral treatment based on a self-help booklet.
- . No significant differences were noted in symptom improvement between the three groups
- . Patient satisfaction was higher in the two groups receiving behavioral training.
- . Consistent with a systematic review published in 2005 that could find no evidence that biofeedback in addition to pelvic floor muscle rehabilitation provided added benefit to pelvic floor muscle rehabilitation alone.

MEDICAL THERAPIES

- Anti-muscarinics (anti-cholinergics)
 - Mechanism of action: inhibition of mainly M2, M3 muscarinic acetyl choline receptor sites
 - Examples: Oxybutynin, Tolterodine, **Trospium**, Solifenacin Darifenacin

MEDICAL THERAPIES

Prospective Randomized Controlled Trial of Extended-Release Oxybutynin Chloride and Tolterodine Tartrate in the Treatment of Overactive Bladder: Results of the OBJECT Study

Rodney A. Appell, MD¹, Peter Sand, MD, Roger Dmochowski, MD, Rodney Anderson, MD², Norman Zinner, MD, Daniel Lama, MD, Martha Roach, MD, John Miklos, MD, Daniel Saltzstein, MD, Timothy Boone, MD, David R. Staskin, MD, Detlef Albrecht, MD for the OBJECT Study Group

- N=378
 - ER oxybutynin 10 mg qd
 - IR tolterodine 2 mg bid
 - Both medications caused decreased DO
 - ER oxybutynin vs IR tolterodine slightly better for mixed incontinence and urinary frequency
 - Dry mouth and central nervous system side effects were similar for both treatment groups.

MEDICAL THERAPIES

ORIGINAL ARTICLES

Minerva Urologica e Nefrologica 2010 December;62(4):355-61

Copyright © 2010 EDIZIONI MINERVA MEDICA

language: English

Overactive bladder syndrome: what is the role of evidence of detrusor overactivity in the cystometric study?

Vecchioli-Scaldazza C.¹, Grinta R.² 

¹ Division of Urology, ASUR, N. 5, Jesi, Ancona, Italy; ² Pharmacoeconomic Assessment Service, ASUR, N. 5, Jesi, Ancona, Italy

- . Relationship between detrusor overactivity on urodynamics and the response to treatment with anticholinergics in patients with OAB.
- . Detrusor overactivity is not found in all subjects with OAB
 - . BUT, when found, respond more favorably to anticholinergic treatment.
- . Author suggests UDS should be considered in all patients with OAB as a predictor for success of therapy.

MEDICAL THERAPIES

thebmj | BMJ 2018;361:k1315 | doi: 10.1136/bmj.k1315

Anticholinergic drugs and risk of dementia: case-control study

Kathryn Richardson,¹ Chris Fox,² Ian Maidment,³ Nicholas Steel,² Yoon K Loke,² Antony Arthur,¹ Phylo K Myint,⁴ Carlota M Grossi,¹ Katharina Mattishent,² Kathleen Bennett,⁵ Noll L Campbell,⁶ Malaz Boustani,⁷ Louise Robinson,⁸ Carol Brayne,⁹ Fiona E Matthews,¹⁰ George M Savva¹

Secondary analyses examined the association between specific classes of anticholinergics as well as cumulative dose within class.

The most consistent evidence for increased dementia risk was found for definite anticholinergic antidepressants, antiparkinsonian drugs, and **drugs to treat urinary incontinence**.

However, no increased risk was found for anticholinergics used to treat gastrointestinal conditions or respiratory agents; the latter category included over-the-counter antihistamines.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Use of drugs with anticholinergic activity is associated with impaired cognition in the short term

It is not known if the reported associations between the use of anticholinergic drugs and future cognitive decline and dementia incidence can be attributed to anticholinergic activity

WHAT THIS STUDY ADDS

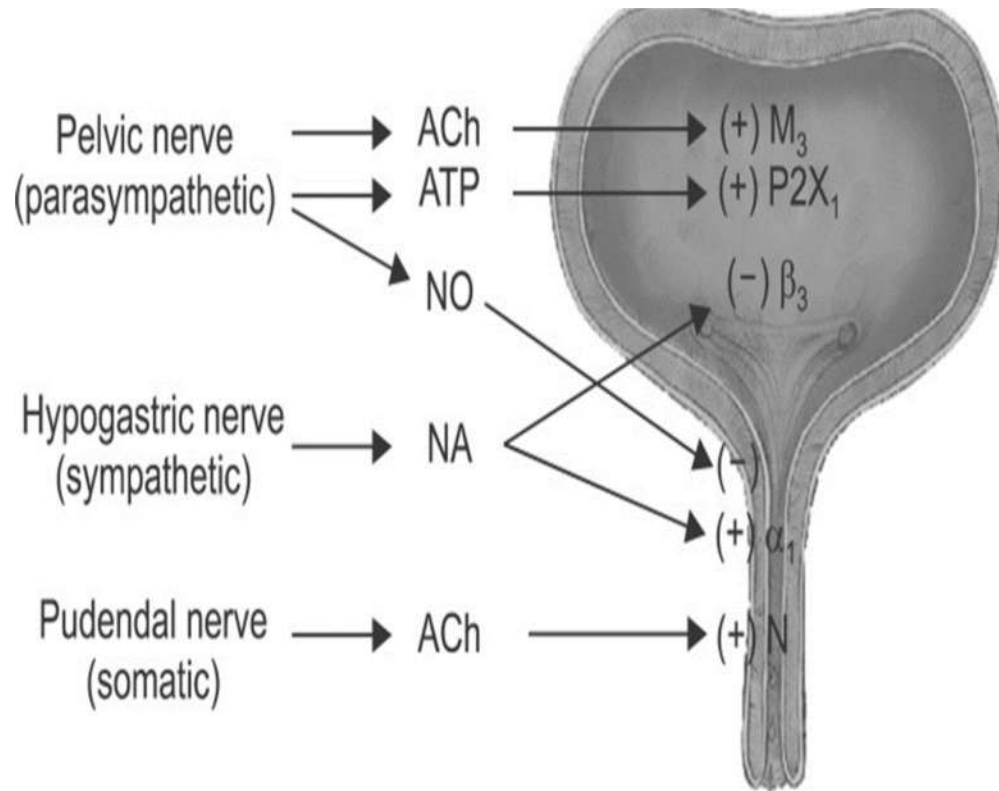
Antidepressant, urological, and antiparkinson drugs with definite anticholinergic activity are linked to future dementia incidence, with associations persisting up to 20 years after exposure

Gastrointestinal and cardiovascular anticholinergic drugs are not positively associated with later dementia incidence

There is no evidence for a cumulative harm of drugs considered possibly anticholinergic

MEDICAL THERAPIES

- . Alpha adrenergic agonists
 - . Mechanism of action: increase urethral closure pressure via alpha-1 adrenergic receptor agonism



MEDICAL THERAPIES

Cochrane Database of Systematic Reviews

Adrenergic drugs for urinary incontinence in adults

Cochrane Systematic Review - Intervention | Version published: 20 July 2005 [see what's new](#)



[View article information](#)

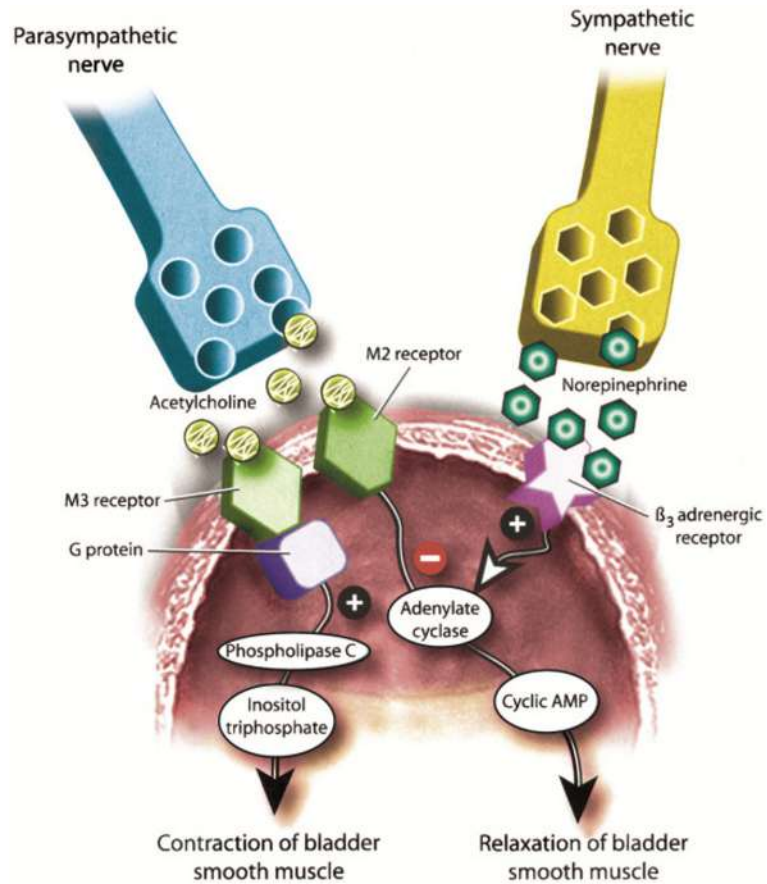
✉ Ammar Alhasso | Cathryn MA Glazener | Robert Pickard | James MO N'Dow

[View authors' declarations of interest](#)

- . 22 RCT, 11 were crossover trials. N=1099 women with N=673 receiving an adrenergic drug
- . 11 phenylpropanolamine, 2 midodrine, 3 norepinephrine, 3 clenbuterol, 1 terbutaline, 1 eskornade
- . limited evidence suggested that an alpha adrenergic agonists are better than placebo in reducing the number of pad changes and incontinence episodes, as well as improving subjective symptoms
- . Increased side effects: insomnia, restlessness and vasomotor stimulation, hypertension

MEDICAL THERAPIES

- Beta adrenergic agonists (Mirabegron)
- Mechanism of action: Beta-3 adrenergic agonist
- B-3 receptors are involved in bladder wall relaxation during the filling and storage phase of micturition.
- Adverse reactions:
 - hypertension, nasopharyngitis, UTI, and headache.
 - not recommended in patients with uncontrolled hypertension
 - blood pressure should be monitored in patients with a diagnosis of hypertension



MEDICAL THERAPIES

Cochrane Database of Systematic Reviews

Beta-3 adrenergic receptor agonist for adult with overactive bladder

Information

DOI:	10.1002/14651858.CD011593 
Database:	Cochrane Database of Systematic Reviews
Version published:	21 March 2015
Type:	Intervention
Stage:	Protocol
Cochrane Editorial Group:	Cochrane Incontinence Group
Copyright:	Copyright © 2015 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

MEDICAL THERAPIES



Urol Int 2014;93:326-337
<https://doi.org/10.1159/000361079>

Original Paper

The Role of Mirabegron in Overactive Bladder: A Systematic Review and Meta-Analysis

Wu T.^a · Duan X.^b · Cao C.-X.^a · Peng C.-D.^a · Bu S.-Y.^a · Wang K.-J.^a

- Mirabegron vs tolterodine:
 - Mirabegron fewer incontinence episodes per 24 hours (MD(mean difference) -0.25; 95% CI -0.43, -0.06; p = 0.009).
- No differences between mirabegron and tolterodine:
 - mean number of micturitions per 24 h (MD -0.17; 95% CI -0.35, 0.01; p = 0.07)
 - OAB-q (MD -1.09; 95% CI -2.51, 0.33; p = 0.13).
- Mirabegron also had a lower adverse reaction rate (OR 0.9; 95% CI 0.8, 1.0; p = 0.04).

MEDICAL THERAPIES

- . Estrogen therapy
- . Mechanism: Locally applied vaginal estrogen may decrease the irritation of the vaginal tissues, and thus the patient perceives a reduction in irritative voiding symptoms rather than a true effect on the lower urinary tract.

MEDICAL THERAPIES

Female Pelvic Med Reconstr Surg, 2016 Jul-Aug;22(4):254-60. doi: 10.1097/SPV.0000000000000256.

Combined Tolterodine and Vaginal Estradiol Cream for Overactive Bladder Symptoms After Randomized Single-Therapy Treatment.

Ellington DR¹, Szychowski JM, Malek JM, Gerten KA, Burgio KL, Richter HE.

- . No difference in symptom bother score improvement between the tolterodine and intravaginal estradiol groups
- . Significant within-group decrease in symptom bother score from baseline to 12 weeks (tolterodine, $P < 0.0001$, and intravaginal estradiol, $P = 0.002$)

ADVANCED THERAPIES - Conservative

- Percutaneous/Posterior Tibial Nerve Stimulation: PTNS
- Mechanism of action:
 - Needle electrode placed near the posterior tibial nerve percutaneously.
 - The electrode is then connected to an external pulse generator which delivers an adjustable electrical pulse that travels to the sacral plexus via the tibial nerve.
 - ?Afferent signals from the tibial nerve to the sacral plexus modulate the upstream and downstream signals to the bladder through the sacral plexus.

ADVANCED THERAPIES



Trusted evidence.
Informed decisions.
Better health.

Non-invasive electrical stimulation for overactive bladder in adults

Published:

9 December 2016

Authors:

Stewart F, Gameiro LF, El Dib R,
Gameiro MO, Kapoor A, Amaro JL

Primary Review Group:

Incontinence Group

- 63 studies (4424 people altogether) comparing electrical stimulation to no treatment or any other available treatment.
- Cochrane group found that electrical stimulation is probably better than sham electrical stimulation or pelvic floor muscle training at reducing symptoms of OAB.
- Low-quality evidence suggested participants receiving ES plus PFMT vs PFMT only, were more than twice as likely to report improvement in UUI (RR 2.82, 95% CI 1.44 to 5.52; n = 51).

ADVANCED THERAPIES

- Sacral Neuromodulation
 - Mechanism of action: Unknown
 - ?blockade of c-afferent fibers, a pathological reflex arc believed to be responsible for incontinence

ADVANCED THERAPIES

- Intravesical Botox Injection
 - Mechanism of action: inhibit release of Acetylcholine

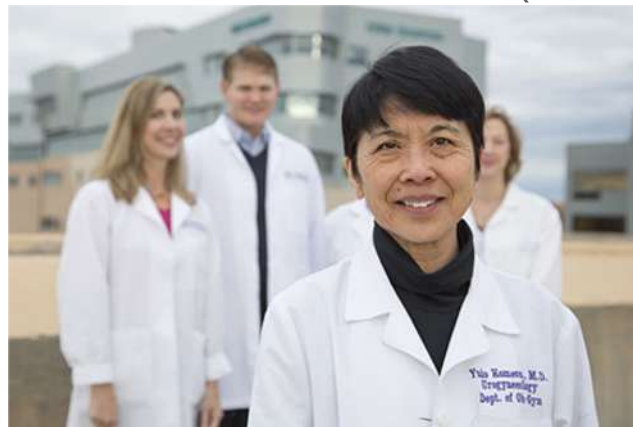
ADVANCED THERAPIES

OnabotulinumtoxinA vs Sacral Neuromodulation on Refractory Urgency Urinary Incontinence in Women:

A Randomized Clinical Trial

Cindy L. Amundsen, MD, Holly E. Richter, PhD, MD, Shawn A. Menefee, MD, Yuko M. Komesu, MD, Lily A. Arya, MD, MS, W. Thomas Gregory, MD, Deborah L. Myers, MD, Halina M. Zyczynski, MD, Sandip Vasavada, MD, Tracy L. Nolen, DrPH, Dennis Wallace, PhD, and Susan F. Meikle, MD, MSPH for the Pelvic Floor Disorders Network

- Rosetta Trial: Cystoscopic intradetrusor injection of 200 U of onabotulinumtoxinA (n = 192) vs sacral neuromodulation (n = 189) for refractory UUI.



ADVANCED THERAPIES

OnabotulinumtoxinA vs Sacral Neuromodulation on Refractory Urgency Urinary Incontinence in Women:

A Randomized Clinical Trial

Cindy L. Amundsen, MD, Holly E. Richter, PhD, MD, Shawn A. Menefee, MD, Yuko M. Komesu, MD, Lily A. Arya, MD, MS, W. Thomas Gregory, MD, Deborah L. Myers, MD, Halina M. Zyczynski, MD, Sandip Vasavada, MD, Tracy L. Nolen, DrPH, Dennis Wallace, PhD, and Susan F. Meikle, MD, MSPH for the Pelvic Floor Disorders Network

- . Botox group > SNM reduction ep. of urgency incontinence per day
 - . (−3.9 vs −3.3 episodes per day; mean difference, 0.63; 95% CI, 0.13 to 1.14; P = .01).
- . Botox group > SNM
 - . improvement in OAB-Q SF symptom bother (−46.7 vs −38.6; mean difference, 8.1; 95% CI, 3.0 to 13.3; P = .002)
 - . treatment satisfaction (67.7 vs 59.8; mean difference, 7.8; 95% CI, 1.6 to 14.1; P = .01)
 - . treatment endorsement (78.1 vs 67.6; mean difference; 10.4, 95% CI, 4.3 to 16.5; P < .001)

ADVANCED THERAPIES

OnabotulinumtoxinA vs Sacral Neuromodulation on Refractory Urgency Urinary Incontinence in Women:

A Randomized Clinical Trial

Cindy L. Amundsen, MD, Holly E. Richter, PhD, MD, Shawn A. Menefee, MD, Yuko M. Komesu, MD, Lily A. Arya, MD, MS, W. Thomas Gregory, MD, Deborah L. Myers, MD, Halina M. Zyczynski, MD, Sandip Vasavada, MD, Tracy L. Nolen, DrPH, Dennis Wallace, PhD, and Susan F. Meikle, MD, MSPH for the Pelvic Floor Disorders Network

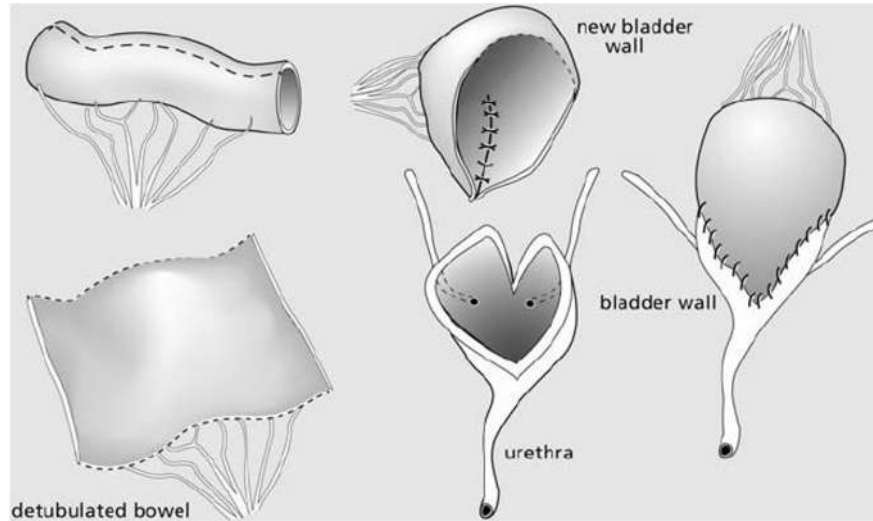
- . SNM group, (3%) had their device revised or removed during the 6-month period.
- . Botox group, 8% required intermittent self catheterization at 1 month, 4% at 3 months, and 2% at 6 months
- . Botox > SNM: Risk of UTI up to 6 months
 - . (35% vs 11%; risk difference, -23%; 95% CI, -33% to -13%; $P < .001$)

SURGICAL INTERVENTION

- Augmentation cystoplasty
 - Method: Bladder is bisected almost completely, and a patch of gut, usually ileum, equal in length to the circumference of the bisected bladder (approximately 25 cm), is sewn in place.
 - May cure symptoms but results in inefficient voiding.
 - May result in strain to void or necessitate clean intermittent self-catheterization
 - Series of 40 patients treated by “clam” ileocystoplasty. Thirty-six patients (90%) were cured of their symptoms, and 30 were able to void spontaneously and efficiently

SURGICAL INTERVENTION

- Augmentation cystoplasty



SURGICAL INTERVENTION

- Bladder transection:
 - above the trigone and ureteric orifices and division of all inferior lateral communications
 - 74% subjective cure rate at 1-year follow-up
- Ingelman-Sundberg procedure: transvaginal partial denervation/transection of inferior hypogastric plexus
 - Successful outcomes have been reported in 50% to 80% of patients.
- Transvaginal infiltration of the pelvic plexus with phenol
 - Only 29% achieved a significant response, and all relapsed during the 22-month follow-up period

