

# Prevenzione, diagnosi e cura dell'incontinenza urinaria

Pazienti incontinenti  
gestione di 2° livello:  
-terapia farmacologica  
-terapia chirurgica

Prof. Enrico Finazzi Agrò  
Dept. of Experimental Medicine and Surgery  
Tor Vergata University  
Unit of Functional Urology  
Tor Vergata University Hospital  
Rome, ITALY



**DALLA PRESTAZIONE ALLA PERFORMANCE**



**74° Congresso Nazionale**  
2-7 ottobre 2017



# Initial Management of Urinary Incontinence in Women

**HISTORY**

**CLINICAL ASSESSMENT**

**PRESUMED DIAGNOSIS**

**MANAGEMENT**

\* Subject to local regulatory approval (see black box warning).

Incontinence on physical activity

Incontinence

Incontinence /

- Gen
- Urin
- vol
- Ass
- Phy
- Cou
- Urin
- If ap
- Ass
- Ass
- Ass

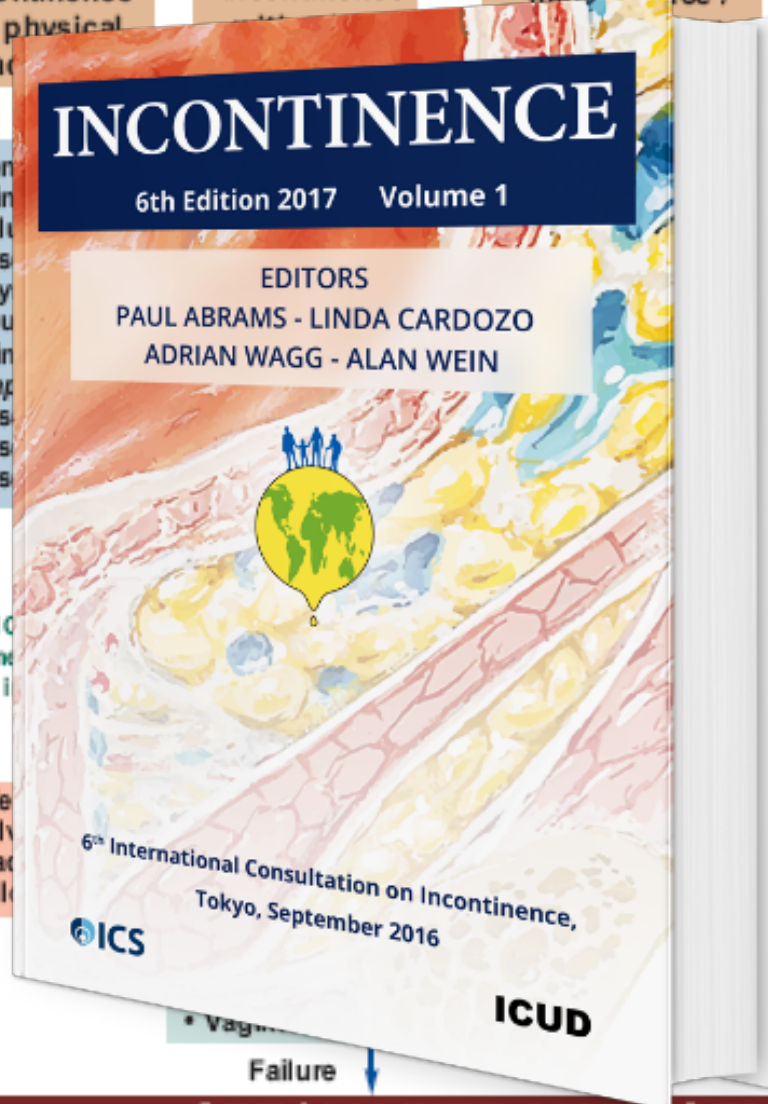
STRESS INCONTINENCE presumed sphincteric

- Life
- Pelv
- Blac
- Dul

Complicated incontinence

- Recurrent incontinence
- Incontinence associated with:
  - Pain
  - Hematuria
  - Recurrent infection
  - Significant voiding symptoms
  - Pelvic irradiation
  - Radical pelvic surgery
  - Suspected fistula

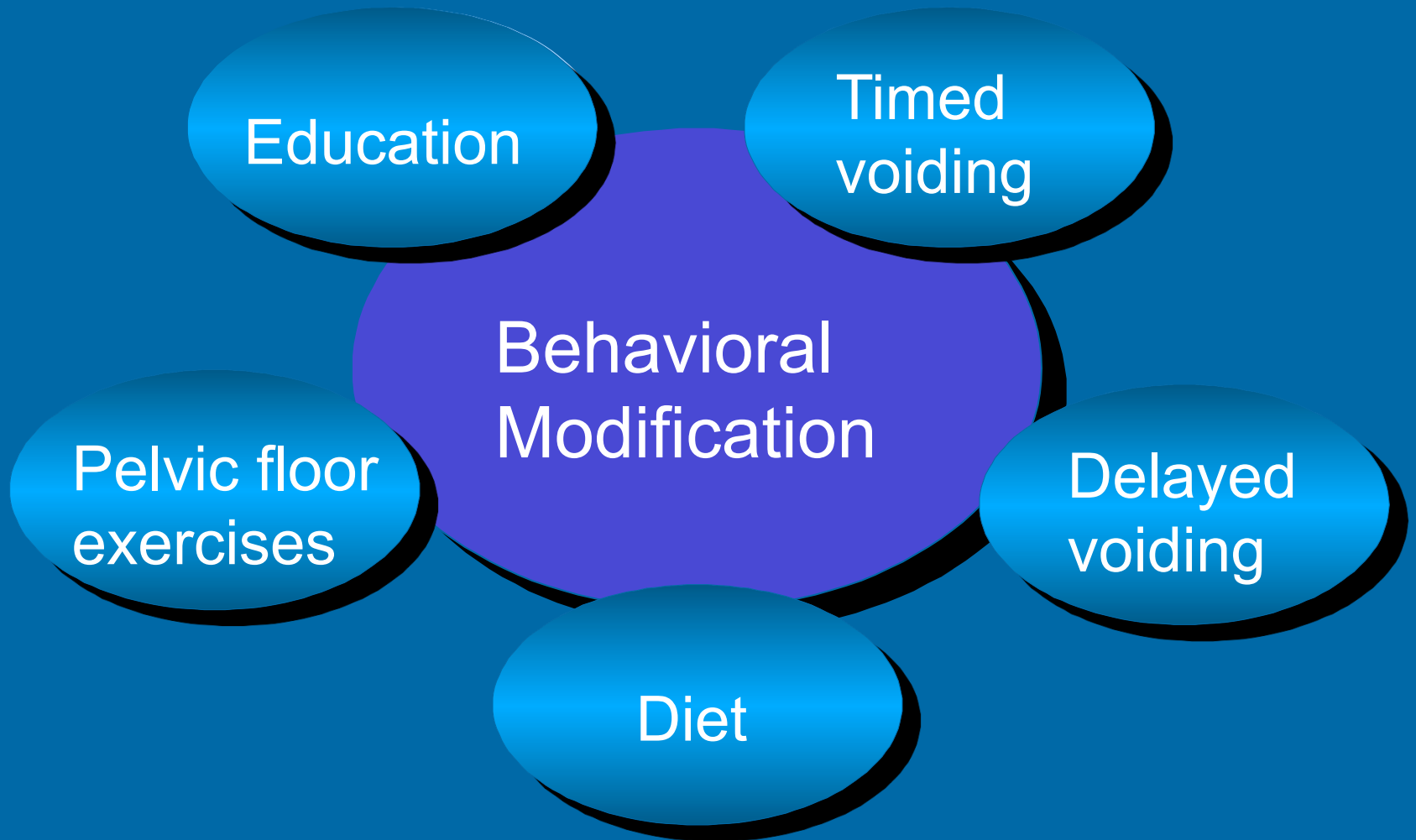
- If other abnormality found e.g.
- Significant post void residual
- Significant pelvic organ prolapse
- Pelvic mass



Failure

**SPECIALIZED MANAGEMENT**

# Behavioral Modification



# Bladder Training

- Modify bladder function
- Methods
  - bladder diary
  - gradually increase void interval
  - teach coping strategies
- Strengthen pelvic floor muscles and improving bladder stability



# Management of Overactive Bladder

- Behavioral therapies<sup>1</sup>
- Pharmacologic therapy
- Combined pharmacologic and behavioral therapy provides improved outcomes<sup>2,3</sup>

1. Mattiasson A. *Urology*. 2000;55(suppl 5a):12-13.

2. Mattiasson A. *Neuro Urodyn*. 2001;20:403-404.

3. Burgio et al. *JAGS*. 2000;48:370-374.

# Drugs used in the treatment of OAB

*There are a number of pharmacological mechanisms that in theory could reduce overactive detrusor muscle activity.*



- *Antimuscarinic drugs*
- *Drugs acting on membrane channels*
- *Drugs with mixed actions*
- *Antidepressants*
- *Alpha-adrenoreceptor antagonists*
- *Beta-adrenoreceptor antagonists*
- *PDE-5 inhibitors (for male LUTS/OAB)*
- *Toxins*
- *Hormones*

**....However**



Drugs	LE	GR
<b>Antimuscarinic drugs</b>		
Tolterodine	1	A
Trospium	1	A
Solifenacin	1	A
Darifenacin	1	A
Fesoterodine	1	A
• Propantheline	2	B
• Atropine, hyoscyamine	3	C
<i>Drugs with mixed actions</i>		
• Oxybutynin	1	A
• Propiverine	1	A
• Dicyclomine	3	C
• Flavoxate	2	

**To date, the only approved treatments with Grade A recommendation based on level 1 evidence are anticholinergic drugs (specifically antimuscarinic)**

# Antimuscarinic drugs on the market



❖ Oxybutynin (IR 7.5-10mg/day, IR 15 mg/day, TDS 3.9-4 mg/day)



❖ Tolterodine (IR 2mg/day, IR 4 mg/day, ER 4mg/day)



❖ Propiverine, (IR 30mg/die, IR 45 mg/die, ER 20mg/die, ER 30 mg/die)



❖ Trospium, (40mg/die)



❖ Solifenacin (5mg/day, 10 mg/day)

❖ Darifenacin (7.15 mg/day, 15 mg/day)



❖ Fesoterodine (4 mg/day, 8 mg/day)

# Rationale for Use of Antimuscarinics in OAB

Effects on afferent activity (myocyte + urothelium)

Effects on voiding contraction

"Therapeutic window"  
for OAB

Concentration of antimuscarinic



# *Safety in patients with BOO*

The role of anticholinergics in men with lower urinary tract symptoms suggestive of benign prostatic hyperplasia: a systematic review and meta-analysis

Benedict T. Blake-James\*, Arash Rashidian†‡, Youko Ikeda\* and Mark Emberton\*†

***The concerns that anticholinergics might be associated with impaired voiding and AUR do not appear to be supported by the evidence from the studies assessed. Anticholinergics are associated with a small rise in PVR, but not an increased rate of AUR.***



# HHS Public Access

Author manuscript

*JAMA Intern Med.* Author manuscript; available in PMC 2015 March 13.

Published in final edited form as:

*JAMA Intern Med.* 2015 March 1; 175(3): 401–407. doi:10.1001/jamainternmed.2014.7663.

## Cumulative Use of Strong Anticholinergic Medications and Incident Dementia

Shelly L. Gray, PharmD, MS<sup>1</sup>, Melissa L. Anderson, MS<sup>2</sup>, Sascha Dublin, MD, PhD<sup>2,3</sup>, Joseph T. Hanlon, PharmD, MS<sup>4</sup>, Rebecca Hubbard, PhD<sup>2,5</sup>, Rod Walker, MS<sup>2</sup>, Onchee Yu, MS<sup>2</sup>, Paul Crane, MD, MPH<sup>6</sup>, and Eric B. Larson, MD, MPH<sup>2,6</sup>

Higher cumulative anticholinergic medication use is associated with an increased risk for dementia



J Alzheimers Dis. 2015;46(4):983-7. doi: 10.3233/JAD-150290.

## How Anticholinergic Drugs Might Promote Alzheimer's Disease: More Amyloid- $\beta$ and Less Phosphatidylcholine.

Wurtman R.J.

### Abstract

Drugs that block muscarinic cholinergic neurotransmission in the brain can, as a consequence, increase the formation of amyloid- $\beta$ , and decrease brain levels of phosphatidylcholine (by slowing its synthesis and accelerating its turnover). Both of these effects might cause a decrease in brain synapses, as characterizes and probably underlies the memory disorder of early Alzheimer's disease.

**KEYWORDS:** Acetylcholine; amyloid; choline; neurotransmission; synapses; synaptic membrane

PMID: [26402628](#) DOI: [10.3233/JAD-150290](#)

[PubMed - indexed for MEDLINE]





Alzheimer's & Dementia: Translational Research & Clinical Interventions 3 (2017) 139-148

Alzheimer's  
&  
Dementia

Featured Article

## Bladder antimuscarinics and cognitive decline in elderly patients

Daniela Claudia Moga<sup>a,b,c,\*</sup>, Erin L. Abner<sup>b,c</sup>, Qishan Wu<sup>b</sup>, Gregory A. Jicha<sup>c,d</sup>

<sup>a</sup>Department of Pharmacy Practice and Science, College of Pharmacy, University of Kentucky, Lexington, KY, USA

<sup>b</sup>Department of Epidemiology, College of Public Health, University of Kentucky, Lexington, KY, USA

<sup>c</sup>Sanders-Brown Center on Aging, University of Kentucky, Lexington, KY, USA

<sup>d</sup>Department of Neurology, College of Medicine, University of Kentucky, Lexington, KY, USA

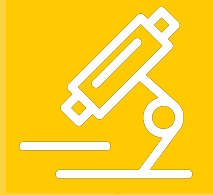
- Association between antimuscarinic initiation and cognitive decline.
- Stronger negative effect on cognitive function to those using nonselective antimuscarinics (Oxybutynin, Tolterodine).
- Higher risk of cognitive decline than possibility of clinical improvement.



Summary of evidence	IE
All antimuscarinic drugs are effective in elderly patients.	1b
In older people, the cognitive impact of drugs which have anticholinergic effects is cumulative and increases with length of exposure.	3
Oxybutynin may worsen cognitive function in elderly patients.	2
Solifenacin, darifenacin and fesoterodine have been shown not to cause increased cognitive dysfunction in elderly people.	1b
There is no evidence as to whether tolterodine and trospium chloride affect cognitive function.	3

## EAU Guidelines on Urinary Incontinence in Adults

# Other drug classes to treat OAB?



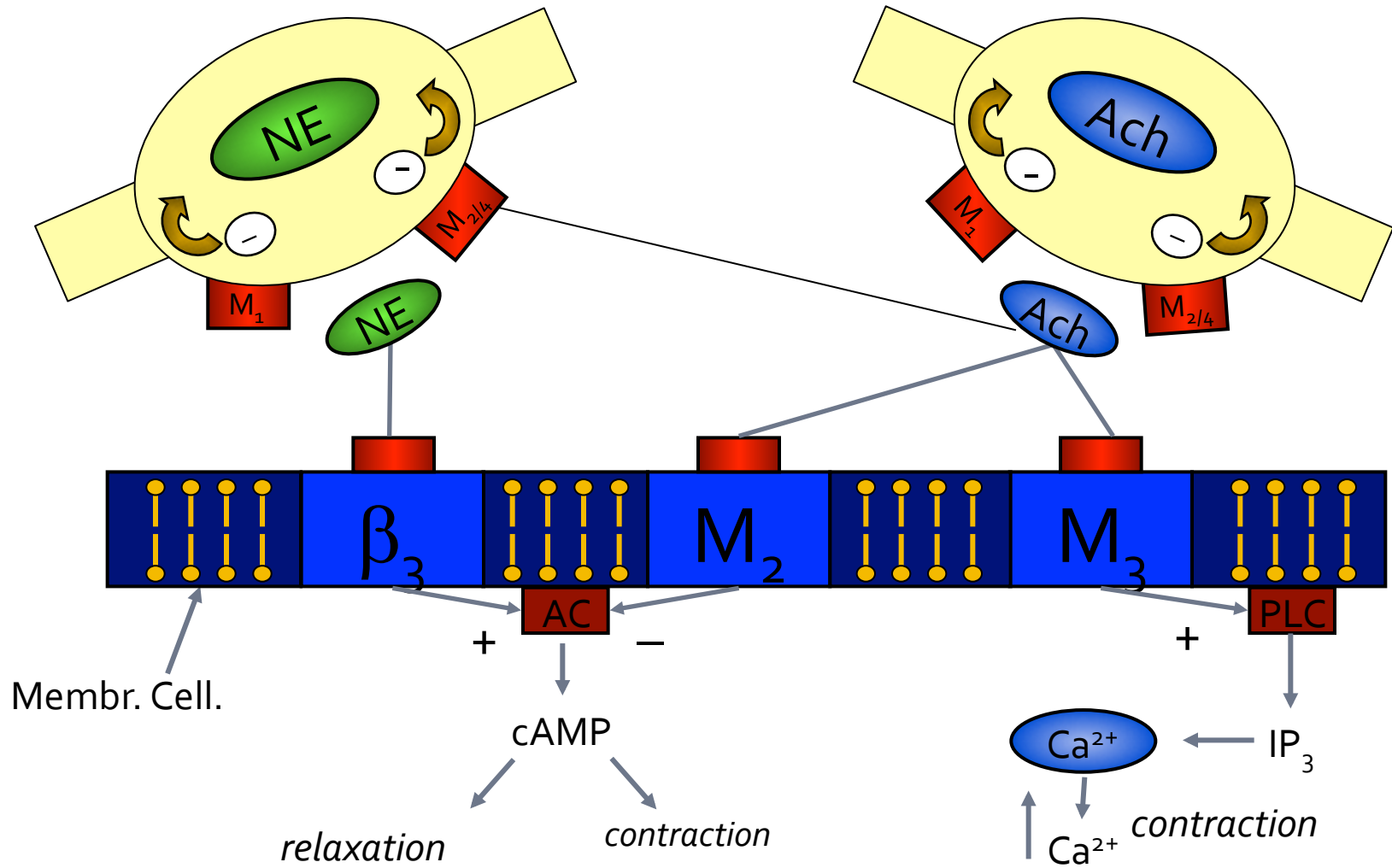
- *“Despite intensive research, few new therapeutic principles have emerged and been demonstrated to have sufficient efficacy and adverse effect profiles to be accepted for approval and clinical use”<sup>1</sup>*
- Research indicated that stimulation of  $\beta_3$ -receptors leads to bladder relaxation
- Discovery of  $\beta_3$ -adrenoceptors, predominately present on the bladder wall → development of  $\beta_3$ -adrenoceptor agonist

FDA-approval  $\beta_3$ -agonist<sup>3</sup>  
**2012**

First FDA-approved antimuscarinic agent<sup>2</sup>  
**1975**

1. Andersson KE. Curr Urol Rep 2013;doi:10.1007/s11934-013-0335-8; 2. Kennelly MJ Rev Urol 2010;12:12-9;
3. [http://www.accessdata.fda.gov/drugsatfda\\_docs/label/2012/202611s000lbl.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/202611s000lbl.pdf)

# Effects of NE e Ach on Bladder activity



Chapple CR. *Urology*. 2000;55:33-46

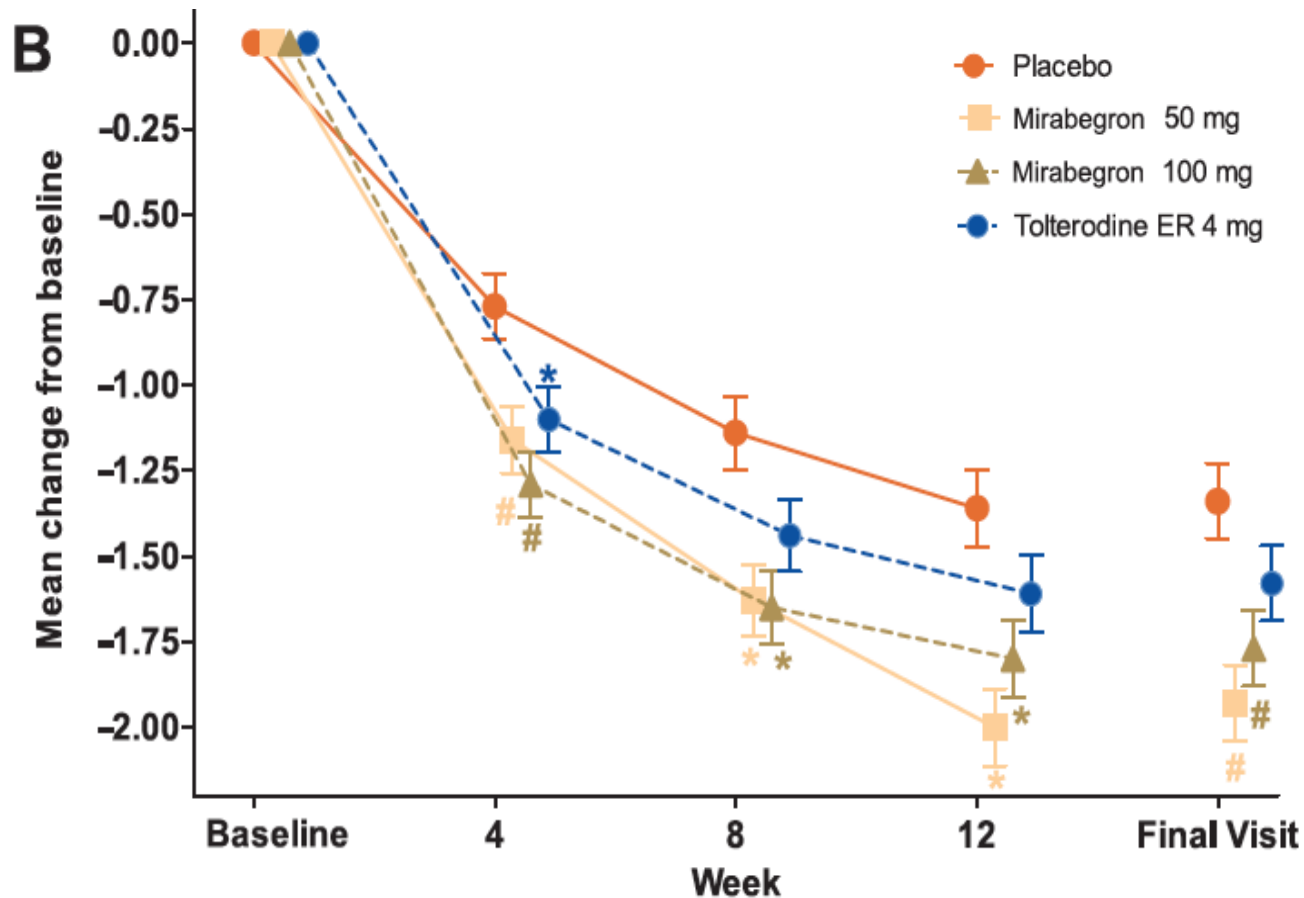
# Binding affinity ( $K_i$ ) of mirabegron for human ARs<sup>1</sup>

Receptor subtype	Mirabegron $K_i$ , nmol/L*
$\beta_1$ -AR	4,200 $\pm$ 900
$\beta_2$ -AR	1,300 $\pm$ 300
$\beta_3$ -AR	40 $\pm$ 20.2

Lower  $K_i$  values represent higher affinity

\* Determined in *in vitro* receptor binding studies using Chinese hamster ovary cells expressing human  $\beta$ -AR subtypes ; values are means of three replicates ( $\pm$  standard error)

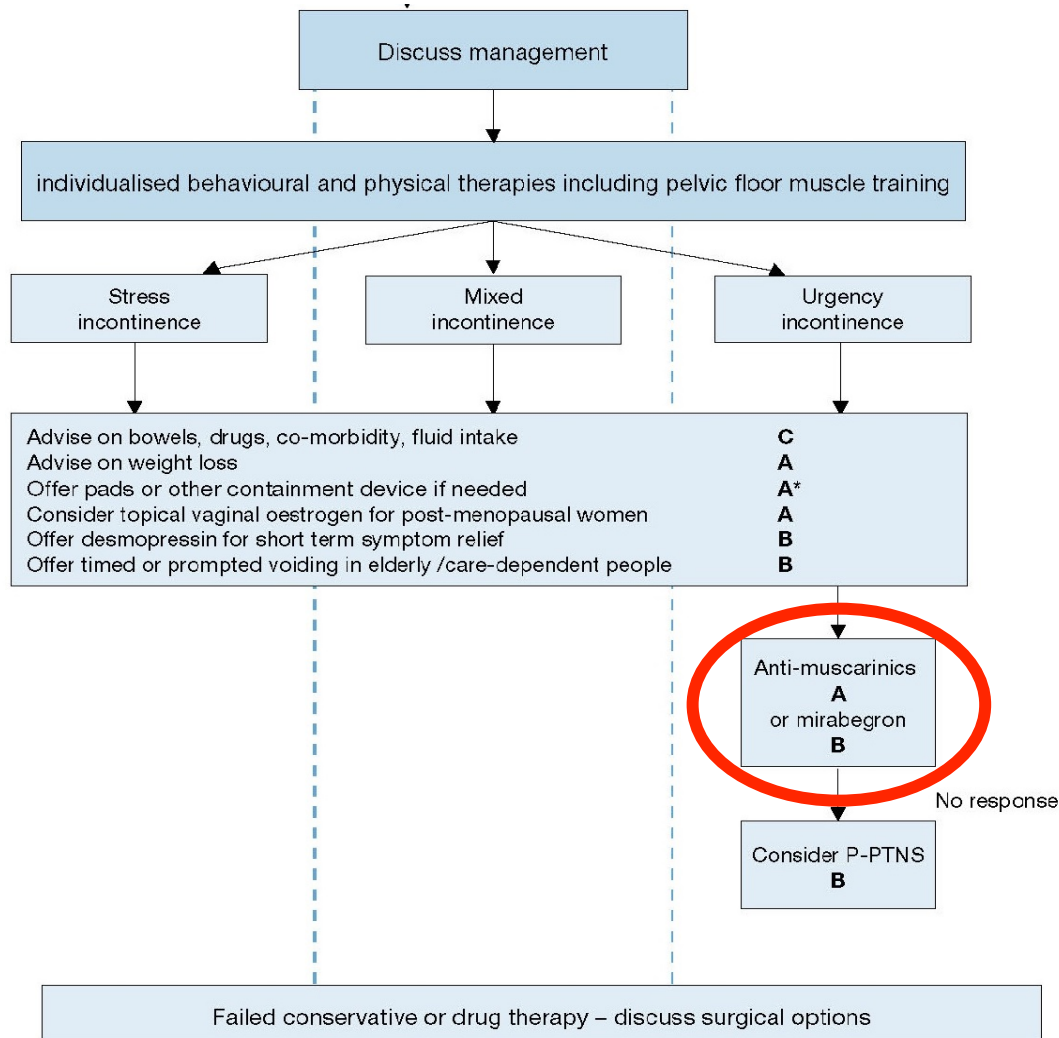
# End-point co-primario: numero medio di minzioni per 24 h



All p values <0.05 for Mirabegron 50 and 100 mg vs placebo

# Women presenting with UI

## EAU guidelines 2016



Search NICE...

Home > NICE Guidance > Conditions and diseases > Urological conditions > Lower urinary tract symptoms

## Mirabegron for treating symptoms of overactive bladder

NICE technology appraisal guidance [TA290] Published date: 26 June 2013

*You should be able to have mirabegron if drugs called 'antimuscarinics' do not work, if they are not suitable for you, or their side effects are unacceptable*

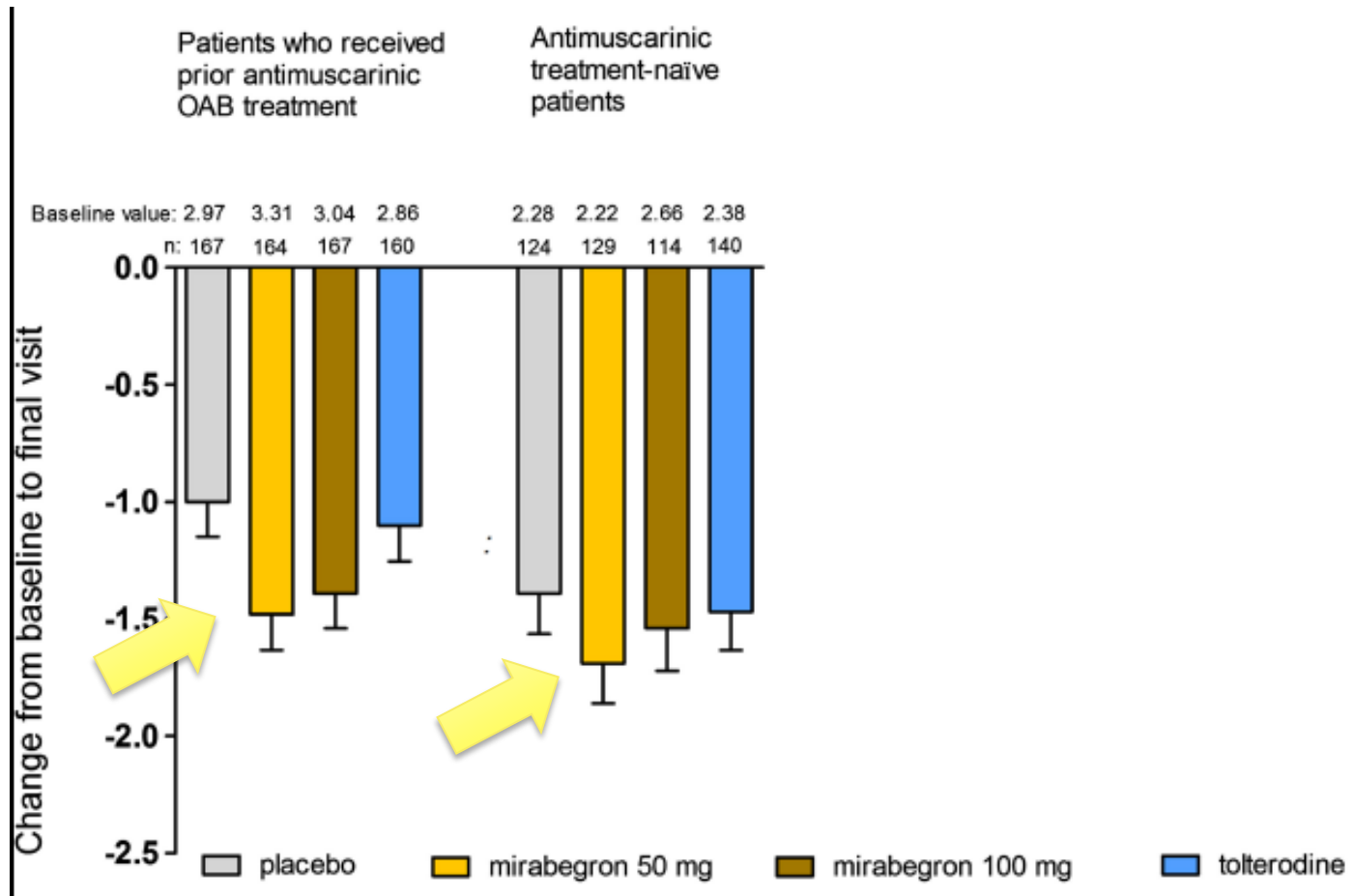
# Beta3Agonista



- Funziona meglio in pazienti non responder a antimuscarinici?

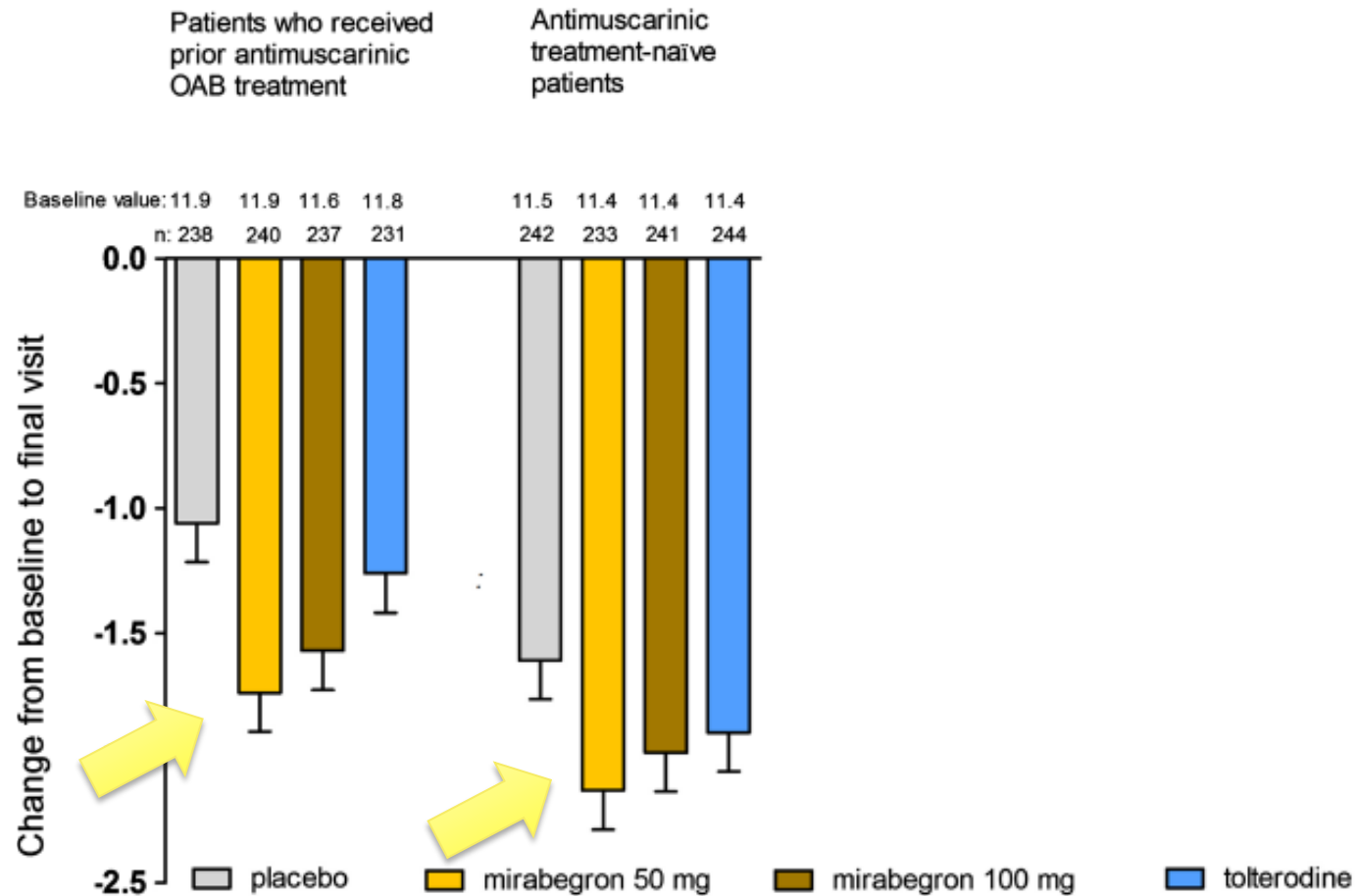
# Prima o seconda linea di terapia?

## Mean number of UI episodes/24 h



# Prima o seconda linea di terapia?

## Mean number of micturitions/24 h



ORIGINAL ARTICLE

# Is mirabegron equally as effective when used as first- or second-line therapy in women with overactive bladder?

**Maurizio Serati<sup>1</sup> · Umberto Leone Roberti Maggiore<sup>2,3</sup> · Paola Sorice<sup>1</sup> ·  
Simona Cantaluppi<sup>1</sup> · Enrico Finazzi Agrò<sup>4</sup> · Fabio Ghezzi<sup>1</sup> · Publication Committee of  
the Italian Society of Urodynamics**



## Seconda linea di trattamento?



## Beta3Agonista


- ◆ Funziona in pazienti non responder a antimuscarinici?
-

## Effect of mirabegron on patients with refractory OAB and on the waiting list for onabotulinumtoxinA (onabotA)



Watcyn-Jones T. Eur Urol Suppl 2014;13(1):e704

- Single-centre study (mean FU 55d)
- N=36 pts with refractory OAB and proven DO
  - 6 males, 30 females (mean age 60 yr) – 86% have UUI
  - on the waiting list for first/repeat onabotA therapy
  - received mirabegron 50 mg od
- Response rate of mirabegron: 67% (24/36 pts)
  - ICIQ-SF score: 13.36 → 9.41 ( $P=0.005$ )
  - 16/24 pts (67%) wanted to be removed from the waiting list, after 2 wk
- 13 of 36 pts (36%) with  $\geq 1$  prior onabotA treatment:
  - 7 wanted to be removed from waiting list, after 2 wk
- AEs:
  - palpitations (2), vomiting (1), rashes (1), lethargy (1), yellow urine (1)



Patients with refractory OAB seem to respond well to mirabegron.  
About one third are willing to be removed from the waiting list for onabotA injections

# Beta3Agonista

EUROPEAN UROLOGY XXX (2016) XXX–XXX

available at [www.sciencedirect.com](http://www.sciencedirect.com)  
journal homepage: [www.europeanurology.com](http://www.europeanurology.com)



**Platinum Priority – Voiding Dysfunction**  
*Editorial by XXX on pp. x–y of this issue*

## **Efficacy and Safety of Mirabegron Add-on Therapy to Solifenacin in Incontinent Overactive Bladder Patients with an Inadequate Response to Initial 4-Week Solifenacin Monotherapy: A Randomised Double-blind Multicentre Phase 3B Study (BESIDE)**

Marcus J. Drake<sup>a,\*</sup>, Christopher Chapple<sup>b</sup>, Ahmet A. Esen<sup>c</sup>, Stavros Athanasiou<sup>d</sup>,  
Javier Cambroner<sup>e</sup>, David Mitcheson<sup>f</sup>, Sender Herschorn<sup>g</sup>, Tahir Saleem<sup>h</sup>,  
Moses Huang<sup>h</sup>, Emad Siddiqui<sup>h</sup>, Matthias Stölzel<sup>i</sup>, Claire Herholdt<sup>h</sup>, Scott MacDiarmid<sup>j</sup>,  
*on behalf of the BESIDE study investigators*

# Beta3Agonista

- ◆ Combination > Solifenacin 5 mg
- ◆ Combination <> Solifenacin 10 mg (with less side effects)

EUROPEAN UROLOGY XXX (2016) XXX-XXX

available at [www.sciencedirect.com](http://www.sciencedirect.com)  
journal homepage: [www.europeanurology.com](http://www.europeanurology.com)

**EAU**  
European Association of Urology



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## Beta3Agonista

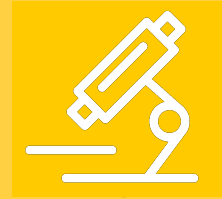
◆ Funziona in pazienti non responder a antimuscarinici?

Sì...

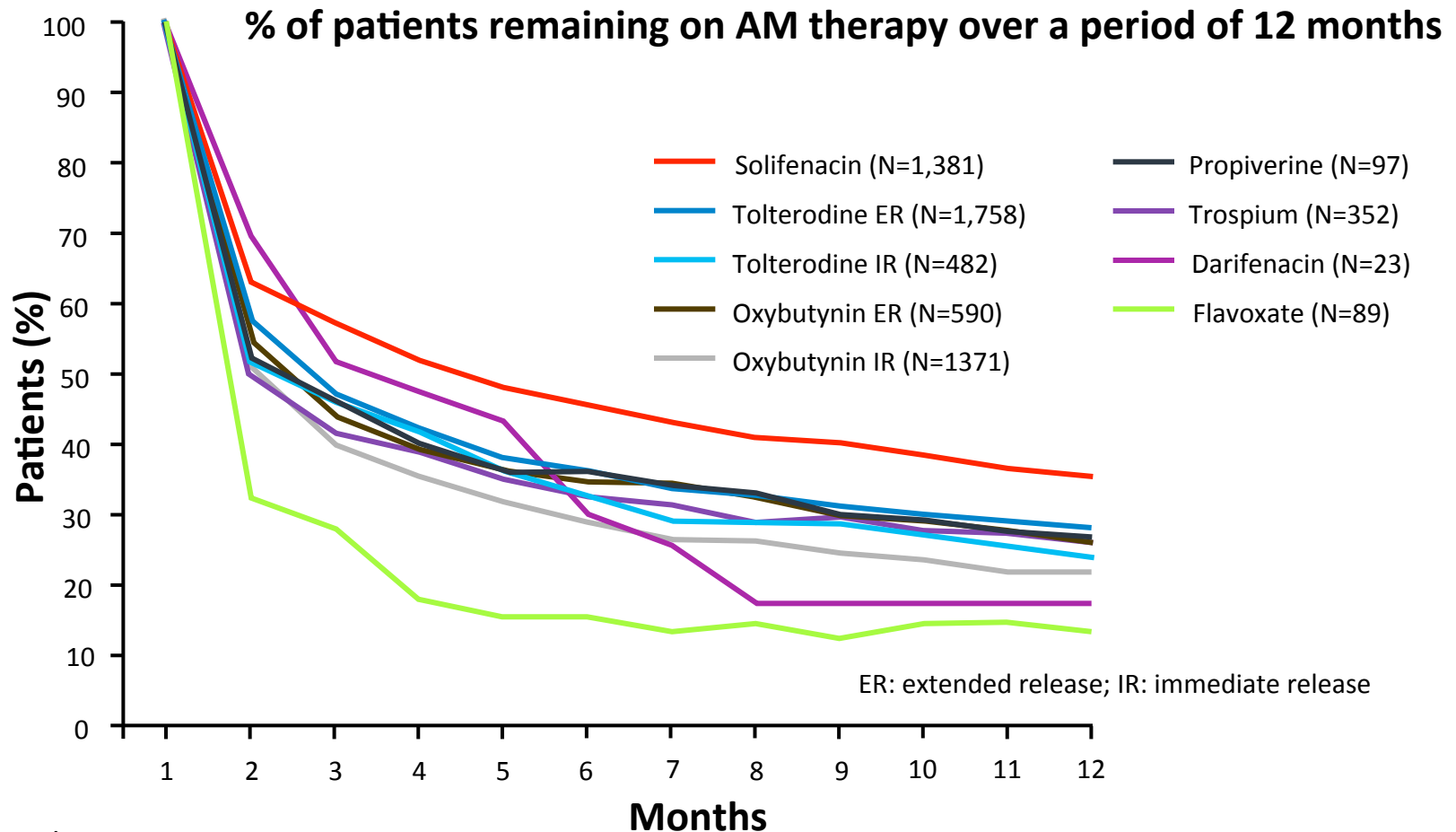
E anche in combinazione!

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# Persistence with antimuscarinic agents is poor



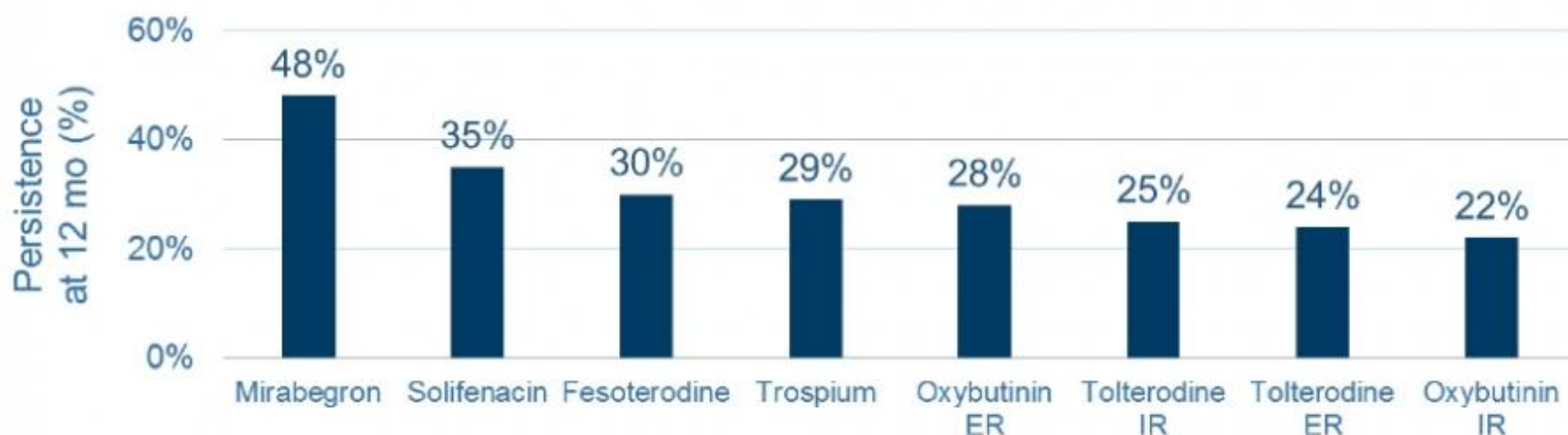
- 12-month UK study on prescription data



## Persistence with mirabegron vs antimuscarinics in OAB

Wagg A. Eur Urol Suppl 2015;14(2):e267

- Analysis of prescription data from a UK longitudinal database: pts starting a new course of OAB therapy (2012-2013) and followed for 12 mo
  - N=10,238 pts receiving antimuscarinics; N=141 pts receiving mirabegron
- Treatment cessation = discontinuation of treatment >1.5 times the expected duration of the previous prescription, including switching to other drug
- Mirabegron had a higher persistence than antimuscarinics at 12 mo:



Mirabegron seems to have a higher persistence rate at 12 mo than antimuscarinics in pts starting a new course of OAB treatment

# Out of pocket...

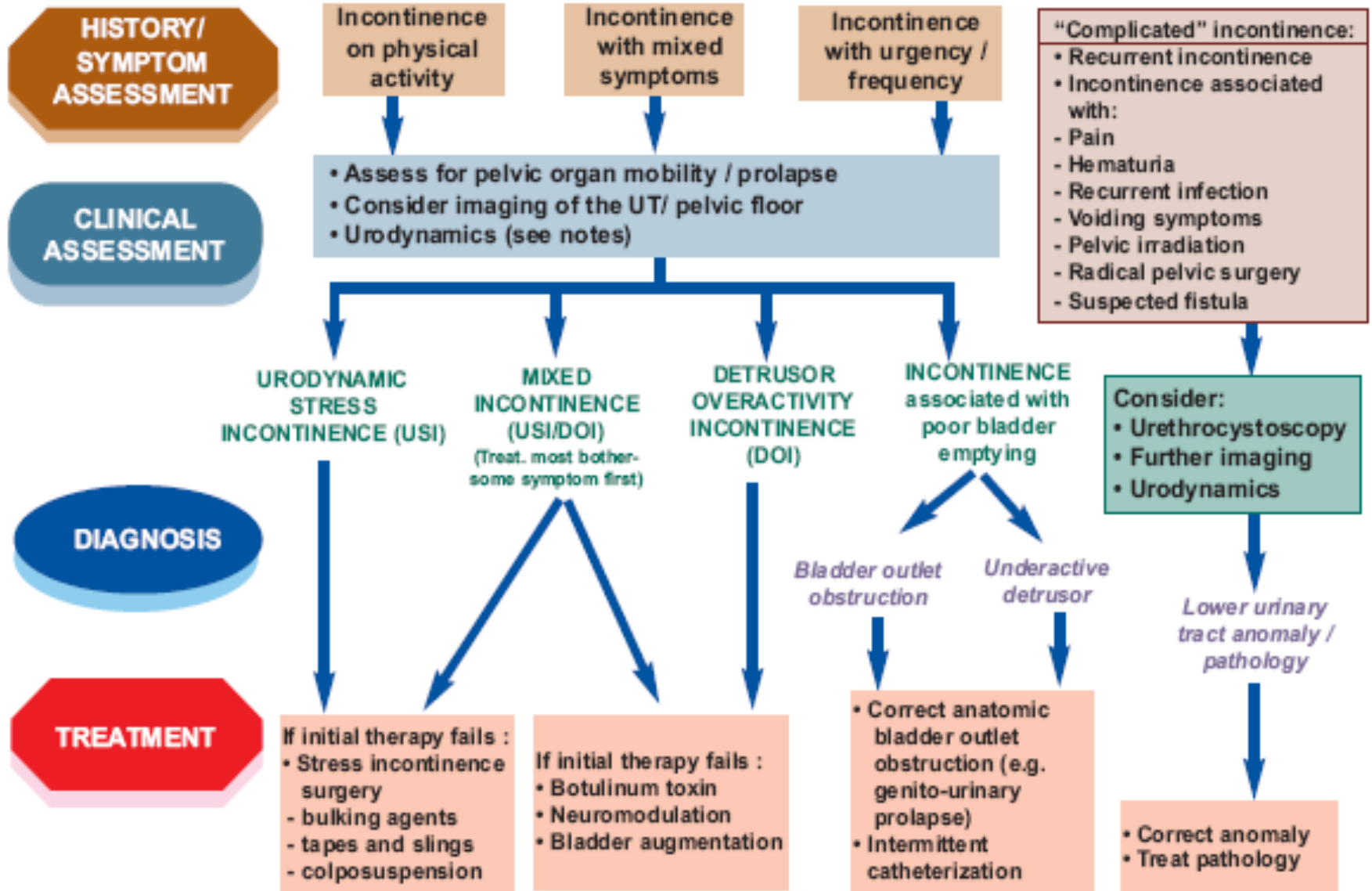




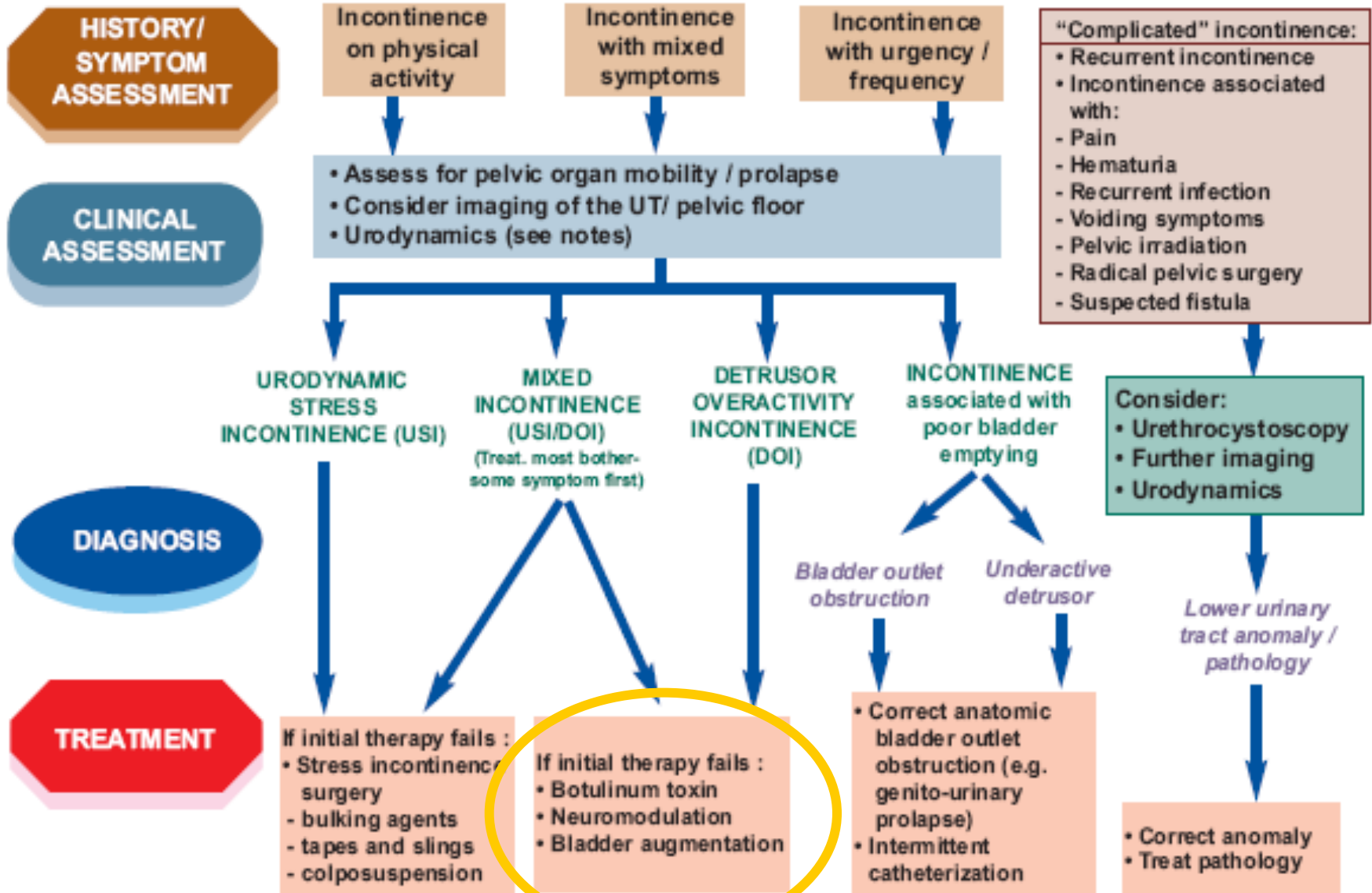
# FARMACI PER L'INCONTINENZA URINARIA

SOTTOGRUPPO «FARMACI» DEL GRUPPO DI LAVORO SUI PROBLEMI  
LEGATI ALL'INCONTINENZA URINARIA E FECALE (D.M. DEL 2  
OTTOBRE 2015)

# Specialized Management of Urinary Incontinence in Women



# Specialized Management of Urinary Incontinence in Women



# Neuromodulazione sacrale

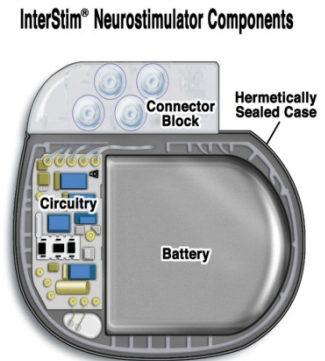
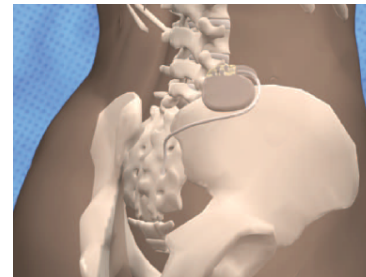
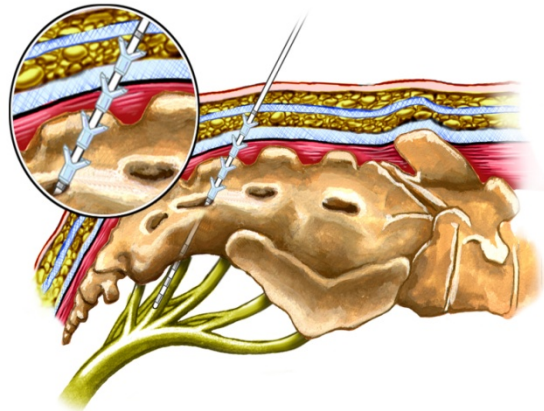
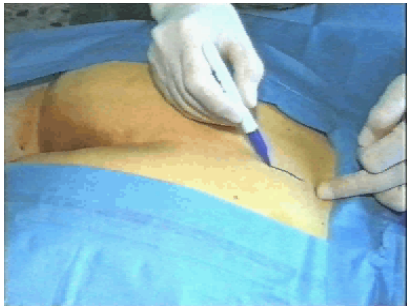
**SISTEMA InterStim®**



# Procedure chirurgiche: neuromodulazione sacrale

- Neuromodulazione sacrale

- Il meccanismo d'azione rimane dibattuto<sup>1</sup>
- Almeno due meccanismi potenziali:<sup>1</sup>
  - Attivazione delle fibre efferenti che arrivano allo sfintere uretrale striato che di riflesso causa il rilassamento del detrusore (secondo Tanagho & Schmidt 1988<sup>2</sup>)
  - Attivazione delle fibre afferenti che causa l'inibizione a livello spinale o soprasspinale (secondo Fowler et al 2000<sup>2</sup>)



1. Groen J, Bosch JLHR. *BJU Int* 2001;87:723–31
2. Tanagho EA, Schmidt RA. *J Urol* 1988;140:1331–9.
3. Fowler CJ, et al. *J Urol* 2000;163:881–3.

## Herbison GP: Cochrane Database Syst Rev. 2009

- Eight reports of randomised studies that evaluated implants which provided continuous stimulation were included.
- It seems clear that continuous stimulation offers benefits for carefully selected people with overactive bladder syndrome and for those with urinary retention.

# SNM for OAB

**Table 5.** Short-term results of treatment with SNM or with placebo among patients with OAB

First author	Follow-up, months	General improvement, %	Voids/day, %	Voided vol., %	IE/day, %	Proportion of group with 100% continence, %	Pads/day, %	MCC, %
Weil [36]	6				-90	56	-92	39
Schmidt [35]	6				-73	47	-82	
Hassouna [40]	12	88	-46	77				
van Kerrebroeck [43]	49		-23	79	-56		-64	
van Voskuilen [44]	64.2	64						
Sutherland [42]	22	69	-35		-88	50	-100	
van Voskuilen [45]	15.5	80	-38	44	-65			
Hijaz [41]	16	75						

# Percutaneous Tibial Nerve Stimulation PTNS

- Neuromodulation  
technique of the lower  
urinary tract obtained with  
electrical stimulation of  
the posterior tibial nerve



# PTNS: procedura



- Trattamento ambulatoriale
- Una seduta di stimolazione a settimana
- 30 minuti
- Periodo di valutazione: 12 settimane

# **Percutaneous Tibial Nerve Stimulation Effects on Detrusor Overactivity Incontinence are Not Due to a Placebo Effect: A Randomized, Double-Blind, Placebo Controlled Trial**

Enrico Finazzi-Agrò,<sup>\*,†</sup> Filomena Petta, Francesco Sciobica, Patrizio Pasqualetti, Stefania Musco and Pierluigi Bove

*From the Department of Surgery/Urology, Tor Vergata University (EFA, FP, FS, PB), SeSMIT, Service for Medical Statistics and Information Technology, AFaR, Fatebenefratelli Hospital, Isola Tiberina (PP) and Fondazione S. Lucia (SM), Rome, Italy*

*North Carolina (SAM)*

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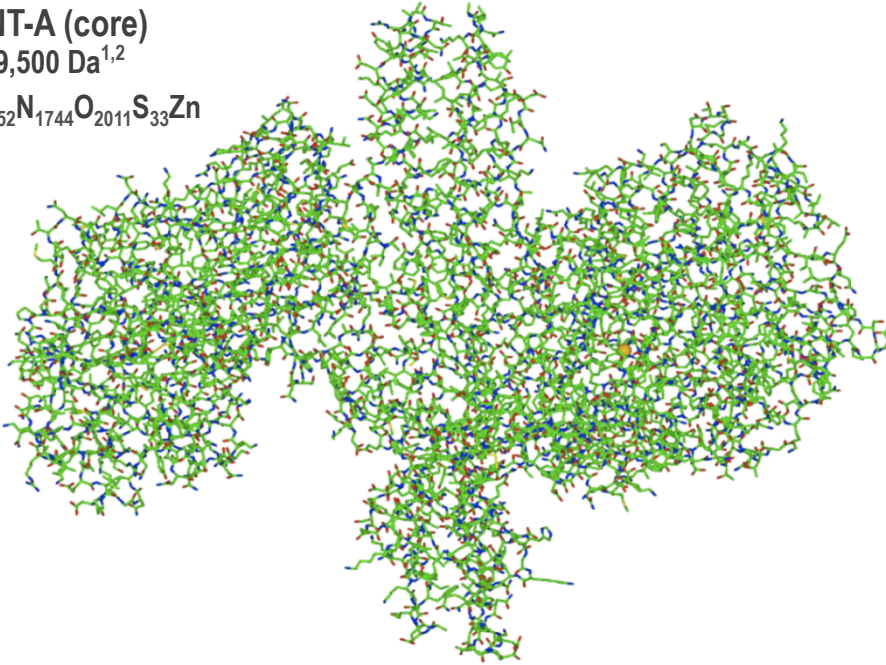
# Guidelines on Urinary Incontinence

M.G. Lucas, J.L.H.R. Bosch, F.R. Cruz, T.B. Madden,  
A. Nambiar, A. Neisius, R.S. Pickard, D.J.M.K. de Ridder,  
A. Tubaro, W.H. Turner

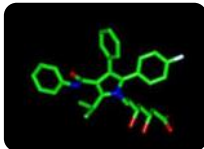
Offer, if available, PTNS as an option for improvement of urgency urinary incontinence in women, but not men, who have not benefited from antimuscarinic medication.

# Tossina botulinica di tipo A: una grande proteina tridimensionale

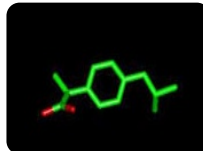
**BoNT-A (core)**  
 149,500 Da<sup>1,2</sup>  
 $C_{6763}H_{10452}N_{1744}O_{2011}S_{33}Zn$



**Lipitor® (Atorvastatina)<sup>3</sup>**  
 559 Da  
 $C_{33}H_{35}FN_2O_5$



**Ibuprofene<sup>3</sup>**  
 206 Da  
 $C_{13}H_{18}O_2$

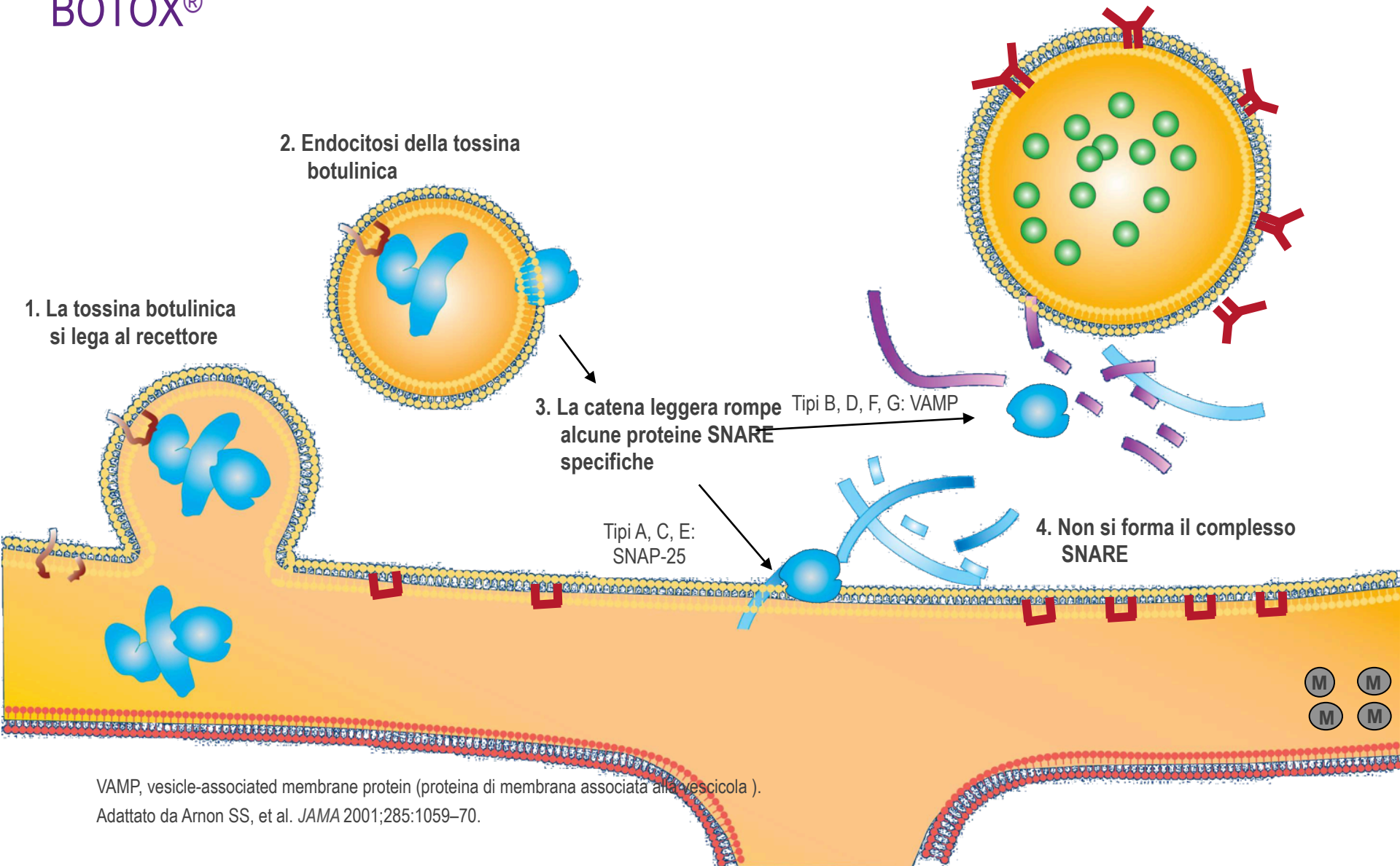


Composto	MW
Aspirina (acido acetilsalicilico)	180 Da <sup>3</sup>
Uraplex® (cloruro di tropsio)	430 Da <sup>3</sup>
Omic® (tamsulosina)	445 Da <sup>3</sup>
Viagra® (citrato di sildenafil)	667 Da <sup>3</sup>
Complesso BOTOX® (tossina botulinica di tipo A)	~900,000 Da <sup>4</sup>

BoNT-A, Tossina botulinica di tipo A; MW, peso molecolare.

1. Lacy DB, et al. *Nat Struct Biol* 1998;5:898–902.
2. Lacy DB, Stevens RC. *J Mol Biol* 1999;291:1091–104.
3. DrugBank. Disponibile su <http://www.drugbank.ca/drugs/DB01076>. Ultimo accesso Febbraio 2013.
4. Schantz EJ, Johnson EA. *Perspect Biol Med* 1997;40:317–27.

# L'inibizione dell'interazione tra le vescicole sinaptiche e le membrane del terminale nervoso è fondamentale per l'azione motoria e sensoriale di BOTOX®



VAMP, vesicle-associated membrane protein (proteina di membrana associata alla vescicola).

Adattato da Amon SS, et al. JAMA 2001;285:1059-70.

# Linee guida che consigliano le iniezioni di tossina botulinica per l'incontinenza neurogena (Grado A)

Linee guida	Livello d'evidenza/Grado di raccomandazione
ICI guidelines 2013 (tossina botulinica [ <i>neurogena</i> ], iniettata nel detrusore) <sup>1</sup>	1A
EAU guidelines 2009 (disfunzione neurogena del basso tratto urinario) <sup>2</sup>	1 A
EAU guidelines 2011 (disfunzione neurogena del basso tratto urinario) <sup>3</sup>	A
EAU guidelines 2011 (incontinenza urinaria) <sup>3</sup>	2 A (neurogena)

EAU, European Association of Urology; ICI, International Continence Society.

1. Abrams P, et al. eds. From the 5th ICI; Health Publication Ltd; 2013.

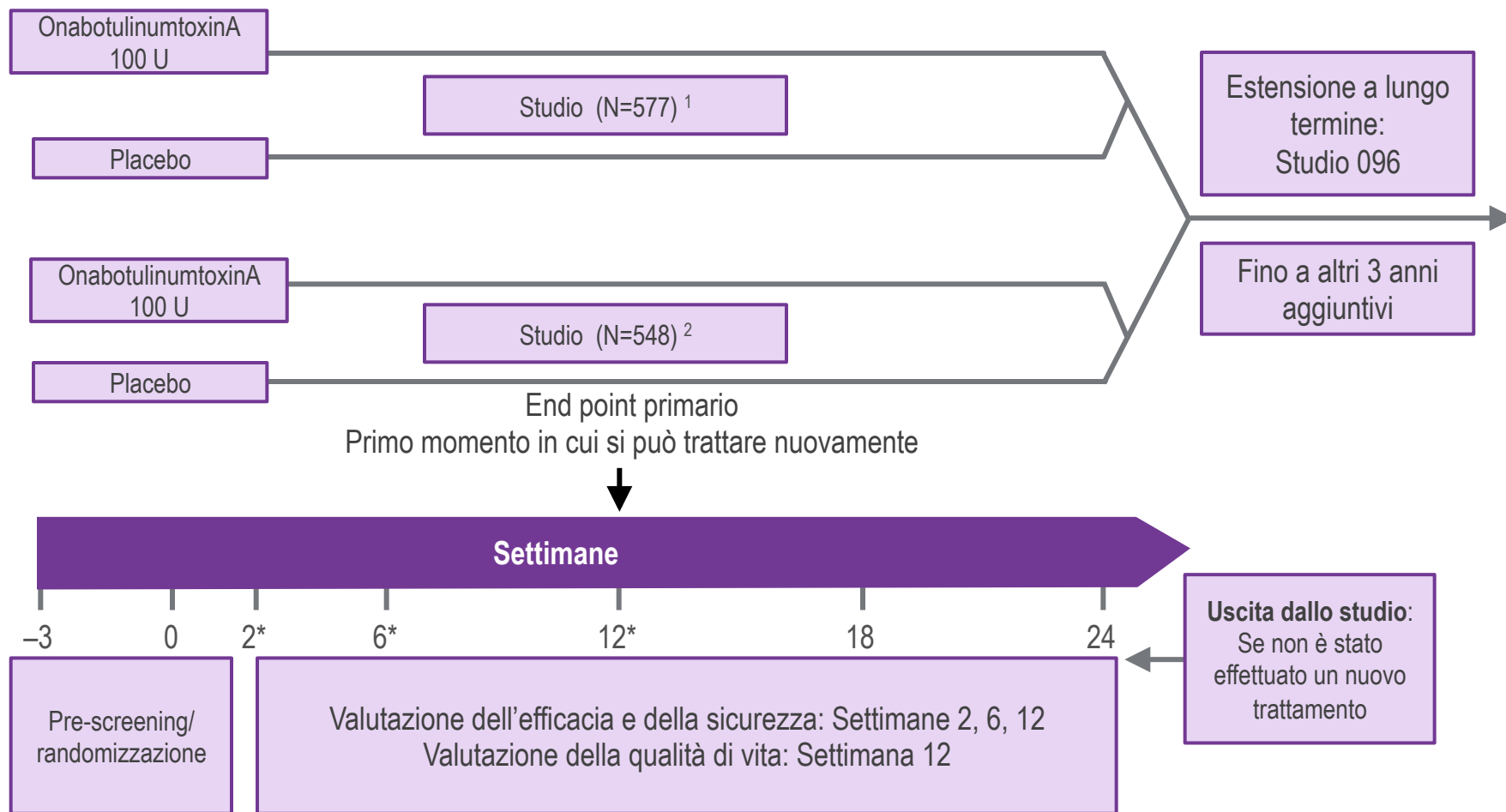
2. Stöhrer M. European Association of Urology. Guidelines on neurogenic lower urinary tract dysfunction. 2009.

Disponibile su [http://www.uroweb.org/fileadmin/tx\\_eauguidelines/2008/Full/Neurogenic\\_LUTS.pdf](http://www.uroweb.org/fileadmin/tx_eauguidelines/2008/Full/Neurogenic_LUTS.pdf). Ultimo accesso Giugno 2011.

3. Pannek J. European Association of Urology. Guidelines on neurogenic lower urinary tract dysfunction. 2011.

Disponibile su [http://www.uroweb.org/gls/pdf/17\\_Neurogenic%20LUTS.pdf](http://www.uroweb.org/gls/pdf/17_Neurogenic%20LUTS.pdf). Ultimo accesso Giugno 2011.

# EMBARC: due studi pivotali di fase III<sup>1,2</sup>

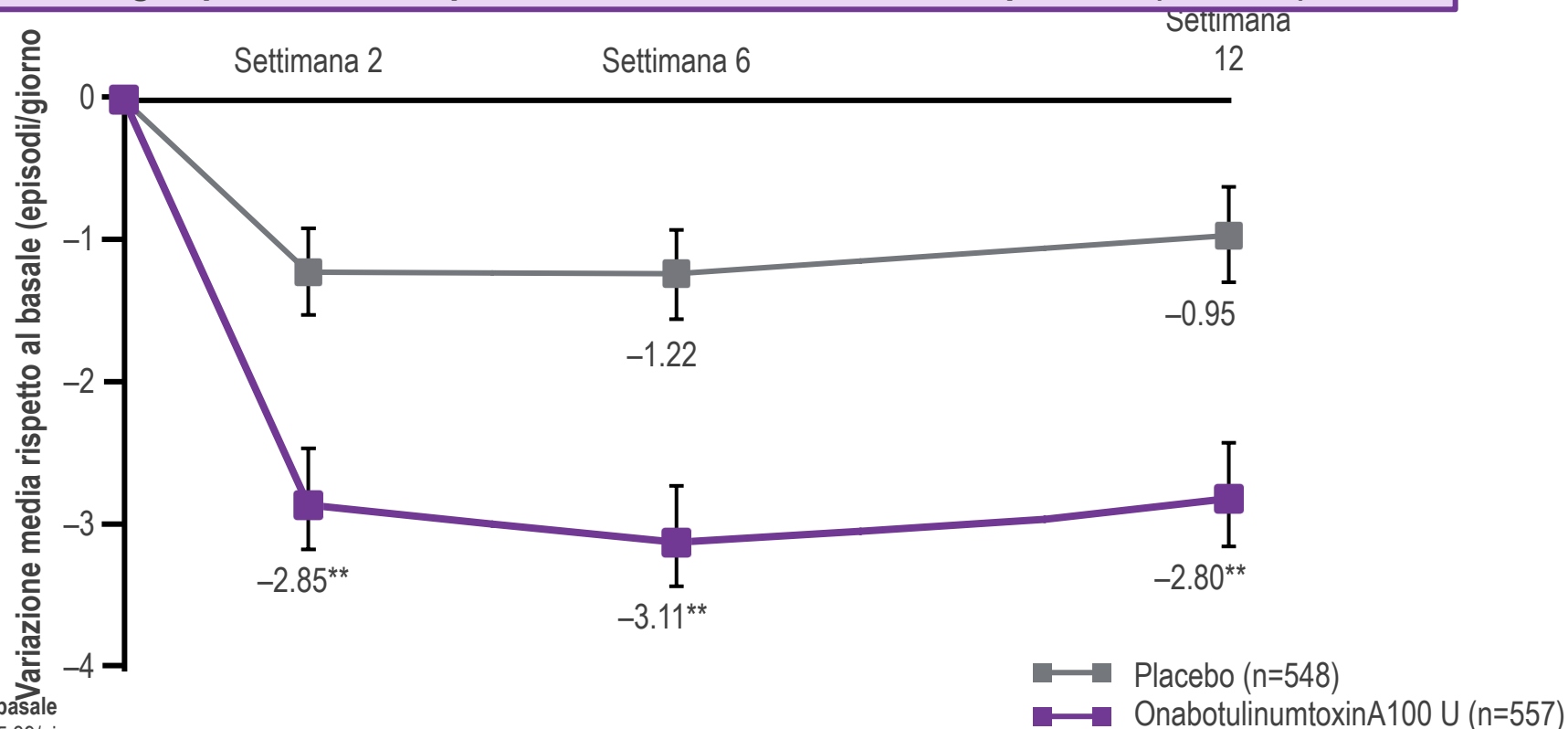


\*Periodo di confronto placebo-controllo.

1. Nitti et al JUrol\_2013
2. Chapple et al EurUrol2013

# Diminuzione significativa degli episodi d'incontinenza urinaria giornaliera rispetto al placebo

Alla 12<sup>a</sup> settimana, OnabotulinumtoxinA consentiva di ottenere il 51% di riduzione degli episodi di UI rispetto al basale contro il 18% col placebo (P<0.001)



Valori al basale

Placebo: 5.39/giorno

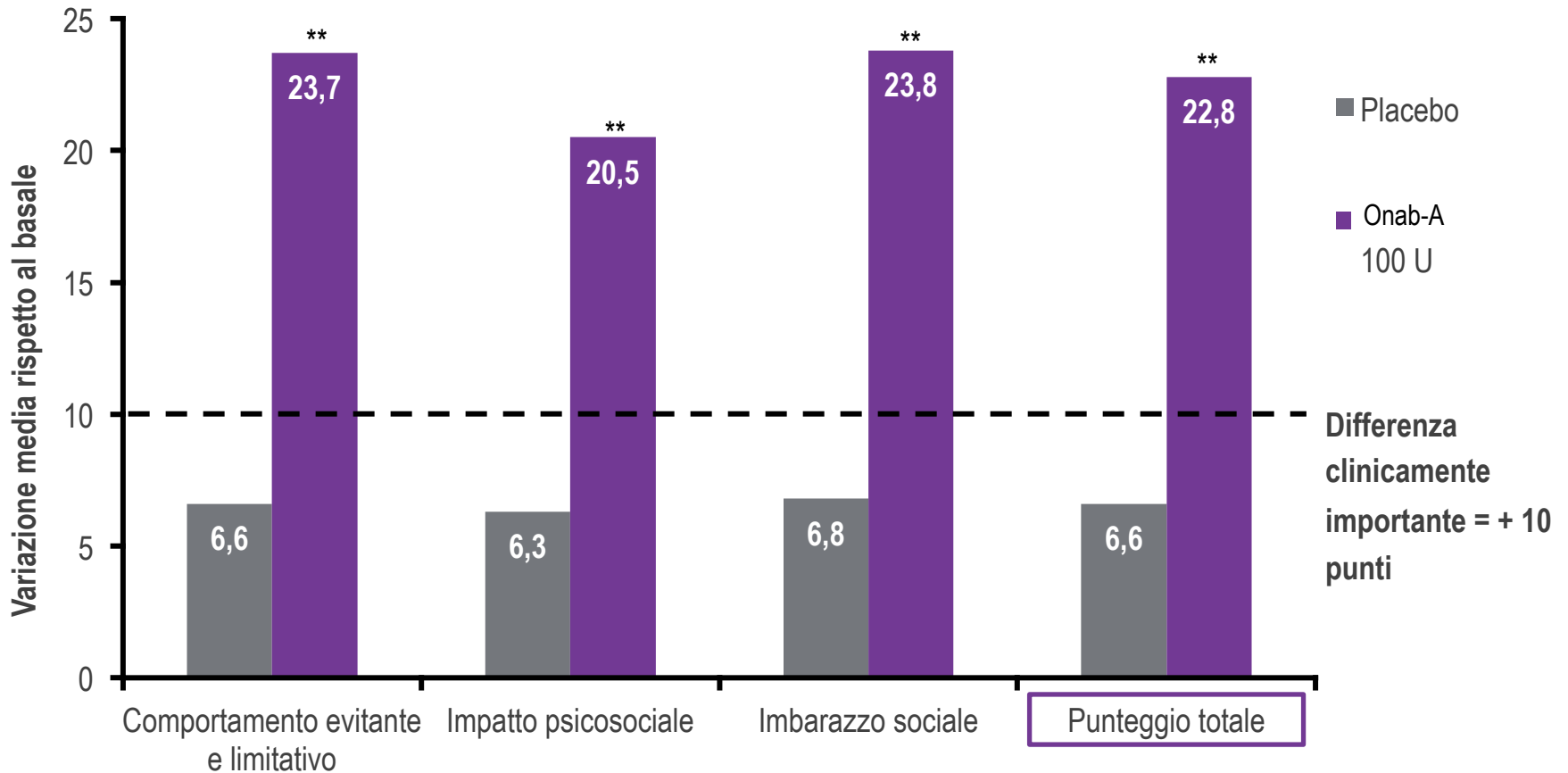
OnabotulinumtoxinA 100 U: 5.49/giorno

\*\*p<0.001 vs. placebo.

UI, incontinenza urinaria.

# Miglioramenti clinicamente significativi in tutti i domini della I-QOL

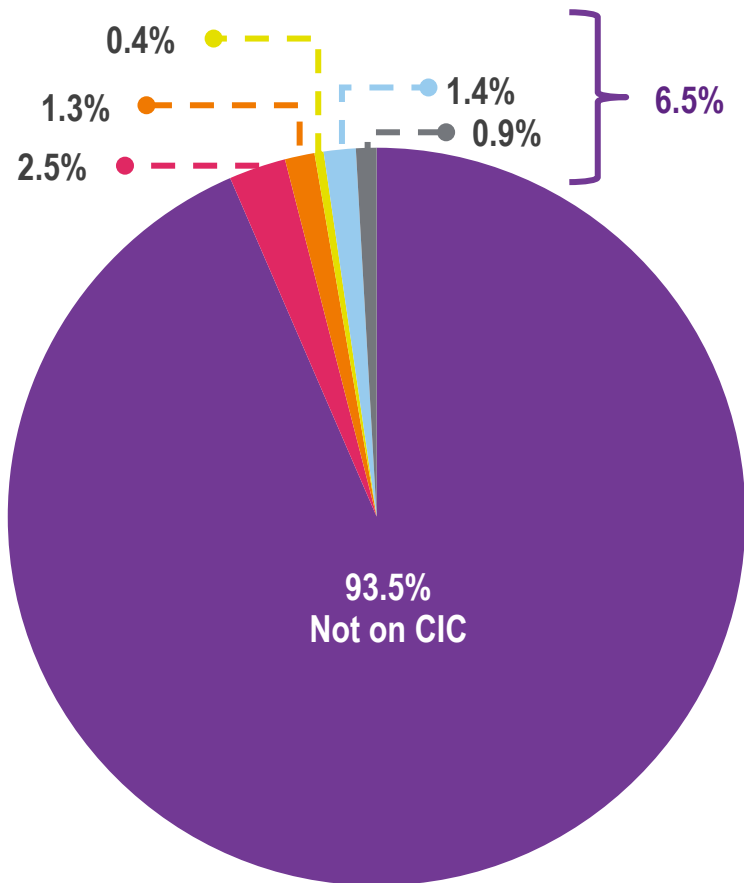
Variatione rispetto al basale dei punteggi della I-QOL alla 12<sup>a</sup> settimana



\*\*p<0.0001 vs. placebo.

I-QOL, Questionario sulla qualità della vita specifico per l'incontinenza ..

# La maggioranza dei pazienti non aveva bisogno del CIC



CIC = 6.5% (36/552 pazienti)\*

## % dei pazienti

- Non ha iniziato il CIC
- Ha usato il CIC ≤6 settimane
- Ha usato il CIC >6 e ≤12 settimane
- Ha usato il CIC >12 e ≤18 settimane
- Ha usato il CIC >18 e ≤24 settimane
- Ha usato il CIC >24 settimane

Le percentuali del CIC sono basse e principalmente transitorie

\*Pazienti che hanno avuto bisogno del CIC in qualsiasi momento durante il 1° ciclo di trattamento.  
CIC, cateterismo intermittente pulito.

Il tempo medio per la richiesta di un nuovo trattamento da parte del paziente è ~6 mesi

**Il tempo medio della durata della risposta dopo inoculo di OnabotulinumtoxinA in base alla richiesta del paziente di un nuovo trattamento, era di 166 giorni (~24 settimane)**

# Gestione dell'incontinenza urinaria: Linee guida EAU 2013<sup>1</sup>

## Tossina botulinica di tipo A (intravesicale; 100–300 U)

Proporre iniezioni intravesicali di tossina botulinica di tipo A ai pazienti affetti da incontinenza urinaria refrattari alla terapia antimuscarinica (A\*)

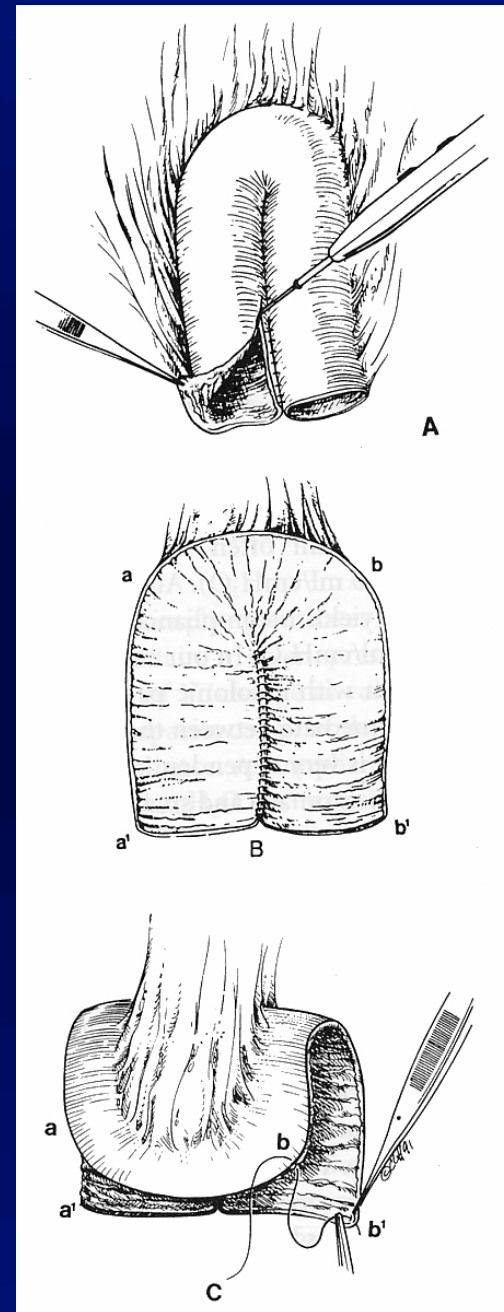
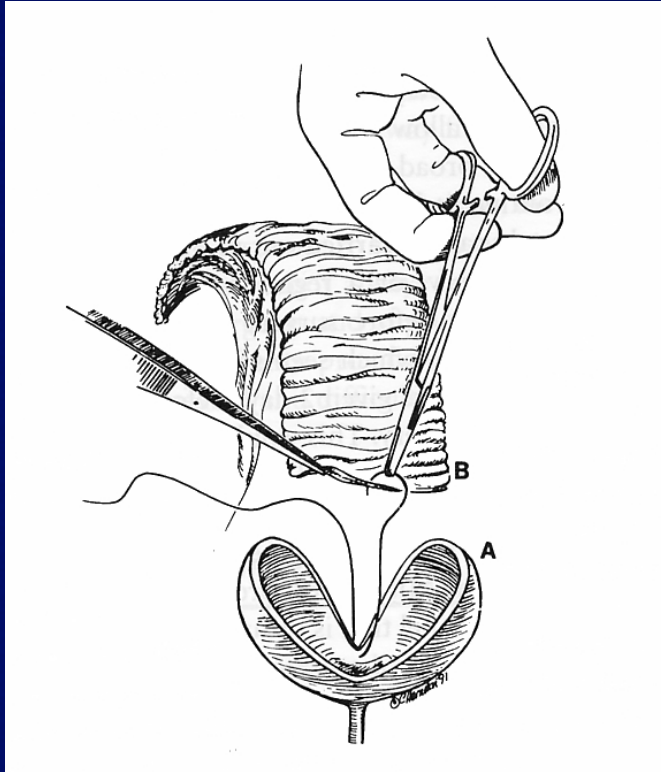
Avvertire i pazienti della durata limitata della risposta, del possibile prolungato bisogno di auto-cateterismo (verificare che siano disposti e capaci di farlo), e del rischio di infezioni delle vie urinarie (A\*)

Inoltre, i pazienti devono essere informati dello stato di autorizzazione della tossina botulinica di tipo A, e che gli effetti negativi a lungo termine, anche se improbabili, rimangono incerti (A\*)

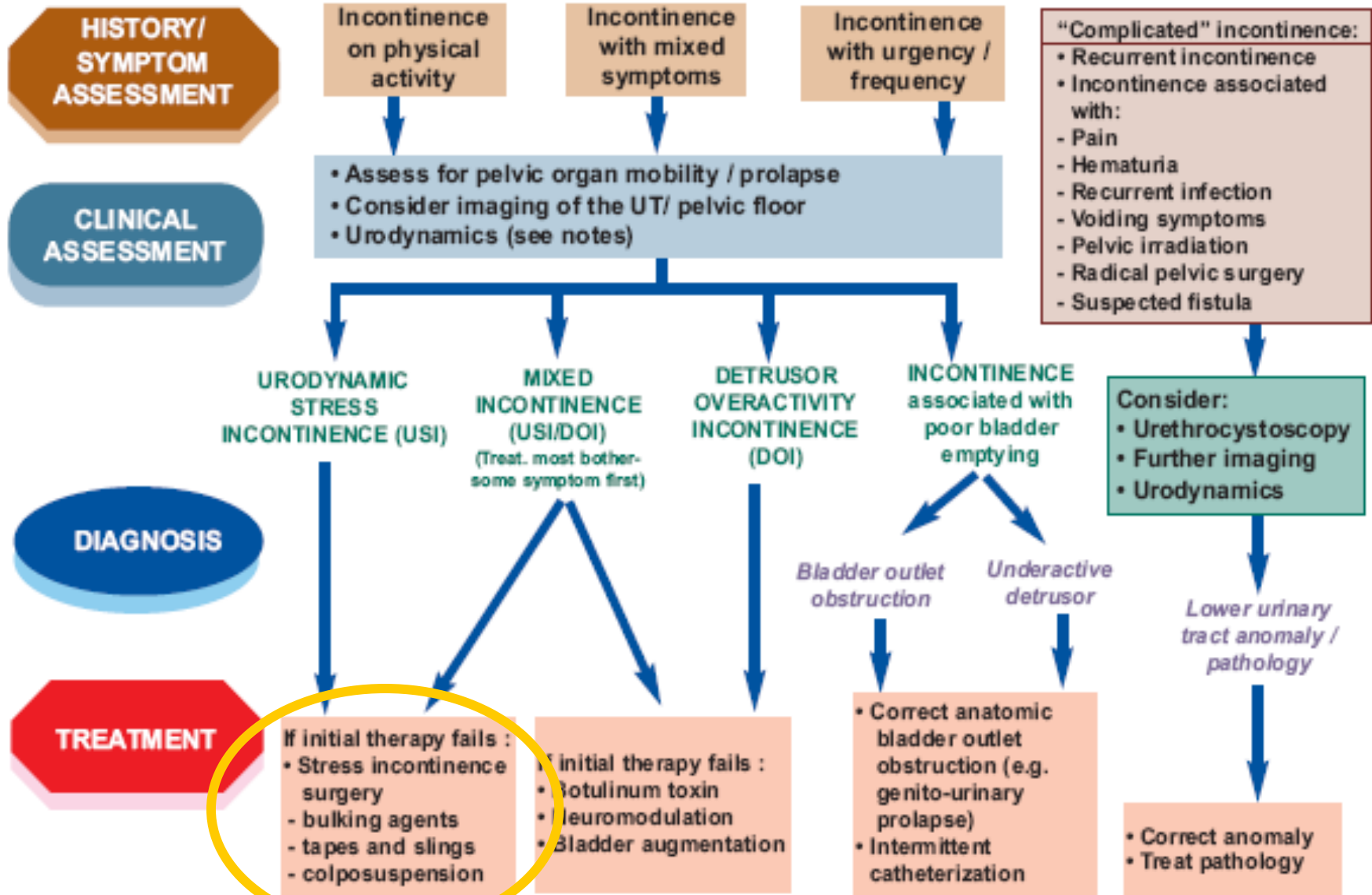
\* Raccomandazione EAU di Grado A: In base a studi clinici di buona qualità e la consistenza riguardo le raccomandazioni specifiche e che includono almeno uno studio clinico randomizzato  
EAU, European Association of Urology.

1. Lucas MG, et al. EAU guidelines on urinary incontinence. 2013.

# ILEOCYSTOPLASTY



# Specialized Management of Urinary Incontinence in Women

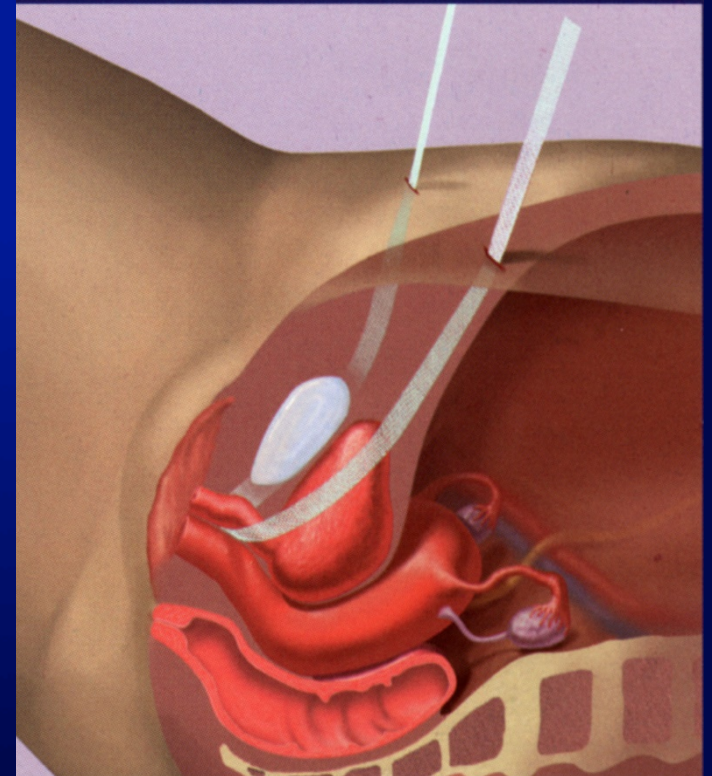
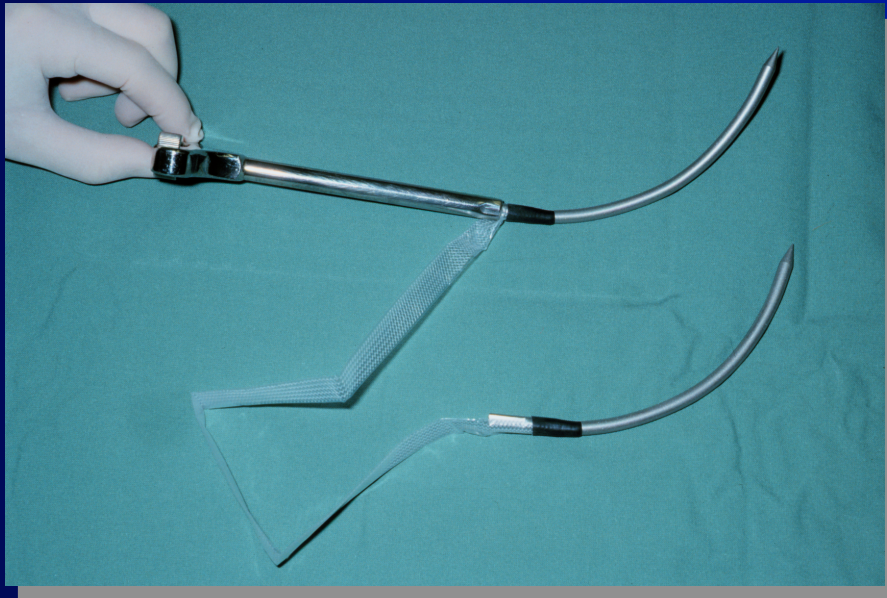


**WHAT CAN WE DO IN WOMEN?**

# Low-tension Mid-Urethral Sling

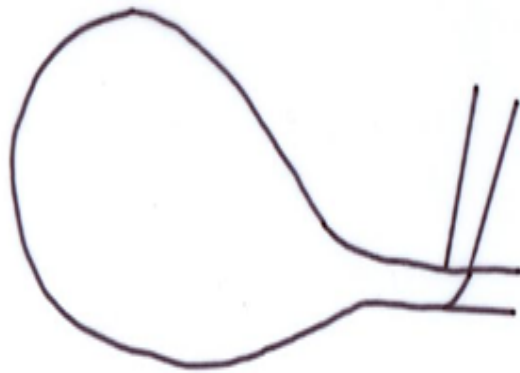
Tension free intravaginal slingplasty

*Ulmsten & Petros 1995*

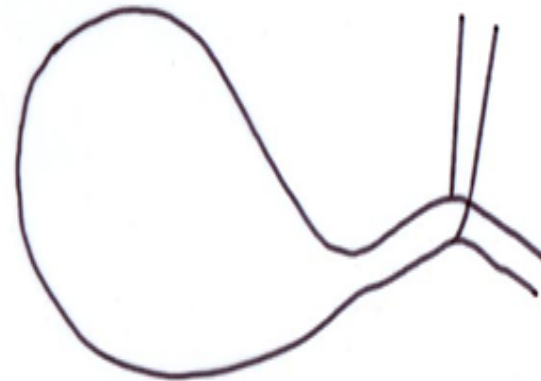


# TVT

## TVT

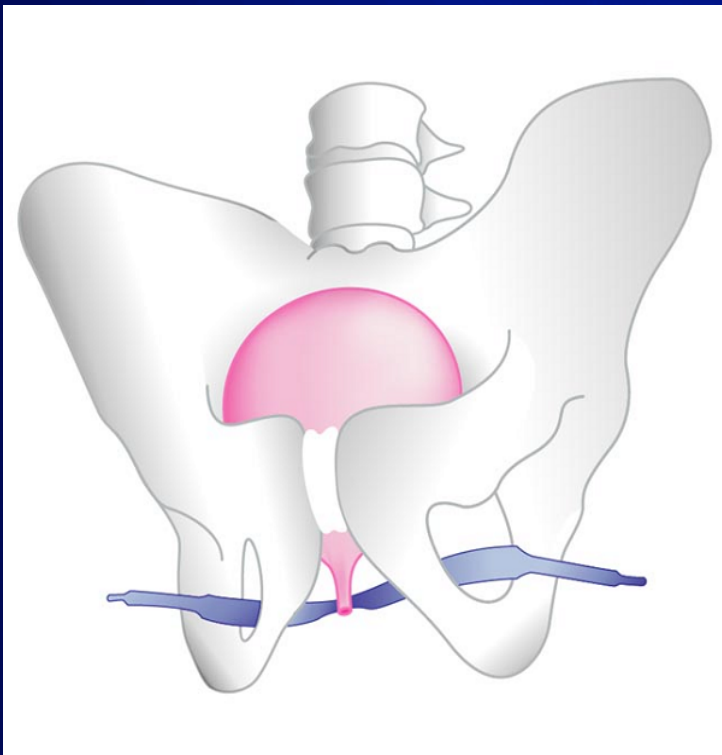


at rest



at stress

# Low-tension Mid-Urethral Sling



TOT -

## TRANSOBTURATOR TAPE

- Tape runs through both obturator foramina
- Cystoscopy not necessary (bladder perforation unlikely)

*Delorme 2001*

# Single-incision mini-sling (SIMS) vs standard midurethral slings (SMUS) for female SUI

Mostafa A. Neurourol Urodyn 2013;32(6):526-8(abs.4)

- Systematic review and meta-analysis of n=25 RCTs including N=3,114 women with SUI (literature search until March 2013)
- SIMS:
  - Mini-Arc: n=6 studies; N=566 women
  - Ajust: n=3 studies; N=350 women
  - Ophira: n=1 study; N=130 women
  - Contasure: n=1 study; N=257 women
  - TFS: n=1 study; N=80 women
  - Solyx: n=1 study; N=30 women
  - TVT-Secur: n= 12 studies; N=1,606 women
- No significant differences between SIMS and SMUS (when excluding TVT-Secur) in patient-reported cure rate and objective cure rate at 12-24 mo FU

RR (95% CI; P value)	SIMS vs SMUS	SIMS excl. TVT-Secur vs SMUS
Patient reported cure rate	0.90 (0.85-0.95; P=0.0003)	0.96 (0.88-1.03; P=0.26)
Objective cure rate	0.90 (0.84-0.95; P=0.0003)	0.97 (0.92-1.02; P=0.26)

RR: relative risk; CI: confidence interval

# Single-incision mini-sling (SIMS) vs standard midurethral slings (SMUS) for female SUI

Mostafa A. Neurourol Urodyn 2013;32(6):526-8(abs.4)

- SIMS vs SMUS
  - Better operative and peri-operative outcomes
  - Earlier return to normal activities and work

SIMS vs SMUS	WMD (95% CI)
Operative time	-2.04 min (-3.51 to -0.58 min)
Postoperative groin pain	-2.51 (-3.62 to -1.40)

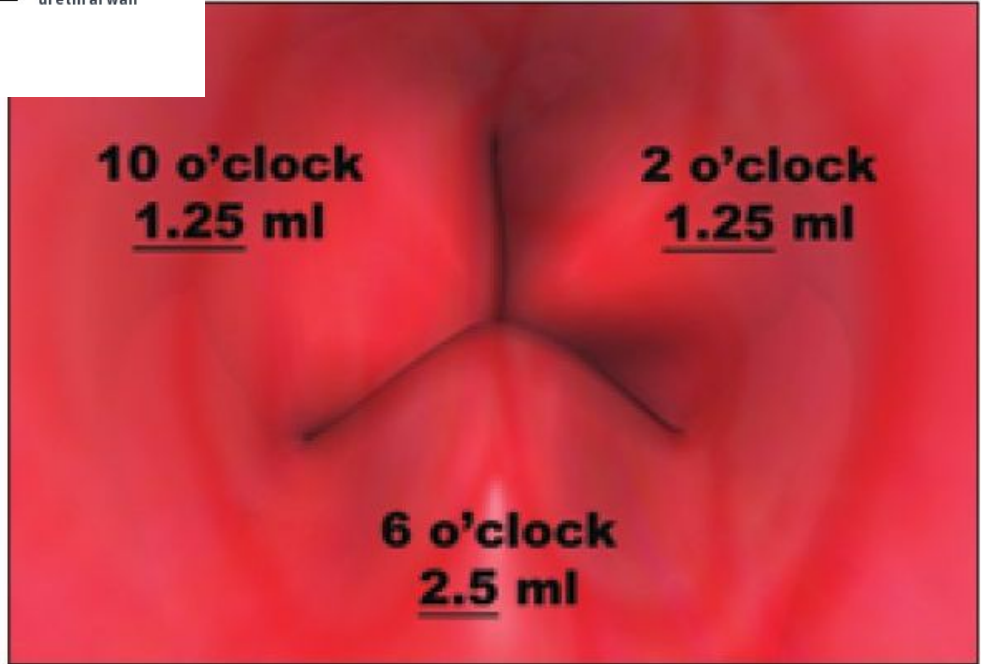
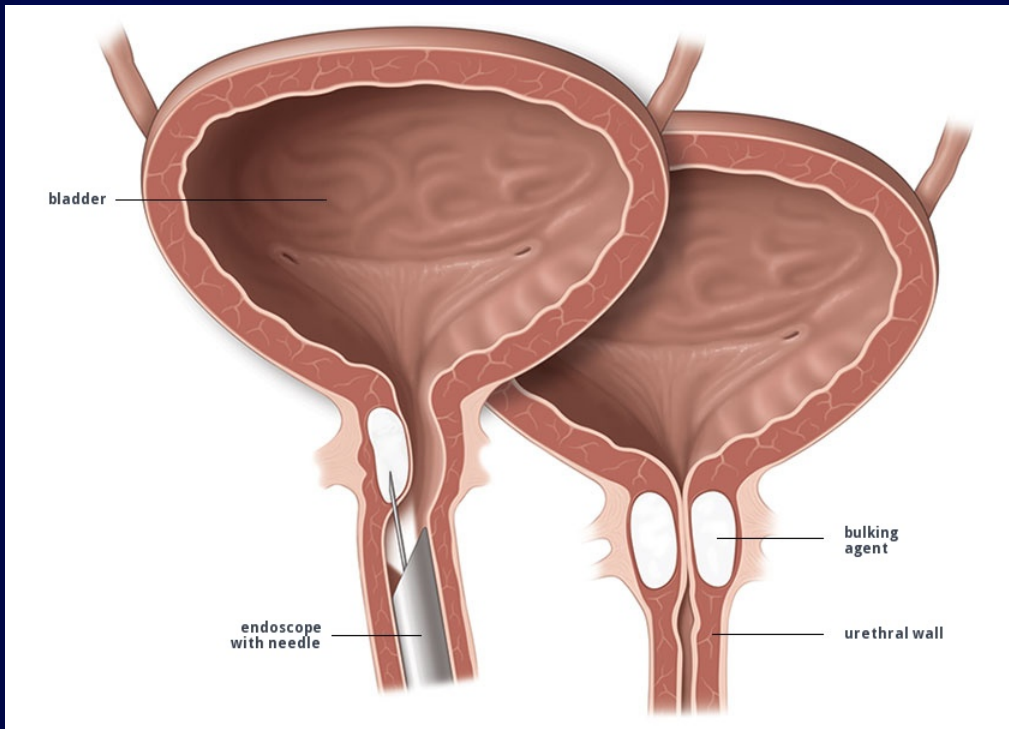
WMD: weighted mean difference; CI: confidence interval

- No difference in lower urinary tract injuries, postoperative voiding difficulties, de-novo urgency/worsening of pre-existing urgency, QoL and sexual function
- Vaginal erosion and repeat continence surgery were significantly higher in the SIMS vs SMUS group but this was mainly due to significant difference in the TVT Secur group

**SIMS, excluding TVT-Secur, seem to have a similar cure rate and better post-operative outcomes vs SMUS at 12-24 mo FU**

Recommendations for surgery for uncomplicated stress urinary incontinence in women	GR
Offer the mid-urethral sling to women with uncomplicated stress urinary incontinence as the preferred surgical intervention whenever available.	A
Warn women who are being offered a retropubic insertion of mid-urethral sling about the relatively higher risk of peri-operative complications compared to transobturator insertion.	A
Warn women who are being offered transobturator insertion of mid-urethral sling about the higher risk of pain and dyspareunia in the longer term.	A
Warn women who are being offered a single-incision sling that long-term efficacy remains uncertain.	A
Do a cystourethroscopy as part of the insertion of a mid-urethral sling.	C
Offer colposuspension (open or laparoscopic) or autologous fascial sling for women with stress urinary incontinence if mid-urethral sling cannot be considered.	A
Warn women undergoing autologous fascial sling that there is a high risk of voiding difficulty and the need to perform clean intermittent self-catheterisation; ensure they are willing and able to do so.	C
Inform older women with stress urinary incontinence about the increased risks associated with surgery, including the lower probability of success.	B
Inform women that any vaginal surgery may have an impact on sexual function.	B
Only offer new devices, for which there is no level 1 evidence base, as part of a structured research programme.	A*
Only offer adjustable mid-urethral sling as a primary surgical treatment for stress urinary incontinence as part of a structured research programme.	A*
Do not offer bulking agents to women who are seeking a permanent cure for stress urinary incontinence.	A*

\* Recommendation based on expert opinion.



Summary of evidence	LE
Peri-urethral injection of bulking agent may provide short-term improvement in symptoms (3 months), but not cure. in women with SUI.	2a
Repeat injections to achieve therapeutic effect are often required.	2a
Bulking agents are less effective than colposuspension or autologous sling for cure of SUI.	2a
Adverse effect rates are lower compared to open surgery.	2a
There is no evidence that one type of bulking agent is better than another type.	1b
Transperineal route of injection may be associated with a higher risk of urinary retention compared to the transurethral route.	2b

# Acceptability of Treatment

	Yes	No
Pelvic floor exercises for 6 months	60%	26%
Pelvic floor exercises for life	41%	44%
Regular drugs for life	14%	69%
Drugs to take as needed	51%	32%
Major operation (85% cure; 2% risk of catheterising)	23%	57%
Minor operation (85% cure; 2% risk of catheterising)	38%	43%
Clinic procedure (60% improvement; no long term risk)	57%	24%
Long term catheter	3%	79%
Learning to self catheterise	11%	73%

**WHAT CAN WE DO IN MEN?**

# Agenda

- Male urinary stress incontinence
  - Bulking agents
  - Fixed male slings
  - Adjustable male slings
  - Compression devices in males
    - Circunferential (AUS)
    - Non Circunferential (Adjust. Balloons)

## EAU Guidelines on Urinary Incontinence in Adults

F.C. Burkhard (Chair), M.G. Lucas, L.C. Berghmans,  
J.L.H.R. Bosch, F. Cruz, G.E. Lemack, A.K. Nambiar,  
C.G. Nilsson, R. Pickard, A. Tubaro  
Guidelines Associates: D. Bedretdinova, F. Farag,  
B.B. Rozenberg

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# Bulking agents

- Few studies
- The only one included in a Cochrane Review was on Macroplastique
  - Bulking agent vs. AUS:  
Continence rate 46% vs. 82%

<b>Evidence summary</b>	<b>LE</b>
There is no evidence that bulking agents cure post-prostatectomy incontinence.	2a
There is weak evidence that bulking agents can offer temporary, short-term, improvement in QoL in men with post-prostatectomy incontinence.	3
There is no evidence that one bulking agent is superior to another.	3

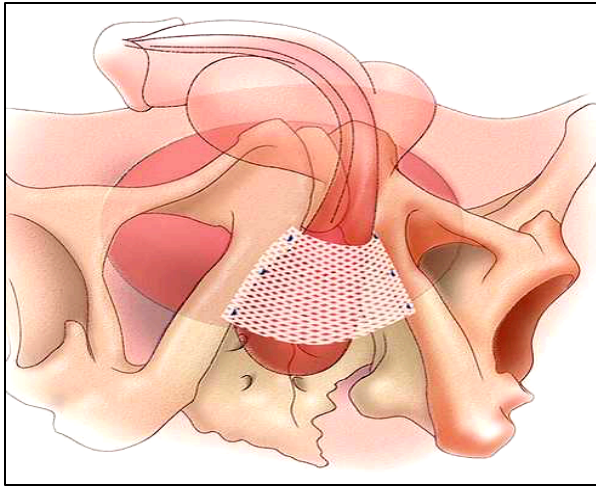
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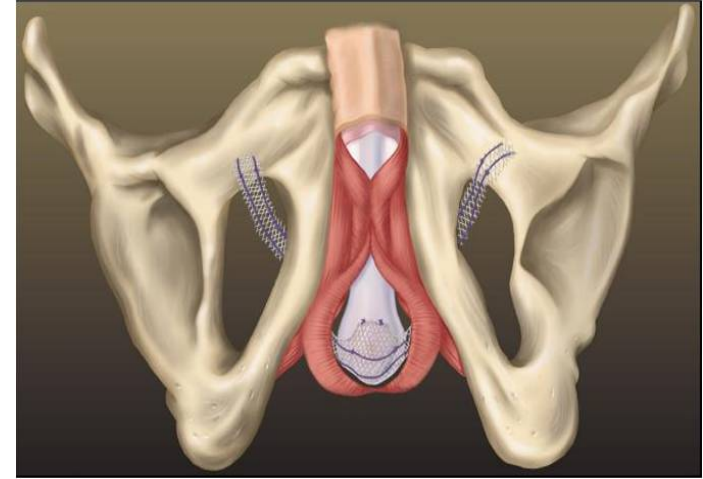
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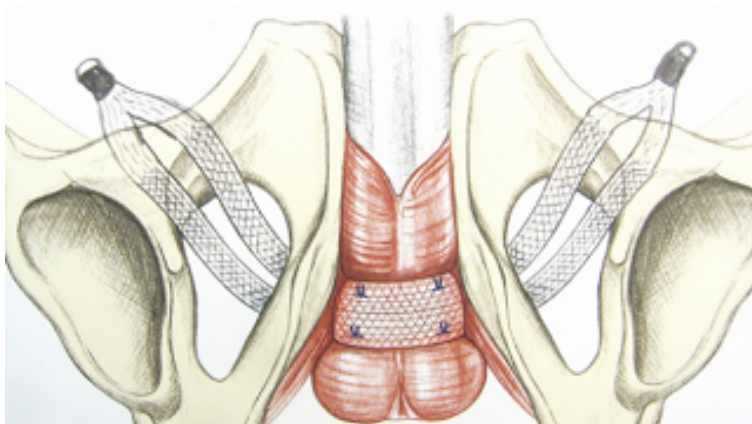
# Non adjustable Slings



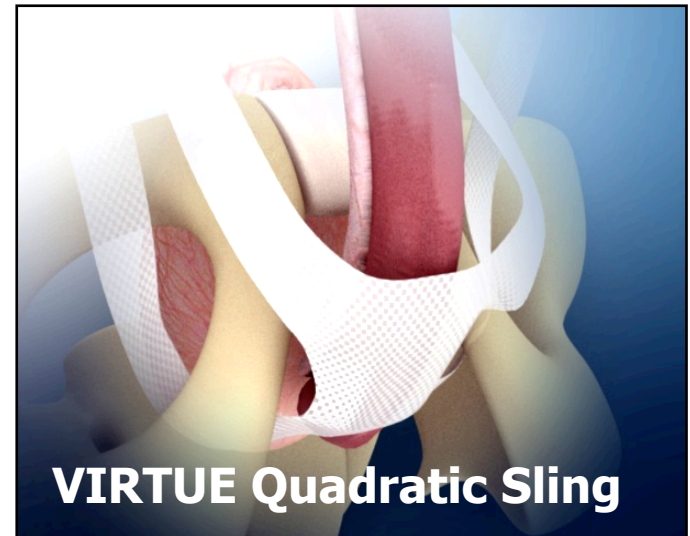
InVance Bone Anchor



AdVance Transobturator



I-STOP TOMS



**VIRTUE Quadratic Sling**

# Fixed Male slings

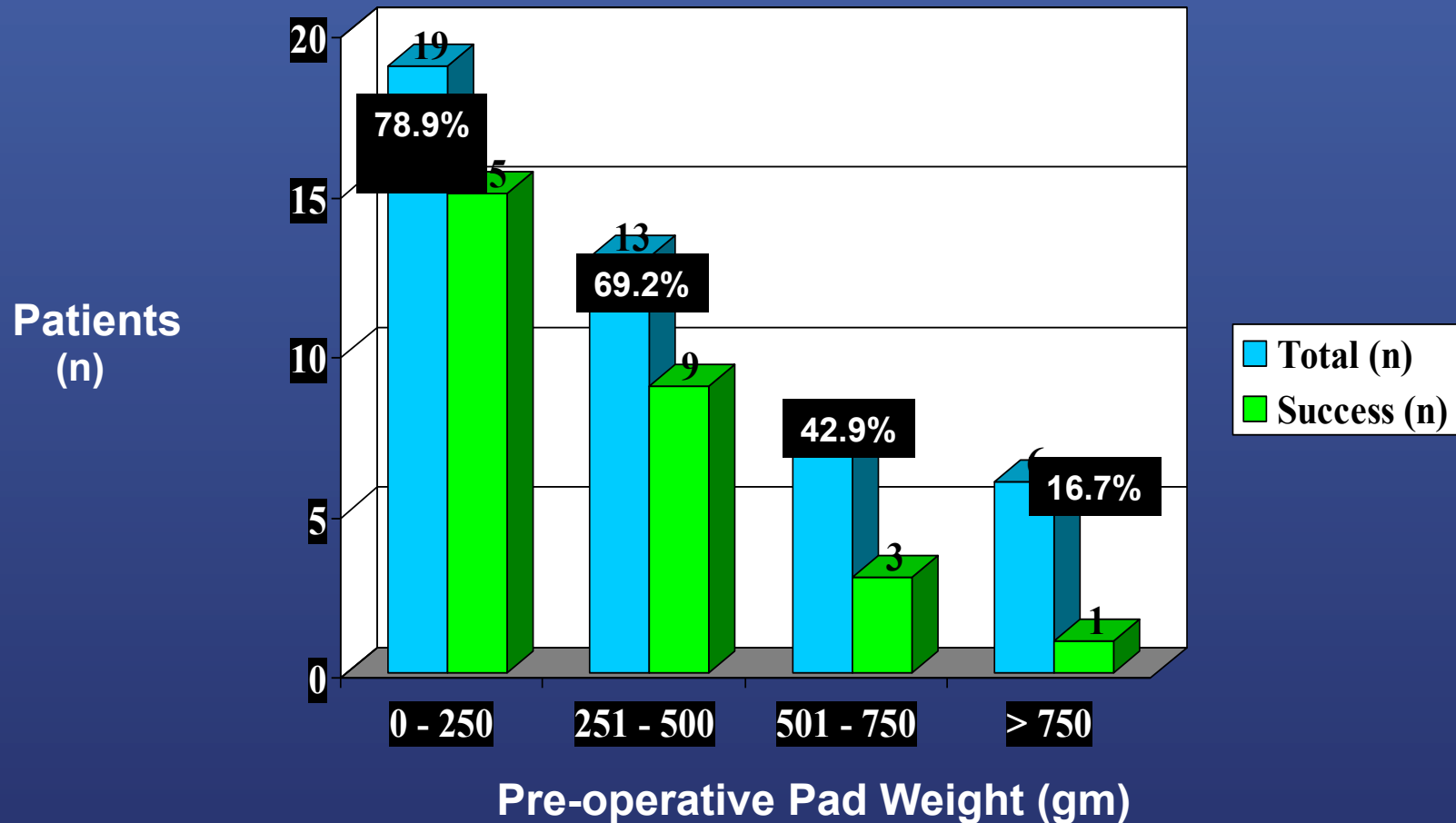
Subjective cure rate: 50%; Improvement 30%; Failure: 20%

<b>Evidence summary</b>	<b>LE</b>
There is limited short-term evidence that fixed male slings cure or improve post-prostatectomy incontinence in patients with mild-to-moderate incontinence.	3
Men with severe incontinence, previous radiotherapy or urethral stricture surgery may have less benefit from fixed male slings.	3
There is no evidence that one type of male sling is better than another.	3

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# Success by Pre-op Pad Weight



Success - 75.8% chance if preoperative *pad weight* < 496 gm  
Odds of a successful surgery if pad wt < 496 gm are 7X greater than  
odds of successful surgery if pad wt > 496 gm

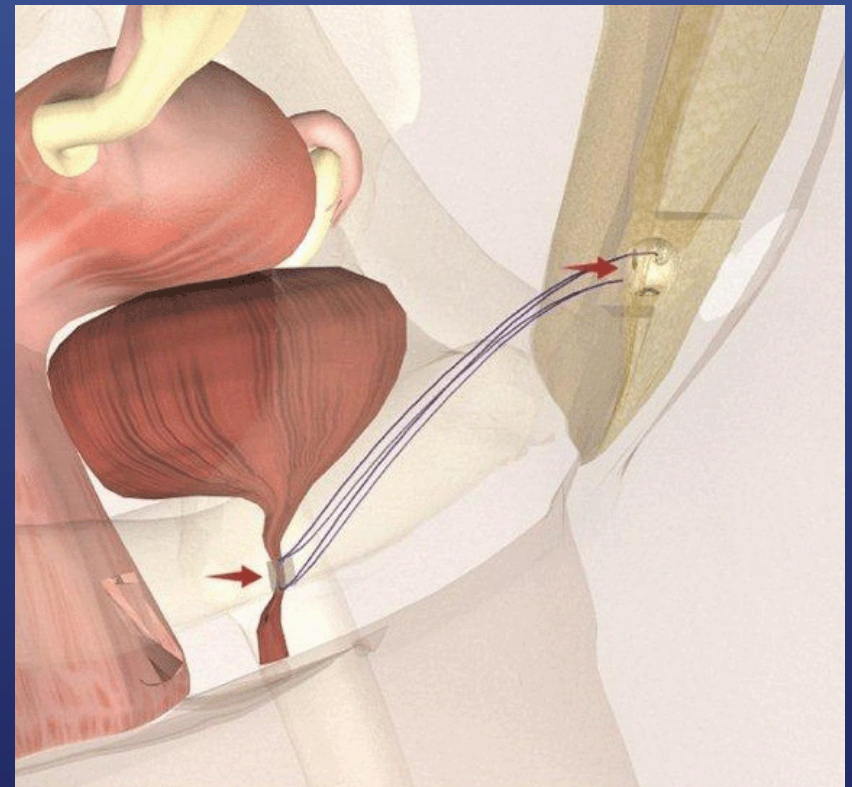
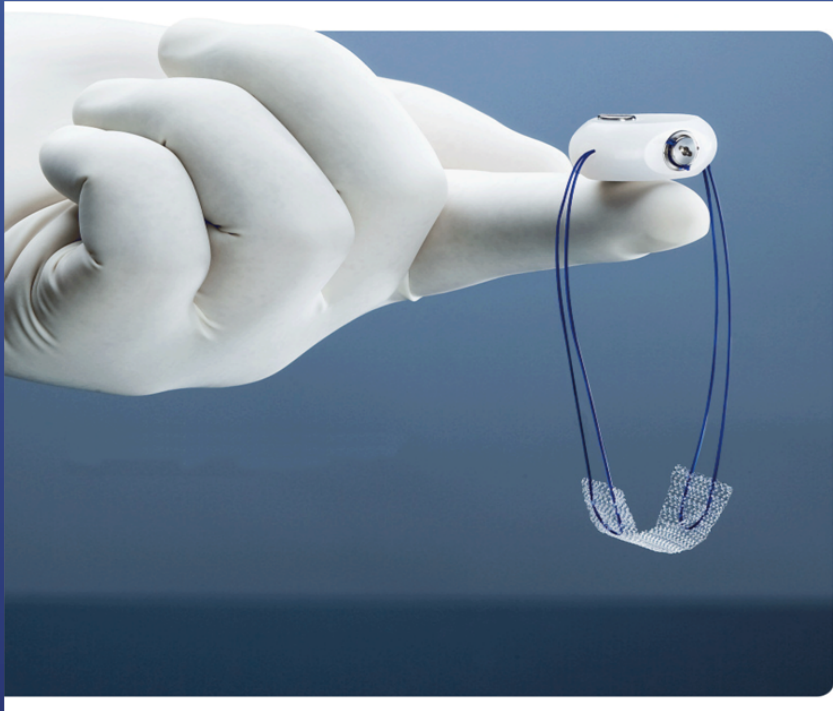
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# Adj. Male Slings Remeex™ (Neomedic)



# Adj. Male Slings

<b>Evidence summary</b>	<b>LE</b>
There is limited evidence that adjustable male slings can cure or improve SUI in men.	3
There is limited evidence that early explantation rates are high.	3
There is no evidence that adjustability of the male sling offers additional benefit over other types of sling.	3

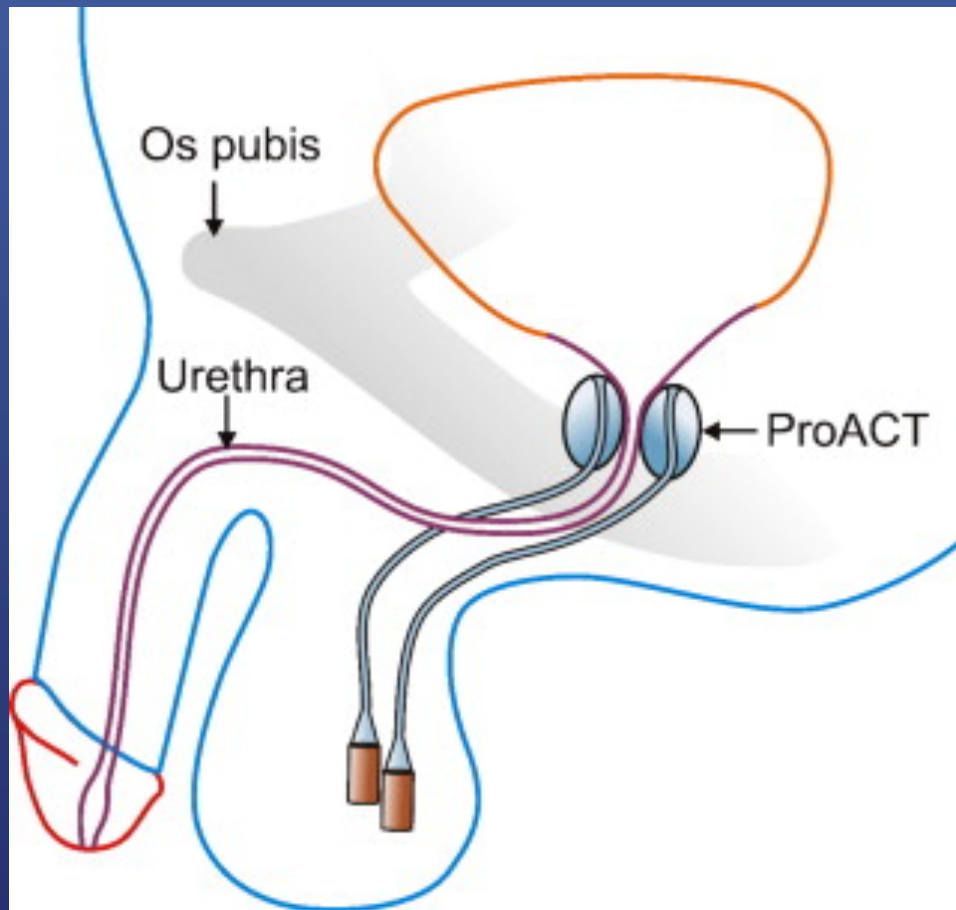
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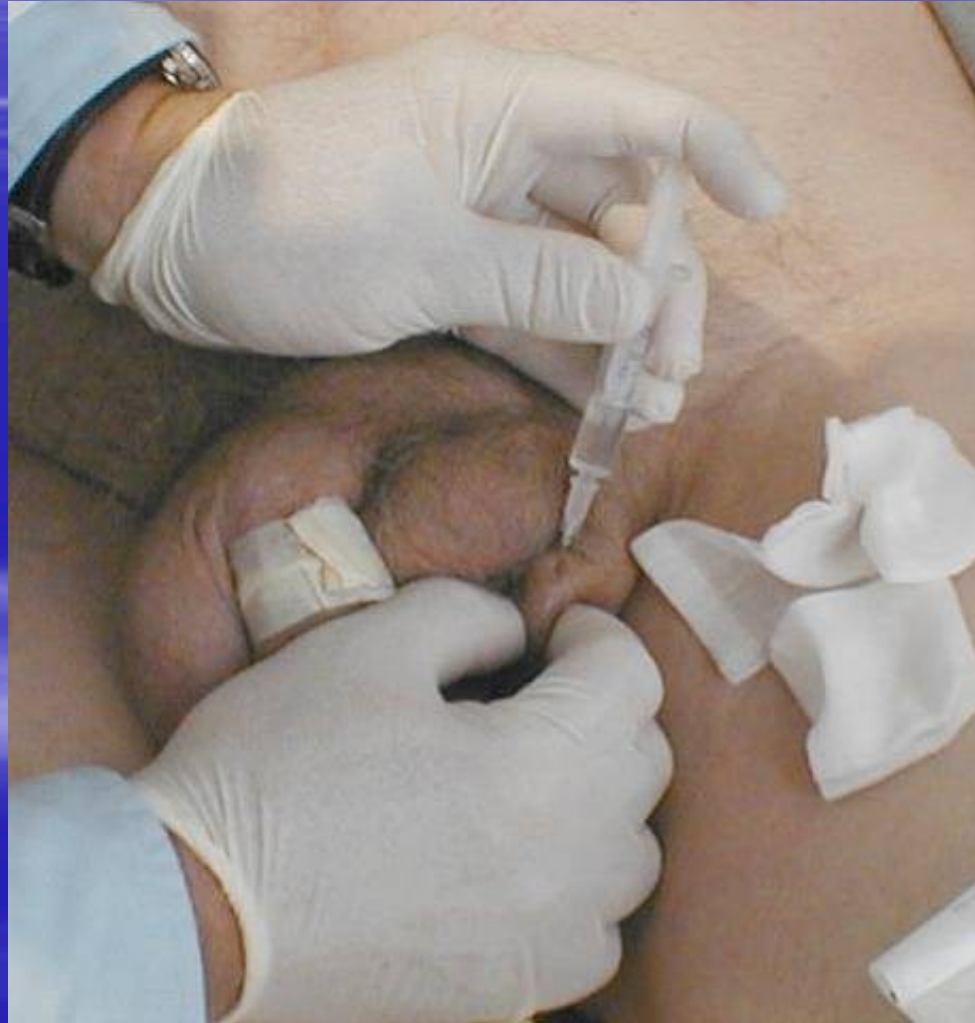
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# Adj. Ballons



# Inflating the balloons...



# Adj. Ballons

Improved pts: 65%

Very limited short-term evidence suggests that the non-circumferential compression device (ProACT <sup>®</sup> ) is effective for treatment of post-prostatectomy SUI.	3
The non-circumferential compression device (ProACT <sup>®</sup> ) is associated with a high failure and complication rate leading to frequent explantation.	3

## EAU Guidelines on Urinary Incontinence in Adults

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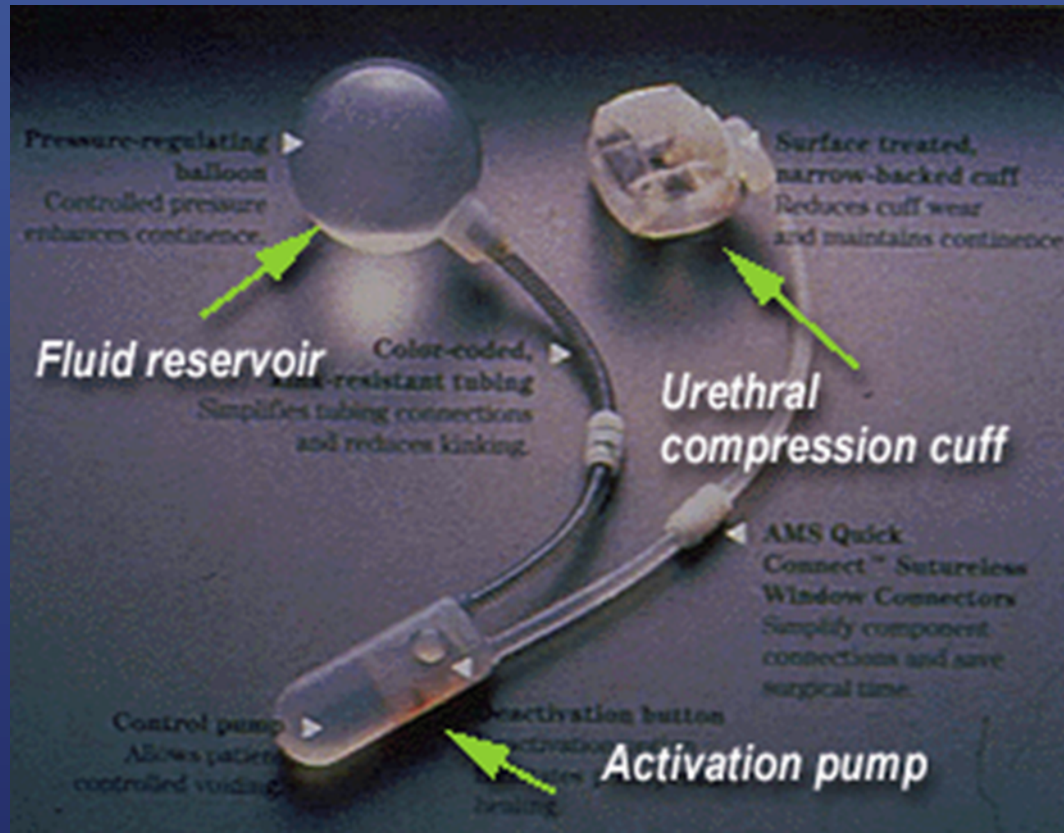
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# AMS 800 (AMS)



# AMS 800 (AMS)

- Two systematic reviews (poor quality studies)
- Continence rate: 80%
  - Lower in pts after RXT
  - More erosion if complete continence
- Effective as «salvage» treatment

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# ICS 2017 FLORENCE

12-15 September

Leading Continence  
Research and Education

Abstracts:  
April 2017

/2017





**SIUD 2018**

**Napoli, 7-9 Giugno**

**Stazione Marittima**

Presidente SIUD  
Enrico Finazzi Agrò

Presidenti del Congresso  
Ferdinando Fusco, Marco Torella

[www.siud.it](http://www.siud.it)  
Scadenza invio abstract  
31 Gennaio 2018