

Functionele urogenitale aandoeningen na de menopauze

De urologische kijk

Elodie Beels
Functionele en Reconstructieve Urologie – Neurourology

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De menopauze

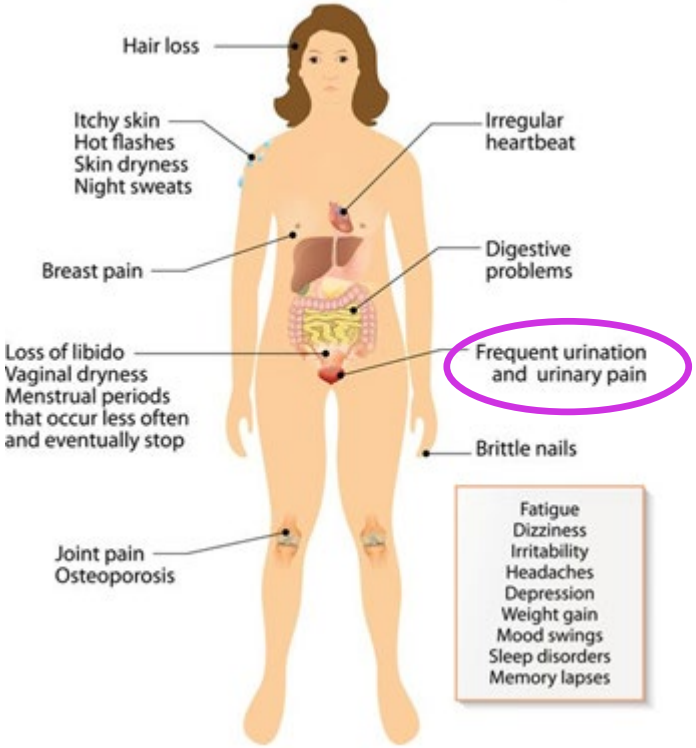
= één precies moment. Exact 1 jaar na de laatste menstruatie.

Gemiddelde leeftijd laatste menstruatie = 51 jaar

De overgang = natuurlijk lichamelijk proces waarbij de menstruele cyclus stopt en de vrouw in haar onvruchtbare periode komt.



Symptomen


Hair loss
Itchy skin
Hot flashes
Skin dryness
Night sweats
Irregular heartbeat
Breast pain
Digestive problems
Loss of libido
Vaginal dryness
Menstrual periods that occur less often and eventually stop
Frequent urination and urinary pain
Brittle nails
Joint pain
Osteoporosis
Fatigue
Dizziness
Irritability
Headaches
Depression
Weight gain
Mood swings
Sleep disorders
Memory lapses


Systemic
- Weight gain
- Heavy night sweats
Headache
Psychological
- Dizziness
- Interrupted sleeping patterns
- Anxiety
- Poor memory
- Inability to concentrate
- Depressive mood
- Irritability
- Mood swings
- Less interest in sexual activity
Palpitations
Breasts
- Enlargement
- Pain
Skin
- Hot flashes
- Dryness
- Itching
- Thinning
- Tingling
Joints
- Soreness
- Stiffness
Back pain
Urinary
- Incontinence
- Urgency
Transitional menstruations
- Shorter or longer cycles
- Bleeding between periods
Vaginal
- Dryness
- Painful intercourse

Prevalentie

Epidemiology of the symptoms of menopause – an

Marta Teresa Makara-Studzińska[1], Kar

Prevalence of menopausal symptoms among mid-life women: findings from electronic medical records

Matthew Sussman, Jeffrey Trocio, Craig Best, Sebastian Mirkin, Andrew G. Bushmakin, Robert Yood, Mark Friedman, Joseph Menzin & Michael Louie

Analysis of quality of life of women in menopause period in Poland, Greece, Belarus and Belgium using MRS Scale. A multicenter study

Krajewska - Ferishah K[1], Krajewska-Kułak E[1*], Terlikowski

Van Damme-Ostapowicz K[1]

Age of menopause and impact of climacteric symptoms by geographical region

S. Palacios, V. W. Henderson, N. Siseles, D. Tan & P. V

Menopausal Symptoms and Women's Quality of Life Outcomes: Literature Review

Rezarta Lalo*, Fatjona Kamberi and Ela Peto

Prevalentie

Analysis of quality of life of women in menopause period in Poland, Greece, Belarus and Belgium using MRS Scale. A multicenter study

Krajewska - Ferishah K[1], Krajewska-Kułak E[1*], Terlikowski S[2], Wiktor H[3], Van Damme-Ostapowicz K[1], Chadzopulu A[4], Adraniotis J[5], Shpakou A[6]

Purpose: Symptomen en QoL vergelijken bij vrouwen in de menopauze uit Polen, Griekenland, Wit-Rusland en België.

Material and Methods: MRS (Menopause Rating Scale) invullen.

Conclusie: Belgische vrouwen vertoonden een belangrijkere impact op QoL als gevolg van een hogere prevalentie en ernst van urogenitale en seksuele symptomen.

Prevalentie

The Menopause Rating Scale (MRS) scores per subscale according to country.

Country	Psychological symptoms	Somatic	Urogenital and sexual symptoms	Total
Poland	4.8 ± 3.4	4.9 ± 3.0	2,5 ± 2.4	12.2 ± 7.6
Belgium	5.0 ± 2.9	5.5 ± 2.7	3,3 ± 2.4 a	13.8 ± 6.5 b
Belorussia	4.1 ± 3.5	5.2 ± 3.7	1,6 ± 2.4	10.8 ± 8.0
Greece	4.7 ± 3.0	5.7 ± 3.1	2,6 ± 2.2	12.9 ± 6.5
Total	4.6 ± 1.15	5.2 ± 1.05	2.5 ± 2.5	

Prevalentie urinaire symptomen:

Laat reproductief stadium: 17%

Vroege menopauzale transitie: 12%

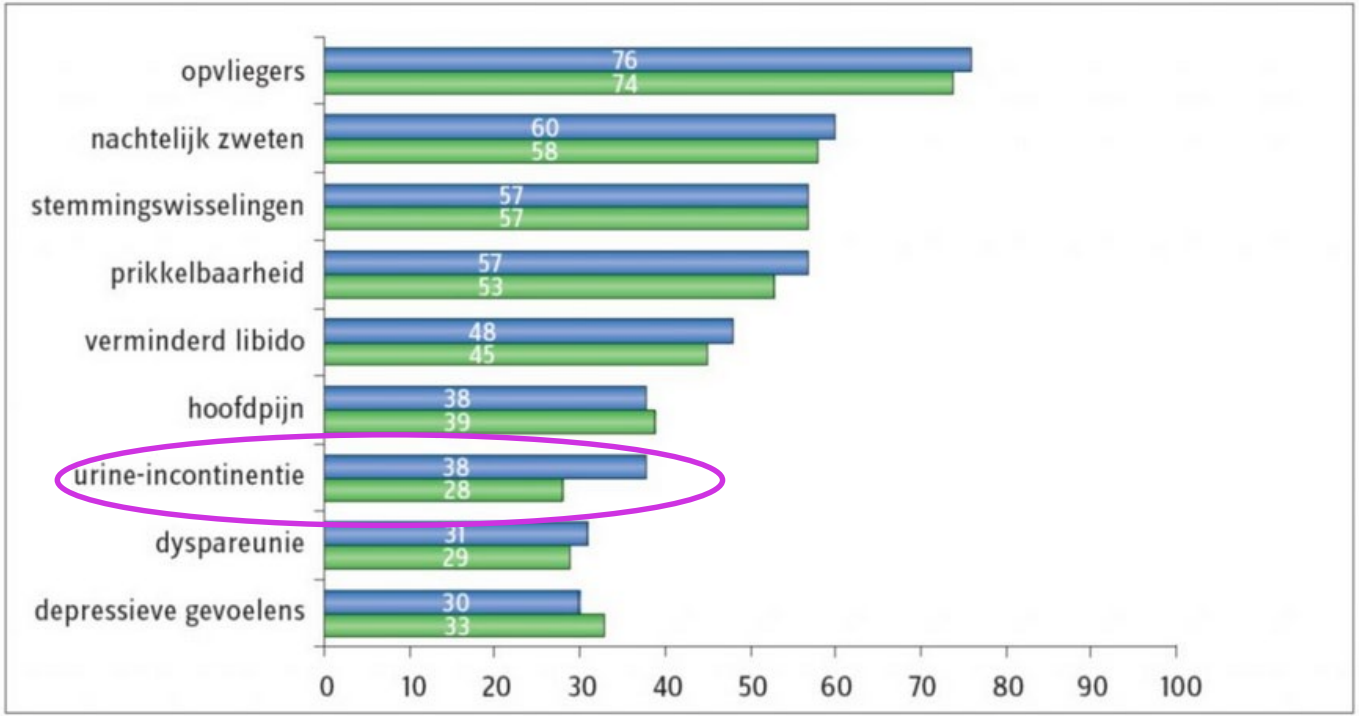
Late menopauzale transitie: 14%

Postmenopauzaal: 14%

Symptoms:

	none	mild	moderate	severe	very severe
Score =	0	1	2	3	4
1. Hot flushes, sweating (episodes of sweating)	☐	☐	☐	☐	☐
2. Heart discomfort (unusual awareness of heart beat, heart skipping, heart racing, tightness)	☐	☐	☐	☐	☐
3. Sleep problems (difficulty in falling asleep, difficulty in sleeping through, waking up early)	☐	☐	☐	☐	☐
4. Depressive mood (feeling down, sad, on the verge of tears, lack of drive, mood swings)	☐	☐	☐	☐	☐
5. Irritability (feeling nervous, inner tension, feeling aggressive)	☐	☐	☐	☐	☐
6. Anxiety (inner restlessness, feeling panicky)	☐	☐	☐	☐	☐
7. Physical and mental exhaustion (general decrease in performance, impaired memory, decrease in concentration, forgetfulness)	☐	☐	☐	☐	☐
8. Sexual problems (change in sexual desire, in sexual activity and satisfaction)	☐	☐	☐	☐	☐
9. Bladder problems (difficulty in urinating, increased need to urinate, bladder incontinence)	☐	☐	☐	☐	☐
10. Dryness of vagina (sensation of dryness or burning in the vagina, difficulty with sexual intercourse)	☐	☐	☐	☐	☐
11. Joint and muscular discomfort (pain in the joints, rheumatoid complaints)	☐	☐	☐	☐	☐

Prevalentie



Figuur 1. Prevalentie van overgangsklachten (%) in een Nederlandse steekproef van 600 vrouwen (blauw) en vergelijking tot vrouwen (N=3601) uit 6 andere landen van de EU (groen) anno 2005.[2]

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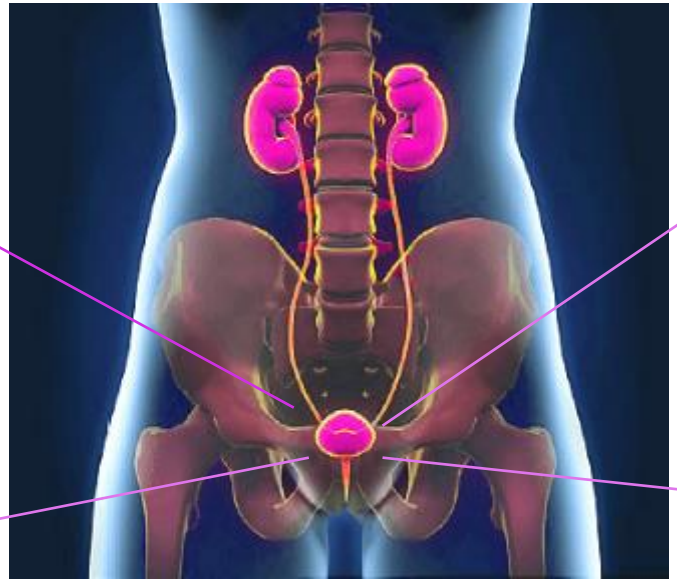
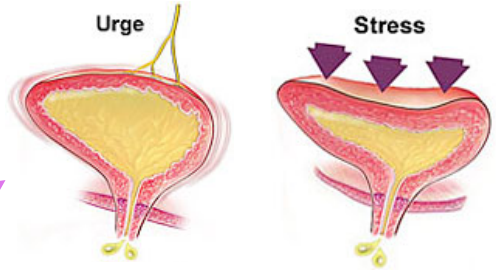
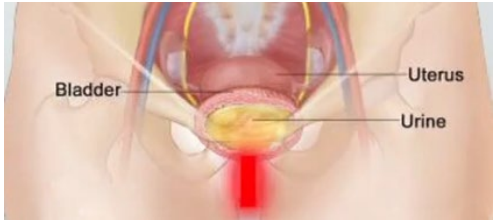






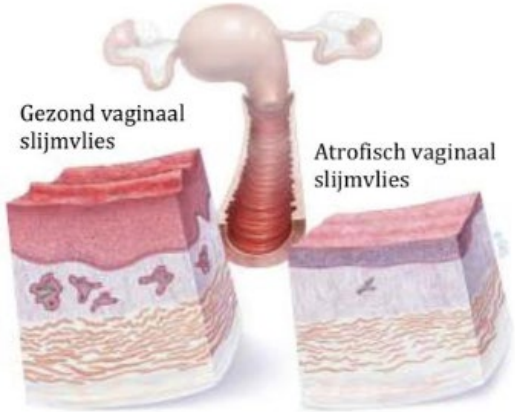


Oorzaak

UROGENITALE ATROFIE (vaginale atrofie, atrofische vaginitis …)

Oestrogeen deficiëntie → bloedflow↓ naar urogenitale organen → ATROFIE

Atrofie = Het slinken en dunner worden van de urogenitale mucosa.



Vaginale droogte

Dyspareunie

Dysurie

Urgency

…

Oorzaak

UROGENITALE ATROFIE (vaginale atrofie, atrofische vaginitis …)

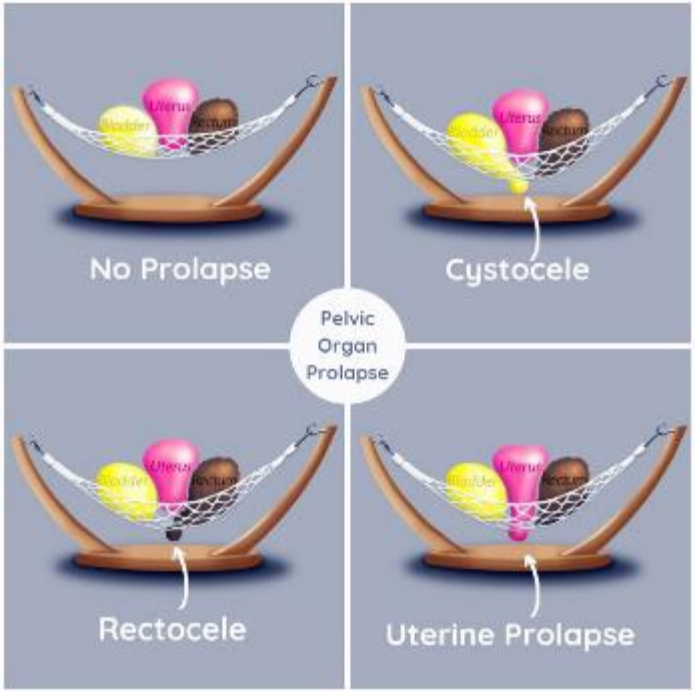


Zwakker worden van blaas en urethra met verlies aan vermogen om urinaire functies te controleren

+

Verandering qua zuurgraad van de vulva en de vagina met toenemende vatbaarheid voor infecties (bacteriën en gisten/schimmels)

Oorzaak



Bekkenbodemspieren = Hangmat

Beschadiging en/of verzwakking

↓

Verlies van ondersteuning/kracht

↓

Prolaps

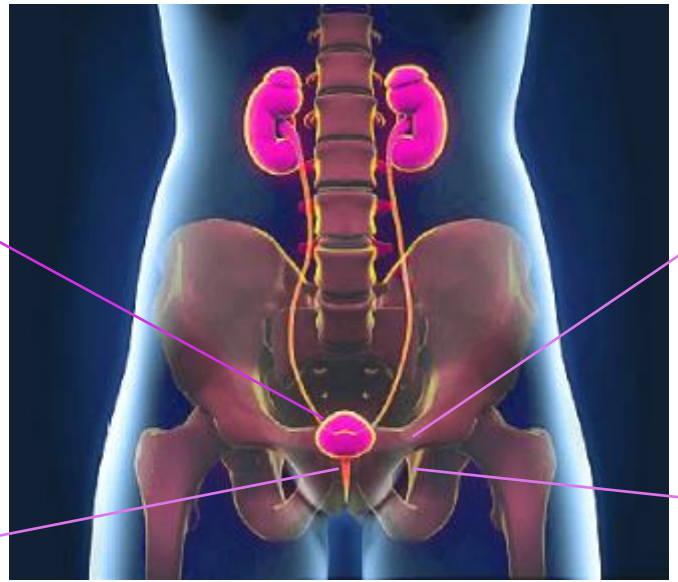
↓

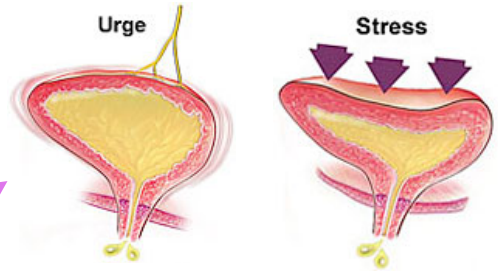
Urologische symptomen

FUNCTIONELE UROLOGISCHE KLACHTEN NA MENOPAUZE











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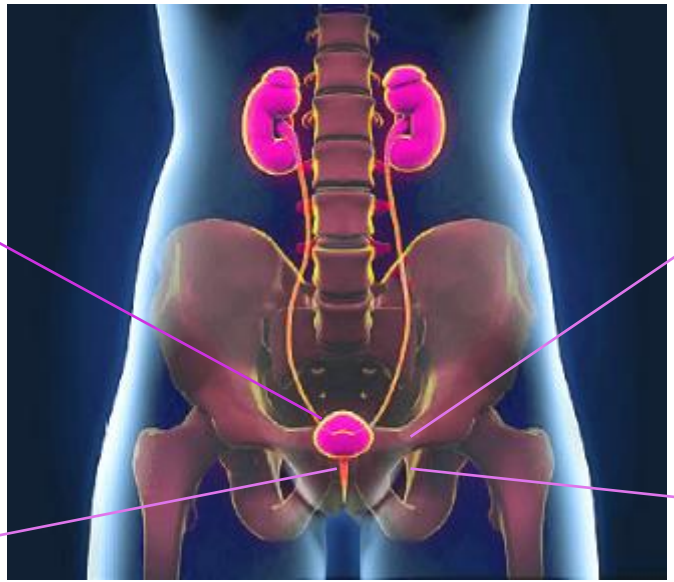
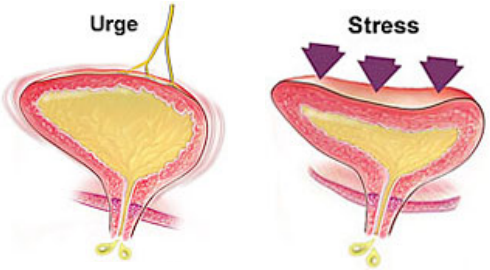








Recidiverende urineweginfecties

EAU guidelines:

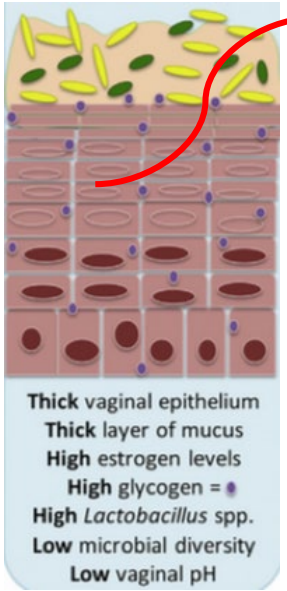
Recurrent UTIs	Recurrences of uncomplicated and/or complicated UTIs, with a frequency of at least three UTIs/year or two UTIs in the last six months.

Risicofactoren:

Young and pre-menopausal women	**Post-menopausal and elderly women**
Sexual intercourse →	History of UTI before menopause
Use of spermicide	Urinary incontinence
A new sexual partner →	Atrophic vaginitis due to oestrogen deficiency
A mother with a history of UTI	
History of UTI during childhood →	Cystocele
Blood group antigen secretory status →	Increased post-void urine volume
	Blood group antigen secretory status
	Urine catheterisation and functional status deterioration in elderly institutionalised women

Oorzaak

Pre-menopauzaal



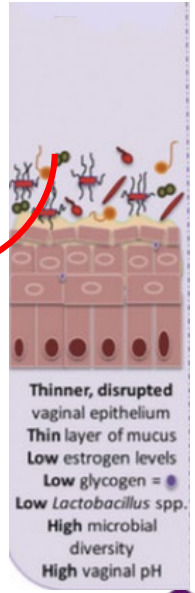
Oestrogenen bevorderen colonisatie van lactobacilli vaginaal.

→ Productie van lactaatzuur uit glycogeen

→ Lage pH

→ Inhibitie van groei van uropathogenen

Post-menopauzaal



Vaginale pH stijgt en lactobacilli verdwijnen.

Vagina wordt gecoloniseerd door Enterobacteriën,

voornamelijk Escherichia coli.

→ Toegenomen vatbaarheid voor UWI

Chan et al. Infect Immun 1985, 47, 84-9
Raz, R., et al. A controlled trial of intravaginal estriol in postmenopausal women with recurrent urinary tract infections. N Engl J Med, 1993. 329: 753.

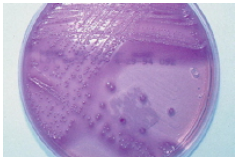
Diagnose

- Medische voorgeschiedenis en anamnese
- Klinisch onderzoek

Urinecultuur

Flow Residu (F/R)







Uitgebreide work-up is niet routine (cystoscopie, beeldvorming, cystografie, (V)UDO…)

→ wel bij atypische presentatie (vb. lithiasis, TCC, outflow obstructie, BPS …)

Behandeling

Levensstijl aanpassingen









Non-antimicrobiële profylaxe

Hormonen

Immunoactive profylaxe

Probiotica, Cranberry en D-Mannose

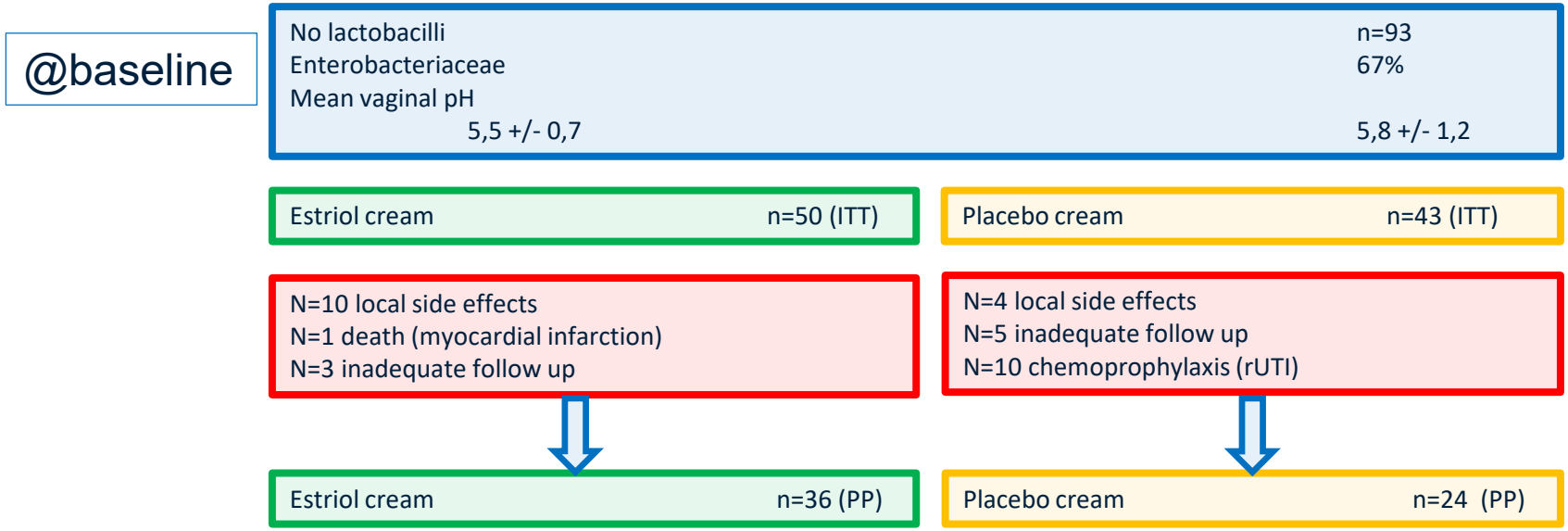
Endovesicale instillaties

Antimicrobiële profylaxe

Non-antimicrobiële profylaxe

Hormonen: Oestrogenen

RCT, postmenopausale vrouwen met rUWI (Raz et al. 1993)



Raz, R., et al. A controlled trial of intravaginal estriol in postmenopausal women with recurrent urinary tract infections. N Engl J Med, 1993. 329: 753.

Non-antimicrobiële profylaxe

Hormonen: Oestrogenen

RCT, postmenopausale vrouwen met rUWI (Raz et al. 1993)

@baseline	No lactobacilli Enterobacteriaceae Mean vaginal pH 5,5 +/- 0,7	n=93 67% 5,8 +/- 1,2
	Estriol cream n=36	Placebo cream n= 24
@ 1M	22/36 (61%) lactobacilli 11/36 (31%) Enterobacteriaceae Mean vaginal pH 3,8 +/- 0,8	0/24 lactobacilli 15/24 (63%) Enterobacteriaceae Mean vaginal pH 6,2 +/- 1,2
@ 8M	21/36 (58%) lactobacilli 10/36 (28%) Enterobacteriaceae Mean vaginal pH 3,6 +/- 1,0	0/24 lactobacilli 17/24 (71%) Enterobacteriaceae Mean vaginal pH 6,1 +/- 2,0

Raz, R., et al. A controlled trial of intravaginal estriol in postmenopausal women with recurrent urinary tract infections. N Engl J Med, 1993. 329: 753.

Non-antimicrobiële profylaxe

Hormonen: Oestrogenen

RCT, postmenopausale vrouwen met rUWI (Raz et al. 1993)

@baseline	No lactobacilli Enterobacteriaceae Mean vaginal pH 5,5 +/- 0,7	n=93 67% 5,8 +/- 1,2
	Estriol cream n=36	Placebo cream n= 24
@ 8M	rUTI 0,5 episodes/patient/year	rUTI 5,9 episodes/patient/year

Conclusie: duidelijk minder UWI aanwezig bij vrouwen onder lokale oestrogenen. Eveneens minder AB gebruik. Lokale oestrogenen zorgen voor een lage pH en toegenomen colonisatie met lactobacilli.

Raz, R., et al. A controlled trial of intravaginal estriol in postmenopausal women with recurrent urinary tract infections. N Engl J Med, 1993. 329: 753.

Non-antimicrobiële profylaxe

Hormonen: Oestrogenen

ALTIJD lokale oestrogenen.





Systemische (orale) oestrogenen:

- Geen reductie in aantal UWI
- Toegenomen risico op veneuze trombose, borstkanker, CVA, coronair lijden

Beerepoot, M.A., et al. Nonantibiotic prophylaxis for recurrent urinary tract infections: a systematic review and meta-analysis of RCTs. J Urol, 2013. 190: 1981.

Non-antimicrobiële profylaxe

Immunoactieve profylaxe (1,2) - Oraal vaccin OM-89 (Uro-Vaxom)

Extract van 18 verschillende serotypes van E. coli.

Goed veiligheidsprofiel en effectiever dan placebo.



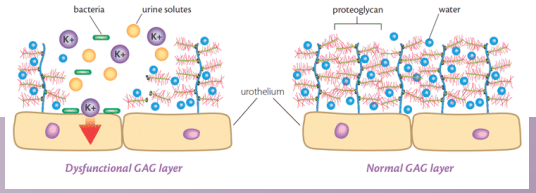
D-Mannose (3)

Dagelijks 2g is superieur tov placebo en even efficient als 50 mg nitrofurantoin

Probiotica (Lactobacillus) (4) Geen overtuigend voordeel

Endovesicale instillaties (5) met hyaluronzuur en chondroitine sulfaat

Herstel van de glycosaminoglycaan laag (GAG)

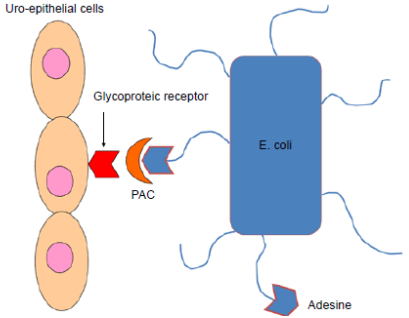


1. Beerepoot, M.A., et al. Nonantibiotic prophylaxis for recurrent urinary tract infections: a systematic review and meta-analysis of RCTs. J Urol, 2013. 190: 1981.
2. Naber, K.G., et al. Immunoactive prophylaxis of recurrent urinary tract infections: a meta-analysis. Int J Antimicrob Agents, 2009. 33: 111.
3. Kranjcec, B., et al. D-mannose powder for prophylaxis of recurrent urinary tract infections in women: a randomized clinical trial. World J Urol, 2014. 32: 79.
4. Schwenger, E.M., et al. Probiotics for preventing urinary tract infections in adults and children. Cochrane Database Syst Rev, 2015: CD008772.
5. Damiano, R., et al. Prevention of rUTIs by intravesical administration of hyaluronic acid and chondroitin sulphate: a placebo-controlled randomised trial. Eur Urol, 2011. 59: 645.

Non-antimicrobiële profylaxe

Cranberry



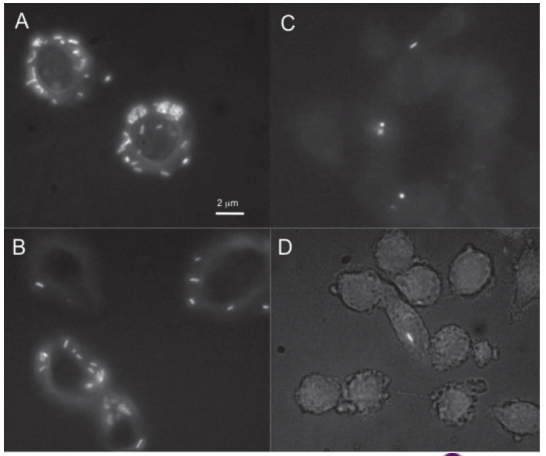


Werking: Proanthocyanidines (PACs) inhiberen de aanhechting van de fimbriae van E. coli aan het uroepitheel.

Waarschijnlijk minder efficient als profylactische AB, maar minder resistentie.

Cave: dosis!

A Placebo
B 18 mg PAC
C 36 mg PAC
D 72 mg PAC



1. Kontiokari, T., et al. Randomised trial of cranberry-lingonberry juice and Lactobacillus GG drink for the prevention of urinary tract infections in women. BMJ, 2001. 322: 1571.
2. Stothers, L. A randomized trial to evaluate effectiveness and cost effectiveness of naturopathic cranberry products as prophylaxis against UTI in women. Can J Urol, 2002. 9: 1558.
3. Jepson, R.G., et al. Cranberries for preventing urinary tract infections. Cochrane Database Syst Rev, 2012. 10: Cd001321.

Antimicrobiële profylaxe

Lage dosis van antibiotica voor een langere periode (3-6m)

OF

Post-coitale prophylaxis

Nitrofurantoine 50mg of 100mg dagelijks

Fosfomycine trometamol 3g om de 10 dagen

Trimethoprim 100mg dagelijks

1. Albert, X., et al. Antibiotics for preventing recurrent urinary tract infection in non-pregnant women. Cochrane Database Syst Rev, 2004: CD001209.
2. Hooton, T.M. Recurrent urinary tract infection in women. Int J Antimicrob Agents, 2001. 17: 259.
3. Rudenko, N., et al. Prevention of recurrent infections by long-term administration of fosfomycin. Double blind, randomized, parallel group, placebo controlled study. Arzneimittelforschung, 2005. 55: 420.

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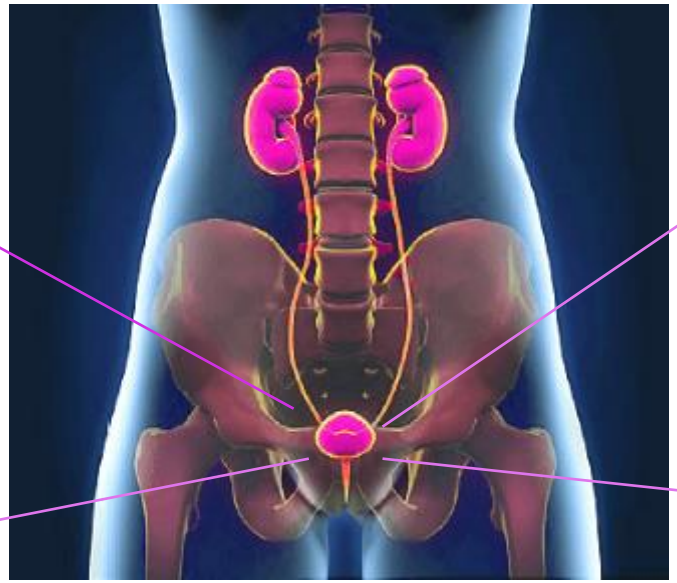
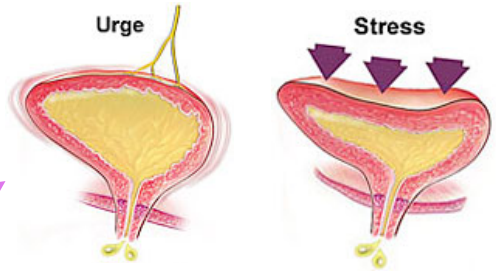








Overactieve Blaas (OAB)

"Urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence (UUI), in the absence of urinary tract infection (UTIs)or other obvious pathology"

Diagnose

Medische voorgeschiedenis en anamnese

Klinisch onderzoek (BBS, atrofie, POP)

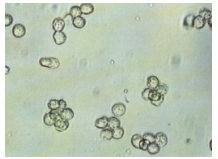
Investigaties

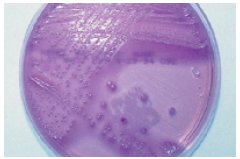
Urine dipstick/microscopie/cultuur

Flow Residu

Plasdagboek







Overdag	Tijd	Drinken (ml)	Hoeveel urine (ml)	Urineverlies Druppels (x) / weinig (xx) / veel (xxx)	Aandrang ja/nee	Opmerkingen?
1	8u10		200 ml		Ja	
2	8u30	250ml				
3	10u00		140 ml	x	Nee	Ik moest hard lachen
4	12u00	250ml				
5	12u35		260 ml		Ja	
6	14u35		185 ml	xxx	Nee	
7	15u50		? ml		Ja	

Frequentie

Plasvolume

24u urine output

Intake

Urineverlies (wegen van pads)



Urineverlies?

Pijn?

Urgency?

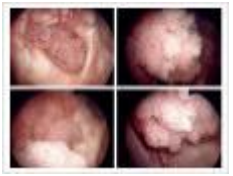
Activiteit?

Bijkomende onderzoeken?

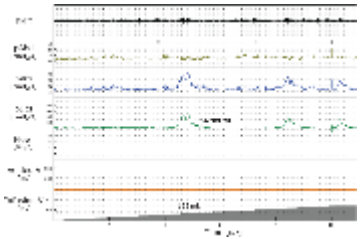
- Na voorafgaande urologische/pelvische chirurgie (radiotherapie)
- Na falen initiële therapie
- Atypische presentatie
- Alarmsymptomen: pijn en hematurie

- **Urine cytologie en Cystoscopie**
- **Urodynamica**
- **Beeldvorming: Echo, RX en/of CT scan**



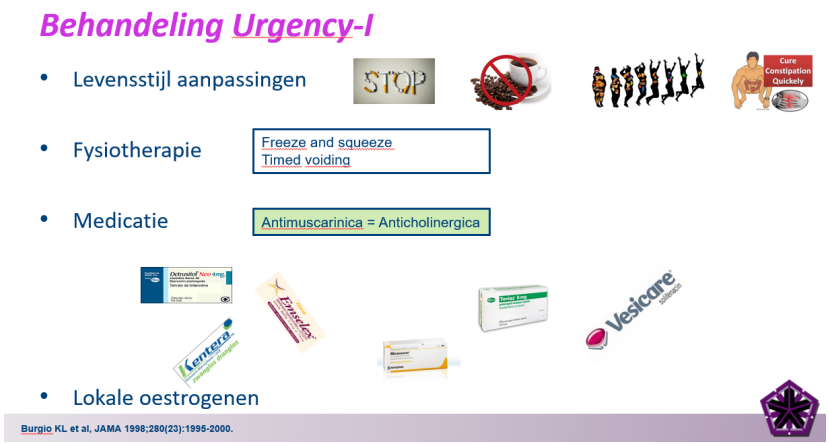






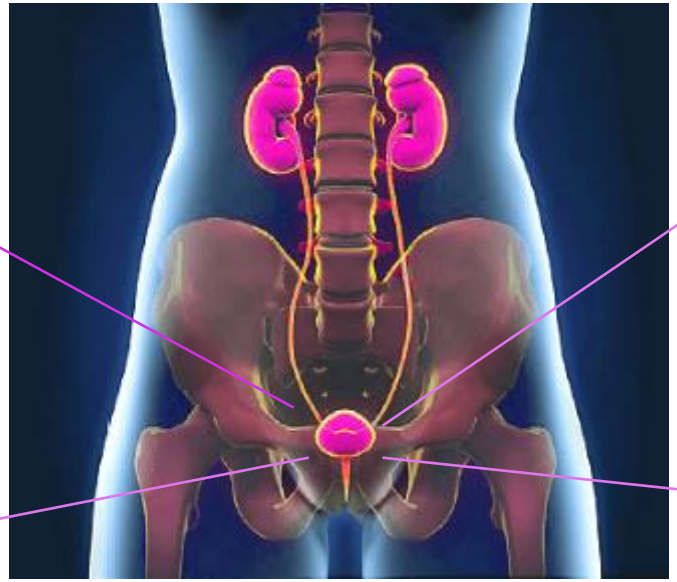
Behandeling

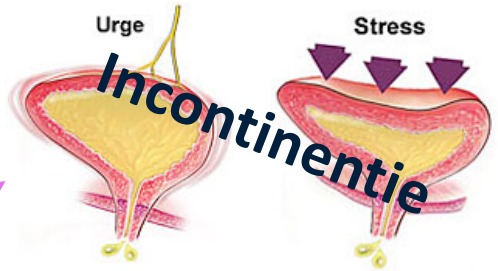
Zie behandeling van urgency - incontinentie.



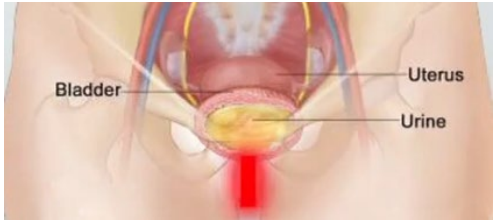
FUNCTIONELE UROLOGISCHE KLACHTEN NA MENOPAUZE







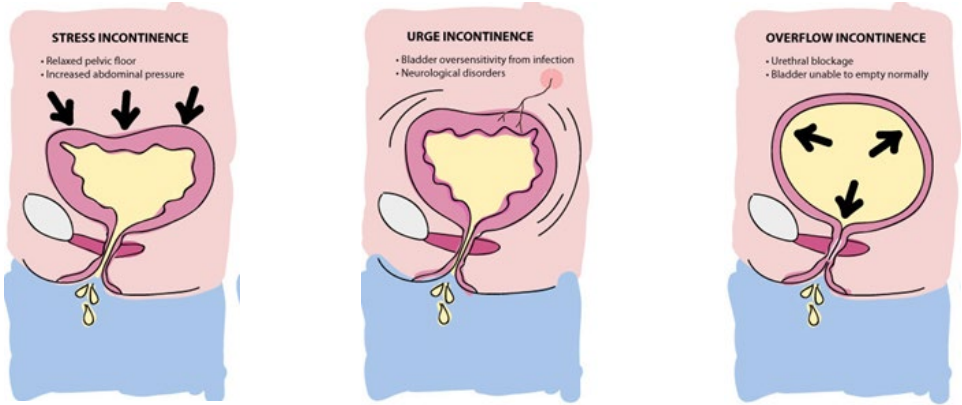




Incontinentie

Symptoom beschrijvend

- Stress: inspanningsgebonden urineverlies
- Urgency: aandrangincontinentie
- Overloopincontinentie



Diagnose

Medische voorgeschiedenis

Obstetrische voorgeschiedenis?

Geboortegewicht kinderen?

Chirurgische voorgeschiedenis?

Radiotherapie?

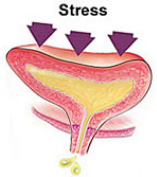
Constipatie? Roken? Obesitas?

Drinkgedrag?

Leeftijd?

Duur van de klachten?

Anamnese



Stress: verlies bij hoesten, lachen, niezen, inspanning… ? Verlies ‘s nachts? Verlies bij zitten in zetel? Achterwege laten van sociale/fysieke activiteiten? Lang bestaand?

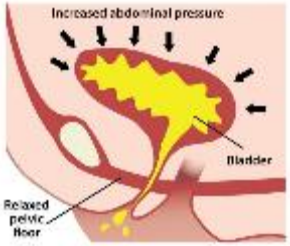


Urgency: angst om niet op tijd toilet te vinden? Nycturie? Verlies ‘s nachts? Verlies bij zitten in de zetel? Frequency?

Mixed

+ objectiveer hoeveelheid urineverlies en wat is de last voor de patient!

Klinisch Onderzoek

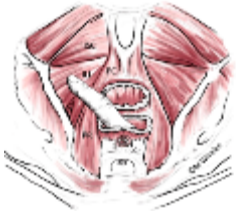


- Confirmeren van diagnose (stress-I)

- Excluderen van geassocieerde pathologie (caruncula, oedeem, prolaps, …)



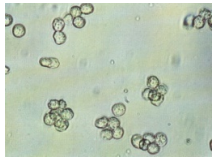
- Atrofe vaginitis?
- Evalueren van de bekkenbodem (kracht, proprioceptie, gevoel)

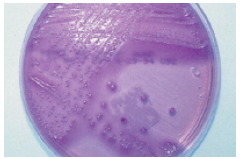


Investigaties

Urine dipstick/microscopie/cultuur







Flow Residu meting

Plasdagboek

Overdag	Tijd	Drinken (ml)	Hoeveel urine (ml)	Urineverlies Druppels (x) / weinig (xx) / veel (xxx)	Aandrang ja/nee	Opmerkingen?
1	8u10		200 ml		Ja	
2	8u30	250ml				
3	10u00		140 ml	x	Nee	Ik moest hard lachen
4	12u00	250ml				
5	12u35		260 ml		Ja	
6	14u35		185 ml	xxx	Nee	
7	15u50		? ml		Ja	



Frequentie

Plasvolume

24u urine output

Intake

Urineverlies (wegen van pads)

Urineverlies?

Pijn?

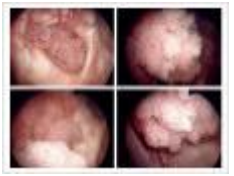
Urgency?

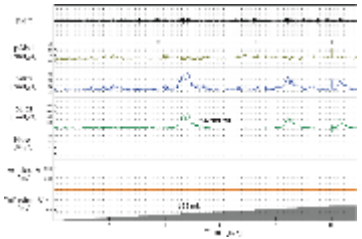
Activiteit?

Bijkomende onderzoeken?

- Onzekerheid over type incontinentie?
- Therapieresistente incontinentie (conservatief/medicatie…)
- Na voorafgaande urologische/pelvische chirurgie (radiotherapie)
- Neurologische aandoeningen
- Alarmsymptomen: pijn en hematurie

- Urine cytologie en Cystoscopie
- Urodynamica
- Beeldvorming: Echo, RX en/of CT scan



Behandeling stress-I

- Levensstijl aanpassingen





- Fysiotherapie



BBSO +
(biofeedback)

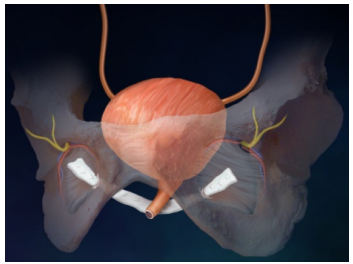
- (Medicatie)

Oestrogenen
Imipramine (Tofranil – TCA)
Alpha agonist

Duloxetine (Yentreve®)

- Chirurgie

Mid urethrale sling procedure





Hay-Smith EJ et al. Cochrane Database Syst Rev 2006; 1:CD005654.
Dahm & Dmochowski eds. Evidence based Urology 2010; chapter 20.

Behandeling stress-I

Level of evidence 1a

Continentie	80%
Verbetering	90%
Autologe sling long term failure	20%
Vaginale erosie	**0-16%**
Urethrale erosie	**0-5%**
De novo urgency	**4-66%**
Revisie	**2-35%**
Long term CIC	2%



Mesh EROSIES

Australian women win landmark vaginal mesh class action against Johnson & Johnson

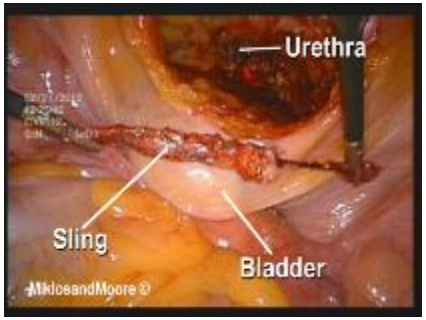
The case was launched on behalf of 700 women who had pelvic mesh and tape products implanted to treat common complications of childbirth



▲ Many woman affected by the vaginal mesh implants were left in severe, debilitating and chronic pain. The Australian class action against companies owned by Johnson & Johnson has been watched closely across the world. Photograph: Emily Critchfield/Duke Health

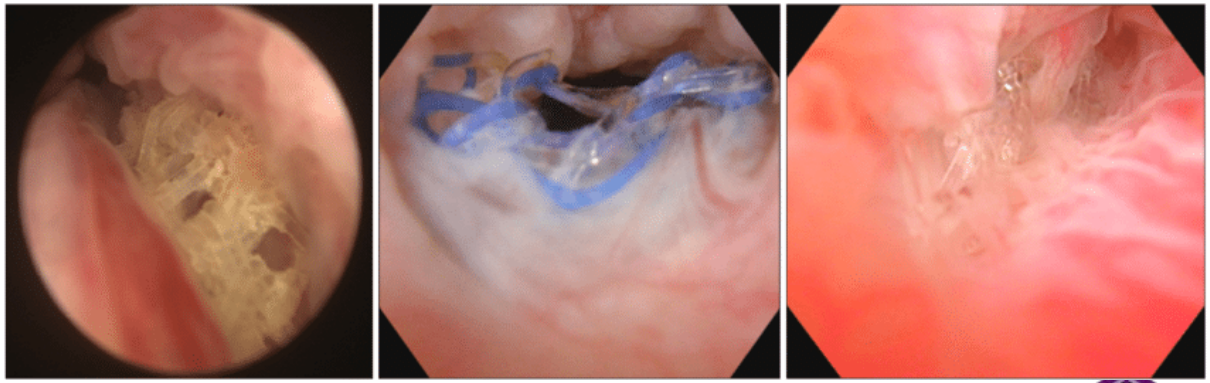
Government halts vaginal mesh surgery in NHS hospitals

Suspension ordered in England to avoid further risk of 'life-changing injuries' to women



Government agrees to temporarily ban vaginal mesh implants for women with urinary incontinence

Campaigners hail decision as 'vindication' for women 'maimed' by operation



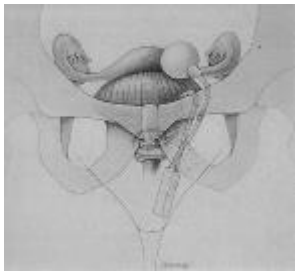
Tweedelijnsbehandeling stress-I

TOA = Trans Obturator Adjustable Sling





AMS sfincterprothese (open of robotisch)









Behandeling Urgency en Urgency-I (wet and dry OAB)

- Levensstijl aanpassingen









- Fysiotherapie

Freeze and squeeze
Timed voiding

- Lokale oestrogenen

- Medicatie

Antimuscarinica = Anticholinergica









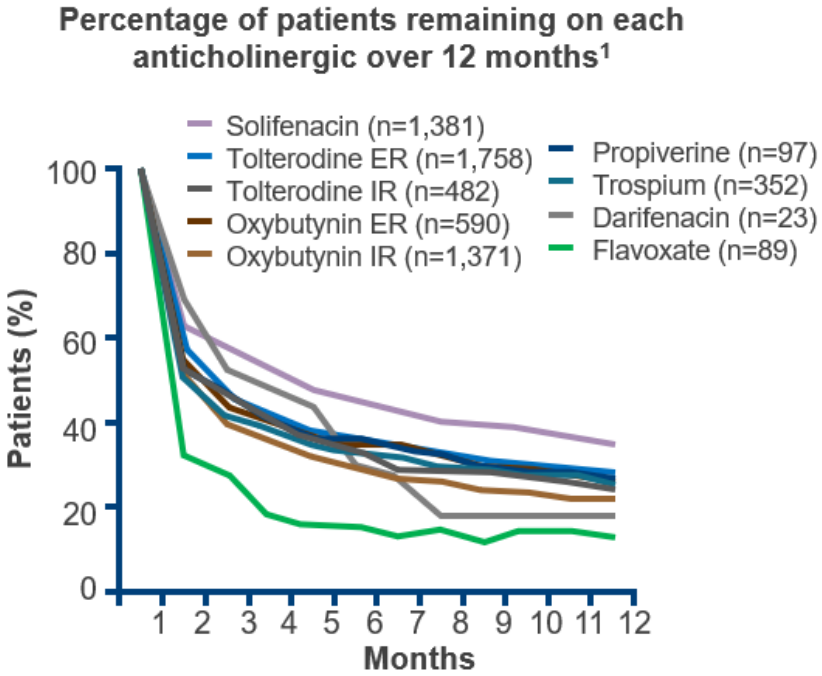




Burgio KL et al, JAMA 1998;280(23):1995-2000.

Behandeling Urgency en Urgency-I (wet and dry OAB)

- 70–90% van de patiënten stoppen therapie binnen 1 jaar[2]
- Voorgaande studies hebben aangetoond dat medicatie al na een maand wordt gestopt[3]
- Voornaamste oorzaken: gebrek aan werkzaamheid en nevenwerkingen[4]



Adapted from: Wagg A, et al. *BJU Int* 2012;110:1767–1774

ER, extended release; IR, immediate release.

1. Wagg A, et al. BJU Int 2012;110:1767–74.
2. D'Souza AO, et al. J Manag Care Pharm 2008;14:291–301.
3. Kelleher C, et al. B J Obstet Gynecol. 1997;104:988–93.
4. Castro D, et al. Acta Urol Esp 2011;35:73–9.

Behandeling Urgency en Urgency-I (wet and dry OAB)

- Medicatie

Antimuscarinica = Anticholinergica

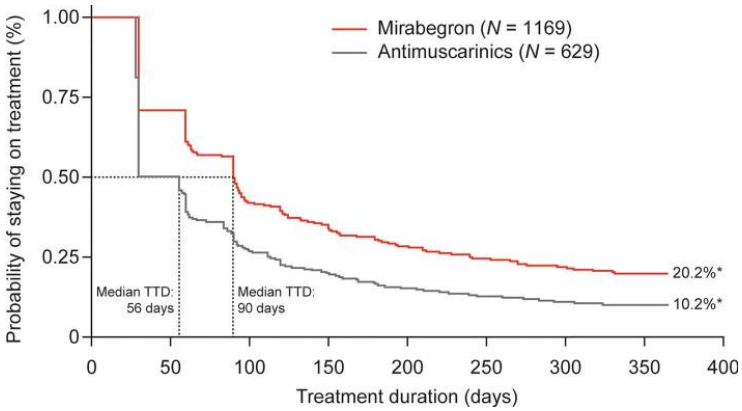
Beta3 adrenoreceptor agonist





CI: ongecontroleerde hypertensie

Weinig nevenwerkingen, maar hoge kostprijs (30 comp aan 54 euro)



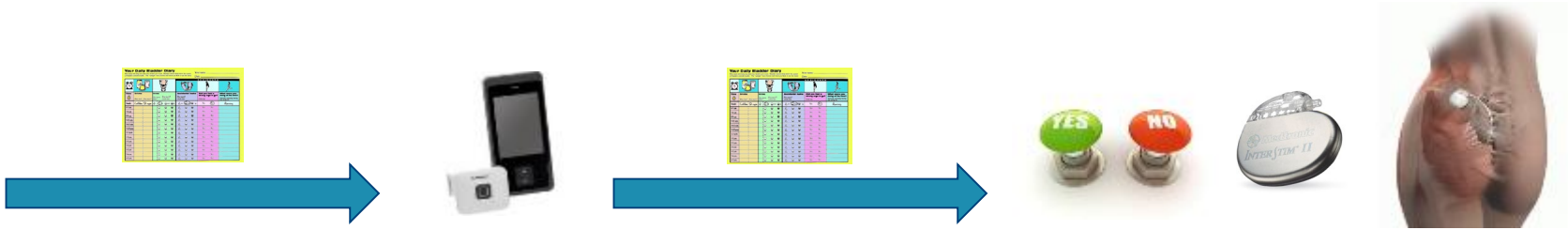
Betere compliantie met Betmiga

TTD = time to treatment discontinuation.

A retrospective study of treatment persistence and adherence to mirabegron vs antimuscarinics. Jameel Nazir et al. BMC Urol 2018.

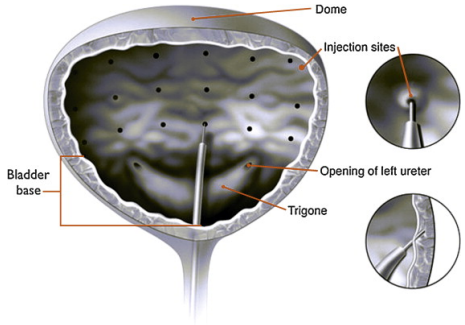
Tweedelijnsbehandeling wet and dry OAB

- Sacrale neuromodulatie



50% verbetering van de klachten (plasdagboek)

- Botox



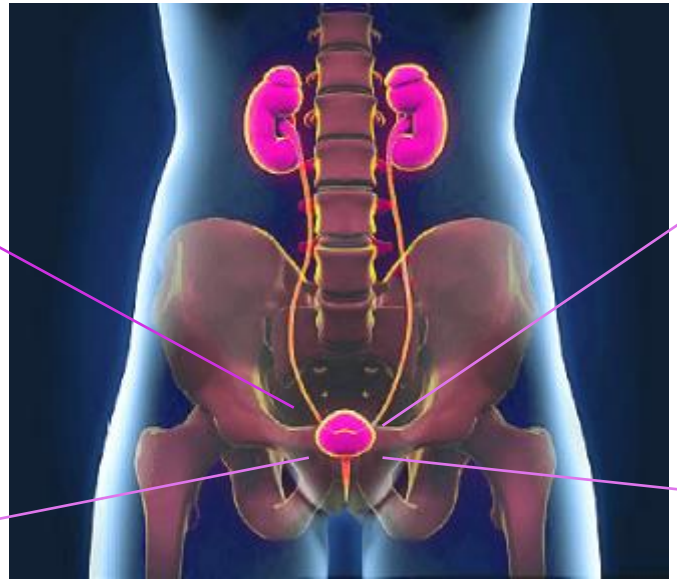
Fowler et al. Eur Urol (2012), doi:10.1016/j.eururo.2012.03.005

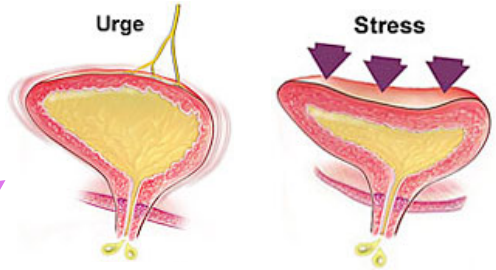
SNM en Botox in UZ Leuven

	Pro	Con
SNM	• Terugbetaald • Langdurig effect • Stop medicatie • 70% kans op verbetering bij refractaire patiënten	• Duur • Meerdere chirurgische ingrepen • Hoge kans op reinterventie • Lage cure rate • Oudere systemen niet MRI compatiebel
Botox	• Stop medicatie • Hoogste cure rate van de gekende behandelingen	• Duur • Reinterventies (gemiddeld jaarlijks) • Nood aan zelfsondage / intermittente sondage (1/20, voor enkele weken!)

FUNCTIONELE UROLOGISCHE KLACHTEN NA MENOPAUZE











Dysurie/mictalgie

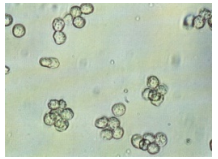
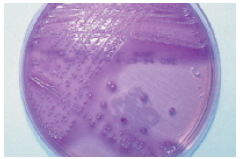
“ Complaint of pain, burning or other discomfort during voiding. Discomfort may be intrinsic to the lower urinary tract (e.g. bladder or urethra), external or referred from other adjacent similarly innervated structures e.g. lower ureter.”

Diagnose

Medische voorgeschiedenis en anamnese

Klinisch onderzoek (BBS, atrofie, POP, andere…)

Investigaties

Urine dipstick/microscopie/cultuur

Zo nodig: vaginale wisser (afscheiding, geur)



Flow Residu

Cytologie en Cystoscopie (TCC, lithiasis, Cis, BPS/IC)

Beeldvorming (Echo, CT, MRI)

Urodynamica

Behandeling

- Infectie te behandelen
- Lokale oestrogenen
- Pijnstilling
- Soms noodzaak tot anticholinergica/Betmiga
- Uropyrine (Fenazopyridine)



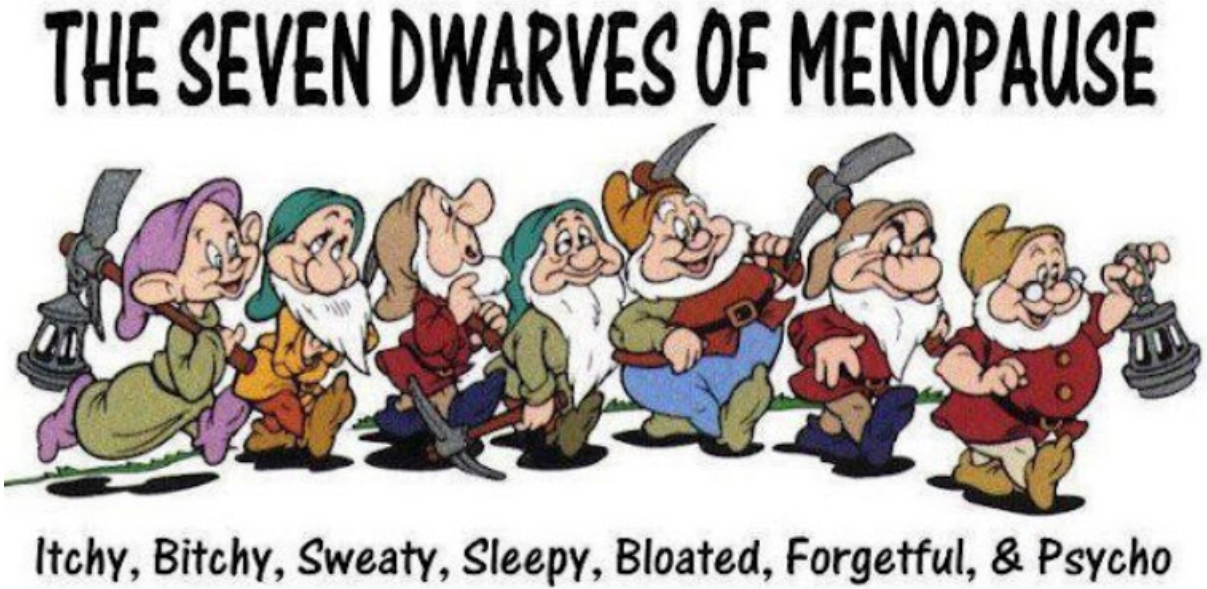
- Behandeling afhankelijk van de diagnose (TCC, Cis, IC, lithiasis…)

Take Home Messages

- Urinaire symptomen frequent bij postmenopauzale vrouwen
- Urogenitale atrofie ligt vaak aan de basis
- Belangrijke plaats voor lokale oestrogenen in de behandeling
- Uitwerken als een urologische klacht
- Let op bij atypische presentatie en alarmsymptomen

Last but not least: goede samenwerking met gynaecologen!

VRAGEN?


THE SEVEN DWARVES OF MENOPAUSE
Itchy, Bitchy, Sweaty, Sleepy, Bloated, Forgetful, & Psycho