Christophe.de.laet@azmonica.be
Christophe.delaet@hotmail.com
03/320.59.64
0499/36.08.54

Geneeskundige dagen:
LUTS en de vergrote prostaat

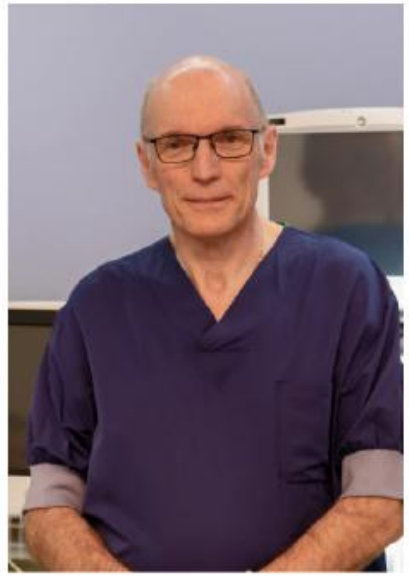
Dr. Christophe De Laet

Uroloog – AZ Monica Deurne/Antwerpen

AZ MONICA

Dr. Christophe De Laet

Algemene en endo-urologie.
Laparoscopie & Robotchirurgie



Dr. Ronny Demeulenaere

Algemene en endo-urologie.
Brachytherapie & oncologische chirurgie

Dr. David Thüer

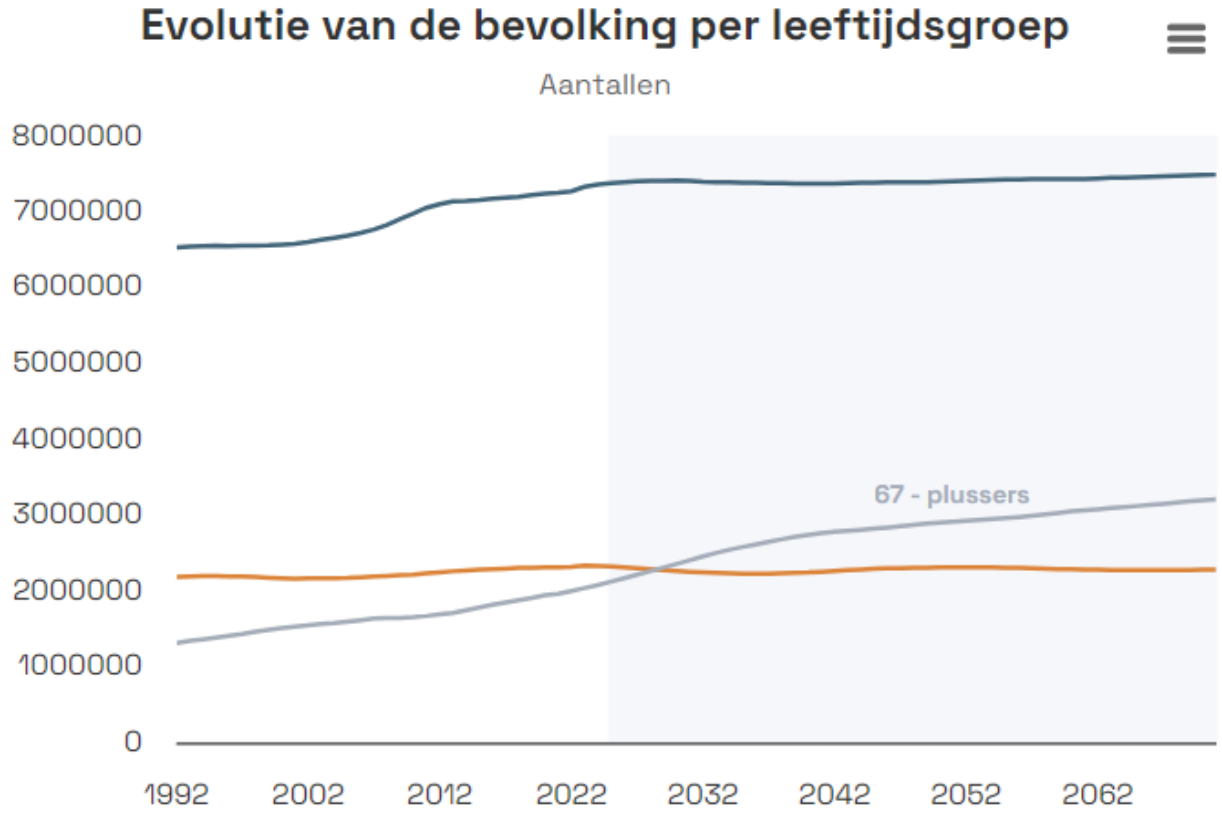
Algemene en endo-urologie.
Incontinentie

Dr. Guillaume Dervaux

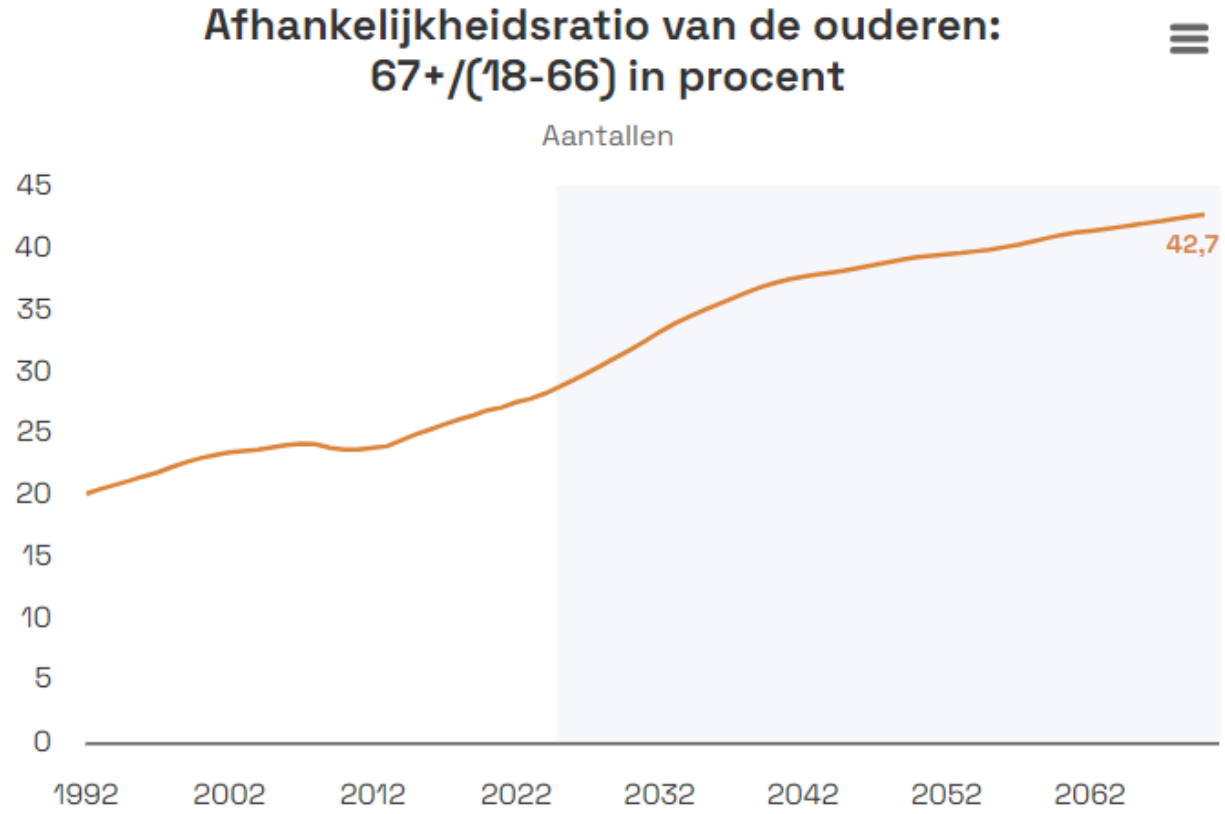
Algemene en endo-urologie.
Steenpathologie

AZ MONICA

Demografie België



Bron: 1992-2023: Statbel. 2024-2070: Demografische vooruitzichten 2024-2070, FPB.



Bron: 1992-2023: Statbel. 2024-2070: Demografische vooruitzichten 2024-2070, FPB.

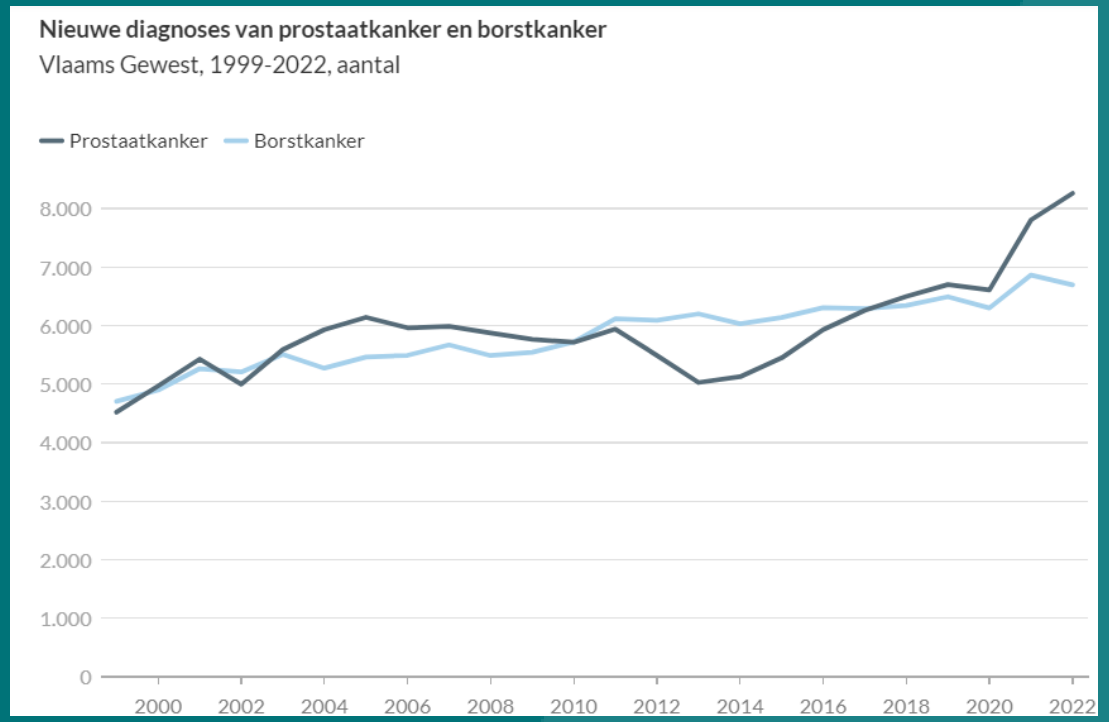
Male LUTS

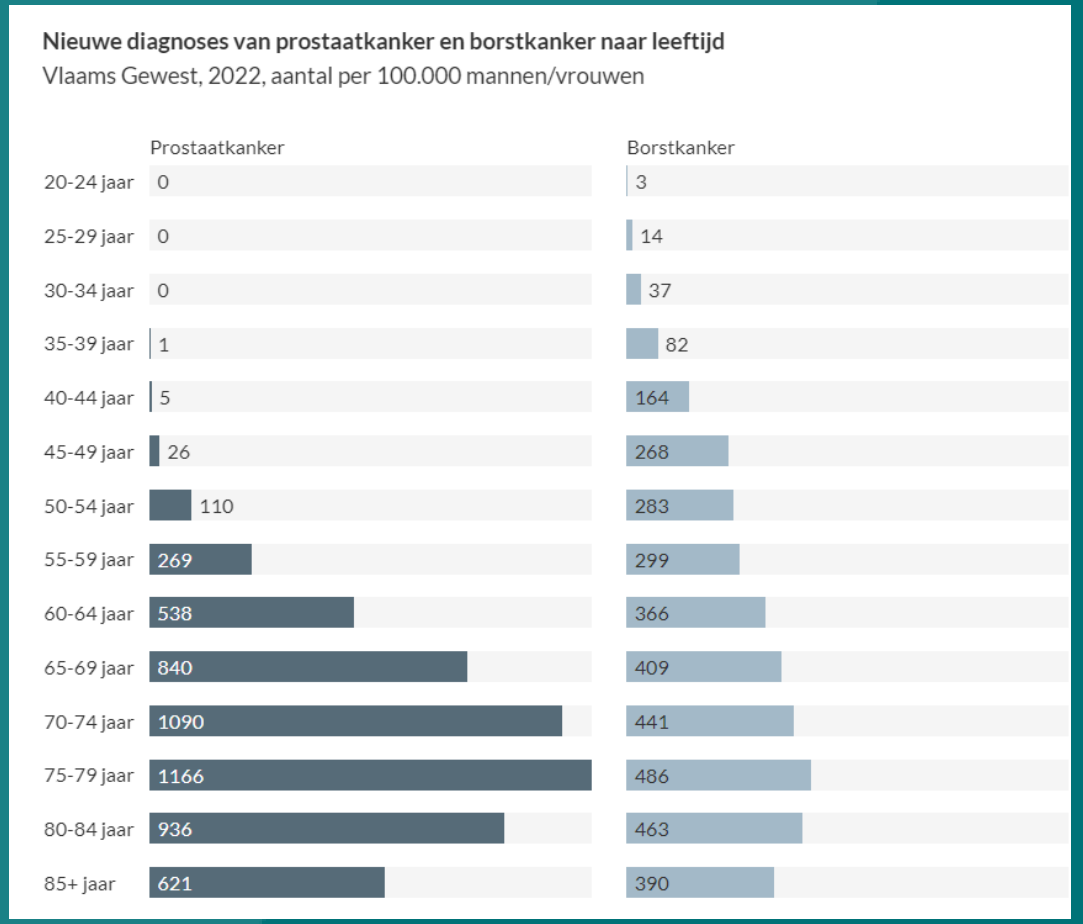
- Prevalentie BPH 30-40% (50-60j) tot 80% (80j+)
- Prevalentie LUTS mid/ernstig 20% (50j) ->30% (60j) ->40% (80j+)

- Impact op QoL ↑, kost ↑ gezien demografie

- Leeftijd ! Metabool syndroom ! (aanpasbaar)

PCa


Nieuwe diagnoses van prostaatkanker en borstkanker
Vlaams Gewest, 1999-2022, aantal
Prostaatkanker
Borstkanker
8.000
7.000
6.000
5.000
4.000
3.000
2.000
1.000
0
2000
2002
2004
2006
2008
2010
2012
2014
2016
2018
2020
2022


Nieuwe diagnoses van prostaatkanker en borstkanker naar leeftijd
Vlaams Gewest, 2022, aantal per 100.000 mannen/vrouwen
Prostaatkanker
Borstkanker
20-24 jaar 0 3
25-29 jaar 0 14
30-34 jaar 0 37
35-39 jaar 1 82
40-44 jaar 5 164
45-49 jaar 26 268
50-54 jaar 110 283
55-59 jaar 269 299
60-64 jaar 538 366
65-69 jaar 840 409
70-74 jaar 1090 441
75-79 jaar 1166 486
80-84 jaar 936 463
85+ jaar 621 390

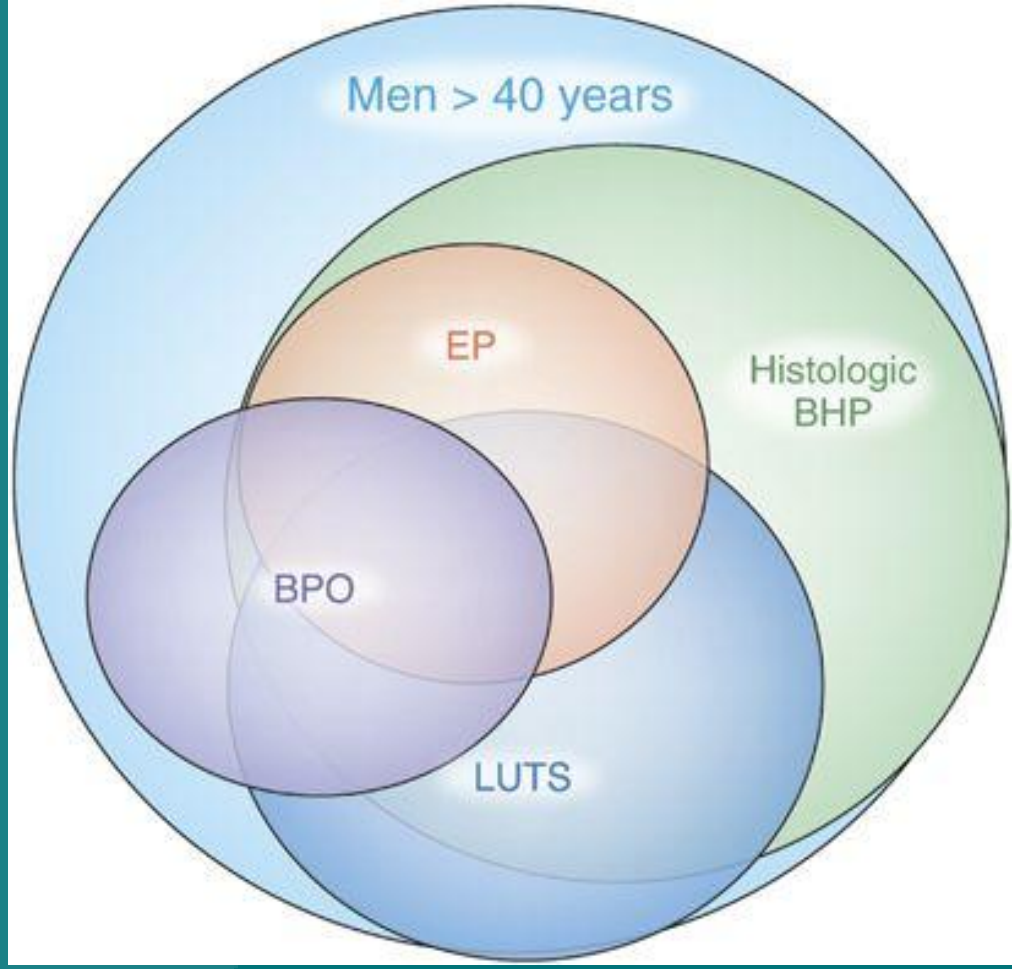
“Same name BUT different diseases”

Incidentiële prostaatkanker bij autopsie: > 50%

11% van alle mannelijke kankers gerelateerde sterfte door Pca.

Definities

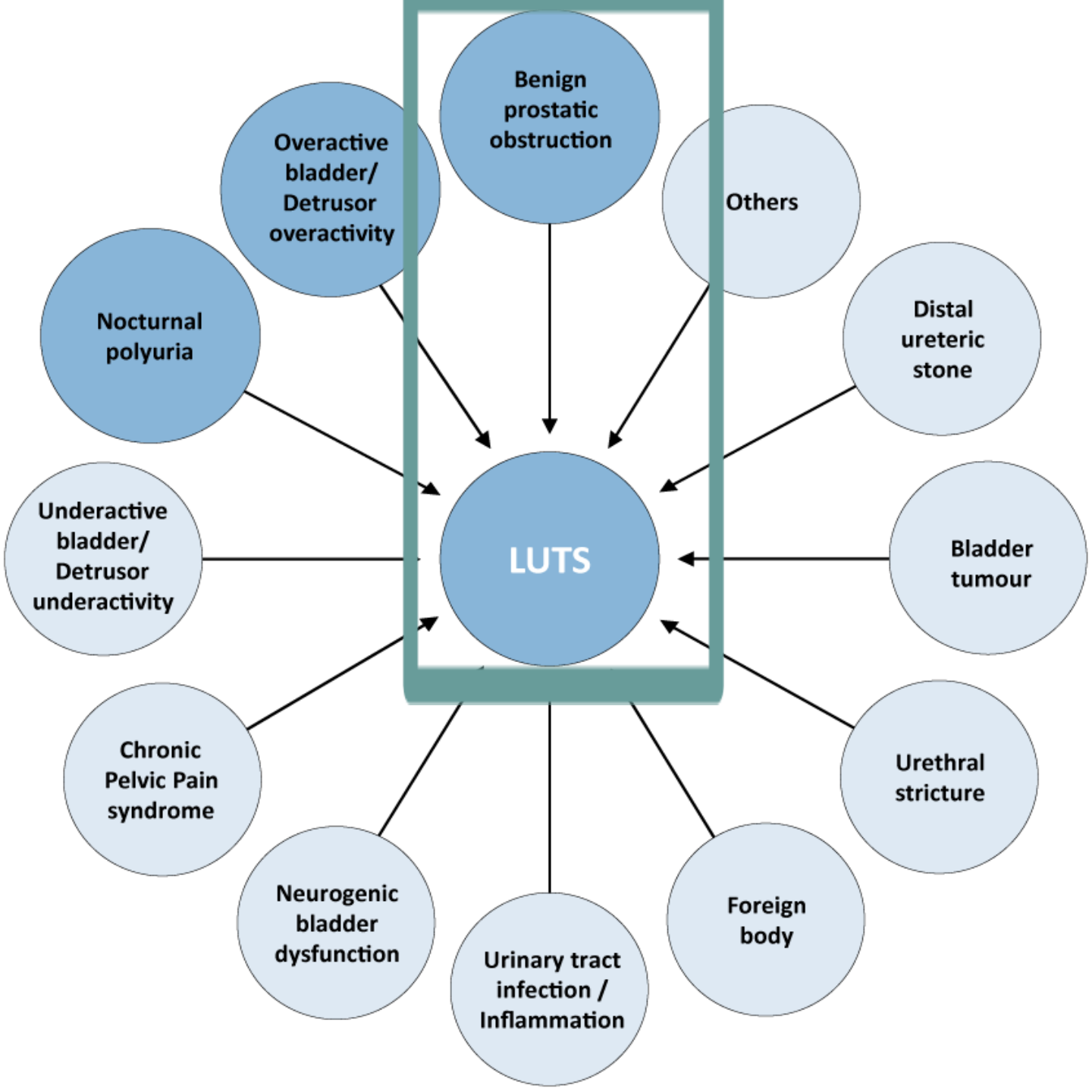
- BPH – Histologisch
- BPE – Klinisch
- LUTS – Klachten



- BOO: bladder outlet obstruction
  - Verhoogde detrusordruk en vertraagde flow
  - BPO: Benign prostatic obstruction dan BPH oorzaak van klachten
  - DOA vs DUA (Detrusor-OnderActiviteit); verminderde druk en vertraagde flow

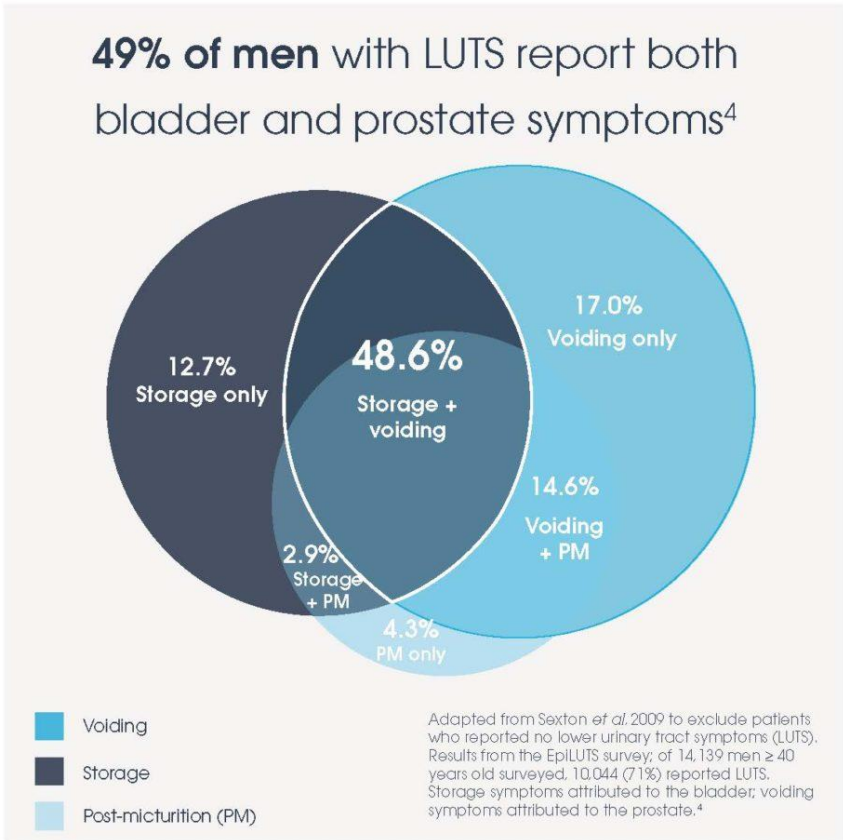
Male LUTS

- Male LUTS zijn multifactorieel, prostaat is slechts 1 factor
- Behandelopties linken aan behandeldoel voor patiënt
  - Overweeg systemische en seksuele impact van behandeling
- Koppel hoog risico patiënten aan laag risico (preventieve) behandelingen en heelkunde


Benign prostatic obstruction
Overactive bladder/ Detrusor overactivity
Others
Nocturnal polyuria
Distal ureteric stone
Underactive bladder/ Detrusor underactivity
LUTS
Bladder tumour
Chronic Pelvic Pain syndrome
Urethral stricture
Neurogenic bladder dysfunction
Urinary tract infection / Inflammation
Foreign body

Epi-LUTS

Fig 1. Results from the EpiLUTS study - LUTS in men[4]



- 2009
- 14,000 mannen
- 40jr+

EPIC-LUTS

- Population-based survey of urinary incontinence, overactive bladder, and other lower urinary tract symptoms in five countries: results of the EPIC study
- 19165 ptn
- 18j+ man en vrouw
- 64,3% - min 1 klacht

LUTS

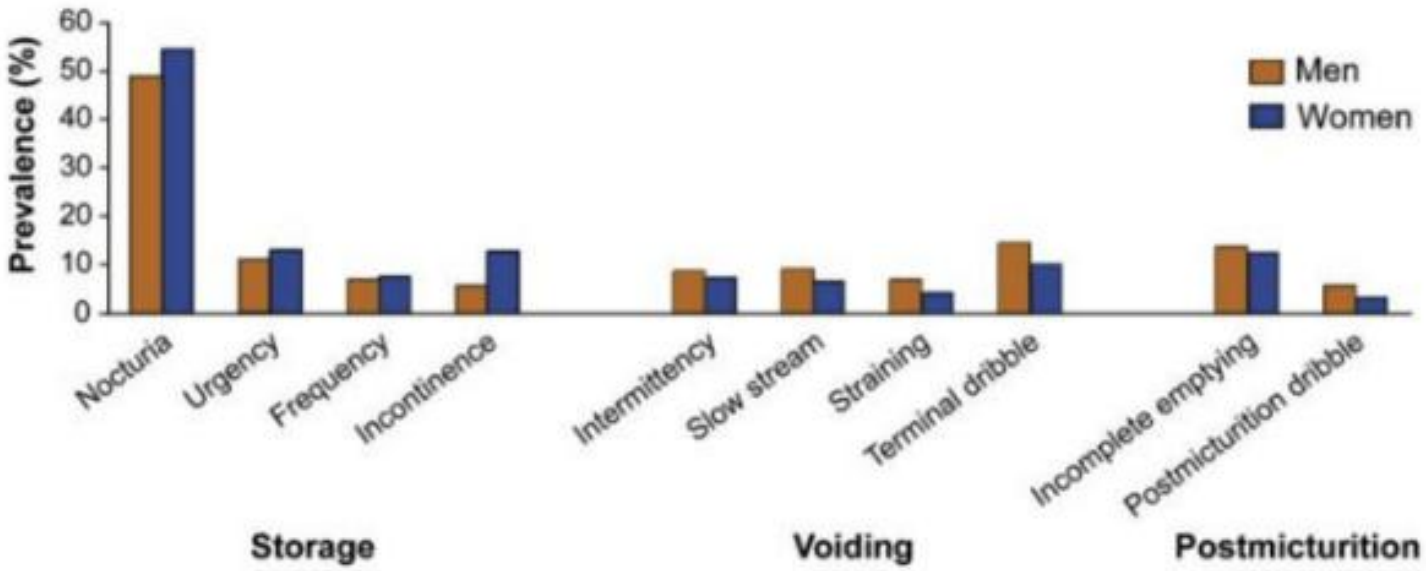
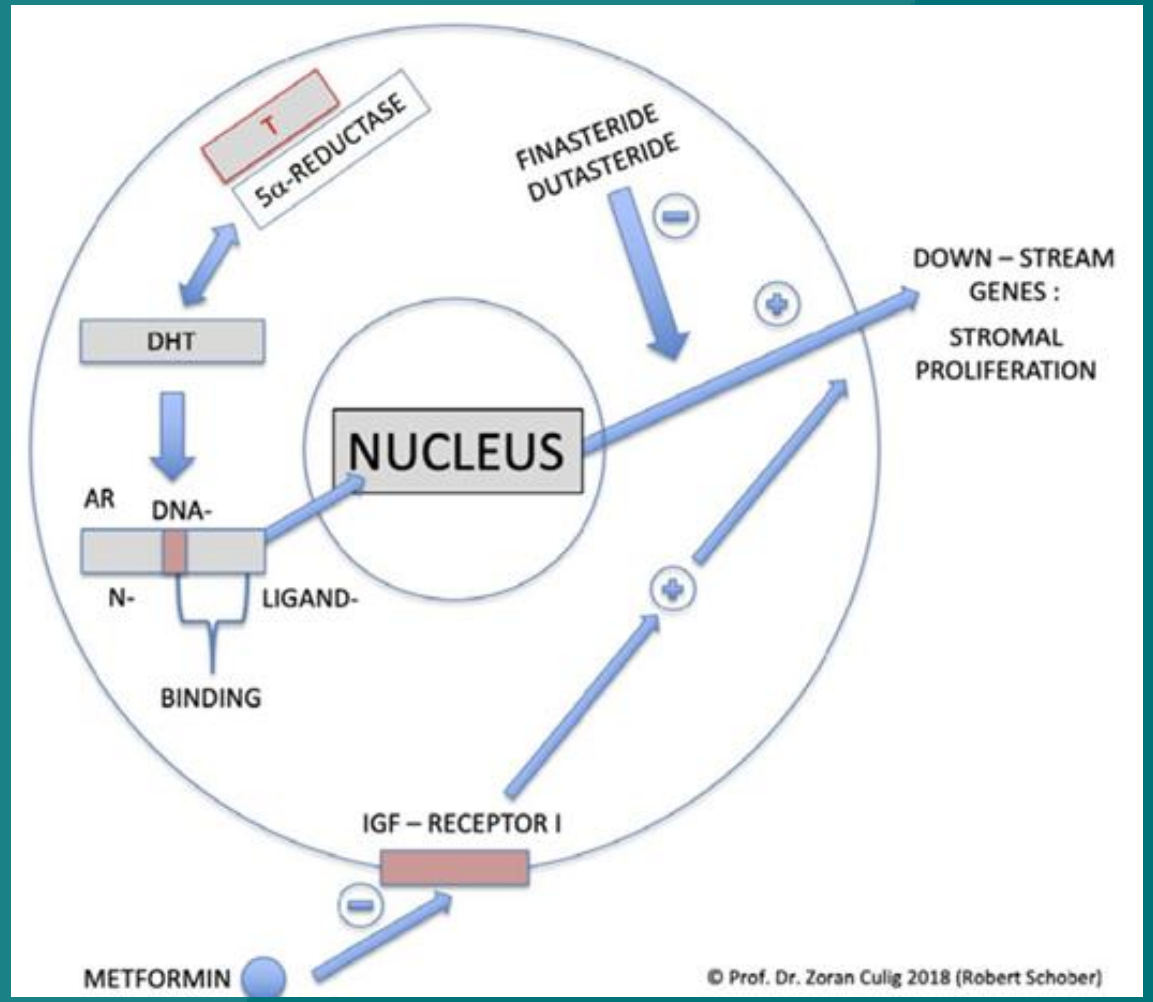


Fig. 4 – Prevalence of storage, voiding, and postmicturition LUTS among men and women using 2002 ICS definitions. ICS = International Continence Society; LUTS = lower urinary tract symptoms.

Pathofysiologie BPH (1)

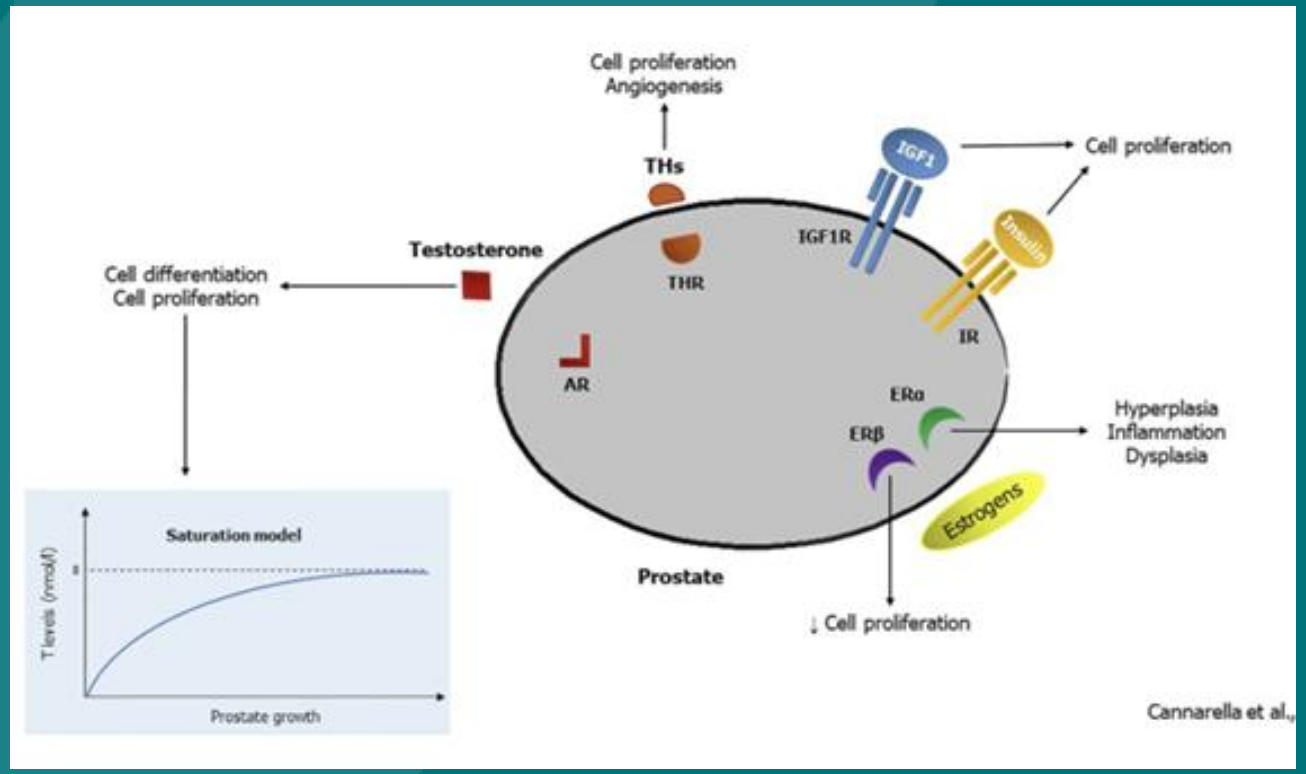
- Andro-/oestrogen receptor
- **Dihydrotestosteron (DHT)** – meest potente androgen
- Groeistimulerende en prodifferentiatie genes

- Aanknopingspunt medicatie

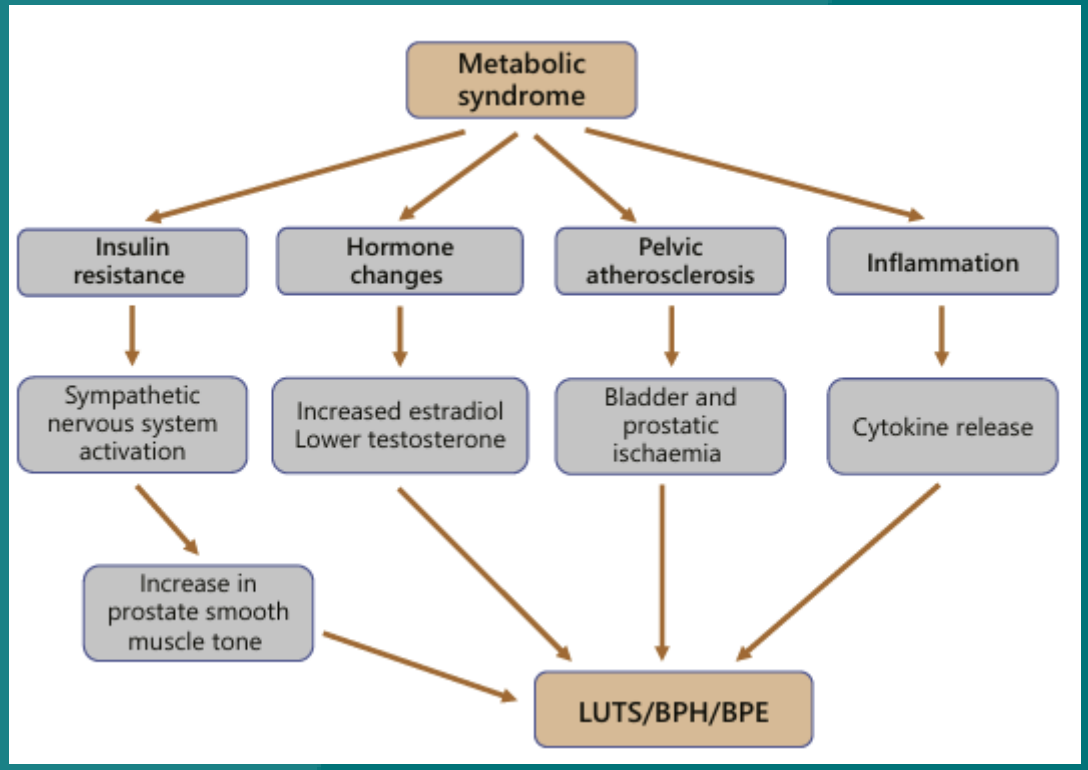


Pathofysiologie BPH (2)

- Relatie prostaat – hormonen
  - Variatie leeftijd
  - Comorbiditeit
- Schildklier -> T3
- Insuline (like-growth factor)
- Oestrogenen
  - PCOS – hormonale en metabole abnormaliteit



- Obesitas 3,5x
- Cyto/chemo-kines + GF
- Geen relatie tot BPH(/LUTS): religie, socio-economisch, vasectomie, seksuele activiteit, roken en alcohol



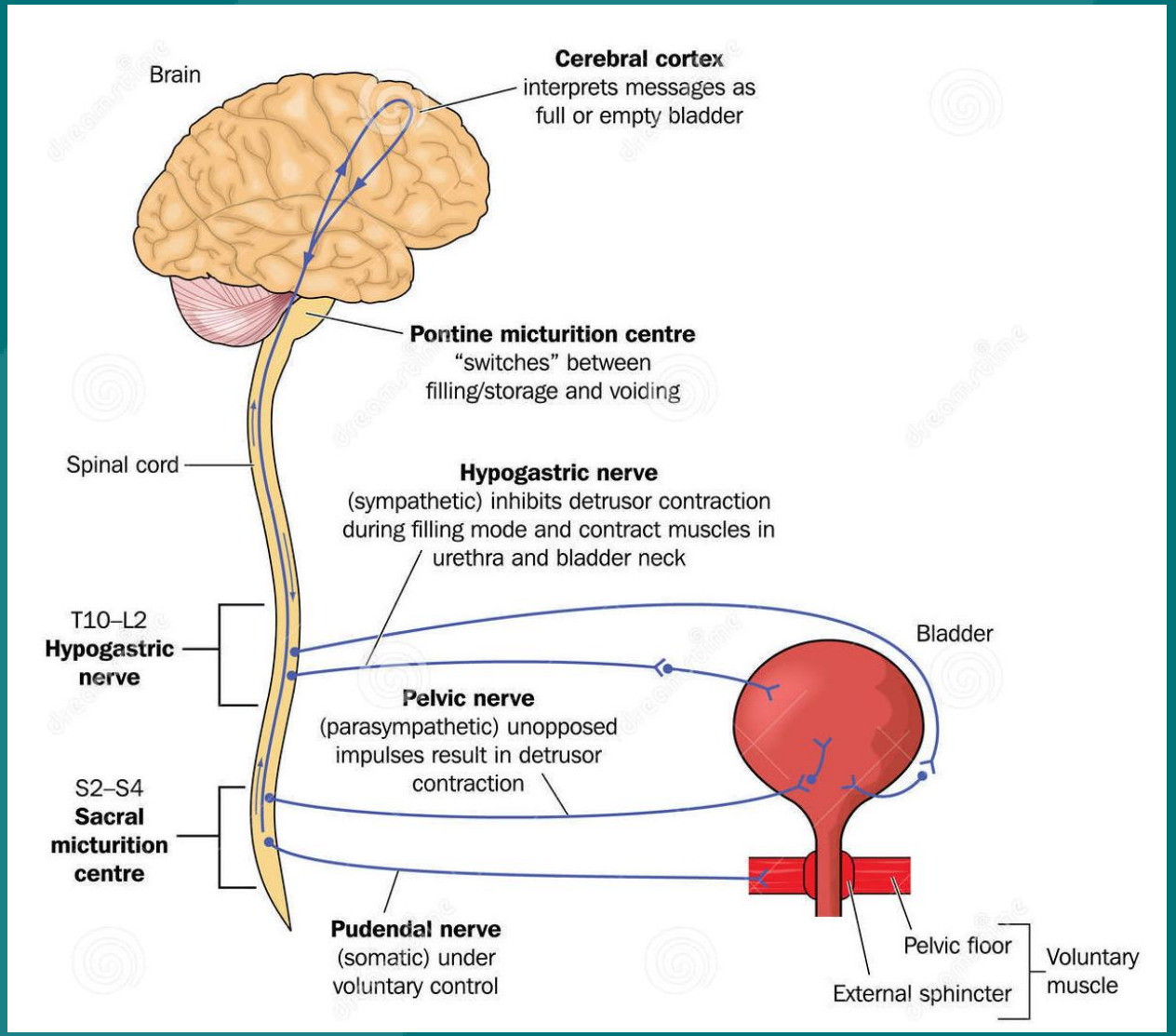
Normale blaas

- Vulling
- Opslag
- Lediging

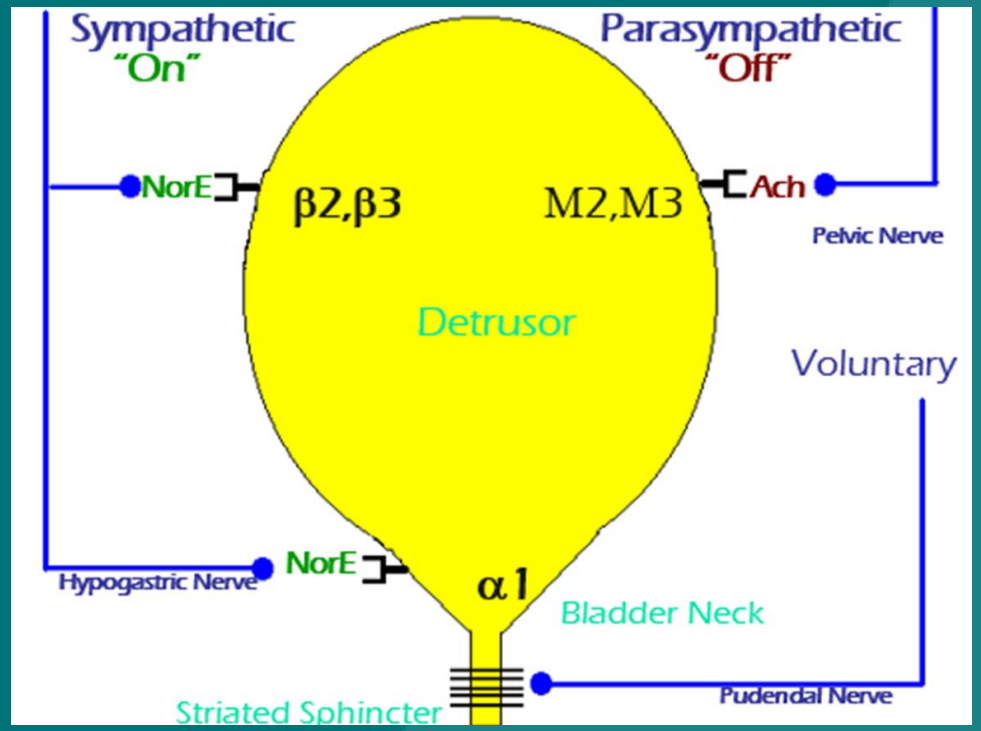
Normale blaas

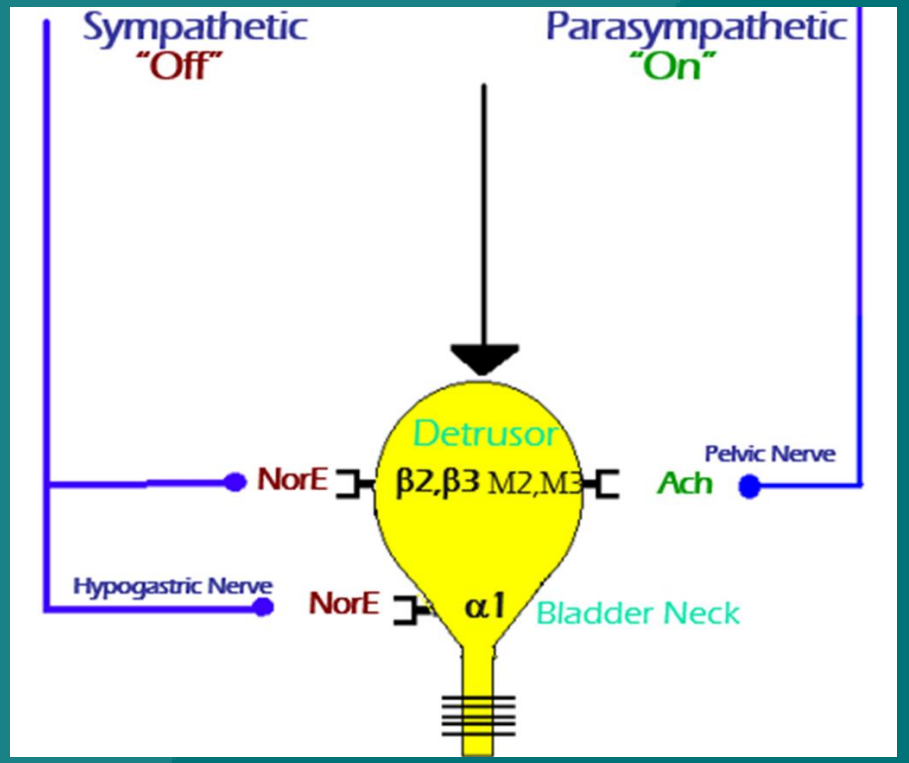
- Vullingsfase
  - Blaas -, sfincter +
  - Duur en capaciteit
- Ledigingsfase
  - Blaas +, sfincter -
  - Duur en ejectiefractie

- Aanknopingspunt medicatie
- Pons + sacraal mictiecentrum



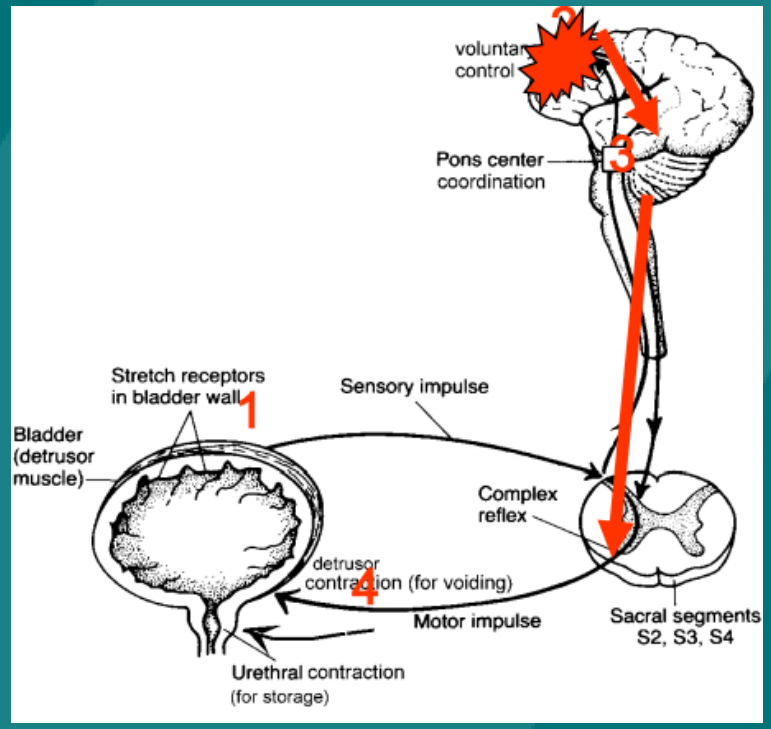
Fysiologie


Sympathetic
"On"
Parasympathetic
"Off"
NorE
β2,β3
M2,M3
Ach
Pelvic Nerve
Detrusor
Voluntary
Hypogastric Nerve
NorE
α1
Bladder Neck
Striated Sphincter
Pudendal Nerve


Sympathetic
"Off"
Parasympathetic
"On"
Detrusor
NorE
β2,β3
M2,M3
Ach
Pelvic Nerve
Hypogastric Nerve
NorE
α1
Bladder Neck

- Controle!!
- Proprioceptie bij vulling

- 1,5L-2,5L per dag urineproductie
- Ledigt 4-6x/dag
- +- 300-500ml per mictie

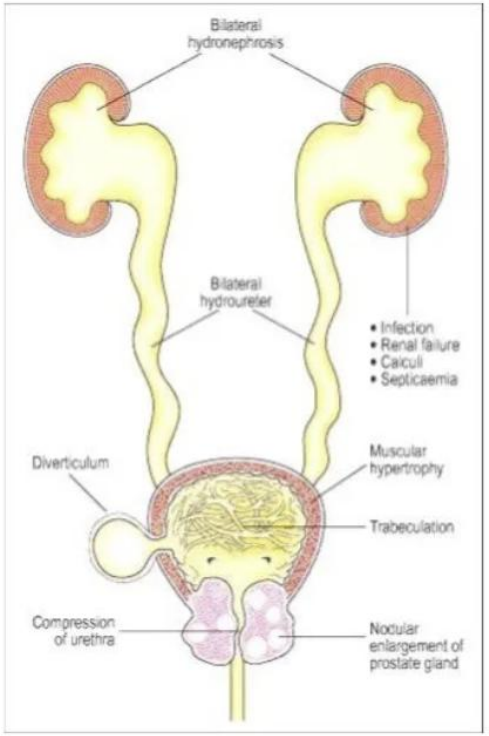


LUTS/BPH

BPH-Complications:

1. Obstructive Uropathy
2. Bladder hypertrophy
3. Trabeculation
4. Diverticula formation
5. Hydroureter – bilateral
6. Hydronephrosis
7. Lithiasis / stone.
8. Secondary infection.

- Not a risk factor for Carcinoma prostate.



- Chronisch en **progressief**

→ retentie, infectie, stenen, hydronefrose, AKI/CNI

- Grote invloed op **kwaliteit van leven**

→ Depressie, schaamte, sociaal isolement

Diagnostiek

Altijd

- Anamnese met VG en IPSS
- Klinisch onderzoek
  - RT → volume < > 50ml
- Mictiedagboek (1-3)
- Flowmetrie + residu
- Urinesediment NVU: niet standaard

Op indicatie

- TRUS: *als prostaatvolume consequenties heeft op beleid*
- UCS / echo nieren (EAU: standaard echo nieren)
- Creatinine

  als NFstoornis verwacht, pré-operatief
- PSA

  NVU: op wens pt, EAU: indien diagnose pca beleid verandert

Polyfarmacie als oorzaak van LUTS

• Opiaten	Ajusted sequence ratio 1,3
• Antipsychotica (levodopa)	ASR 1,8
• SSRI’s (paroxetine, fluvoxamine)	ASR 1,7 – 2,1
• Benzodiazepine (diazepam)	ASR 1,44
• Antiarrytmica / cardiac stimulants	ASR 2,97

- Hashimoto et al. 2015. J of farmalogical heathcare

IPSS

- Ernst
  - 1-7 mild
  - 8-19 matig
  - 20-35 ernstig
- Predominante klacht
- QoL

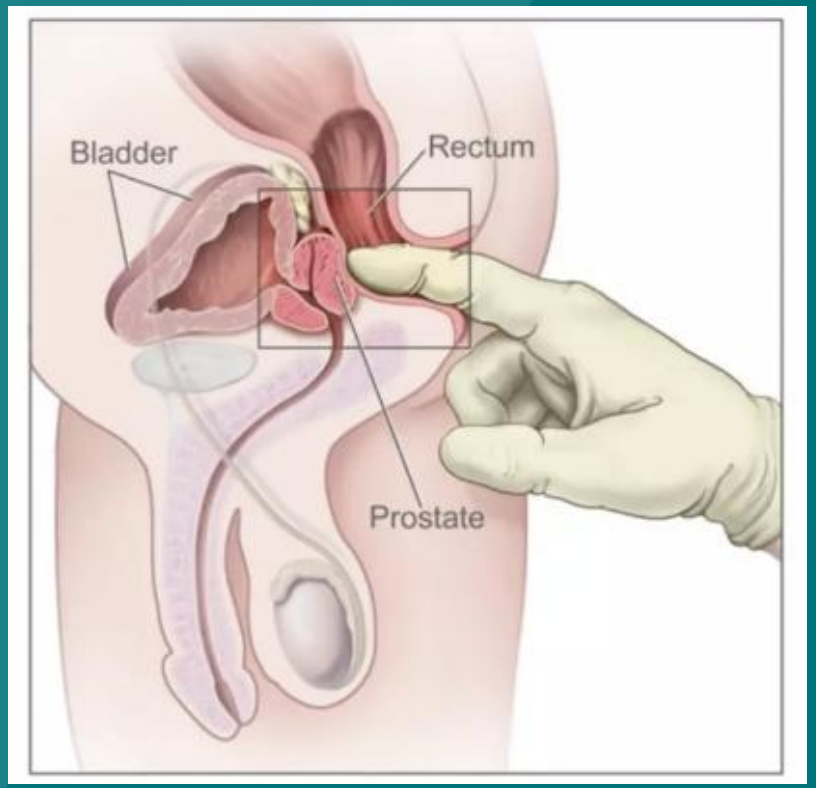
- Niet geslacht, leeftijd, ziekte gerelateerd
- Her-evaluatie!

International Prostate Symptom Score (I-PSS)							
In the past month:	**Not at All**	**Less than 1 in 5 times**	**Less than Half the Time**	**About Half the Time**	**More than Half the Time**	**Almost Always**	**Your Score**
1. Incomplete Emptying How often have you had the sensation of not emptying your bladder?	0	1	2	3	4	5	
2. **Frequency** How often have you had to urinate less than every two hours?	0	1	2	3	4	5	
3. Intermittency How often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
4. Urgency How often have you found it difficult to postpone urination?	0	1	2	3	4	5	
5. Weak Stream How often have you had a weak urinary stream?	0	1	2	3	4	5	
6. Straining How often have you had to strain to start urination?	0	1	2	3	4	5	
	None	**1 time**	**2 times**	**3 times**	**4 times**	**5 times**	
7. Nocturia How many times did you typically get up at night to urinate?	0	1	2	3	4	5	
Total I-PSS Score							
Score:	1-7 Mild		8-19 Moderate		20-35 Severe		
		The first seven questions of the I-PSS are from the American Urological Association (AUA) Symptom Index					
Quality of Life Due to Urinary Symptoms							
	Delighted	**Pleased**	**Mostly Satisfied**	**Mixed**	**Mostly Dissatisfied**	**Unhappy**	**Terrible**
If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?	**0**	**1**	**2**	**3**	**4**	**5**	**6**

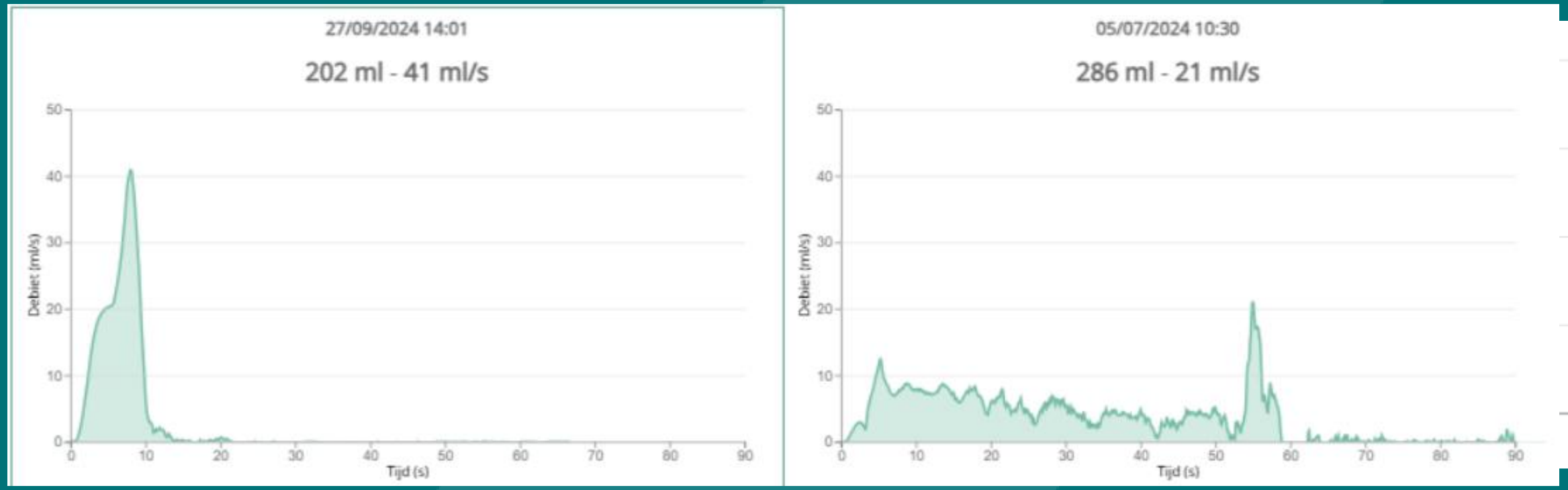
Klinisch onderzoek

- Meest effectieve methode voor detectie

  RT + PSA
- Abdominaal nazicht (NSP, retentie,..)
- + lab



Flowmetrie


27/09/2024 14:01
202 ml - 41 ml/s
Debiet (ml/s)
Tijd (s)
05/07/2024 10:30
286 ml - 21 ml/s
Debiet (ml/s)
Tijd (s)
80

UDO – urodynamisch onderzoek

- Gouden standaard voor bewijs obstructie

- Doel?
- Bij wie?
- Belasting?
- Onderzoeksafhankelijk

UDO

- Mogelijke voorspellers voor falen spontane mictie na TURP:
  - Afwezigheid van DO
  - Grote blaascapaciteit
  - Lagere maximale detrusordruk

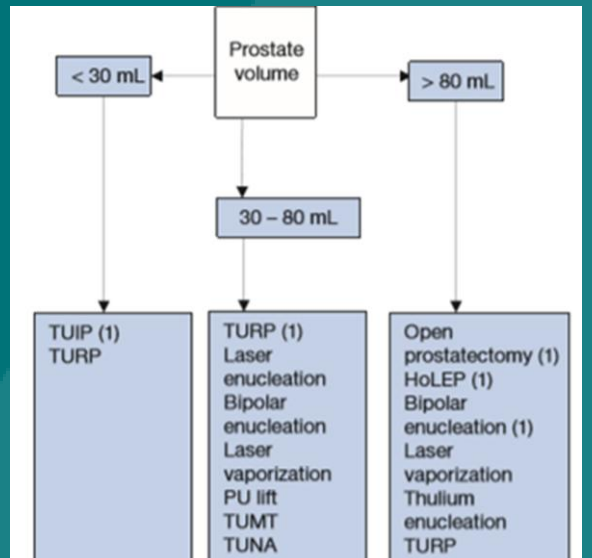
- Maar: DO tijdens vullingsfase lijkt niet voorspellend voor QoL en LUTS nadien

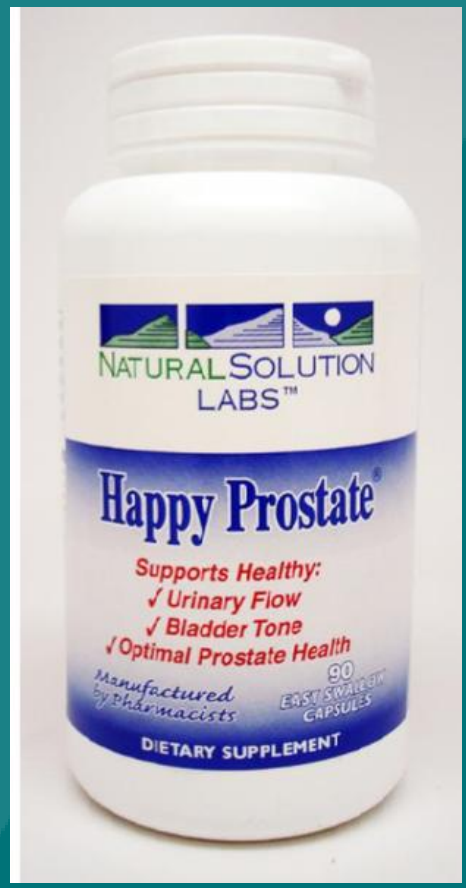
Bron: Djovan 1997, Cho 2013, Mitchell 2014, Huang 2015

Recommendations	Strength rating
Perform pressure-flow studies (PFS) only in individual patients for specific indications prior to invasive treatment or when evaluation of the underlying pathophysiology of LUTS is warranted.	Weak
Perform PFS in men who have had previous unsuccessful (invasive) treatment for LUTS.	Weak
Perform PFS in men considering invasive treatment who cannot void > 150 mL.	Weak
Perform PFS when considering surgery in men with bothersome predominantly voiding LUTS and Q_{max} > 10 mL/s.	Weak
Perform PFS when considering invasive therapy in men with bothersome, predominantly voiding LUTS with a post void residual > 300 mL	Weak
Perform PFS when considering invasive treatment in men with bothersome, predominantly voiding LUTS aged > 80 years.	Weak
Perform PFS when considering invasive treatment in men with bothersome, predominantly voiding LUTS aged < 50 years.	Weak

Behandeling

- Watchful waiting
- Levensstijl
- Medicamenteus
  - Phytotherapie
  - α-blokkers, 5-ARI, anti-cholinergica, B3M,..
- Operatief
  - PV < 80ml
  - PV > 80ml





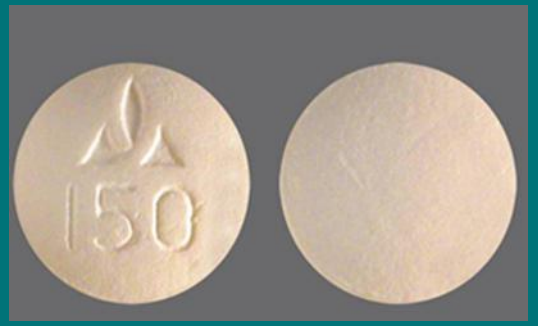
Gedrags- en dieetaanpassing

- Educatie + geruststelling
- Levensstijladvies
  - Periodiek drinken – “Timed” voiding
  - Vermindering cafeïne en alcohol
  - Behandeling constipatie
  - Leegstrijken penis, perineum melken
  - Medicatie

Medicamenteuze behandeling

- 1ste keus: alfablokker
- Prostaat 40+ml = 5ARI (extra of 1ste keuze?)
- Opslagproblematiek: Beta-3-agonist of anticholinergicum

- Combinatie indien onvoldoende effect
- Cave: (geriatrisch) profiel en residu > 150ml



Alpha1-adrenoreceptorblokkers (α1-blokkers)

- Werkingsmechanisme: Remmen de werking van noradrenaline op gladde spiercellen in de blaashals/UP, verminderen hierdoor outflow obstructie.
- Geen effectiviteitsverschil in beschikbare medicijnen
- Effectiviteit: Vermindert IPSS met 30-40%, verhoogt Qmax met 20-25%.
- Nevenwerking: Duizeligheid, (orthostatische)hypotensie, retrograde ejaculatie.

5α-reductase inhibitoren

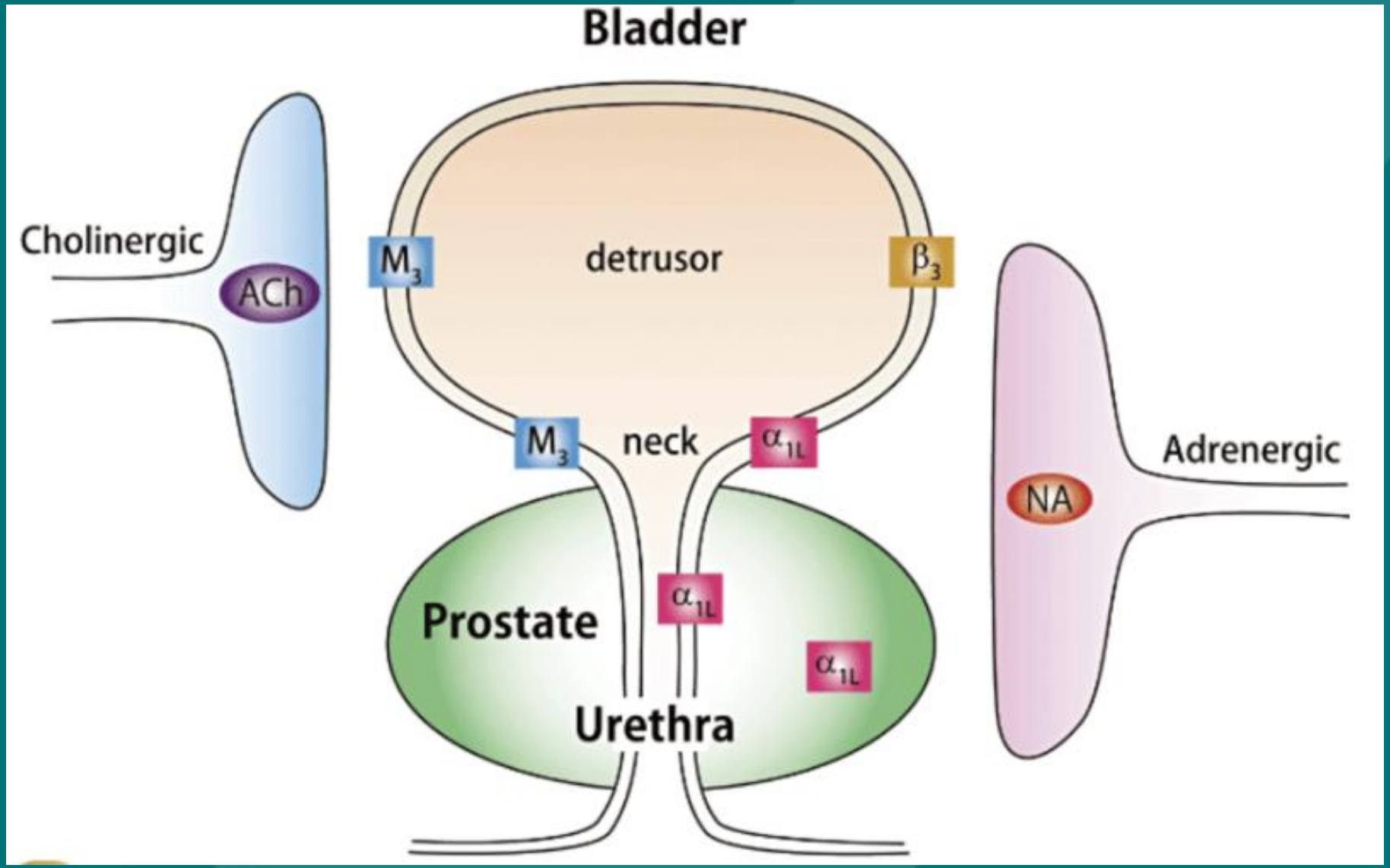
- Werkingsmechanisme: Remmen omzetting van testosteron naar dihydrotestosteron. Best voor prostaten >40cc
- Effectiviteit: Verminderen prostaatvolume (20%) en daarmee IPSS + verhogen Qmax CAVE minstens 6M behandeling.
- Nevenwerkingen: libidoverlies, erectiele dysfunctie, gynaecomastie (1-2%)

Muscarinereceptor antagonisten

- Werkingsmechanisme: Blokkeren muscarinereceptoren (M3) op gladde spiercellen in de blaas.
- Effectiviteit: Verbeteren storage LUTS, verminderen frequentie, urgentie en UUI.
- Nevenwerkingen: Droge mond(16%), constipatie(4%), voiding dysfunction (2%)

Beta-3-agonisten

- Werkingsmechanisme: Stimuleren β-3-adrenoreceptoren, ontspannen de detrusor.
- Effectiviteit: Verbeteren storage-LUTS, inclusief frequentie, urgentie en UUI.
- Nevenwerkingen: hypertensie, UWI, hoofdpijn, nasopharnyngitis


Bladder
Cholinergic
ACh
M3
detrusor
β3
M3
neck
α1L
Adrenergic
NA
Prostate
α1L
α1L
Urethra

Fosfodiësterase 5-remmers (PDE5i's)

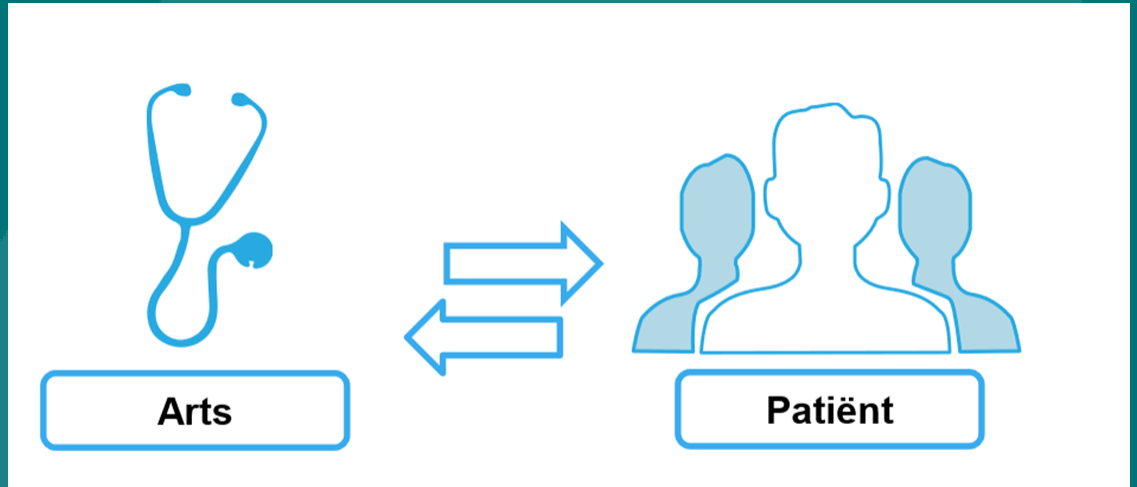
- "Tadalafil 5mg"
- Werkingsmechanisme: vermindering van de gladde spiertonus van de detrusor, prostaat en urethra.
- Efficiëntie: Goede subjectieve verbetering: IPSS verminderen, storage-en voiding-LUTS verbeteren.
- Qmax weinig verschil van placebo.
- Nevenwerkingen: blozen, GER, hoofdpijn, dyspepsie, rugpijn en neusverstopping.

	placebo	α1-blokker	5-ARI	Combinatie
IPSS	**-20%**	**-30/40%**	**-30/40%**	**-40%**
Qmax	**+0,5 ml/s**	**+1,5-2,0 ml/s**	**+1,5-2,0 ml/s**	**+2,5 ml/s**
Start werking		Dagen - weken	2-6 mnd	combi
PSA	Geen effect	Geen effect	50% daling	50% daling
progressie		IPSS minder	IPSS,AUR,operatie	IPSS,AUR,operatie
prostaatvol	Geen effect	Geen effect	20-25% minder	20-25% minder
bijwerkingen		vasculair (α1b) ejaculatie (α1a)	libodo	combi

Combinatietherapie: α-blokker + 5ARI / + muscarinereceptorA / + β3 agonist
Cave hoge kost en geen tussenkomst (30-70€/maand)

Take-home messages

- LUTS/BPH veel voorkomend
- Breed diagnostische uitwerking
- Verschillende medicamenteuze en operatieve technieken voor BPH
- Size does matter…
- De “beste behandeling” is voor iedere patiënt anders
  → Shared decision making



NEWS

Europe recommends screening programmes for prostate cancer

20 September 2022

Long campaign by Europa Uomo bears fruit

Europa Uomo has welcomed the European Commission's announcement that it will extend recommended population-based cancer screening programmes in Europe to prostate cancer.

The announcement follows a long campaign by Europa Uomo and the European Association of Urology (EAU) calling on the European Commission to extend its 2003 screening guidelines, which recommended organised, population-based screening programmes for breast, cervical and colorectal cancer. Europa Uomo said that the recommendation should be extended to include prostate cancer to take account of recent evidence which changed the balance of risks and benefits.

LATEST NEWS

Excellent response to Europa Uomo partners' study
First EU-PROPER results due to be presented in April
24/01/2024

National prostate screening programme underway in Czech Republic
Innovative pilot scheme follows new EU recommendation on early detection
12/01/2024

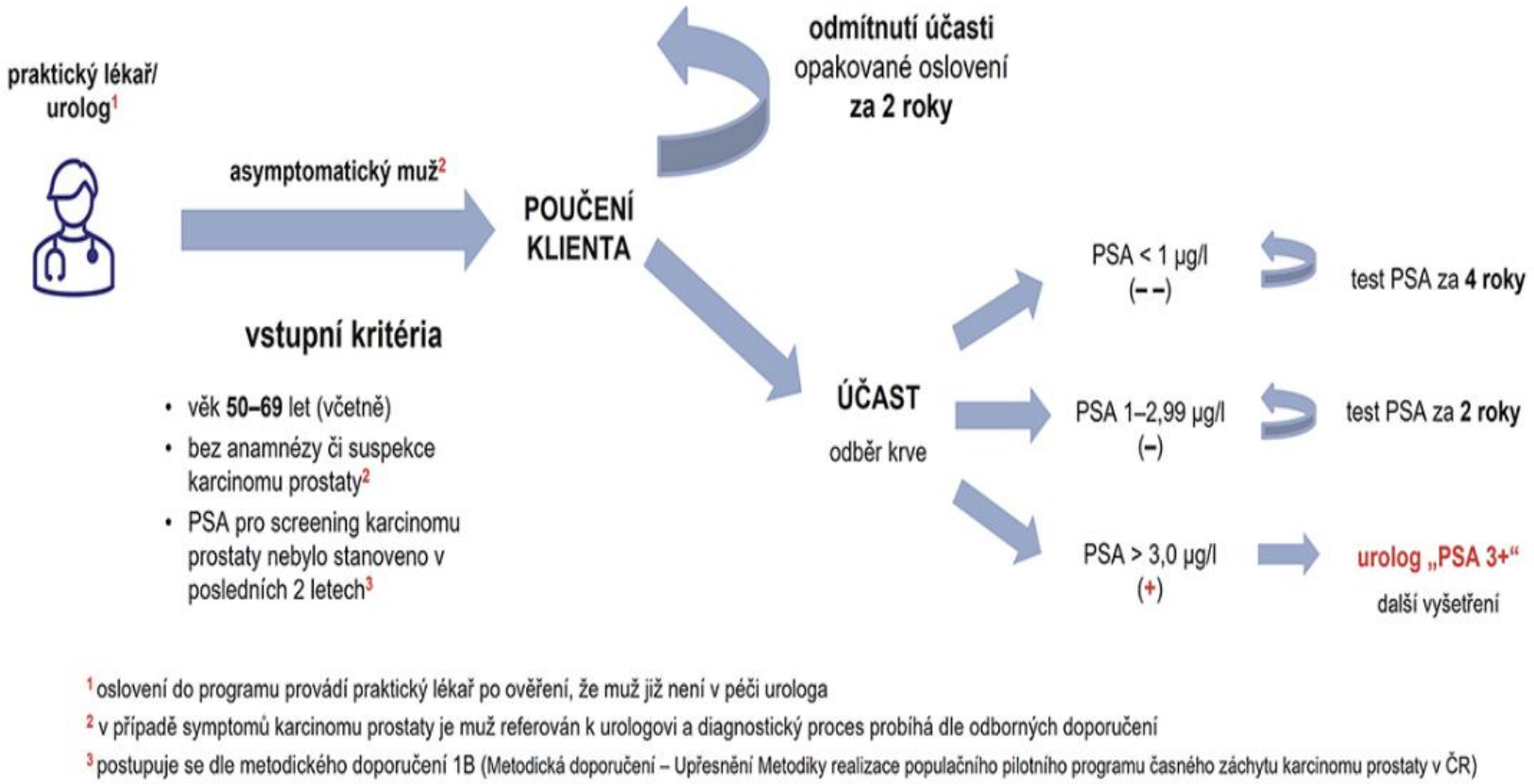
Europa Uomo celebrates 20th anniversary

New EU wide project to reduce prostate cancer mortality through smart early detection

26 April 2023
The EU4Health programme has approved PRAISE-U (PRostate cancer Awareness and Initiative for Screening in the European Union), an ambitious three-year project involving 25 institutions from 12 countries. PRAISE-U's mission is to design a nationally tailored cost-effective early detection algorithm for prostate cancer screening in the EU to reduce morbidity and mortality caused by prostate cancer while avoiding overdiagnosis and overtreatment.

Prostate cancer is the number 1 and 2 cancer killing men in northern and western Europe respectively. It is the most frequent male cancer in Europe with important consequences for healthcare systems. Every year, around 450,000 European men are diagnosed with prostate cancer. Delayed diagnosis can lead to higher rates of metastasised disease, which is a disease state that coincides with a high mortality rate and a prolonged negative impact on the quality of life. It has been shown that organised repeated screening results in early detection that can reduce suffering and dying from prostate cancer. Modern tools and strategies can streamline the process to detect cancer when it poses a threat to the patient.

vyšetření a rozhodne o dalším sledování a vyšetřeních.



[1] oslovení do programu provádí praktický lékař po ověření, že muž již není v péči urologa

[2] v případě symptomů karcinomu prostaty je muž referován k urologovi a diagnostický proces probíhá dle odborných doporučení

[3] postupuje se dle metodického doporučení 1B (Metodická doporučení – Upřesnění Metodiky realizace populačního pilotního programu časného záchytu karcinomu prostaty v ČR)

Pozn: Urolog PSA 3+ = certifikované pracoviště ČUS ČLS JEP, které provádí muže celým screeningovým programem; PSA = prostatický specifický antigen.