



PROSTATE CANCER

STATE OF THE ART IN SCREENING, DIAGNOSTICS AND TREATMENTS

Harm van Melick, Urologist

Amsterdam 11-11-2021



santeon

ST ANTONIUS

oncomid
oncologie midden-nederland

ABOUT ME

Harm van Melick

- Oncologic urologist St. Antonius Nieuwegein-Utrecht
- Train residents
- Researcher oncologic urology
- Chair scientific committee Dutch Urologic Association
- Medical advisor Netherlands Comprehensive Cancer Organization (IKNL)



NEDERLANDSE VERENIGING VOOR UIROLOGIE



WHAT IS THIS TALK ABOUT?

Screening, diagnostics and treatments

- About the prostate and PSA
- Facts and numbers of prostate cancer
- Imaging and prostate biopsies
- Treatments
- Screening

EAU - EANM - ESTRO - ESUR - ISUP - SIOG Guidelines on Prostate Cancer

N. Mottet (Chair), P. Cornford (Vice-chair), R.C.N. van den Bergh, E. Briers, Expert Patient Advocate (European Prostate Cancer Coalition/Europa UOMO), M. De Santis, S. Gillissen, J. Grummet, A.M. Henry, T.H. van der Kwast, T.B. Lam, M.D. Mason, S. O'Hanlon, D.E. Oprea-Lager, G. Ploussard, H.G. van der Poel, O. Rouvière, I.G. Schoots, D. Tilki, T. Wiegel
Guidelines Associates: T. Van den Broeck, M. Cumberbatch, A. Farolfi, N. Fossati, G. Gandaglia, N. Grivas, M. Lardas, M. Liew, L. Moris, P-P.M. Willemse

 European Association of Urology



 European Society for Radiotherapy & Oncology

 European Association of Nuclear Medicine

 INTERNATIONAL SOCIETY OF GERIATRIC ONCOLOGY

 EUROPA UOMO
The Voice of Men with Prostate Cancer in Europe



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VOTE FOR SCREENING

Before presentation

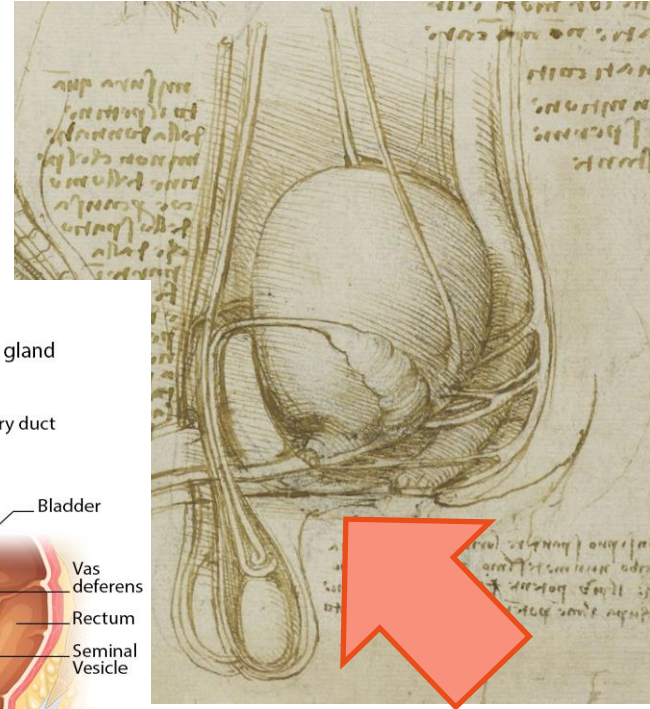
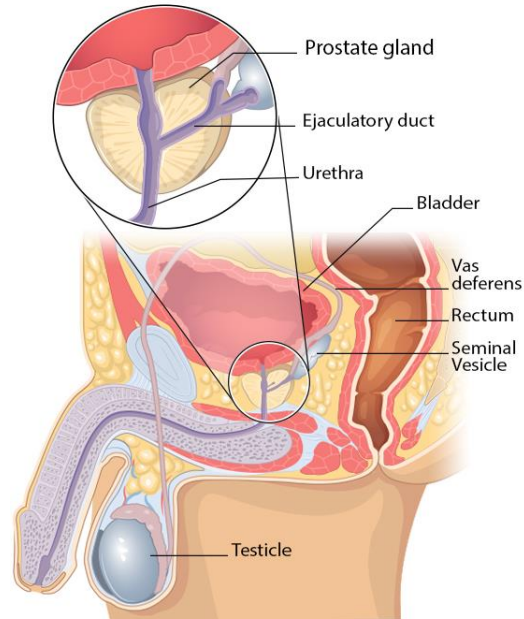
Who votes for screening for prostate cancer in the Netherlands?



PROSTATE

Anatomy & functioning

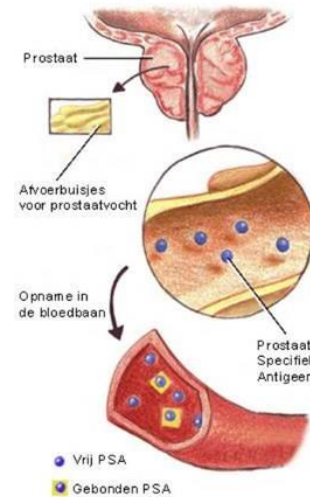
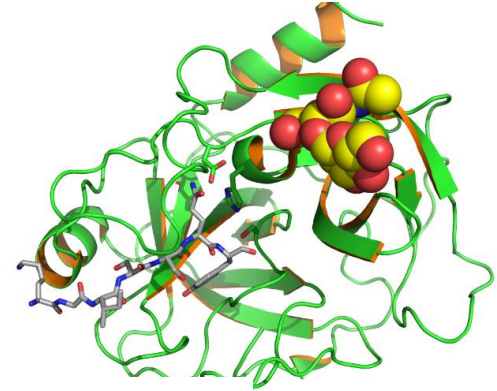
- PRO STATE gland (voorstander klier)
- Reproductive system
- Seminal fluid
- Fully encloses urethra



PSA HISTORY

- Glycoprotein that liquefies seminal fluid
- Discovered by Richard Ablin 1970
- Papsidero 1980 blood test
- Clinically available about 1990

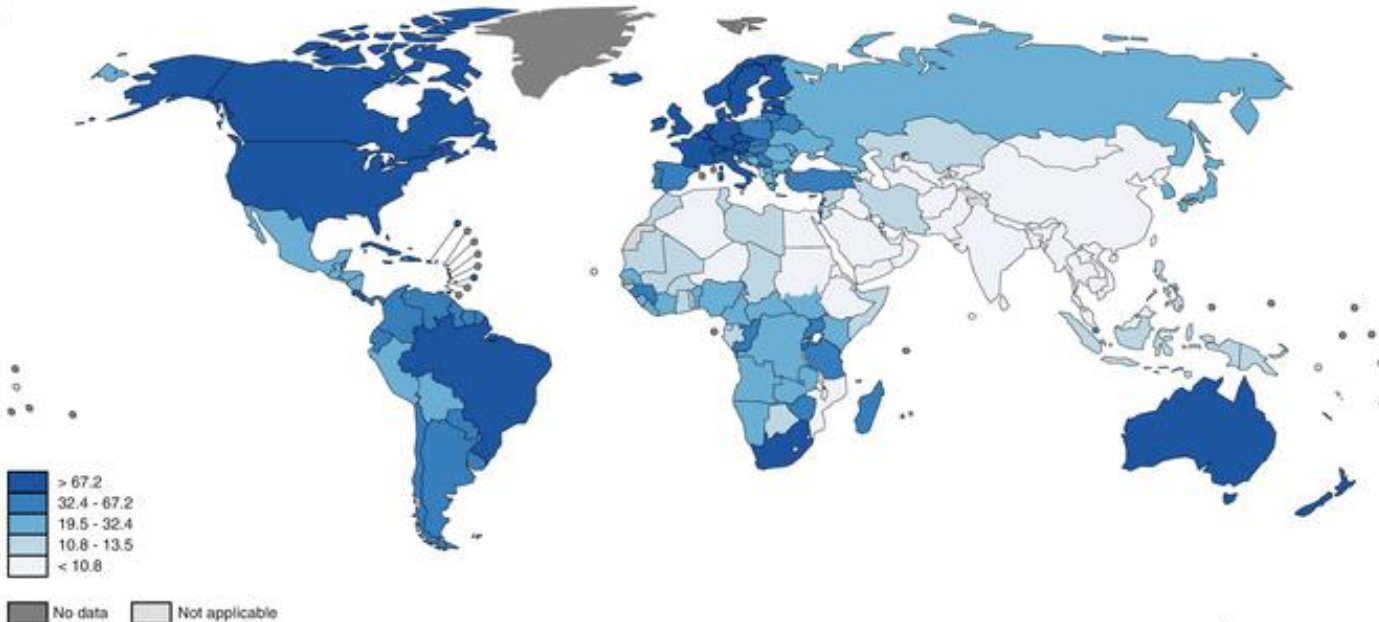
- Specific for prostate, not cancer



PROSTATE CANCER INCIDENCE

World wide

a



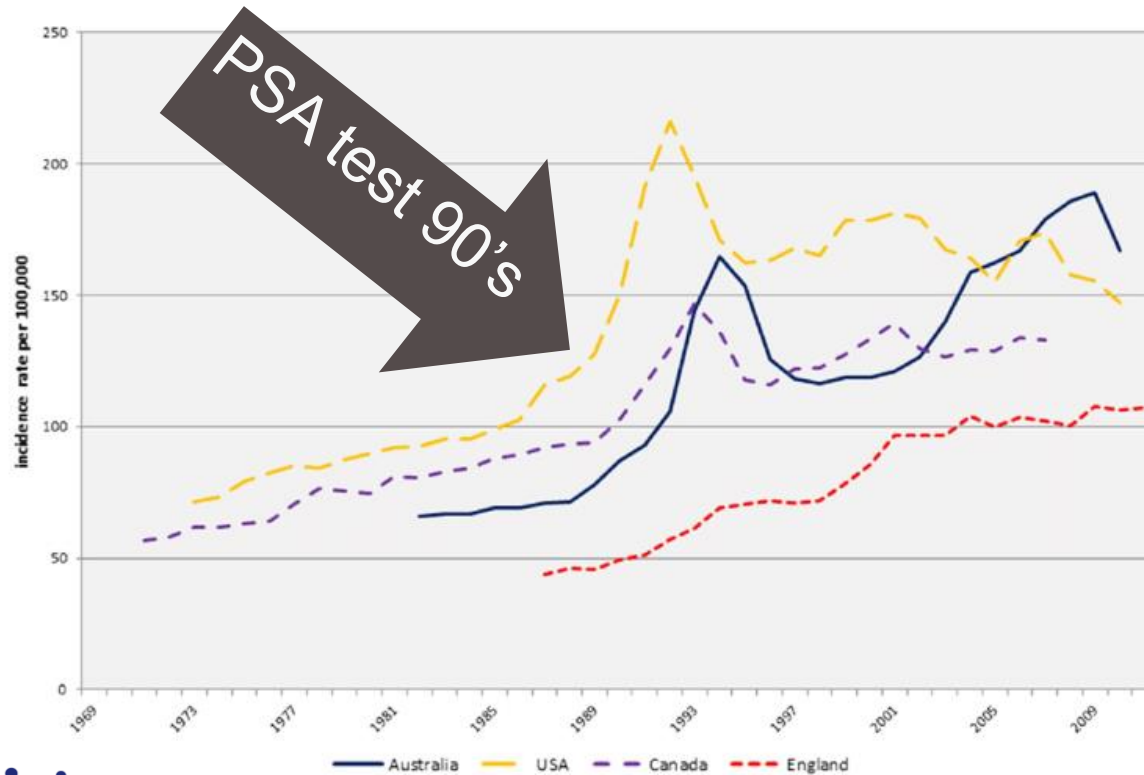
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data source: GLOBOCAN 2012
Map production: IARC
World Health Organization

 **World Health Organization**
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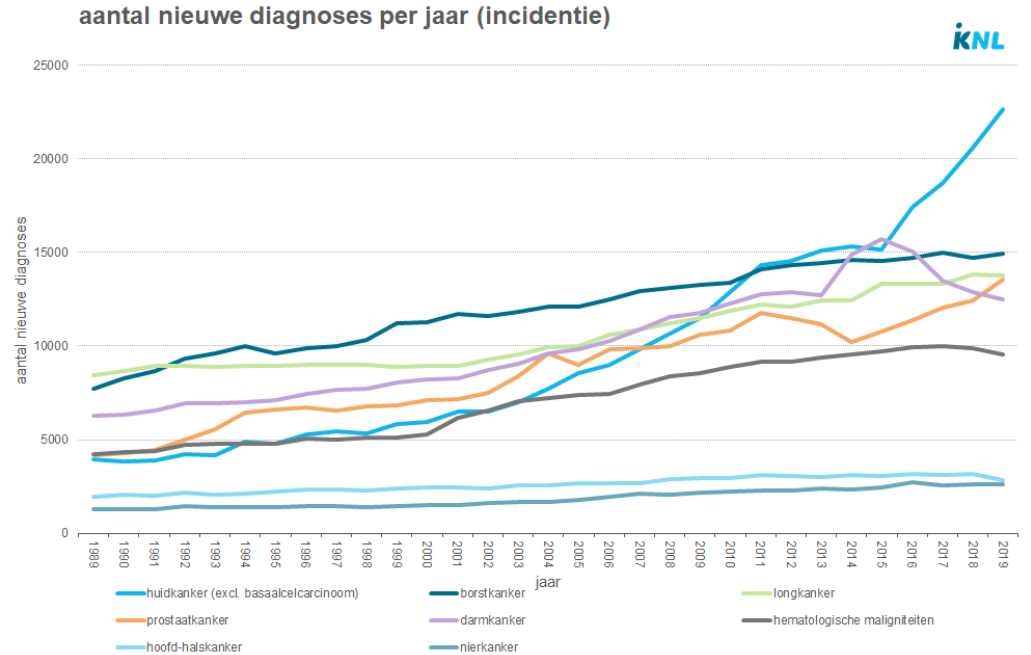
PROSTATE CANCER INCIDENCE

Incidence western world



PROSTATE CANCER INCIDENCE

Netherlands



PROSTATE CANCER INCIDENCE

Netherlands

Nederlandse Kankerregistratie



Aantal nieuwe kankerpatienten* in 2020 t.o.v. 2019

	2020	2019	
plaveiselcelcarcinoom van de huid	14.900	14.700	+
longkanker	13.900	14.200	-
borstkanker	13.200	14.900	---
prostaatkanker	12.800	13.500	--
darmkanker	11.700	12.800	--
hematologische maligniteiten	9.900	10.300	-
melanoom van de huid	6.800	7.000	-
blaaskanker**	3.700	3.600	+
slokdarmkanker (incl. cardia)	3.100	3.100	0
hoofd-halskanker	3.000	3.100	--
alvleesklierkanker	2.700	2.800	-
nierkanker	2.600	2.700	-
baarmoederkanker	2.100	2.100	0
eierstokkanker (incl. eileider)	1.400	1.500	--
hersentumor	1.400	1.400	0
maagkanker	1.000	1.100	--
totaal***	115.000	119.000	-

* invasieve tumoren ** incl. nierbekken/urineleider

*** excl. basaalcarcinoom van de huid

bron IKNL

legenda

- 0 = gelijk
- + = toename <5%
- = afname <5%
- = afname 5-10%
- = afname >10%

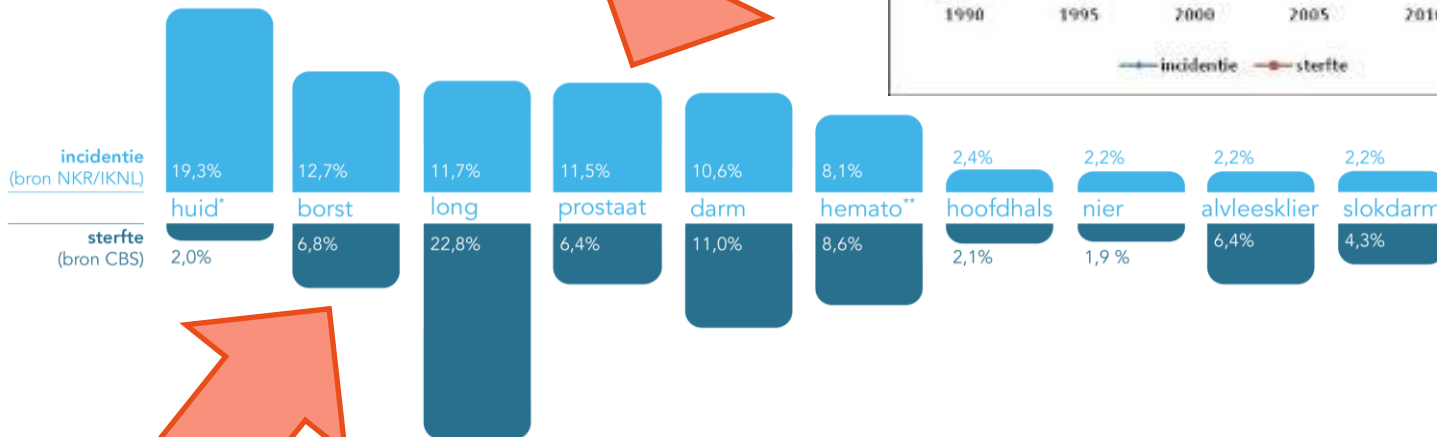
⬇️ = sterke daling t.o.v. 2019 door de tijdelijke onderbreking van de bevolkingsonderzoeken naar borst- en darmkanker

MORTALITY

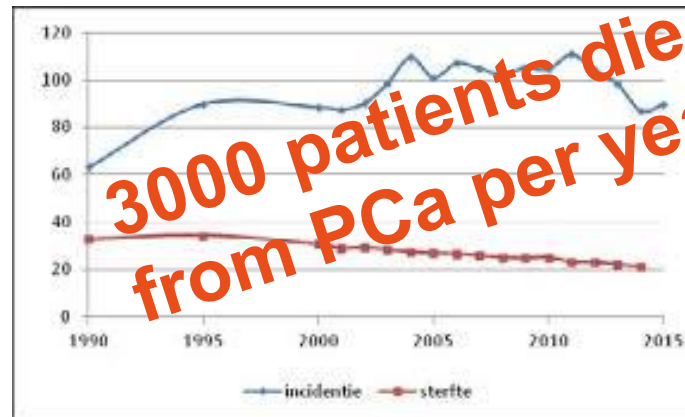
NL

TIEN MEEST VOORKOMENDE KANKERSOORTEN

percentage van alle nieuwe kankerdiagnoses (incidentie) in 2019 en percentage van de kankersterfte in 2018

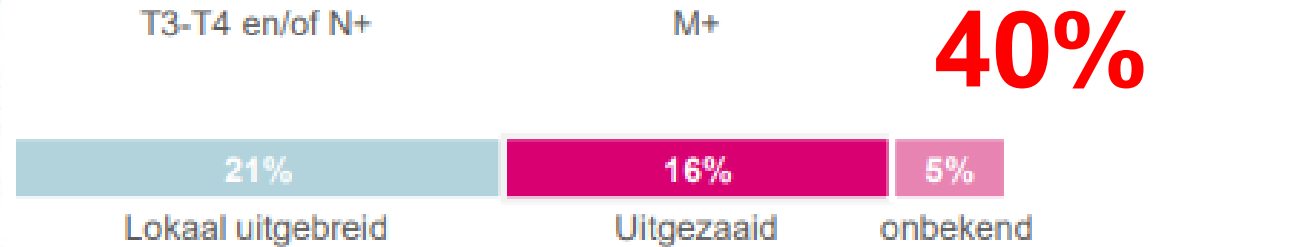
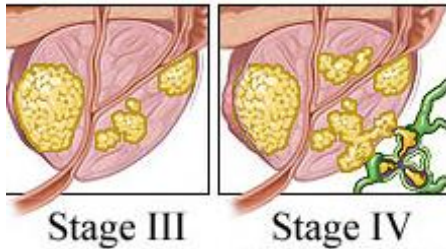
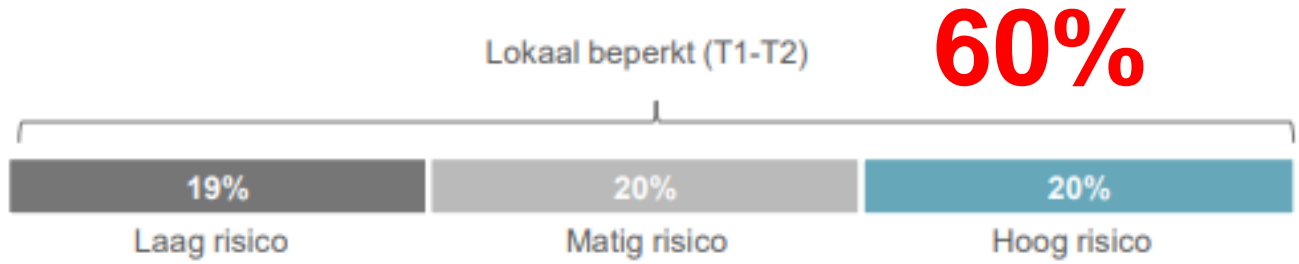
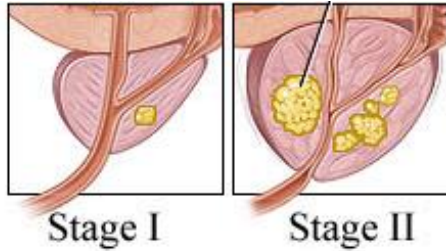


* exclusief basaalcelcarcinoom, ** hematologische maligniteiten



Nederlandse Kankerregistratie (NKR), beheerd door Integraal Kankercentrum Nederland (IKNL)

RISK CLASSIFICATION



CONCLUSIONS STATISTICS

- Nr 1 male cancer (*1 out of 8 men*)
- Incidence increasing; about 13.000/yr NL
- Mortality of 3.000/yr NL (*equal to breast cancer*)
- Large variability in mortality (*stage dependant*)

**Willet Whitmore 80's
quote 'more men die
with prostate cancer
than from prostate
cancer'**

Diagnosis for Prostate Cancer



Digital
rectal
examination



Trans
rectal
ultrasound
(TRUS)



MRI
Fusion
biopsy



PCA3
(Prostate
CANCER
gene 3)



Prostate-specific
antigen
blood test (PSA)

© www.medindia

DIAGNOSTICS

When a man goes to his GP

DON'T FEAR THE FINGER.



- 'I have urinary problems. Do I have prostate cancer?'
- 'My friend told me I should test my PSA'

DIAGNOSTICS

When a man goes to his GP

Ideally GP tells his patient about the pro's and cons of PSA testing; **decision aid** available



Testen op prostaatanker?

Start de keuzehulp

Voorlezen Print E-mail

Keuzehulp

Testen op prostaatanker?

Veel mannen denken: hoe eerder ik weet dat ik prostaatanker heb, hoe beter. Dat hoeft niet altijd zo te zijn. Het heeft voor- en nadelen om te weten of u prostaatanker heeft. Deze keuzehulp helpt u een persoonlijke keuze te maken of u zich wel of niet laat testen.

Deze keuzehulp is bedoeld voor mannen van 50 tot 75 jaar die erover denken om hun PSA te laten controleren. De keuzehulp is niet bedoeld voor mannen met verhoogde kans op prostaatanker. U gaat in 5 stappen door de keuzehulp heen. In de laatste stap zet de keuzehulp u op een rij wat u belangrijk vindt. Dit wordt gebruikt om de keuzehulp uit te printen en meenemen naar het gesprek met uw arts als u dat wilt.

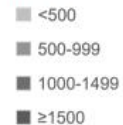


PRACTICE VARIATION

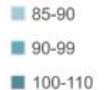
- Patient variation
 - Socio-economic status
 - Educational level
- GP variation ?!



Absoluut aantal mannen



Incidentie per 100.000 inwoners, gestandaardiseerd naar leeftijd (ESR)

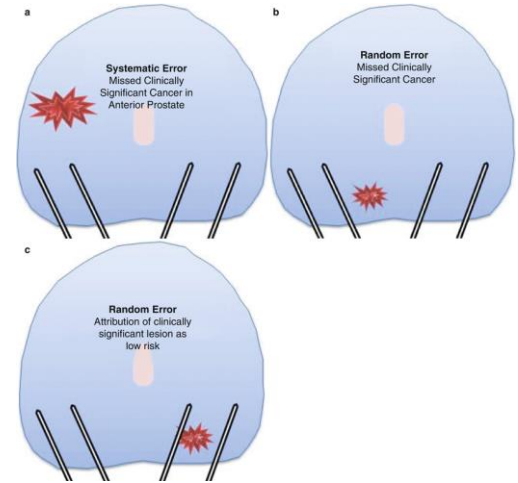
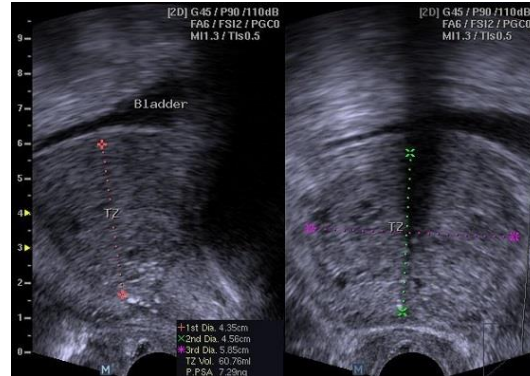
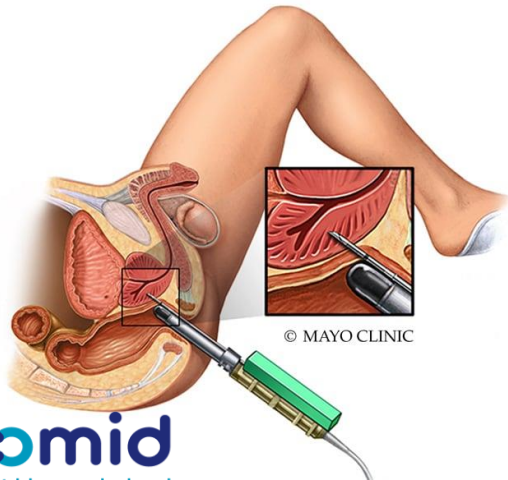


DIAGNOSTICS

urologist

Major changes last 5-10 years

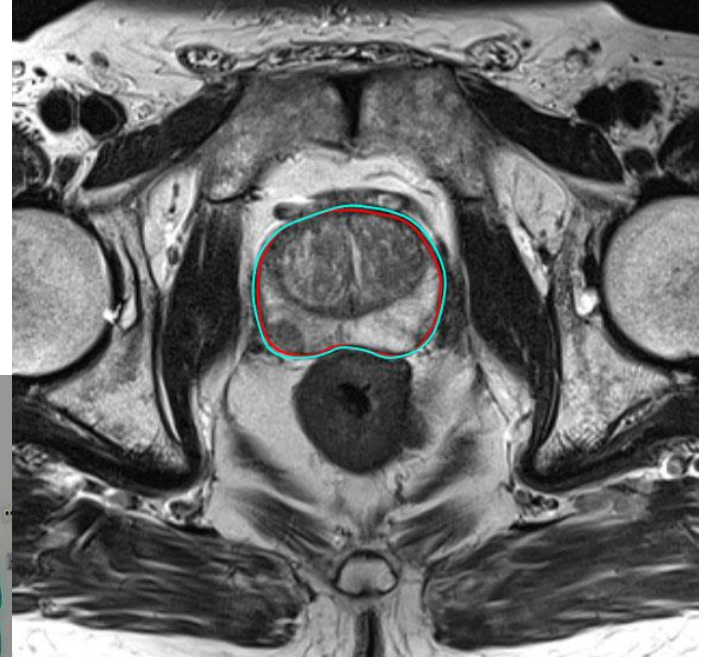
Old school: ultrasound random biopsies



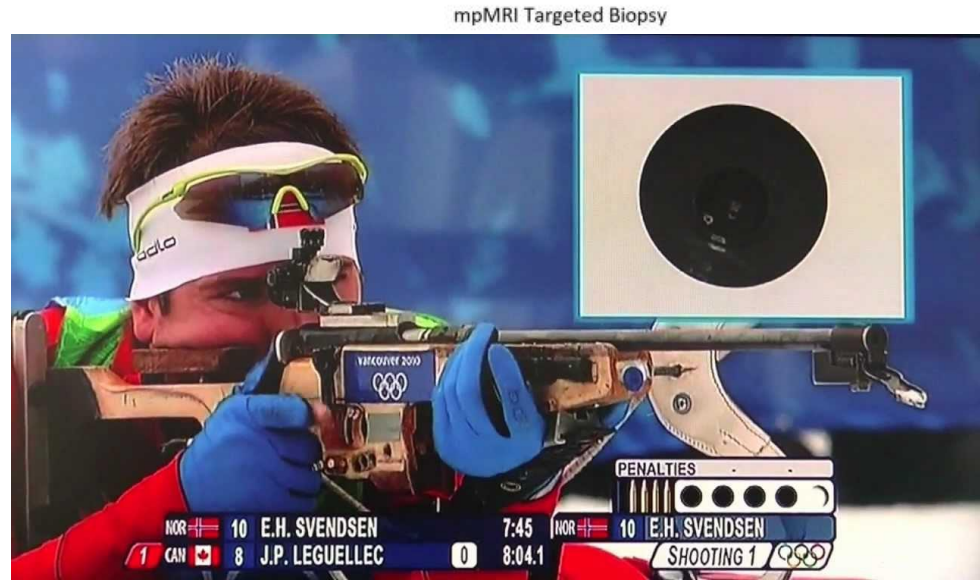
DIAGNOSTICS: REVOLUTION

MRI prostate

Since 2019 in EAU guidelines:
MRI before biopsy

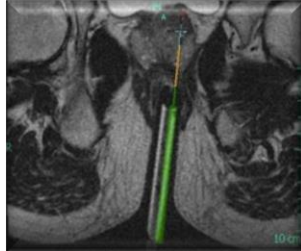


RANDOM VERSUS TARGET BIOPSY



TARGET BIOPSY TECHNIQUES

In-bore MRI



Pro

precision

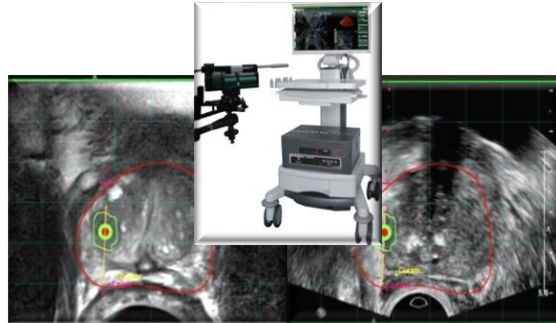
Contra

expensive

availability

time consuming

MRI-US fusion



Pro

office based (possible)

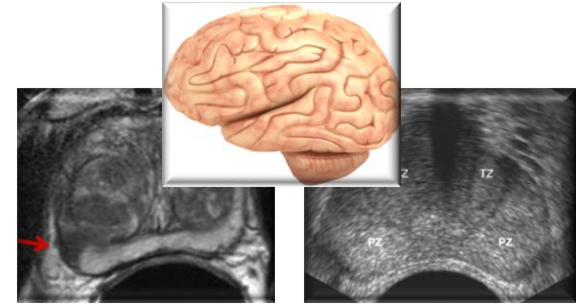
urologist

Contra

learning curve?

expensive

Cognitive fusion



Pro

office based

cheap

urologist

Contra

precise?

DIAGNOSTICS

MRI prostate and target biopsy



MRI-Targeted or Standard Biopsy for Prost

V. Kasivisvanathan, A.S. Rannikko, M. Borghi, V. Panebianco, L.A. Mynderse, G. Hellawell, R.G. Hindley, M.J. Roobol, S. Eggener, M. Ghei, A. Villers, F. Bi G. Robert, P.B. Singh, W. Venderink, B.A. Hadaschik, A. Ruffion, J.C. Hu, S.S. Taneja, P. Pinto, I. Gill, C. Allen, F. Giganti, A. Freeman, S. Morris, S. Pur J. Deeks, Y. Takwoingi, M. Emberton, and C.M. Moore, for the PRECISION

Platinum Priority – Prostate Cancer – Editor's Choice
Editorial by Derek J. Rosario, Thomas J. Walton and Steven J. Kennish on pp. 579–581 of this issue

Head-to-head Comparison of Transrectal Ultrasound-guided Prostate Biopsy Versus Multiparametric Prostate Resonance Imaging with Subsequent Magnetic Resonance-guided Biopsy in Biopsy-naïve Men with Elevated Prostate-specific Antigen: A Large Prospective Multicenter Clinical Study

Marloes van der Leest^a, Erik Cornel^b, Bas Israël^a, Rianne Hendriks^c, Anwar R. Padhani^d, Martijn Hoogenboom^e, Patrik Zamecnik^f, Dirk Bakker^g, Anglita Yanti Setiasti^h, Jeroen Veltmanⁱ, Huib van den Hout^j, Hans van der Lelij^k, Inge van Oort^l, Sjoerd Klaver^m, Frans Debruyneⁿ, Michiel Sedelaar^o, Gerjon Hanink^p, Maroeska Rovers^q, Christina Hulsbergen-van de Kaa^r, Jelle O. Barentsz^{s,t,u}

Advantages MR guided target biopsy

	MR TBx	Standard	
No biopsies performed	31%	6%	Less biopsies needed
Significant PCa	38%	26%	More significant cancers
Gleason 6 PCa	9%	22%	Less overdiagnosis
Overall PCa	47%	48%	

BIOPSY ROUTE

Transrectal versus transperineal

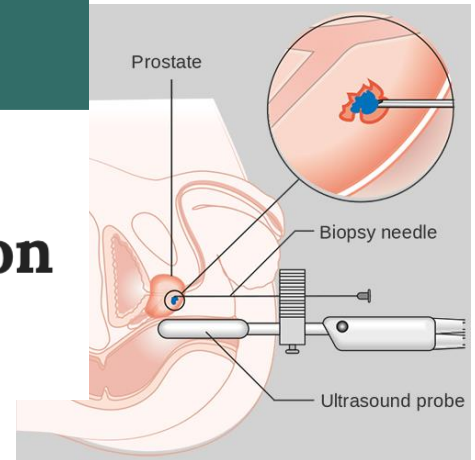


MENU ▾

Prostate Cancer and Prostatic Diseases

Perspective | [Open Access](#) | Published: 13 January 2020

“TREXIT 2020”: why the time to abandon transrectal prostate biopsy starts now



CONCLUSIONS DIAGNOSIS

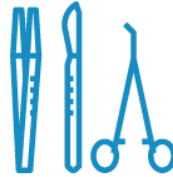
- Major improvement due to MRI (image) guided biopsy
- Less men need biopsies
- More accurate
- Less low-risk cancers (less overdiagnosis)
- More finding of the cancers that are relevant
- Change to perineal biopsy route

PROSTATE CANCER POSSIBLE TREATMENT OPTIONS*

*Some of the most chosen options for treating prostate cancer depending on its stage



**Active
surveillance**



**Surgery of the
prostate**



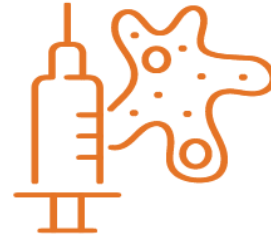
**Hormonal
treatments**



Radiotherapy



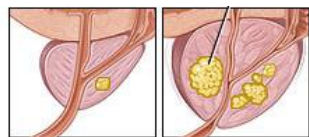
Chemotherapy



Immunotherapy

TREATMENTS

Many options, many choices

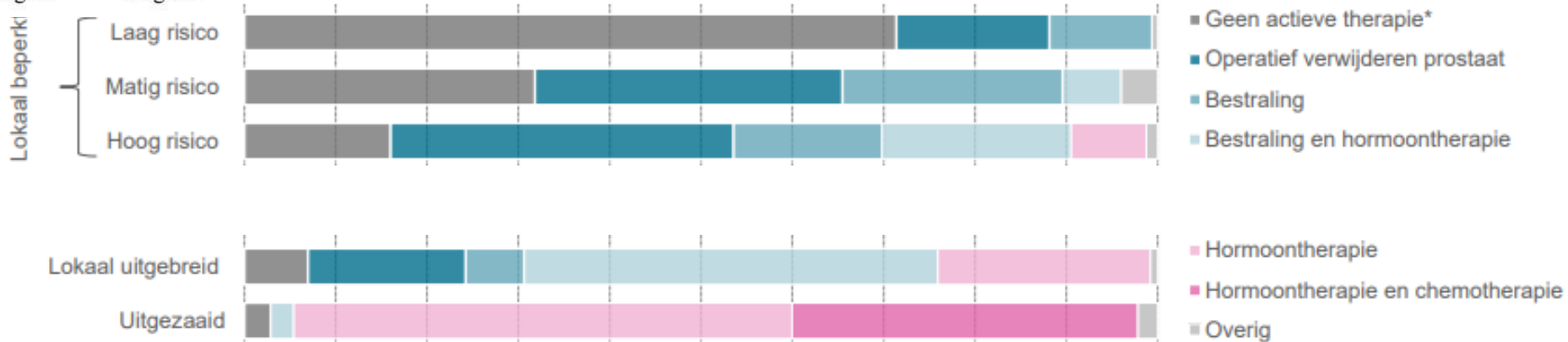


Stage I

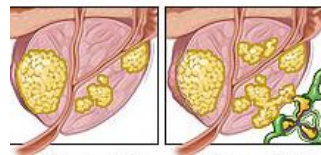
Stage II

Behandeling van patiënten met prostaatkanker (%) per stadium en risicoprofiel

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%



*Geen actieve therapie omvat zowel actief volgen als een afwachtend beleid



Stage III

Stage IV

© Healthwise, Incorporated

TREATMENTS

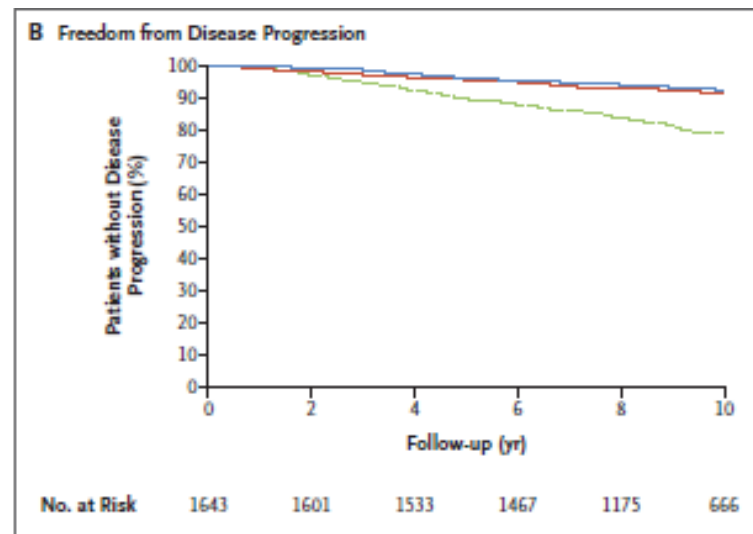
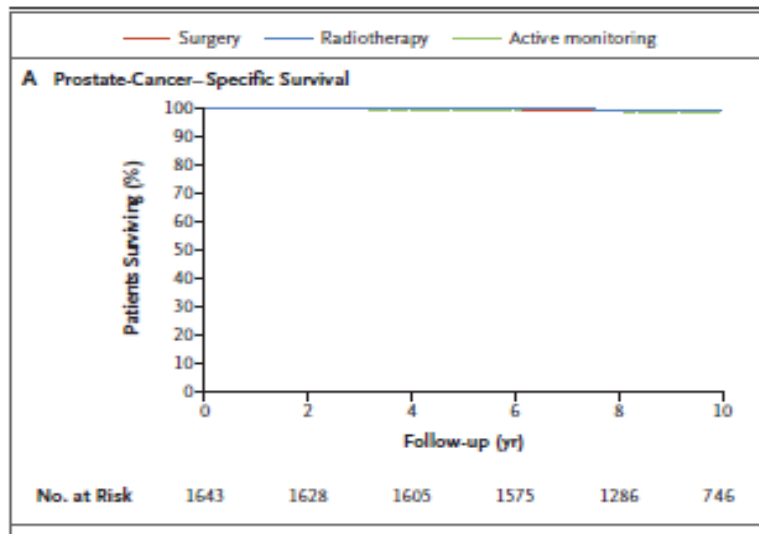
low risk disease: do we treat?



10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer

F.C. Hamdy, J.L. Donovan, J.A. Lane, M. Mason, C. Metcalfe, P. Holding, M. Davis, T.J. Peters, E.L. Turner, R.M. Martin, J. Oxley, M. Robinson, J. Staffurth, E. Walsh, P. Bollina, J. Catto, A. Doble, A. Doherty, D. Gillatt, R. Kockelbergh, H. Kynaston, A. Paul, P. Powell, S. Prescott, D.J. Rosario, E. Rowe, and D.E. Neal, for the ProtecT Study Group*

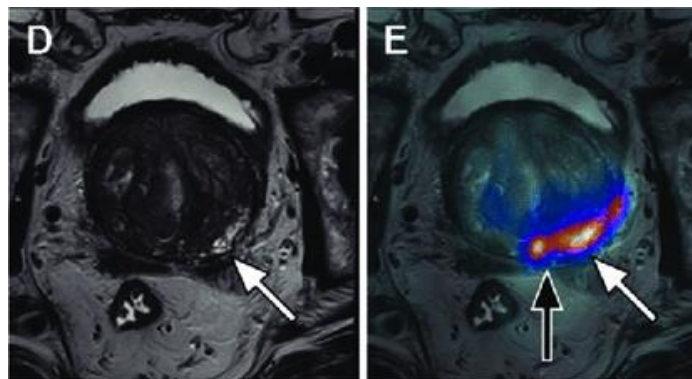
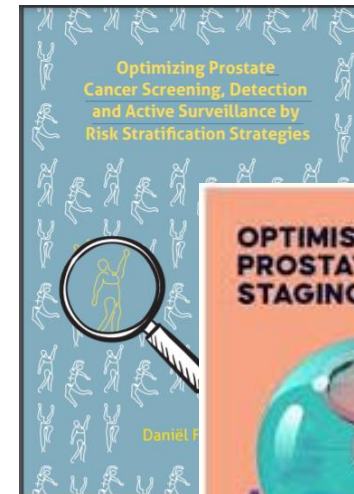
Majority low-risk



TREATMENTS

Active surveillance

- First choice for low-risk disease
- Important: Good Selection & Good Follow-up
- 2 PhD's last week
- Innovative studies: PASPORT trial 1/2



TREATMENTS

Intermediate and high risk prostate cancer



TREATMENTS

Surgery and radiotherapy outcomes



JAMA Oncology

[View Article](#)

JAMA Oncol. 2019 Feb; 5(2): 213–220.

Published online 2018 Nov 15. doi: [10.1001/jamaoncol.2018.4836](https://doi.org/10.1001/jamaoncol.2018.4836)

PMCID: PMC6439553

PMID: [30452521](https://pubmed.ncbi.nlm.nih.gov/30452521/)

Oncological outcomes

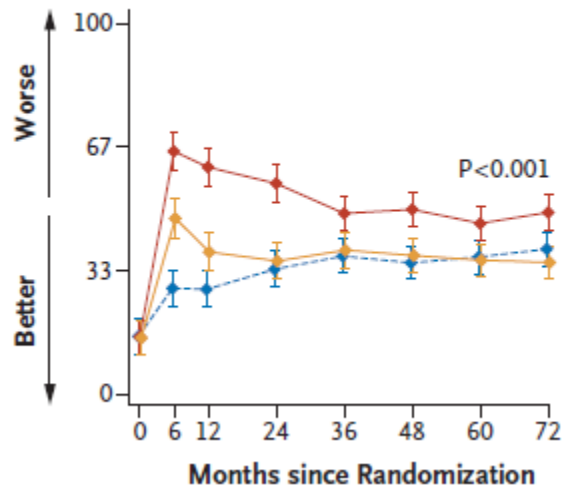
Functional outcomes

- Urinary problems
- Bowel problems
- Incontinence
- Erectile dysfunction

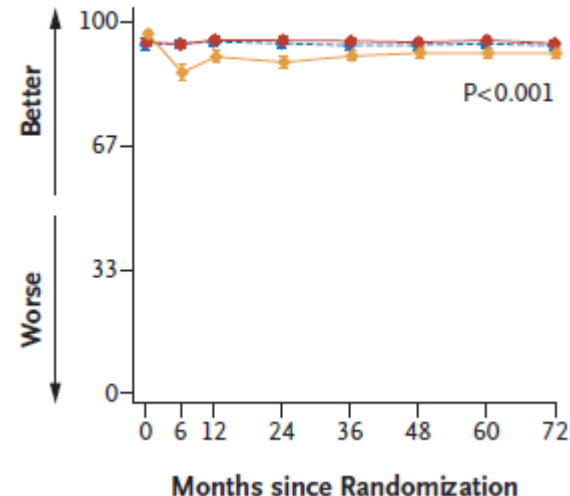
Surgery vs Radiotherapy in the Management of Biopsy Gleason

Score 8-10 Prostate Cancer and the Risk of Mortality

Problem with Erectile Dysfunction

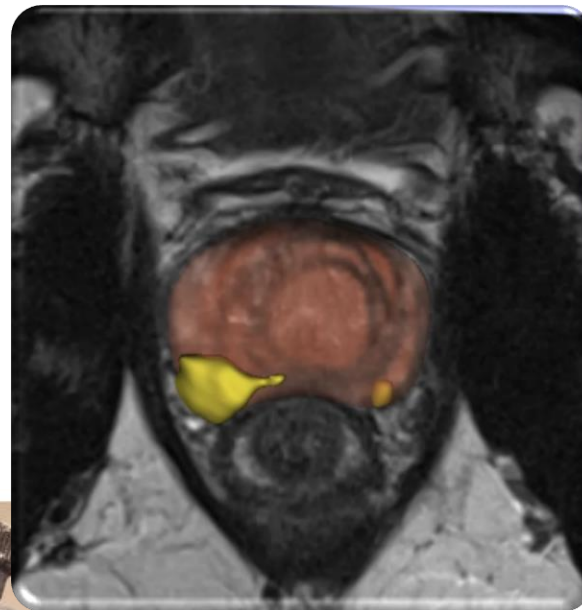
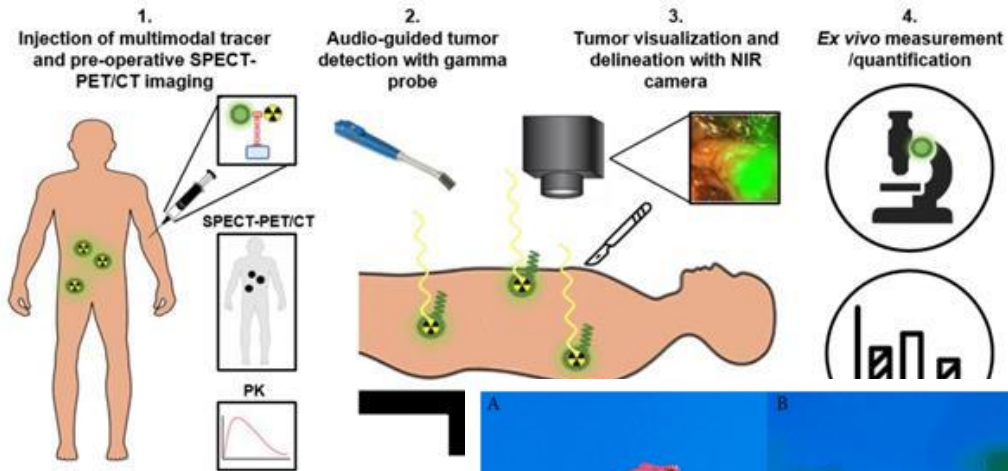


Bowel Bother Score



TREATMENTS

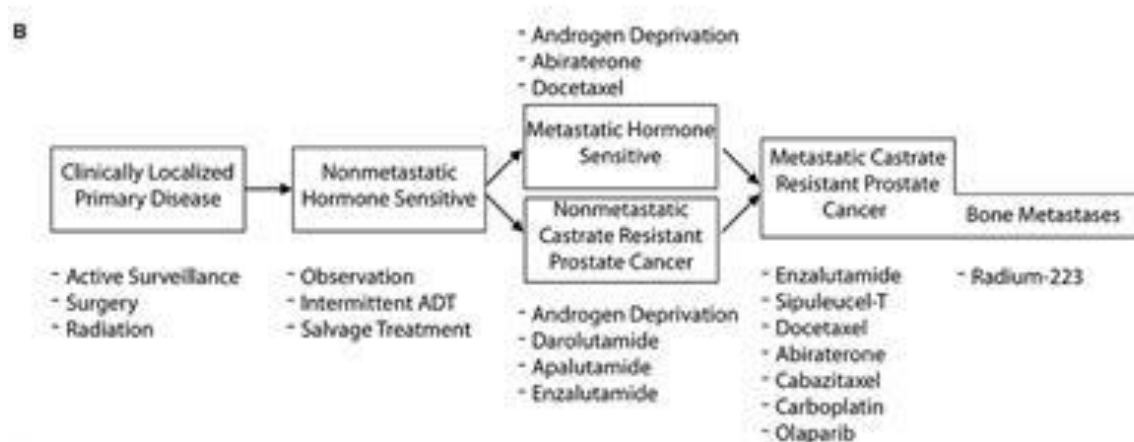
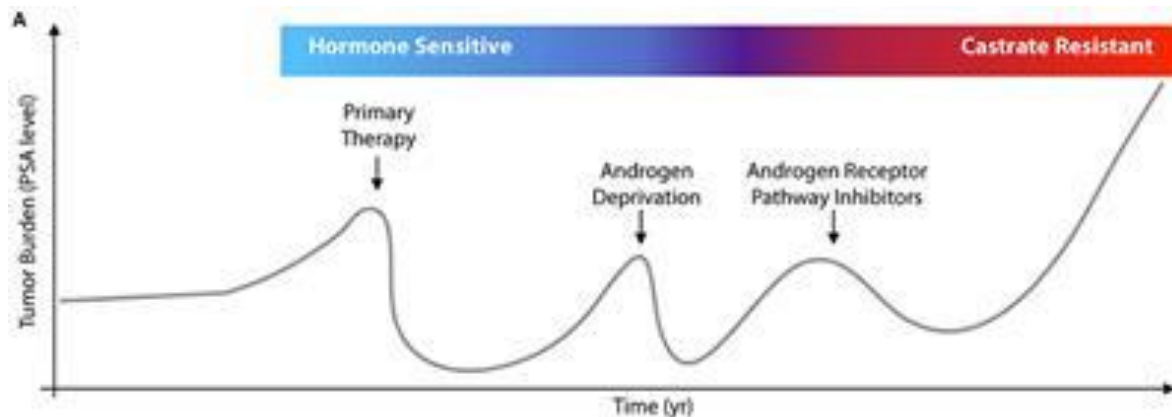
Developments surgery



TREATMENTS

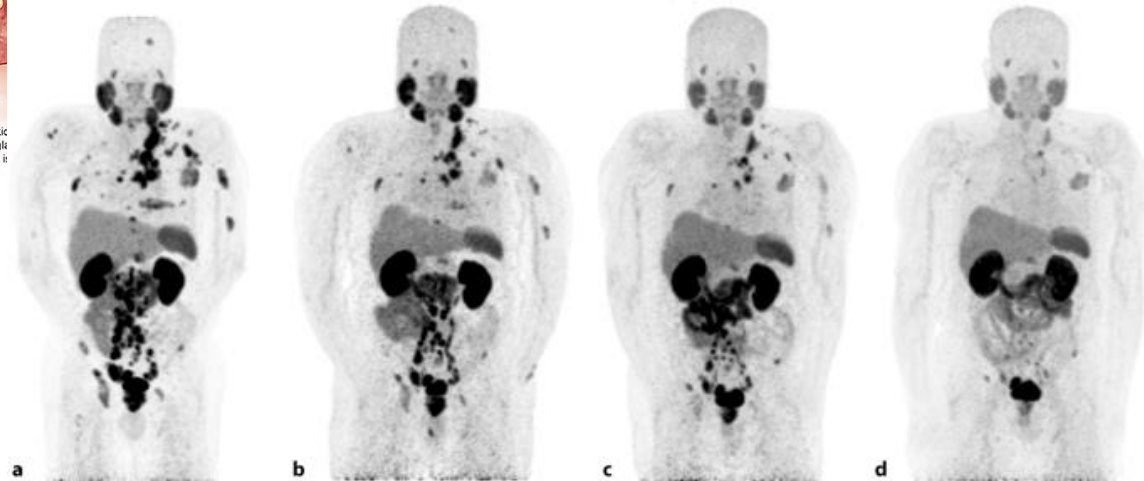
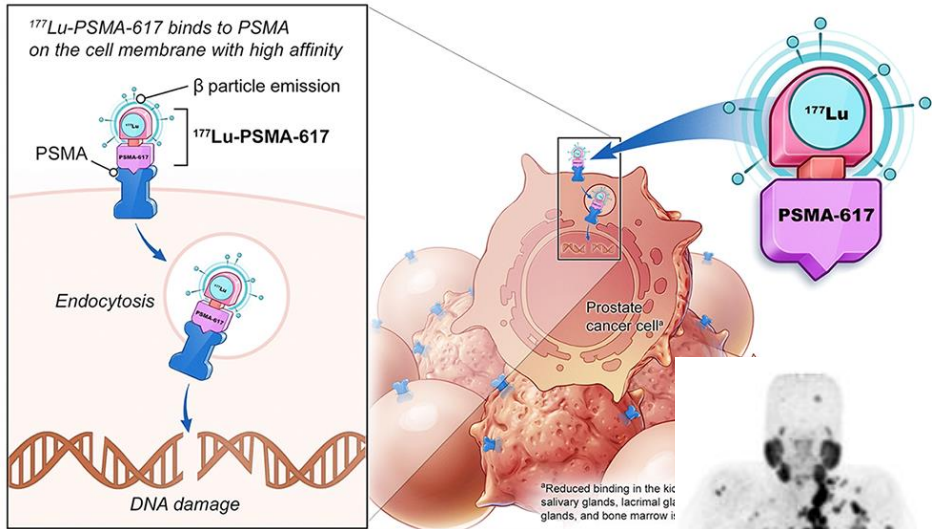
Metastatic disease

- 16% M1 at diagnosis
- Progression to M1 disease



INNOVATIVE THERAPY

PSMA-Lutetium



TREATMENTS

Evaluating new modalities



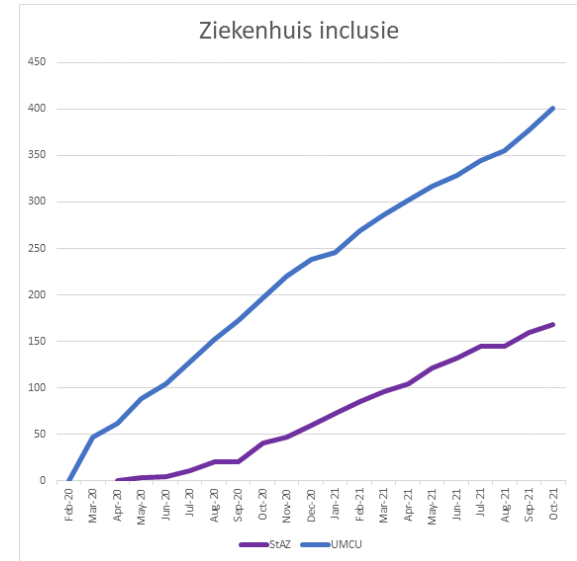
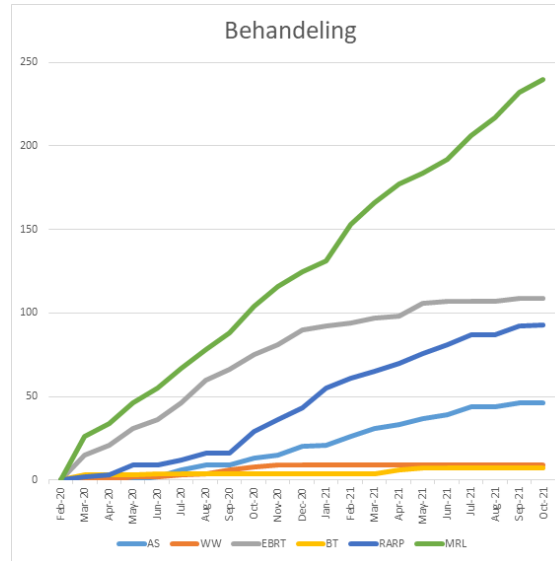
UTRECHT
PROSTAAT
COHORT

- Start 2020 UMCU and St. Antonius
- All patients with local Pca included
- All data in prospective database including imaging and PROMS (!)
- All treatments identical data collection to make meaningful comparison possible

UPC

Inclusion

- 600+ patients included



CONCLUSION TREATMENTS

- Good staging very important
- NOT treating in low-risk disease: active surveillance
- Different options in intermediate-high risk disease
 - RT innovation: MR-Linac
 - Surgical innovation: image guided surgery
- Combination (systemic) treatments in metastatic disease
 - Innovative: Lu-PSMA

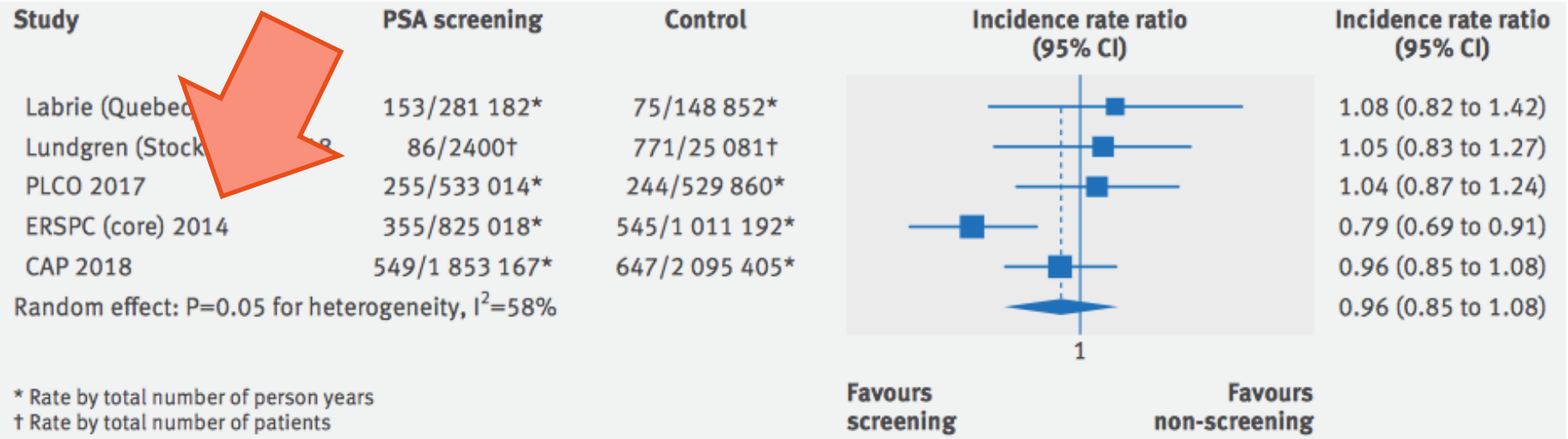
SCREENING



SCREENING

- Males complain: females have nation wide screening for breast cancer en cervical cancer
- In 2019 died 2954 men from prostate cancer and 3050 women from breast cancer
- So why is there no screening program for men?

RESULTS SCREENING STUDIES



ERSPC

Lancet 2014

n >270.000

8 countries

Median FU 13 yrs

Reduction risk death = 21%

NNI = 781

NND = 27

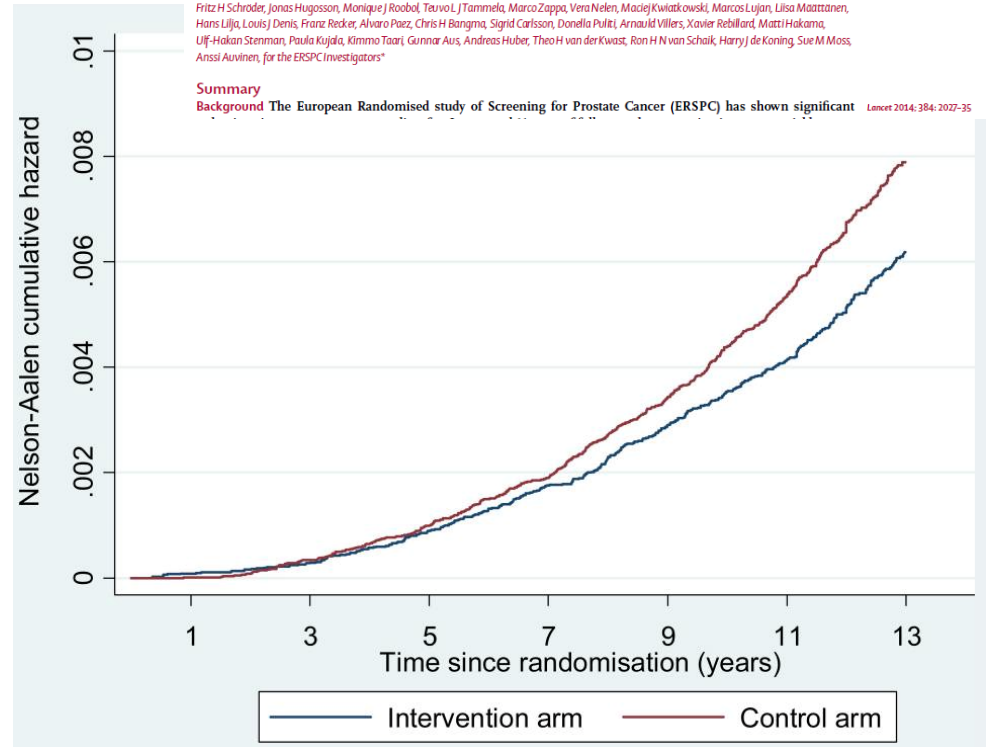
Screening and prostate cancer mortality: results of the European Randomised Study of Screening for Prostate Cancer (ERSPC) at 13 years of follow-up



Fritz H Schröder, Jonas Hugosson, Monique J Roobol, Teuvo L J Tammela, Marco Zappa, Vera Nelen, Maciej Kwiatkowski, Marcos Lujan, Liisa Maattänen, Hans Lilja, Louis J Denis, Franz Redeker, Alvaro Paez, Chris H Bangma, Sigrid Carlsson, Donella Puliti, Arnould Villers, Xavier Rebillard, Matti Hakama, Ulf-Hakan Stenman, Paula Kujala, Kimmo Taari, Gunnar Aus, Andreas Huber, Theo H van der Kwast, Ron H N van Schaik, Harry J de Koning, Sue M Moss, Anssi Auvinen, for the ERSPC Investigators*

Summary

Background The European Randomised study of Screening for Prostate Cancer (ERSPC) has shown significant [Lancet 2014; 384: 2027-35](#)



2018 REQUEST PILOT STUDY NETHERLANDS

- Health council (Gezondheidsraad) refused license for pilot screening study
- Reasons, advantages do not counterbalance disadvantages:
 - High number of **overdiagnosis**
 - High percentage of **overtreatment** (of low risk disease)
 - **Psychological burden** and **stress** for patients

FINETUNING ERSPC

1. Screening the right way
2. Correction population data
3. Secondary endpoints
4. Improvements since ERSPC

FINETUNING ERSPC

1. Screening the right way

Gothenburg

- N = 20.000
- Reduction risk death = 35% (vs 21%)
- NNI = 231 (vs 781)
- NND = 10 (vs 27)

Differences from ERSPC:

- Age: 50–64
- Screening every 2 years
- Long follow-up
- (High participation)
- (Low contamination)

FINETUNING ERSPC

Comparing to other types of screening

				Prostate	
	Breast	Cervix	Colorectal	ERSPC	Gothenburg
Reduction risk death	15-20%	20-60%	15%	27%	35%
NNI	100-2000	1140 (10 yrs)	600-1200 (17 yrs)	781	231
NND	10	?	?	27	10

FINETUNING ERSPC

Correction of population data

ERSPC overall:

- Non-participation: Mortality reduced 21% > 27%

Simulation:

- Non-participation: 20% > 27%
- Additional contamination: 27% > 29-31%

FINETUNING ERSPC

Secondary endpoint

Metastases

- 30% risk reduction
- Less hormones / palliative treatment

Quality of life

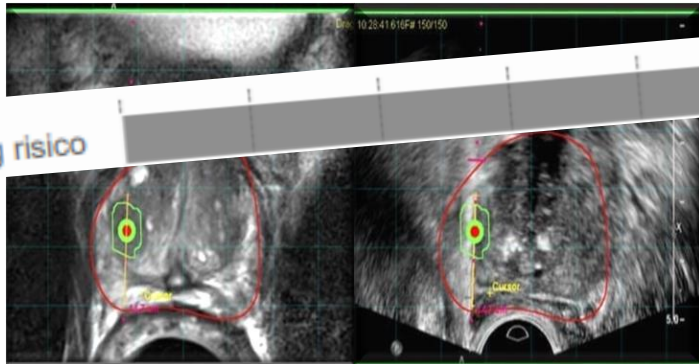
- Quality adjusted life years (QALYs) gained per 1000 men being screened (every year screening): 56

FINETUNING ERSPC

Improvements since ERSPC

ERSPC started in the 90s; it's history!

ERSPC = no MRI, no target biopsies, fe



Post-ERSPC era

Less biopsies needed

More significant cancers

Less overdiagnosis

More Active Surveillance

SCREENING IN MODERN TIMES

Awareness

DISCLAIMER

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Onafhankelijke informatie is niet gratis. Het NTVG investeert veel geld om het hoge niveau van haar artikelen te waarborgen, door een proces van peer-review en redactievoering. Het NTVG kan alleen bestaan als er voldoende betaalde abonnementen zijn. Het is niet de bedoeling dat onze artikelen worden verspreid zonder betaling. Wij rekenen op uw medewerking.



'Intelligente opsporing' van prostaatkanker

Een alternatief voor bevolkingsonderzoek

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EAU
European Association of Urology

Platinum Opinion

Early Detection of Prostate Cancer in 2020 and Beyond: Facts and Recommendations for the European Union and Commission

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Prostaatkankerstichting

EUROPA UOMO
The Voice of Men with Prostate Cancer in Europe

EUPROMS 2.0

How's your quality of life cancer?

In coalition for prostate cancer we are asking men who have prostate cancer to complete our online survey.

by: <https://euproms.ydeal.dev>

www.europa-uomo.org

The advertisement features a man in a blue shirt and shorts hiking on a path through a green field. A purple banner at the top right says 'EUPROMS 2.0'. A yellow banner in the center asks 'How's your quality of life cancer?'. Below it, text encourages men with prostate cancer to complete an online survey. A purple banner at the bottom provides the survey link, and a small purple banner at the bottom right shows the website.

ST ANTONIUS
een santeon ziekenhuis

CONCLUSIONS

State of the art in screening, diagnostics and treatments

- Rising incidence and mortality; variations in NL
- Diagnostic revolution: MRI selection and MRI target biopsy
- Innovative therapy
 - Image guided radiotherapy
 - Image guided surgery
 - New (combinations) systemic therapy
- Screening discussion completely different from 1990 ERSPC

VOTE FOR SCREENING

End of presentation

Who votes for screening for prostate cancer in the Netherlands?

