

Screening prostate cancer in 2025 What is the most optimal approach?

16th May 2025

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Conflicts of interest

I have the following potential conflict(s) of interest to report

Type of affiliation / financial interest	Name of commercial company
Receipt of grants/research supports:	Astellas, Janssen
Receipt of honoraria or consultation fees:	Astellas, Bayer, Janssen



Main disclosure – Case 1

- Man, 62 years old, LUTS, abnormal DRE, PSA 32, PSMA M1a disease
- Has until now never heard of the word 'PSA'...



(this does not mean I advocate for screening in everyone)



Main disclosure – Case 2

- Man, 83 years old, friends recommended PSA, PSA 4.7, gets MRI
- 1 biopsy 2 mm ISUP GG 2, radiation, soiling, impacts his hobbies



UNACCEPTABLE

(this does not mean individual early detection is always useless)



Screening: Pandora's box?



Screening: Double-edged sword?



Screening: Karma

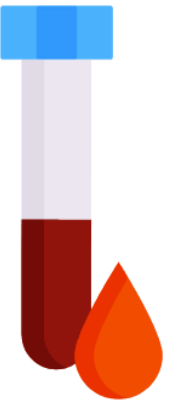


Screening: Taming the beast



Main messages

- PSA is an easily accessible and extremely powerful tool to reduce the burden of prostate cancer in an individual!
- Are we able to actively apply PSA in such a way that the benefits outweigh the harms on a population level?



Changing ways of entering the pathway

LUTS -> PSA

Ask for PSA

Lesion FDG

PSA via
internal medicine

Screening



LUTS -> PSA

Ask for PSA

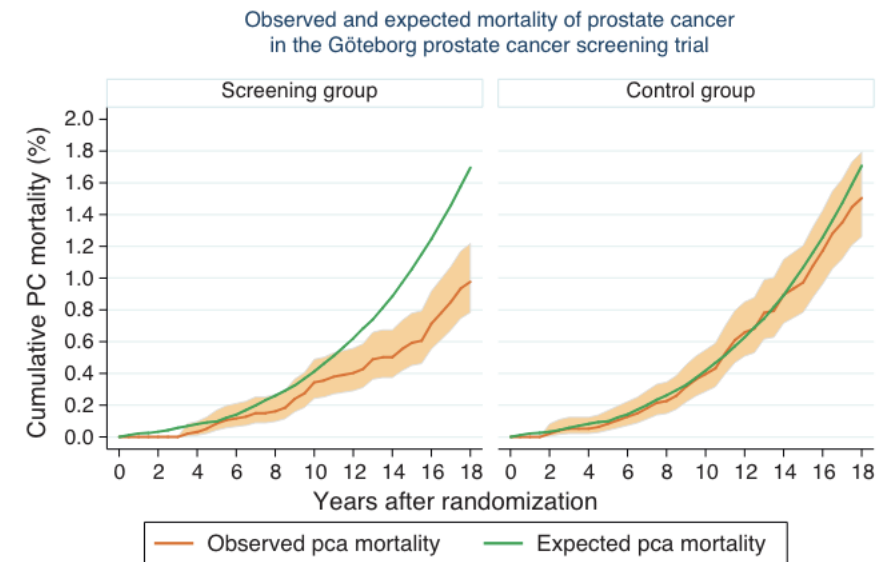
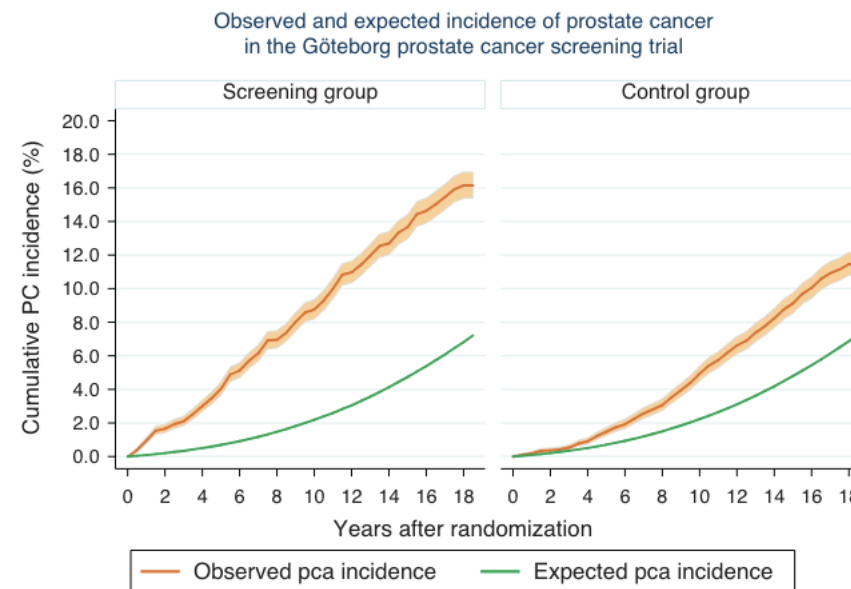
Lesion FDG

PSA via
internal medicine

Screening

Opportunistic (PSA-) screening

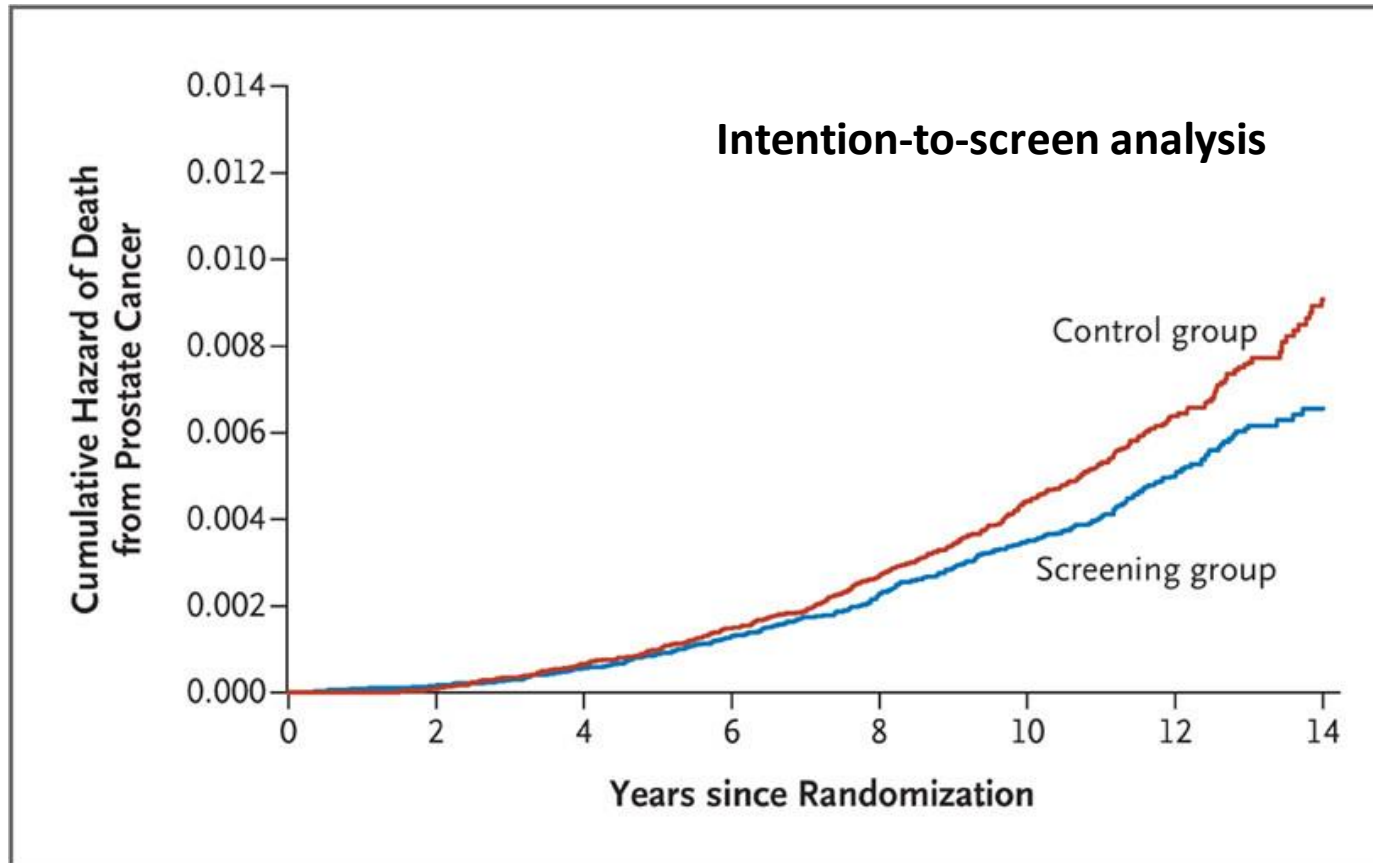
- Little impact PCa mortality
- High overdiagnosis rates



ERSPC started in 1991



PCa mortality reduction 20%



1 - Men not participating

2 - Invited men who had PSA before

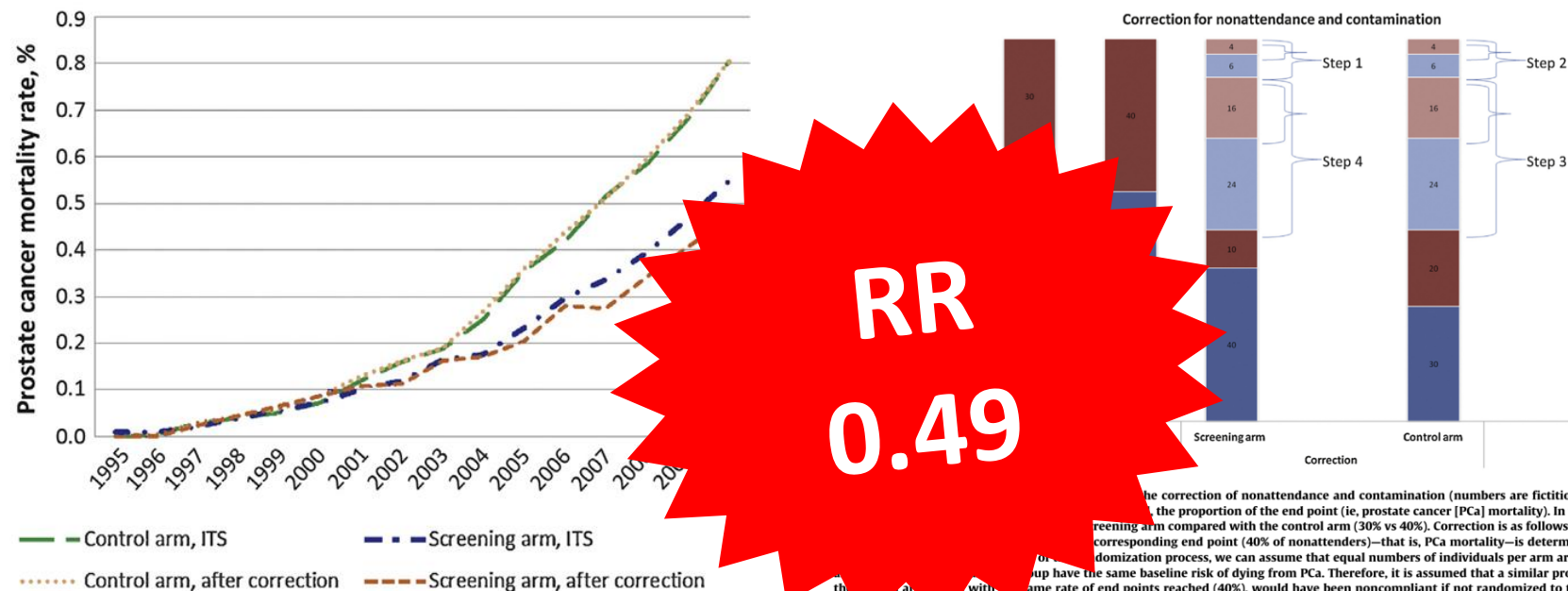


Intention-to-screen → individual

- Correct for

1 - Men not participating

2 - Invited men who had PSA before

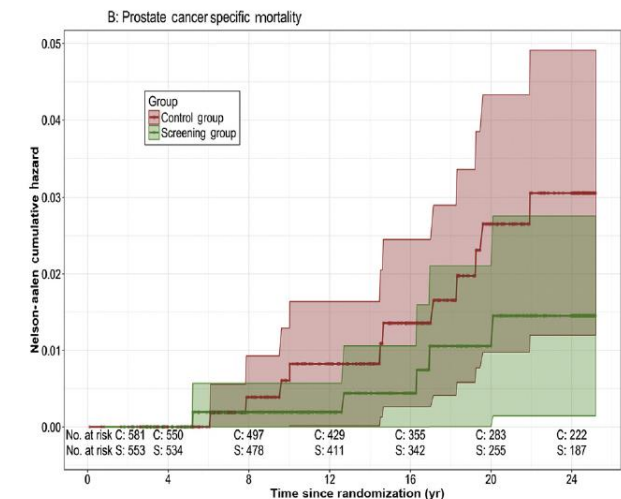
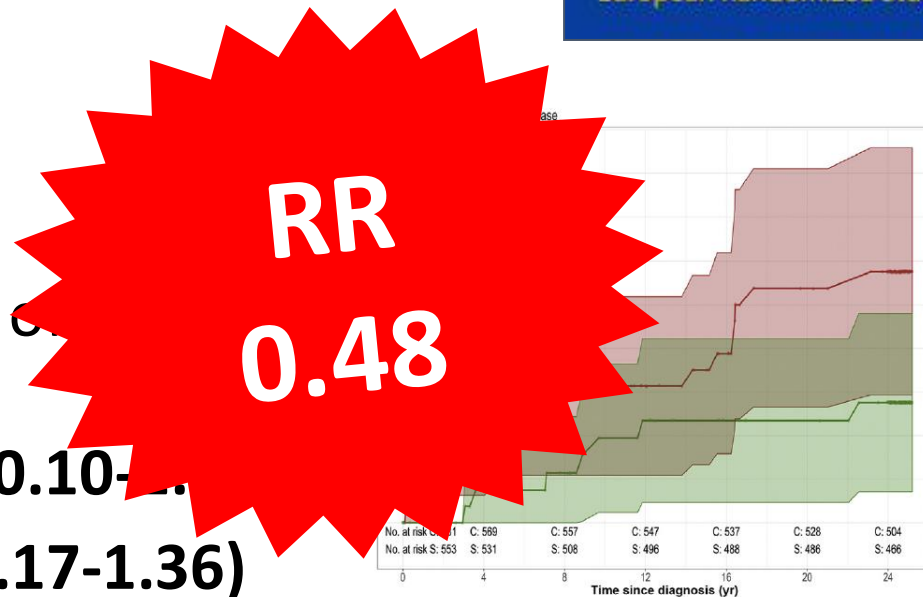


RR
0.49

Fig. 3 – Absolute risk of dying from prostate cancer per arm for the intention to screen (ITS) analysis and after correction for nonattendance and prostate-specific antigen contamination. Results are given for different years of ending follow-up.

ERSPC 1st cohort

- 1991-1992, no contamination
- N=1134, RCT screening vs SOC
- PSA >10 excluded
- 55-74 yr
- PSA >3, biopsy
- At time of analysis, 63% of control group had died.
- **RR M+ disease 0.46 (CI 0.10-1.96)**
- **RR PCa death 0.48 (CI 0.17-1.36)**



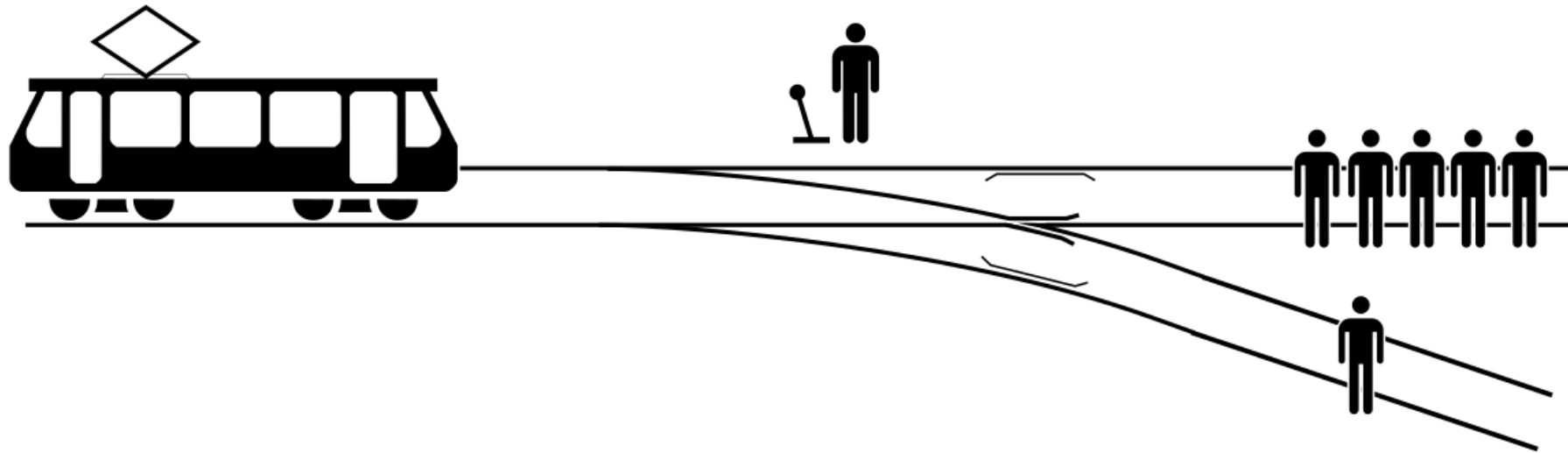
PSA is very powerful!



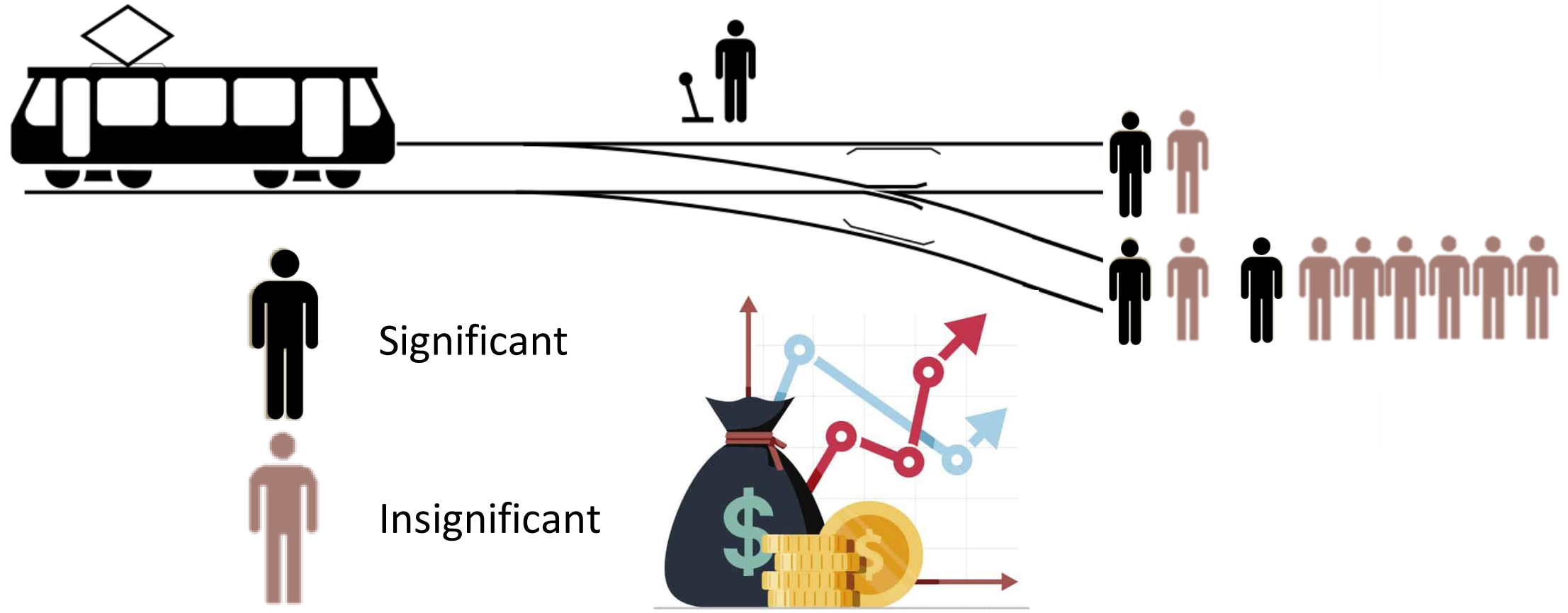
Catch significant disease, leave rest undetected



The trolley dilemma



What do we accept?



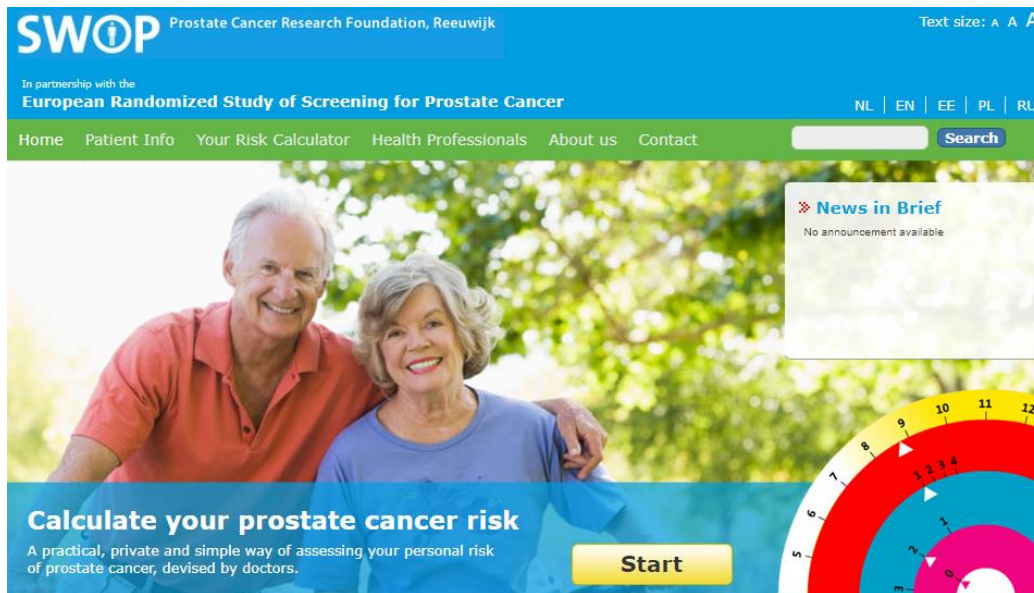
Risk stratification tools

CLASSIC	Pros	Cons
PSA	High sensitivity, cheap	Low specificity
DRE	High specificity, cheap	Low sensitivity, physical exam
PSA-density	Cheap, easy	Physical exam

NOVEL	Pros	Cons
MRI	Increases specificity	Availability, quality, costs, stage shift
Micro ultrasound	Increases specificity	Availability, quality, costs, stage shift
Biomarkers (STHLM3, kallikrein panel)	Increases specificity	Availability, costs



Risk calculators ↓ unnecessary testing



SWOP Prostate Cancer Research Foundation, Reeuwijk

In partnership with the
European Randomized Study of Screening for Prostate Cancer

NL | EN | EE | PL | RU

Home Patient Info Your Risk Calculator Health Professionals About us Contact

News in Brief
No announcement available

Calculate your prostate cancer risk
A practical, private and simple way of assessing your personal risk of prostate cancer, devised by doctors.

Start

PCPT Risk Calculator Home Map Add to phone ▾

Characteristics

Race
▾

Age
▾

PSA [ng/ml]
▾

Family History of Prostate Cancer
▾

Digital rectal examination
▾

Prior biopsy
▾

☐ Percent free PSA available?

☐ PCA3 available?

☐ T2:ERG available?

Calculate Risk

MRI



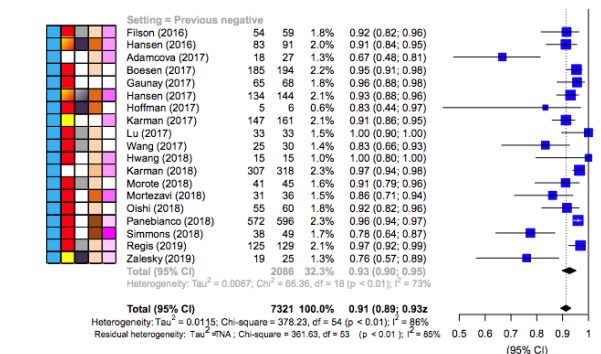
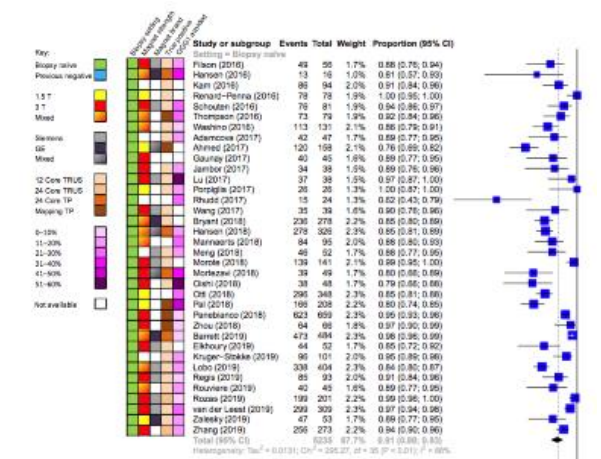
Review: NPV mpMRI 91%, but variability

Biopsy naïve:
NPV 91% (95% CI 88%-93%)

- ✗ Miss rate =
- ✗ False negative 9%

Prior negative biopsy
NPV 93% (95% CI 90%-95%)

- ✗ Miss rate =
- ✗ False negative 7%



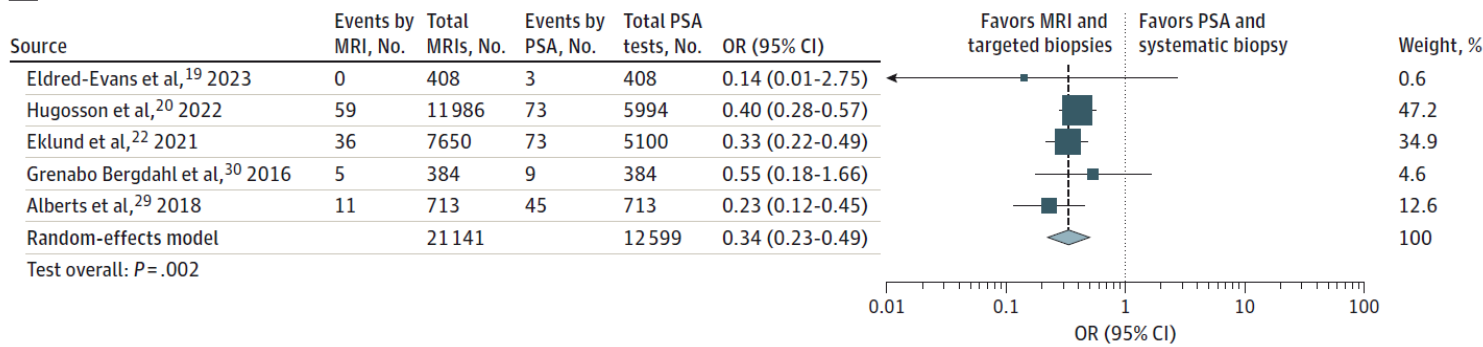
MRI in screening vs standard screening - review

JAMA Oncology | Original Investigation

Magnetic Resonance Imaging in Prostate Cancer Screening A Systematic Review and Meta-analysis

Tamás Fazekas, MD; Sung Ryul Shim, MPH, PhD; Giuseppe Basile, MD; Michael Baboudjian, MD; Tamás Kói, PhD; Mikolaj Przydacz, MD, PhD, DSc; Mohammad Abufaraj, MD; Guillaume Ploussard, MD, PhD; Veeru Kasivisvanathan, MD, PhD; Juan Gómez Rivas, MD, PhD; Giorgio Gandaglia, MD; Tibor Szarvas, MD, PhD; Ivo G. Schoots, MD, PhD; Roderick C. N. van den Bergh, MD, PhD; Michael S. Leapman, MD, MHS; Péter Nyirády, MD, PhD, DSc; Shahrokh F. Shariat, MD, DDr(hc); Pawel Rajwa, MD, PhD

A CDR of clinically insignificant prostate cancer



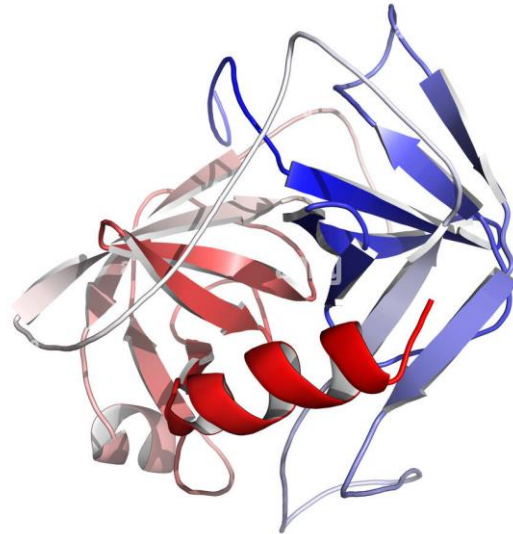
Lower odds of insignificant PCa detection
OR: 0.34 (95% CI: 0.23-0.49)

Similar clinically significant PCa detection
OR: 1.02 (95% CI: 0.75-1.37)

Lower odds of biopsies
OR 0.28 (95% CI: 0.22-0.36)

Higher PPV
OR: 4.15 (95% CI: 2.93-5.88)

Biomarkers



New algorithms

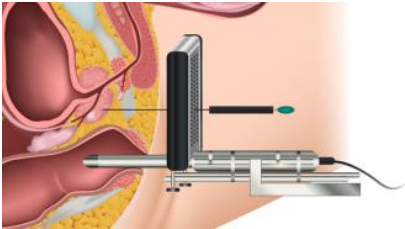


The perfect protocol does not exist

- The perfect algorithm may be different for:
 - Country, region, hospital
 - Patient group (age, screening vs clinical)
- The perfect algorithm may depend on:
 - Availability
 - Costs
 - Quality



Any new protocol outperforms PSA-only



SWOP Prostate Cancer Research Foundation - Belgium
SWOP Prostate Cancer Research Foundation - Belgium
Calculate your prostate cancer risk
PCPT Risk Calculator Home Map Add to phone
Start

Characteristics

Race

Age

PSA [ng/ml]

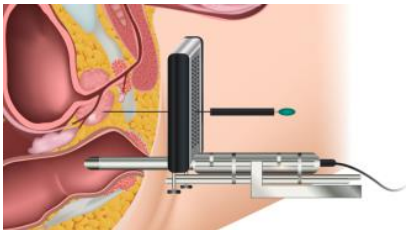
Family History of Prostate Cancer

Digital rectal examination

Prior biopsy

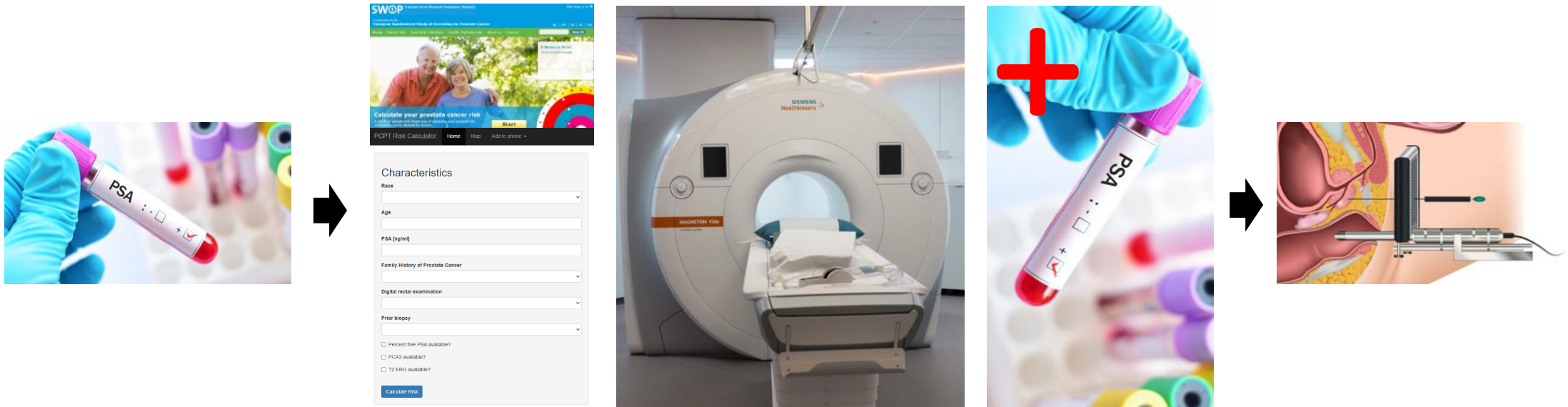
☐ Percent free PSA available?
☐ PCAs available?
☐ T2 ERG available?

Calculate Risk



Improved but more complicated algorithm

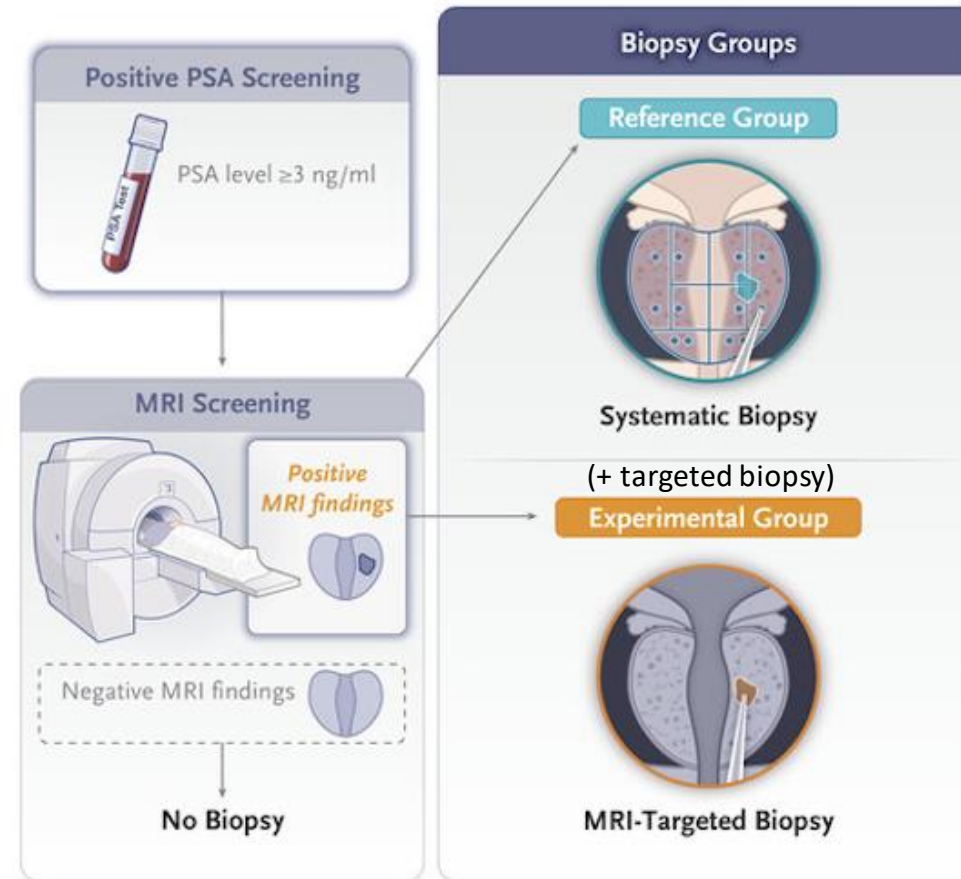
- Risk calculator: validation, calibration?
- MRI: availability, costs, quality, team, logistics, biopsy protocols?
- Serum biomarkers: availability, costs?



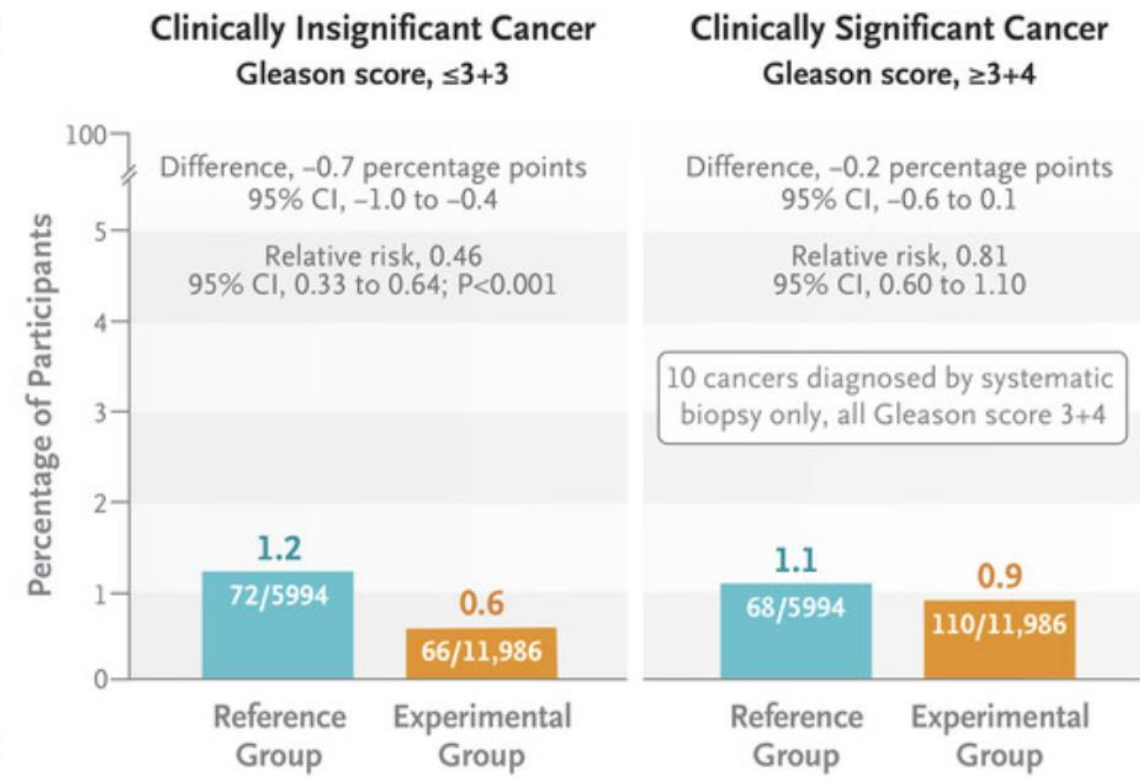
Risk-stratified screening

Study	Lead investigator, country	Intervention
PROBASE	Peter Albers, Germany	PSA, 45 vs. 50
Goteborg-2	Jonas Hugosson, Sweden	PSA + mpMRI, 3 vs 1.8 ng/mL
STHLM3-MR-2	Tobias Nordstrom, Sweden	PSA + STHLM3 + mpMRI, 3 vs. 1.5 ng/mL, 11% STHLM3
PROSCREEN	Anssi Auvinen, Finland	PSA + 4Kscore + mpMRI
IP1-PROSTAGRAM	David Eldred-Evans, UK	PSA + TRUS + mpMRI
Nanjing	Jingyan Shi, China	PSA + mpMRI, 4 ng/mL
MVP	Robert Nam, Canada	PSA vs. mpMRI
ReIMAGINE	Caroline Moore, UK	PSA + mpMRI
VISIONING-1	Cyrill Rentsch, Switzerland	PSA + bpMRI
PROFILE	Rosalind Eeles, UK	PSA + mpMRI, high genetic risk
BARCODE-1	Rosalind Eeles, UK	SNPs + mpMRI, top 10% genetic risk
ProCaRis	Jacob Fredsoe, Denmark	PSA + SNPs
Screening in men w germline BRCA2	Preston Sprenkle, US	PSA + DRE + mpMRI
IMPACT study	Rosalind Eeles, UK	BRCA1/2
Screening men w high risk gen predis	David Margel, Israel	BRCA1/2, PSA + mpMRI

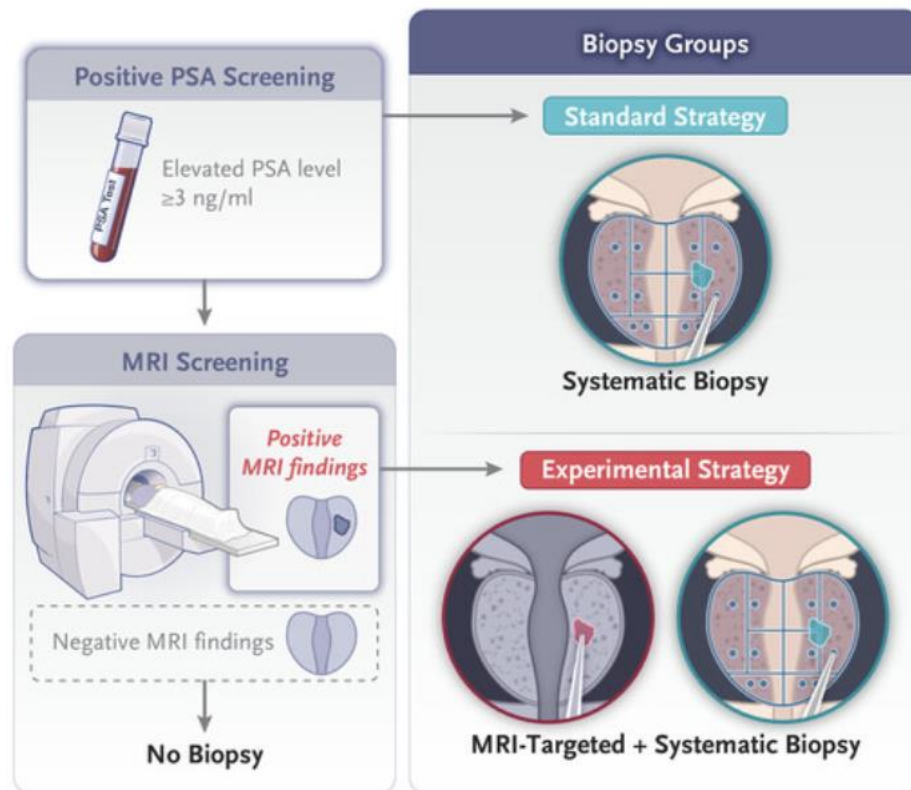
Göteborg-2



• N=17,980, 50-60 yrs



STHLM3-MRI trial

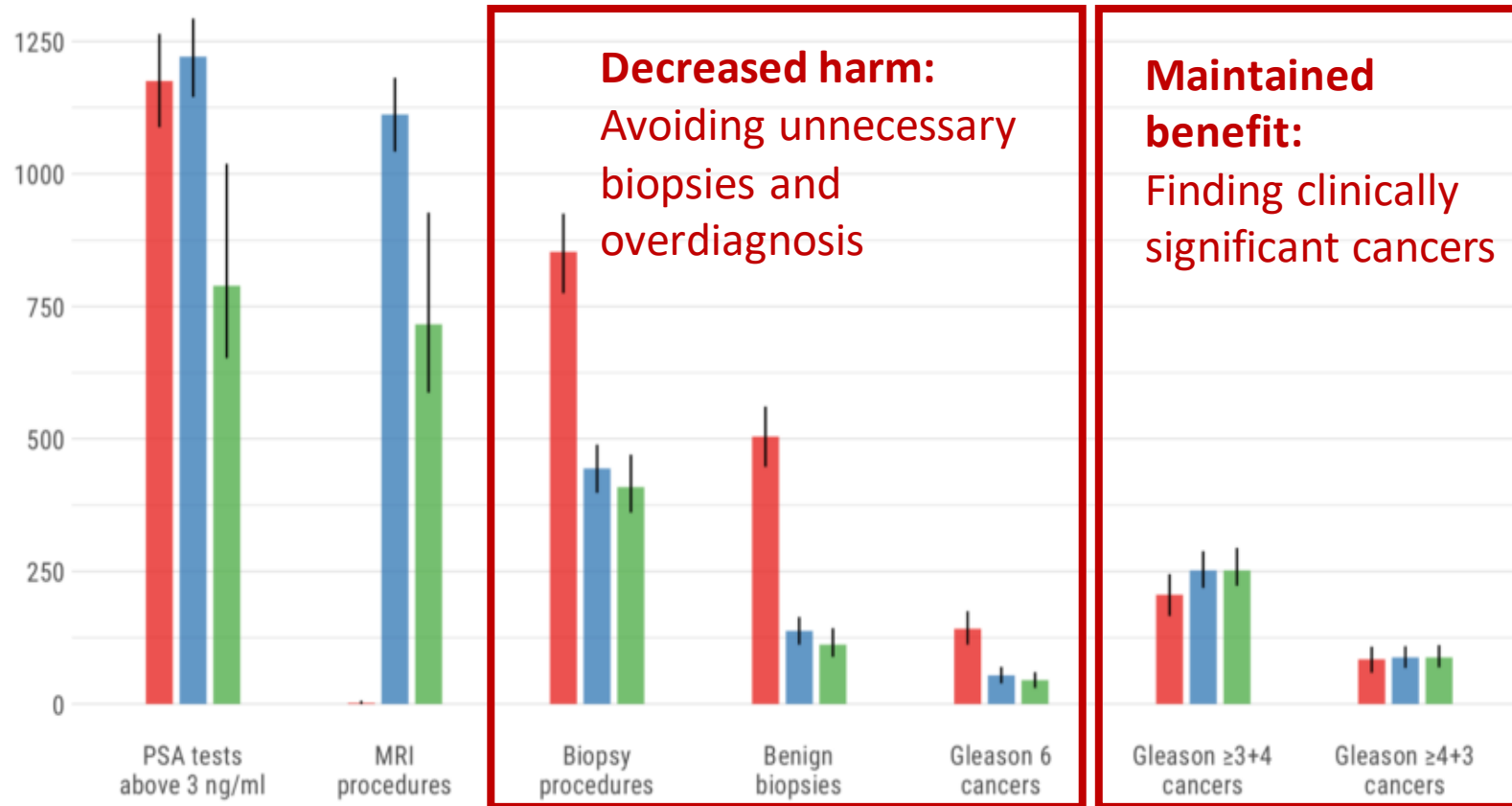


Standard strategy
(PSA ≥ 3)

MRI-enhanced
strategy (PSA ≥ 3)

MRI-enhanced
strategy (STHLM3 ≥ 0.15)

STHLM3-MRI trial



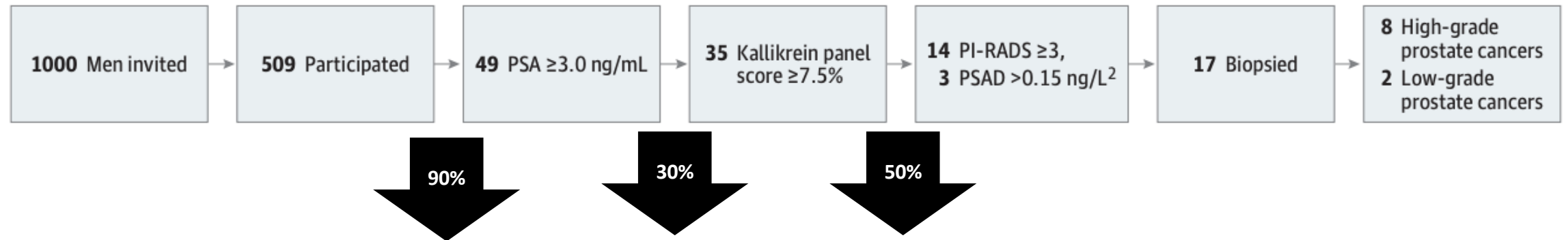
Standard strategy
(PSA ≥ 3)

MRI-enhanced
strategy (PSA ≥ 3)

MRI-enhanced
strategy (STHLM3 ≥ 0.15)

PRO SCREEN

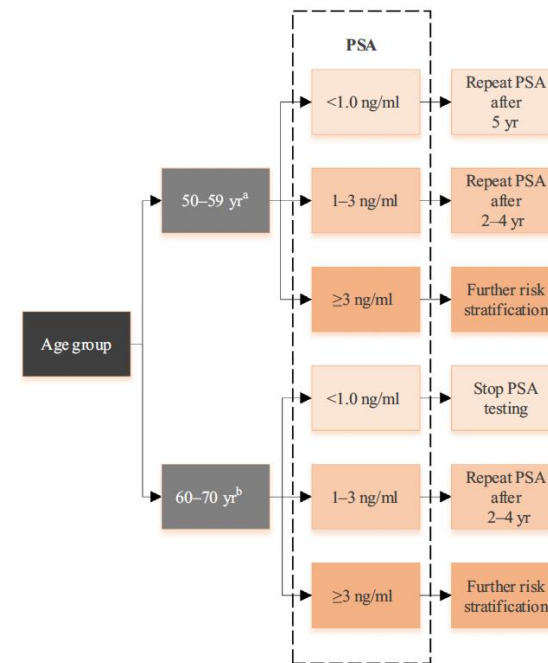
- N=61.193, 50-63 yrs
- PSA >3 → 4-kallikrein panel >7.5% → MRI PIRADS 3-5 → target Bx
- 51% participation
- Risk difference 0.11% for low grade, 0.51% for high grade



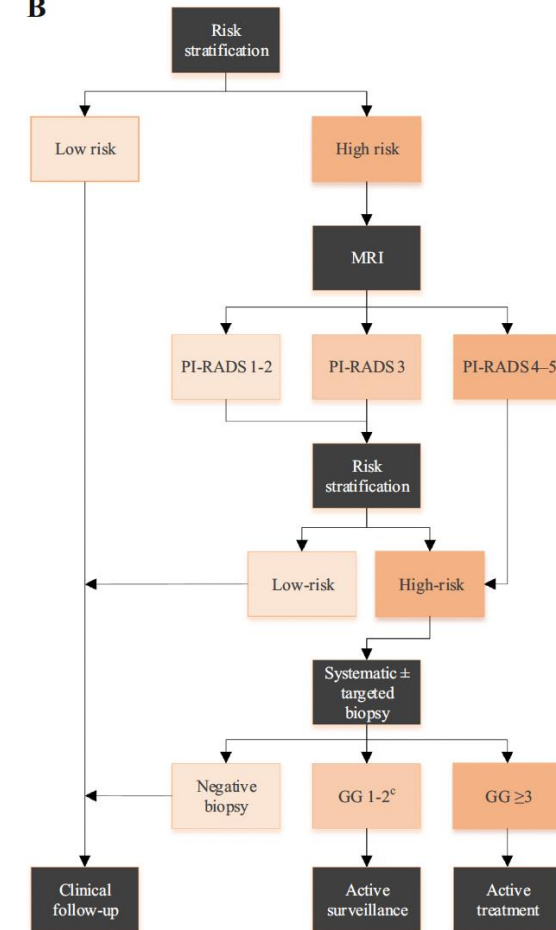
Risk-adapted protocols

- Risk stratification with calculator after PSA
- MRI-based biopsy indication
- Age- and PSA-specific PSA retesting interval

A



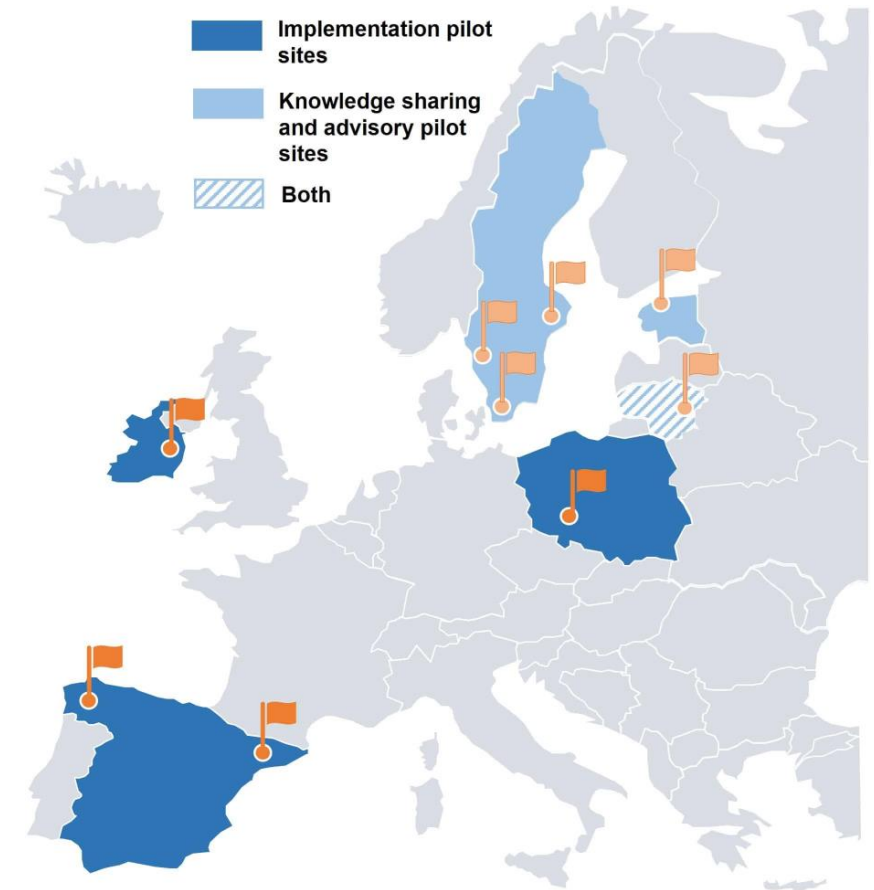
B



Prostate cancer Awareness and Initiative for Screening in the EU

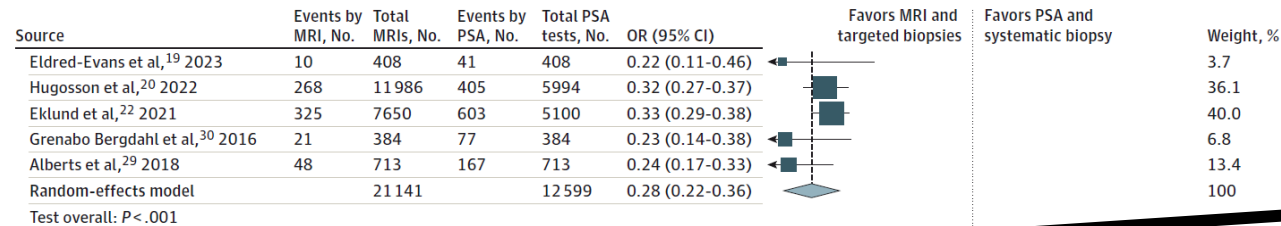
- Screening in Europe:
 - State of play
 - Acceptance
 - Risk-based screening
- 5 x pilot
 - Ireland
 - Spain 2 x
 - Lithuania
 - Poland

Praise u
SMART EARLY DETECTION OF PROSTATE CANCER

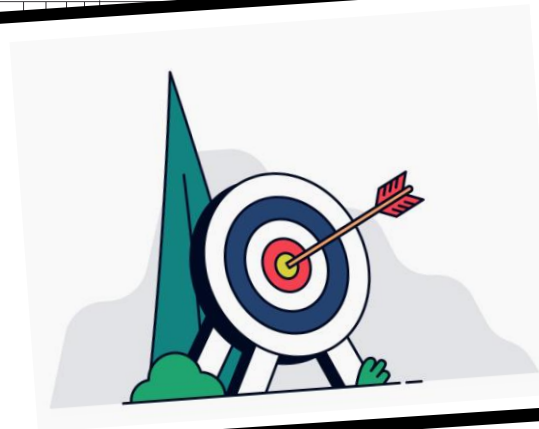


Pathology is NOT only valid endpoint

B Biopsy indication rates



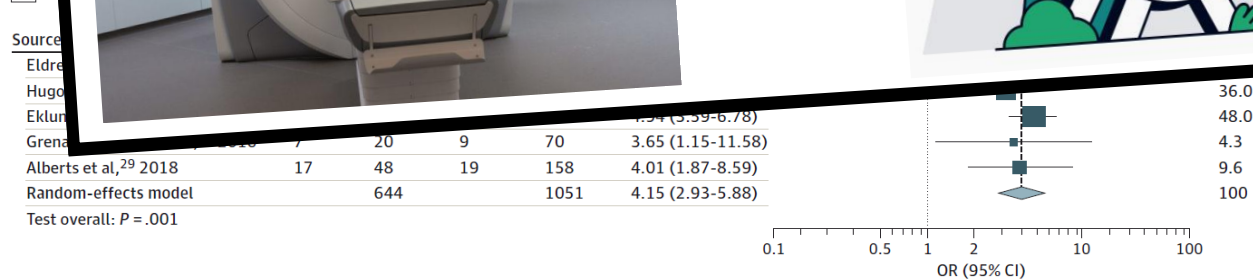
Biopsies
OR 0.28 (95% CI: 0.22-0.36)



on
.49)

PPV clinically significant PCa
OR: 4.15 (95% CI: 2.93-5.88)

C PPV clinically significant PCa



Adapt sequencing of risk stratification



SWOP Swedish Prostate Cancer Risk Calculator

Calculate your prostate cancer risk
with the SWOP risk calculator. Results are provided
as a percentage of risk.

PORT Risk Calculator [Home](#) [Help](#) [Add to device](#)

Characteristics

Race

Age

PSA (ng/ml)

Family history of Prostate Cancer

Digital rectal examination

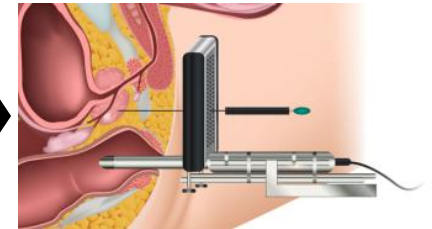
Prior biopsy

☐ Percent free PSA available?

☐ PCA3 available?

☐ T2 ERG available?

[Calculate Risk](#)



Screening is more than a diagnostic algorithm

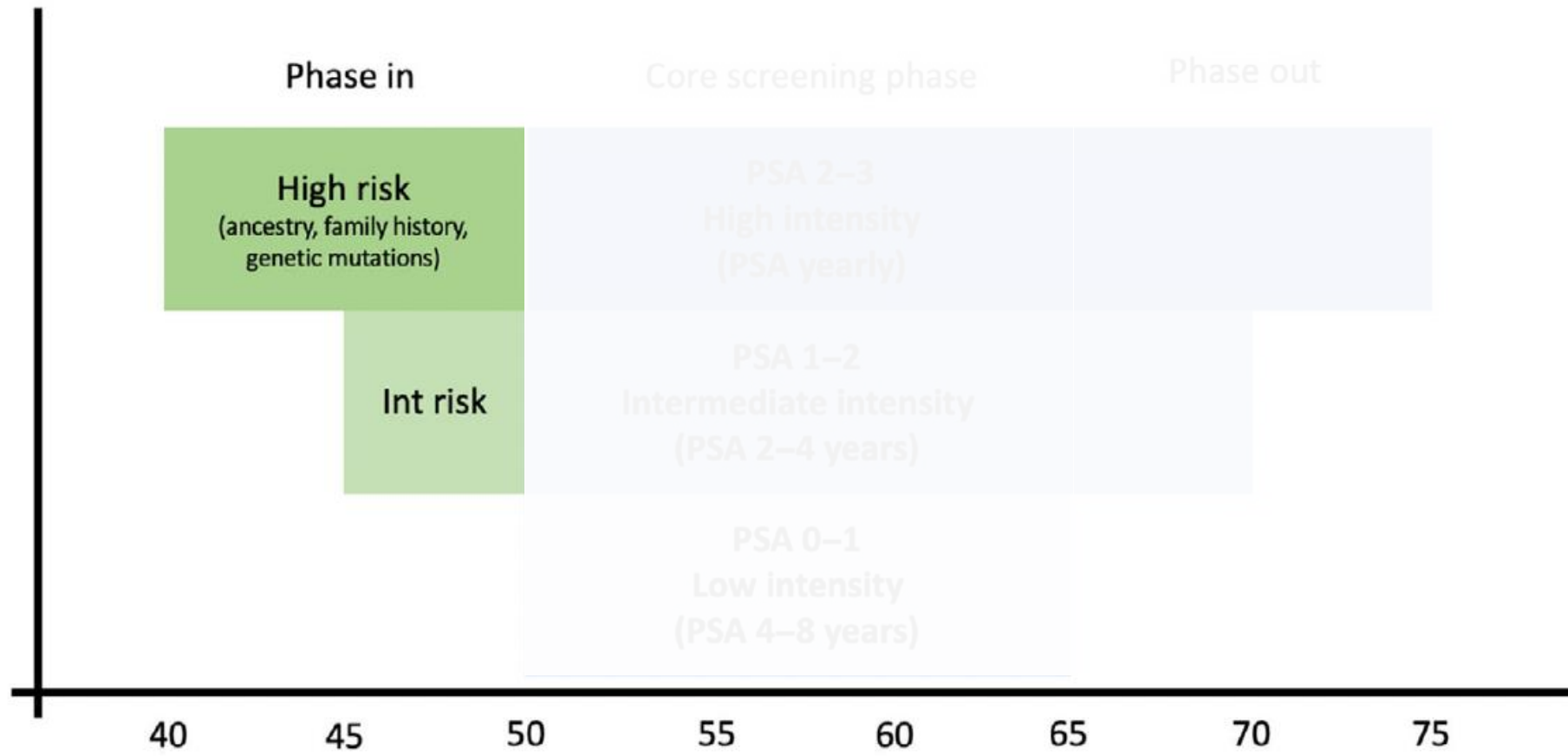
- Support from policy makers?
- Resources?
- Participation?
- Compliance?
- Active surveillance?
- Opportunistic screening?
- ...



More improvements than MRI and biomarkers

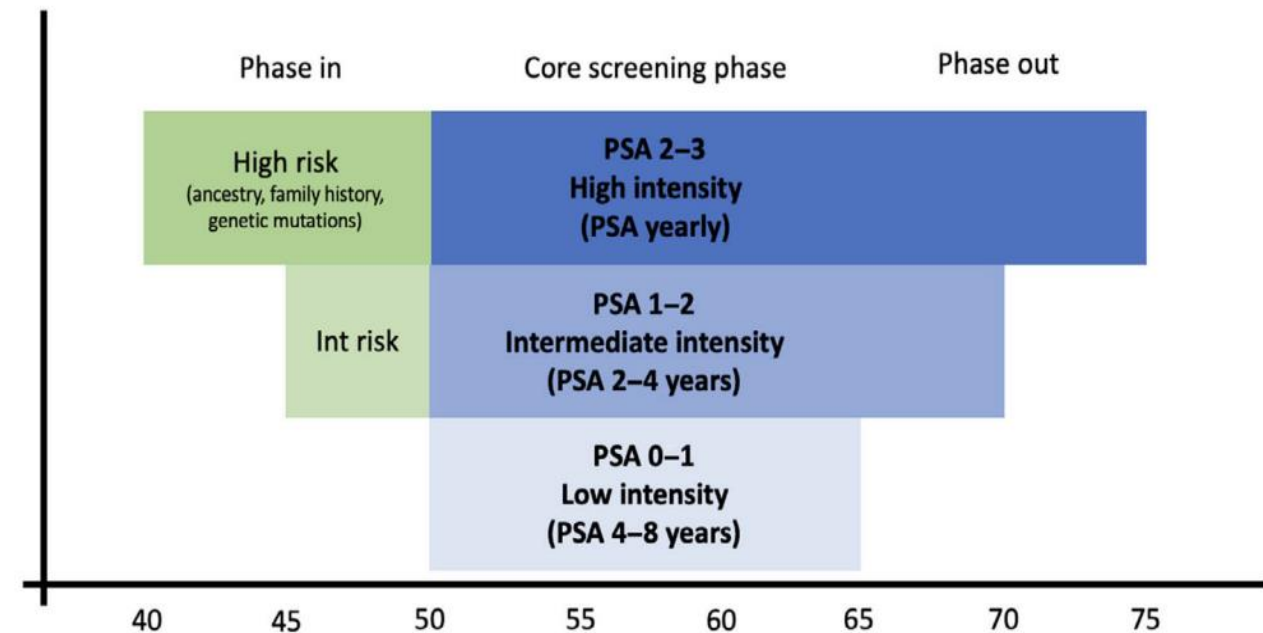
	Classic algorithm for screening, diagnosis, and treatment	Modern algorithm for screening, diagnosis, and treatment	Impact
Starting age	Fixed	Individualised, based on risk groups	Increase efficacy
Stopping age	Fixed	Individualised, based on last PSA	Reduce overdiagnosis
Risk groups	Age only	Age, optional: baseline PSA, family history, genetic profile	Early identification of men who benefit most
Re-testing interval	Standard re-testing 2–4 years	Individualised, based on	Relax testing in low risk, intensify testing in high risk

Phase-in, phase-out according to risk



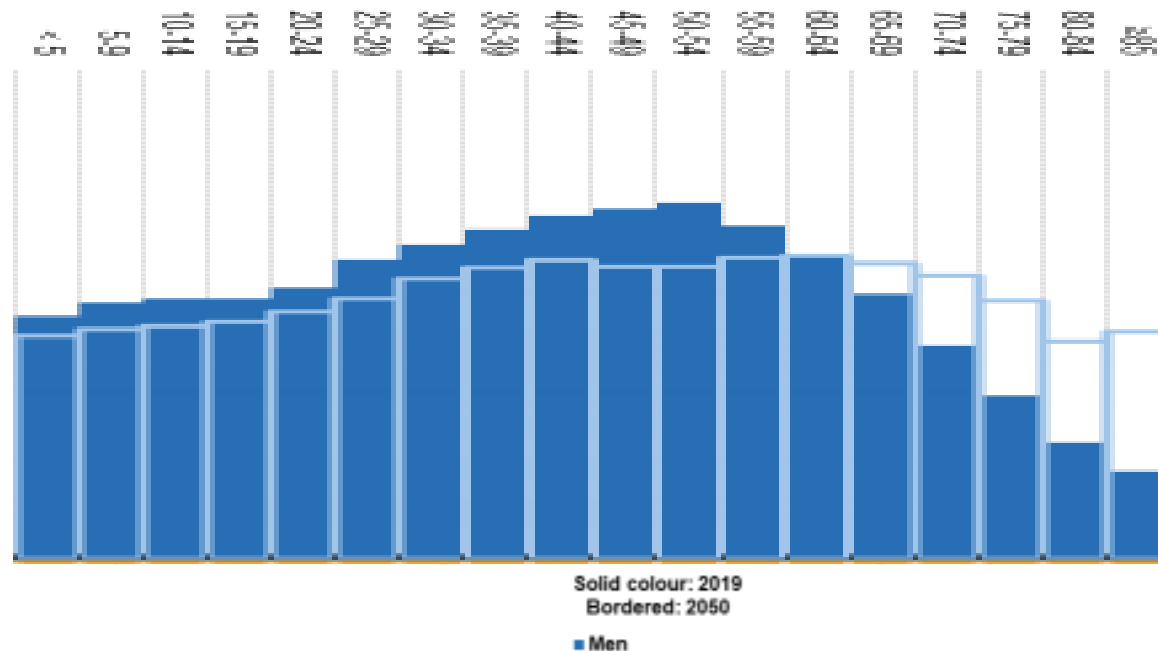
Perfect screening (phase in – phase out)

- Invite high-risk population
- High acceptance (awareness)
- Acquire early baseline PSA
- Early phase in for high risk
- Risk estimation biopsy
 - calculator/MRI
- Individual retesting
 - PSA <1 → 5 yr, PSA 1-3 → 2 yr
- Early phase out for low risk
- Low opportunistic screening

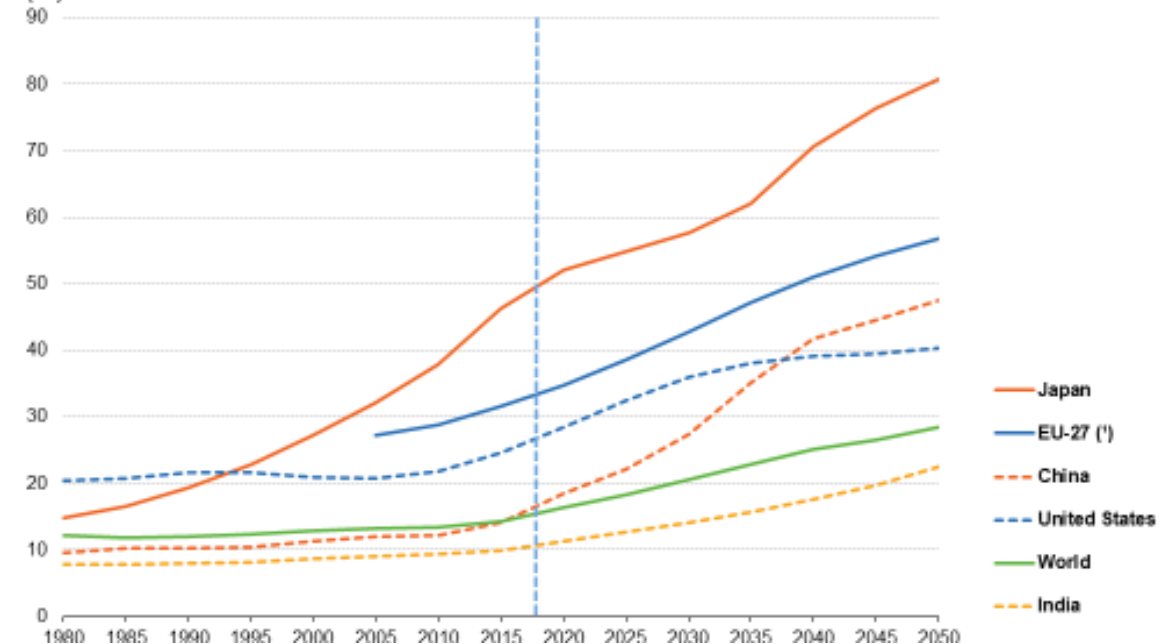


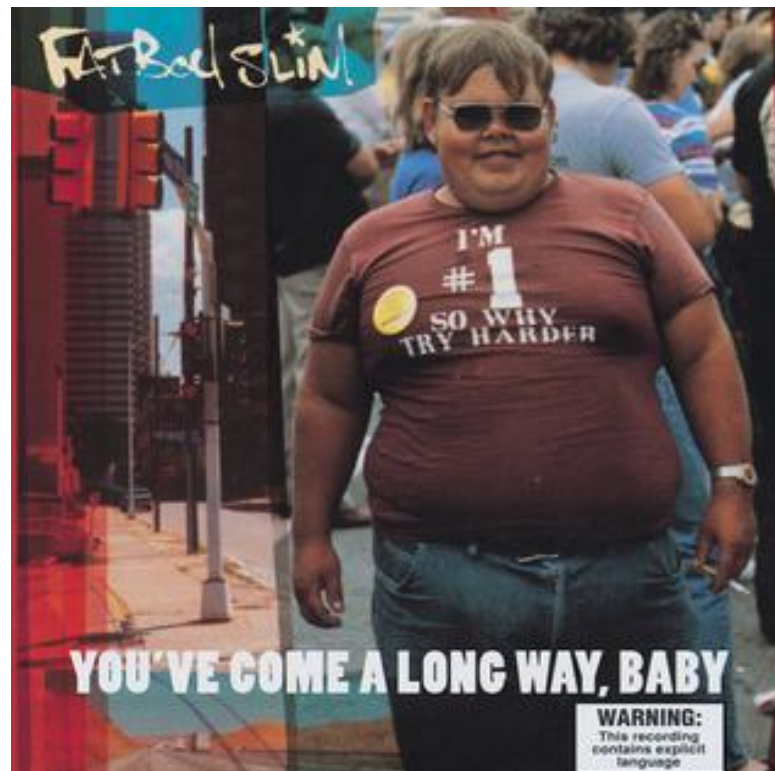
Rising age, PCa tsunami

Population pyramids, EU-27, 2019 and 2050
(% share of total population)



Old-age dependency ratio, 1980-2050
(%)





Take home – Developments in screening

- A huge potential in improving biopsy indication
- May turn the tide for screening
- Should be put into perspective with risk calculator
- Choice and sequencing may differ per country
- Screening may reduce opportunistic testing
- Organised screening may be needed
- **‘The optimal approach’ is more than just the diagnostic algorithm**



