PROSTAFORUM 2022

WHAT IS THE EVIDENCE ON PROSTATE CANCER SCREENING?

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Why prostate cancer screening?


BMJ

LONDON, SATURDAY 13 FEBRUARY 1993

Prostate cancer: to screen or not to screen?

It's happening, but the case has not been made

Prostate cancer: to screen or not to screen?

Schröder FH, 1993

Journal: BMJ

Reference: 306:407-8.

Written in 1993

About 50-60% of all cases of prostate cancer in the European Community present with obvious metastases or are locally too advanced for potentially curative management. Of those cancers that seem to be limited to the prostate clinically, 25-35% will have lymph node metastases.[2] Of the remainder, another 25-35% will be too advanced for curative treatment and will turn out to be unresectable if surgery is attempted.[3]

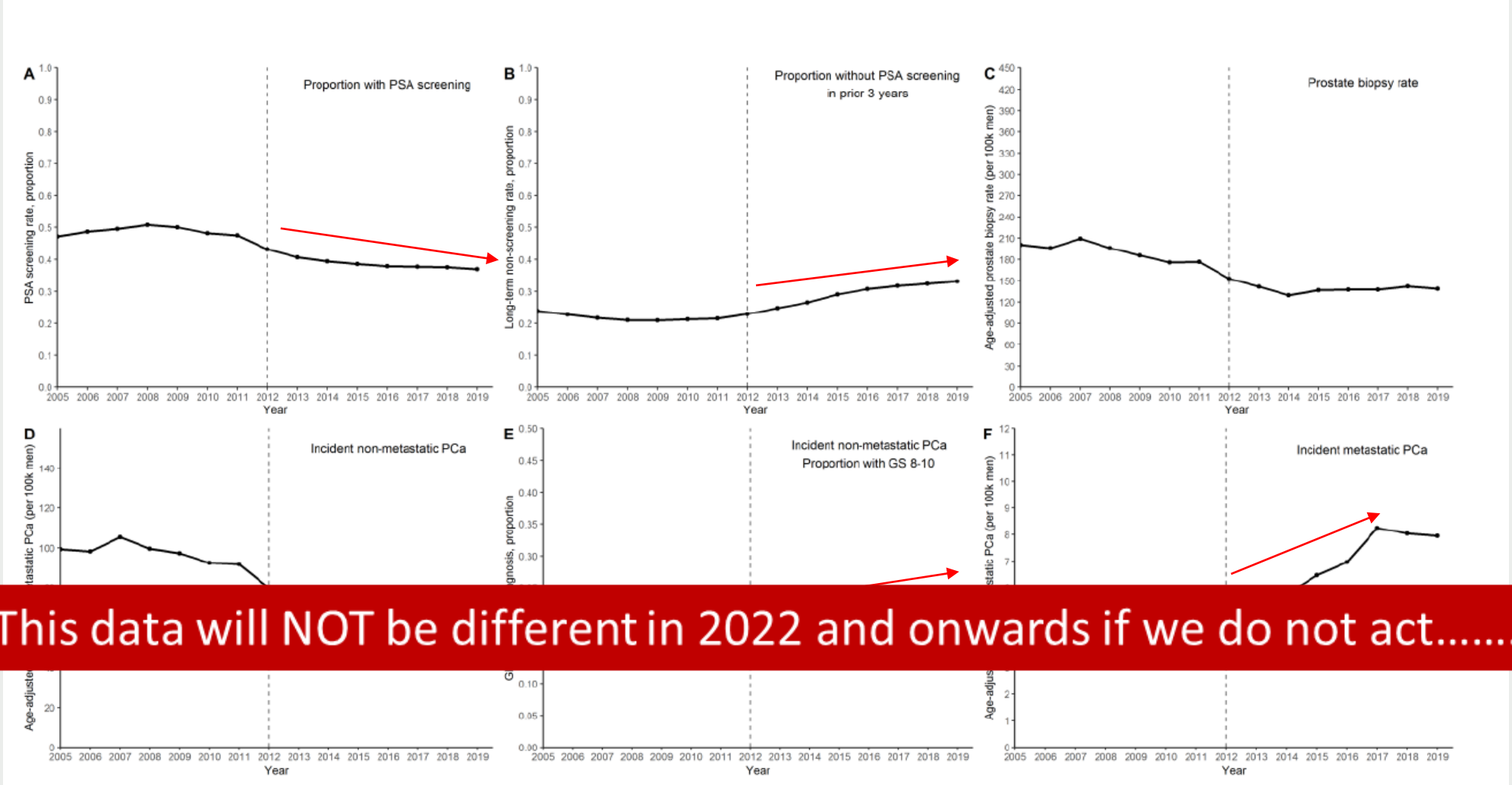
This data will NOT be different in 2022 and onwards if we do not act…….

Published October 24,2022
Data from 5,371,701 men in the US.
In 2012 the USPSTF recommended against PSA screening

JAMA Oncology | Original Investigation

Association of Prostate-Specific Antigen Screening Rates With Subsequent Metastatic Prostate Cancer Incidence at US Veterans Health Administration Facilities

Alex K. Bryant, MD, MAS; Kyung Min Lee, PhD; Patrick R. Alba, MS; James D. Murphy, MD, MS; Maria Elena Martinez, PhD; Loki Natarajan, PhD; Michael D. Green, MD, PhD; Robert T. Dess, MD; Tori R. Anglin-Foote, MHA; Brian Robison, MPH; Scott L. DuVall, PhD; Julie A. Lynch, PhD; Brent S. Rose, MD



This data will NOT be different in 2022 and onwards if we do not act.....

Screening trials initiated in the 90s

Study	Setting, country	Enrolment criteria	Study conducted	No of men randomised (intervention/control)	Screening method	Screening frequency	Primary outcomes	Secondary outcomes
ERSPC (core)[31]	RCT, multicentre, 9 European countries	Men aged 55-69 years	1993-2003, 13 year follow-up	72 891/89 352	PSA ± DRE. If PSA ≥3 ng/mL standardised prostate biopsy	Screening every 2-4 years	Prostate cancer-specific mortality	All-cause mortality, prostate cancer incidence, clinical stage, quality of life, harms
Labrie (Quebec)[33]	RCT, Quebec, Canada	Men aged 45-80 years	1988-1999, 11 year follow-up	31 133/15 353	PSA ± DRE. If PSA ≥3 ng/mL standardised prostate biopsy	Annual screening	Prostate cancer-specific mortality	Prostate cancer incidence, clinical stage
Lundgren (Stockholm)[23]	RCT, Stockholm, Sweden	Men aged 55-70 years	1988-2003, 20 year follow-up	2400/25 081	PSA, DRE, TRUS. Biopsy depended on DRE and TRUS findings, PSA >10 ng/mL	One-time screening	Prostate cancer-specific mortality	All-cause mortality, prostate cancer incidence
PLCO[32]	RCT, multicentre, US	Men aged 55-74 years	1993-2001, 15 year follow-up	38 340/38 343	PSA, DRE	Annual screening	Prostate cancer-specific mortality	All-cause mortality, prostate cancer incidence, clinical stage, Gleason grade, harms

RCT=randomised controlled trial. PSA=prostate-specific antigen. DRE=digital rectal examination. TRUS=transrectal ultrasound.

To assess the effect of PSA based screening on prostate cancer-specific mortality more than 300,000 men were included in studies

The PLCO in the US

NATIONAL CANCER INSTITUTE
PLCO
Prostate, Lung, Colorectal & Ovarian
CANCER SCREENING TRIAL

Compliance and Contamination

- Screening before entry (screening/control)
  - PSA test — DRE
    - Once: 34.6/34.3 — 32.8/31/9
    - Two or more: 9.4/9.8 — 22.2/22.0
- Compliance
  - PSA 85%; DRE 86%
- Testing in the control group
  - PSA: 40% in first year to 52% in sixth year
  - DRE: Range from 41 to 46%

PLCO Screening Centers

10 centers

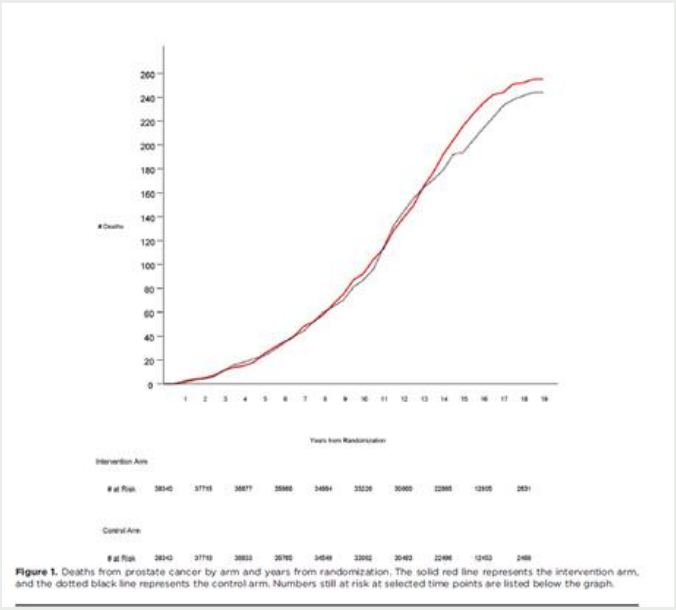


Figure 1. Deaths from prostate cancer by arm and years from randomization. The solid red line represents the intervention arm, and the dotted black line represents the control arm. Numbers still at risk at selected time points are listed below the graph.

15 yr of FU, RR 1.04 (0.87-1.24) p=0.67

PLCO		
76,693 men		
Age 55-74		
No difference in PCa mortality		
Upfront: 34% contamination During trial: 52% contamination		

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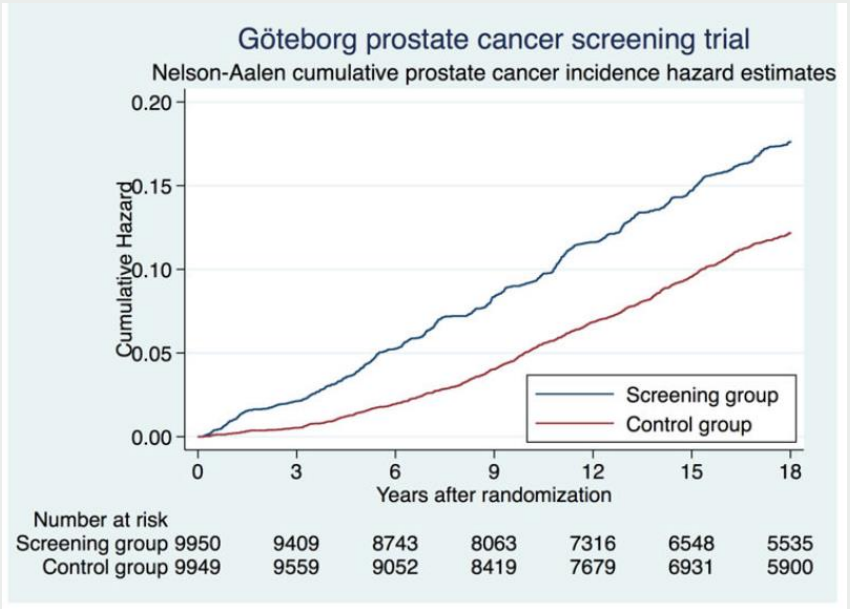
Cancer . 2017 Feb 15;123(4):592-599. doi: 10.1002/cncr.30474.

The Goteborg Screening trial

Sahlgrenska University, Goteborg, Sweden



18 yr of FU, RR 0.65 (0.49-0.87) p< 0.001

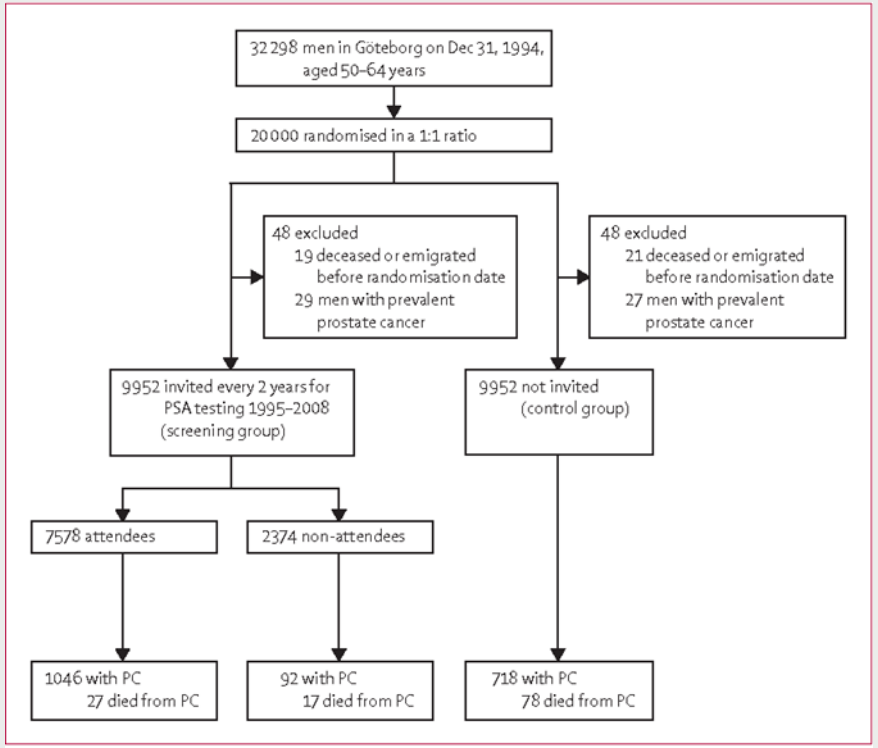


Figure 1: **Trial profile**
PSA=prostate-specific antigen. PC=prostate cancer.

PLCO	Goteborg	
76,693 men	20,000 men	
Age 55-74	Age 50-64	
No difference in PCa mortality	**35%** PCa mortality **reduction**	
Upfront: 34% contamination During trial: 52% contamination	To avoid one death: Screen 231 men Extra diagnoses: 10 men	

Lancet Oncol . 2010 Aug;11(8):725-32.

The ERSPC

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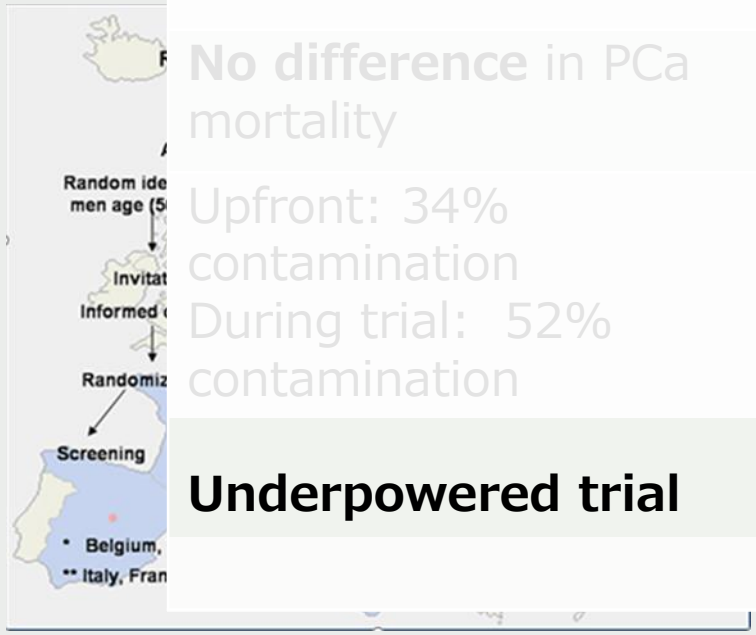
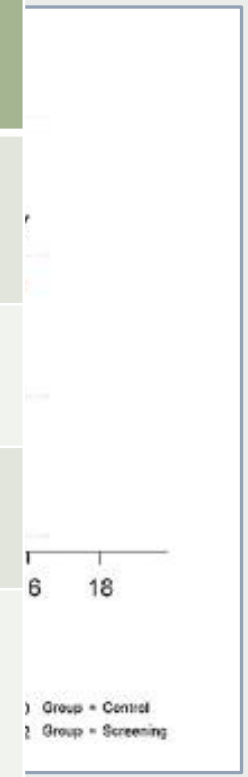


PLCO	Goteborg	ERSPC
76,693 men	20,000 men	182,160 men
Age 55-74	Age 50-64	Age 55-70
No difference in PCa mortality	**35%** PCa mortality **reduction**	**20%** PCa mortality **reduction**
Upfront: 34% contamination During trial: 52% contamination	To avoid one man dying and suffering from Prostate cancer	To avoid one man dying and suffering from Prostate cancer
Underpowered trial	Screen: 231 Extra diagnose: 10	Screen: 570 Extra diagnose: 18

p< 0.001



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Eur Urol 2019 Jul;76(1):43-51

ERSPC Rotterdam : 1993 - ongoing

A total of 42,376 men included

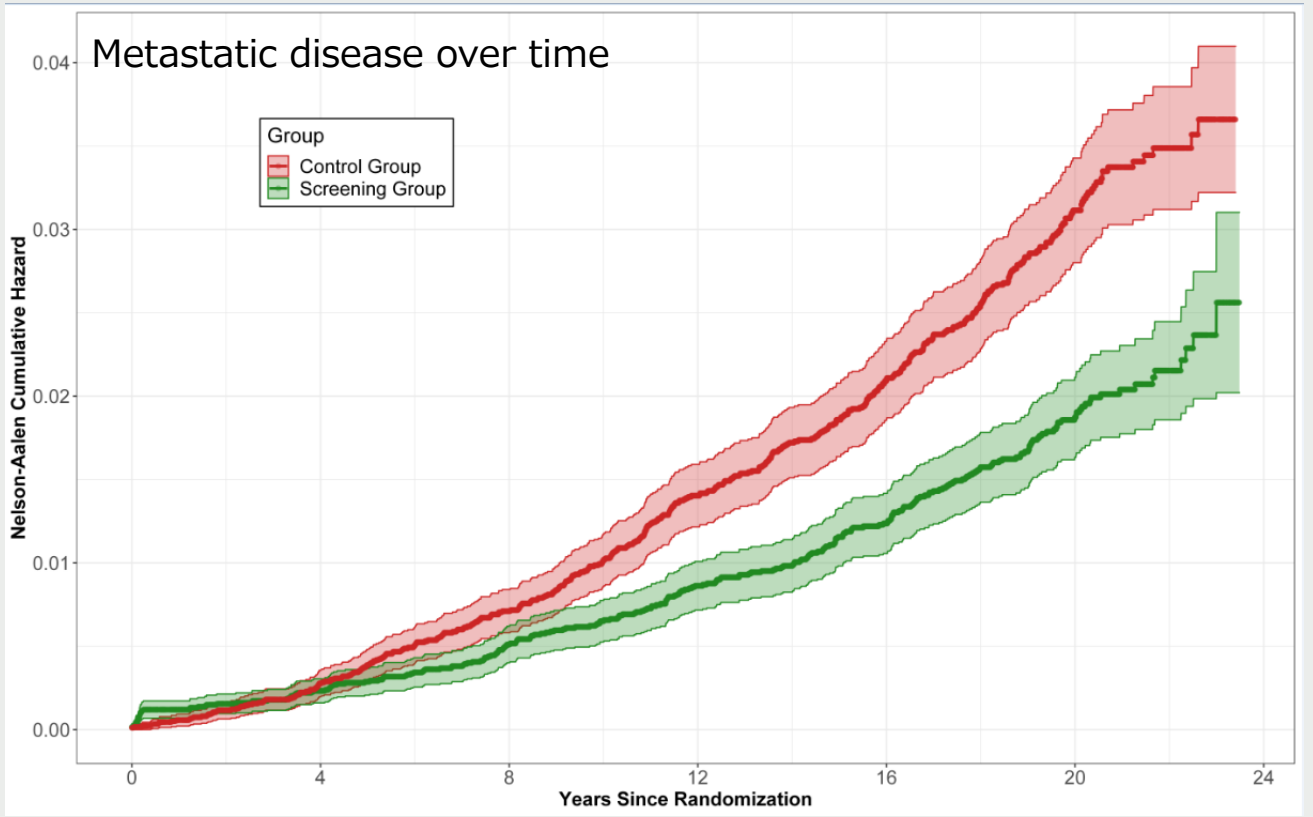
Complete follow up on screening history, treatment(s), progression, metastases and (PCa) mortality in both arms

Data on PSA testing and prostate biopsy outside the study available at an individual level

In addition: From 1991 – 1993 there were 5 pilot studies

Pilot 1 1991/1992: N= 1,134

ERSPC Rotterdam N=42,376 men



Median follow-up 18-year

41% reduction in men diagnosed with metastatic disease

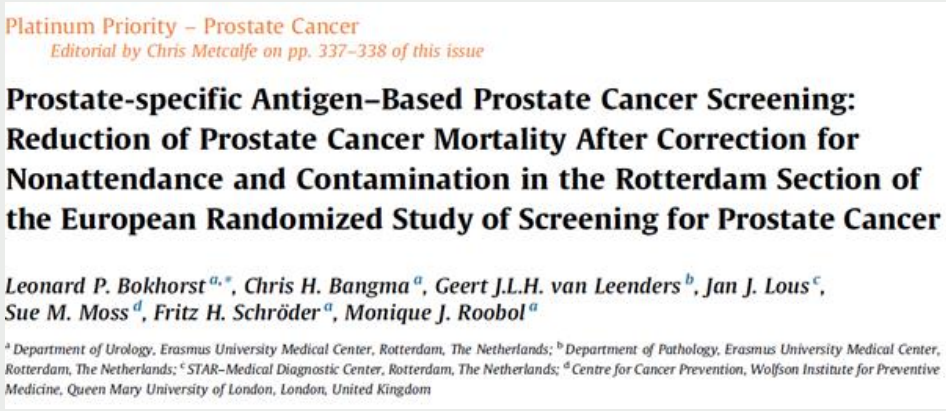
Eur Urol 2013 Oct;64(4):530-9.

ERSPC Rotterdam: screening versus no screening

In a screening trial:

Non-attendance: men do not show up for PSA testing or prostate biopsy

Contamination: men are screened while in control arm or during the interval period while in screening arm



Platinum Priority – Prostate Cancer

Editorial by Chris Metcalfe on pp. 337–338 of this issue

Prostate-specific Antigen–Based Prostate Cancer Screening: Reduction of Prostate Cancer Mortality After Correction for Nonattendance and Contamination in the Rotterdam Section of the European Randomized Study of Screening for Prostate Cancer

Leonard P. Bokhorst [a,], Chris H. Bangma [a], Geert J.L.H. van Leenders [b], Jan J. Lous [c], Sue M. Moss [d], Fritz H. Schröder [a], Monique J. Roobol [a]*

[a] Department of Urology, Erasmus University Medical Center, Rotterdam, The Netherlands; [b] Department of Pathology, Erasmus University Medical Center, Rotterdam, The Netherlands; [c] STAR-Medical Diagnostic Center, Rotterdam, The Netherlands; [d] Centre for Cancer Prevention, Wolfson Institute for Preventive Medicine, Queen Mary University of London, London, United Kingdom

Conclusion:
Comparing men screened multiple times as compared to men NOT screened at all results in **50% of PCa deaths avoided**

	PCa mortality reduction
Intention to screen analysis	32%
Correction for non-attendance	33%
Correction for PSA contamination	39%
Correction for biopsy contamination	47%

The first ERSPC Pilot study in Rotterdam (1991)

- 63% of cohort initially screened in 1991/1992 has died by now
- Contamination up to now: 4.5%
- **53% PCa mortality reduction**
- **58% reduction of metastatic disease**

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Brief Correspondence

Results of Prostate Cancer Screening in a Unique Cohort at 19 yr of Follow-up

Daniël F. Osses[a,b,*], *Sebastiaan Remmers*[a], *Fritz H. Schröder*[a], *Theo van der Kwast*[c,d], *Monique J. Roobol*[a]

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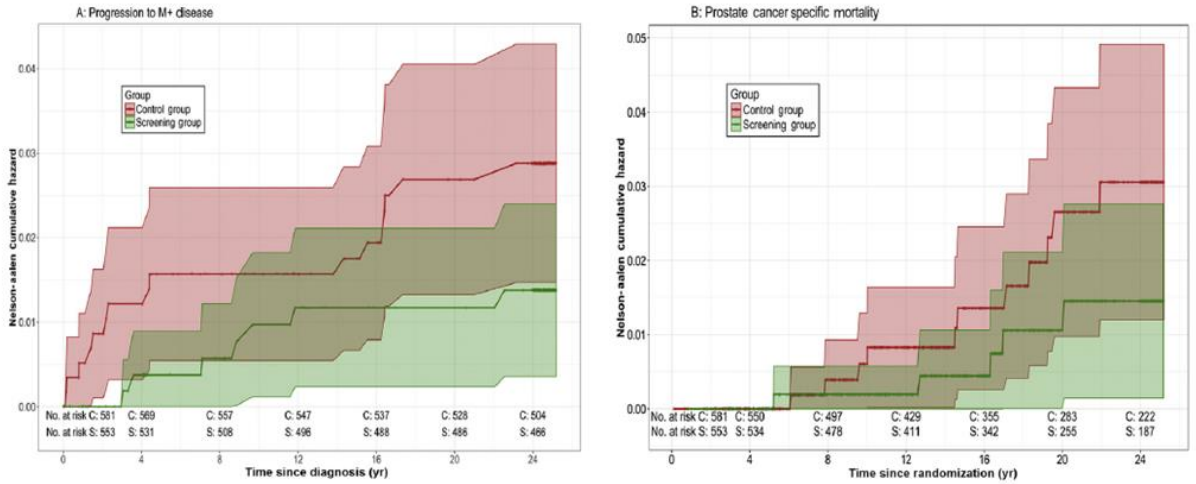
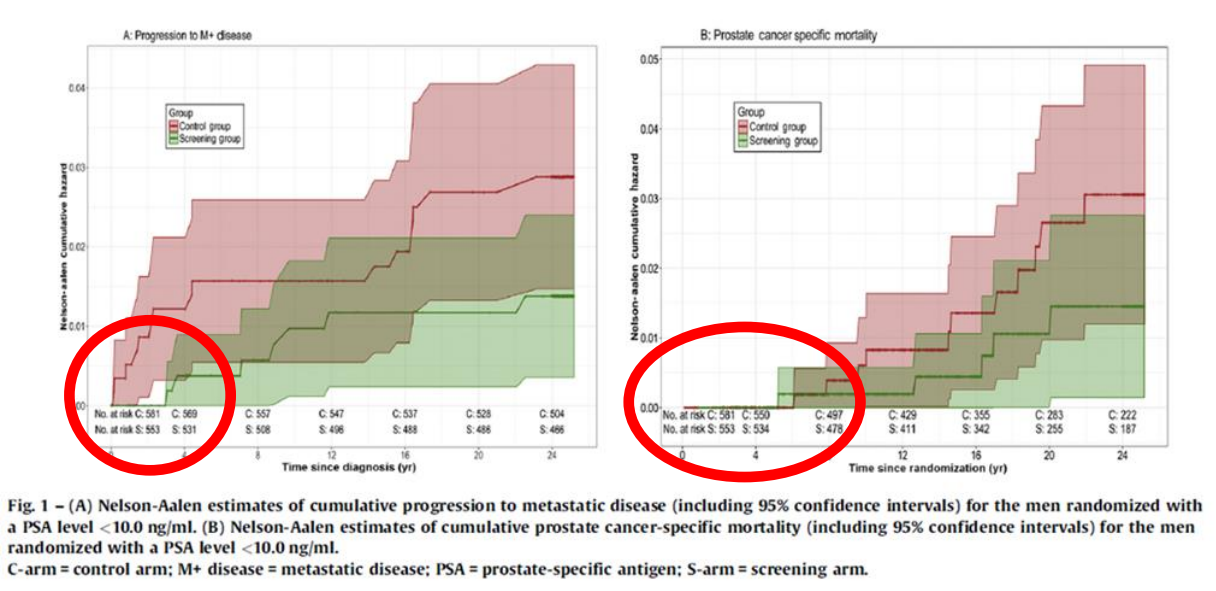


Fig. 1 – (A) Nelson-Aalen estimates of cumulative progression to metastatic disease (including 95% confidence intervals) for the men randomized with a PSA level <10.0 ng/ml. (B) Nelson-Aalen estimates of cumulative prostate cancer-specific mortality (including 95% confidence intervals) for the men randomized with a PSA level <10.0 ng/ml.
C-arm = control arm; M+ disease = metastatic disease; PSA = prostate-specific antigen; S-arm = screening arm.

Effect of screening: ongoing initiatives

1. Stage shift
2. Reduction in metastatic disease
3. Effect on PCa mortality



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C-arm = control arm; M+ disease = metastatic disease; PSA = prostate-specific antigen; S-arm = screening arm.

T-stage at diagnosis	Screening arm	Control arm
Per 1000 PCa detected		
T1/T1A/T1B	35	64
T1C	576	419
T2	293	307
T3	85	174
T4	11	36

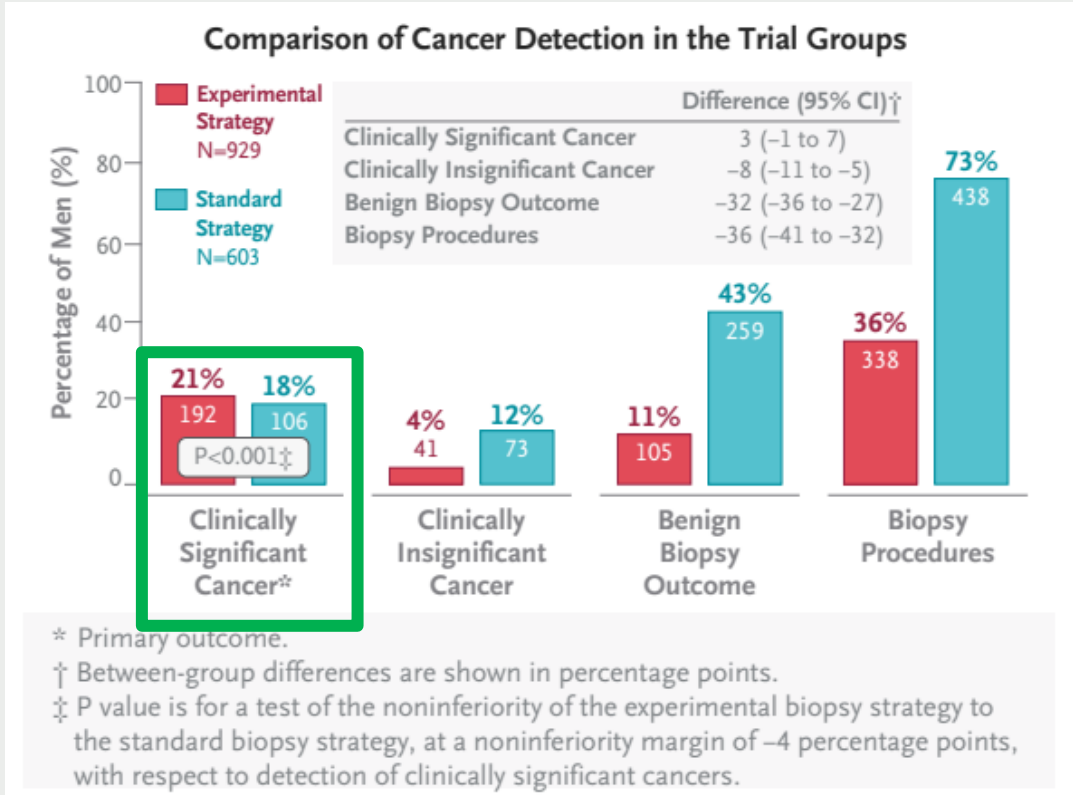
Gleason at diagnosis	Screening arm	Control arm
Per 1000 PCa detected		
6	588	352
7	165	185
> 7	61	106

ERSPC Rotterdam data and ERSPC data 2009 NEJM

STHLM-3-MRI screening trial

- From February **2018 through March 2020**, a total of 49,118 men were invited to participate; 12,750 men consented to screening
- **1532** men had PSA level of 3.0 ng/ml or higher
- Randomised to a 10-12 core standard biopsy (**standard biopsy group**)
- or MRI, with targeted and standard biopsy if the MRI positive (experimental biopsy group).

Favorable results regarding tumor characteristics at diagnosis!!



CONCLUSIONS

In an organized, population-based prostate cancer screening program, an experimental MRI-targeted biopsy strategy was noninferior to standard biopsy in detecting clinically significant prostate cancer while resulting in less detection of clinically insignificant cancer.

Eklund M et al. DOI: 10.1056/NEJMoa2100852

Conclusions

- Data from **pre-PSA era** show that PCa is a disease often related to a lot of suffering over a considerable period
- 2 out of 3 men diagnosed with PCa died of their disease
- We now know that:
- Organized screening with the use of the PSA test reduces suffering and dying from PCa
- Potential harms (unnecessary testing /over diagnosis and over treatment) can be largely avoided with current knowledge and results of the first contemporary population-based screening trial shows favorable results

The way forward

It is time to organize all relevant stakeholders and start implementing our knowledge to avoid further suffering and lives lost

Why Urology ? why Prostate Cancer?

- The text from my inaugural address:

- **Why urology?**
- Not the most appealing subject to talk about at a birthday party, unless it is a joke….
- Just because urological problems are not or rarely discussed it is a fascinating part of medicine.
- In particular **prostate cancer** often has **a long-lasting considerable impact on daily life**.
- Patients often **suffer in silence** and feel they are **alone**

- To help these men is a privilege

- *Working at the department of Urology since September 1991.*

Thank you for listening