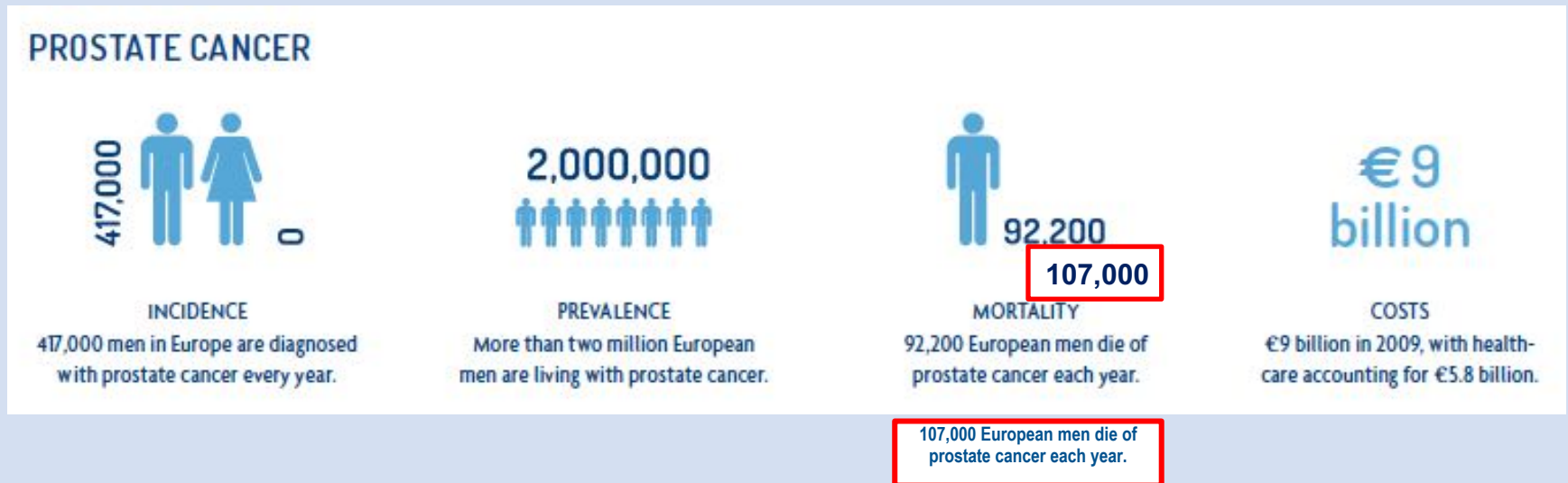


Has the time come to introduce Early Detection of Prostate Cancer?

**By Prof. Em. Hein Van Poppel
Adjunct-Secretary General for Education of
the European Association of Urology (EAU)**

Prostate Cancer in the European Society



Prostate cancer is the most common cancer in Europe for males

- Per year 336.000 men are diagnosed with prostate cancer in the EU-27
- 1 in 7 men in Europe will develop prostate cancer before the age of 85
- More than two million men living with prostate cancer
- 107,000 European men died of the disease in 2018
- The yearly costs of PCa in Europe is over 9 billion euros

Prostate Cancer in Belgium

- Incidence in Belgium decreasing 2006-2017
- Prostate cancer is the most common male cancer in Belgium

EU
160/100,000
37/100,000 PCa deaths
107.000 deaths/y

BE
147/100,000
32/100,000 PCa deaths
1500 deaths/y

- 5 year PCa Specific survival:

1. Cyprus	(99,2%)
2. Lithuania	(94,3%)
3. Belgium	(>90%)

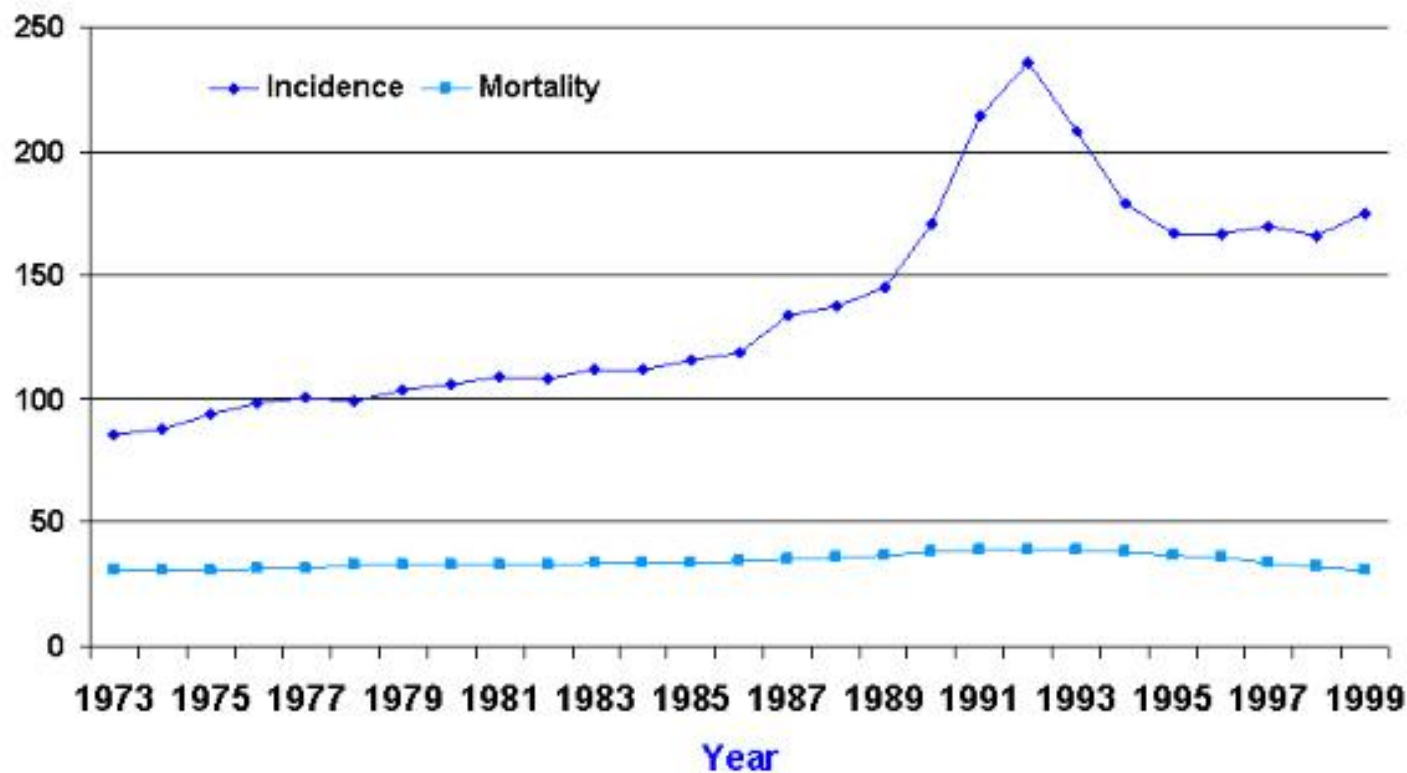
Table IV. MORTALITY-INCIDENCE RATE RATIOS¹ IN 13 COUNTRIES DURING 1973–77 TO 1988–92

Countries	1973–77 ¹	1978–82	1983–87	1988–92
High risk				
U.S. blacks	0.35	0.33	0.39	0.25
U.S. whites	0.28	0.25	0.23	0.16
Canada	0.36	0.29	0.25	0.20
Sweden	0.49	0.43	0.38	0.38
Australia			0.41	0.33
France			0.53	0.36
Medium risk				
Denmark			0.59	0.60
England and Wales			0.60	0.57
Italy			0.45	0.41
Spain	0.70	0.61	0.47	0.48
Israel	0.48	0.46	0.48	0.38
Low risk				
Singapore	0.40	0.44	0.55	0.38
Japan	0.49	0.44	0.42	0.42
Hong Kong	0.41	0.39	0.36	0.35

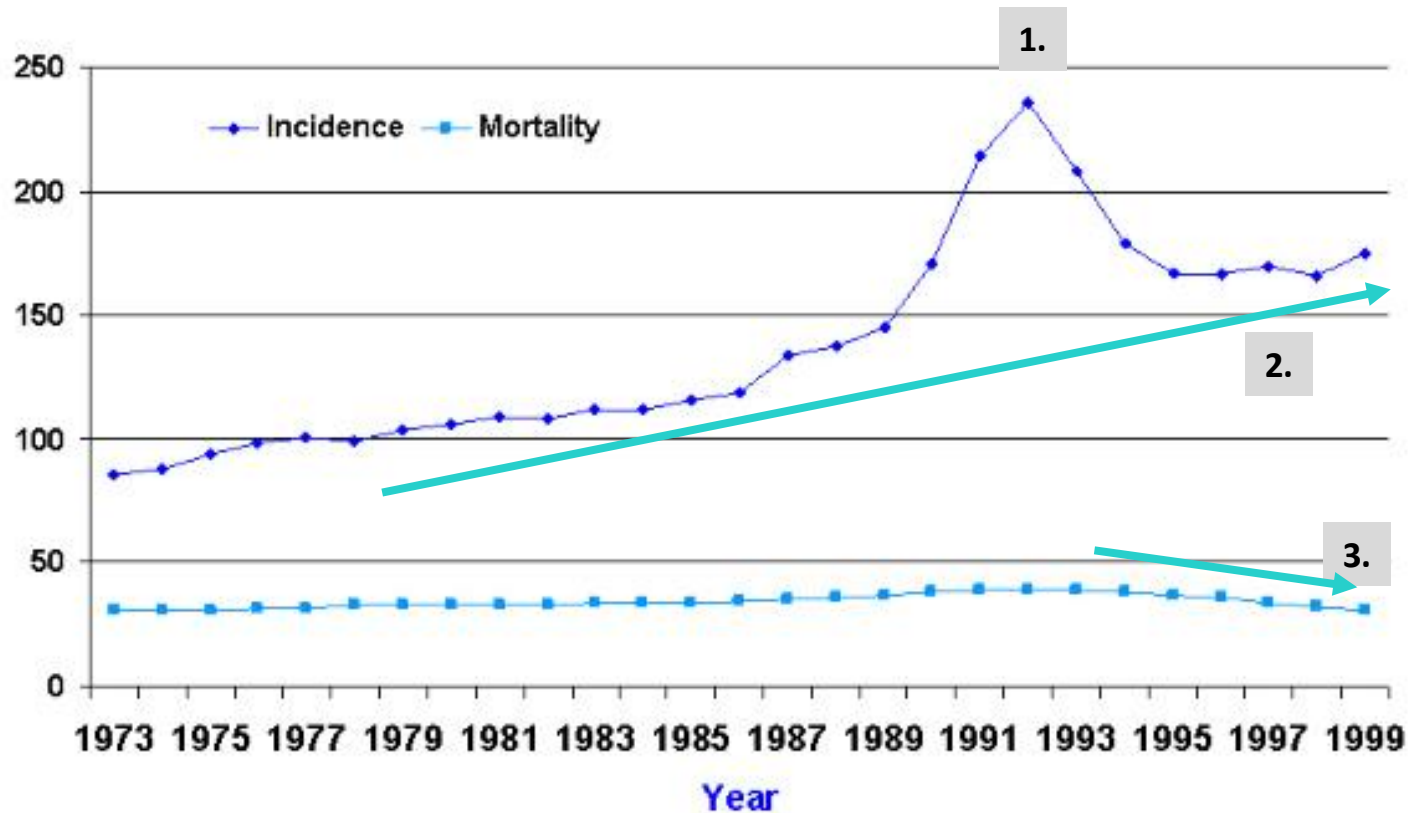
**In the pre-screening era,
1 out of 2 to 3 PCa patients
died of their disease**

¹ The ratio of mortality to incidence in each country, by time period.

Then PSA was introduced ...



Then PSA was introduced ...



What we all know about PSA?

- It can be used for early detection
- Population based screening:
 - results in stage migration at diagnosis
 - decreases prostate cancer death
 -

Changes of Cancer Mortality

5-Year Rate Changes - Mortality
United States, 2005-2009
All Ages, Both Sexes, All Races (incl Hisp)

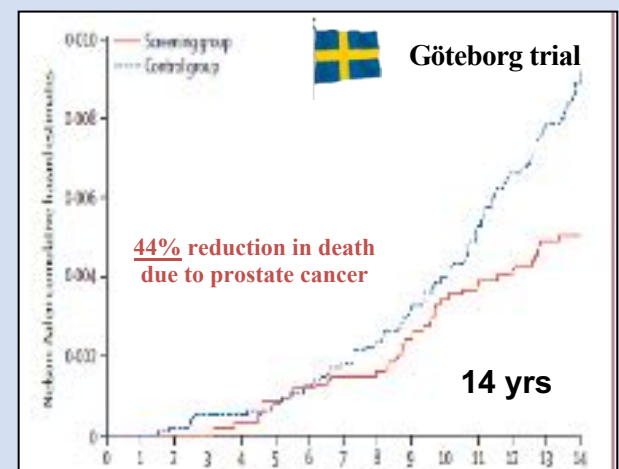
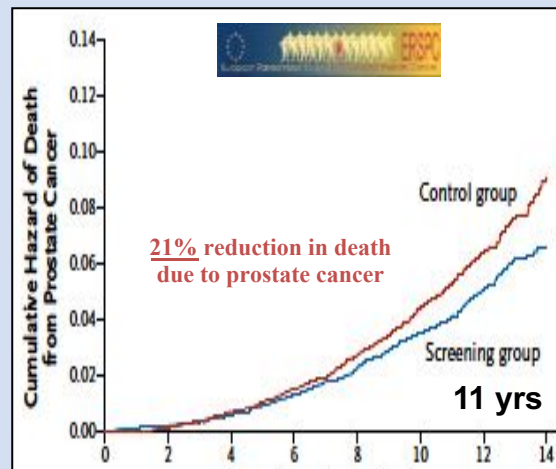
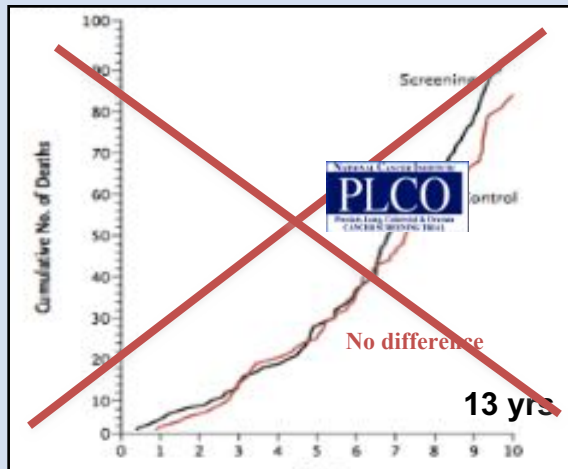


Changes of Cancer Mortality

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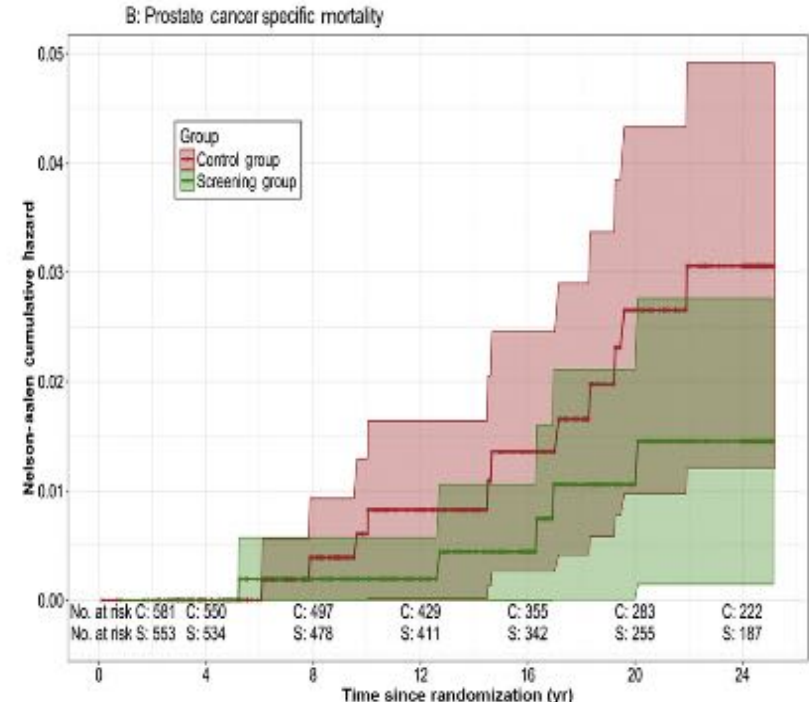
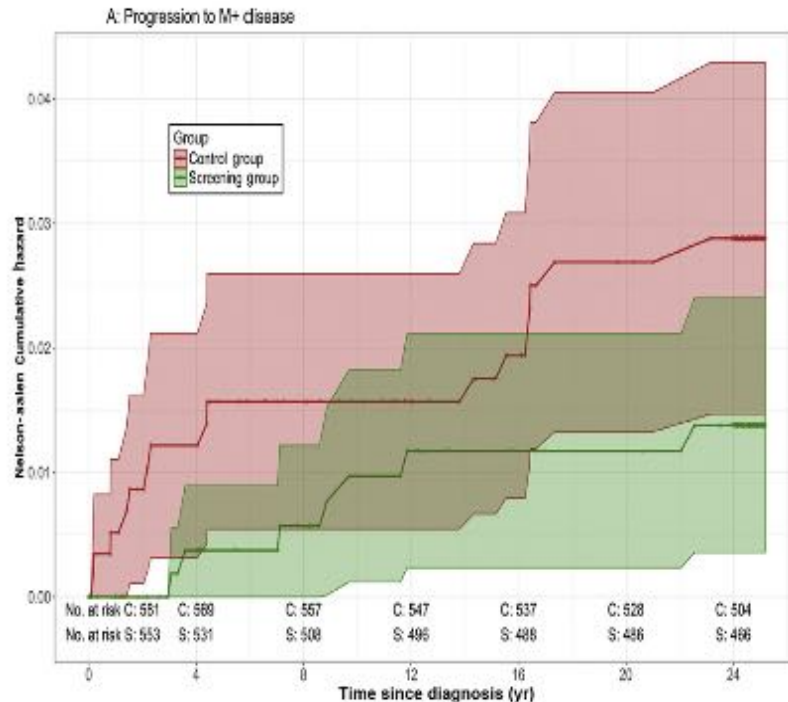
Prostate Cancer Screening RCT's



	PLCO	ERSPC	Göteborg
	76,693 men	182,000 men	20,000 men
	negative	NNS=1055 NNT=37	NNS=293 NNT=12
	52% contamination 30% dilution → underpowered	relaxed screening	---

Screening decreases M+ and PCa death

- longest follow-up, and...+/- no contamination



19y FU R'Dam cohort: - 54% M+ and - 52% PCa Death

Osses et al. Eur. Urol. 2019

What we all know about PSA?

1. It can be used for early detection
2. Population based screening:
 - results in stage migration at diagnosis
 - decreases prostate cancer death
 - ***exposes to over diagnosis and overtreatment***

Same name but different diseases

Yes indeed...



**Incidental prostate
cancer at autopsy: > 50%**

But do not forget...



**11% of all male cancer
deaths are PC related**

Siegel et al., CA Cancer Clin. 2019

What we also know

1. Early detected disease can be cured
2. Treatment of early disease has less side effects : better QoL
 - Less incontinence/impotence after RPr
 - No need of hormones in case of RT
3. Treatment of more advanced disease has more side effects, impacts heavily on QoL and does often not cure
4. Treatment of metastatic disease is extremely expensive



Cost of “too late” detected PCa Care

The total cost of this man with PCa was close to **300.000€** over 18 years.

Surgery
€5,000



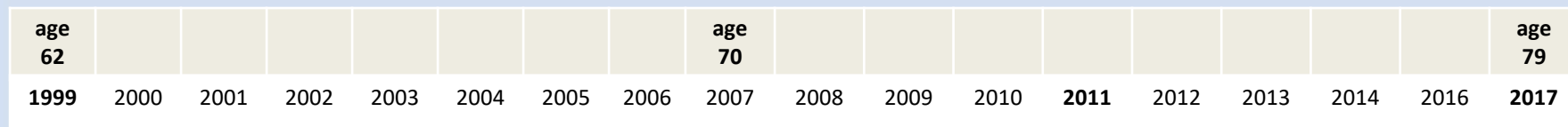
Relapse:
Radiotherapy
€5,000



Medical Castration
€ 11,000

€240,000
for drugs and supportive care
last 2-4 years of life

Radium 223
Cabazitaxel
Enzalutamide
Docetaxel
Abiraterone
Denosumab
Palliative
Radiotherapy



Then, why was PSA testing discouraged?

1. Prostate cancer is said not to be a killing disease:
 - “You will die with, not from PCa”
2. Treatment can lead to unpleasant side effects while, if not detected/treated, you might never experience any complaint
3. PCa diagnosis automatically led to active treatment

Because, we were not able to discriminate between significant and insignificant cancer

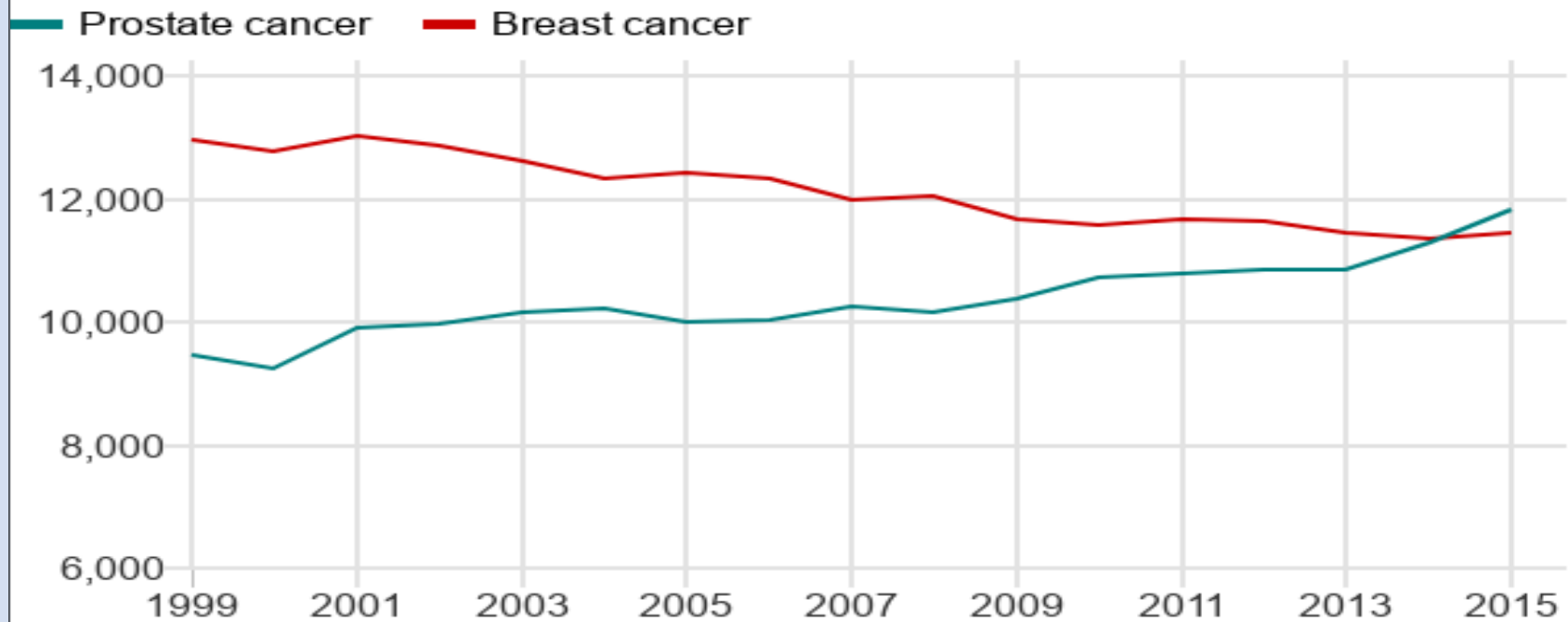
Anti - PSA Propaganda !

What happened with less PSA testing?

UK: PCa death increased by 17% in 10 years

More people now die from prostate than breast cancer

UK prostate and breast cancer deaths, 1999-2015



Source: Prostate Cancer UK

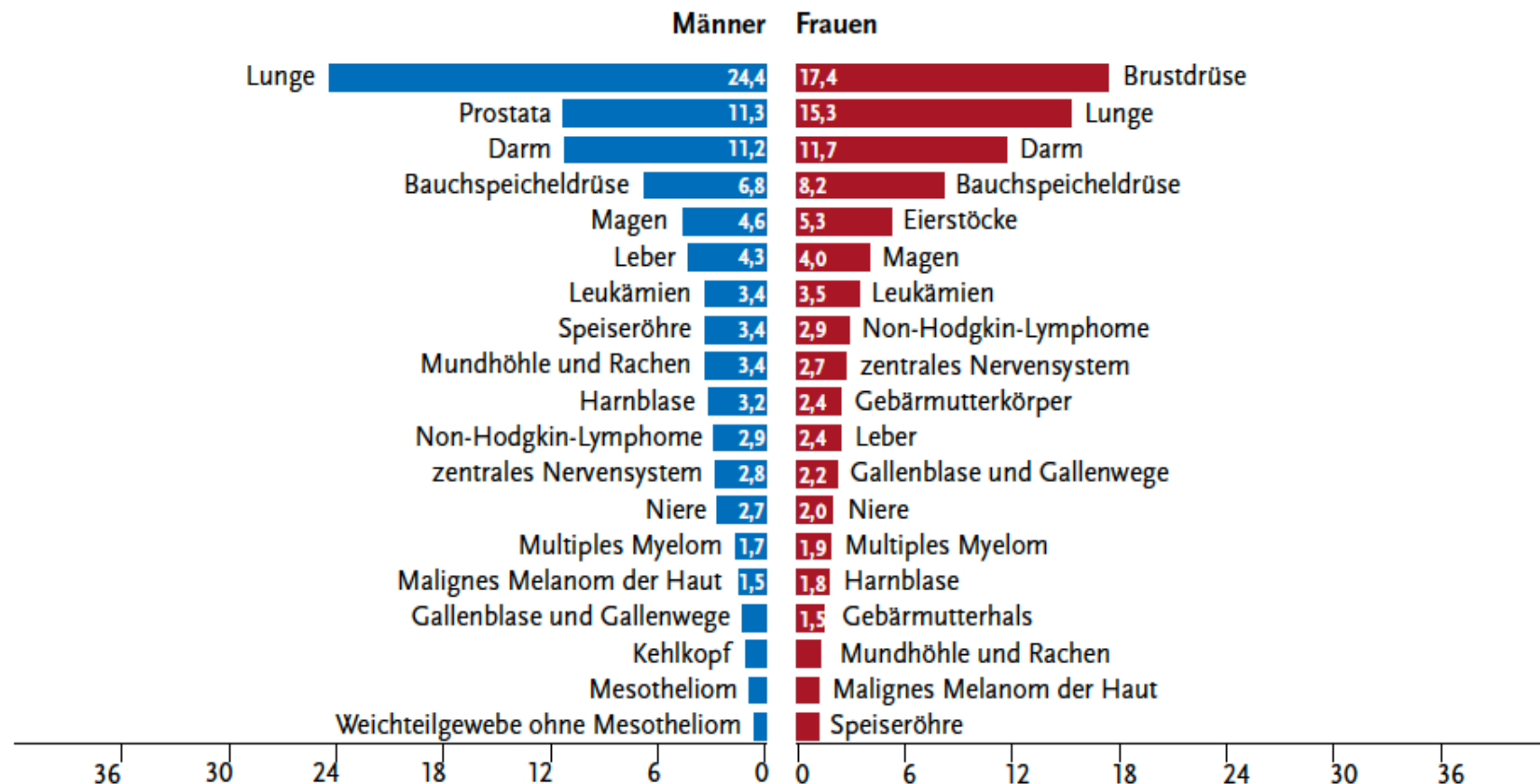
BBC

<http://spcsg.ca/reading-material/prostate-cancer-deaths-overtake-breast-cancer/>

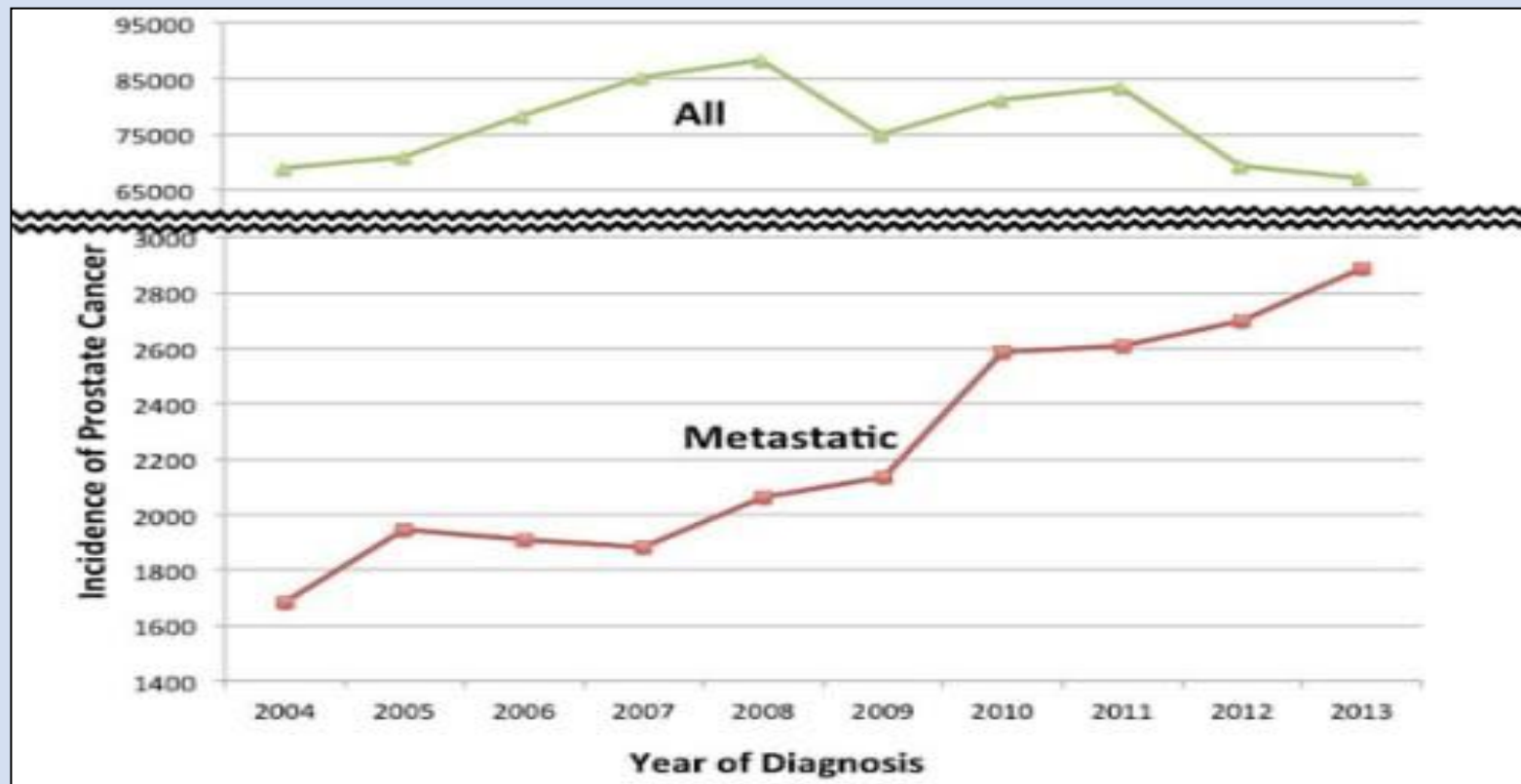
Germany : PCa Mortality ranks 2nd

Abbildung 3.0.2

Prozentualer Anteil der häufigsten Tumorlokalisationen an allen Krebssterbefällen in Deutschland 2014

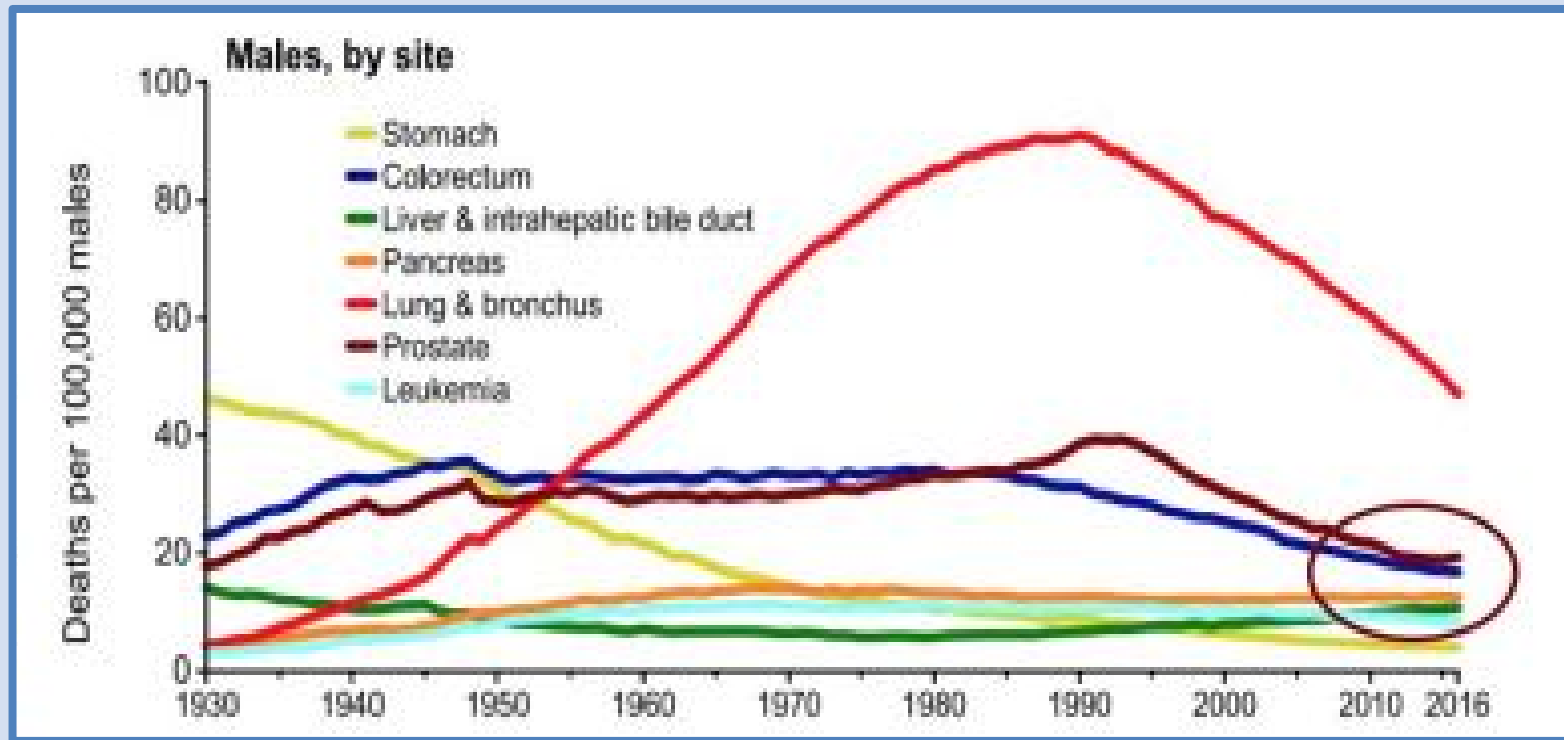


Cases of aggressive prostate cancer on the rise



Weiner A. et al., Prostate Cancer and Prostatic Diseases, 2016

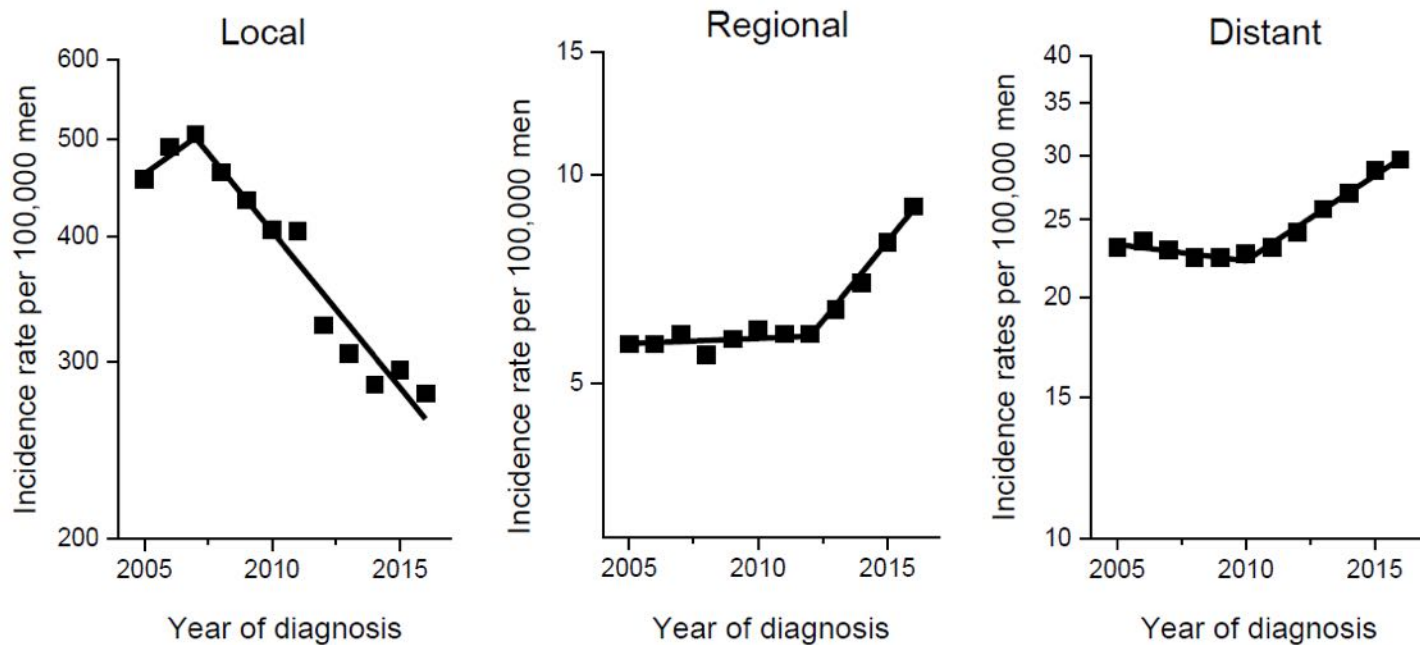
What has been the consequence of less PSA testing?



Overall, the ever decreasing mortality rate from PCa has come to a stop

And we let this happen!

PCa Incidence 5 years after USPSTF recommendations against Screening



- A. Jemal et al. JNCI, 2020
- doi: 10.1093/jnci/djaa068

What happens today with less PSA testing?

1. UK: PCa is diagnosed in more advanced or metastatic stages (>65%)
 - More men are incurable (... will become CRPC)
 - PCa death increased by 17% in 10 years
2. USA: More patients are primarily diagnosed in a metastatic – incurable stage: “reverse migration”
 - Increasing incidence of distant stage PCa from 4 in 2001 to 8% in 2017
 - PCa death increased with 5% in 1 year
3. Germany: T3 at diagnosis 29% (2008), 49% (2017)

Hu et al., JAMA Oncol. 2017
Lenzen-Schulte, Dtsch Arztebl. 2020

And COVID19...?

Butler et al., Cancer 2020
Am. Cancer Society 2020
D.Siegel et al., MMWR 2020

Times have changed !

1. We are able to avoid over diagnosis:

- Better use of PSA: age-related PSA, PSA Density
- Risk Calculators (PCPT and ERSPC) +/- Molecular Biomarkers

- **mp(bp)MRI before** biopsy

Mannaerts et al., Eur. Urol. Oncol. 2018

....decrease of number of biopsies

.....detect more significant and less insignificant cancers



Amin et al., J. Urol. 2020

2. We reduce overtreatment:

- Application of Active Surveillance in 65% of low & intermediate risk



Nomogram to predict disease progression for men on AS

Van Hemelrijck, EAU20

Costs versus Savings

1. PSA: €10/x
2. mpMRI: €136 (bp as good?)
3. Early detected significant PCa
€10-15,000

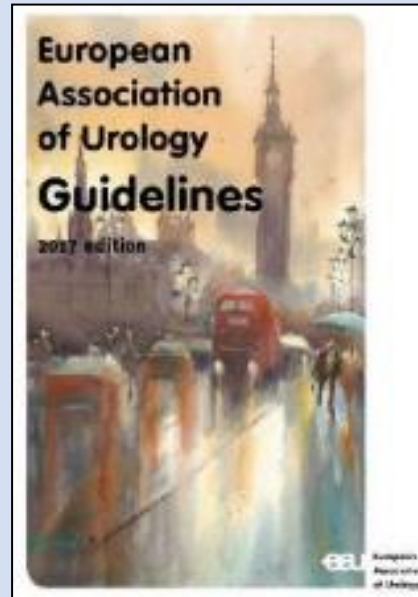
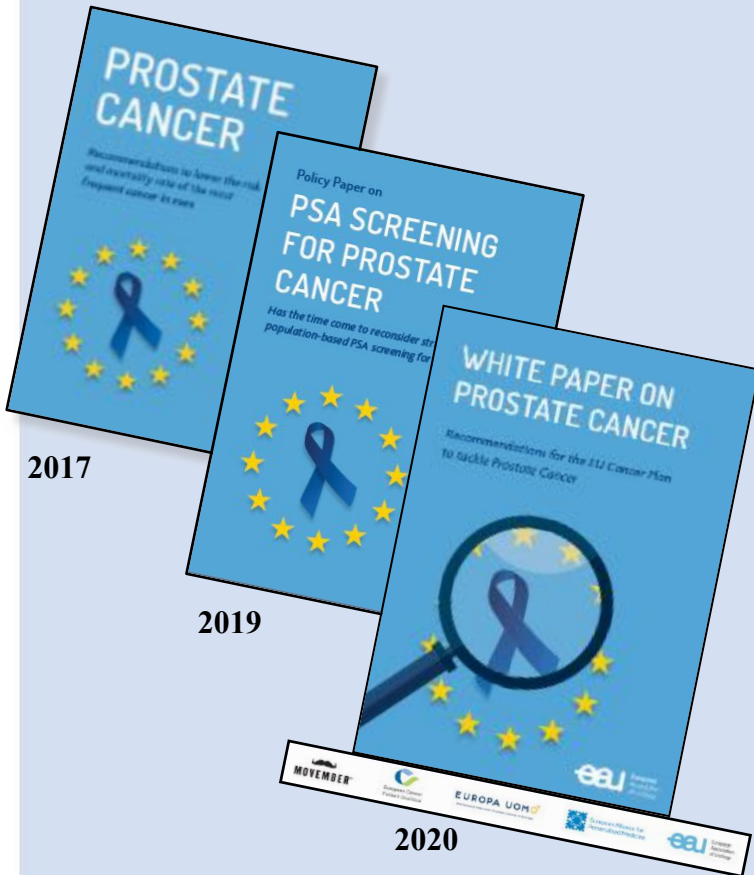
1. Less biopsies, less complications of biopsies and treatments
2. Less over-diagnosis, avoiding over-treatment
3. No costly treatment of castrate refractory disease (€240,000)
4. Less PCa deaths > increased professional life spent
5. Better QoL

In Summary

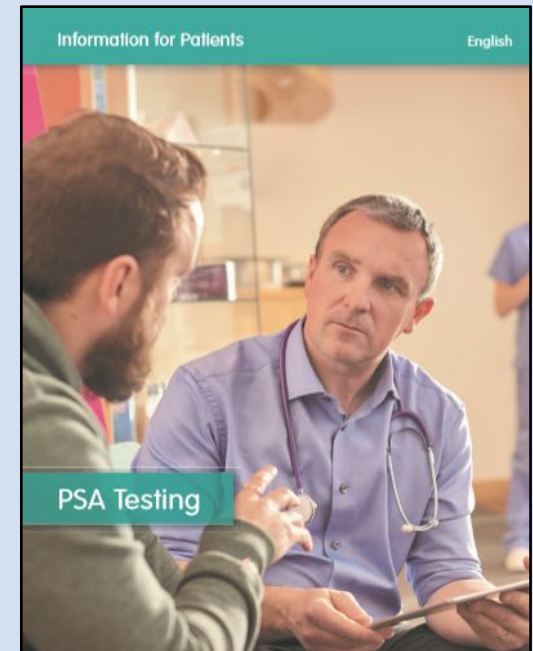
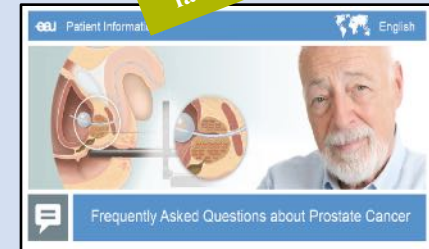
- **Early detection saves lives and saves money**
- **Late detection - increases the risk of dying from PCa**
 - = poor QoL**
 - = more costly (non-curative) treatment**
- **Late stage M+ PCa is very costly + miserable for men**

EAU initiatives

18+
languages



Endorsement of 58 National Societies





Prostate Cancer Screening
Bucharest, Romania 4-6-2019



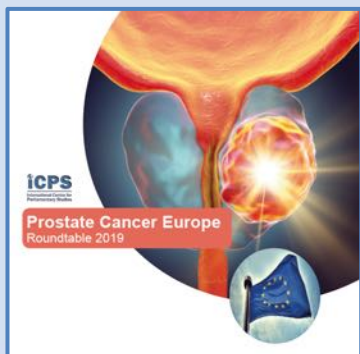
Vlaams Parlement
Freia Saeys



Early Detection WP5 conference
Budapest, Hungary 20-5-2019



2017
2019-
2020(!)

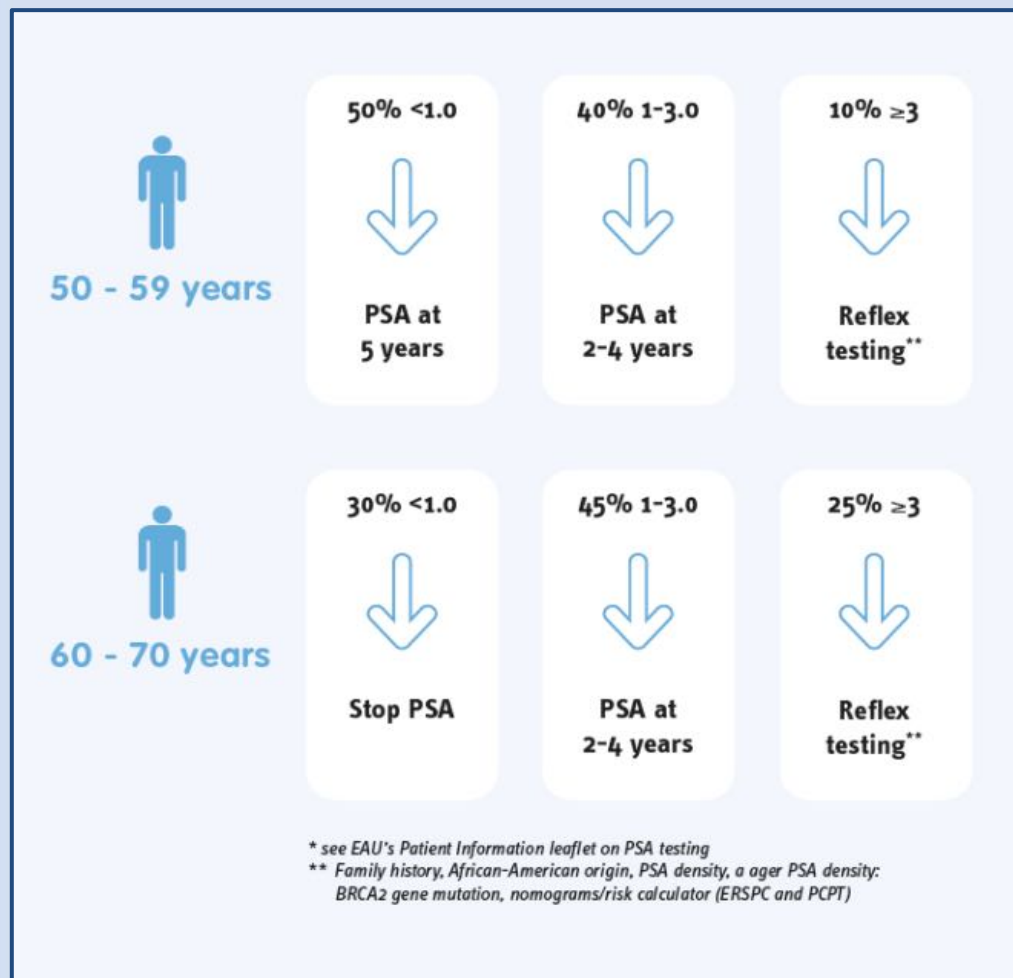


2016
2017
2018
2019
2020(!)



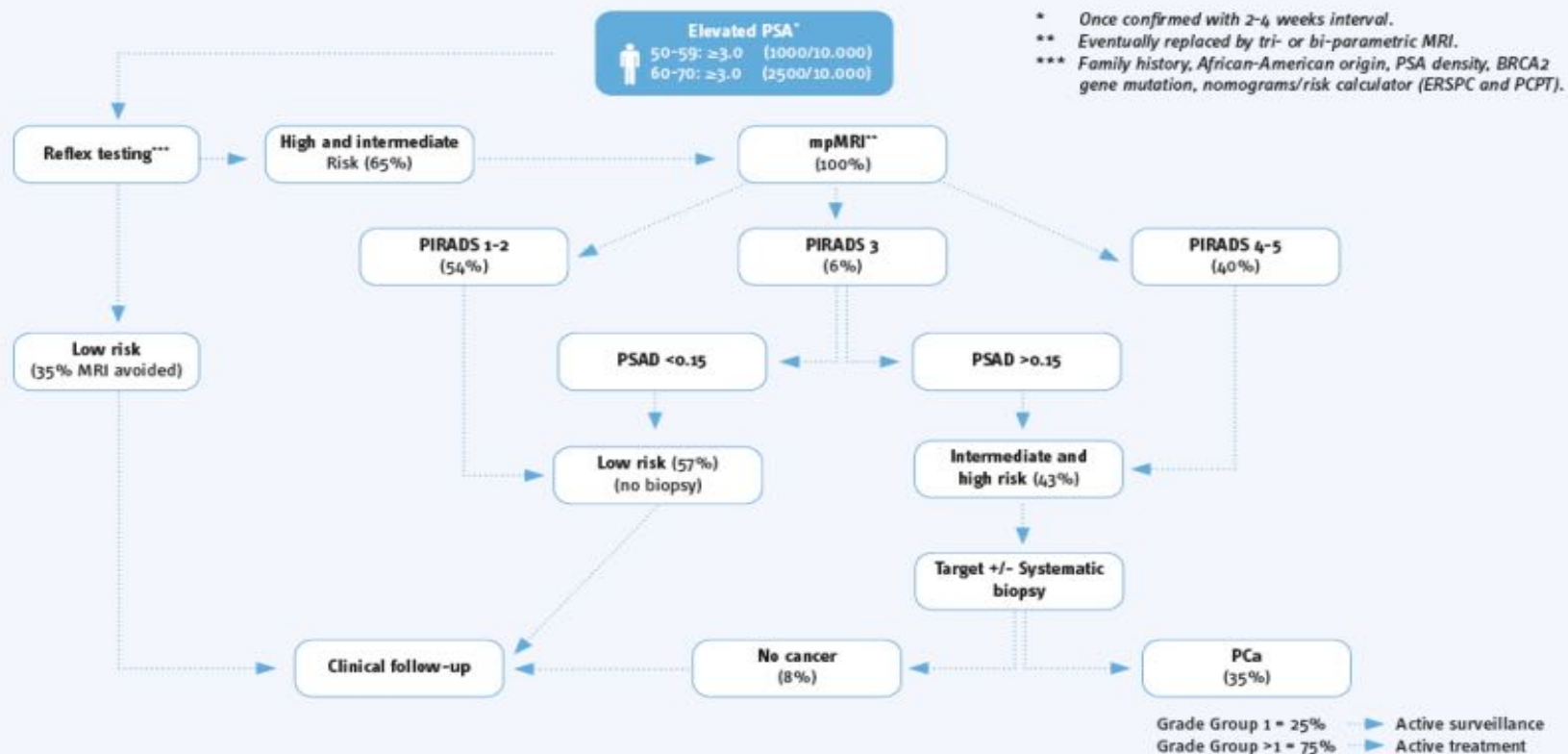
24-03-2020
Croatian Presidency of the
Council of the European Union
PARLIAMENTARY DIMENSION

Risk stratified early detection



Risk Calculators: ERSPC and PCPT





How to eliminate the 2nd MAJOR CANCER KILLER of men in Europe?



The way forward for the EU

Europe's Beating Cancer plan



• Prevention

- Reduce tobacco consumption
- Improve (healthy) diets
- Reduce alcohol consumption
- Increase physical activity
- Reduce obesity
- Increase vaccination against Human papillomaviruses and Hepatitis B
- Avoid excessive exposure to sunlight (including sunbeds)
- Protection from exposure to certain chemicals that can cause cancer
- Other

Please describe

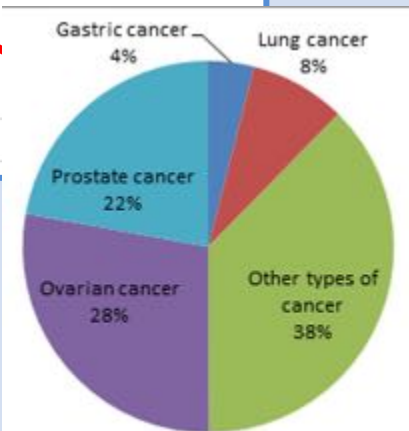
600 character(s) maximum

• Screening and early diagnosis

- Improving the participation to breast, cervical, and colorectal cancer screening
- Extension of screening to other cancer type
- Other

Please describe

600 character(s) maximum



- **Public consultation on European Commission's Plan to Beat Cancer**
We try to include early diagnosis of PCa

Our recommendations



- Use PSA testing properly
 - well-informed men 45-50 till >10 y life expectancy
 - risk calculators, age-related PSA, PSAD, (biomarkers) and MRI
 - Biopsy those at risk for significant cancer
 - Treat actively (RPr or RT) those at risk to die from PCa
 - Manage with active surveillance those with low (and some with intermediate) risk
- ➡ Decrease PCa cost, decrease mortality and improve Quality of Life

Conclusions



1. Early detection saves lives
2. Prostate cancer deaths can (rather easily) be dramatically reduced
3. Our adult male population and GP's need to be informed (WONCA)
 - “If you do not want to die from PCa ...”
 - No uninformed mass screening
 - A well informed healthy men should be offered early detection