Smart Prostate Cancer Screening

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Research Center for EBM

- Noting for disclosure

Introduction

- Prostate cancer will account for ~ 26,000 deaths in the United States in 2017
- The current, age-adjusted mortality of 19 per 100,000 men is a 50% improvement compared with the early 1990s.

Siegel RL, Miller KD, Jemal A. Cancer statistics, 2017. CA Cancer J Clin2017;67(1):7–30.

Cancer Statistics Review, 1975-2013-SEER Statistics. Available at: https://seer.cancer.gov/csr/1975_2013/. Accessed March 7, 2017.

Introduction

- Autopsy studies have identified prostate cancer in:
- ~ 5% of specimens from men younger than 30 to
- ~60% from those aged greater than 79 years.

- The addition of PSA to the digital rectal examination (DRE) significantly improved the sensitivity of screening, and as early as 1992

- The latter half of the 1990s showed declining rates of prostate cancer mortality and advanced disease, but there was a disproportionately larger increase in cancer incidence and use of radical treatment.

Factors affecting PSA

- Age
  - Age-adjusted PSA[1]
    - 40 to 49 - 0.0 to 2.5
    - 50 to 59 - 0.0 to 3.5
    - 60 to 69 - 0.0 to 4.5
    - 70 to 79 years - 0.0 to 6.5

Prostate size:

Percent free/total PSA [2]

25% cutoff: 95% sensitivity & eliminates 20% of unnecessary biopsies

< 15% Suspicious for cancer

> 24% Suggests benign disease

15-24% Grey area

Medications

5-alpha reductase inhibitors

Oral Estrogen agents

LHRH agonists and antagonists

1. Oesterling, JAMA 1993
2. Catalona, JAMA, 1998

Serum PSA as a Screening Test for Prostate Cancer

PSA accuracy in detecting cancer:

Sensitivity	79%
Specificity	59%
PPV	40%
NPV	89%
Overall accuracy	64%

(Catalona, NEJM, 1991)

Concerns????

- Overdiagnosis & Overtreatment

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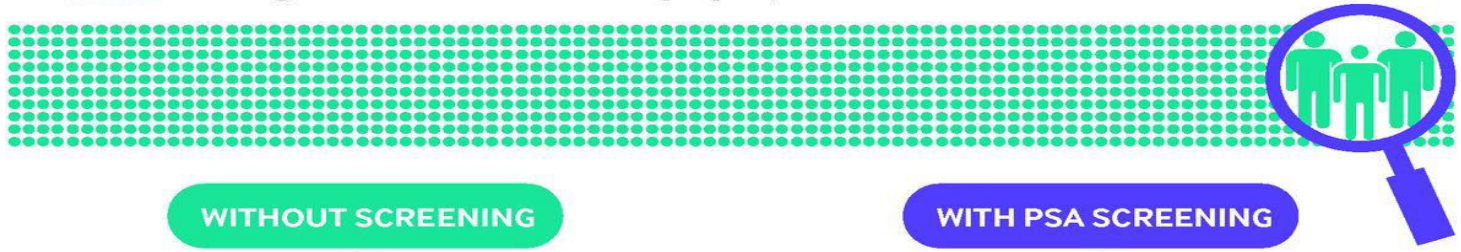
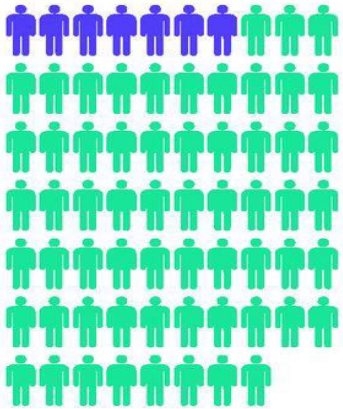
PROSTATE SCREENING IN MEN

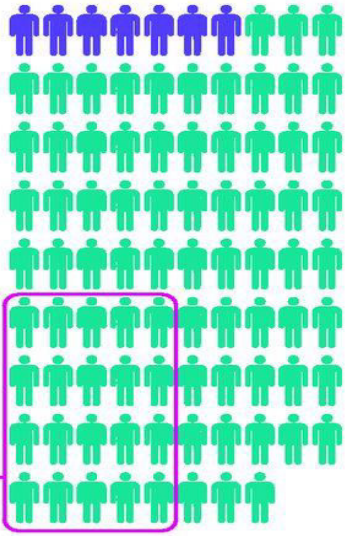
IF THERE WAS A PSA PROSTATE CANCER SCREENING PROGRAMME

Of 1000 men aged 45-80, without any symptoms...



WITHOUT SCREENING	WITH PSA SCREENING
68 will be diagnosed with prostate cancer	88 will be diagnosed with prostate cancer
7 will die of prostate cancer	7 will die of prostate cancer
61 will be treated and survive their cancer	81 will be treated and survive their cancer
	20 of the 81 will be overdiagnosed. These are cancers that would not have caused any harm.*
	0 lives will be saved as a result of screening





DUE TO SCREENING
No lives will be saved and around 20 men will be diagnosed with cancers that would not have caused them any harm

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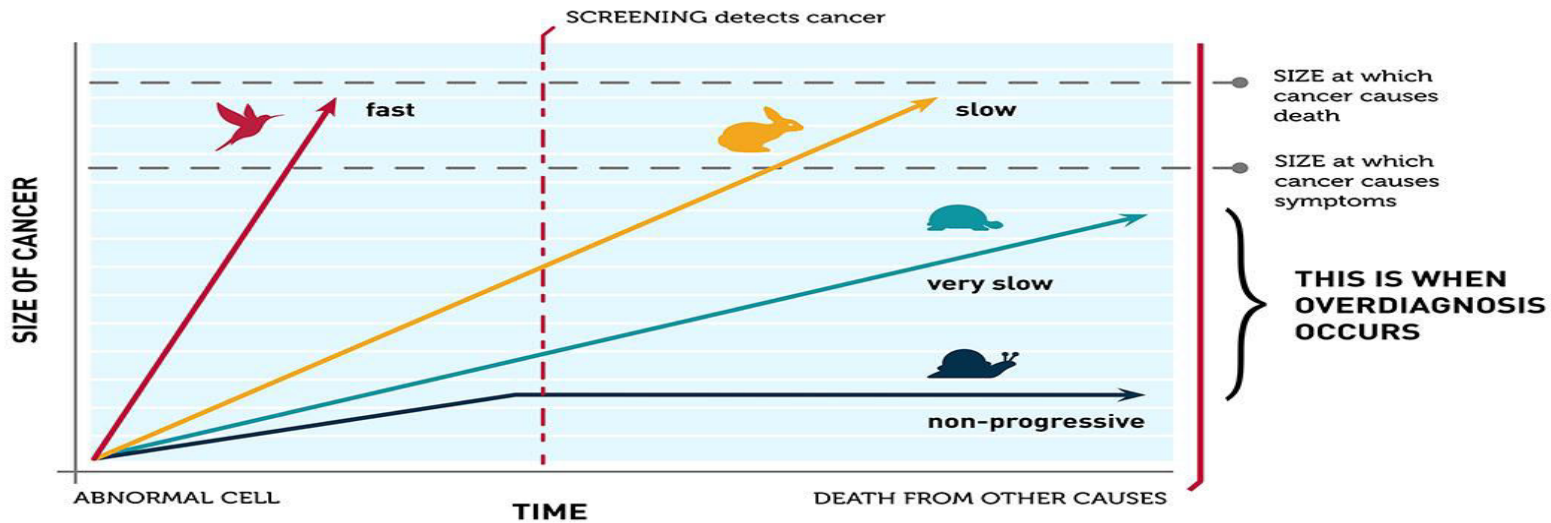
NATIONAL CANCER INSTITUTE

OVERDIAGNOSIS

occurs when screen-detected cancers are either
non-growing or so **slow-growing**
that they would never cause medical problems



Adapted from a figure courtesy of
H. Gilbert Welch, Dartmouth Medical School

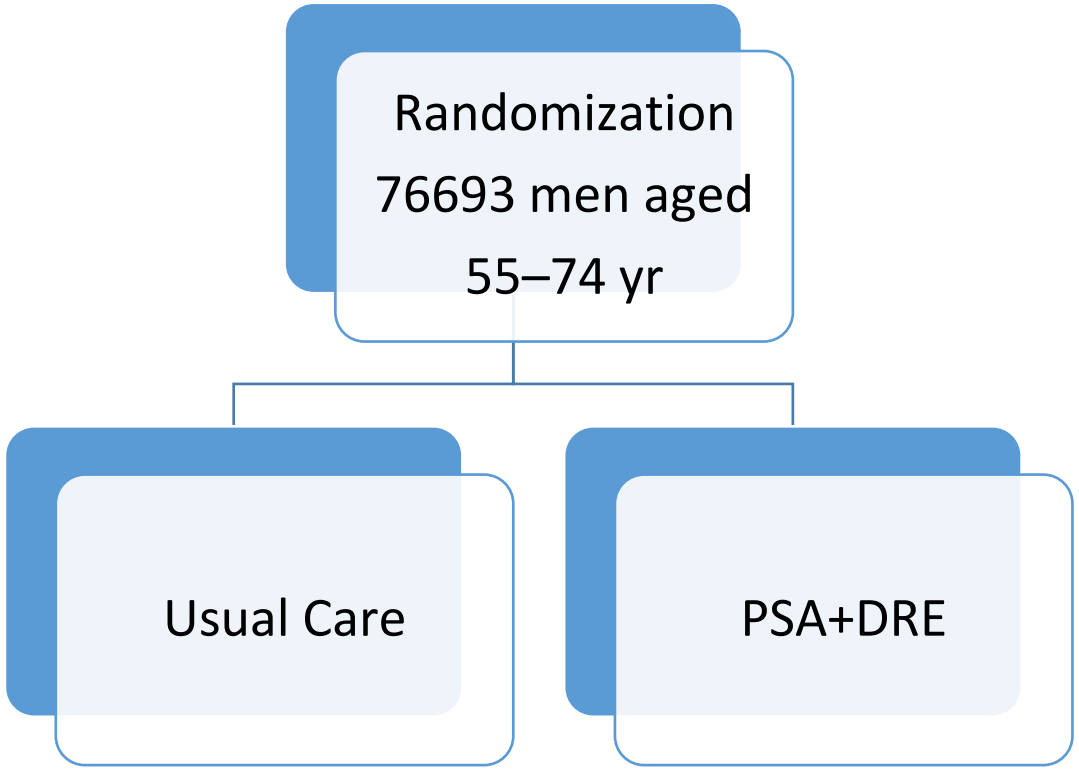
prevention.cancer.gov
NCI Division of Cancer Prevention

Overtreatment

- **Prostate biopsy complications and surgery:**
- Infection
- 10% risk of blood transfusion
- Wound infection
- Rectal injury (<1%)
- Urinary incontinence (~10%)
- Erectile dysfunction
- (variable but common)
- Anesthetic related

Complication of radiation:
Hematuria
Radiation proctitis
    Loose, bloody stools
Urinary retention
Strictures (urethra and ureter)
Erectile dysfunction
Secondary malignancies
    Bladder, rectal, hematological

The PLCO study



Primary Outcome Measure: Pca Specific Mortality

The PLCO study

- After 13 years of follow-up, the investigators did not find a statistically significant difference between the disease-specific mortality rates of the screening and control groups

(RR, 1.09; 95% CI, 0.87–1.36).

In 2012, the US Preventive Services Task Force (USPSTF) discouraged PSA-based prostate cancer screening.

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JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

National Prostate Cancer Screening Rates After the 2012 US Preventive Services Task Force Recommendation Discouraging Prostate-Specific Antigen–Based Screening

Michael W. Drazer, Dezheng Huo, and Scott E. Eggener

- **A trend analysis to showed: Prostate cancer screening significantly declined among men older than age 50 years**

J Clin Oncol. 2015 Aug 1;33(22)

The PLCO study

- High contamination rate of 40% to 52% per year in the control group (74% of men in the usual care arm were screened at least once).
- The estimated mean number of screening PSAs (DREs) was 2.7 (1.1) in the control arm and 5.0 (3.5) in the screened arm.

- In a subset analysis a 44% decrease in the risk of prostate cancer-specific death was observed in men with no or minimal comorbidity assigned to screening compared to control.
- The numbers needed to screen and **treat** to prevent one death were 723 and **5**, respectively.
- This benefit was not found among men with one or more significant comorbidities.

Randomization

182,000 men aged 50–74 yr in 7 European countries

Usual Care

PSA (every 4 years) +DRE

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ERSPC Study

- During a median follow-up of 11 years, the investigators concluded that the PSA-based screening program reduced mortality from prostate cancer by 21%.

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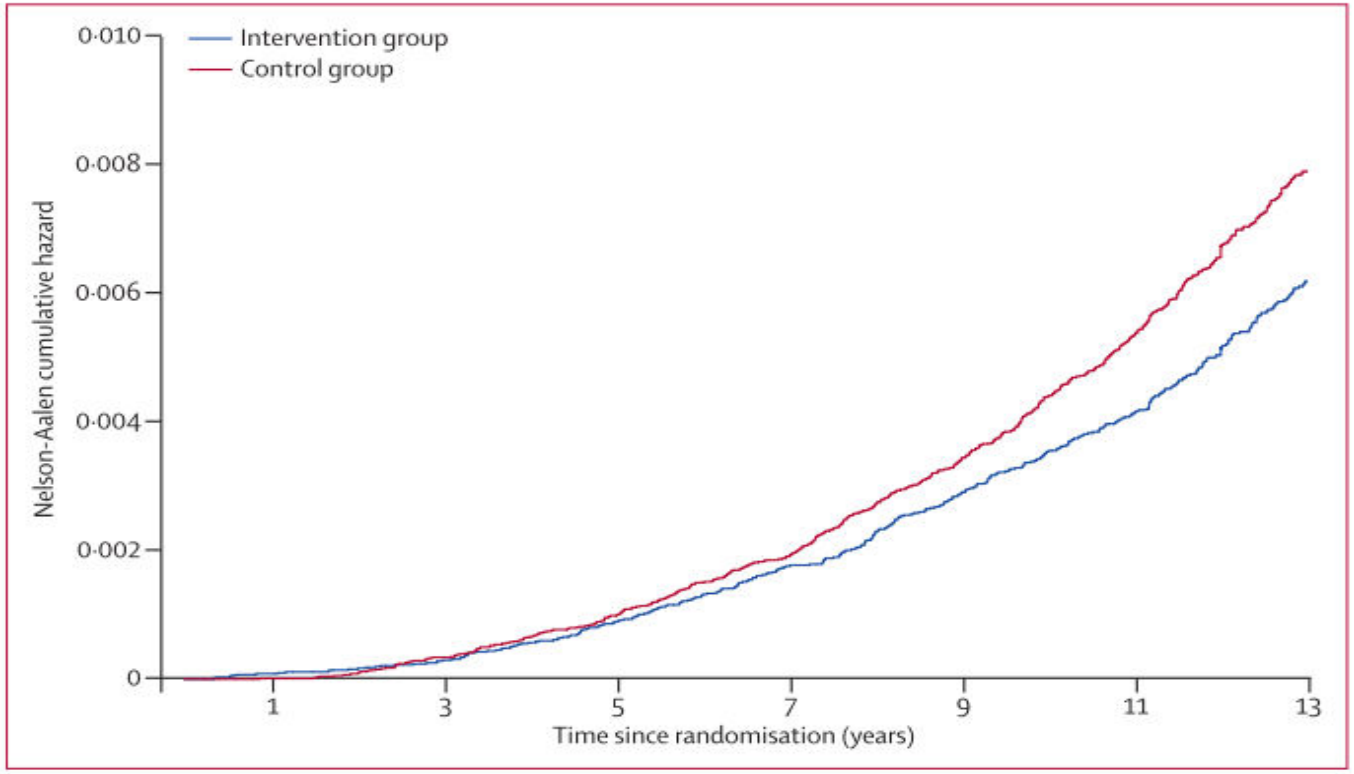
Screening and prostate cancer mortality: results of the European Randomised Study of Screening for Prostate Cancer (ERSPC) at 13 years of follow-up

*Fritz H Schröder, Jonas Hugosson, Monique J Roobol, Teuvo L J Tammela, Marco Zappa, Vera Nelen, Maciej Kwiatkowski, Marcos Lujan, Liisa Määttänen, Hans Lilja, Louis J Denis, Franz Recker, Alvaro Paez, Chris H Bangma, Sigrid Carlsson, Donella Puliti, Arnauld 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**

Lancet 2014; 384: 2027–35

- The third update of the ERSPC trial at 13 years' follow-up confirms the widely quoted figure of a substantial 21% reduction in prostate-cancer mortality



Lancet 2014; 384: 2027–35

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ERSPC Study

- **This extended follow up, showed that the number needed to screen and to treat is decreasing, and is now below the number needed to screen**

	Number needed to screen	Number needed to treat
9 years of follow-up	1410	48
11 years of follow-up	979	35
13 years of follow-up	781	27

ERSPC Study

- The control patients were far more likely to receive initial treatment with androgen-deprivation monotherapy for equivalent risk disease, a very inferior treatment compared with radiation plus androgen-deprivation therapy.
- Some of this 21% difference between screened and control patients might be attributable to increased prostate-cancer mortality in the control group

Summery

- The contradictory results of PLCO and ERSPC can be explained by high rates of PSA testing in the United States around the study period contaminating the control arm.
- Contamination in PLCO has been estimated to be as high as 90%.
- In addition, participant survey data reveal that when considering the 3 years before PLCO randomization, the control patients had more cumulative PSA testing than those assigned to screening.
- **In contrast, contamination in ERSPC is estimated to be 23% to 40%**

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Conclusion

- **Controversy goes on!**
- **Mass screening of PCa is not indicated.**

Overdiagnosis

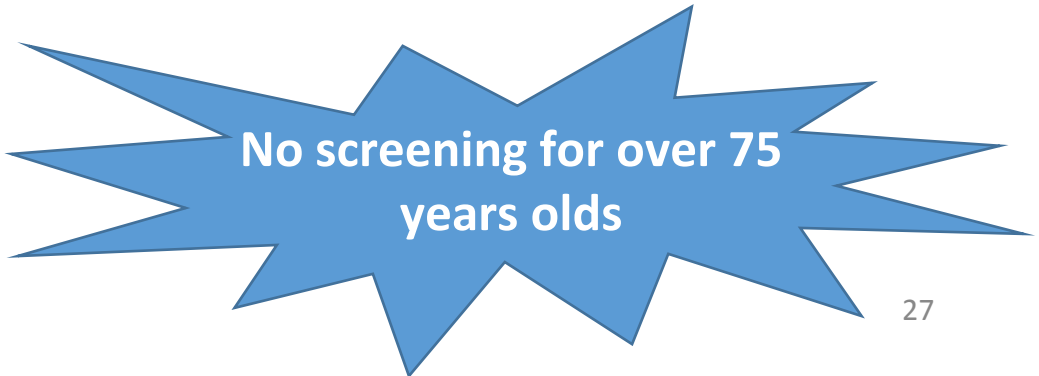
- The proportion of all screen-detected prostate cancer in the United States during 1988 to 2000 that was overdiagnosed was estimated to be:

22.9% (SCANS), 28.0% (PSAPC),
and 42.0% (MISCAN-PRO)

Regardless of the value of the lead time, the relatively high probability for the overdiagnosis of prostate cancer

Cont.

- Estimates of overdiagnosis depend on age and screening interval screening at older ages was associated with a higher estimated overdiagnosis
- Longer interval between screening was associated with a lower estimated frequency of overdiagnosis.



Kaiser Permanente EPC/University of Arizona.Prostate Cancer Screening Overdiagnosis

Cont.

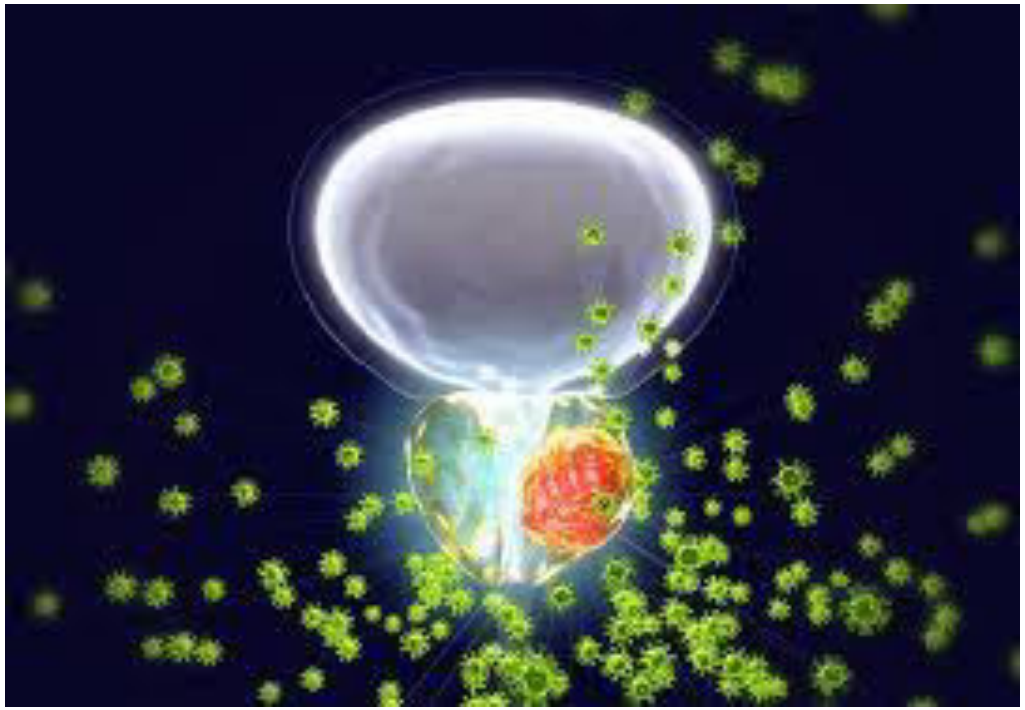
- **There is several modeling studies for screening.**
- **Modeling** studies suggested that raising the PSA threshold, lengthening the interval of screening, and lowering the age to stop screening would all reduce the frequency of overdiagnosis.

- *No screening strategy can eliminate the problem of overdiagnosis*.

Kaiser Permanente EPC/University of Arizona.Prostate Cancer Screening Overdiagnosis

Cont.

- Factors that affect overdiagnosis such as
- age,
- PSA level,
- clinical stage of the cancer,
- Gleason score,
- and patient’s comorbidities,



Overtreatment prevention

- Less aggressive management of screen-detected cancer—greater use of new biomarkers and active surveillance in low-risk cancers— might preserve the benefit of screening while reducing harms.

But

- The use of the data from modeling studies to select men who

could enter active surveillance in clinical populations has not yet been evaluated

Kaiser Permanente EPC/University of Arizona.Prostate Cancer Screening Overdiagnosis

Furthermore:

- Overdiagnosis can result in psychosocial morbidity,
- A burden of testing, and the diagnosis of cancer may have financial implications even beyond increased costs of medical care.
- Given the range of potential sequela from overdiagnosis, the true disutility of overdiagnosis is not known and has not been measured empirically.

- *Therefore, the balance of benefits to harms is, in part, dependent on the (differences) in preferences and values related to avoiding overdiagnosis.*

Kaiser Permanente EPC/University of Arizona.Prostate Cancer Screening Overdiagnosis

2017 USPSTF Screening Update

- **Men ages 55–69**
- The decision about whether to be screened for prostate cancer should be an individual one. The USPSTF recommends that clinicians inform men ages 55 to 69 years about the potential benefits and harms of prostate-specific antigen (PSA)–based screening for prostate cancer. Screening offers a small potential benefit of reducing the chance of dying of prostate cancer. However, many men will experience potential harms of screening, **including false-positive results that require additional workup, overdiagnosis and overtreatment, and treatment complications such as incontinence and impotence.** The USPSTF recommends individualized decision-making about screening for prostate cancer after discussion with a clinician, so that each man has an opportunity to understand the potential benefits and harms of screening and to incorporate his values and preferences into his decision.
- **Recommendation Grade C** (Offer or provide this service for selected patients depending on individual circumstances)

- **Men age 70 and older**
- **The USPSTF recommends against PSA-based screening for prostate cancer in men age 70 years and older.**
- **Recommendation Grade D** (Discourage the use of this service)

https://screeningforprostatecancer.org/#utm_source=google&utm_medium=cpc&utm_campaign=recommendation&utm_term=branded&utm_content=draft_uspstf

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EUROPEAN UROLOGY 71 (2017) 618–629

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

European Association of Urology

Guidelines

EAU-ESTRO-SIOG Guidelines on Prostate Cancer. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent

Nicolas Mottet[a,*], *Joaquim Bellmunt*[b,c], *Michel Bolla*[d], *Erik Briers*[e], *Marcus G. Cumberbatch*[f], *Maria De Santis*[g], *Nicola Fossati*[h,i], *Tobias Gross*[j], *Ann M. Henry*[k], *Steven Joniau*[l], *Thomas B. Lam*[m,n], *Malcolm D. Mason*[o], *Vsevolod B. Matveev*[p], *Paul C. Moldovan*[q], *Roderick C.N. van den Bergh*[r], *Thomas Van den Broeck*[l], *Henk G. van der Poel*[s], *Theo H. van der Kwast*[t], *Olivier Rouvière*[q], *Ivo G. Schoots*[u], *Thomas Wiegel*[v], *Philip Cornford*[w]

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Table 4 – Guidelines for screening and early detection

Recommendation	LE	GR
Do not subject men to PSA testing without counselling them about the potential risks and benefits.	3	B
Offer an individualised risk-adapted strategy for early detection to a well-informed man with a good performance status and a life expectancy of at least 10–15 yr.	3	B
Offer PSA testing in men at elevated risk of having PCa: • Men aged >50 yr • Men aged >45 yr and a family history of PCa • African American men aged >45 yr • Men with a PSA level >1 ng/ml at age 40 yr • Men with a PSA level >2 ng/ml at age 60 yr	2b	A
Offer a risk-adapted strategy (based on initial PSA level), with follow-up intervals of 2 yr for those initially at risk: • Men with a PSA level >1 ng/ml at age 40 yr • Men with a PSA level >2 ng/ml at age 60 yr Postpone follow-up to 8 yr in those not at risk.	3	C
Decide on the age at which early diagnosis of PCa should be stopped based on life expectancy and performance status; men who have a life expectancy <15 yr are unlikely to benefit.	3	A

GR = grade of recommendation; LE = level of evidence; PCa = prostate cancer; PSA = prostate-specific antigen.


فرش