Prostate Cancer Screening: Perspectives in 2023

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MedNet21
Center for Continuing Medical Education

The Ohio State University Wexner Medical Center

Case presentation

- A 45 year old healthy Black male presents to your office for his annual health assessment.
- He denies any urinary symptoms and has no family history of cancer.
- Should we screen him for prostate cancer?

Objectives

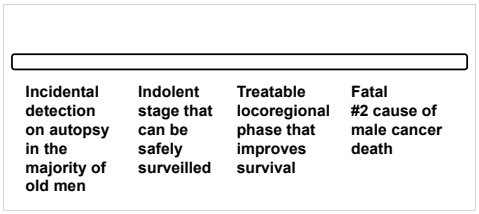
- What is prostate cancer screening?
- Why should we screen for prostate cancer?
- Who, when, how, and where should we screen for prostate cancer?

Prostate cancer is important!

- #1 most common cancer
- #2 cause of male cancer death
- In the US (2023):
  - 288,300 cases
  - 34,700 deaths

American Cancer Society Statistics, CA Cancer J Clin 2023, non-melanoma skin not included

Prostate cancer is a spectrum



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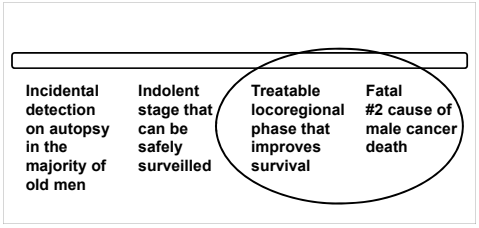

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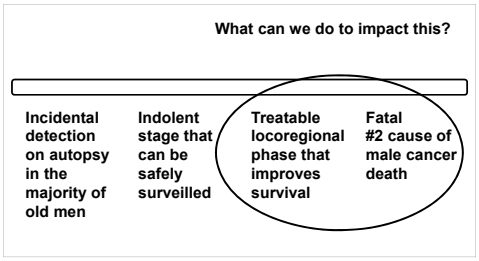

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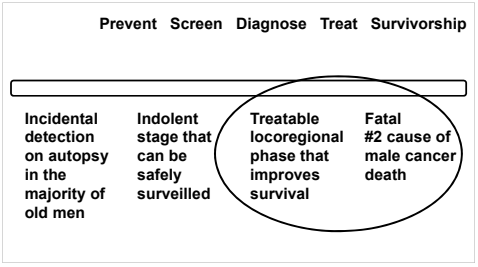

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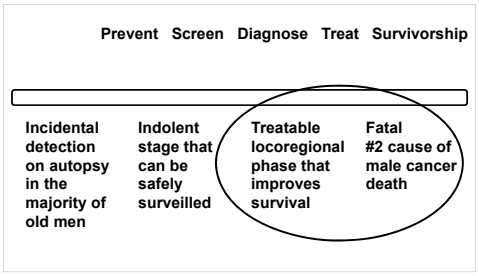
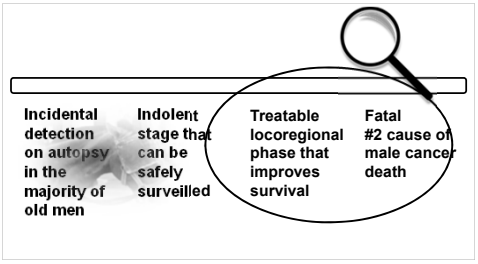


Screening



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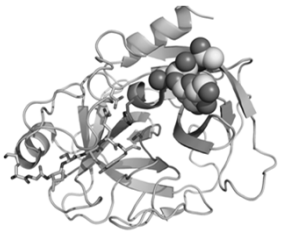
Screening = PSA*



*Pretty Much

Modern PSA screening is based on large part on certain key events…

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PSA: Historical Perspective

1960
1970
1980
1990
2000
2012
2019

Flocks identifies that the human prostate has unique antigens

Rao et al. BJU Int 2008

PSA: Historical Perspective

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Hara identifies a unique antigen in the semen

Rao et al. BJU Int 2008

PSA: Historical Perspective

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Ablin discovers PSA – prostate specific antigen

Rao et al. BJU Int 2008

PSA: Historical Perspective

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Wang & Chu improve our understanding of PSA and optimize clinical testing

Rao et al. BJU Int 2008

PSA: Historical Perspective

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Stamey publishes a clinical report on the use of PSA in the New England Journal of Medicine
-correlation with stage and tumor volume
-correlation with treatment response

Rao et al. BJU Int 2008

PSA: Historical Perspective

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FDA approval of PSA for the early detection of prostate cancer
Numerous nonrandomized studies supporting its use

Rao et al. BJU Int 2008

PSA: Historical Perspective

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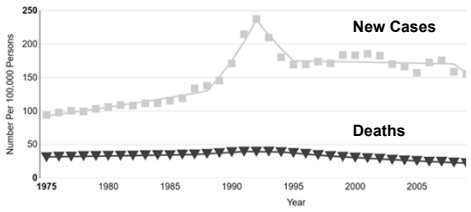
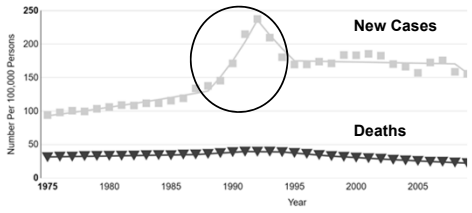
Widespread screening and treatment

What has PSA done?



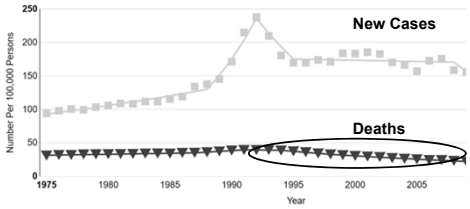
SEER Registry Public Data

Screening dramatically increased incidence



SEER Registry Public Data

Prostate cancer mortality has halved

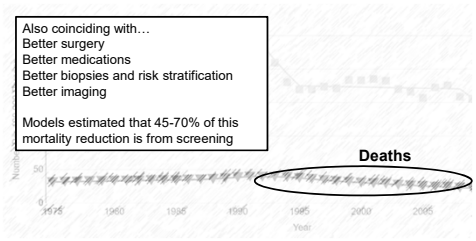


SEER Registry Public Data

Prostate cancer mortality has halved

Also coinciding with…
Better surgery
Better medications
Better biopsies and risk stratification
Better imaging

Models estimated that 45-70% of this mortality reduction is from screening



Cancer Causes Control. 2008 Mar;19(2):175-81. Epub 2007 Nov 20.

PSA has profoundly impacted medicine

Prostate cancer is the most common cancer in men and the second most common cause of cancer death in men

Models estimated that 45-70% of a two-fold reduction in prostate cancer mortality relates to PSA screening

Cancer Causes Control. 2008 Mar;19(2):175-81. Epub 2007 Nov 20.
American Cancer Society Statistics, CA Cancer J Clin 2023, non-melanoma skin not included

The END

What's the problem – why not just do it??
Why are we even talking about this?

PSA: Historical Perspective

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FDA approval of PSA for the early detection of prostate cancer
Numerous nonrandomized studies supporting its use

Rao et al. BJU Int 2008

PSA: Historical Perspective

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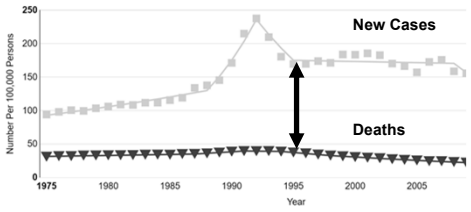
USPSTF Grade I – insufficient evidence for PSA

A gap between incidence and mortality



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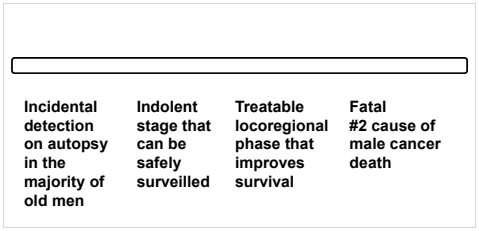

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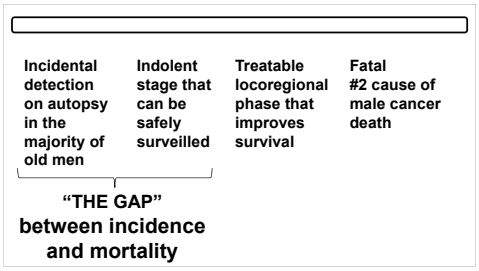


Prostate cancer is a spectrum

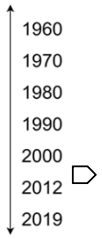
PSA has profoundly impacted medicine

Prostate cancer is the most common cancer in men and the second most common cause of cancer death in men

We were screening many men and treating most men with prostate cancer with expensive and toxic treatments, without high-level evidence of benefit

American Cancer Society Statistics, CA Cancer J Clin 2019, non-melanoma skin not included

PSA: Historical Perspective



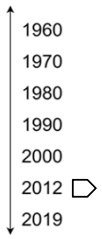
2 major randomized screening studies reported in the New England Journal of Medicine

Schroder et al NEJM 2009, Andriole et al NEJM 2009

2009 Revelations

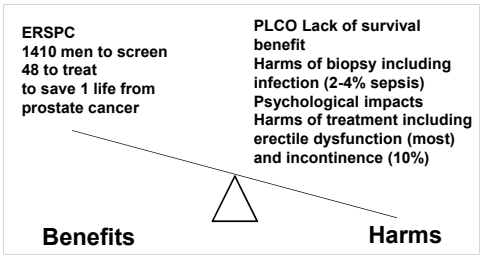
Trial	PLCO	ERSPC
Location	US	Europe
Participants	76,685 men 55-74	162,243 men 55-69
Intervention	Annual PSA	PSA every 4 years
Finding	**No impact** on prostate cancer mortality	Reduction of 1 prostate cancer death per 1410 screened and 48 treated

PSA: Historical Perspective

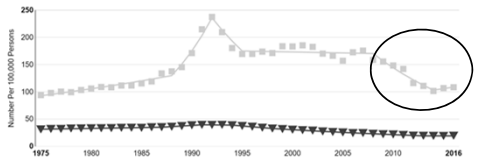


USPSTF – grade "D" recommendation, the harms outweigh the benefits without regard to age, race, family history

The USPSTF Decision



Reduced screening decreased incidence



We have MANY studies that show that screening, biopsies, diagnoses of prostate cancer decreased following the 2012 recommendations.

This was even more pronounced in high-risk groups (African American men, those with a family history)

Eapen Curr Op Urol (2017)

USPSTF Skepticism

- The USPSTF had no representation from any doctor who actually deals with prostate cancer (urologist, medical oncologist, radiation oncologist).
- Those who dealt with the disease had concerns…

What about this?

Deaths per 100,000

Incidence of more aggressive cancer declined by 25%
→ What will happen to these undetected cases??

Prostate biopsy series started showing a 33% higher rate of more aggressive disease
→ Can these patients be as successfully managed??

Metastatic prostate cancer increased by 92% from 2004 to 2013 and median PSA at presentation of doubled
→ Does this relate to changes in screening practice??

Barocas J Urol (2015); Banerji J Urol (2016); Weiner Pros Can Pros Dis (2016)

PLCO Death Knell

1960
1970
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We realize 90% of men in the non-screening arm of the PLCO had a PSA before or during the trial (Shoag et al. NEJM 2016)

90% rate of contamination in PLCO trial

Shoag NEJM (2016)

2019 Revelations

Trial	PLCO	ERSPC
Location	US	Europe
Participants	76,6[illegible]74	162,243 men 55-69
Intervention	Annua[illegible]	PSA every 4 years
Finding	No im[illegible] pro[illegible]ce mortality	Reduction of 1 prostate cancer death per ~~1410~~ 570 screened and ~~48~~ 18 diagnosed

A changing tide

1960
1970
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2019

USPSTF – grade "C" recommendation, shared decision making on PSA screening

In 2023 screening is looking better and better

Trial	ERSPC Pilot	Goteborg	ERSPC Rotterdam	ERSPC
Location	Rotterdam	Goteborg	Netherlands	Europe

Hugosson Eur Urol (2019), Franlund J Urol 2022, De Vos Eur Urol 2023, Hugosson Eur Urol (2018)

In 2023 screening is looking better and better

Trial	ERSPC Pilot	Goteborg	ERSPC Rotterdam	ERSPC
Location	Rotterdam	Goteborg	Netherlands	Europe
Follow-up	19 years	22 years	21 years	16 years
Number to screen	101	221	246	570
Number to diagnose	3	9	14	18

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In 2023 recommendations against screening are looking worse

Since 2010 the incidence of metastatic prostate cancer has increased by 5-7% annually

Desai JAMA Netw Open (2022)

In 2023 diagnosis has also changed

- Using MRI following elevated PSA:
  - reduces biopsy by 28% and insignificant cancer by 13%
  - increases significant cancer diagnosis by 12%
- Additional biomarkers may
  - reduce biopsy rates by 24-34%
- Biopsy via the perineum (transperineal) rather than rectum (transrectal) reduces post-biopsy infection
  - From 2-4% (transrectal) to <<1%

Kasivisvanathan NEJM (2018), Sathianathen J Urol (2018), Stefanova J Urol (2019)

By 2023 treatment has also changed

- Multiple large studies now show appropriate patients have a clear benefit to treatment (SCPG4, PROTECT)
- Active surveillance is being increasingly employed for low-risk cases – overtreatment reduced
- Surgery and radiation advances continue to reduce morbidity

Butler NEJM (2019), Wilt NEJM (2016), Hamdy NEJM (2016), Bil-Axelson NEJM (2018)

Earlier screening

We can stratify men by a baseline PSA in their 40s:

PSA > 1.7 ng/dL - 8.7 odds of lethal prostate cancer

82% deaths in those with PSA above median (0.7 ng/dL)

In African American men, PSA > 1.7 ng/dL - odds 174 for aggressive prostate cancer compared to those under 0.7 ng/dL

Preston JCO (2016), Preston Eur Urol (2019)

Increasing recognition of high-risk groups

Certain men are at high risk

- African American men
  - incidence 60% higher, death rate is double
- BRCA / Lynch
  - 2-6 fold risk
- Family history
  - Father or brother – 2 fold risk
  - 2 first degree relatives – 5 fold risk

Only 4% in PLCO were African American and 7% had a family history. We can move up discussions of screening to 40 (multiple guidelines are supportive).

Segal Ca J Clin (2019) Schroder NEJM (2009) Steinberg GD Prostate (1990) Castro JCO (2013)

Principles of a good screening test

1. Important disease…second leading cause of cancer death in men
2. Acceptable treatment…improving
3. Access to diagnosis and treatment…improving
4. Recognizable early stage…improved understanding of indolence
5. Suitable test…improving use of tests other than PSA
6. Acceptable test…improving use of MRI, transperineal biopsy
7. Understood natural history…improving
8. Agreed on policy on whom to treat as patients…improving
9. Acceptable cost…generally
10. Continuous process…improving understanding when to start/stop

- Wilson, James Maxwell Glover, Gunnar Jungner, and World Health Organization. "Principles and practice of screening for disease." (1968).

Screening recommendations (Average Risk)

Society	Summary of recommendation
USPSTF	Men 55-69 shared decision making
AUA	Men 45-69 shared decision making
NCCN	Men 45-75 shared decision making
ACS	Men starting at 50 shared decision making
ACP	Men 50-69 shared decision making
AAFP	Men 55-69 shared decision making

Society Websites

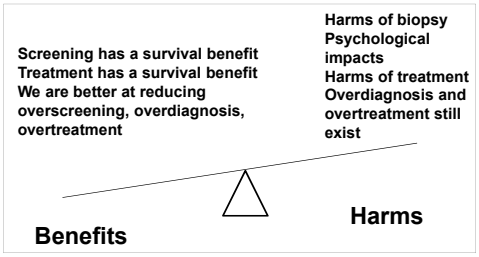
Screening recommendations (High Risk)

Black
Family history
Germline predisposition (e.g. BRCA 2)

Society	Start screening
AUA	40
NCCN	40
ACS	40-45

Society Websites

Shared decision making



Use of the digital rectal exam

- The data doesn't show a benefit for DRE in the *screening* setting
- Optional … but we definitely see many high-grade tumors with a low PSA and abnormal DRE
- It is more valuable in the workup of an elevated PSA

Naji Ann Fam Med (2018)

Practical recommendations

- Discussion regarding screening beginning in the 40s, continue until 70s
  - Focus on younger rather than older
- Interval can be varied based on risk – between 1 and 4 years
  - Yearly may just be the most practical
- Be more vigilant in those at risk (Black, FHx, BRCA)
- Double PSA in those on finasteride (Proscar) or dutasteride (Avodart)
- Repeat the PSA in 4-6 weeks if elevated
- Perform DRE for an elevated PSA
- Do not perform PSA with an acute UTI or recent Foley

Back to the case…

Recommendation: Shared decision making on PSA

Discuss it before you do it, as well as the rationale and limitations. May use a decision aid if visit time is limited.

Back to the case…

Indications for urology referral:

Know your urologist's practice patterns. Err on the side of referring; most of us don't biopsy or subsequently treat unless necessary.

PSA>2 in 40s

PSA>3 in 50s and 60s

PSA>4 in 70s

Abnormal digital rectal exam

Please err on the side of screening and referring Black men, family history & susceptible germlines.

My indications to biopsy are higher but I would order an MRI in many of these men