



## Prostate Cancer Screening: Perspectives in 2023

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*The Ohio State University Wexner Medical Center*

**MedNet21**  
Center for Continuing Medical Education



## 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

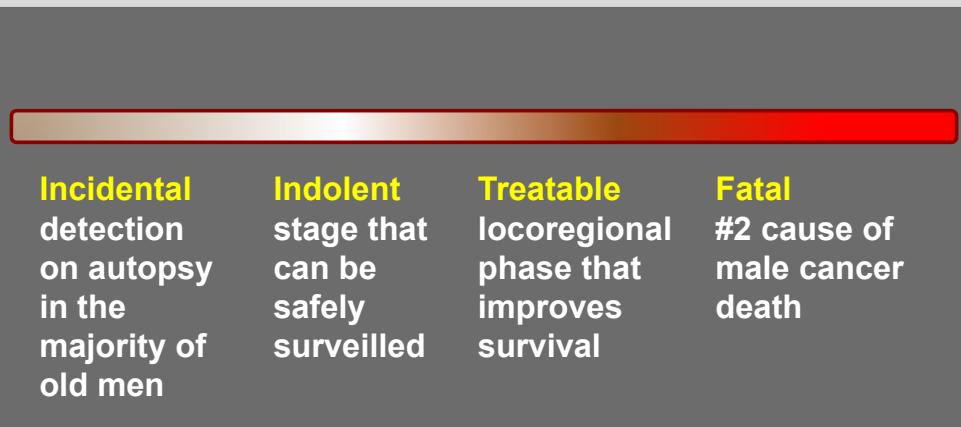
- What is prostate cancer screening?
- Why should we screen for prostate cancer?
- Who, when, how, and where should we screen for prostate cancer?

## Prostate cancer is important!

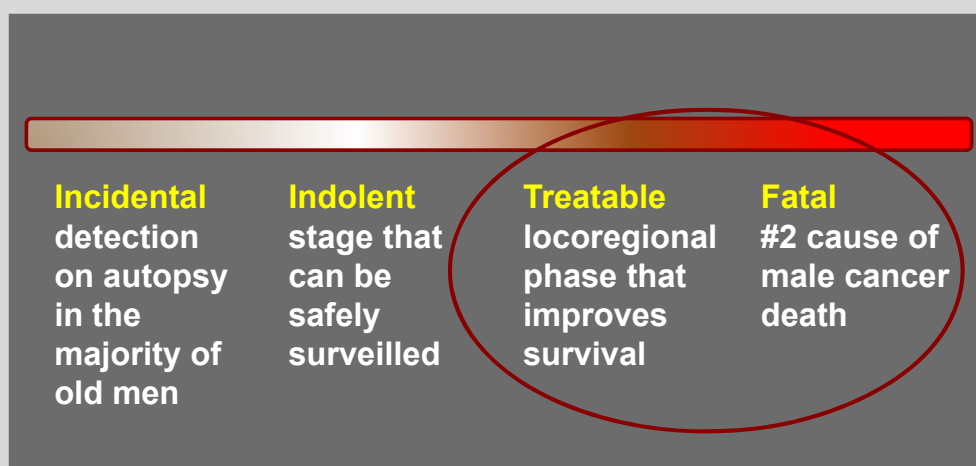
- #1 most common cancer
- #2 cause of male cancer death
  
- In the US (2023):
  - 288,300 cases
  - 34,700 deaths

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

## Prostate cancer is a spectrum

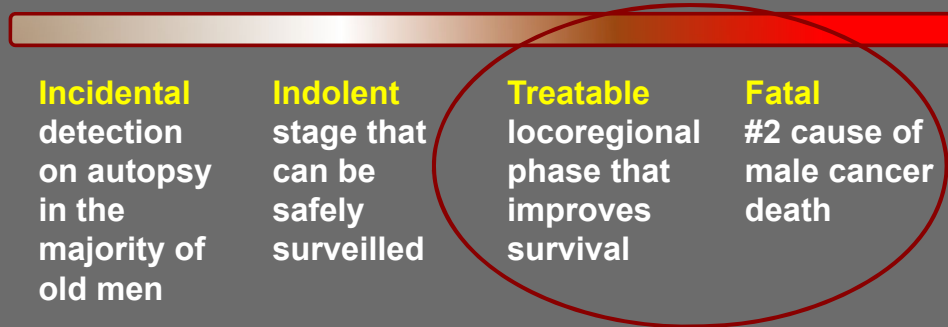


## Prostate cancer is a spectrum



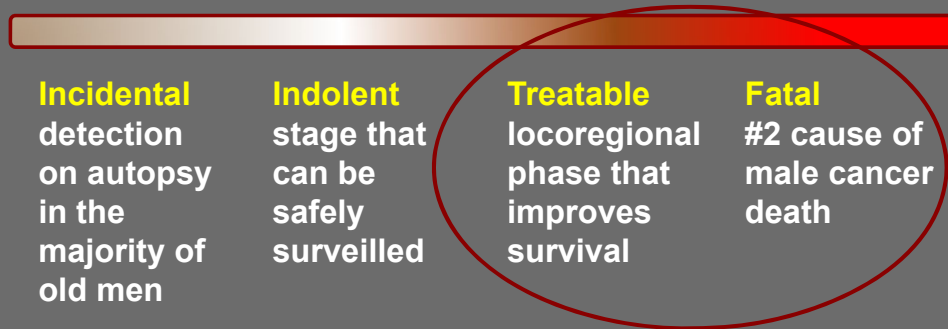
## Prostate cancer is a spectrum

What can we do to impact this?



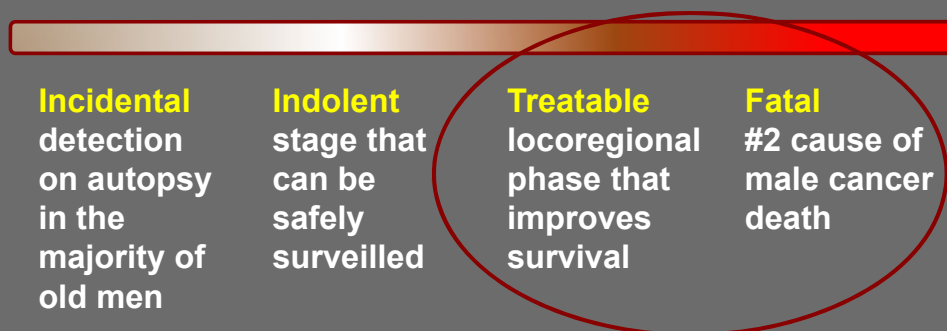
## Prostate cancer is a spectrum

Prevent Screen Diagnose Treat Survivorship

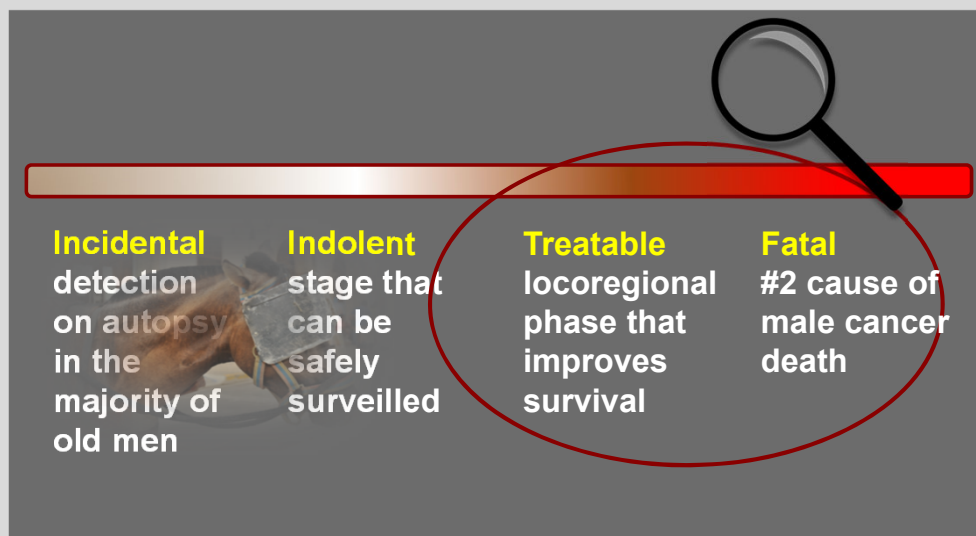


## Prostate cancer is a spectrum

Prevent **Screen** Diagnose Treat Survivorship

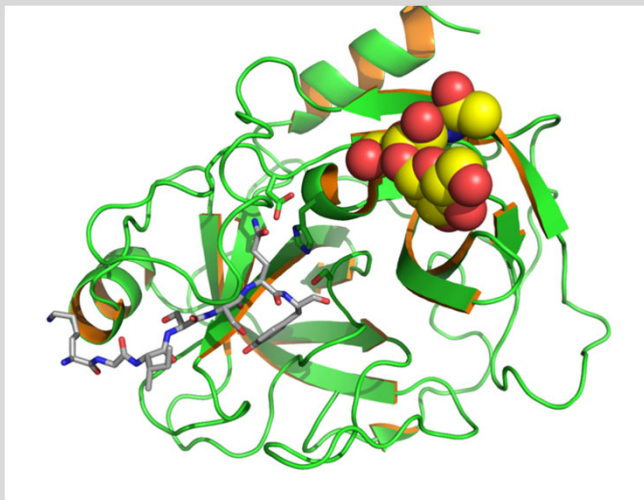


## Screening



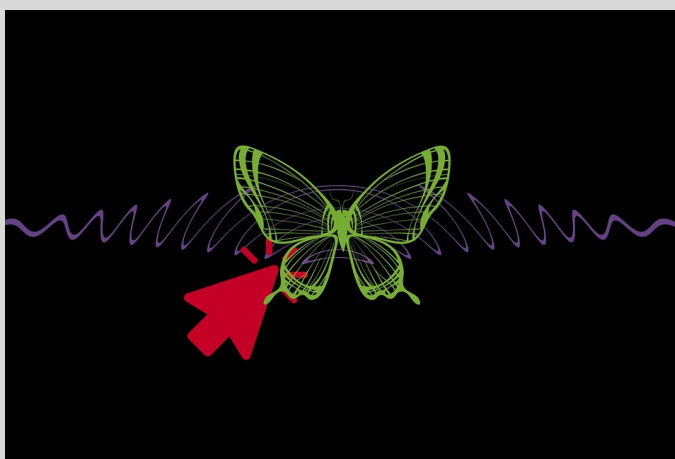
Google Images: Permission to Reuse

# Screening = PSA\*



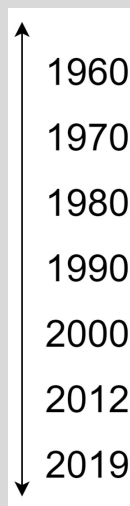
\*Pretty Much

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



Google Images: Permission to Reuse

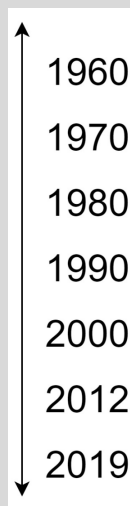
## PSA: Historical Perspective



**Flocks identifies that the human prostate has unique antigens**

Rao et al. BJU Int 2008

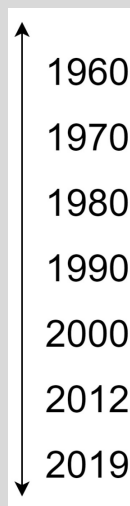
## PSA: Historical Perspective



**Hara identifies a unique antigen in the semen**

Rao et al. BJU Int 2008

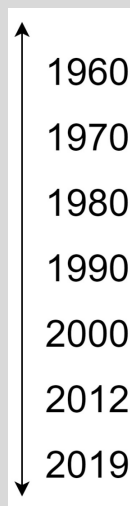
## PSA: Historical Perspective



**Ablin discovers PSA – prostate specific antigen**

Rao et al. BJU Int 2008

## PSA: Historical Perspective

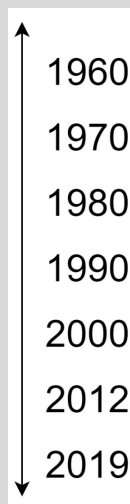


**Wang & Chu improve our understanding of PSA and optimize clinical testing**

Rao et al. BJU Int 2008



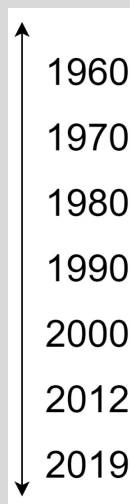
## PSA: Historical Perspective



**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



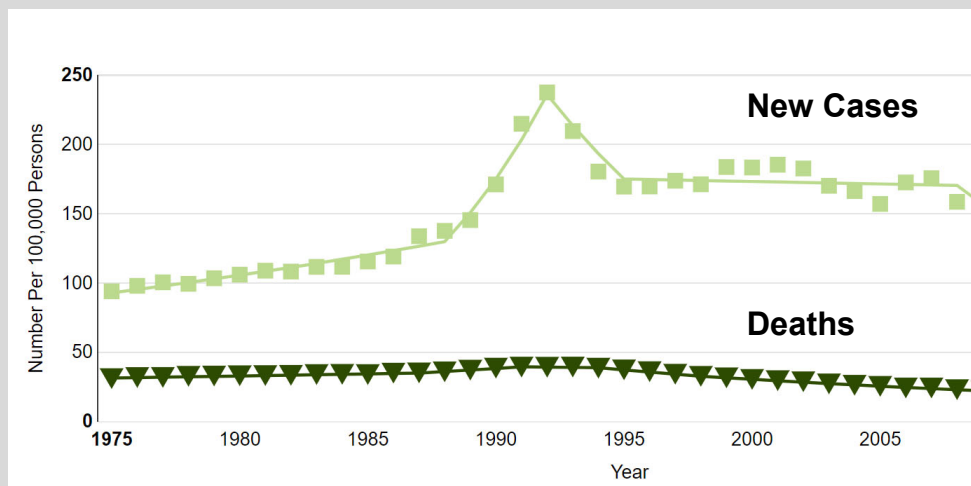
**FDA approval of PSA for the early detection of prostate cancer**  
Numerous nonrandomized studies supporting its use

Rao et al. BJU Int 2008

## PSA: Historical Perspective

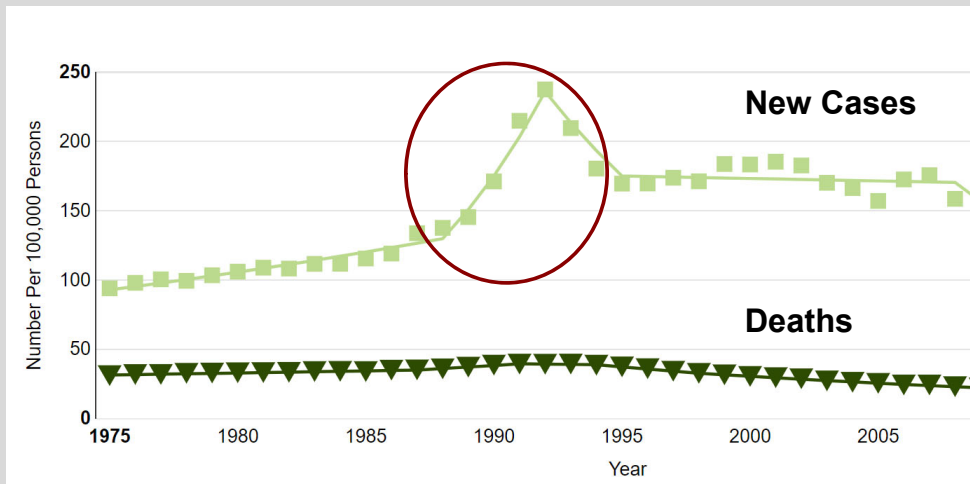


## What has PSA done?



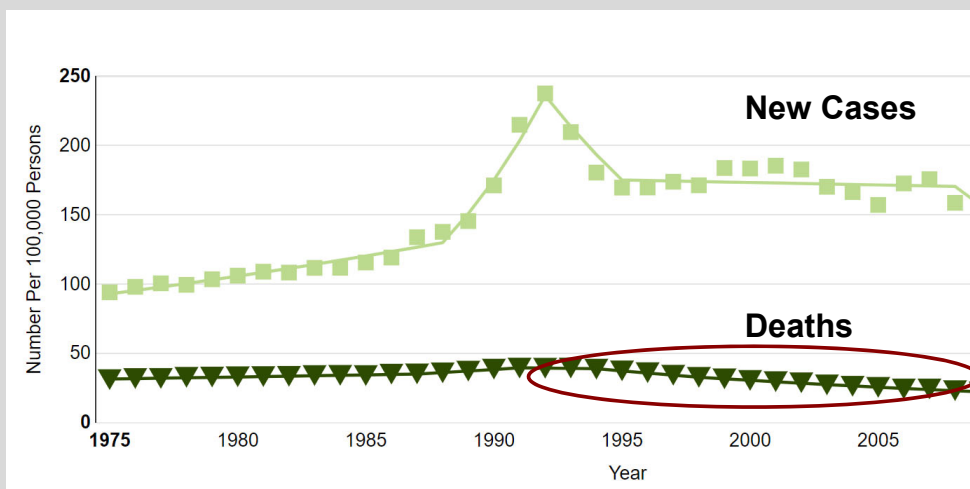
SEER Registry Public Data

## Screening dramatically increased incidence



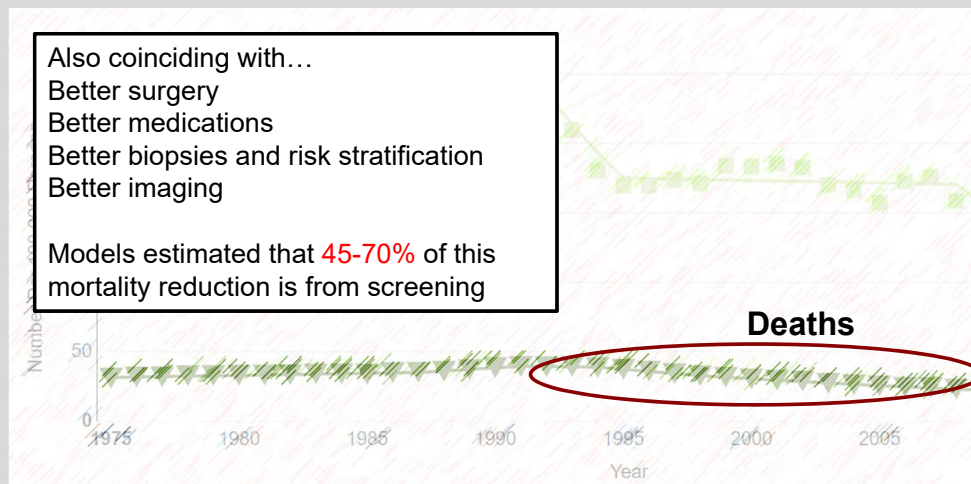
SEER Registry Public Data

## Prostate cancer mortality has halved



SEER Registry Public Data

## Prostate cancer mortality has halved



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

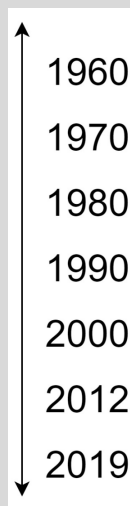
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American Cancer Society Statistics, CA Cancer J Clin 2023, non-melanoma skin not included

# The END

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

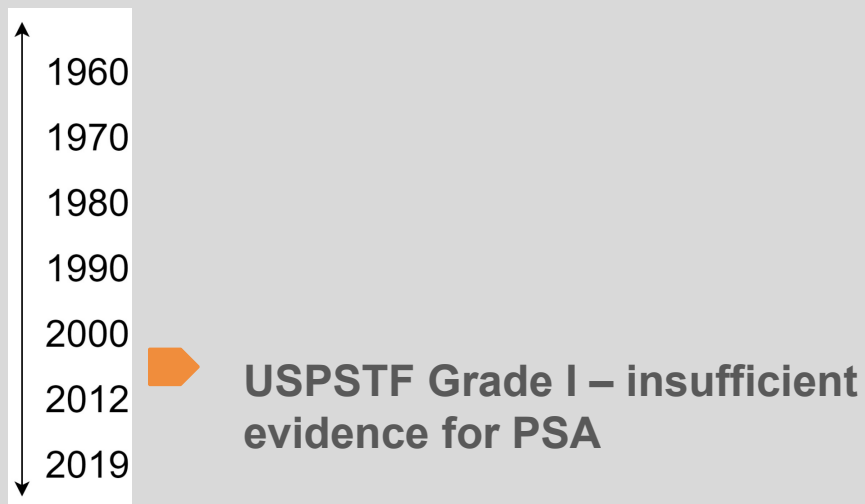
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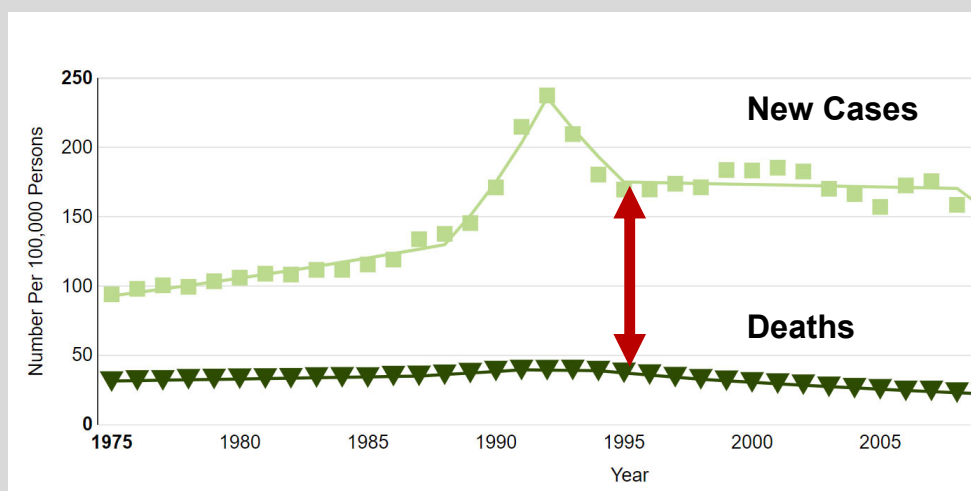
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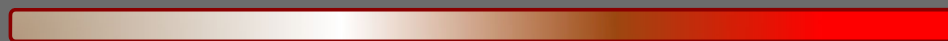


## A gap between incidence and mortality



SEER Registry Public Data

## Prostate cancer is a spectrum



### **Incidental**

detection  
on autopsy  
in the  
majority of  
old men

### **Indolent**

stage that  
can be  
safely  
surveilled

### **Treatable**

locoregional  
phase that  
improves  
survival

### **Fatal**

#2 cause of  
male cancer  
death

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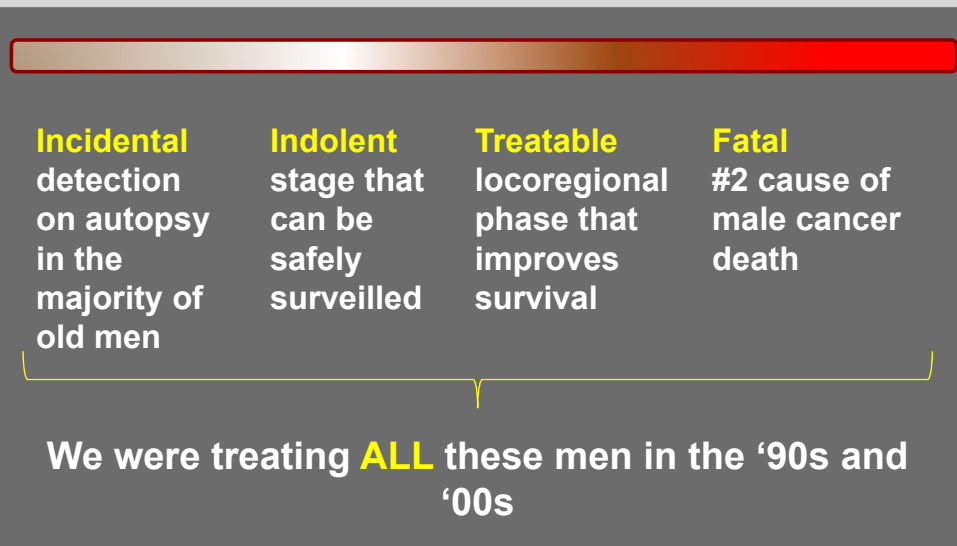
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“THE GAP”  
between incidence  
and mortality

## Prostate cancer is a spectrum



## PSA has profoundly impacted medicine

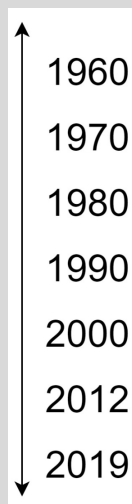
Prostate cancer is the most common cancer in men and the second most common cause of cancer death in men

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



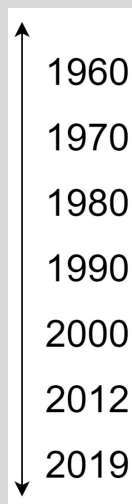
2 major randomized screening studies reported in the New England Journal of Medicine

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	<b>No impact</b> on prostate cancer mortality	Reduction of <b>1</b> prostate cancer death per <b>1410</b> screened and <b>48</b> treated

## PSA: Historical Perspective



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

## The USPSTF Decision

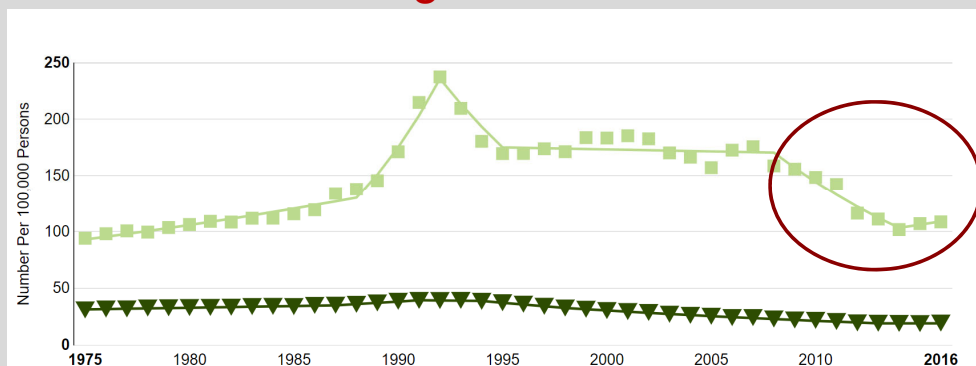
**ERSPC**  
 1410 men to screen  
 48 to treat  
 to save 1 life from  
 prostate cancer

**PLCO** Lack of survival  
 benefit  
 Harms of biopsy including  
 infection (2-4% sepsis)  
 Psychological impacts  
 Harms of treatment including  
 erectile dysfunction (most)  
 and incontinence (10%)

Benefits

Harms

## 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



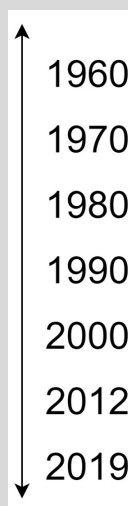
Incidence of more aggressive cancer declined by 25%  
→ **What will happen to these undetected cases??**

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



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)

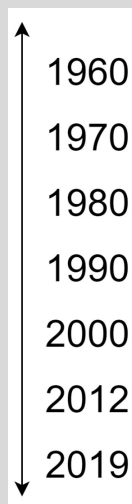
# 90% rate of contamination in PLCO trial

Shoag NEJM (2016)

## 2019 Revelations

Trial	PLCO	ERSPC
Location	US	Europe
Participants	76,674	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 4818 diagnosed

## A changing tide



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-Axelsson 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

Screening has a **survival benefit**  
 Treatment has a **survival benefit**  
 We are better at reducing  
 overscreening, overdiagnosis,  
 overtreatment

Harms of biopsy  
 Psychological  
 impacts  
 Harms of treatment  
 Overdiagnosis and  
 overtreatment still  
 exist

Benefits

Harms

## 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**