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PROGRESS AND PROMISE AGAINST CANCER WEBINAR SERIES

# PROSTATE CANCER SCREENING: AN UPDATE

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## Disclosures



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# The U.S. Preventive Services Task Force (USPSTF)

Grade D: *recommends against prostate-specific antigen (PSA)-based screening for prostate cancer*



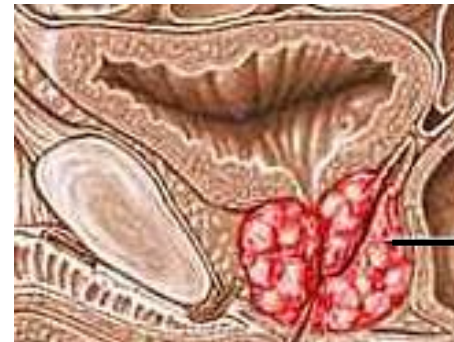
- ...the reduction in prostate cancer mortality after 10 to 14 years is, at most, very small, even for men in what seems to be the optimal age range of 55 to 69 years...
- ...no apparent reduction in all-cause mortality...
- ...harms associated with the diagnosis and treatment of screen-detected cancer are common, occur early, often persist, and include a small but real risk for premature death...
- ...more men in a screened population will experience the harms of screening and treatment of screen-detected disease than will experience the benefit...
- The USPSTF concluded that there is moderate certainty that the benefits of PSA-based screening for prostate cancer do not outweigh the harms.

## Prostate Cancer in the United States

- Prostate cancer is the most commonly diagnosed life-threatening cancer in men (180,890 cases and 26,120 deaths in 2016)
- Small prostate cancers are present in 29% of men between ages 30 and 40 and 64% of men between ages 60 and 70
- The lifetime risk of a prostate cancer diagnosis is about 1 in 8
- The lifetime risk of dying from prostate cancer is about 1 in 37



normal  
prostate



prostate  
cancer

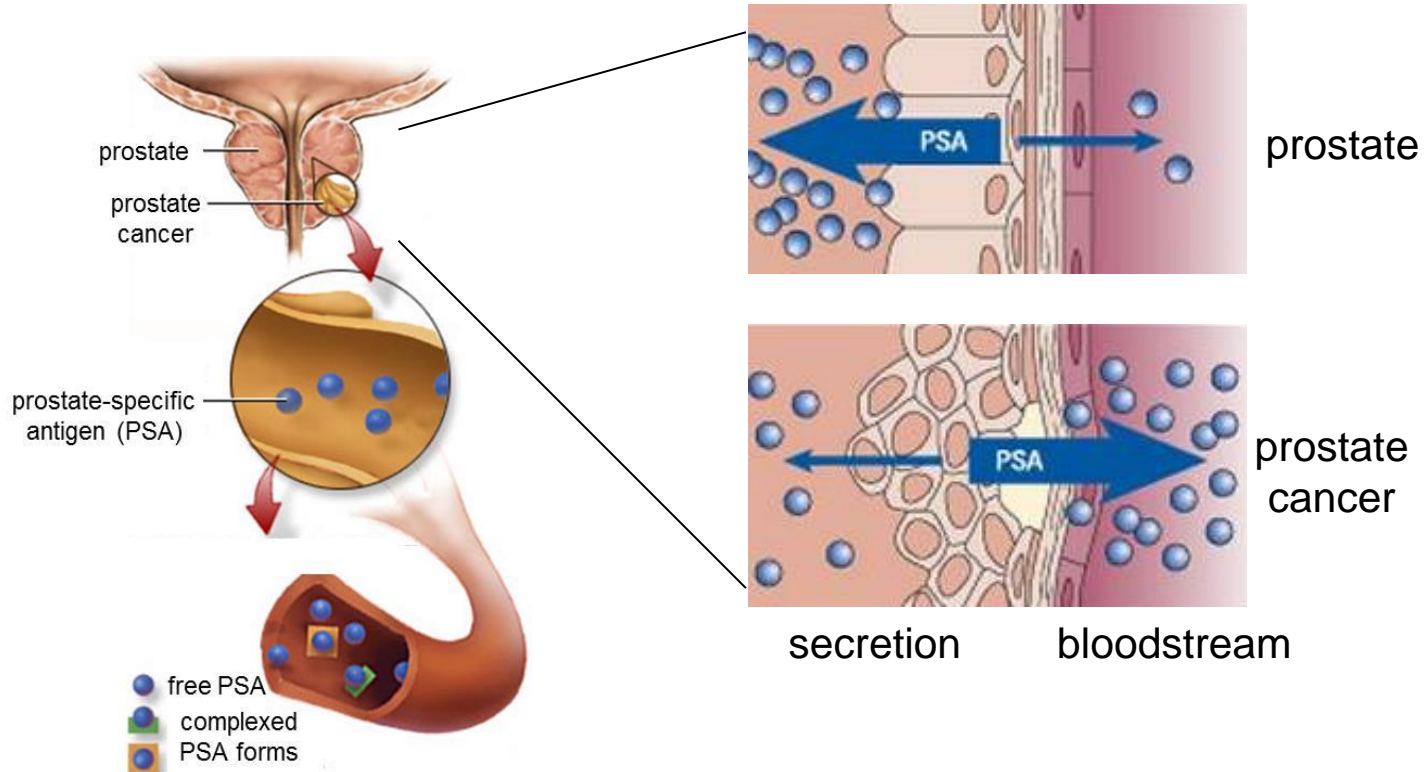
# PSA-Based Screening Recommendations of Other Organizations

(American Cancer Society, American Urological Association,  
American Society of Clinical Oncology)

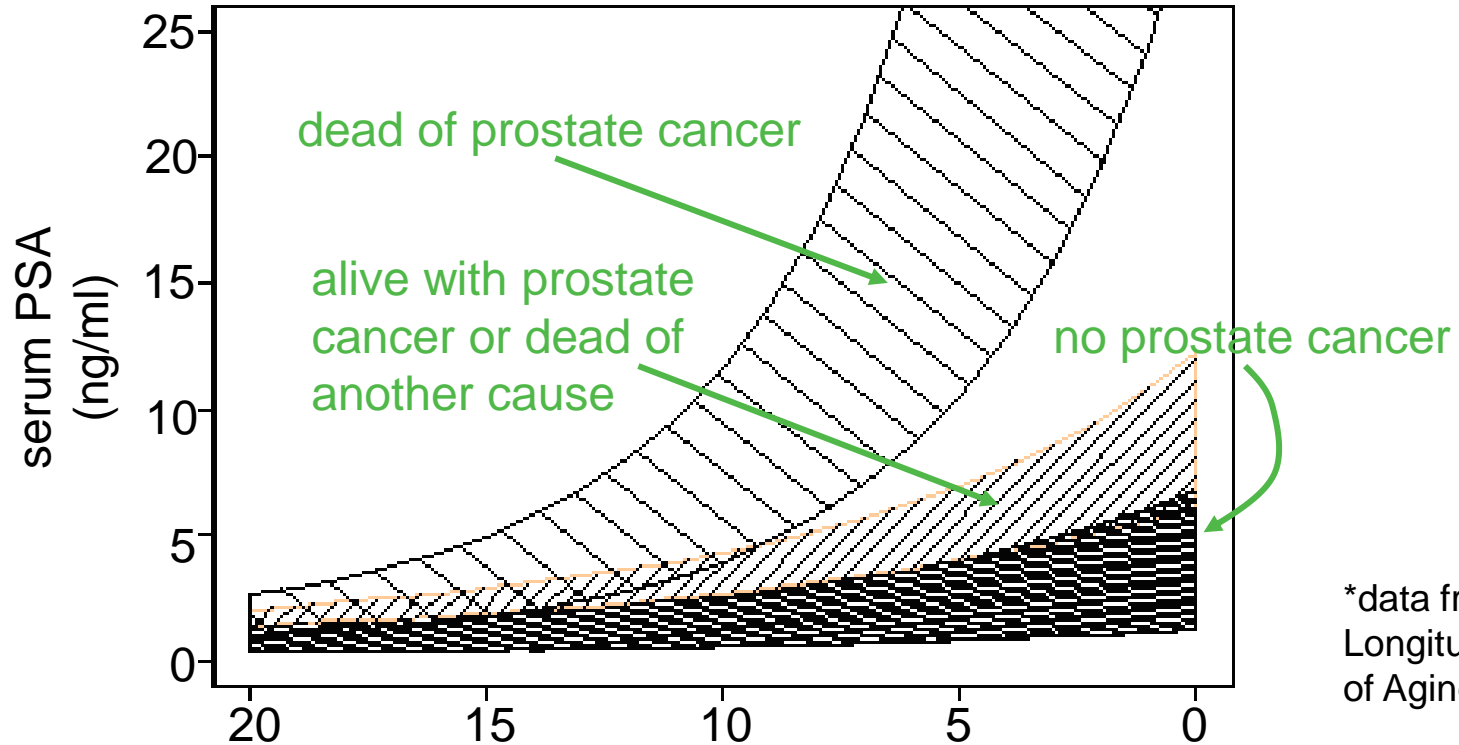


- PSA-based screening should be offered to all men beginning at age 50-55 years
- PSA-based screening should be considered before age 50 years for African-American men
- PSA-based screening should be considered before age 50 years for me with a strong family history of prostate cancer
- All men at risk for prostate cancer should participate in shared decision-making with physicians to ensure that the benefits and harms of screening are well understood before pursuing serum PSA testing

# Prostate-Specific Antigen (PSA) is an Enzyme Normally Secreted into the Ejaculate that Appears in the Bloodstream of Men with Prostate Cancer



# The Rise of Serum (Blood) PSA Predicts Life-Threatening Prostate Cancer when Cure may be Possible\*



\*data from Baltimore Longitudinal Study of Aging (2005)

# European Randomized Study of Prostate Cancer Screening (ERSPC)\*

(162,388 European men randomized to PSA testing every 4 years with a cut-off value of 3 ng/mL for biopsy)



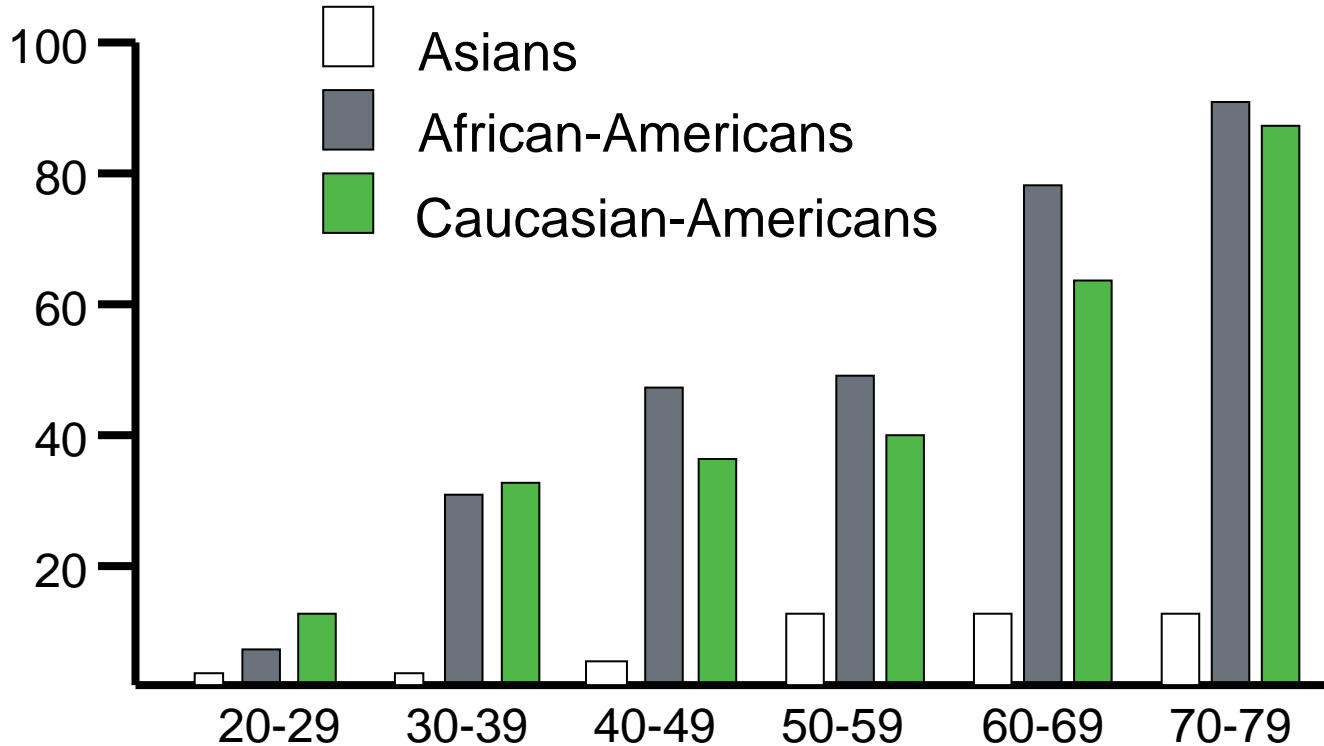
## Results:

- 40% reduction in metastatic prostate cancer
- 21% reduction in mortality at 13 years
- 781 men needed to be screened and 27 men diagnosed/treated to prevent one prostate cancer death
- Screening cost-effectiveness was \$73,000 per quality-adjusted life-year gained
- Screening above age 63 not cost effective because of over-diagnosis

\*Schroder FH *et al.* Lancet 384: 6-12 (2014); Buzzone C *et al.* Eur Urol 68: 895-90 (2015); Heijnsdijk EA *et al.* J Natl Cancer Inst 10: 366 (2014)



# Prevalence of Prostate Cancer at Autopsy\*



\*Sakr WA *et al.* In Vivo 8: 439-43, (1984); Gu FL *et al.* Urology 44: 688-91 (1994); Lee YS and Shanmugaratnam K Singapore Med J 13: 1321-6 (1972); Miller GJ *et al.* J Urol 151: A204 (1994); DeSantis C *et al.* CA J Cancer Clin (2013)

# Unsuspected Prostate Cancers in Healthy Men Over Age 55 Years: Results of the Prostate Cancer Prevention Trial (PCPT)\*



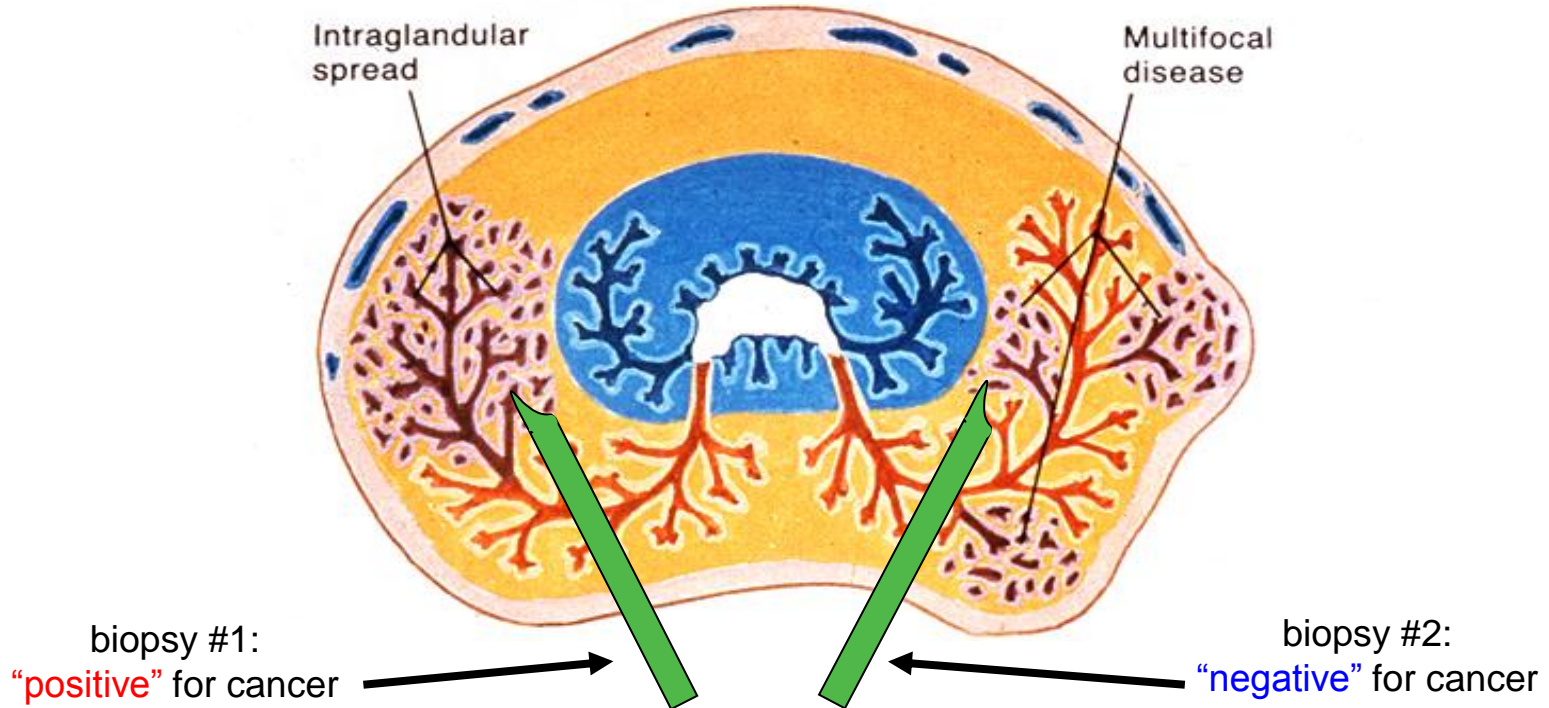
Serum PSA level (at study entry)	Number of men biopsied from the placebo group	Number of men with prostate cancer**
0.0-1.0 ng/mL	2196	357 (16.3%)
1.1-2.0 ng/mL	1647	457 (27.7%)
2.1-3.0 ng/mL	848	332 (29.3%)
3.1-4.0 ng/mL	1	1 (100%)

\*\*63% of prostate cancer diagnoses made at end-of-study biopsy

\*Thompson IM *et al.* New Engl J Med, 349: 215-24 (2003)

# Core Needle Biopsies of the Prostate

## Random Sampling of the Peripheral Zone



# United States Food and Drug Administration Approval of a DNA (Methylation) Test for Prostate Cancer: Pivotal Registration Trial Data\*

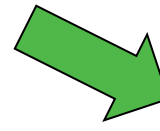
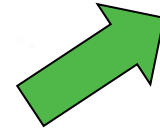
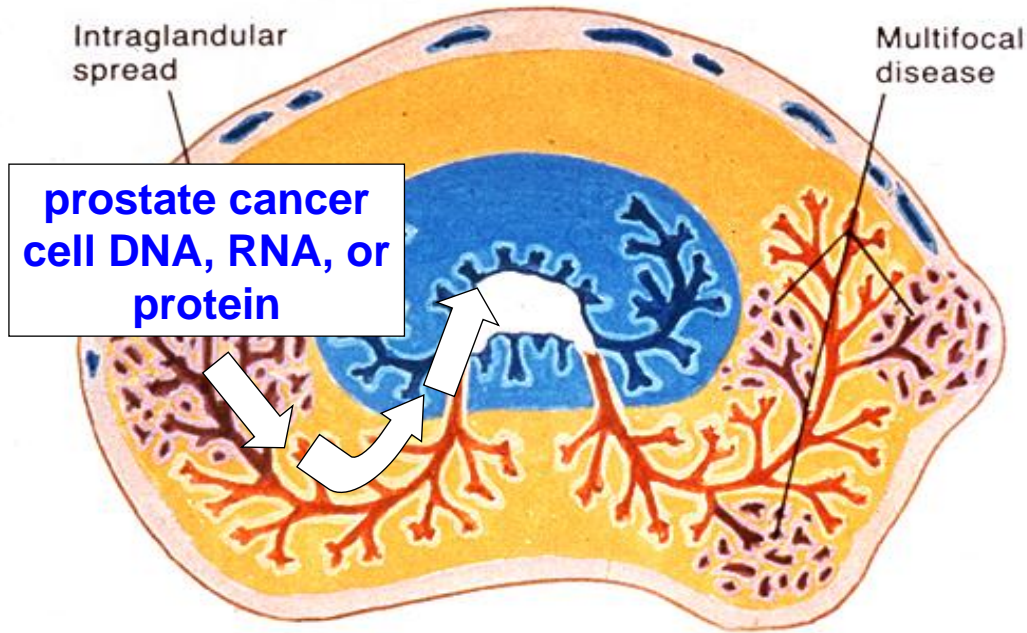


Investigators	Study	Number of Men	Odd Ratio for Cancer on Second Biopsy	Negative Predictive Value
Steward GD <i>et al.</i> (2013)	MATLOC	498	3.17 (95% CI of 1.81-5.53)	90% (95% CI of 87-93)
Partin AW <i>et al.</i> (2014)	DOCUMENT	350	2.69 (95% CI of 1.60-4.51)	88% (95% CI of 85-91)



\*Steward GD *et al.* J Urol 189: 1110-6 (2013)  
Partin AW *et al.* J Urol 192: 1081-7 (2014)

# Prostate Cancer DNA, RNA, or Protein in Prostate Secretions/Urine: Can a **New Molecular Test** be Used for Prostate Cancer Screening/Early Detection?



urine test



blood test

# Decline in Prostate Cancer Mortality: Result of PSA Screening?



- Prostate cancer mortality rates since 1995 are below those for 1986 when serum PSA testing was rare
- Mortality decline is attributable to a decrease in the incidence of advanced/metastatic prostate cancer  
Chu KC *et al.* *Cancer*, 97: 1507-16 (2003)
- Mortality rates are lowest in areas where the rates of advanced stage prostate cancer are lowest, and advanced stage prostate cancer is lowest in areas with highest PSA utilization  
Jemal A *et al.* *Cancer Epidemiol Biomarkers Prev*, 14: 590-5 (2005)
- 2 of 3 randomized clinical trials of prostate cancer screening have shown reductions in prostate cancer mortality  
Schroder FH *et al.* *New Engl J Med* 360: 1320-8 (2009); Andriole GL *et al.* *New Engl J Med* 360: 1310-9 (2009); Hugosson J *et al.* *Lancet Oncol*, 11: 725-32 (2010)

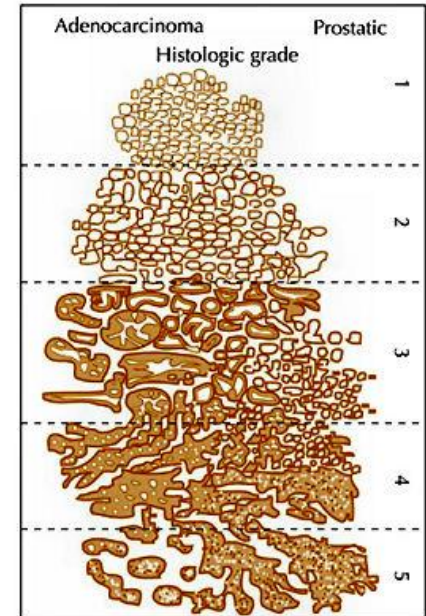
# Active Surveillance of Low-Risk Prostate Cancer

Candidate men with prostate cancer for active surveillance

- low-risk (Gleason score  $\leq 6$ ) localized prostate cancer
- low-volume intermediate-risk (Gleason  $3 + 4 = 7$ ) prostate cancer

Active surveillance regimen

- serum PSA testing at 3-6 month intervals
- digital rectal examination (DRE) annually
- follow-up biopsies at 2-4 year intervals
- imaging and genomic tests were recommended only for discordant clinical and/or pathologic findings
- curative intervention reserved for men reclassified to a higher-risk category (Gleason score  $\geq 7$ ) and/or for men with an increase in the extent of low grade cancer on surveillance biopsies.



(Gleason score is the sum of the two most common grades)