

Prostate Cancer Screening Update 2019



Brian Helfand MD, PhD

Chief, Division of Urology

NorthShore University HealthSystem

Ronald L. Chez Family and Richard Melman Family Endowed Chair of Prostate Cancer

Clinical Associate Professor

University of Chicago, Pritzker School of Medicine

Relevant Disclosures

- Ambry Genetics -- speaker
- Blue Earth Diagnostics – speaker and investigator
- Genomic Health -- speaker

Learning Objectives

- Understand the most recent changes in the USPSTF's decision for PSA screening
- Understand the value and limitations of PSA based screening
- Understand the benefits of newer tests used to supplement PSA screening and help guide in the decision for prostate biopsy
- Understand how genetic risk assessment may contribute to identifying men who are most at risk of prostate cancer and how it may contribute to more accurate screening methodologies

Facts About Prostate Cancer

Myth: Every man is develops prostate cancer at some point

Prostate Cancer

Did you know? About **1 in 7** men will be diagnosed with prostate cancer during his lifetime.



Are you at risk? As your age increases so does your risk



1 in 9 men 70 and older

1 in 16 men 60 to 69

1 in 38 men 40 to 59

1 in 10,000 men under 40

Family History:

- If your **father or brother** has had prostate cancer, your risk of getting prostate cancer more than doubles.



Race:

- African-American men are more than **1 ½ times** more likely to get prostate cancer and more than **2 times as likely to die of prostate** cancer as Caucasian men.

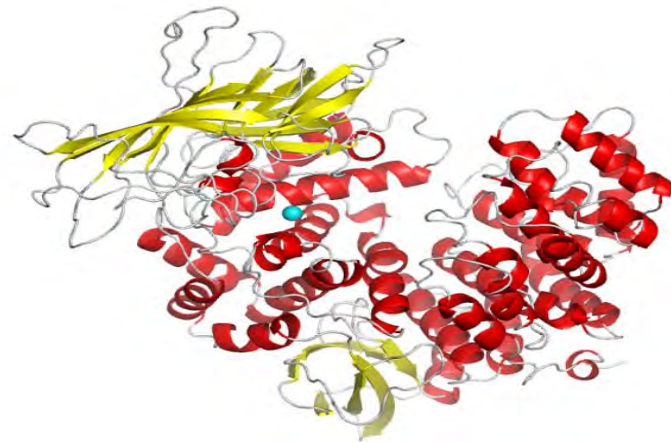


Prostate Cancer Screening

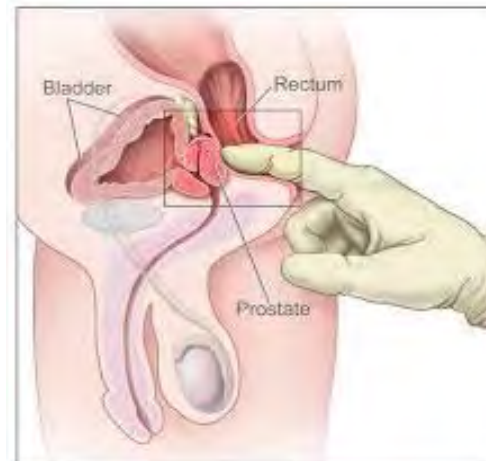
2 Critical Components

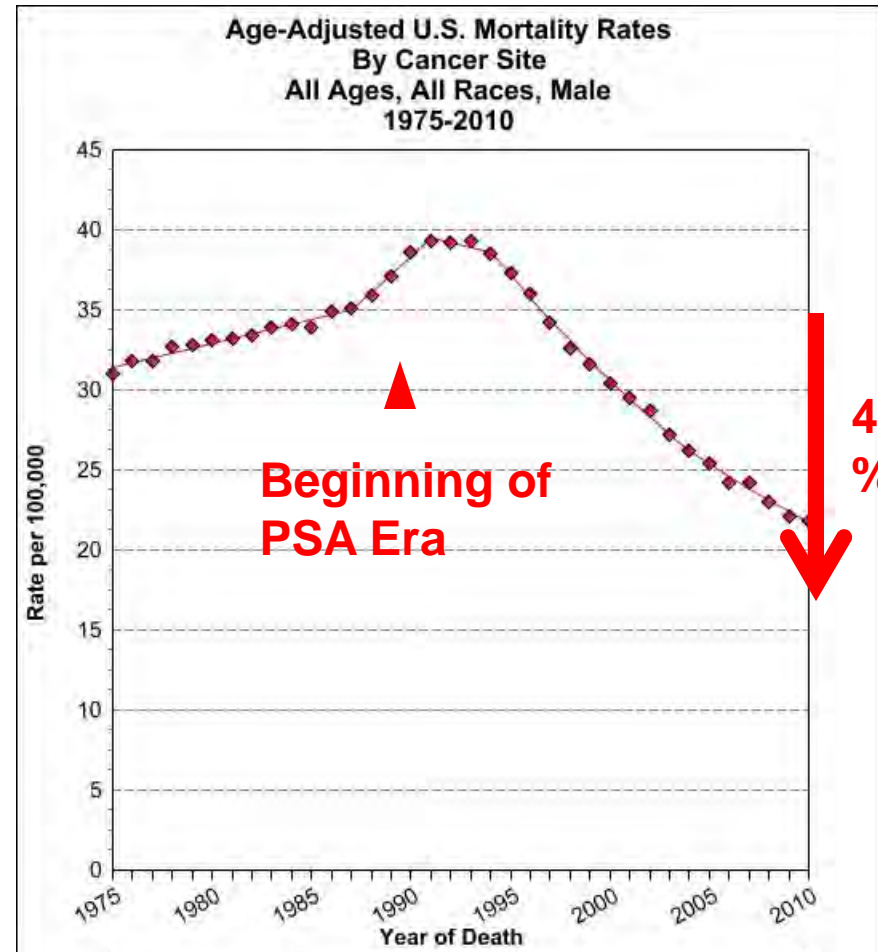
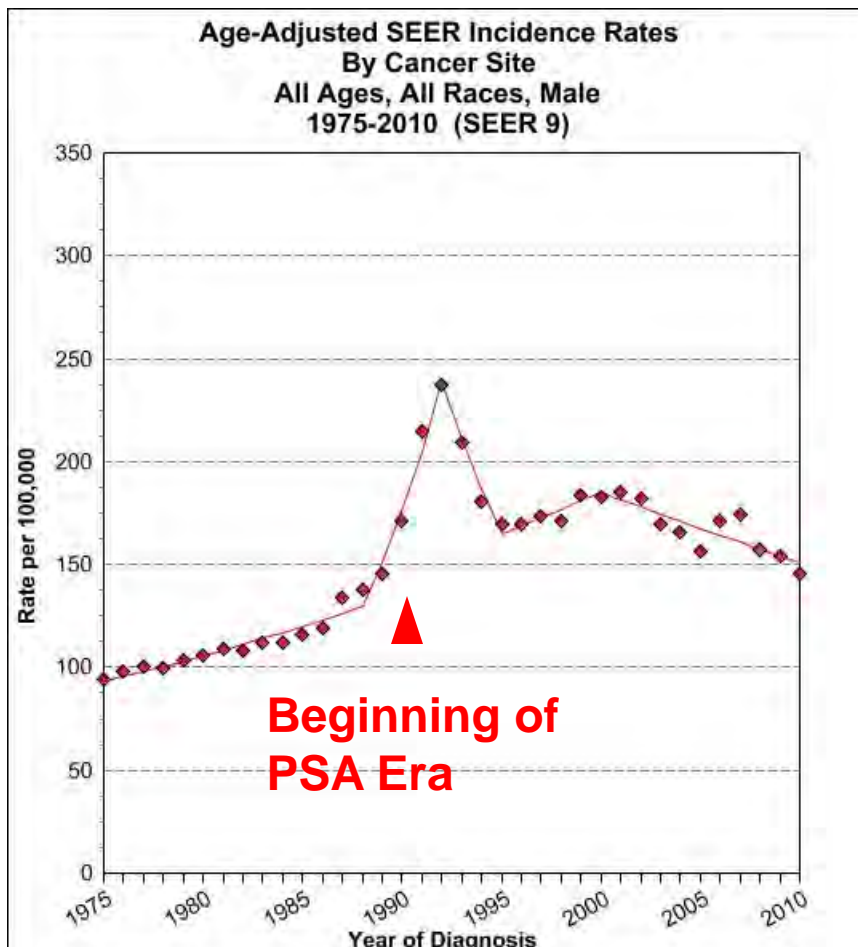
- Discovered in 1970
 - Most widely used oncologic biomarker
 - Member of the human kallikrein family of glycoproteins
 - Liquefies semen to improve sperm mobility
-
- ~10-15% of men have normal PSA and nodule
 - Higher likelihood that more aggressive

Prostate Specific Antigen



Digital Rectal Exam





After its introduction, PSA testing was widely adopted in the U.S. (> 50% of men were tested), resulting in an increase in the detection of prostate cancer followed by a dramatic decrease in the age-adjusted prostate cancer mortality rate

PSA Screening: The Good

- From 1990-2012
 - There was 80% decrease in the percentage of patients with metastases at diagnosis
 - 45% decrease in prostate cancer-specific mortality rate

PSA Screening: The Bad

- PSA often detects slow growing, non-aggressive prostate cancers
- Other factors that affect PSA:
 - Infection/Inflammation/Instrumentation
 - Urinary retention
 - Sexual activity
 - Exercise
 - Ejaculation/Vigorous massage
 - Advanced age/Benign enlargement
- Must screen ~150-200 men and treat 5-9 men to prevent one death
- PSA may miss rapidly growing, life threatening prostate cancers
- 30% of men with prostate cancer and PSA >4.0 ng/mL already have disease beyond the prostate and may be incurable

Prostate Cancer Screening (USPSTF May 2018)

Shared Decision Making is Key

<u>Age</u>	<u>Recommendation</u>	<u>Grade</u>
Men 55-69 y/o	The decision to undergo periodic PSA-based screening should be an individual one and involve shared decision making (SDM) based on patient values and preferences	C

*Men <55 years old can be offered earlier screening after shared decision making

Relevant for men with increased risk including:

Family history of prostate cancer or other related cancers
(breast, ovarian, pancreatic, colon, endometrial, melanoma)

African American race

Prostate Cancer Screening

(USPSTF May 2018)

<u>Age</u>	<u>Recommendation</u>	<u>Grade</u>
Men >70 y/o	Recommended AGAINST PSA-based screening	D

*This is based upon average life expectancy of 80years

PS Prostate Cancer Screening Summary

1. Prostate cancer screening should be performed and should include PSA and DRE
2. Screening is associated with significantly lower metastasis and mortality
3. Understand limitations of PSA including the fact that other factors contribute to elevation in PSA values

PSA Screening Alternatives

- PSA has limitations
- PSA can vary based upon clinical situation and therefore other tests have been developed to aid in screening
- PSA kinetics; PHI, 4K score, Prostarix, Polygenic Risk Scores, Prolaris, Genomic Oncotype DX Score, ProstaVysion, Metamark Biopsy Test, Progenesa PCA3, TMPRSS-ERG/ETS fusions, ConfirmMDx, *SPOP*, expressed prostatic secretions biomarkers

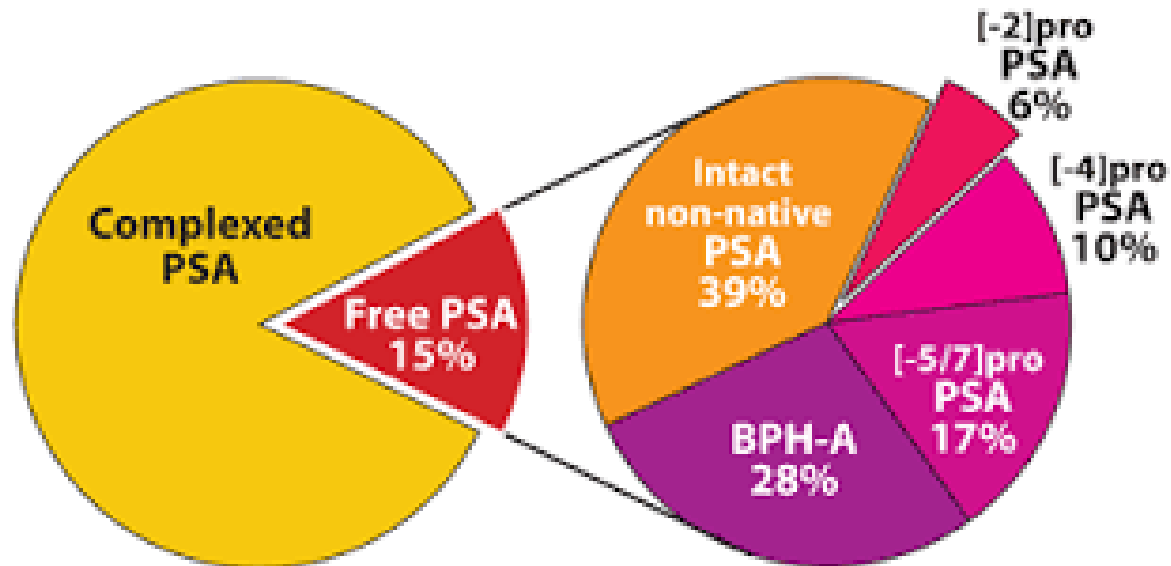
Single PSA blood test prior to age 50

Total PSA (ng/mL)	25 Year-Probability of Developing Prostate Cancer (%)
0.0 – 0.5	4
0.5 – 1.0	8
1.0 - 2.0	20
2.0 – 3.0	41
> 3.0	60

Lilja, H, et al.: J. Clin, Oncol. 25:431, 2007

Prostate Health Index

A More Sensitive and Specific Alternative to PSA



$$phi = \frac{p2PSA}{fPSA} \cdot \sqrt{tPSA}$$

Prostate Health Index Test Results

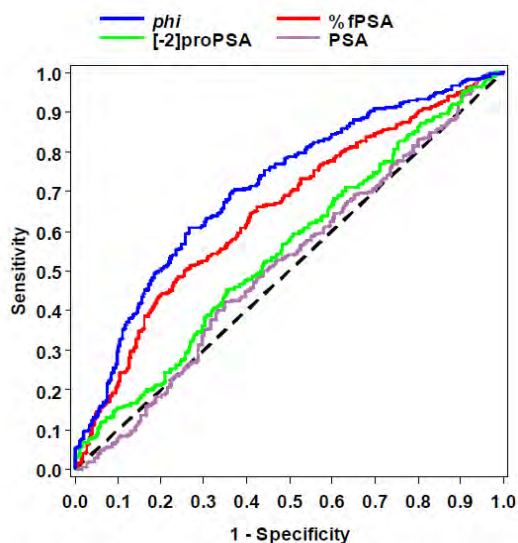
Interpretation

<i>phi</i> Score	Probability of Cancer
0 – 26.9	9.8%
27 – 35.9	16.8%
36 – 54.9	33.3%
55+	50.1%

PHI identifies significant prostate cancer

PHI is more sensitive and specific than PSA

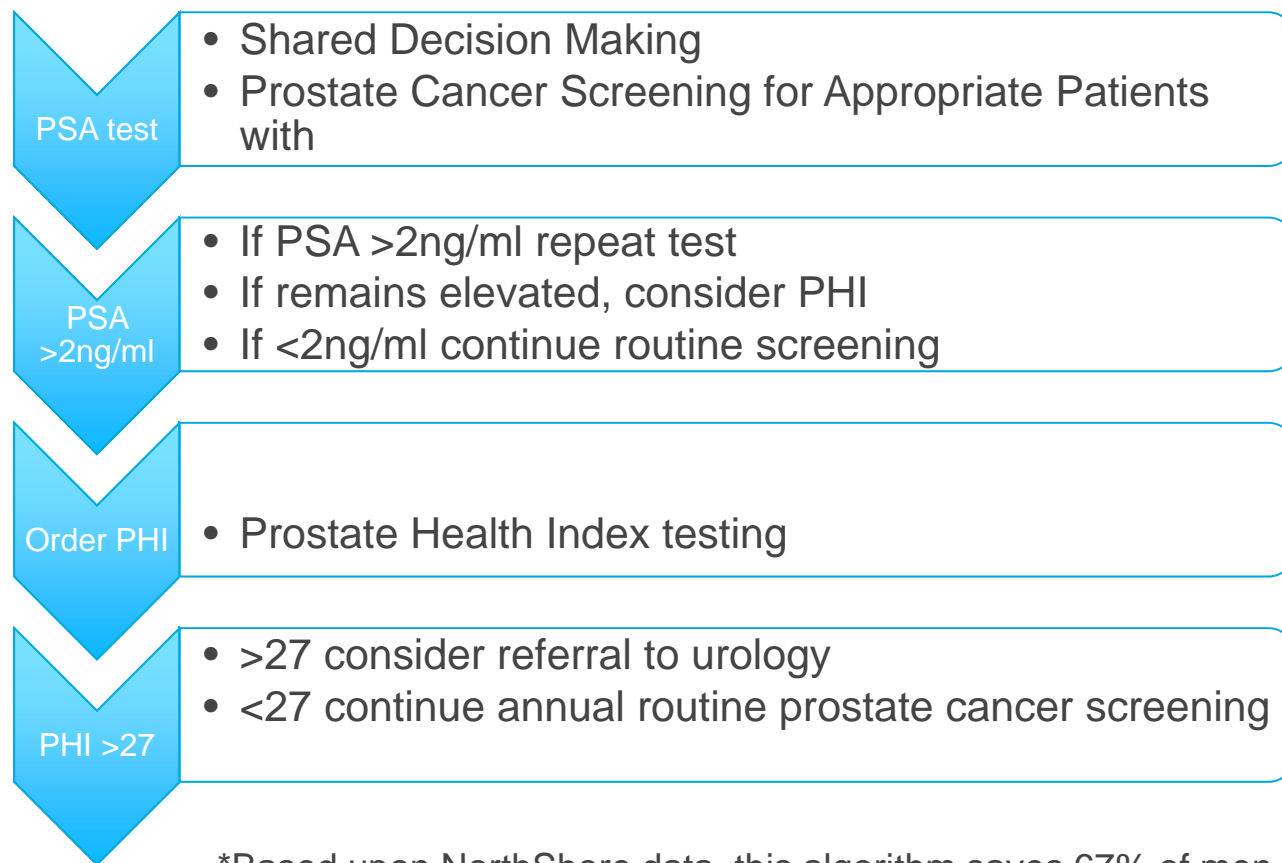
- › 658 men from prospective multi-institutional US trial
- › Inclusion criteria
 - Age ≥ 50 , PSA 4–10 ng/mL (Hybritech calibration) and negative DRE, initial (79%) or repeat (21%) biopsy
- › PHI cutoff at **28** can avoid 30.1% unnecessary biopsy



J Urol. 2015;193:1163-69.

	PHI	%fPSA	PSA
GS ≥ 7	0.787	0.661	0.551
Epstein significant	0.718	0.654	0.549

Algorithm for PCPs incorporating PHI



*Based upon NorthShore data, this algorithm saves 67% of men prostate biopsy

A large, bold, light blue letter 'G' is positioned on the left side of the slide, partially overlapping the title text.

Advances in Genetics Helps Guide Prostate Cancer Screening

A large, bold, light blue letter 'R' is positioned on the left side of the slide, partially overlapping the title text.

1. Currently family history and race are only known factors that associated with increased risk
2. Many limitations to family history data
3. Prostate cancer is one of most heritable tumors
4. Knowledge of genetics can help identify who is most likely to develop prostate cancer

Genetics of Prostate Cancer

- Prostate cancer is considered to be one of the most heritable of all cancers
- Heritability can be assessed using 3 components:
 - Family history based information
 - Rare pathogenic mutations (e.g. *BRCA2*)
 - Common prostate cancer specific single nucleotide polymorphisms

Prostate Cancer Risk SNPs

- Common genetic variation; variations known as SNPs
- About 10 million SNPs in the human genome
- Certain combinations of SNPs can be used to estimate risk for a specific diseases
- Explain >40% of hereditary disease risk

What is a Genetic Risk Score?

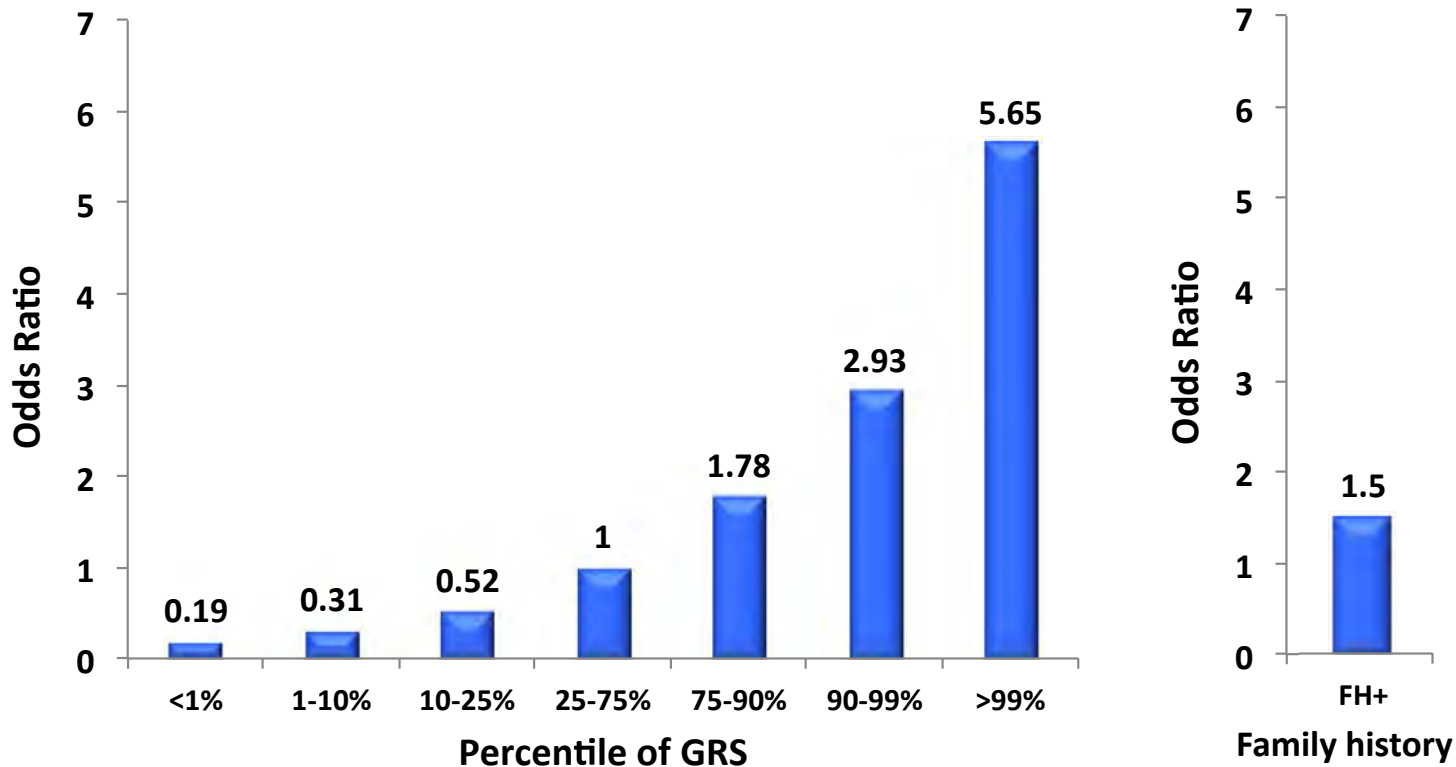
Genetics of Prostate Cancer for Screening



- A number calculated based on the cumulative variation across multiple SNPs, which is then used to provide an estimate of disease risk
- GRS is simple to interpret
 - GRS = 1.0 indicates an average risk
 - GRS > 1.0 indicates higher risk
 - GRS < 1.0 indicates lower risk

Genetic Risk Score is More Informative than Family History

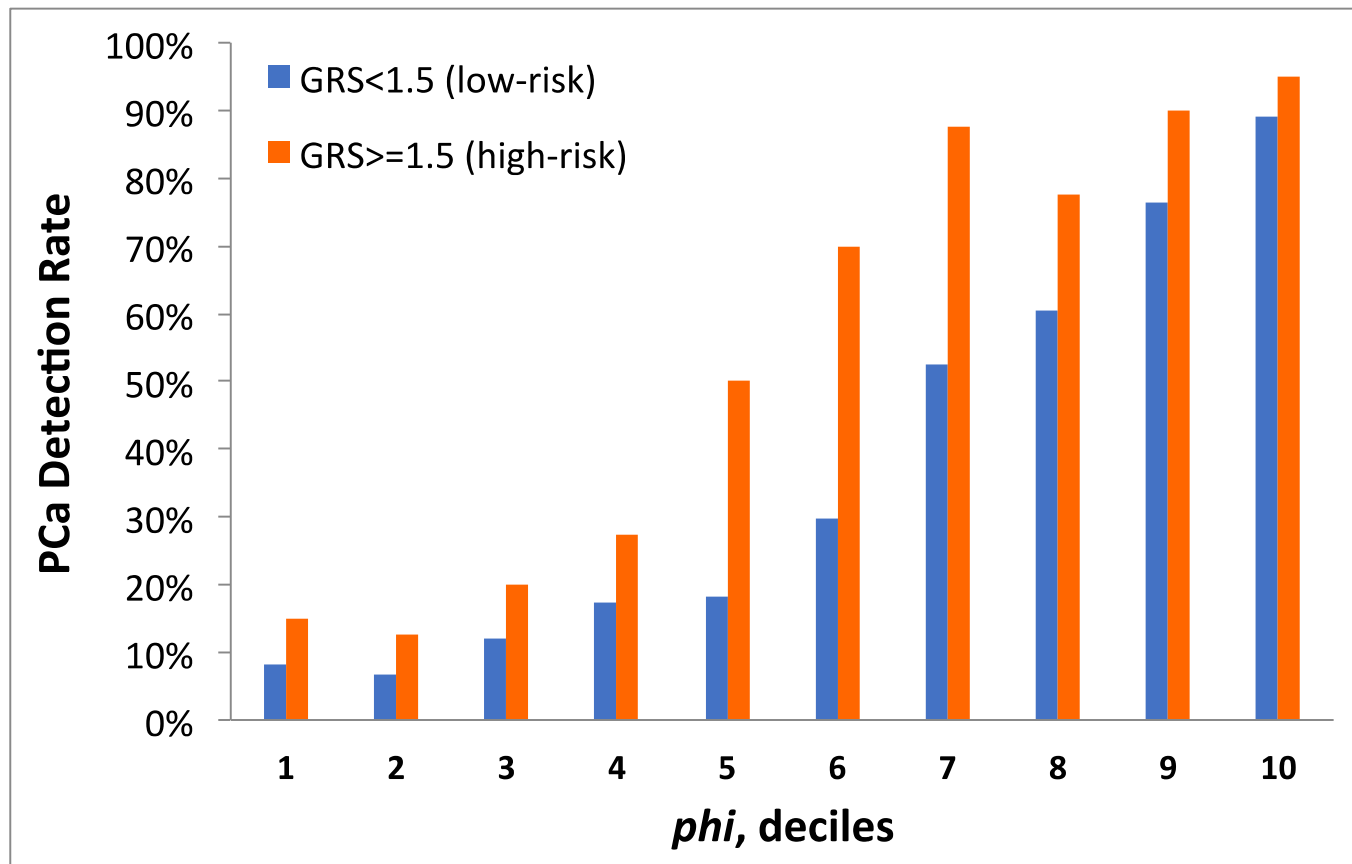
43,303 sporadic prostate cancer cases and 43,737 controls



Al Olama, et al., 2014

Combining phi and Genetic Risk Score

PCa Detection Rate by *phi* and GRS in a Biopsy Cohort (N=1,887)



Prostate Cancer Screening Summary

1. Prostate cancer screening should be discussed with appropriately aged men
2. Understand limitations of PSA screening
3. If elevated PSA → repeat and consider more advanced testing
4. Phi and GRS are newer tests that can improve upon prostate cancer screening and identify men most at risk of harboring tumors and aggressive disease