

PSA levels during midlife and risk of aggressive prostate cancer in African American men

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HARVARD T.H. CHAN
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BRIGHAM AND
WOMEN'S HOSPITAL



Screening for Prostate Cancer: U.S. Preventive Services Task Force Recommendation Statement

Virginia A. Moyer, MD, PhD, on behalf of the U.S. Preventive Services Task Force*

Description: Update of the 2008 U.S. Preventive Services Task Force (USPSTF) recommendation statement on screening for prostate cancer.

Methods: The USPSTF reviewed new evidence on the benefits and harms of prostate-specific antigen (PSA)-based screening for prostate cancer, as well as the benefits and harms of treatment of localized prostate cancer.

Recommendation: The USPSTF recommends against PSA-based screening for prostate cancer (grade D recommendation).

This recommendation applies to men in the general U.S. population, regardless of age. This recommendation does not include the use of the PSA test for surveillance after diagnosis or treatment of prostate cancer; the use of the PSA test for this indication is outside the scope of the USPSTF.

Ann Intern Med. 2012;157:120-134.

www.annals.org

For author affiliation, see end of text.

* For a list of the members of the USPSTF, see **Appendix 1** (available at www.annals.org).

This article was published at www.annals.org on 22 May 2012.

Recommendation Summary

Population	Recommendation	Grade (What's This?)
Men, Screening with PSA	The U.S. Preventive Services Task Force (USPSTF) recommends against prostate-specific antigen (PSA)-based screening for prostate cancer.	D

USPSTF Summary of benefits and harms

What are the benefits of screening men aged 55–69 yr with a PSA test every 1–4 y for 10 y?

Benefits

Possible benefit of screening

Reduced 10 y risk for dying of prostate cancer

Men, *n*

Die of prostate cancer with no screening	5 in 1000
Die of prostate cancer with screening	4–5 in 1000
Do not die of prostate cancer because of screening	0–1 in 1000



0-1 men of 1000 screened are saved

Harms of screening

Harms

At least 1 false-positive screening PSA test result

Most positive test results lead to biopsy. Of men having biopsy, up to 33% will have moderate or major bothersome symptoms, including pain, fever, bleeding, infection, and temporary urinary difficulties; 1% will be hospitalized.

100–120 in 1000

Prostate cancer diagnosis

Although a diagnosis of prostate cancer may not be considered a harm, currently 90% of diagnosed men are treated and, thus, are at risk for the harms of treatment. A large majority of the men who are being treated would do well without treatment; a substantial percentage of the men who would have remained asymptomatic for life.

110 in 1000



110 men of 1000 screened are “overdiagnosed”; most men are treated

Complications of treatment (among men who are treated)

Develop serious cardiovascular disease due to treatment	
Develop deep venous thrombosis or pulmonary embolus due to treatment	1 in 1000
Develop erectile dysfunction due to treatment	29 in 1000
Develop urinary incontinence due to treatment	18 in 1000
Die due to treatment	<1 in 1000

Need for “Smarter Screening” strategies

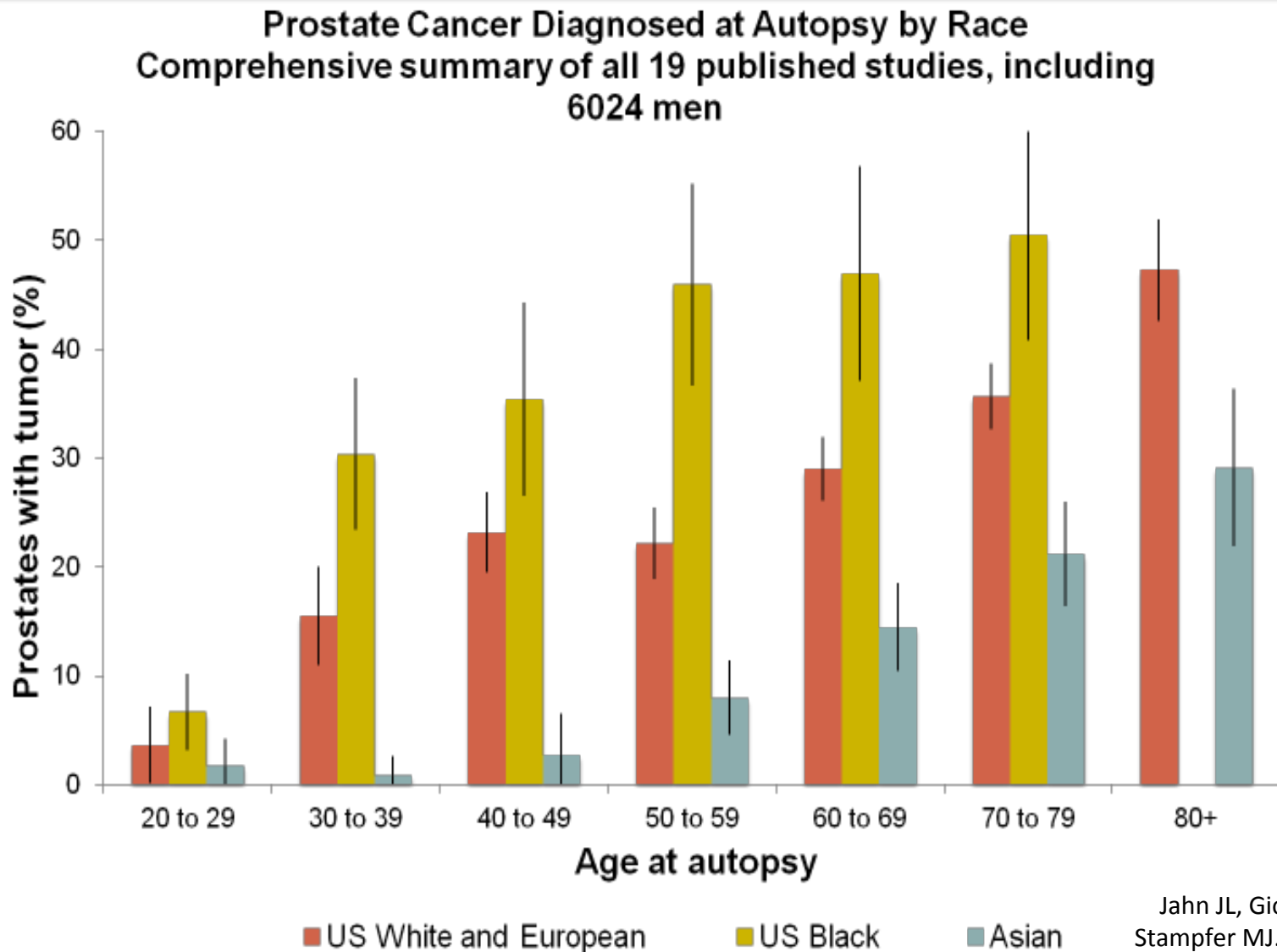
“Baseline PSA”

One measure of PSA in midlife, at age 40 or 45

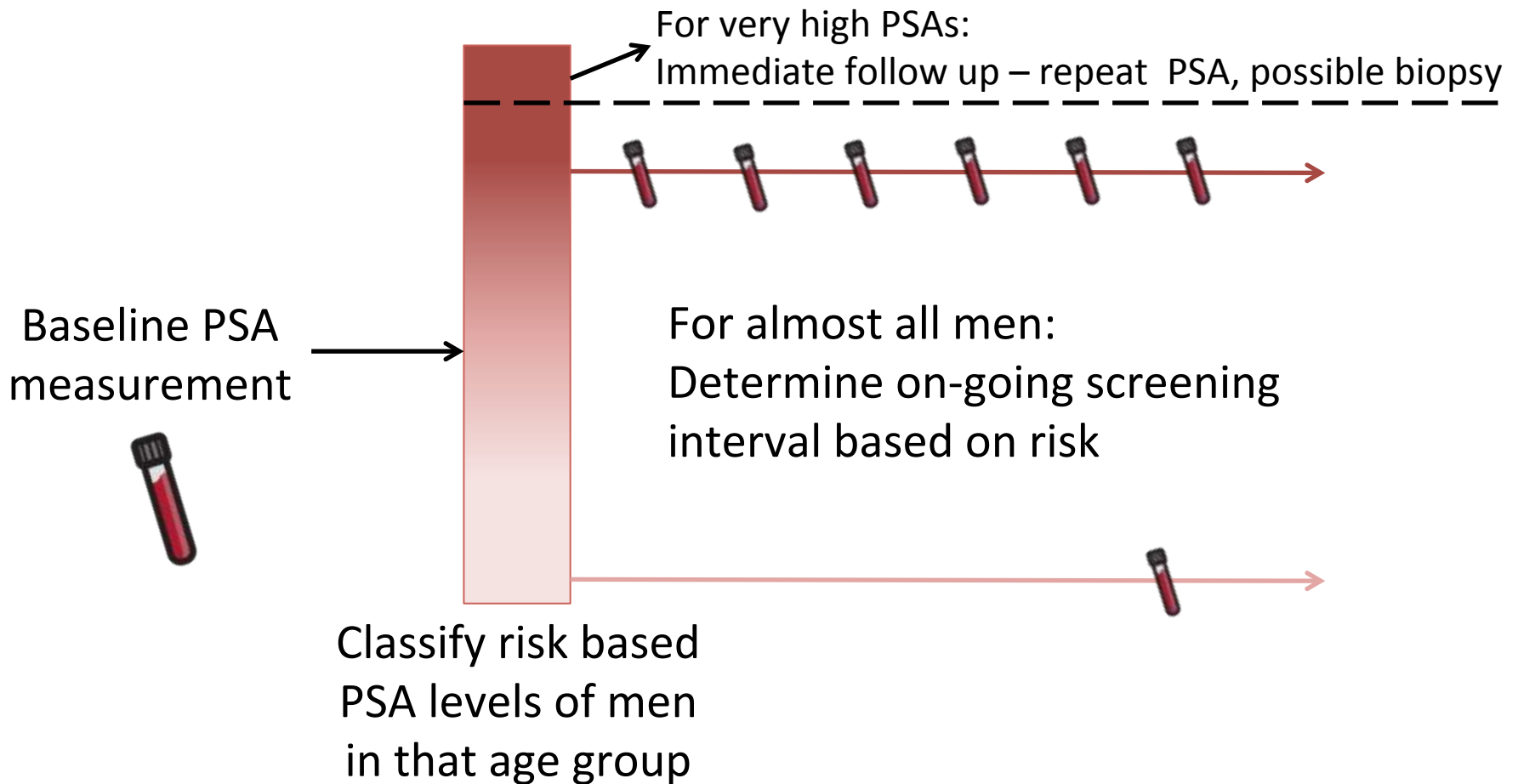
Goals:

- Predict future risk of prostate cancer
 - Personalize on-going screening recommendations
- *Not* aiming to diagnose cancer or do biopsies at this point

Motivation for baseline PSA testing: Prostate cancer starts at a young age



Baseline PSA screening strategy



Baseline PSA and lethal prostate cancer

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ORIGINAL REPORT

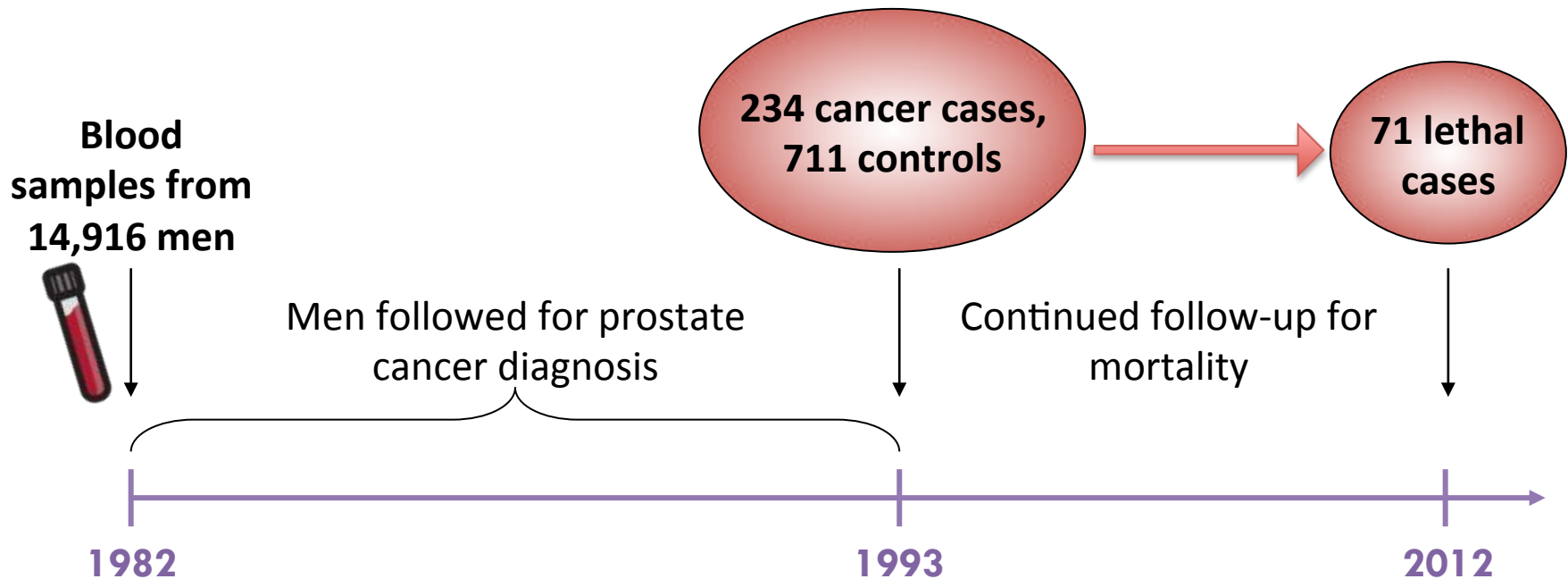
Baseline Prostate-Specific Antigen Levels in Midlife Predict Lethal Prostate Cancer

Mark A. Preston, Julie L. Batista, Kathryn M. Wilson, Sigrid V. Carlsson, Travis Gerke, Daniel D. Sjoberg, Douglas M. Dahl, Howard D. Sesso, Adam S. Feldman, Peter H. Gann, Adam S. Kibel, Andrew J. Vickers, and Lorelei A. Mucci

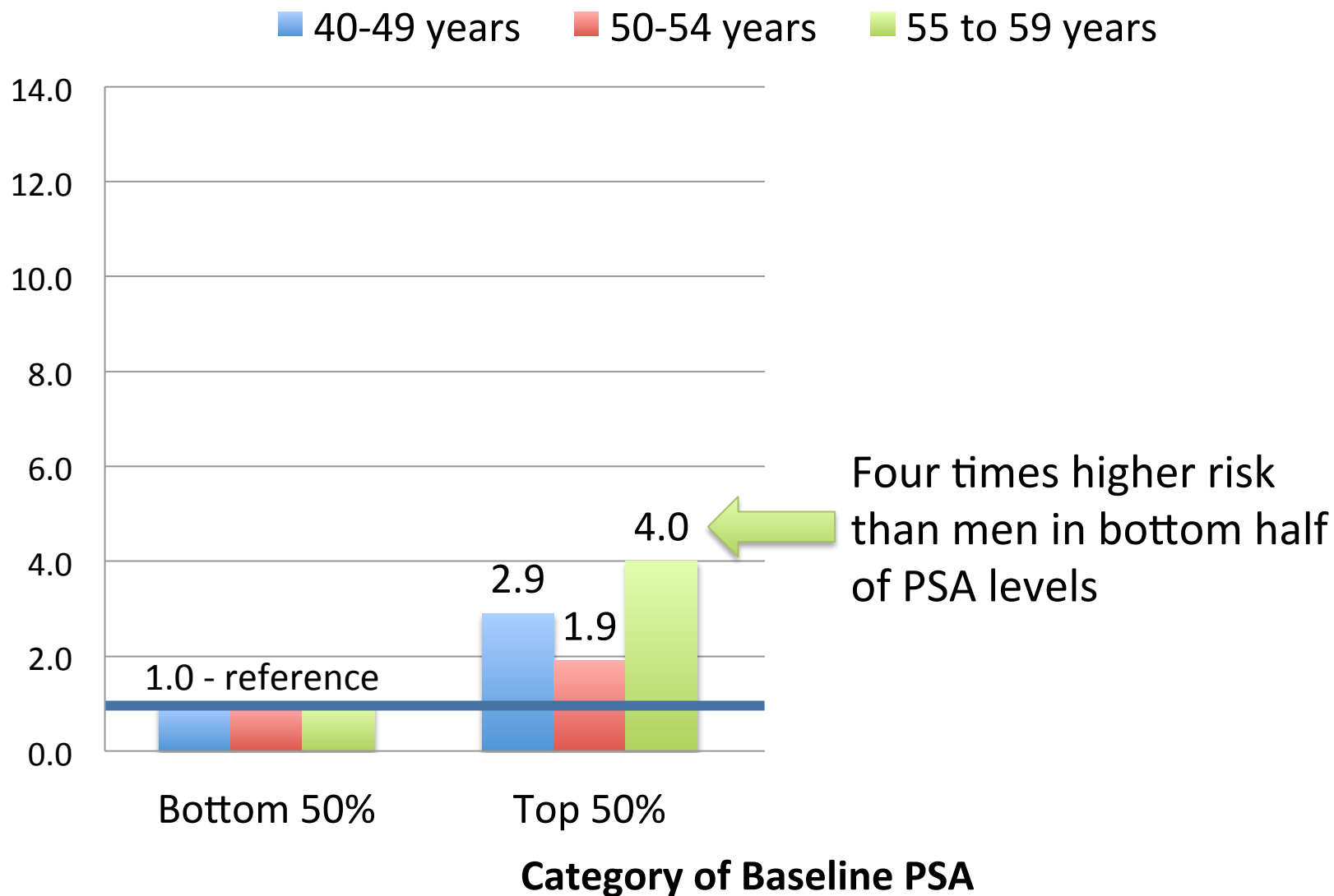
Physicians' Health Study

Randomized trial of aspirin and beta-carotene among 22,071 US male physicians started in 1982

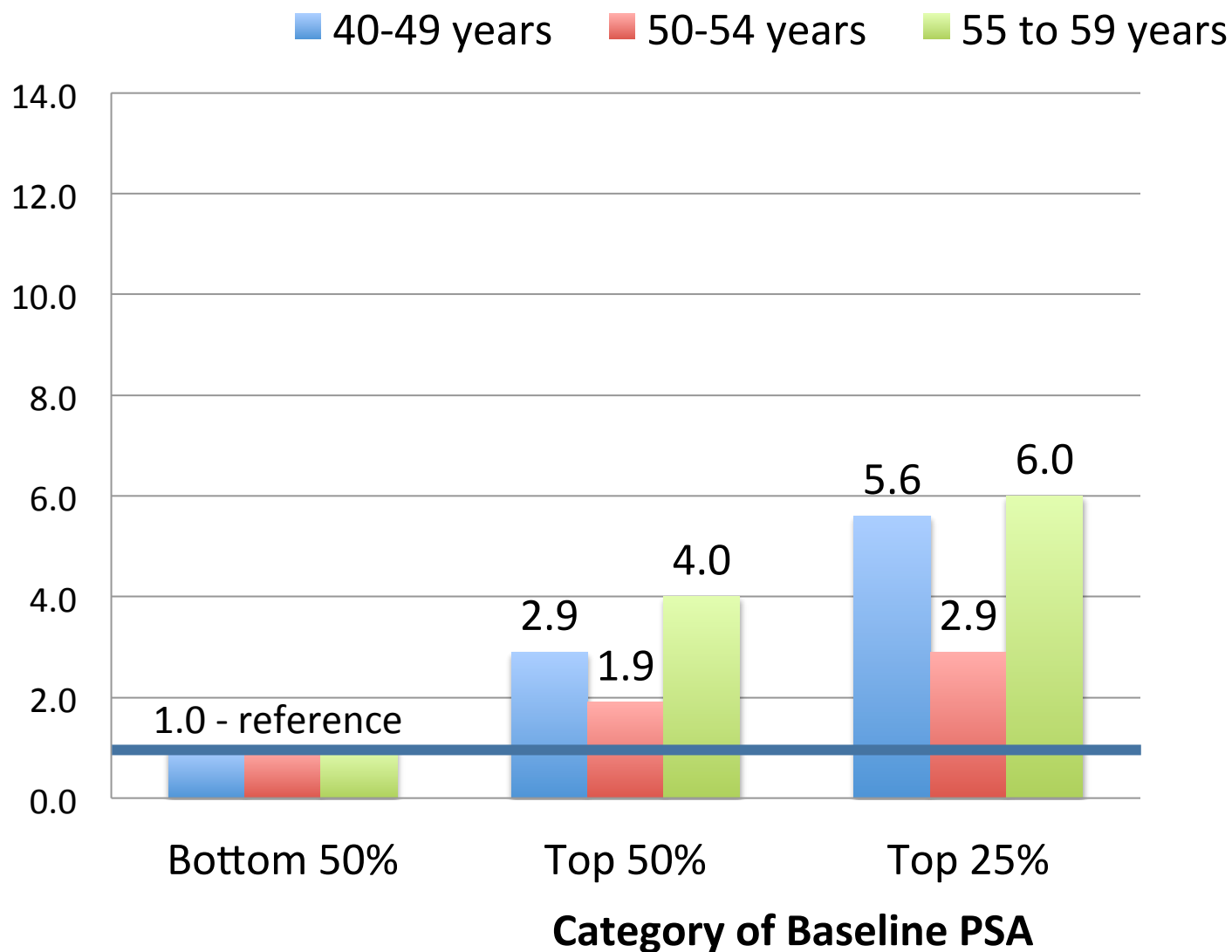
- For this study: Focus on men age 40-59 in 1982, followed for prostate cancer mortality for 30 years



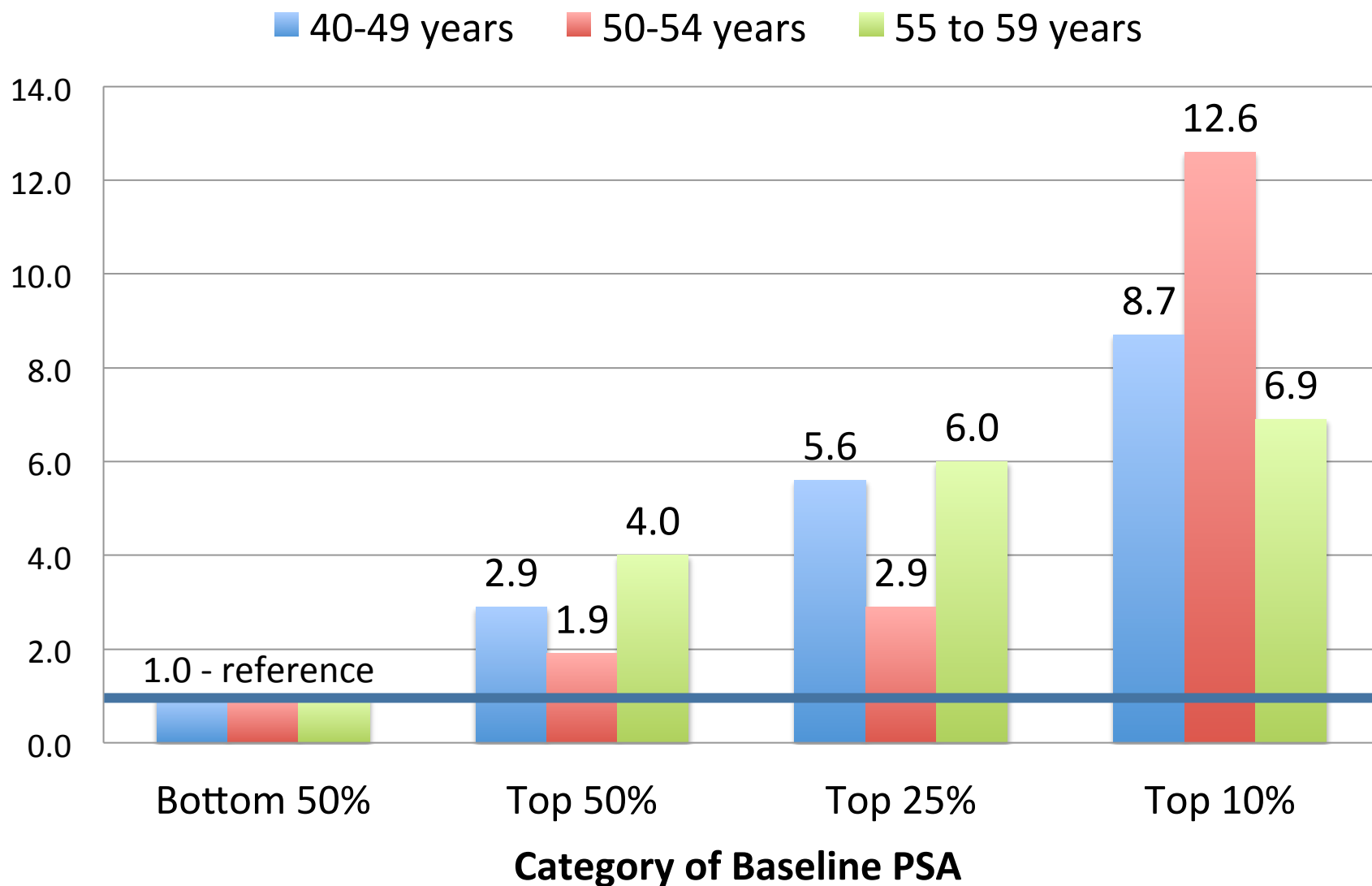
Odds ratio for lethal prostate cancer by baseline PSA



Odds ratio for lethal prostate cancer by baseline PSA

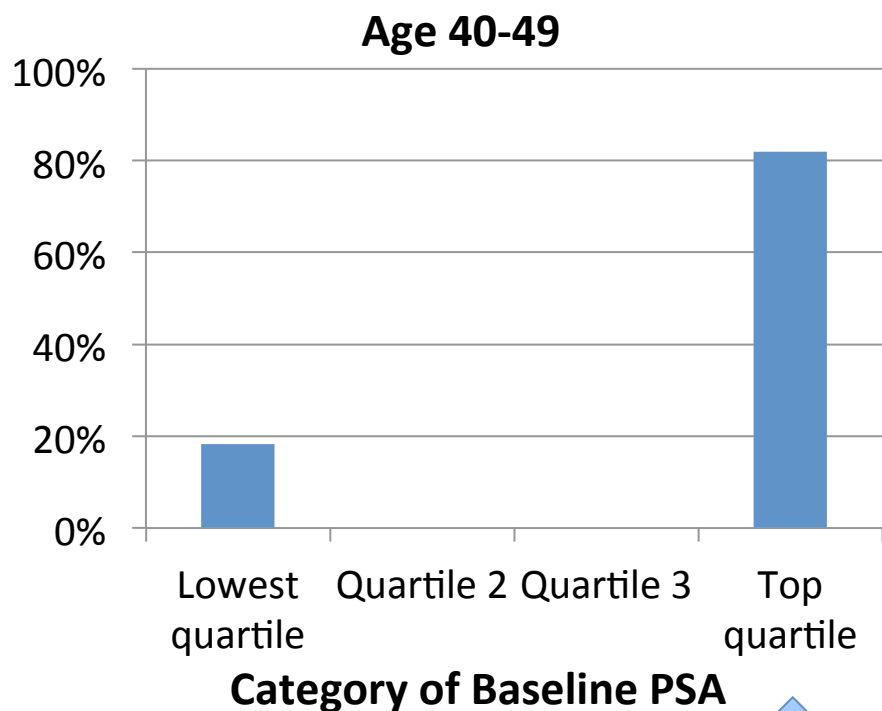


Odds ratio for lethal prostate cancer by baseline PSA

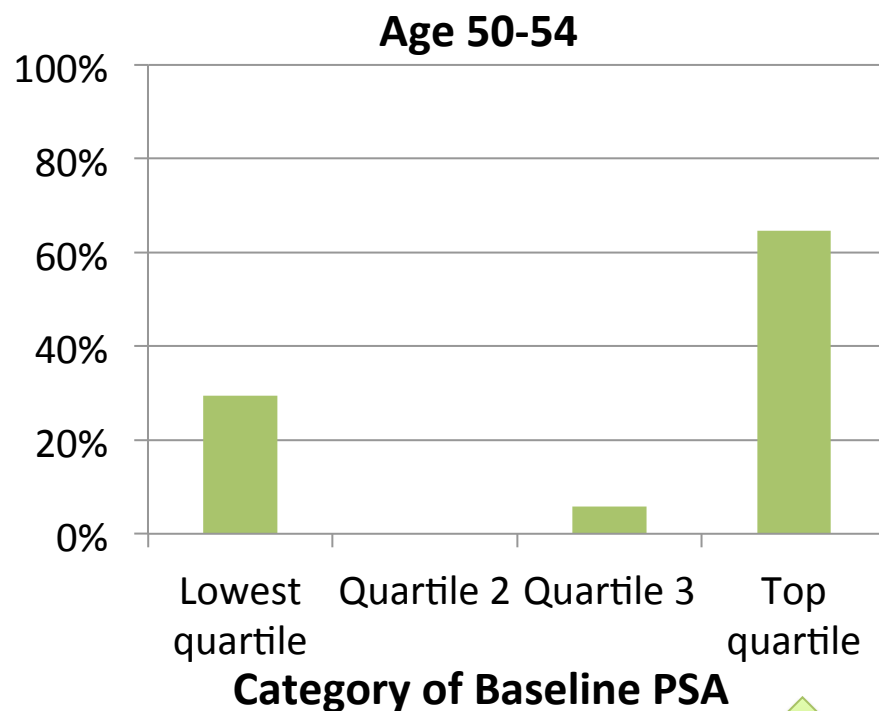


How well does baseline PSA classify men?

Percent of lethal prostate cancer from each category of baseline PSA



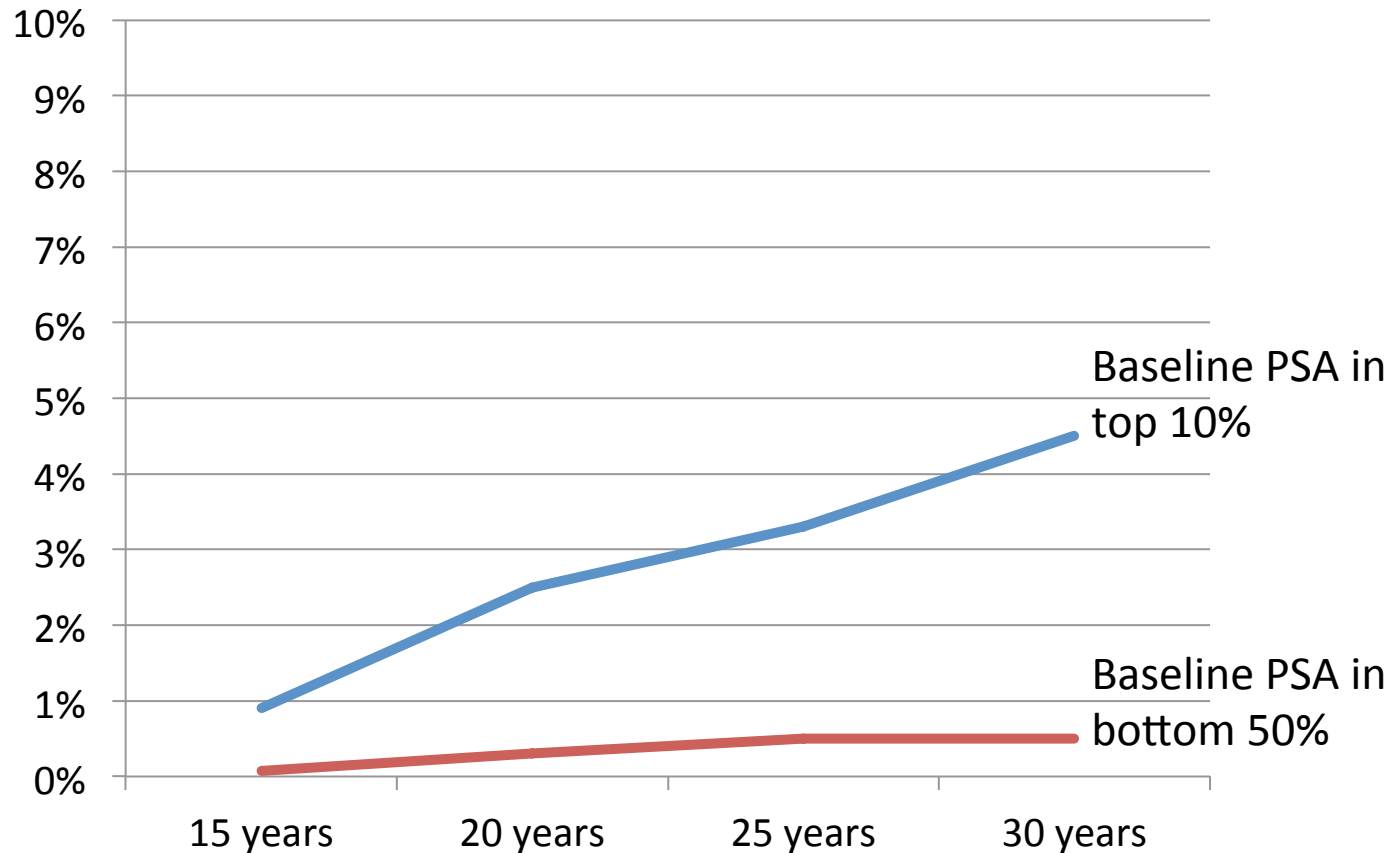
82% of lethal cases were among men in the top quarter of PSA values



62% of lethal cases were among men in the top quarter of PSA values

Long-term risk of lethal prostate cancer

Cumulative risk of lethal prostate cancer according to PSA at age 45-49



Are these results relevant for African American men?

Our PSA study was in a cohort that is 95% white

Recommendation Summary		
Population	Recommendation	Grade (What's This?)
Men, Screening with PSA	The U.S. Preventive Services Task Force (USPSTF) recommends against prostate-specific antigen (PSA)-based screening for prostate cancer.	D



Based mainly on 2 trials:

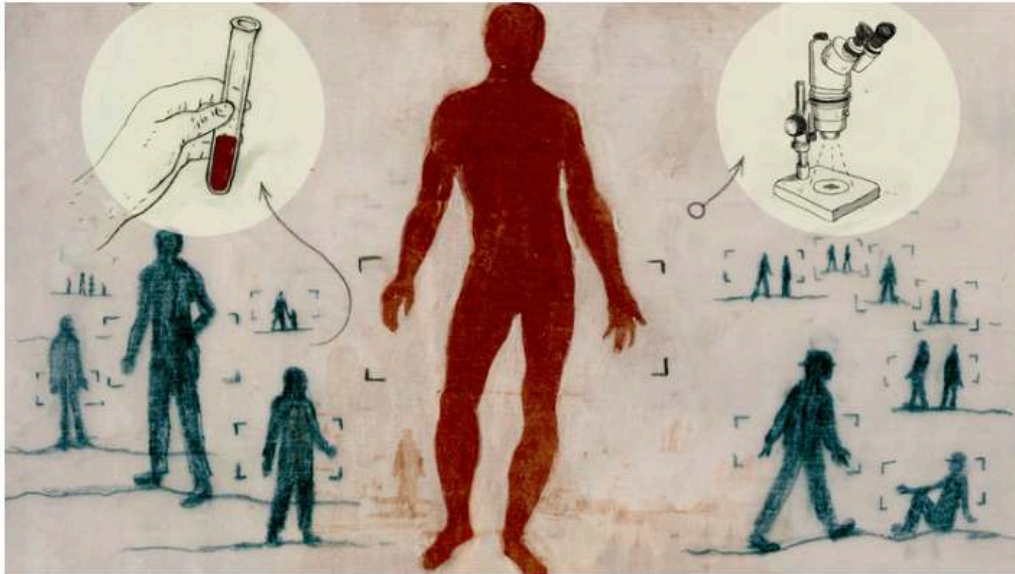
- US trial: 4% of men were African American
- European trial: didn't report on race

Prostate cancer and race

The New York Times

Prostate Cancer Isn't Colorblind

By LANNIS HALL, ARNOLD D. BULLOCK, ANGELA L. BROWN and GRAHAM COLDITZ JULY 27, 2016



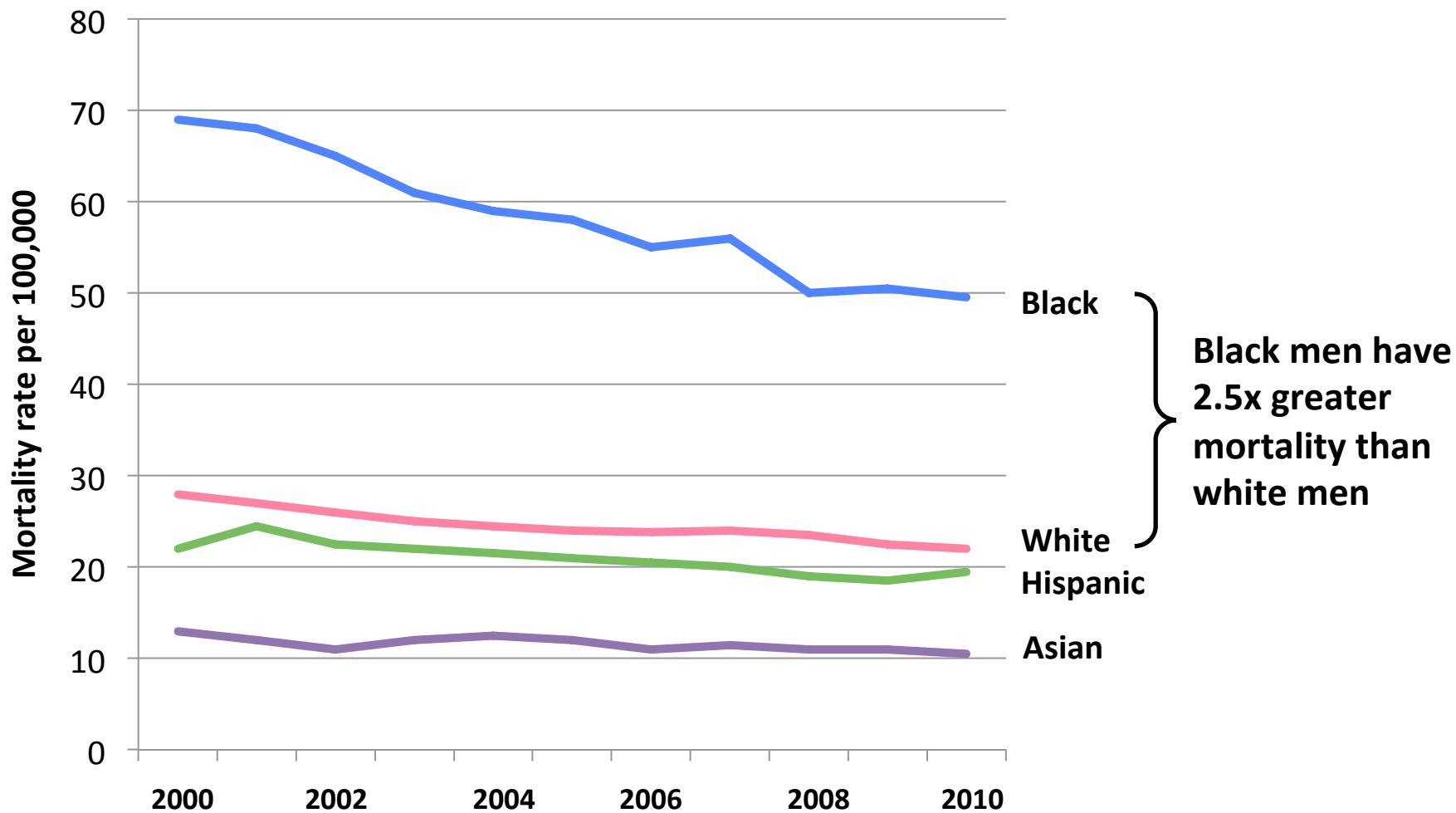
Jonathon Rosen

“The risks facing African-Americans are shocking: They have the highest incidence of prostate cancer and the highest mortality rate from the disease of any ethnic or racial group in the United States.

**1 in 6 will get prostate cancer
1 in 23 will die from it”**

ST. LOUIS — In 1966, the Rev. Dr. Martin Luther King Jr. [said](#), “Of all the forms of inequality, injustice in health care is the most shocking and inhuman.” While major advances have been made in health care, ethnic and racial disparities remain in the prevention, diagnosis and treatment of

Trends in U.S. prostate cancer mortality by race and ethnicity



Southern Community Cohort Study



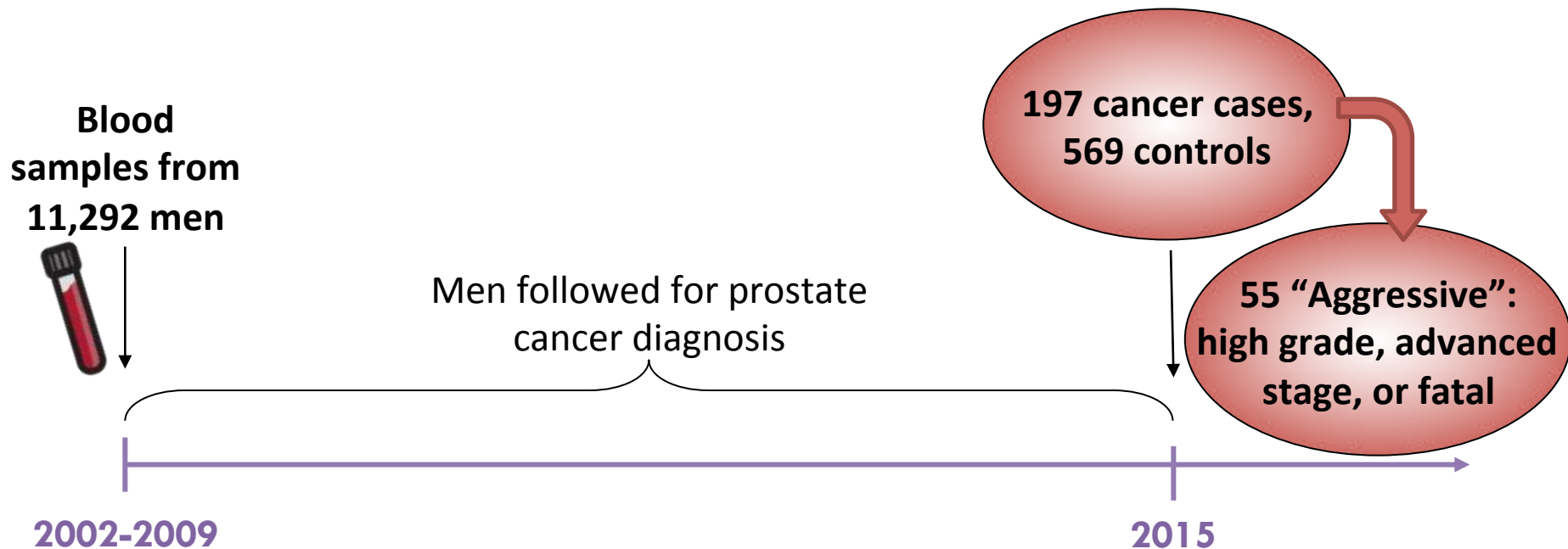
Cohort of 85,000 men and women recruited from community health centers in the Southeastern U.S.

- Enrollment from 2002-2009
- Two-thirds of participants are African American, with 22,905 African American men
- Average 51 years old at start

Southern Community Cohort Study

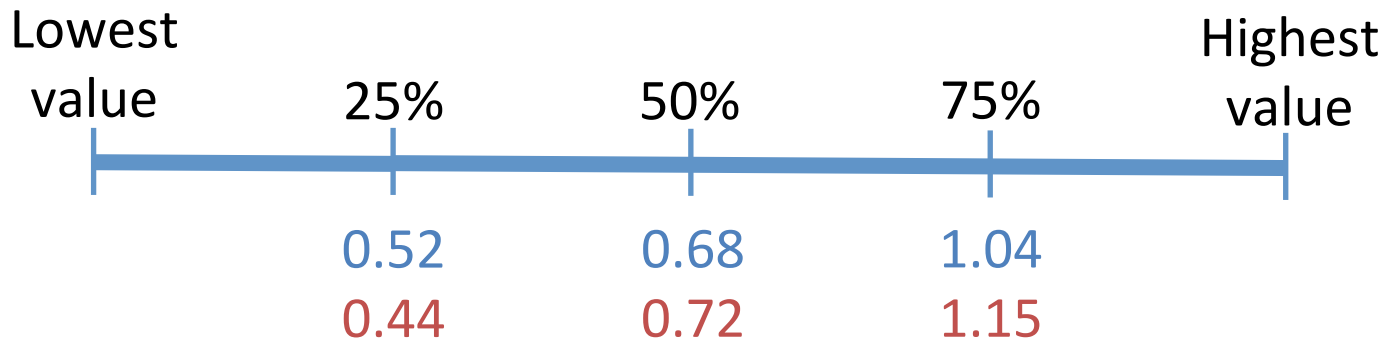
Study population: African American men age 40-64 at start of study

- Median follow-up of 9 years



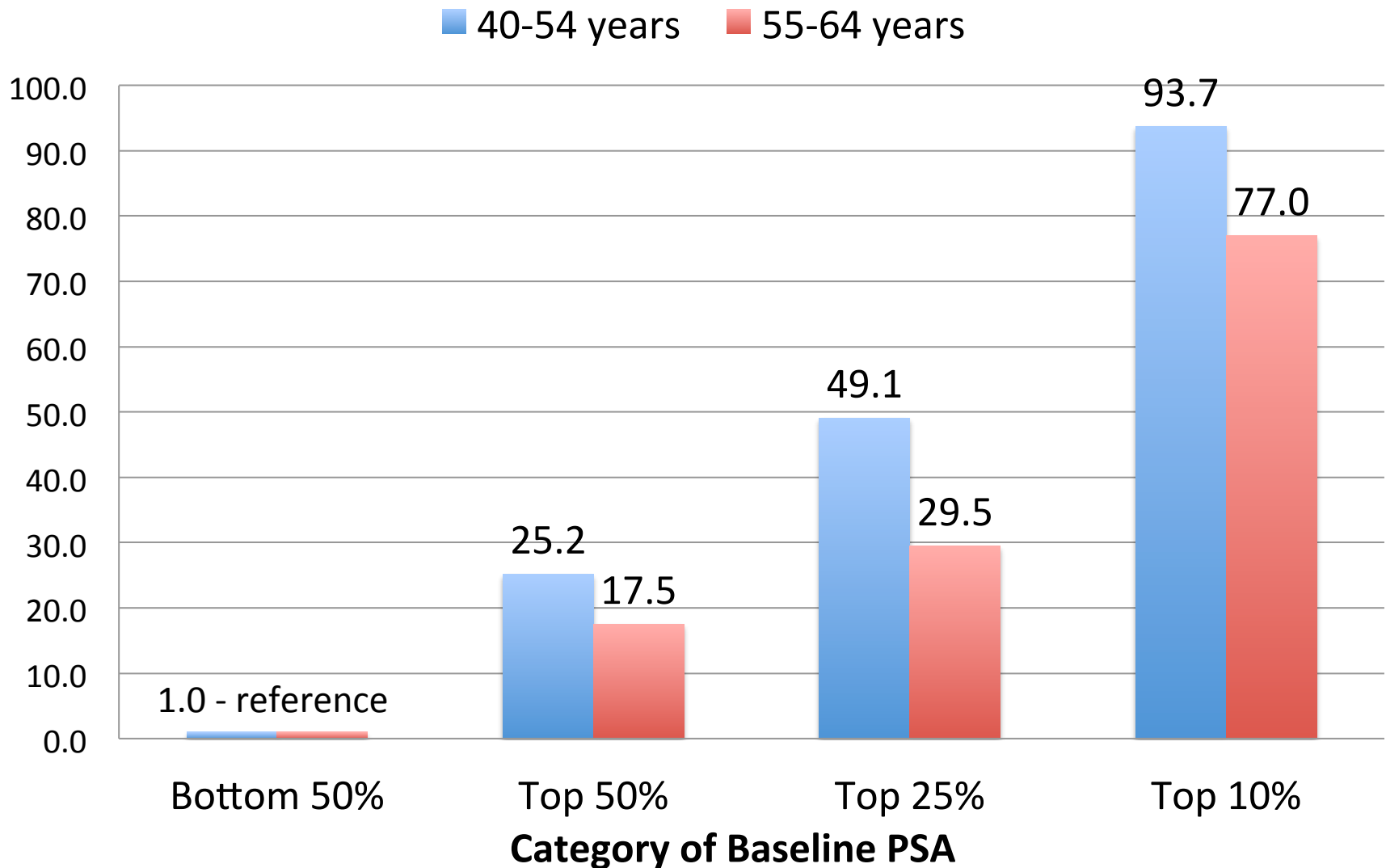
PSA Levels among controls age 40-49 years

Percentiles of PSA (ng/mL) in: Physicians' Health Study Southern Community Cohort Study

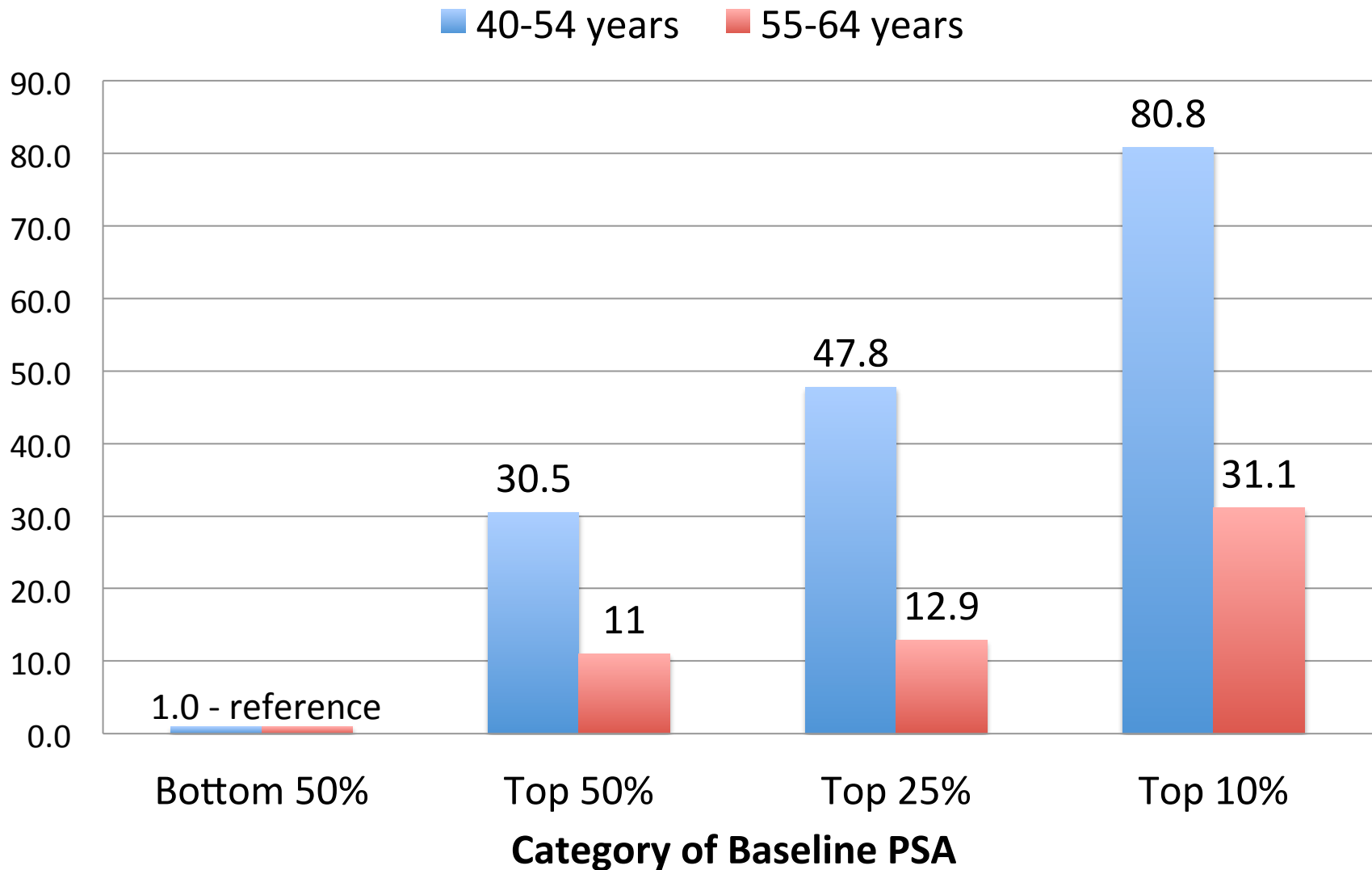


→ PSA levels at age 40-49 among men who remained free of prostate cancer are very similar in the two cohorts

Odds ratio for total prostate cancer by baseline PSA in African American men



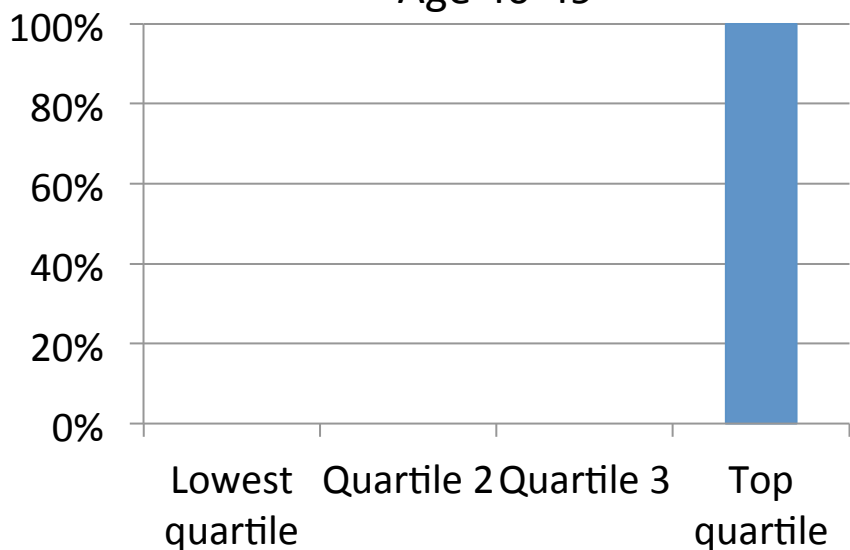
Odds ratio for aggressive prostate cancer by baseline PSA in African American men



How well does baseline PSA classify men by future risk?

Percent of aggressive prostate cancer from each category of baseline PSA

Age 40-49

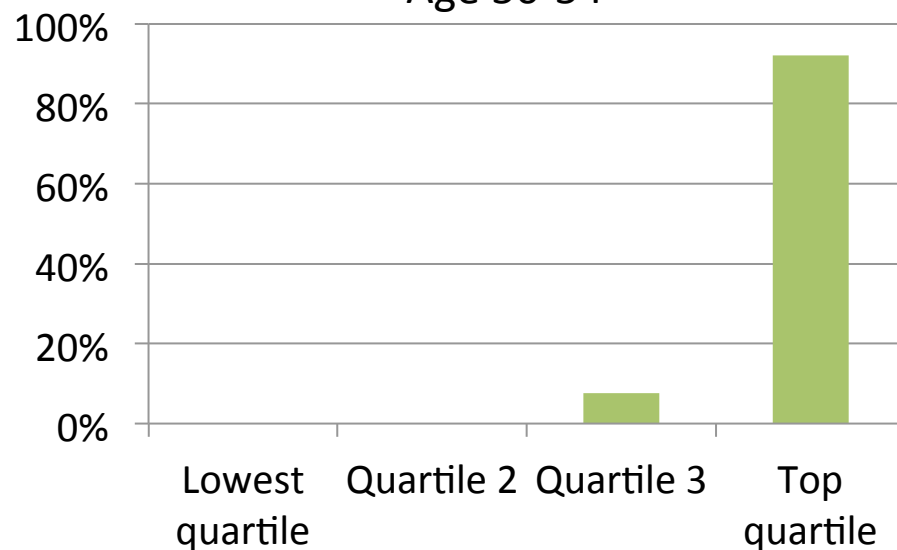


Category of Baseline PSA



ALL aggressive cases were among men in the top quarter of PSA values

Age 50-54



Category of Baseline PSA



92% of aggressive cases were among men in the top quarter of PSA values

Summary

- Midlife PSA levels strongly predict risk of:
 - Lethal prostate cancer in a cohort of largely white men over several decades of follow-up
 - Aggressive prostate cancer in a cohort of African American men over about one decade of follow-up
- PSA levels in midlife among men who did not get diagnosed with prostate cancer were very similar in the two cohorts
- A midlife measurement of PSA may allow for risk-stratified screening strategies and more effective use of PSA screening for prostate cancer

Thank you!

Collaborators:

Mark Preston

Lorelei Mucci

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PHS Table 1

Table 1: Characteristics of prostate cancer cases and controls, Physicians' Health Study

	Original case-control study		Updated case-control study	
	Controls (n= 711)	Total Cases (n= 234)	Controls for Lethal Cases (n=213)	Lethal Cases (n=71)
Study period	1982-1993		1982 - 2012	
Mean age at blood draw (SD)	54.5 (4.1)	54.5 (4.1)	55.0 (4.1)	54.9 (4.1)
<45 years, n (%)	20 (2.8)	7 (3.0)	3 (1.4)	1 (1.4)
45-<50 years, n (%)	84 (11.8)	27 (11.5)	28 (13.2)	10 (14.1)
50-<55 years, n (%)	202 (28.4)	70 (29.9)	51 (23.9)	17 (24.0)
55-<60 years, n (%)	405 (57.0)	130 (55.6)	131 (61.5)	43 (60.6)
Mean BMI at baseline (SD)	24.7 (2.5)	24.9 (2.6)	24.7 (2.5)	25.4 (2.7)
< 25 kg/m ² , n (%)	408 (57.4)	123 (52.6)	123 (57.8)	31 (43.7)
≥25 kg/m ² , n (%)	303 (42.6)	111 (47.4)	90 (42.3)	40 (56.3)
Caucasian race, n (%)	659 (93.6)	224 (96.1)	201 (94.8)	69 (97.2)
Smoking status at baseline				
Never, n (%)	338 (47.5)	111 (47.4)	102 (47.9)	31 (43.7)
Past, n (%)	314 (44.2)	102 (43.6)	98 (46.0)	31 (43.7)
Current, n (%)	59 (8.3)	21 (9.0)	13 (6.1)	9 (12.7)
Median PSA at baseline [IQR]	0.89 [0.58-1.45]	2.34 [1.34-4.78]	1.04 [0.63-1.68]	2.96 [1.31-6.56]

SCCS Table 1

	Cases N=197	Controls N=569	Aggressive cases N=55
African-American, %	100	100	100
Follow-up time, years, median [IQR]	9.0 [7.0,11.0]	9.0 [7.0,11.0]	9.0 (7.0,10.0)
Blood markers, median [IQR]			
Total PSA	3.50 [2.08,6.48]	0.83 [0.51,1.40]	3.61 [2.02,11.90]
Free PSA	0.57 [0.35,0.93]	0.25 [0.17,0.38]	0.58 [0.34,1.09]
Age at blood draw, N (%)			
40-49 years	36 (18%)	110 (19%)	9 (16%)
50-54 years	45 (23%)	143 (25%)	13 (24%)
55-59 years	59 (30%)	172 (30%)	15 (27%)
60-64 years	57 (29%)	144 (25%)	18 (33%)
Ever had DRE by baseline (%)	67%	63%	74%
Ever had PSA test by baseline (%)	58%	57%	48%
Marital Status, N (%)			
Married	77 (39%)	175 (31%)	17 (31%)
Separated/Divorced	79 (40%)	243 (43%)	30 (55%)
Widowed	11 (6%)	31 (43%)	3 (6%)
Single, Never Married	30 (15%)	120 (21%)	5 (9%)
Education, N (%)			
< 9 years	20 (10%)	71 (12%)	6 (11%)
9-11 years	53 (27%)	154 (27%)	16 (29%)
High school/GED	71 (36%)	189 (33%)	21 (38%)
Vocational school/Some college	31 (16%)	116 (20%)	6 (11%)
College/Graduate school	22 (11%)	39 (7%)	6 (11%)
BMI at baseline, N (%)			
< 25 kg/m ²	63 (32%)	198 (35%)	23 (42%)
25-29 kg/m ²	69 (35%)	203 (36%)	18 (33%)
≥30 kg/m ²	65 (33%)	168 (30%)	14 (25%)
Smoking status at baseline, N (%)			
Never	38 (19%)	128 (23%)	4 (7%)
Past	62 (31%)	137 (24%)	14 (25%)
Current	97 (49%)	304 (53%)	37 (67%)
Pack-years among ever smokers, mean	24.2	22.8	25.1

SCCS Table 1, continued

	Cases	Aggressive Cases
Case Characteristics		
Age at diagnosis, median [IQR]	60.4 [55.5,64.3]	60.5 [56.3,65.3]
Time to diagnosis, years, median [IQR]	4.4 [2.2,6.1]	5.0 [2.5,6.3]
Diagnosed within 1 yr of blood draw	17 (9%)	5 (9%)
Diagnosed within 2 yrs of blood draw	46 (23%)	12 (22%)
Lethal cases¹, N (%)	17 (9%)	17 (31%)
Aggressive cases², N (%)	55 (28%)	--

SCCS Table 2

Table 2. Distribution of total PSA by age group among controls

	10th percentile	25th percentile	50th percentile	75th percentile	90th percentile
Age 40-49	0.32	0.44	0.72	1.15	1.68
Age 50-54	0.33	0.46	0.80	1.08	1.85
Age 55-59	0.36	0.52	0.94	1.65	2.73
Age 60-64	0.39	0.64	1.03	1.89	3.33

	PSA level (ng/mL)	Proportion of cancers in category	
		Total prostate cancer	Aggressive prostate cancer
40-49 years			
Top 10th percentile	≥ 1.68	86%	100%
Top quartile	≥ 1.15	92%	100%
Above median	≥ 0.72	94%	100%
Below median	< 0.72	6%	0%
Bottom quartile	< 0.44	0%	0%
Bottom 10th percentile	< 0.32	0%	0%
50-54 years			
Top 10th percentile	≥ 1.85	69%	46%
Top quartile	≥ 1.08	91%	92%
Above median	≥ 0.80	98%	100%
Below median	< 0.80	2%	0%
Bottom quartile	< 0.46	0%	0%
Bottom 10th percentile	< 0.33	0%	0%
55-59 years			
Top 10th percentile	≥ 2.73	66%	73%
Top quartile	≥ 1.66	86%	80%
Above median	≥ 0.94	93%	87%
Below median	< 0.94	7%	13%
Bottom quartile	< 0.52	3%	7%
Bottom 10th percentile	< 0.36	0%	0%
60-64 years			
Top 10th percentile	≥ 3.33	68%	61%
Top quartile	≥ 1.89	88%	83%
Above median	≥ 1.03	96%	94%
Below median	< 1.03	4%	6%
Bottom quartile	< 0.64	4%	6%
Bottom 10th percentile	< 0.39	2%	6%