

Biomarkers of Lethal Prostate Cancer

Example of Baseline PSA level in midlife

IX International Congress of Uro-Oncology
Sao Paulo Brazil

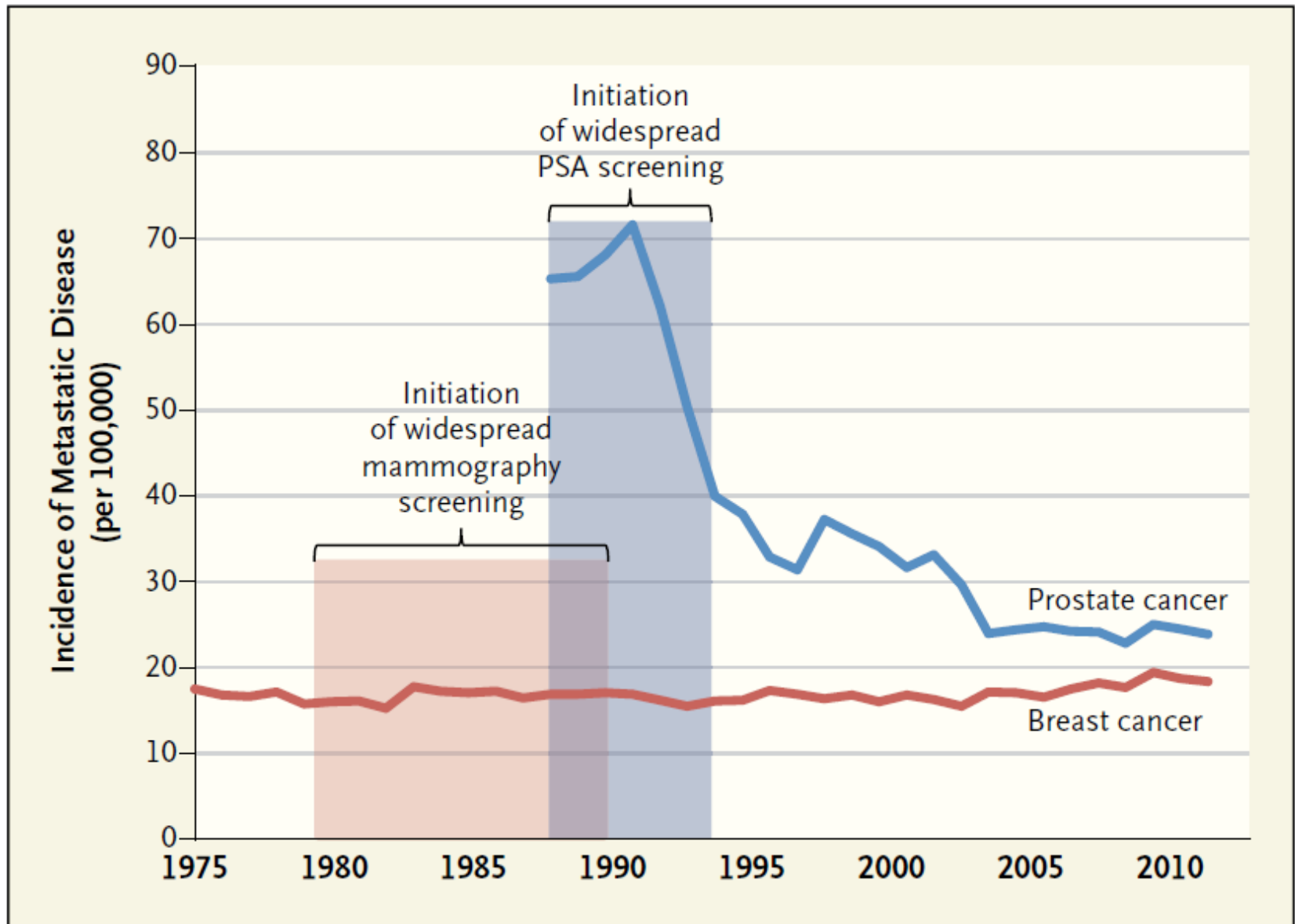
Lorelei Mucci, ScD
Associate Professor of Epidemiology
Harvard TH Chan School of Public Health

Leader, Cancer Epidemiology
Dana-Farber/Harvard Cancer Center

@loreleimucci



Metastatic Cancer Incidence at Presentation in the U.S.

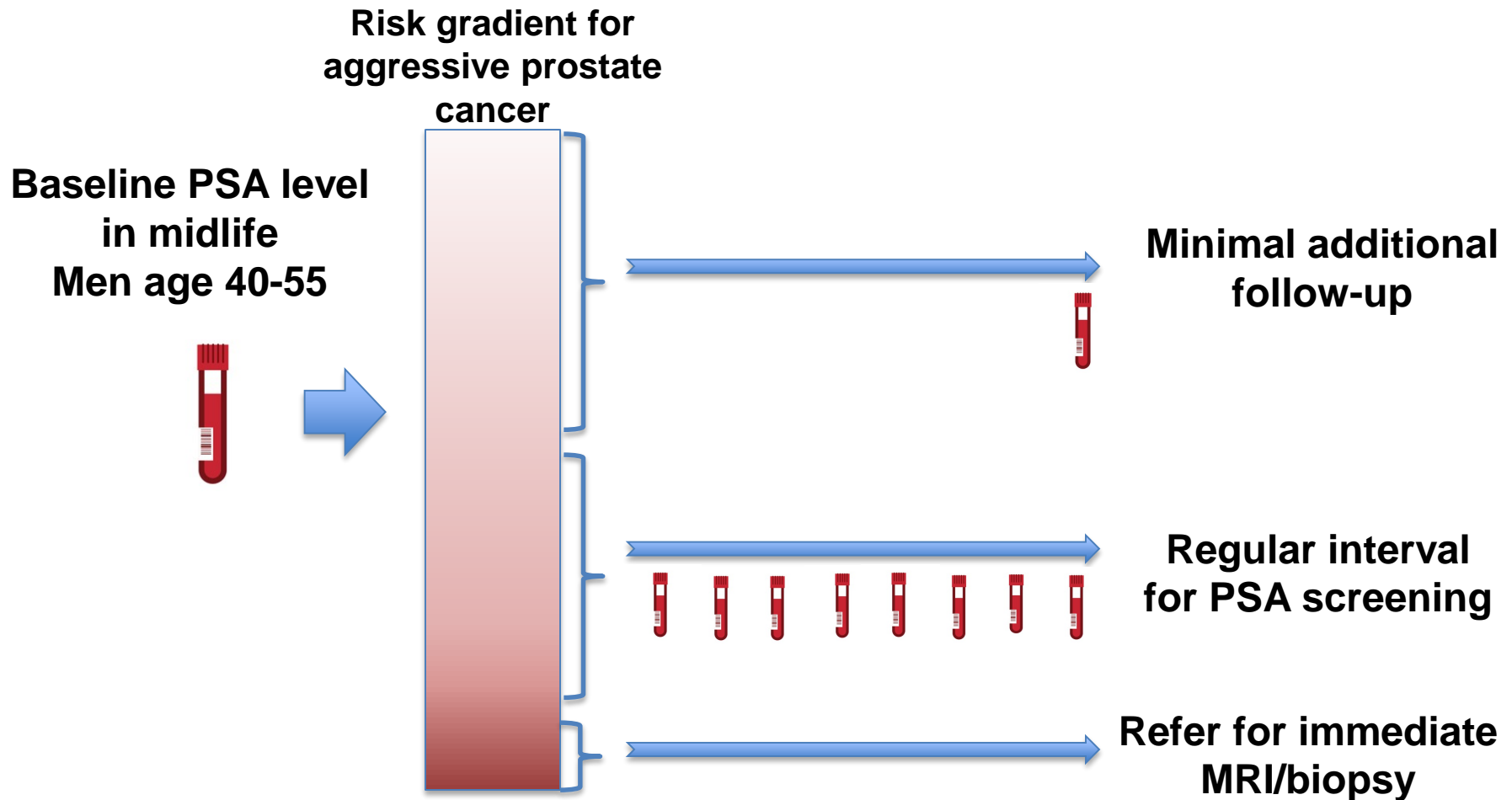


Background: PSA as a screening tool

Prostate cancer screening using **prostate-specific antigen (PSA)** is controversial:

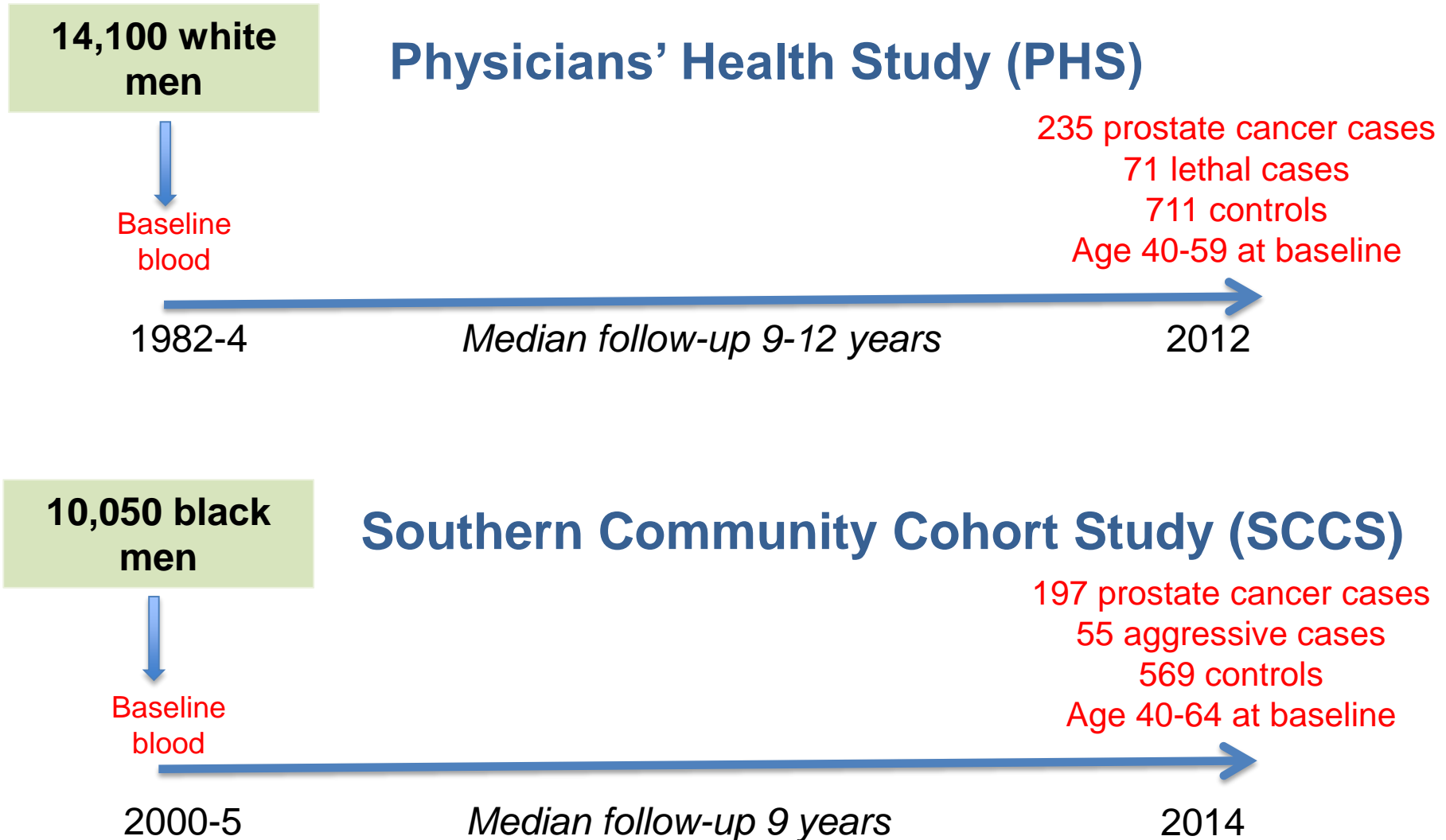
- European trial of PSA screening demonstrated significant reduction in prostate cancer mortality.
- U.S. PLCO trial failed to show survival benefit, although may be benefit when accounting for contamination of screening in control arm.
- Widespread use has led to many unnecessary biopsies as well as overdiagnosis of indolent prostate cancer.
 - In U.S., 1 million men undergo prostate biopsy each year, 80% do not have cancer.
 - Only 1 in 4 with an initial negative biopsy will eventually be diagnosed with cancer.
- Some cancers still detected too late, after they have metastasized.
- **Urgent need for reliable predictors of future risk – particularly for high-risk disease.**

Is there an alternate, risk-stratified screening strategy?



Preliminary studies:

Baseline PSA in midlife and aggressive prostate cancer



Distribution of baseline PSA values in midlife among controls

		Total PSA, ng/mL				
Age group	Race	Study population	25th percentile	50th percentile	75th percentile	90th percentile
40-49 years						
40-49	Black	SCCS	0.44	0.72	1.15	1.68
40-49	White (94%)	PHS	0.52	0.68	1.04	1.68
45-49	White	Malmo	0.41	0.60	0.94	-
50-55 years						
50-54	Black	SCCS	0.46	0.80	1.08	1.85
50-54	White (94%)	PHS	0.59	0.88	1.40	1.96
51-55	White	Malmo	0.52	0.84	1.36	-
55-59 years						
55-59	Black	SCCS	0.52	0.94	1.65	2.73
55-59	White (94%)	PHS	0.60	0.96	1.64	2.88

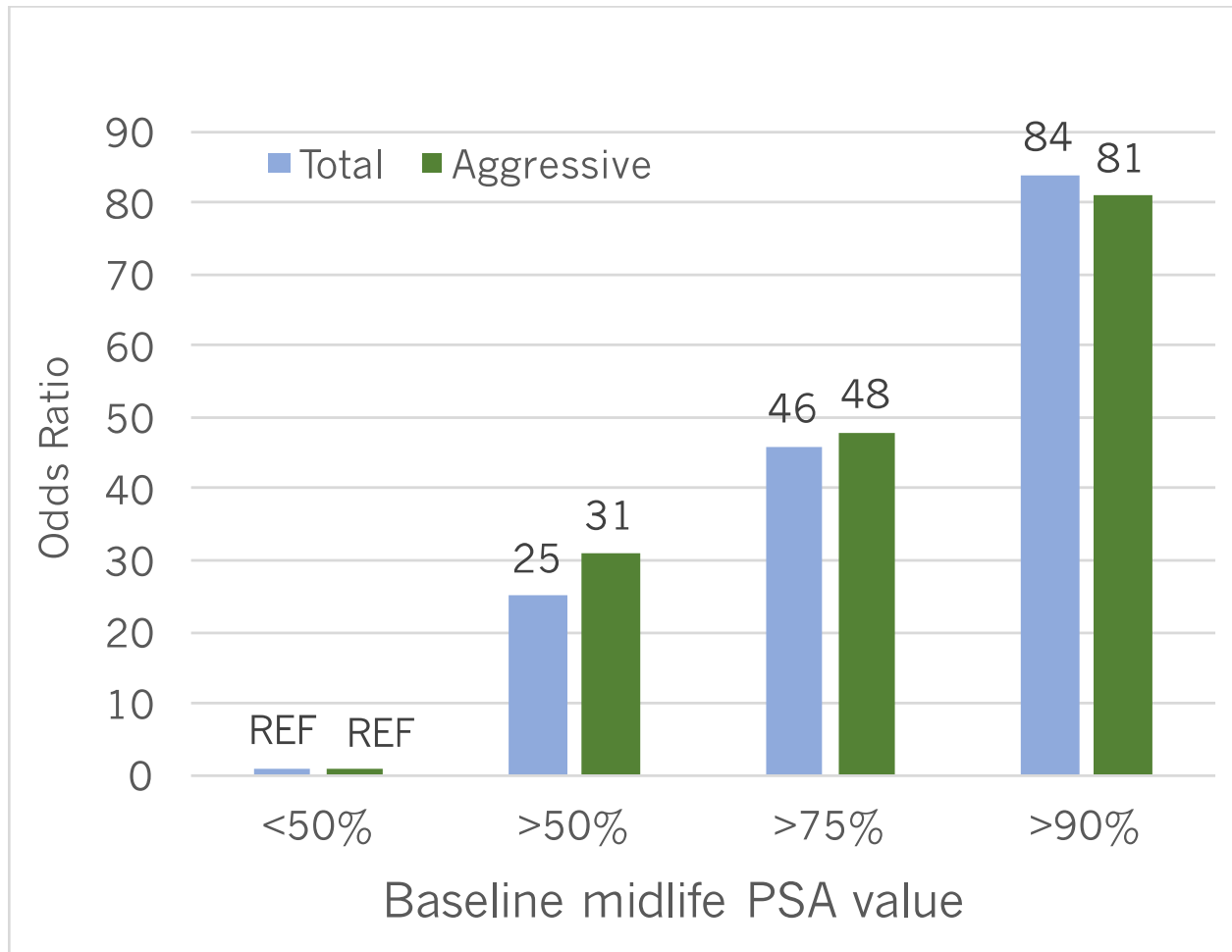
Physicians' Health Study

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

Age group	Median PSA level	% cases with PSA above median	RR (95% CI) >90% vs below median
		Total	Total
40 to 49 years	0.68 ng/ml	95%	32.4 (7.1,149.0)
50 to 54 years	0.88 ng/ml	94%	34.6 (11.5,103.6)
55 to 59 years	0.96 ng/ml	96%	30.3 (13.5,67.7)

Baseline PSA in midlife and prostate cancer risk in SCCS



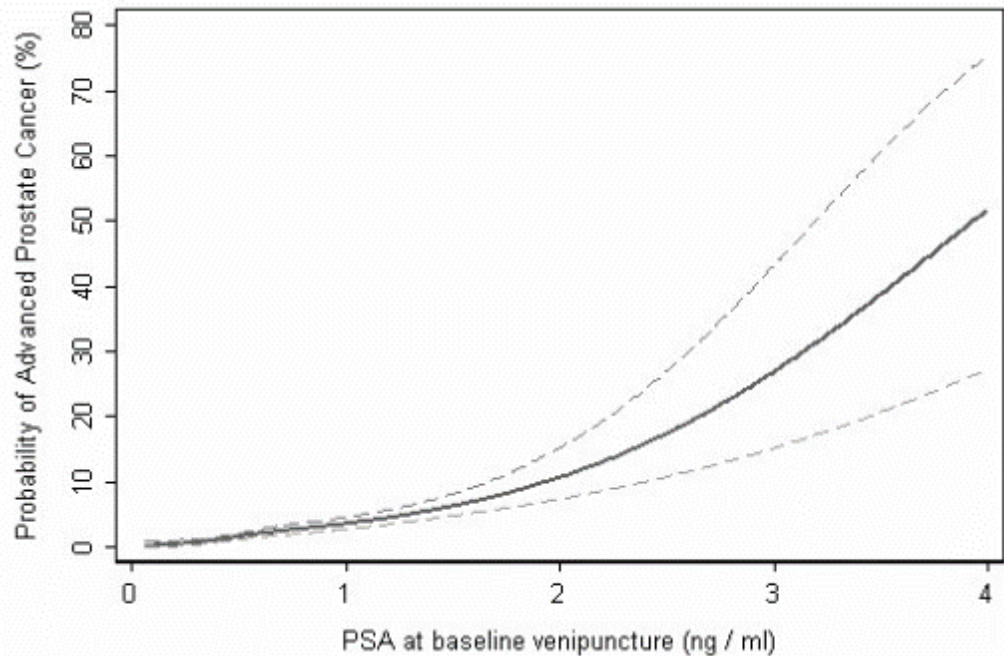
Relative risks remain high excluding cases diagnosed in first 5 years of blood draw

Proportion of total and aggressive cancers captured by PSA percentiles - SCCS

	PSA level (ng/mL)	Total prostate cancer	Aggressive prostate cancer
40 to 49 years			
Top 10th percentile	>1.68	86%	100%
Top quartile	>1.15	89%	100%
Above median	>0.72	94%	100%
Below median	≤0.72	6%	0%
50 to 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%
55 to 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%

Additional Studies on baseline midlife PSA

- Whittemore *et al*, 2005
 - Blood among men at [median age 34 years](#)
 - Median PSA in whites, 0.37 ng/ml and in blacks, 0.33 ng/ml
 - Relative risks of ~7 for high vs. low baseline PSA
- Lilja *et al*, 2007
 - Blood among men age 44 to 50 years



Unanswered questions

- Can pre-diagnostic PSA level in midlife predict future risk of aggressive or lethal prostate cancer
 - Yes, but based on observational data
- Can prediction be further refined?
 - A small proportion of patients with “low” baseline PSA will be diagnosed with aggressive cancer in future
 - Some patients with an elevated PSA have indolent or no cancer
- Why is the PSA elevated in midlife?
- Can a baseline PSA level in midlife be used to identify cohort of patients who are still treatable?

Acknowledgements

Harvard TH Chan School of Public Health

Kathy Wilson

Sarah Markt

Meir Stampfer

Lisa Signorello

Moffitt Cancer Center

Travis Gerke

Vanderbilt-Ingram Cancer Center

William Blot

Mark Steinwandel

Brigham and Women's Hospital

Mark Preston

Adam Kibel

Quoc Trinh

Memorial Sloan Kettering

Hans Lilja

Andrew Vickers

Sigrid Carlsson

PRACTICAL/PROTeCT

Ros Eeles

David Neal

Funding

- National Institutes of Health/National Cancer Institute
- Dana-Farber/Harvard Cancer Center Mazzone Awards Program
- Dana-Farber/Harvard Cancer Center SPORE in Prostate Cancer
- Prostate Cancer Foundation Young Investigator Awards
- American Urological Association Urology Care Foundation Scholar Award