

Not Just Black and White: Disparities in Prostate Cancer Management in the US

Alicia Morgans, MD, MPH

Associate Professor of Medicine

Robert H. Lurie Comprehensive Cancer Center

Northwestern University Feinberg School of Medicine

Disclosures

- Honoraria from Bayer, Janssen, Astellas, AstraZeneca
- Research funding from Bayer, Genentech, Seattle Genetics

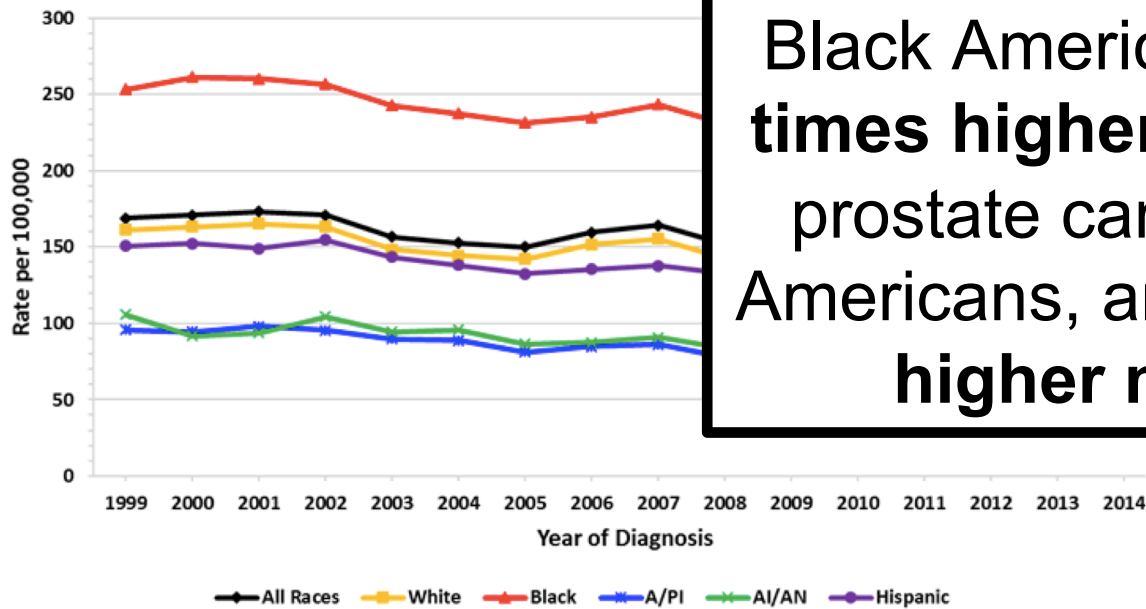
Outline

- Background: Not just black and white
- Disparities in personalized medicine
- Biology vs Access: Can improved access overcome biology?
- Efforts to make a difference
- Conclusions

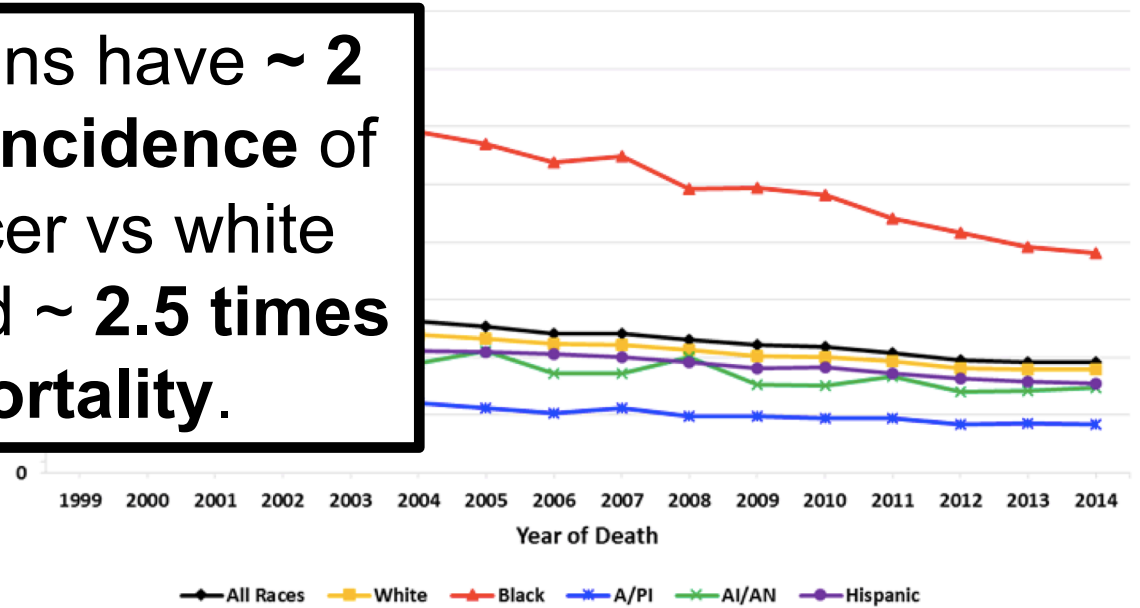
Background

- 174,650 new diagnoses of prostate cancer in 2019 in the US

Incidence in the US by Race

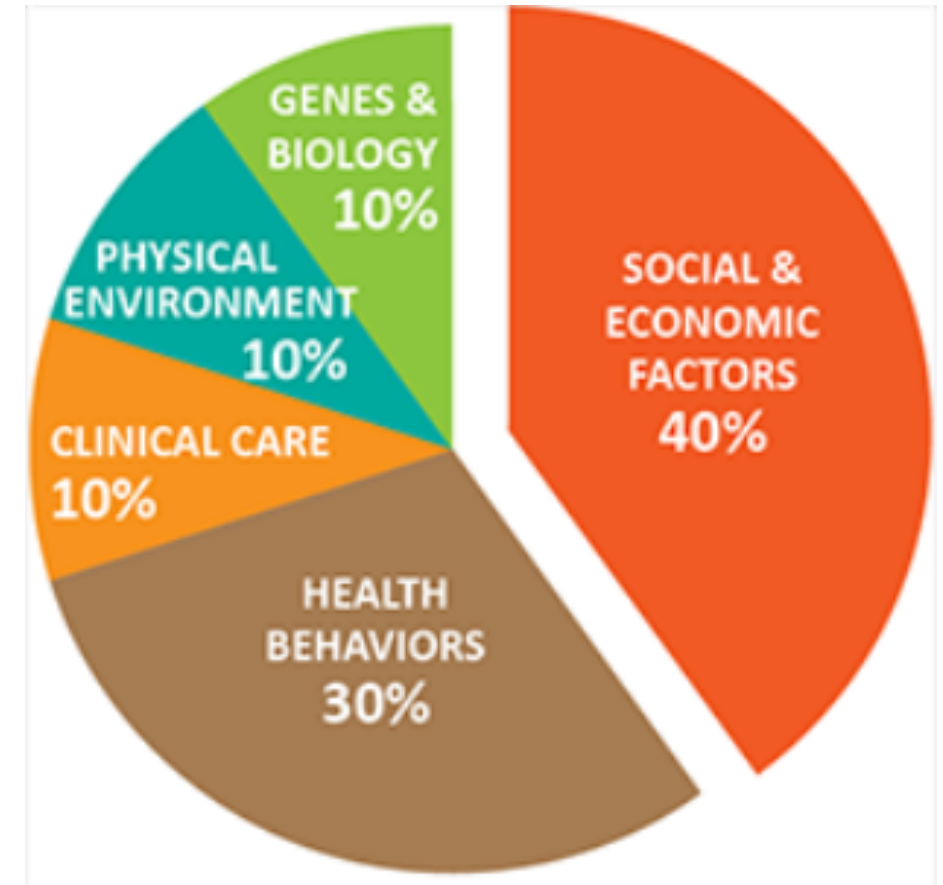
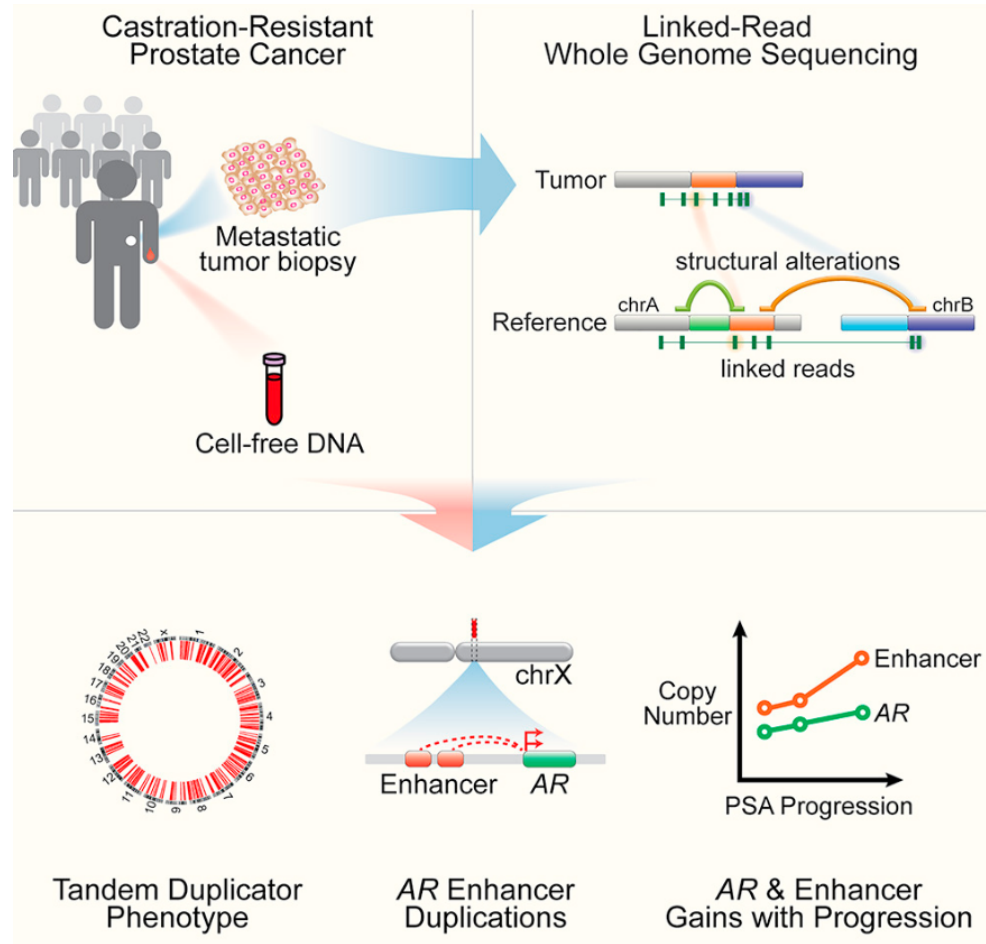


Death in the US by Race



Black Americans have ~ **2 times higher incidence** of prostate cancer vs white Americans, and ~ **2.5 times higher mortality**.

Biology or Other Factors?



Social Determinants of Health

Viswanathan SR, et al. Cell. 2018.

http://images.huffingtonpost.com/2016-08-05-1470421229-8733640-socialdeterminants_health250.PNG

Not Just Black and White

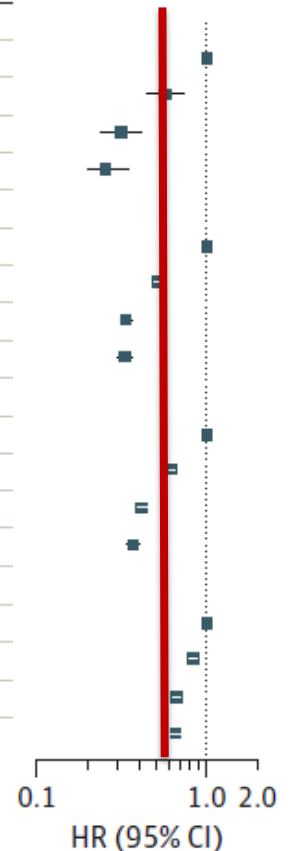
- Disparities exist by **race**, **socioeconomic status**, **age**, **geography**, **education** and others
- Disparities in both cancer specific outcomes and supportive care delivery

Disparity by Age:

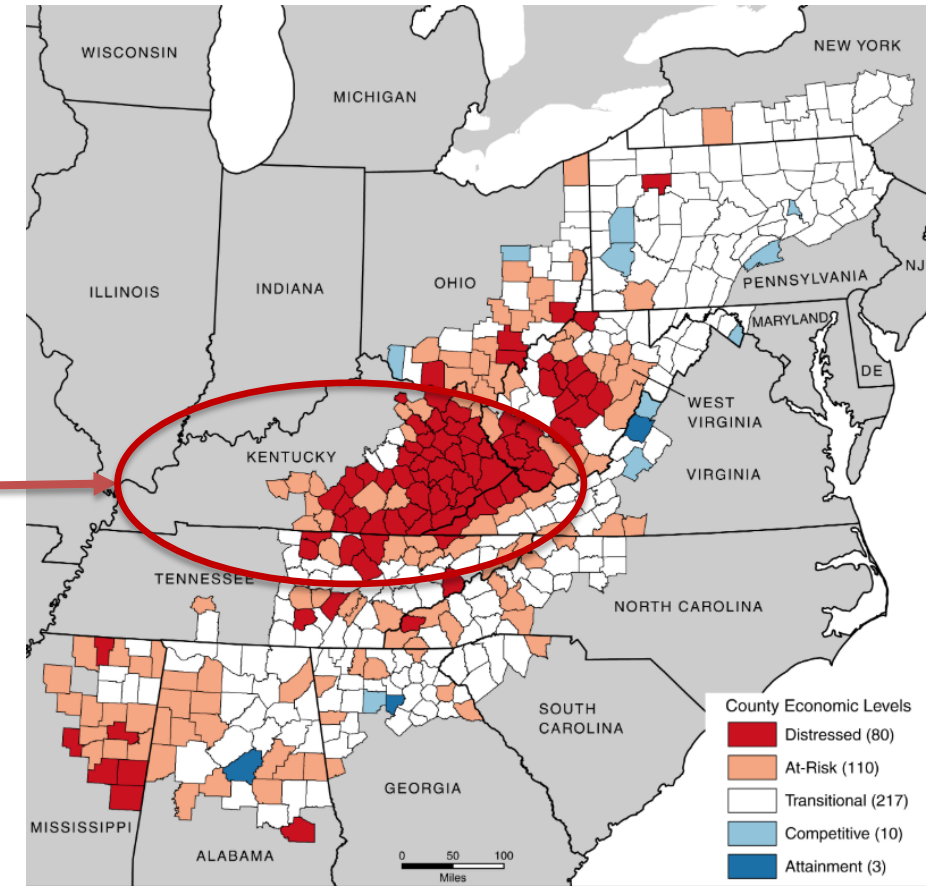
Improvements in survival more pronounced for younger than older men

F Prostate ($P = 3.58 \times 10^{-89}$)

Age groups, y	HR (95% CI)
20-49	
1990-1994	1 [Reference]
1995-1999	0.57 (0.45-0.73)
2000-2004	0.31 (0.24-0.41)
2005-2009	0.25 (0.18-0.35)
50-64	
1990-1994	1 [Reference]
1995-1999	0.52 (0.49-0.55)
2000-2004	0.33 (0.31-0.36)
2005-2009	0.32 (0.30-0.36)
65-74	
1990-1994	1 [Reference]
1995-1999	0.62 (0.60-0.65)
2000-2004	0.41 (0.39-0.44)
2005-2009	0.37 (0.34-0.40)
75-85	
1990-1994	1 [Reference]
1995-1999	0.83 (0.79-0.87)
2000-2004	0.66 (0.63-0.70)
2005-2009	0.65 (0.61-0.70)



Appalachia: Education and Poverty Drive Disparities



Created by the Appalachian Regional Commission, June 2019
Data Sources:
Unemployment data: U.S. Bureau of Labor Statistics, LAUS, 2015–2017
Income data: U.S. Bureau of Economic Analysis, REIS, 2017
Poverty data: U.S. Census Bureau, American Community Survey, 2013–2017

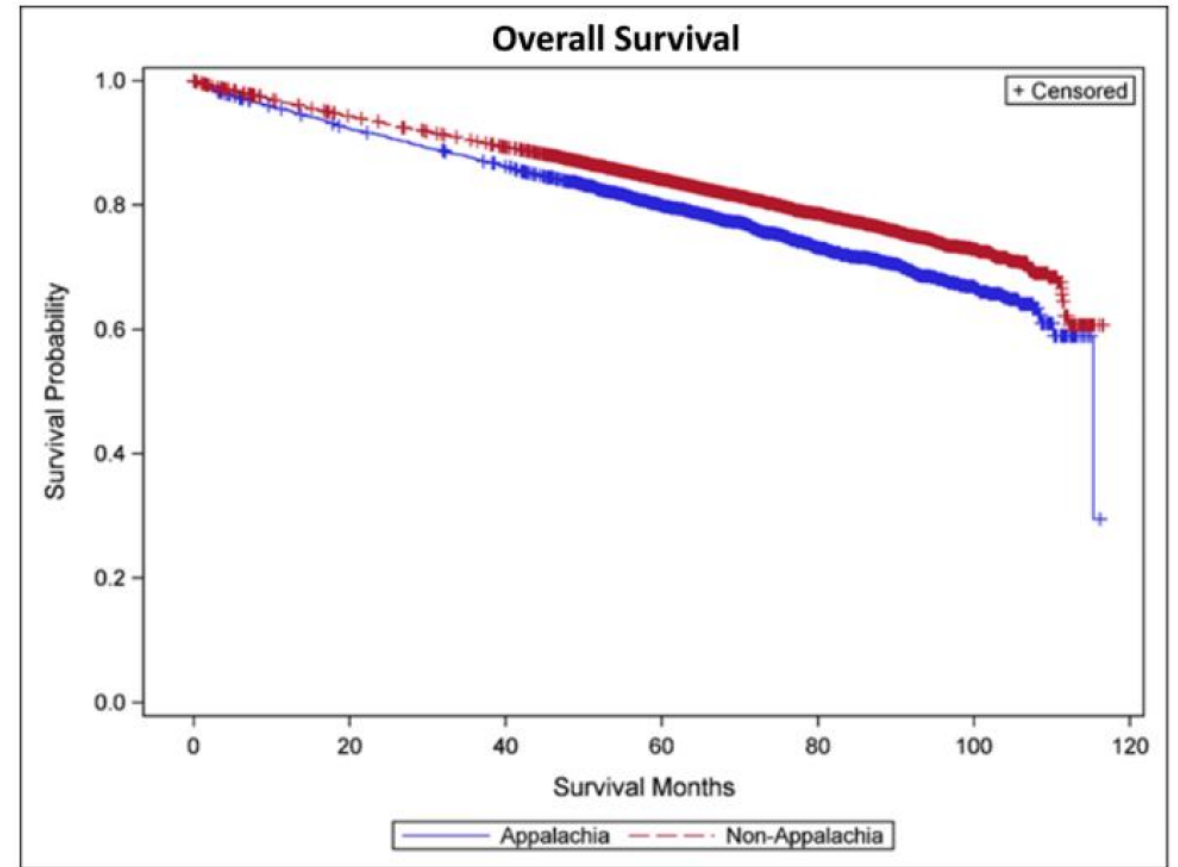
Effective October 1, 2019
through September 30, 2020

<https://www.worldatlas.com/maps/united-states.html>

Appalachia Regional Commission

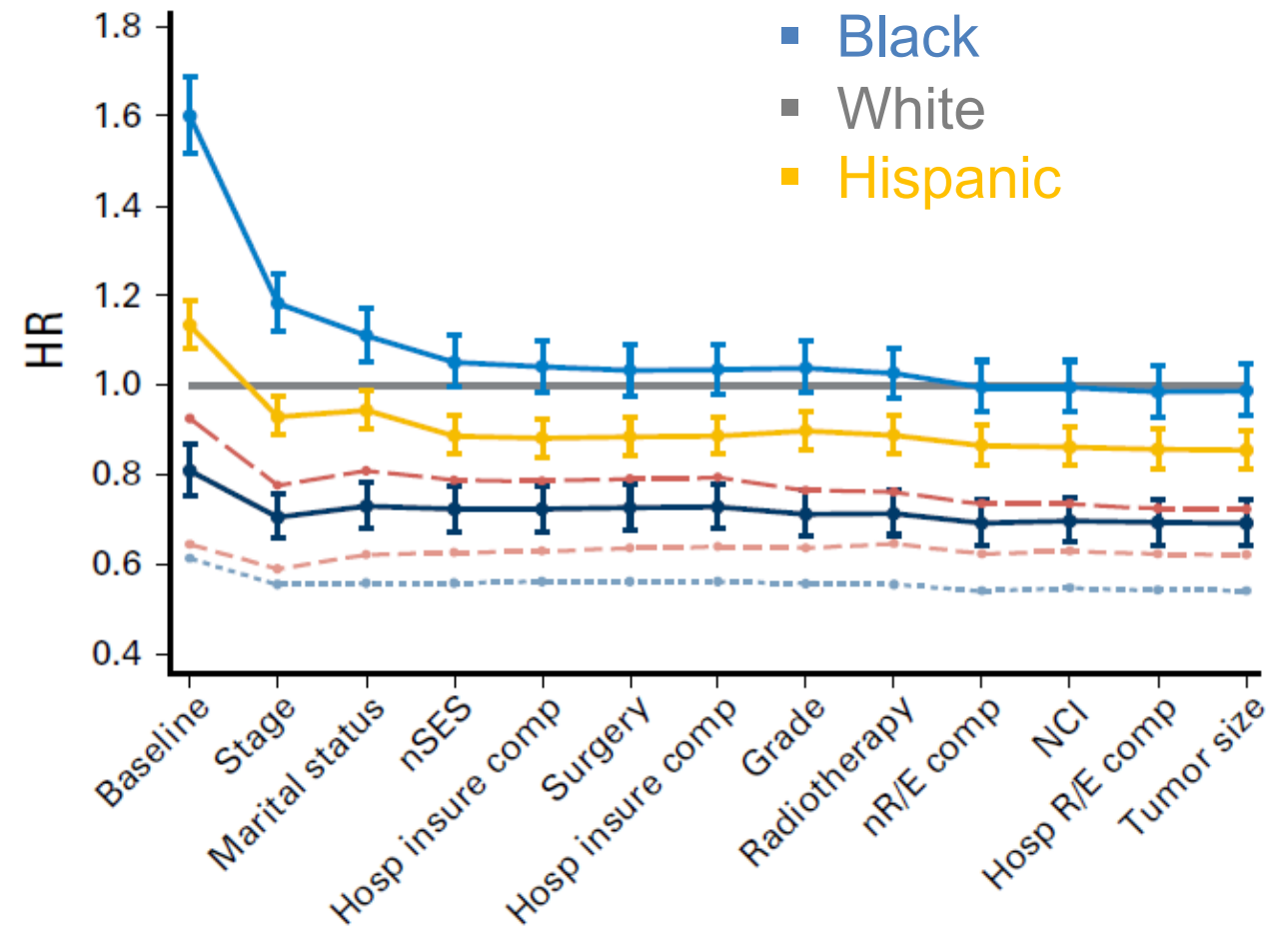
Appalachia: Education and Poverty Drive Disparities

- 12,871 men with prostate cancer
- Compared survival between men from Appalachia vs non-Appalachian Kentucky
- Poorer survival in men from Appalachia
 - Associated with lower education attainment, higher poverty, and greater number of comorbid illnesses



California: Stage, Marital Status, and Neighborhood SES

- 270,101 men with prostate cancer
- Performed mediation analysis to identify factors associated with differential outcomes
- Black men had poorer survival than other ethnic groups
- Predominantly due to **stage at diagnosis** (24% of disparity)
- Also associated with **marital status**, **neighborhood socioeconomic status**, and **hospital insurance composition**

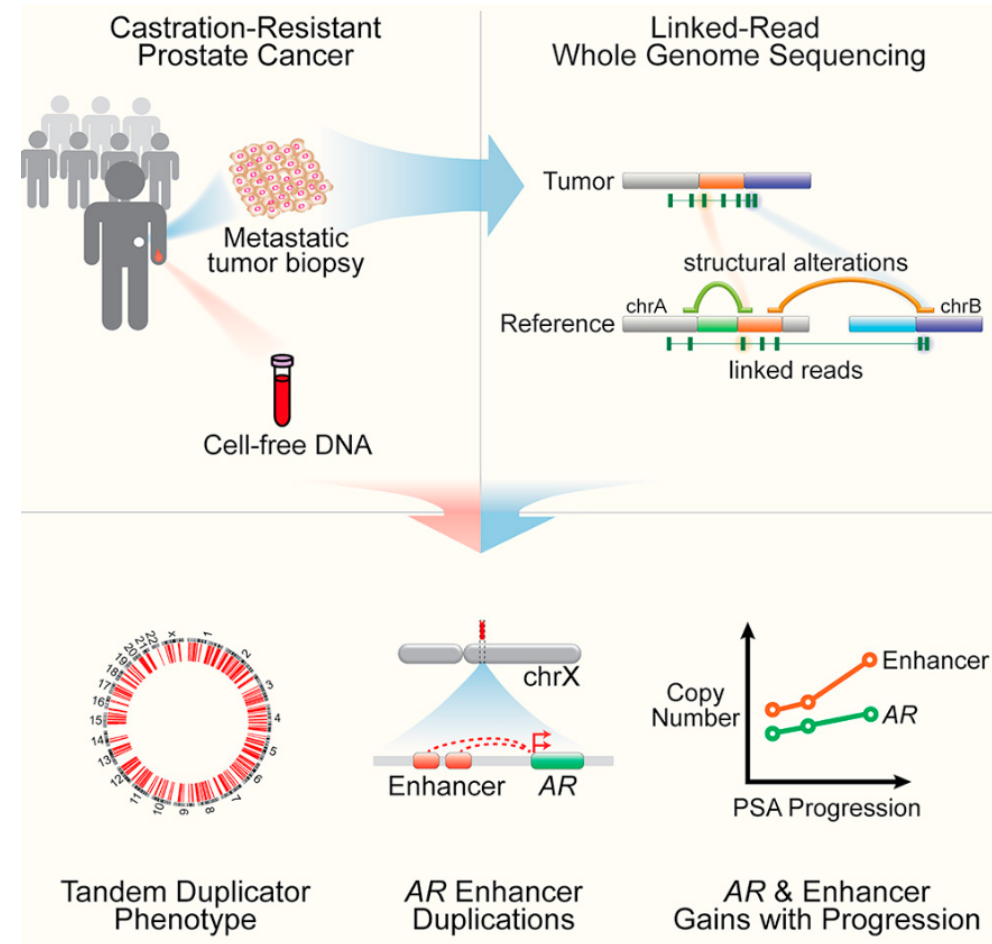


DEXA Use Disparities by Age, Race, SES

Characteristic	No. of Patients (%)	Percentage That Received Bone Density Testing	<i>P</i> ^a	Adjusted OR	95% CI	<i>P</i> ^b
Total	28,960 (100)	10.2				
Age, y			.003			
66-69	4304 (15)	10.9		1.00		Ref
70-74	7224 (25)	10.5		0.99	0.86-1.13	.88
75-79	8167 (28)	10.1		0.96	0.86-1.07	.43
80-84	6119 (21)	10.6		0.98	0.84-1.14	.76
→ ≥85	3146 (11)	8.3		0.76	0.65-0.89	< .001
Race			< .001			
Non-Hispanic white	22,115 (76)	10.1		1.00		Ref
→ Non-Hispanic black	2710 (9)	6.5		0.72	0.61-0.86	< .001
Hispanic	1763 (6)	11.2		0.96	0.80-1.15	.65
Other	1314 (5)	16.4		1.39	1.13-1.71	.002
Unknown	1058 (4)	12.6		0.97	0.83-1.13	.69
Marital status			< .001			
Married	18,132 (63)	10.7		1.00		Ref
Unmarried	6084 (21)	8.3		0.82	0.72-0.93	.002
Unknown	4744 (16)	10.9		1.07	0.92-1.24	.41
Percentage of high school graduates in census tract of residence			< .001			
→ Quartile 1: Lowest	8201 (28)	8.5		1.00		Ref
Quartile 2	7388 (26)	9.4		1.13	1.02-1.25	.02
Quartile 3	7143 (25)	10.9		1.30	1.14-1.49	< .001
Quartile 4: Highest	6186 (21)	12.8		1.44	1.25-1.66	< .001

Disparities in Personalized Medicine

- Genetic/genomic sequencing are increasingly integrated into clinical practice, and affect treatment decisions



Racial/Ethnic Disparities in Genomic Sequencing

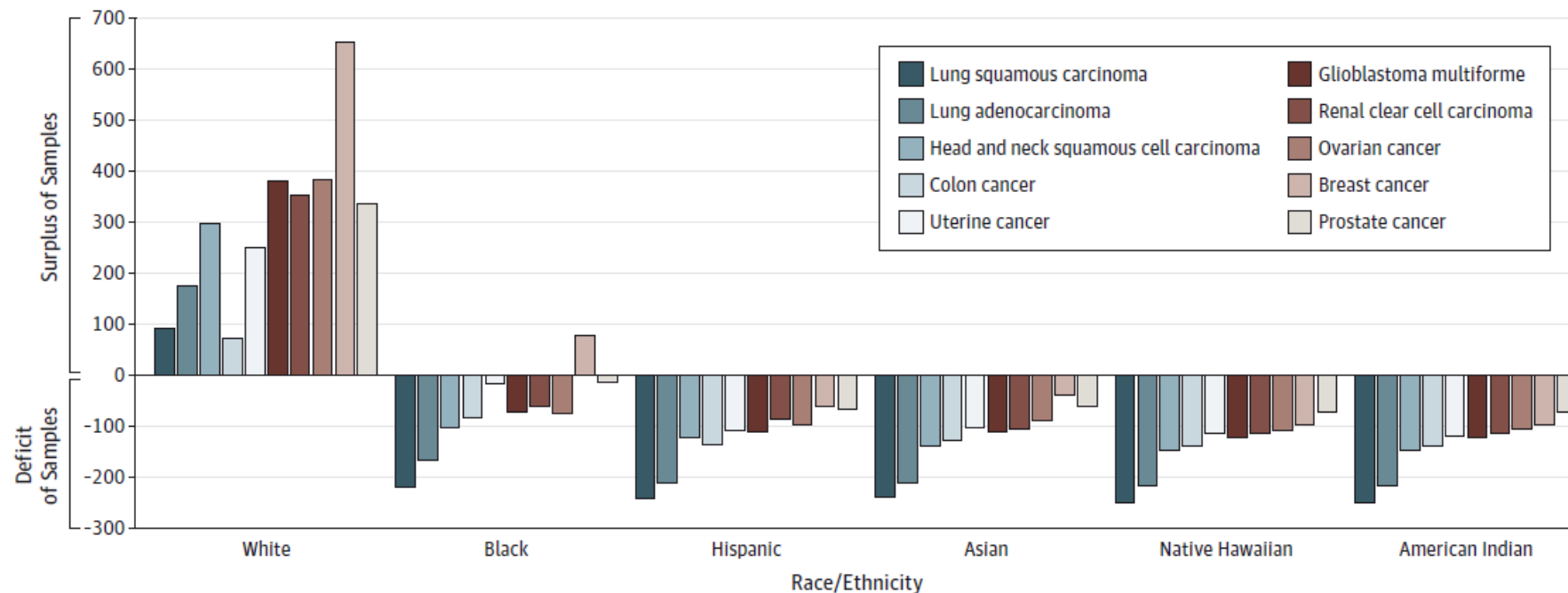
Daniel E. Spratt, MD; Tiffany Chan, MA; Levi Waldron, PhD; Corey Speers, MD; Felix Y. Feng, MD; Olorunseun O. Ogunwobi, MD, PhD; Joseph R. Osborne, MD, PhD

- TCGA data analyzed for multiple tumor types (5729 samples)
- Samples were sufficient to detect mutations in white men with Pca, but insufficient for other races

Breakdown of samples

77% white
12% black
3% Asian
3% Hispanic

A No. of samples needed to detect a 10% mutational frequency rate



Prevalence of Germline Variants in Prostate Cancer and Implications for Current Genetic Testing Guidelines

Piper Nicolosi, PhD; Elisa Ledet, PhD; Shan Yang, PhD; Scott Michalski, MS, LCGC; Brandy Freschi, MS, CGC; Erin O'Leary, MS, CGC; Edward D. Esplin, MD, PhD; Robert L. Nussbaum, MD; Oliver Sartor, MD

Breakdown of samples

72% white

6% black

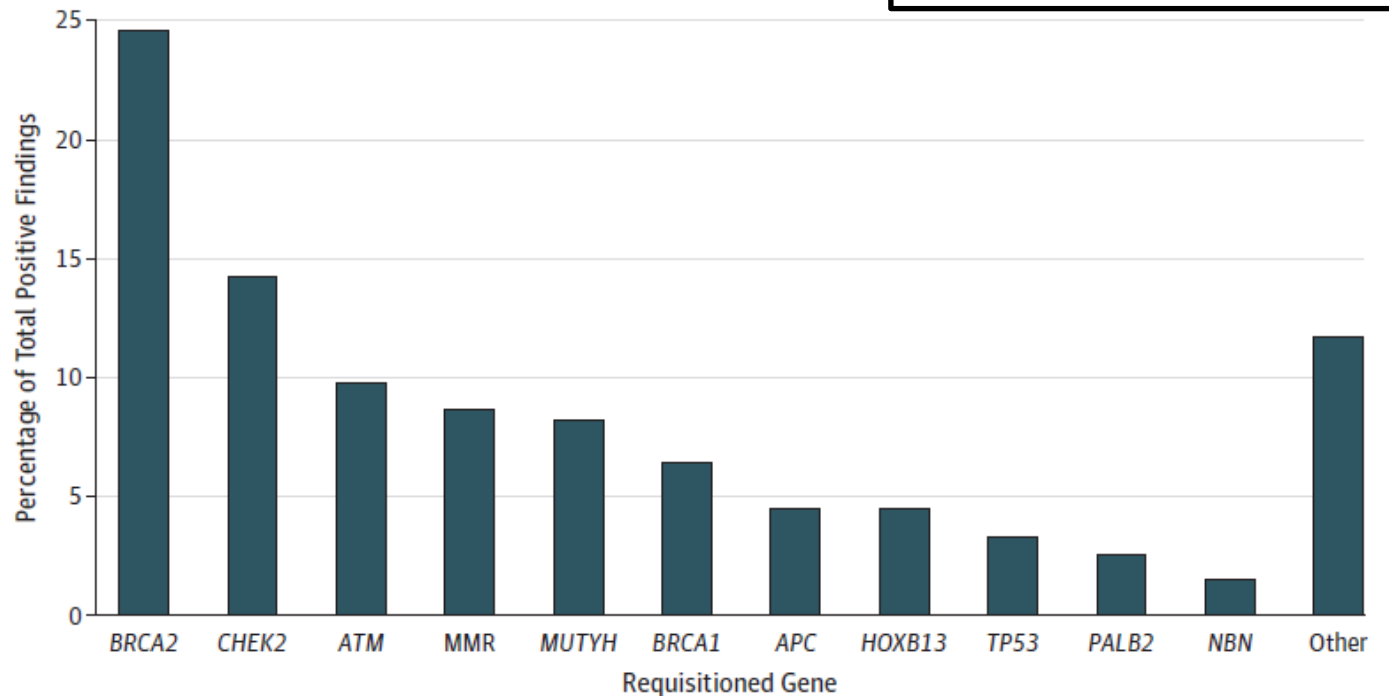
6% Ashkenazi Jewish

2% Hispanic

2% Asian

- Invitae data analyzed for men receiving germline sequencing for prostate cancer (3607 samples)
- Few actionable mutations were identified in black patients – 4% of total mutations

Figure. Frequency by Gene of Pathogenic, Likely Pathogenic, and Increased-Risk Allele Variants Detected in This Study



Disparities in Castration-Resistant Prostate Cancer Trials

Daniel E. Spratt and Joseph R. Osborne, *Memorial Sloan Kettering Cancer Center, New York, NY*

Table 1. Summary of Enrollment of Black Men Onto CRPC Trials

Enrollment	Sipuleucel-T	Radium-223 Chloride	Enzalutamide (pre-chemo)	Enzalutamide (post-chemo)	Abiraterone (pre-chemo)	Abiraterone (post-chemo)	Cabazitaxel	All Patients With CRPC in RCTs	Expected Black Enrollment*
Total patients	512	809	1,717	1,199	1,195	1,088	755	7,275	
Random assignment	2:1	2:1	1:1	2:1	2:1	1:1	1:1	—	
Percent black	5.8	2.0	2.0	3.9	3.6	2.8	5.3	3.3	15.8
No. of black patients	30	16	34	47	43	30	40	240	1,149
No. of black patients receiving trial drug	23	11	21	31	29	15	20	150	673

Abbreviations: chemo, chemotherapy; CRPC, castration-resistant prostate cancer; NCI, National Cancer Institute; RCT, randomized controlled trial.

*Based on (1) conservative NCI enrollment data that 66% of the available black population enrolls onto NCI clinical trials; (2) the US population is approximately 12% black; (3) there is a greater than two-fold increase in the incidence of lethal prostate cancer in black men.^{1a,9}

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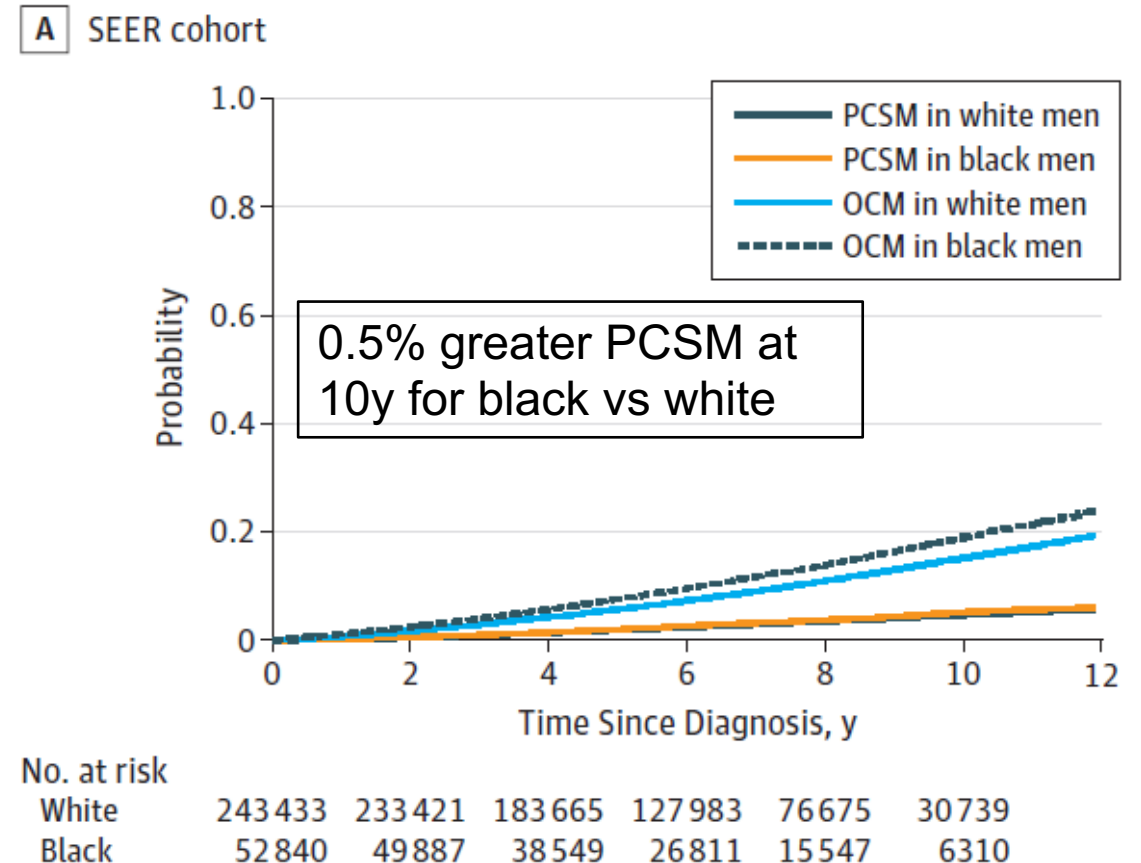
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Can Improved Access Overcome Biology?

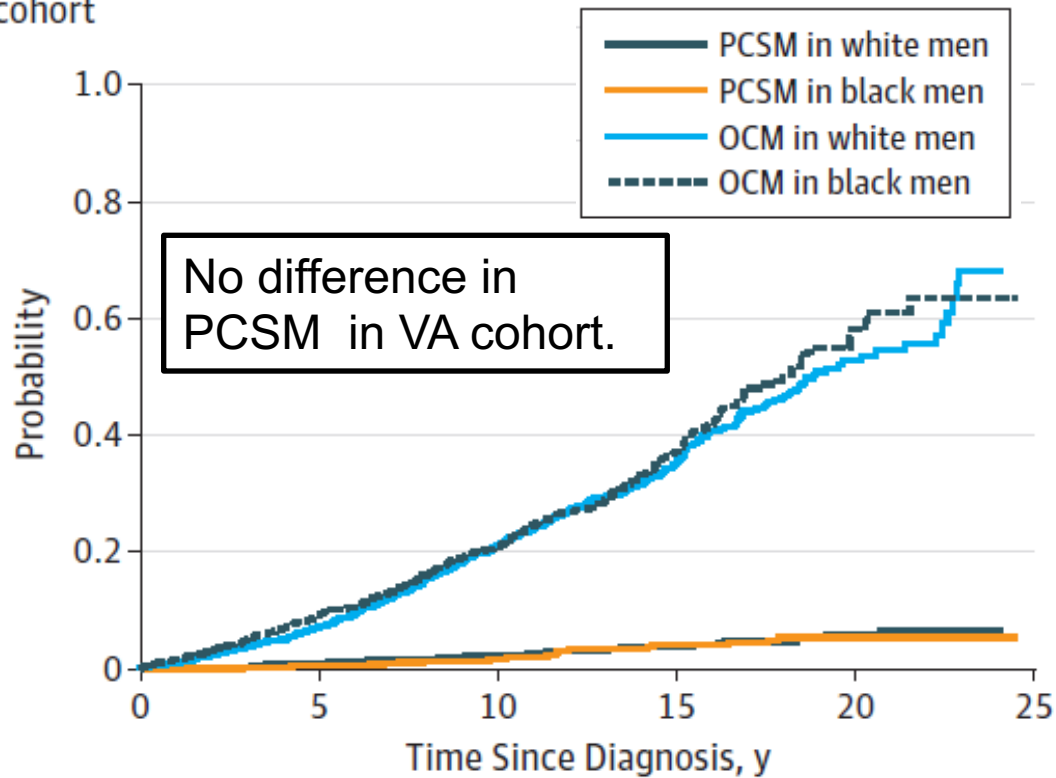
Figure 1. Cumulative Incidence of Prostate Cancer-Specific Mortality (PCSM) and Other-Cause Mortality (OCM) After Inverse Probability Weighting

- Multiple-cohort study
 1. SEER population-based cohort
 2. Veterans Administration cohort
 3. Randomized controlled trial cohort



Can Improved Access Overcome Biology?

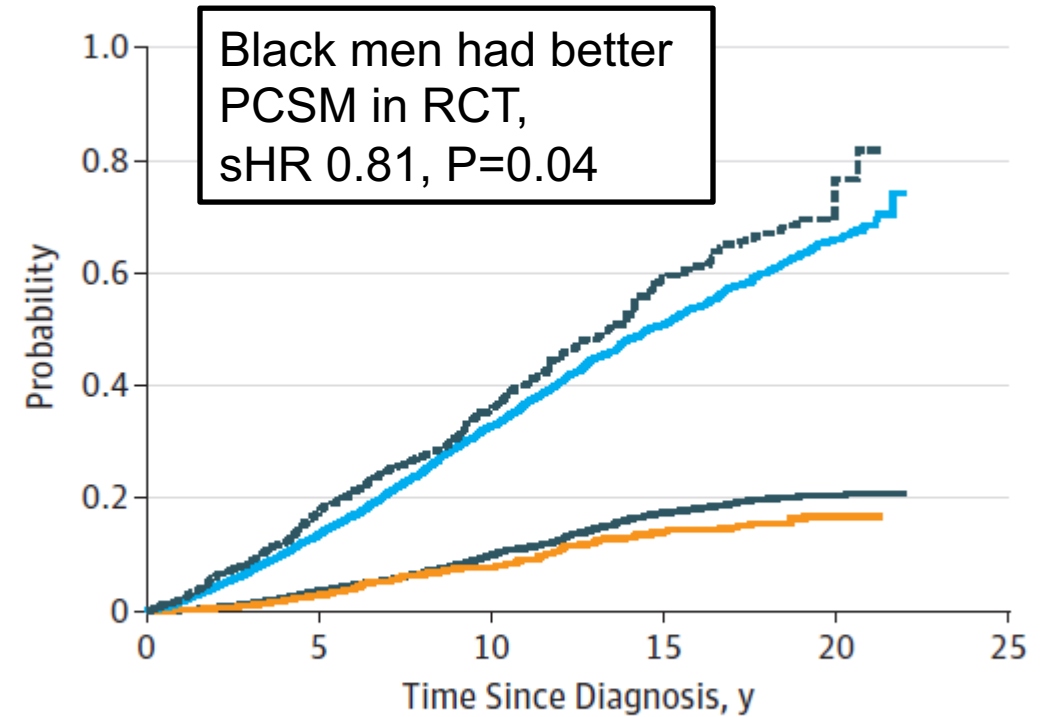
B VA cohort



No. at risk
White
Black

2459	1863	946	301	52
1513	1074	550	186	33

C RCT cohort



No. at risk
White
Black

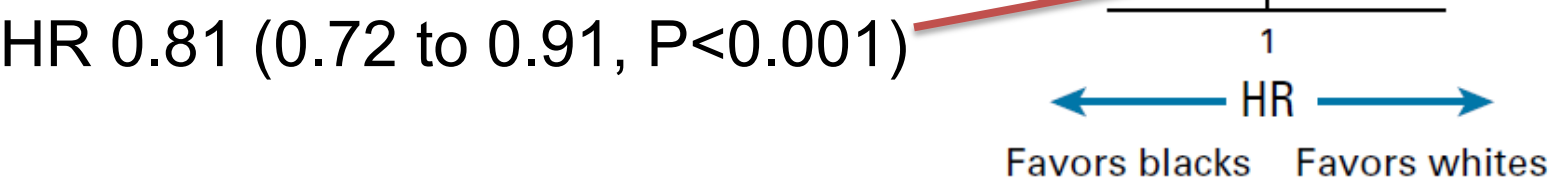
4724	3783	1681	484	63
1129	851	383	92	3

Overall Survival of Black and White Men With Metastatic Castration-Resistant Prostate Cancer Treated With Docetaxel

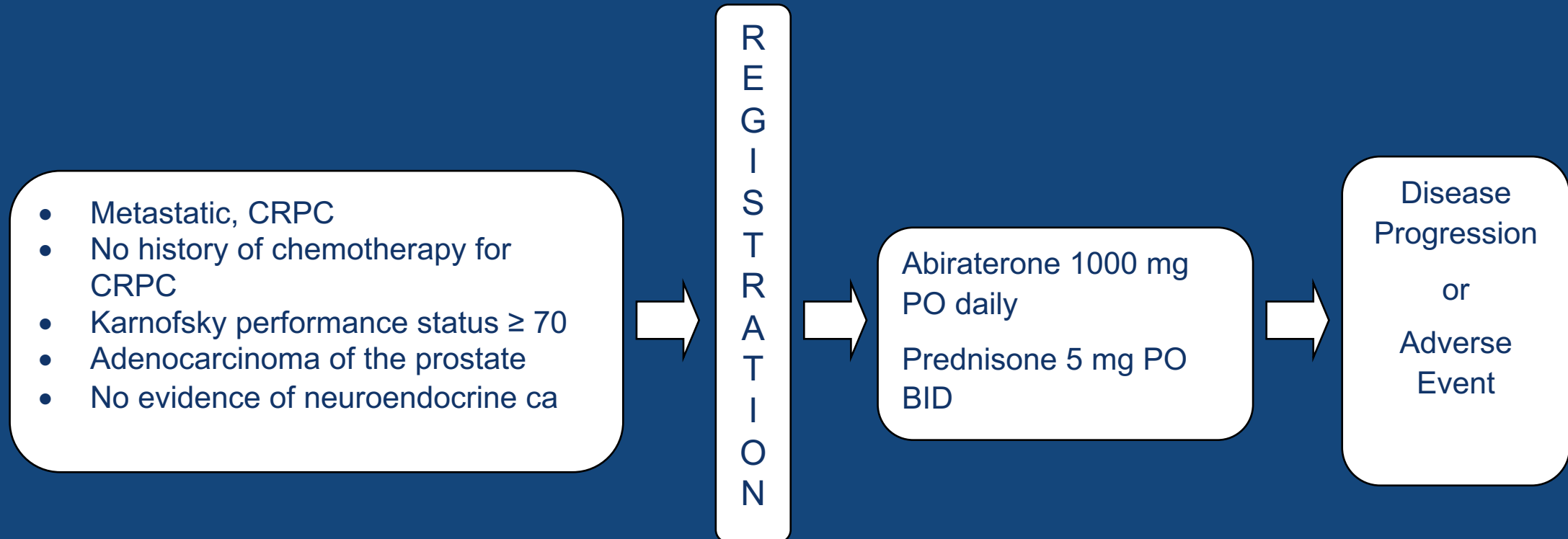
Trial (ClinicalTrials.gov Identifier)	Total Sample Size, No.	Calendar Year of Recruitment	Treatment Arms (No. of patients)
SWOG 9916 ²⁴ (NCT00004001)	674	Oct 1999-Jan 2003	Docetaxel + estramustine (n = 338) Mitoxantrone + prednisone (n = 336)
TAX 327 ²³	1,006	Mar 2000-Jun 2002	Docetaxel + prednisone (n = 669) Mitoxantrone + prednisone (n = 337)
CALGB 90401 ²⁶ (NCT00110214)	<ul style="list-style-type: none"> • 8,820 men • 9 phase III RCTs • All received docetaxel or docetaxel containing regimens 		Docetaxel + prednisone + bevacizumab (n = 524) Docetaxel + prednisone (n = 526)
SWOG 0421 ²⁸ (NCT00134056)			Docetaxel + prednisone (n = 498) Mitoxantrone + prednisone (n = 496)
VENICE ²⁹ (NCT00519285)			Docetaxel + prednisone + aflibercept (n = 612) Docetaxel + prednisone + placebo (n = 612)
ENTHUSE 33 ²⁷ (NCT00617669)			Docetaxel + prednisone + entinostat (n = 524) Docetaxel + prednisone + placebo (n = 528)
READY ³⁰ (NCT00744497)		Oct 2008-Apr 2011	Docetaxel + dasatinib (n = 762) Docetaxel + placebo (n = 760)
MAINSAIL ³¹ (NCT00988208)	1,059	Nov 2009-Nov 2011	Docetaxel + prednisone + lenalidomide (n = 533) + placebo (n = 526)
SYNERGY ³² (NCT01188187)	1,022	Aug 2010-Apr 2014	Docetaxel + prednisone + custirsen (n = 510) Docetaxel + prednisone (n = 512)

- Black men were younger, had poorer ECOG PS, higher PSA and T, lower Hgb
- Median OS ~ 21 mo for black and white men

Trial	Median OS, Months (95% CI)		HR (95% CI)
	Whites (n = 7,528)	Blacks (n = 500)	
SWOG 9916	17 (16 to 20)	24 (14 to 26)	0.8 (0.5 to 1.4)
No. of patients (No. of deaths)	290 (190)	40 (20)	
TAX 327	20 (18 to 22)	NR (14 to NR)	0.5 (0.2 to 1.1)
No. of patients (No. of deaths)	624 (340)	16 (7)	
CALGB 90401	22 (21 to 23)	23 (20 to 29)	0.8 (0.6 to 1)
No. of patients (No. of deaths)	923 (870)	110 (101)	
SWOG 0421	18 (17 to 20)	19 (17 to 23)	0.7 (0.6 to 0.9)
No. of patients (No. of deaths)	809 (640)	137 (102)	
VENICE	24 (22 to 25)	25 (19 to 33)	1.1 (0.7 to 1.7)
No. of patients (No. of deaths)	1,112 (788)	32 (27)	
ENTHUSE 33	19 (18 to 21)	25 (22 to NR)	0.5 (0.3 to 0.9)
No. of patients (No. of deaths)	676 (366)	39 (16)	
READY	22 (21 to 24)	18 (14 to 22)	1.1 (0.8 to 1.5)
No. of patients (No. of deaths)	1,301 (769)	57 (43)	
MAINSAIL	18 (17 to NR)	18 (13 to NR)	1.1 (0.6 to 2)
No. of patients (No. of deaths)	869 (183)	46 (11)	
SYNERGY	22 (21 to 24)	17 (13 to NR)	0.8 (0.5 to 1.4)
No. of patients (No. of deaths)	924 (557)	23 (15)	
Overall	21 (21 to 22)	21 (19 to 23)	0.81 (0.72 to 0.91); <i>P</i> < .001

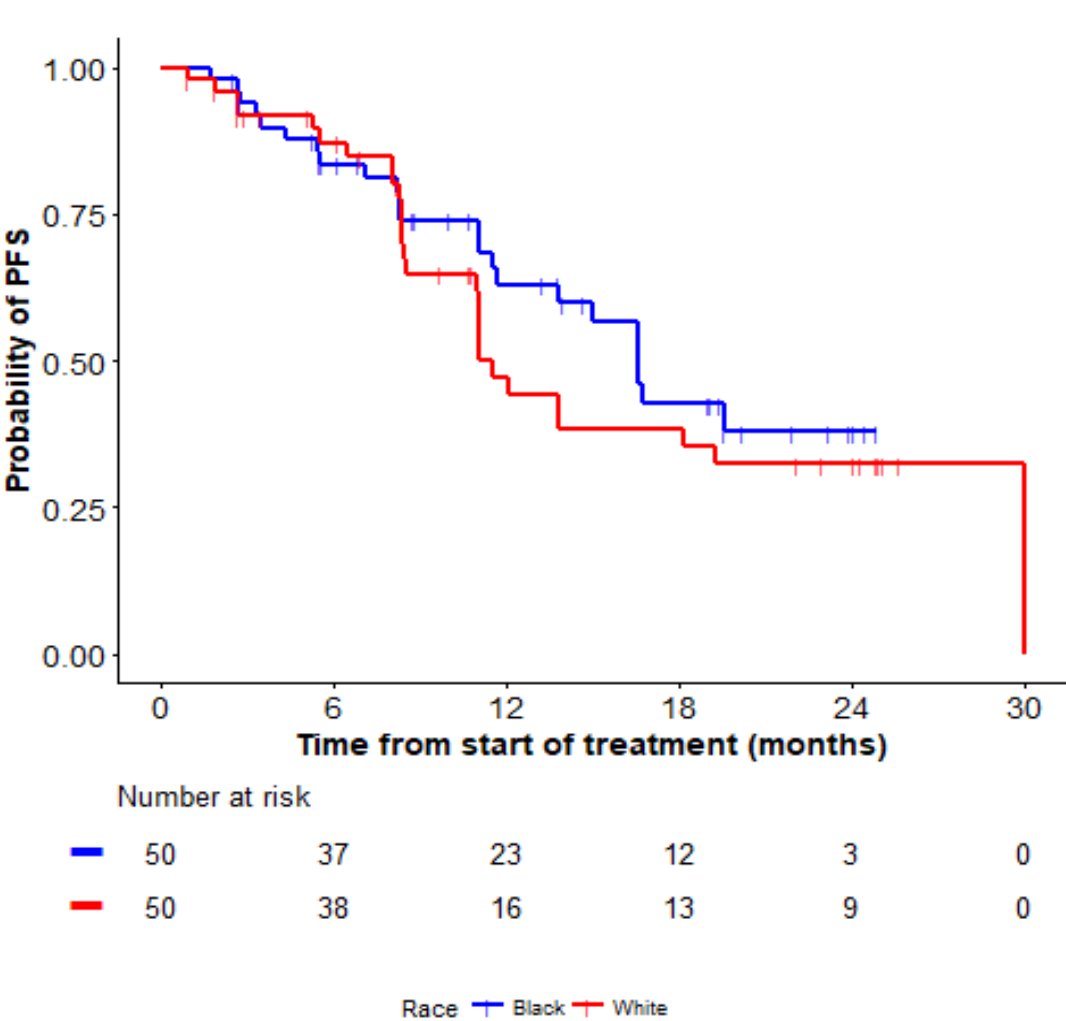


Abi Race Schema



Statistical Design: non-comparative pilot open-label, parallel arm study of AP in 100 men (50 B, 50 W) with mCRPC, self-identified race.

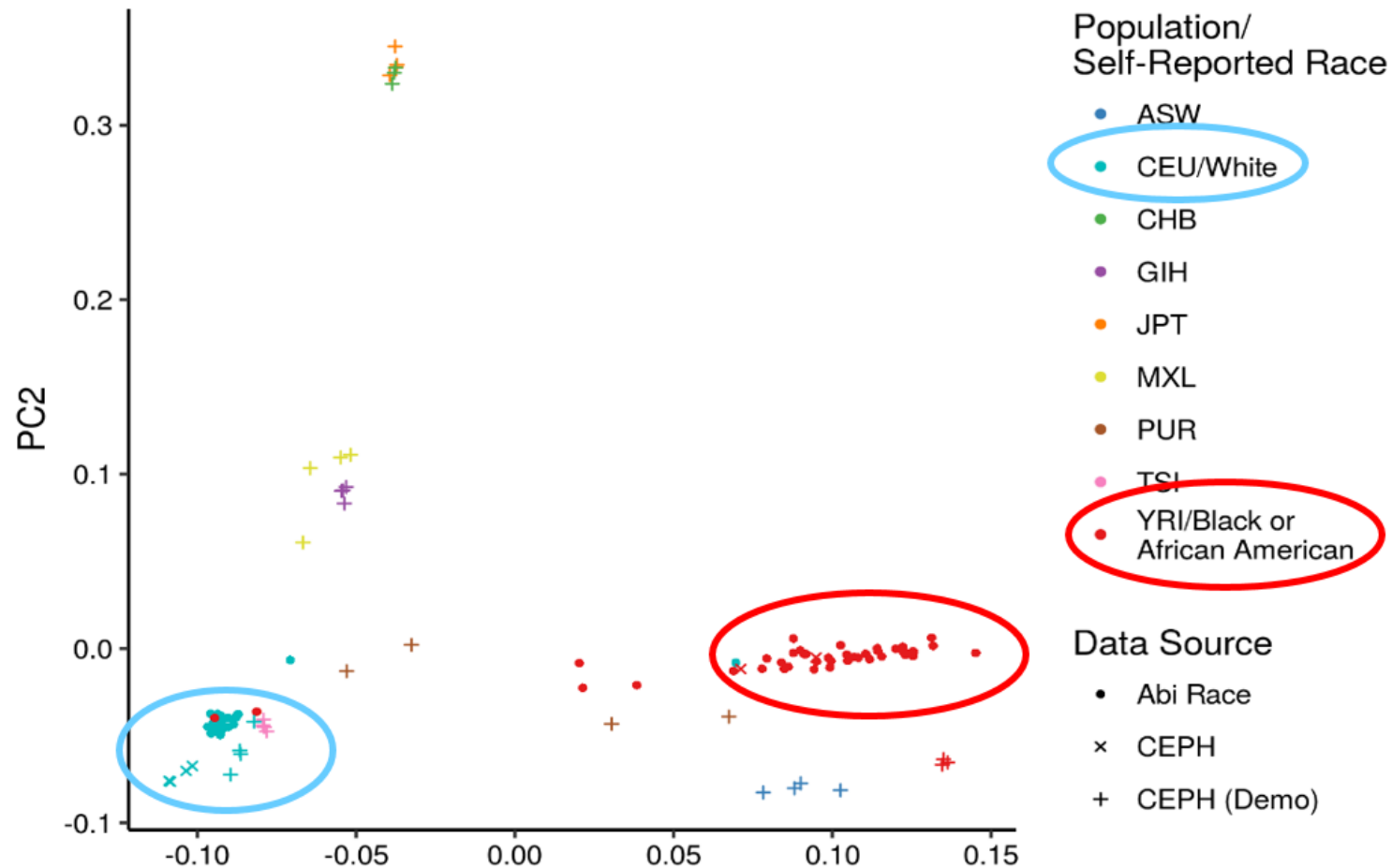
PSA Progression Free Survival: Longer PSA PFS by Race?



	AbiRace		COU-AA-302
	Black	White	
≥30% PSA Decline (%)	82	78	NR
≥50% PSA Decline (%)	74	66	68
≥90% PSA Decline (%)	48	38	NR
Tumor Flare (%)	16	4	NR
Median PSA PFS (mo)	16.6	11.5	11.1

NR = not reported.

Distinctly Different Genotypic Clusters: SNP Genetic Ancestry Analysis by EIGENSTRAT Method



Adapted from original slide courtesy of Dan George, Presented by A Morgans, ASCO 2018.

Does Different Biology = Superior Outcomes?

Author	Intervention	Population	Endpoint	HR for Black men
Quinn et al	Sipuleucel-T in mCRPC	Pooled analysis, N=33 Black men	OS	0.49 (95% CI 0.26–0.91) p=0.02
Halabi et al	Docetaxel in mCRPC	Pooled analysis, N=500 Black men	OS	0.81 (95% CI, 0.72 to 0.91) p<0.001
Dess et al	Radiotherapy in localized prostate cancer	Pooled analysis, N=52,840 Black men	PCSM	0.81 (95% CI, 0.66-0.99) p = .04

Courtesy of Hala Borno, Presented at ASCO Annual Meeting 2019.

Quinn D, et al J Clin Oncol. 2017.

Halabi S, et al. J Clin Oncol. 2019.

Dess, et al. JAMA Oncol. 2019.

Efforts to Include

IRONMAN Registry

- * 5,000 men
- * 10 countries
- * Includes clinical outcomes, genomics, patient reported data to determine optimal treatment strategies for advanced prostate cancer



Efforts to Include



Metastatic Prostate Cancer Project

Data Release Learn More **count me in**

You can have a direct impact on the future of men with prostate cancer

The Metastatic Prostate Cancer Project is a nationwide genomic research study for men with advanced or metastatic prostate cancer. We seek to generate the most comprehensive database that will be shared with the entire research community to accelerate discoveries.

The banner image shows a diverse group of men silhouetted against a bright sunset. One man in the center is raising his arms in a gesture of triumph or hope. A blue circular button with a white downward arrow is positioned at the bottom center of the banner.



<https://mpcproject.org/home>

Conclusions

- Disparities in prostate cancer in the US come in many forms
 - Both biology and social determinants of health contribute
 - Other disparities (age, geography, education, socioeconomic status) exist
 - Lack of inclusion in clinical trials and genomic sequencing worsens disparities
- Differences in biology and access to care
 - Some biologic differences may be associated with improved outcomes!
- Efforts to enhance inclusion in clinical trials and improve access to genomic sequencing are underway

Issues of disparity must be tackled not just in the US, but around the world! Improvements in