Dana-Farber Cancer Institute

Minimizing the Impact of Biological and Social Drivers on Cancer Disparities: Prostate Cancer

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MADCaP NETWORK

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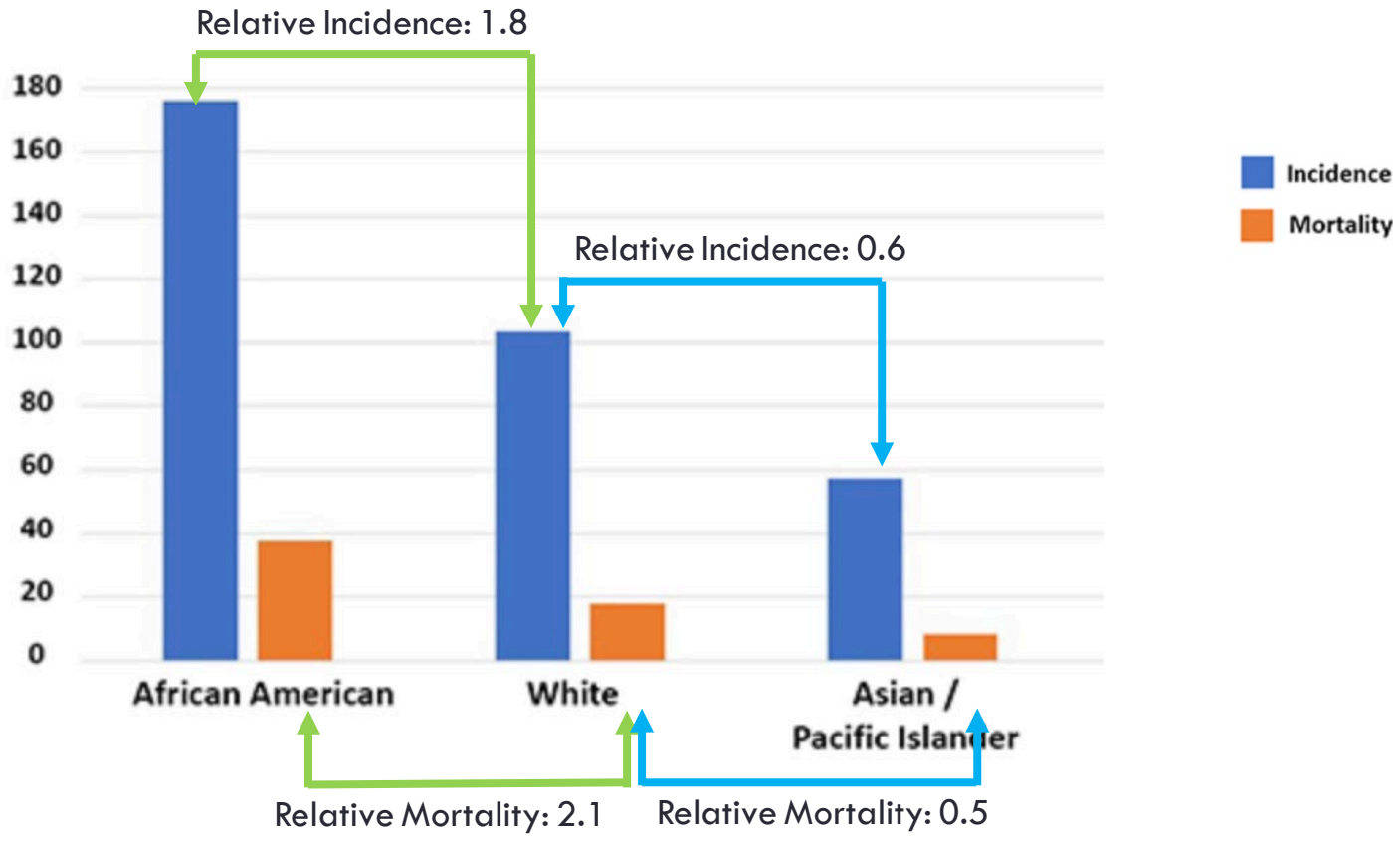
BROAD INSTITUTE

Cancer Health Disparities:

- Exist At All Phases Of The Cancer Continuum
- May Determined By Complex Effects Of Biological And Social Drivers
- Require Interventions Tailored To These Influences And The Timing Of Their Effects

Prostate Cancer Incidence and Mortality



Siegel et al., Sung et al. *CA Cancer J Clin* 2021

Why Do Prostate Cancer Disparities Exist?

- Biology, Genetics?
- Social Drivers & Consequences of Systemic Racism?
  - Risk Factors & Lifestyle?
  - Prevention & Early Detection?
  - Treatment?

Prostate Cancer Risk Factors

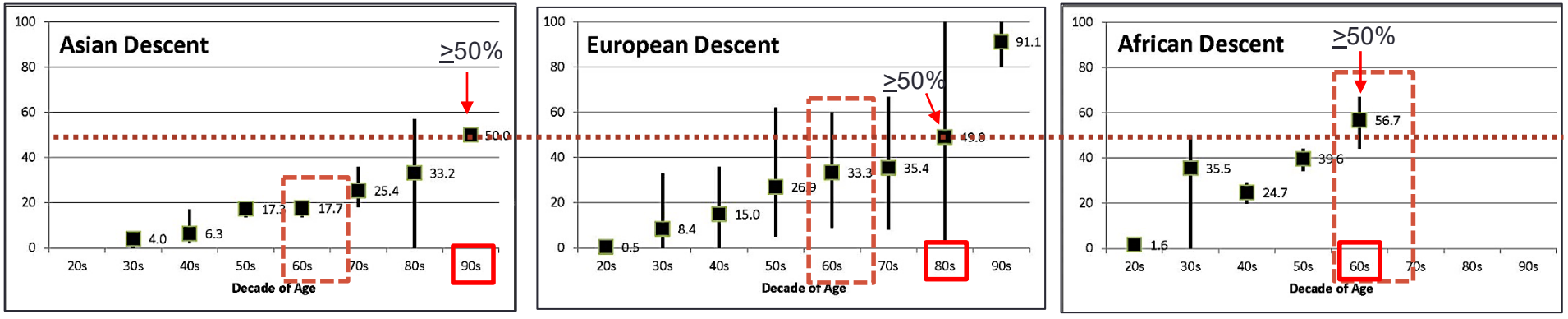
Age
Family History
Self-Identified Race/Ethnicity
Height

Obesity (Aggressive Disease)

Kensler & Rebbeck *CEBP* 2020

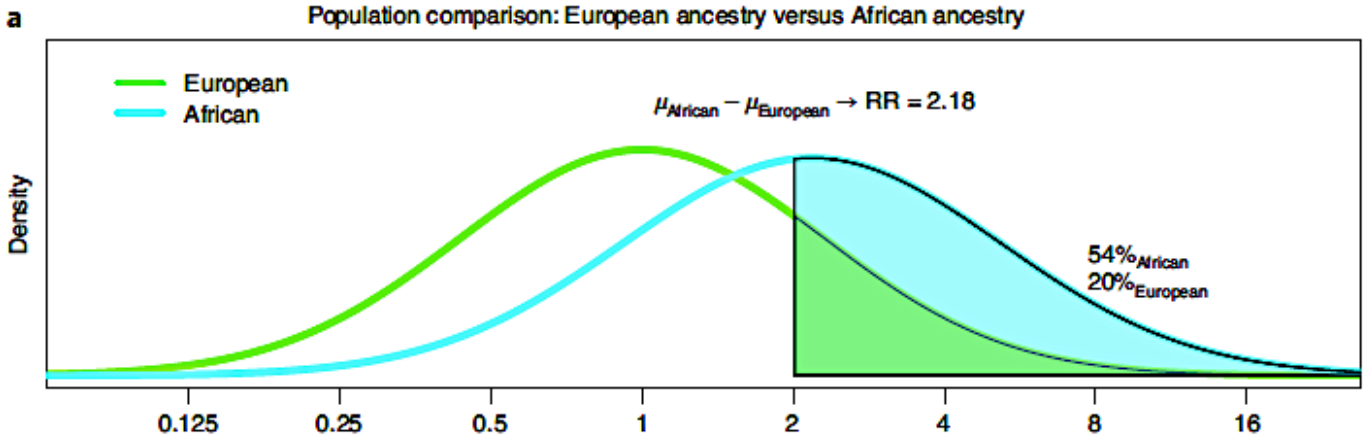
Disparities Exist Even Before Diagnosis

Autopsy Prevalence of Latent Prostate Cancer

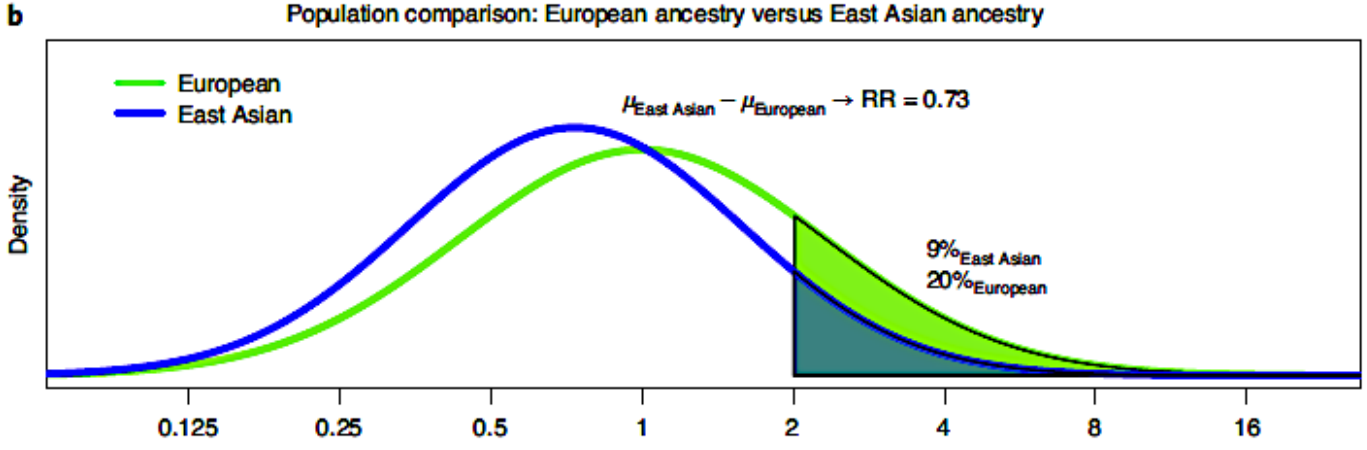


Rebbeck and Haas, *Can J Urol* 2014

Multiethnic Prostate Cancer Genomic Risk Scores
(NB: Heritability of PCa=57%, N=451 GWAS SNPs)



NHW vs. Black

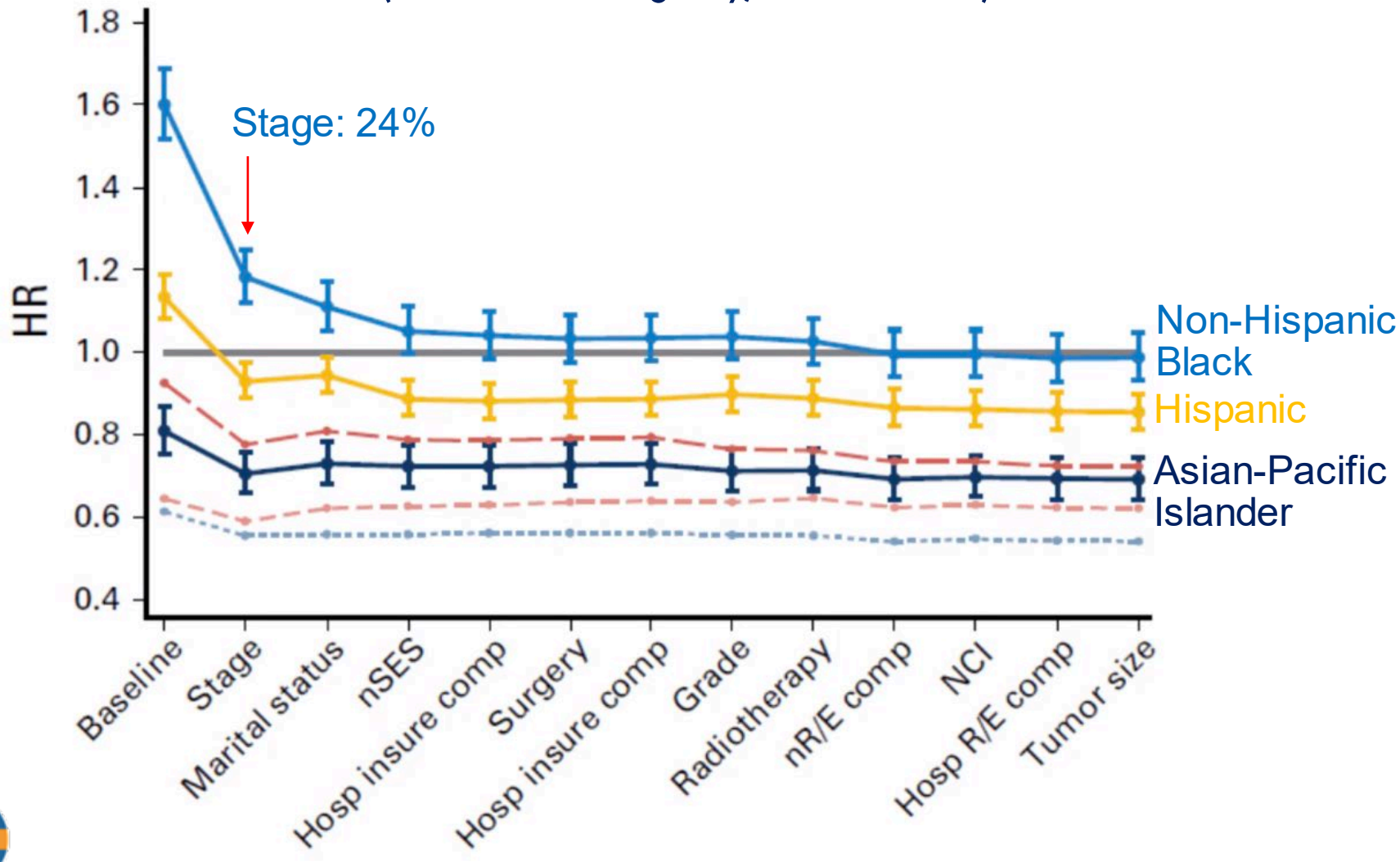


NHW vs. Asian

~1/3 of familial risk explained by PRS

Conti et al. *Nat Genet* 2021

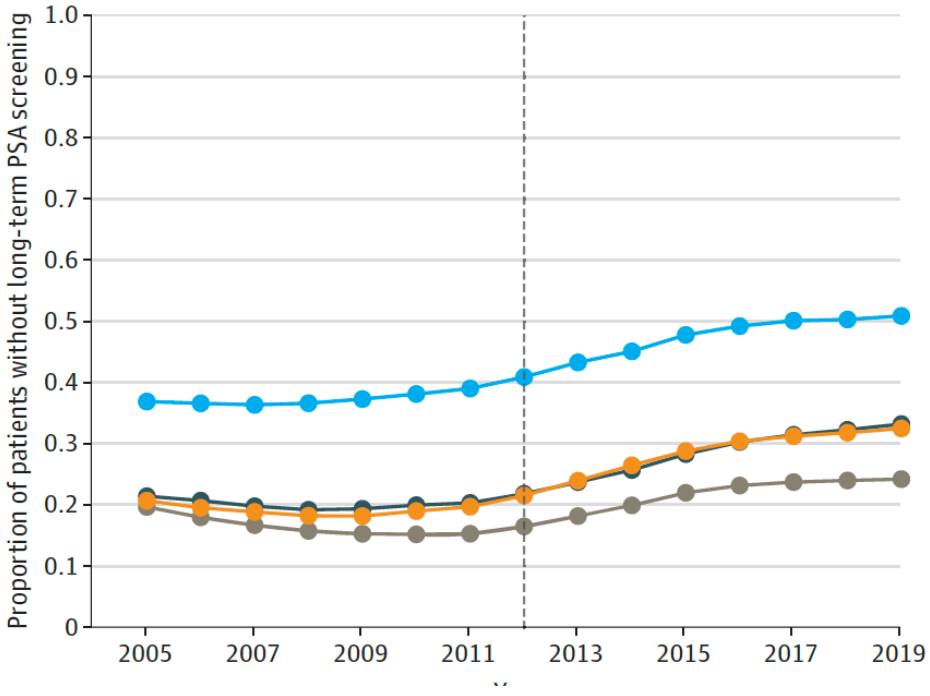
Relative Impact of Factors on Prostate Cancer Mortality by Race/Ethnicity Compared with Non-Hispanic Whites (CA Cancer Registry, 2000-2013)



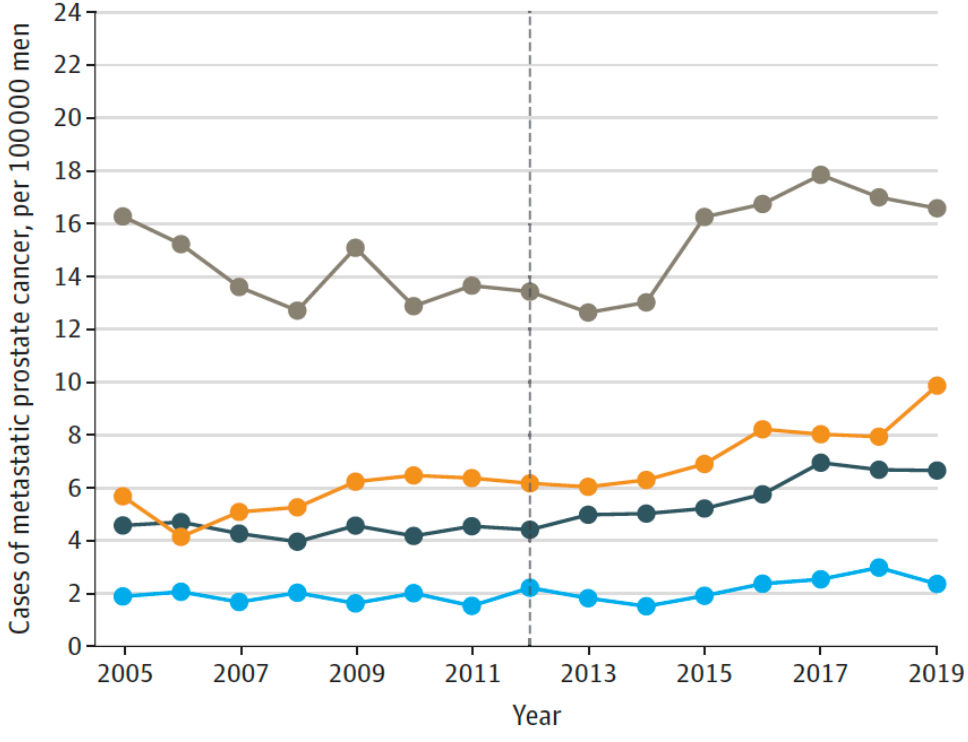
Ellis et al., *JCO* 2018

PSA Screening and Metastatic Prostate Cancer Incidence
128 VA Hospitals, 2005-2019

Long-Term Prostate Cancer Non-Screening Rates



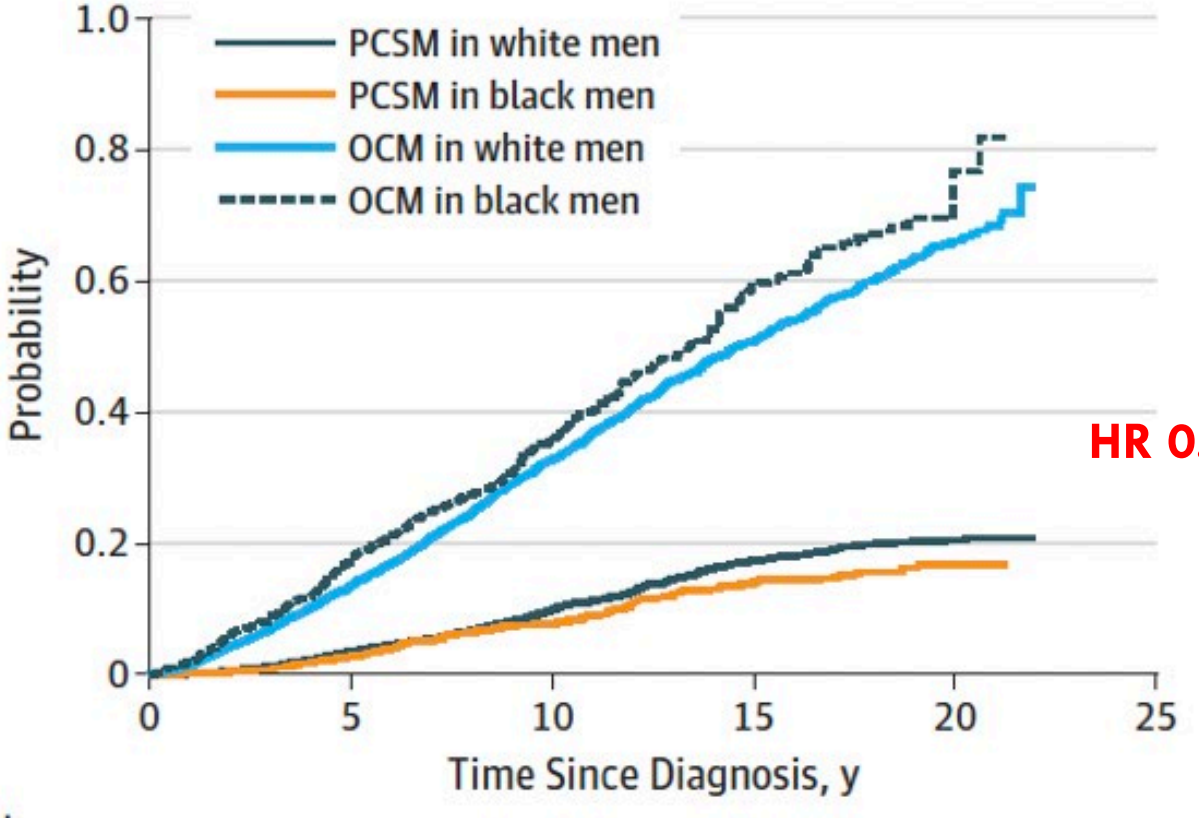
Metastatic Prostate Cancer Incidence Rates
(Age-Adjusted)



- Non-Hispanic Black
- Hispanic
- Asian
- Non-Hispanic White

Bryant et al., *JAMA Onc* 2022

RTOG RCT: Black Race is Associated With Lower Risk Of Prostate Cancer-Specific Mortality In M0 Prostate Cancer



HR 0.81 (0.66, 0.99)

No. at risk					
White	4724	3783	1681	484	63
Black	1129	851	383	92	3

Dess R et al, *JAMA Onc* 2019

Some Prostate Tumor Subtypes Differ by Race

Subtype classification	Odds ratio (95% confidence interval)[a]			p_{het}
	Total population	Black	White	
Zhang subtypes				0.20
Luminal	Reference	Reference	Reference	
Basal	1.44 (1.07–1.94)	1.86 (1.14–3.03)	1.24 (0.85–1.81)	
Tomlins subtypes				0.007
ERG$^+$	Reference	Reference	Reference	
ETS$^+$	0.61 (0.40–0.92)	0.13 (0.03–0.64)	0.82 (0.52–1.28)	
SPINK1$^+$	0.52 (0.29–0.90)	0.28 (0.12–0.69)	0.70 (0.26–1.70)	
Triple negative	0.63 (0.45–0.88)	0.32 (0.16–0.62)	0.86 (0.57–1.30)	
You subtypes				0.001
PCS1	Reference	Reference	Reference	
PCS2	0.40 (0.26–0.60)	0.69 (0.29–1.65)	0.27 (0.16–0.45)	
PCS3	0.49 (0.35–0.69)	1.05 (0.58–1.92)	0.29 (0.18–0.45)	
Kamoun subtypes				0.01
S1	Reference	Reference	Reference	
S2	0.50 (0.33–0.75)	0.98 (0.39–2.45)	0.39 (0.23–0.62)	
S3	0.56 (0.40–0.78)	0.46 (0.23–0.92)	0.66 (0.44–0.98)	
Alshalalfa subtypes				0.96
Adenocarcinoma	Reference	Reference	Reference	
Neuroendocrine	2.42 (1.15–5.02)	2.38 (0.86–6.59)	2.46 (0.83–6.98)	

p_{het} = p value for heterogeneity from a likelihood ratio test of race × subtype product terms.

[a] Odds ratios and 95% confidence intervals were estimated from logistic regression models including race, subtype, age, Gleason group, prostate-specific antigen level, extraprostatic extension, seminal vesicle invasion, and lymph node invasion.

Kensler et al., *Eur Urol* 2022

Priorities for Interventions to Reduce Prostate Cancer Disparities:

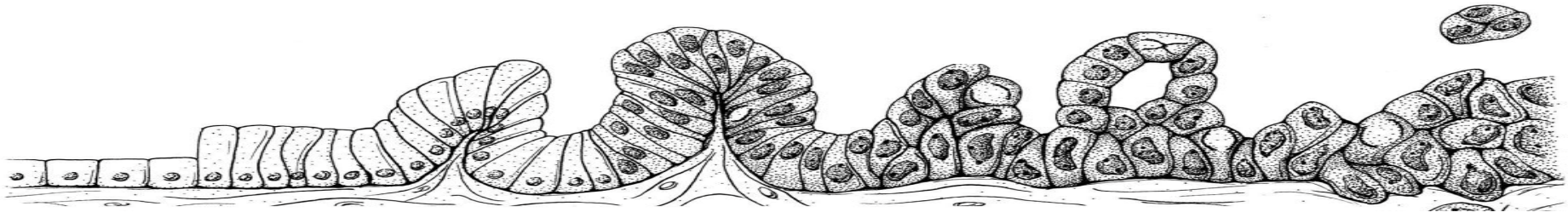
- Risk stratification (multivariate genetics and social drivers)
- Implications of tumor heterogeneity
- Risk-adaptive screening tools and care pathways
- Equity in treatment benefit

Normal

Pre-Cancer

Incident Cancer

Metastasis
Mortality



SOCIAL DRIVERS

GENETICS, BIOLOGY

Risk Stratification ★

Prevention

Early Detection ★★

Treatment ★

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