

# The Causes and Consequences of Cancer Health Disparities

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# Overview

**Part 1: Discussion of key cancer health disparities in the US**

**Part2: Discussion on key factors that contribute to disparities**

# Race and Ethnicity

**Race:** Biological differences between groups assumed to have different bio-geographical ancestries or genetic makeup

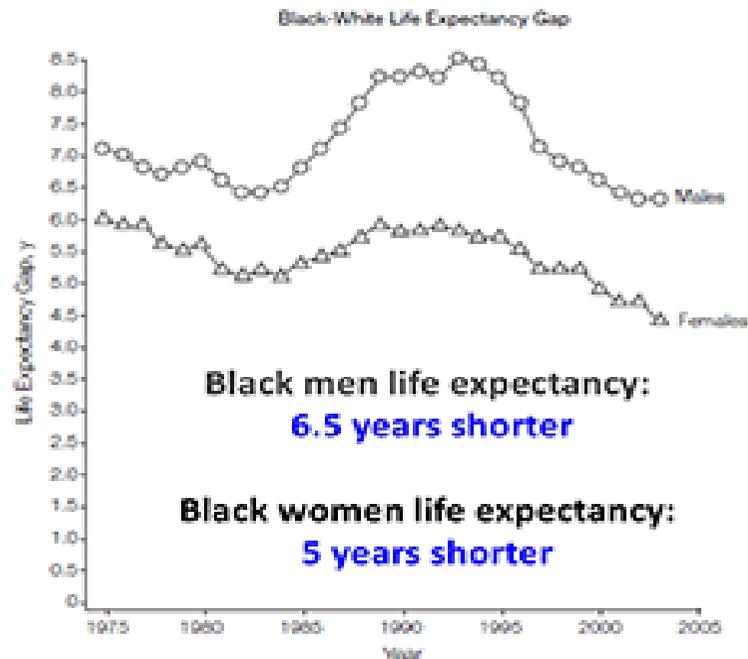
**Ethnicity:** A multi-dimensional construct reflecting biological factors, geographical origins, historical influences, shared customs, beliefs and traditions among populations that may not have common genetic origin

Both are important factors to consider in trying to research, understand and diminish cancer disparities

# Health Disparities in the United States

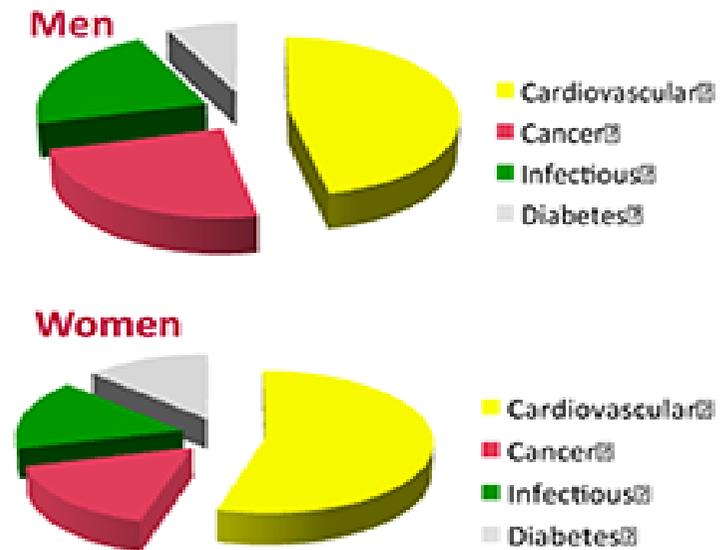
## Health Disparities in the United States

Racial differences in life expectancy in the United States



NATIONAL CANCER INSTITUTE

Contributing Factors



Adapted from JAMA 2007 297:11 1227

# Cancer Disparities: Definition

The NCI defines “cancer health disparities as:

“differences in the incidence, prevalence, mortality and burden of cancer and related adverse health conditions that exist among specific population groups in the United States”

# **Cancer Disparities: Definition**

## **Excess Burden of Cancer in the African-American Community**

**African-Americans have the highest death rates from all cancer sites combined, and from malignancies of the lung, colon and rectum, breast, prostate, and the cervix of all racial groups in the united States”**

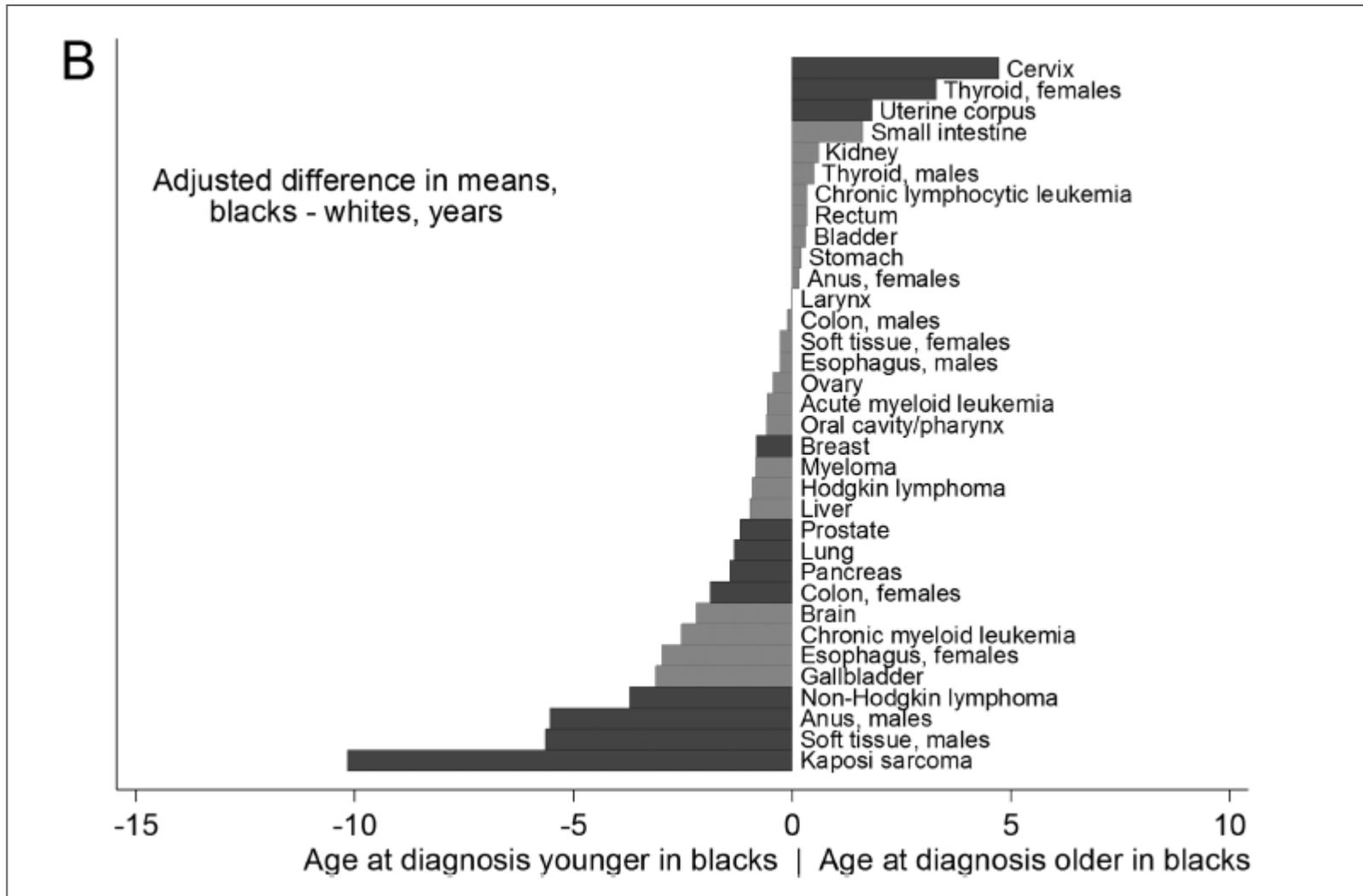
**Incidence Rates by Race/Ethnicity and Sex, U.S., 1999-2012**

# Cancer disparities

## Cancer Disparities



# Younger age at diagnosis for most cancers



# Younger age at diagnosis for most cancers

Cancers mainly diagnosed at younger age in black men and women

NHL, anal cancer, Kaposi sarcoma and soft tissue

Etiologic heterogeneity

Cause of the cancer differs across groups, causes cancer at different ages

Subtypes can be caused by different factors – can contribute to disparities

Timing or intensity of exposure

For example, exposure to tobacco could occur earlier in one population

Timing, prevalence and frequency of early cancer detection

Screening, or through follow after an incidental finding

NCI Early Onset Malignancy Initiative

The Center for Cancer Genomics (CCG) in collaboration with the Division of Cancer Prevention's NCI Community Oncology Research Program (NCORP) invited the twelve Minority/Underserved NCORP sites to participate in this project

## S Cancer Health Disparities: Second cancers

African Americans also have a higher risk of certain second cancers

Site-specific risk of second primary cancer in women with endometrial cancer according to race (1973-2007)

Second Cancer Site	White (n = 10,584)	Black (n = 463)
	SIR (95% CI)	SIR (95% CI)
All sites (N = 11,047)	0.85 (0.84–0.87)	1.19 (1.08–1.31)
Solid tumors (N = 9744)	0.85 (0.83–0.87)	1.19 (1.08–1.31)
Digestive system (N = 2854)	0.97 (0.93–1.01)	1.37 (1.16–1.61)
Colon and rectum (N = 1949)	1.02 (0.97–1.07)	1.53 (1.24–1.87)
Liver (N = 40)	0.58 (0.41–0.80)	1.17 (0.32–2.99)
Pancreas (N = 356)	0.88 (0.79–0.98)	0.97 (0.56–1.55)
Respiratory system (N = 1382)	0.72 (0.68–0.76)	1.09 (0.84–1.39)
Breast (N = 3448)	0.98 (0.95–1.01)	1.01 (0.82–1.23)
Female genital system (N = 448)	0.65 (0.59–0.71)	1.48 (1.03–2.07)
Urinary system (N = 801)	1.19 (1.11–1.28)	1.80 (1.25–2.52)

Digestive system: esophagus, stomach, small intestine, colon and rectum, liver, gallbladder, and pancreas.

Respiratory system: lung and bronchus.

Female genital system: ovary, cervix, vagina, and vulva.

Urinary system: urinary bladder, ureter, kidney, and renal pelvis.

INTERNATIONAL JOURNAL OF GYNECOLOGICAL CANCER

# Secondary cancer racial disparity

Table 2 Risk of site-specific second primary cancers among women with first primary stages I-III breast cancer by race/ethnicity in the Surveillance, Epidemiology and End Results 15 Registries, 2001-2010

Second primary cancer site	Non-Hispanic White		Black		Hispanic		Asian/Pacific Islander	
	SIR	95 % CI	SIR	95 % CI	SIR	95 % CI	SIR	95 % CI
All sites*	1.08*	1.06-1.10	1.47*	1.38-1.56	1.04	0.97-1.11	1.51*	1.42-1.61
Breast	1.17*	1.12-1.21	2.16*	1.96-2.36	1.39*	1.24-1.54	1.80*	1.62-2.00
All solid tumors	1.10*	1.07-1.12	1.48*	1.39-1.57	1.05	0.98-1.13	1.51*	1.41-1.62
Oral cavity	1.22	1.02-1.45	1.44	0.78-2.41	0.78	0.36-1.48	1.79	1.06-2.84
Esophageal	1.27	0.94-1.68	1.34	0.54-2.76	1.08	0.29-2.76	0.80	0.10-2.89 <sup>b</sup>
Stomach	0.99	0.80-1.22	1.50	0.96-2.23	1.70	0.95-2.80	1.64*	1.13-2.29
Colon and rectum	1.00	0.93-1.08	1.13	0.93-1.37	0.99	0.78-1.25	1.23	1.00-1.51
Liver	0.58*	0.40-0.83	0.36	0.07-1.04 <sup>b</sup>	1.61	0.74-3.06	0.86	0.48-1.43
Pancreatic	1.08	0.95-1.22	1.06	0.72-1.51	0.95	0.58-1.46	1.34	0.90-1.93
Lung and bronchus	1.01	0.95-1.07	1.05	0.86-1.26	0.63*	0.49-0.81	1.29	1.04-1.59
Cervical	0.55*	0.39-0.75	0.59	0.24-1.21	0.32	0.07-0.94	0.63	0.26-1.31
Uterine	1.22*	1.12-1.33	1.16	0.87-1.53	0.99	0.74-1.31	1.71	1.33-2.16
Ovarian	1.05	0.92-1.19	1.14	0.70-1.76	1.25	0.85-1.78	1.52	1.02-2.19
Bladder	1.05	0.91-1.20	0.84	0.43-1.47	0.58	0.29-1.04	1.03	0.49-1.89
Kidney	1.00	0.85-1.17	1.17	0.75-1.73	0.85	0.48-1.40	1.86*	1.16-2.81
Thyroid	1.50*	1.32-1.69	2.19*	1.51-3.08	1.39	0.96-1.96	1.78*	1.29-2.38
Lymphoma	0.87	0.77-0.97	1.08	0.70-1.60	0.80	0.53-1.16	1.26	0.86-1.78
Hodgkin lymphoma	0.61	0.30-1.08	0.55	0.01-3.05 <sup>b</sup>	0.92	0.11-3.34 <sup>b</sup>	1.01	0.03-5.65 <sup>b</sup>
Non-Hodgkin lymphoma	0.88	0.78-0.99	1.13	0.72-1.68	0.79	0.52-1.16	1.27	0.87-1.81
Myeloma	0.90	0.71-1.11	1.08	0.68-1.62	0.67	0.24-1.45	1.20	0.55-2.27
Leukemia	1.33*	1.17-1.51	2.52*	1.74-3.52	1.19	0.74-1.82	3.20*	2.21-4.47
Acute lymphocytic leukemia	1.29	0.59-2.46	1.52	0.04-8.48 <sup>b</sup>	1.22	0.03-6.81 <sup>b</sup>	1.36	0.03-7.59 <sup>b</sup>
Chronic lymphocytic leukemia	0.65*	0.49-0.86	0.83	0.23-2.12 <sup>b</sup>	0.13	0.01-0.73 <sup>b</sup>	0.54	0.01-3.02 <sup>b</sup>
Acute myeloid leukemia	2.31*	1.92-2.76	4.86*	3.05-7.36	2.62*	1.43-4.40	5.00*	3.26-7.32
Chronic myeloid leukemia	1.43	0.97-2.03	2.11	0.57-5.39 <sup>b</sup>	1.85	0.50-4.74 <sup>b</sup>	1.46	0.18-5.26 <sup>b</sup>

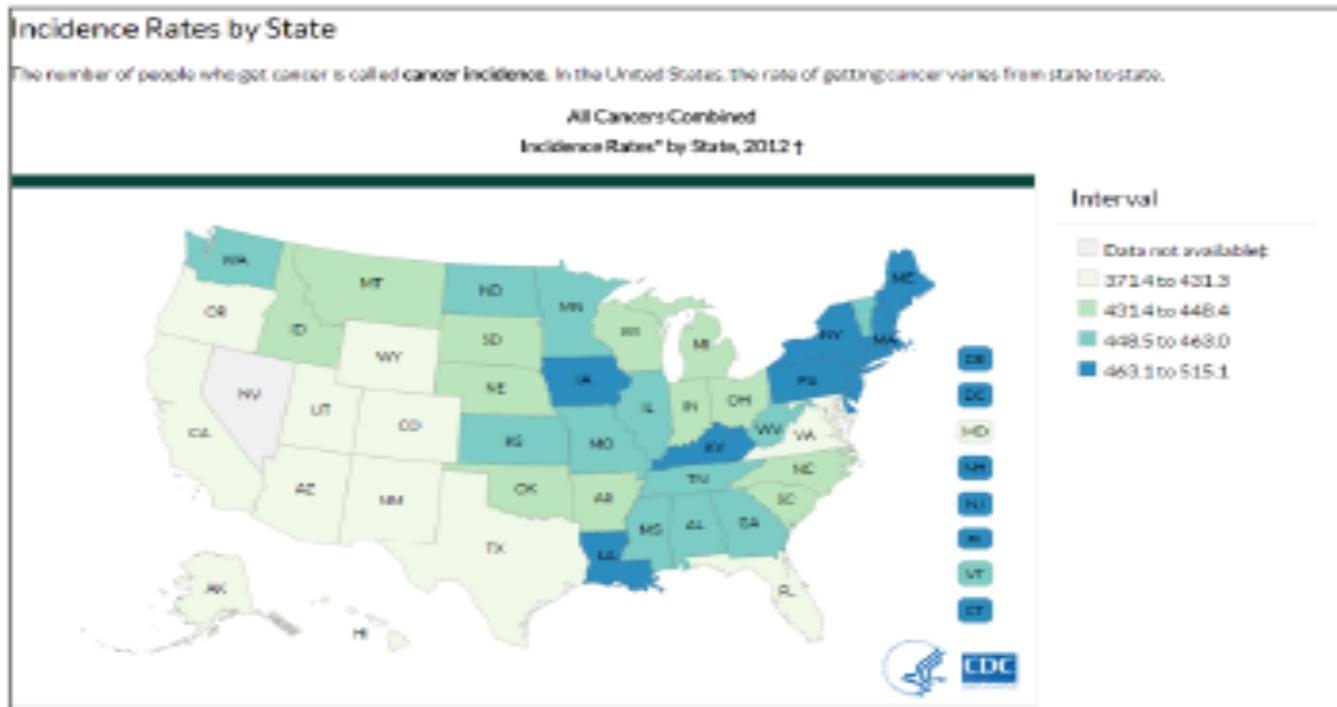
\* Indicates risk estimate is statistically significant at  $P < 0.001$

<sup>a</sup> Excludes non-melanoma skin cancer

<sup>b</sup> SIR based on  $<5$  second primary cancer cases

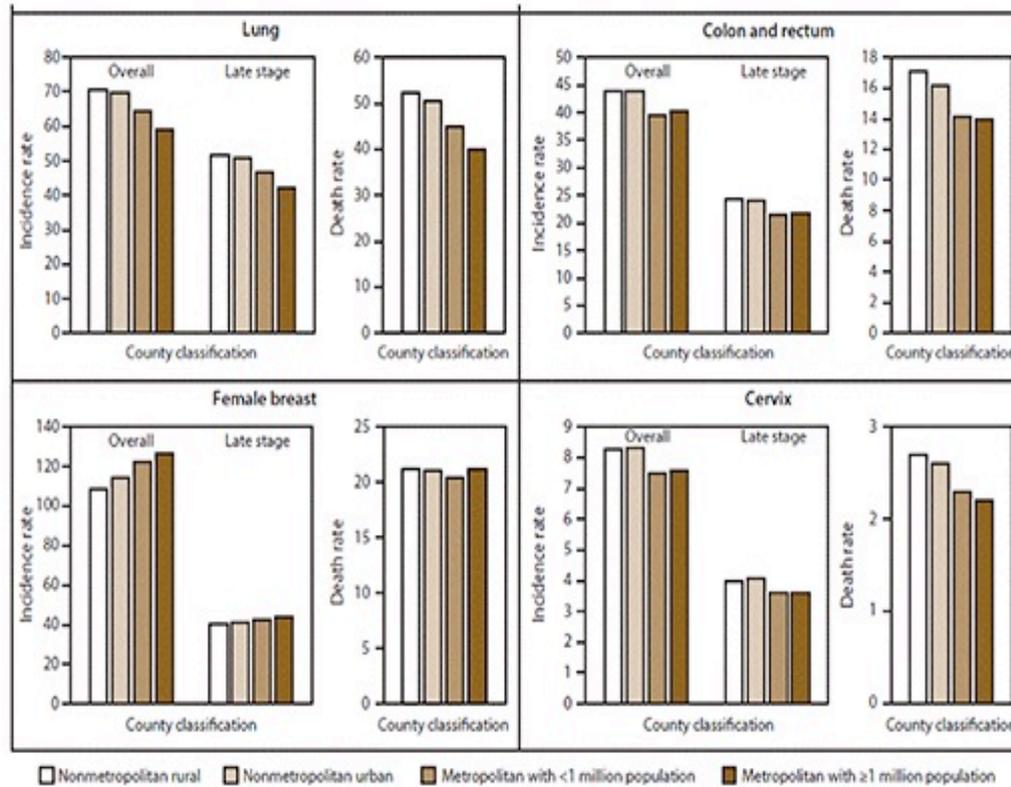
# Geographical factors

## Geographical factors contribute to cancer disparities



# Rural-urban disparities

## Rural-Urban Disparities in Cancer Mortality



# Geographical factors

## Geographical factors contribute to cancer disparities

- A low socioeconomic status (SES) neighborhood confers additional incidence or mortality risk beyond individual SES (*J. Epidemiol. Community Health* 2003, 57:444-52)
  - Unequal burden of pollution
  - Access to preventative services (eg tobacco cessation)
  - Areas with the highest percentage of African Americans have the highest exposure to cancer-associated pollutants (*Environ Health Perspect.* 2005 113(6): 693–699)
  
- Rural populations are more likely to have increased cancer incidence, unequal burden of pollution
  - Forego medical care and prescriptions due to cost
  - Report fair/poor health and health-related unemployment
  - Experience psychosocial distress

# Survival Health Disparities by Cancer Site

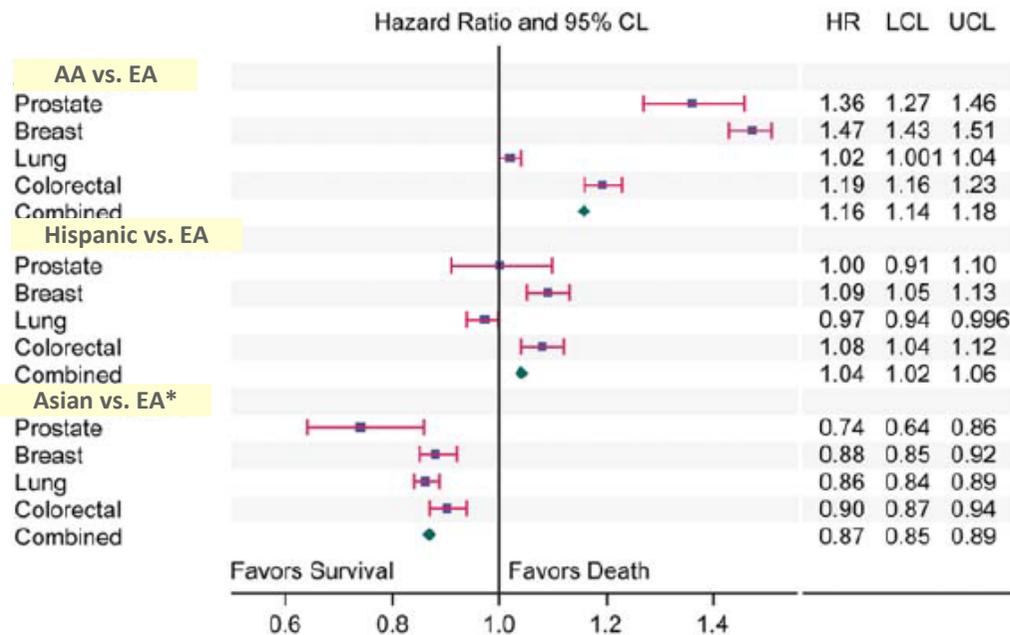
African Americans have the highest rate of cancer specific mortality

Racial differences are not reducing over time (overall)

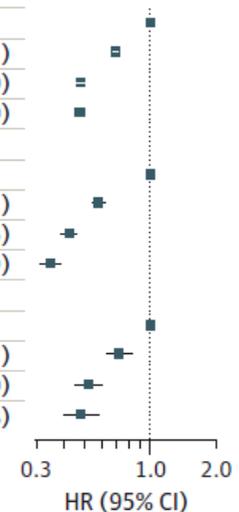
Breast cancer—disparities might be increasing

Prostate cancer<sub>s</sub>—disparities might be improving

r



Race	HR (95% CI)
<b>White</b>	
1990-1994	1 [Reference]
1995-1999	0.69 (0.67-0.71)
2000-2004	0.48 (0.46-0.50)
2005-2009	0.47 (0.45-0.50)
<b>Black</b>	
1990-1994	1 [Reference]
1995-1999	0.58 (0.54-0.62)
2000-2004	0.42 (0.39-0.46)
2005-2009	0.35 (0.31-0.39)
<b>Asian</b>	
1990-1994	1 [Reference]
1995-1999	0.72 (0.63-0.82)
2000-2004	0.53 (0.45-0.60)
2005-2009	0.48 (0.40-0.58)



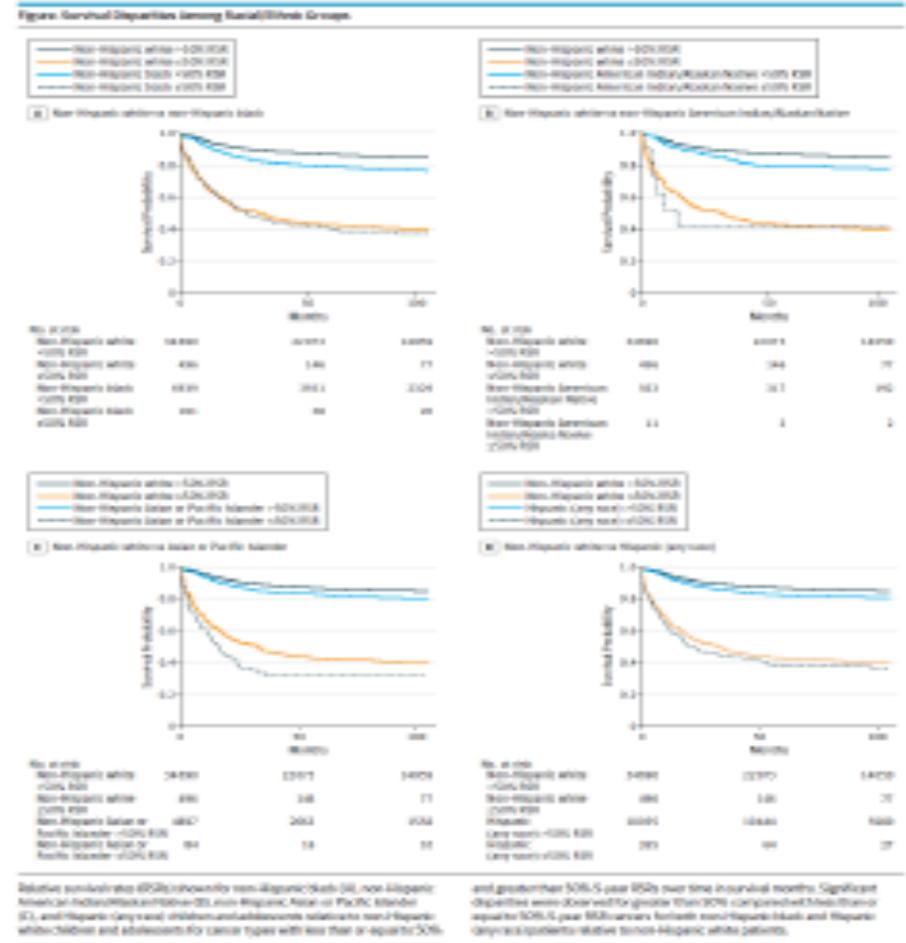
merican

# Childhood and adolescent cancer survival

Evidence for racial/ethnic disparities in childhood and adolescent cancer survival for non-Hispanic black, non-Hispanic American Indian/Alaskan Native, non-Hispanic Asian or Pacific Islander, and Hispanic (any race) patients.

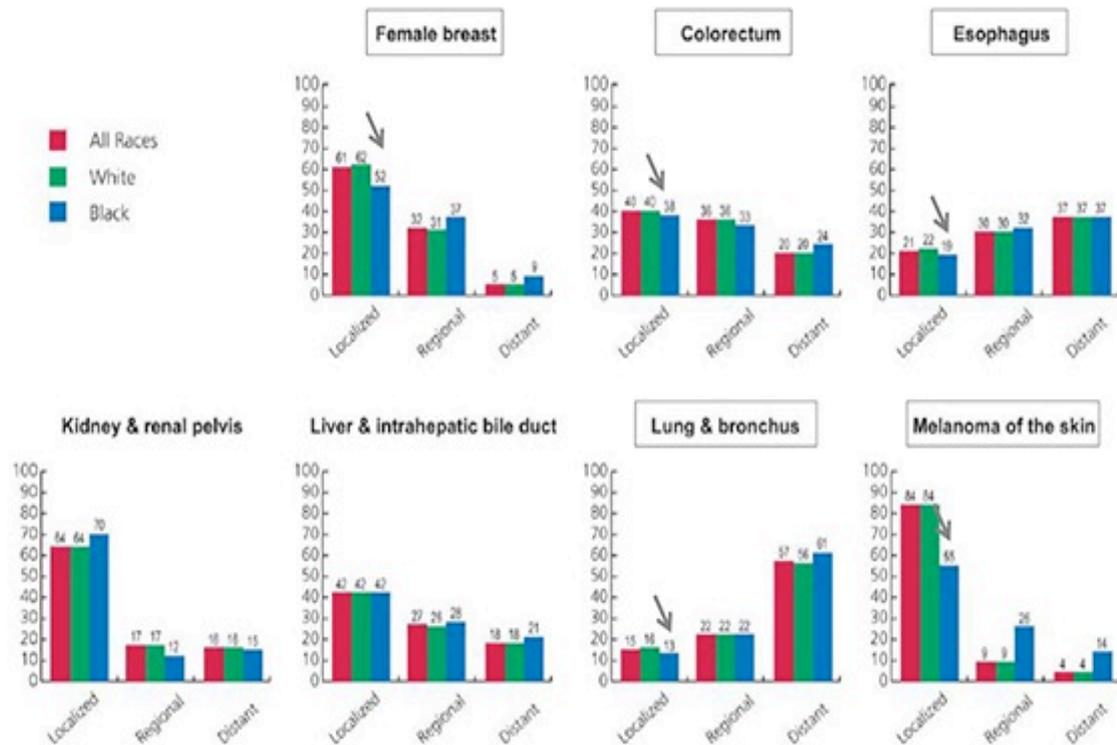
These disparities were larger overall for more survivable cancer types, which are generally more amenable to medical intervention.

As childhood and adolescent cancer treatment continues to advance, the risk of leaving disadvantaged groups behind grows. Efforts should be made to promote health equity by race/ethnicity among all children and adolescents with cancer in the United States.



# Disparities in cancer mortality

Some of the reasons for disparities in cancer mortality: Lack of early detection?



## ➤ **Some of the reasons for disparities in cancer mortality: Access to screening?**

Possibly for some cancers

Breast cancer mammography use similar in equal access to care setting (Cancer 2013 Oct 1;119(19):3531-8)

Colorectal cancer screening is lower among African Americans even in an equal access to care setting (Cancer. 2013; 4(3): 270–280)

Uptake of screening for other cancers, such as HPV, may also be lower in minority populations

But the differences exist even in cancers where there is no validated screening modality (liver, esophagus, etc)

# Lung cancer screening

## Lung Cancer Screening

**Table 2** Numbers and per cent of lung cancers diagnosed in the NCI-MD case-control study from 1998 to 2015 that fall within guidelines for lung cancer screening

	Criteria					
	NLST*		USPSTF†		CMS‡	
	EA	AA	EA	AA	EA	AA
All (n=1141 EA, n=517 AA)	381 (33.4%)	161 (31.1%)	449 (39.4%)	176 (34.0%)	421 (36.9%)	171 (33.1%)
p Value	0.355		<b>0.036</b>		0.134	
Men (n=600 EA, n=270 AA)	231 (38.5%)	98 (36.3%)	269 (44.8%)	110 (40.7%)	255 (42.5%)	105 (38.9%)
p Value	0.392		0.119		0.168	
Women (n=541 EA, n=247 AA)	150 (27.7%)	63 (25.5%)	180 (33.3%)	66 (26.7%)	167 (30.9%)	66 (26.7%)
p Value	0.350		<b>0.007</b>		0.083	

Bold signifies statistical significance.

Data based on smoking status, pack-years of smoking, time since quitting and age.

\*NLST criteria: aged 55–74, current or former smoker, at least 30 pack-years of smoking, if former smoker, having quit within the last 15 years.

†USPSTF criteria: aged 55–80, current or former smoker, at least 30 pack-years of smoking, if former smoker, having quit within the last 15 years.

‡CMS criteria: aged 55–77, current or former smoker, at least 30 pack-years of smoking, if former smoker, having quit within the last 15 years.

AA, African American; CMS, Centers for Medicare & Medicaid Services; EA, European Americans; NLST, National Lung Screening Trial; USPSTF, US Preventive Services Task Force.

# Lung cancer screening

## Lung Cancer Screening: Example of guidelines that trend towards disproportionately excluding some populations

Table 2. Reasons for USPSTF Lung Cancer Screening Ineligibility for SCCS Smokers With Lung Cancer

Characteristic <sup>a</sup>	SCCS Smokers, No. (%)			P Value
	White	African American	Total	
<b>All cancer cases</b>				
No.	478	791	1269	NA
Age <55 y	91 (19)	192 (24)	283 (22)	.03
<30 Pack-years	77 (16)	358 (45)	435 (34)	<.001
Smoking cessation >15 y	43 (9)	47 (6)	90 (7)	.04
<b>Ineligible lung cancer cases</b>				
No.	208	536	744	NA
Age <55 y	91 (44)	192 (36)	283 (38)	.046
<30 Pack-years	77 (37)	358 (67)	435 (58)	<.001
Smoking cessation >15 y	43 (21)	47 (9)	90 (12)	<.001

Abbreviations: NA, not applicable; SCCS, Southern Community Cohort Study; USPSTF, United States Preventive Services Task Force.

<sup>a</sup> Categories are not mutually exclusive.

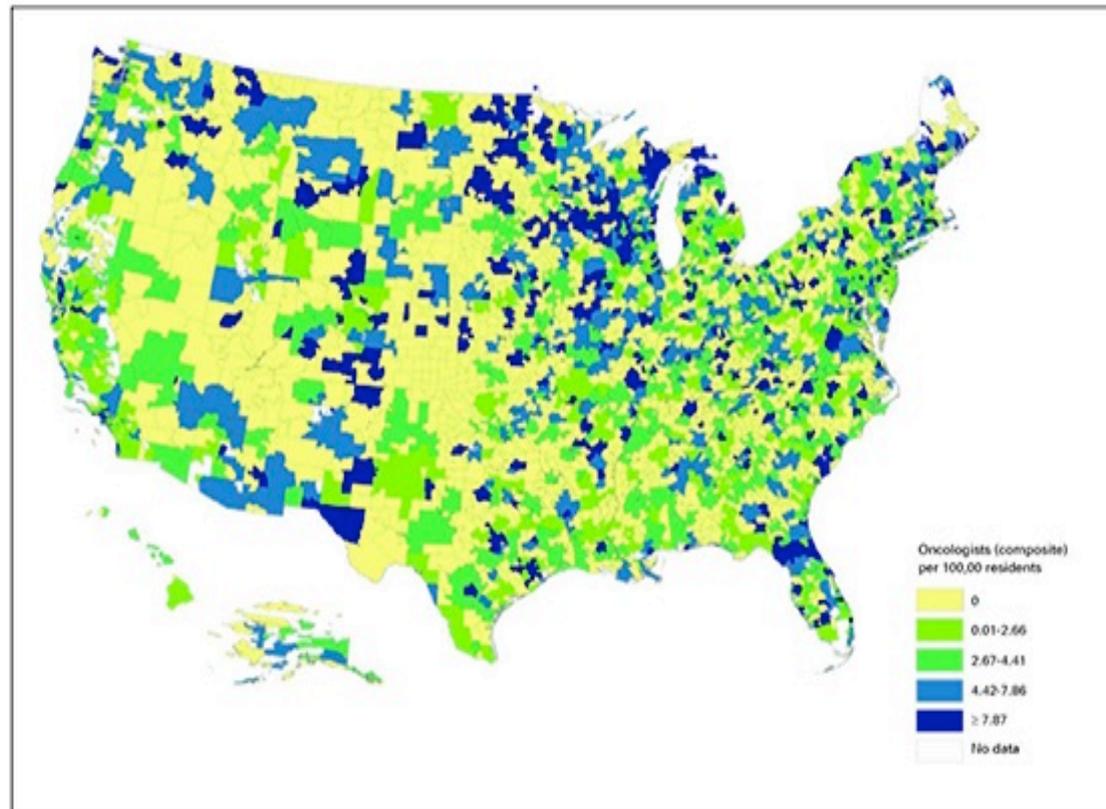
# Access to screening

## **Some of the reasons for disparities in cancer survival: Access to screening?**

- **Barriers to screening include residence in a rural area and access to screening services**
- **Uptake of screening for other cancers can vary**
  - Breast cancer mammography use similar in equal access to care setting (Cancer 2013 119(19):3531-8)
  - Colorectal cancer screening is lower among African Americans even in an equal access to care setting (Cancer. 2013; 4(3): 270–280)
  - Lung cancer screening similar to lower among African Americans
  - Specificity of screening criteria
- **But mortality differences exist even in cancers where there is no validated screening modality (liver, esophagus, etc)**

# Oncologist map

Oncologists per 100,000 residents by hospital service area



JOURNAL OF CLINICAL ONCOLOGY ASCO

Chun Chieh Lin et al. JCO doi:10.1200/JCO.2015.61.1558

# Disparities and health insurance.

Nearly half of the observed racial/ethnic disparities in higher stage at breast cancer diagnosis are mediated by health insurance coverage.

In multivariable analyses, after adjusting for demographic and clinical characteristics and county-level SES factors (Table 3), racial/ethnic minority women all had between a 2-fold and 4-fold higher odds of being uninsured or having Medicaid at the time of breast cancer diagnosis compared with NHW women

**Table 3. Results From Multivariable Logistic Models Associating Race/Ethnicity With Health Insurance Status (Uninsured or Medicaid Coverage vs Insured)**

AJCC Stage III vs Stages I or II	Crude Model		Adjusted Model			
	OR (95% CI)	P Value	Multivariable <sup>a</sup>		Multivariable and SES <sup>b</sup>	
	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value
White	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA
Black	2.85 (2.75-2.96)	<.001	2.85 (2.74-2.96)	<.001	2.11 (2.02-2.21)	<.001
American Indian or Alaskan Native	6.11 (5.42-6.91)	<.001	4.37 (3.78-5.05)	<.001	3.46 (2.96-4.06)	<.001
Asian or Pacific Islander	1.72 (1.65-1.80)	<.001	1.90 (1.82-1.99)	<.001	2.32 (2.21-2.44)	<.001
Hispanic	4.22 (4.08-4.36)	<.001	4.15 (4.00-4.30)	<.001	4.21 (4.05-4.38)	<.001

Abbreviations: AJCC, American Joint Committee on Cancer; NA, not applicable; OR, odds ratio; SEER, Surveillance, Epidemiology, and End Results Program; SES, socioeconomic status.

<sup>a</sup> Multivariable model adjusted for age, SEER registry, year of diagnosis,

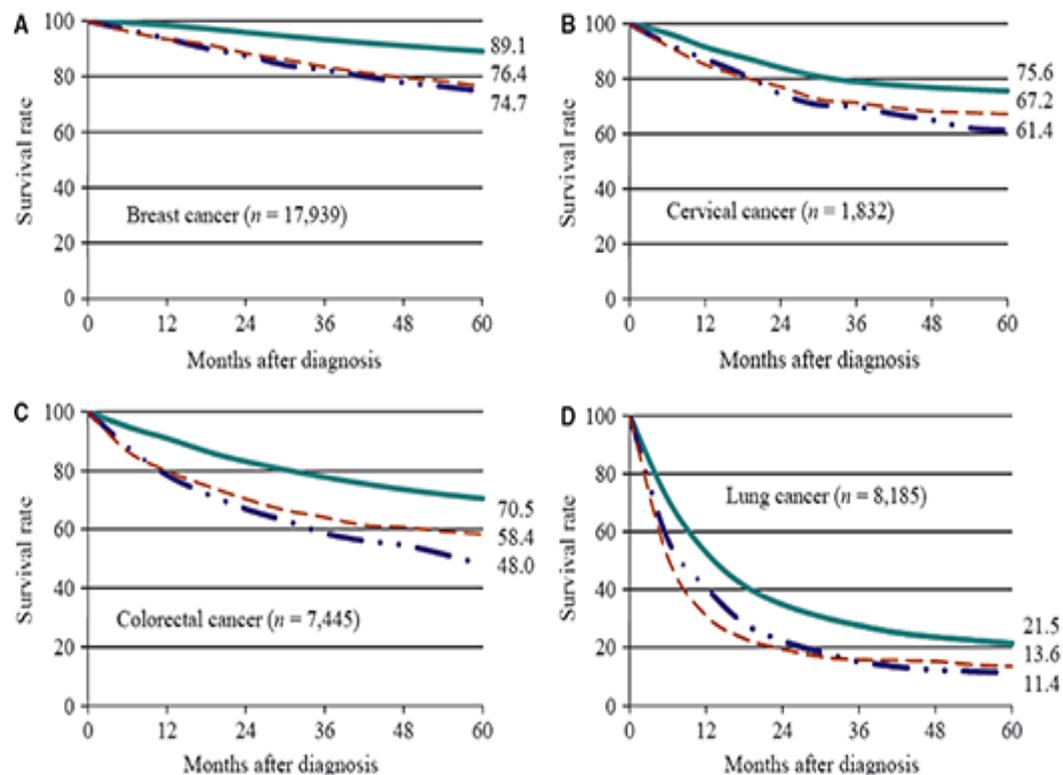
and breast cancer subtype.

<sup>b</sup> Multivariable model additionally adjusted for marital status and county-level SES variables (median income, educational level, poverty level, language isolation, and urban residence).

• PMID: 31917398

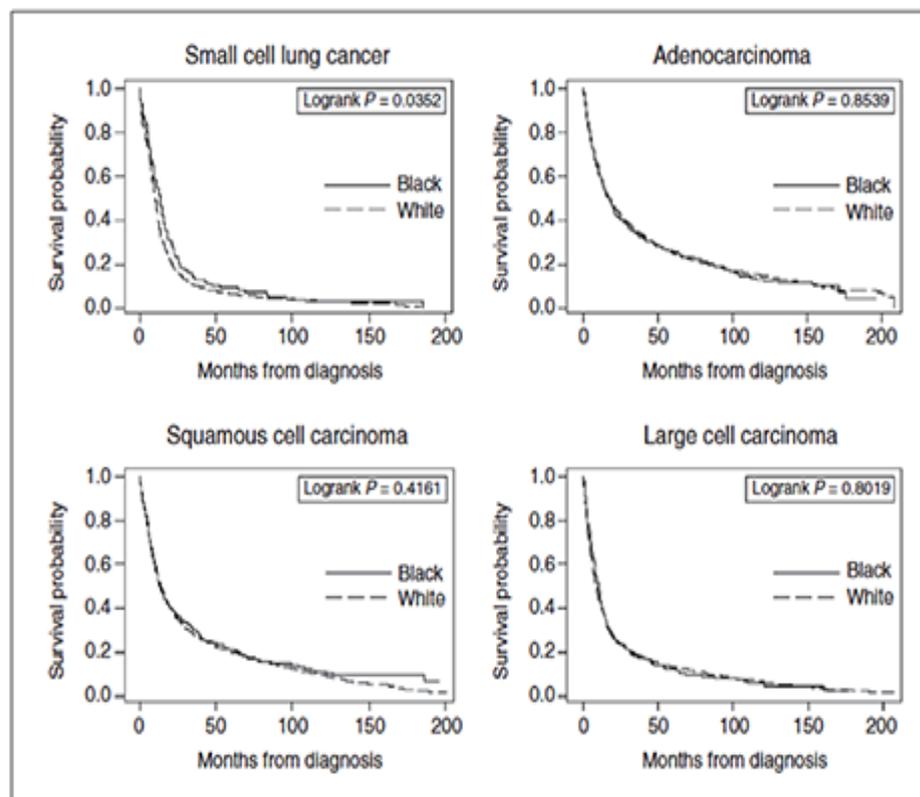
# Access to care

Some of the reasons for disparities in cancer mortality: Access to care?



# Access to care

Some of the reasons for disparities in cancer mortality: Access to care?

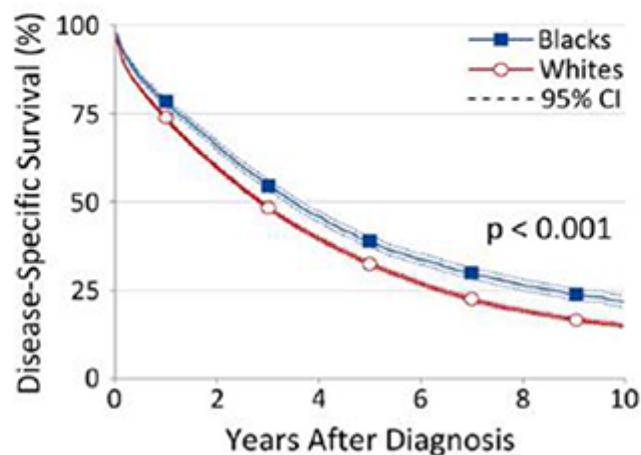


# Access to care

## Some of the reasons for disparities in cancer mortality: Access to care?

### Multiple myeloma

Increased incidence among African Americans but adverse disparities in outcome not observed  
African Americans may have a more indolent form of MM



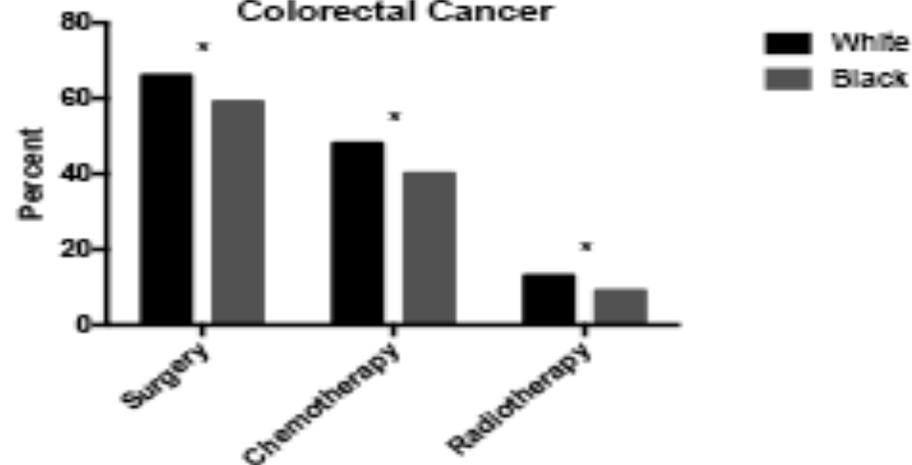
AA patients with myeloma have better survival than EA patients

# Care versus quality care

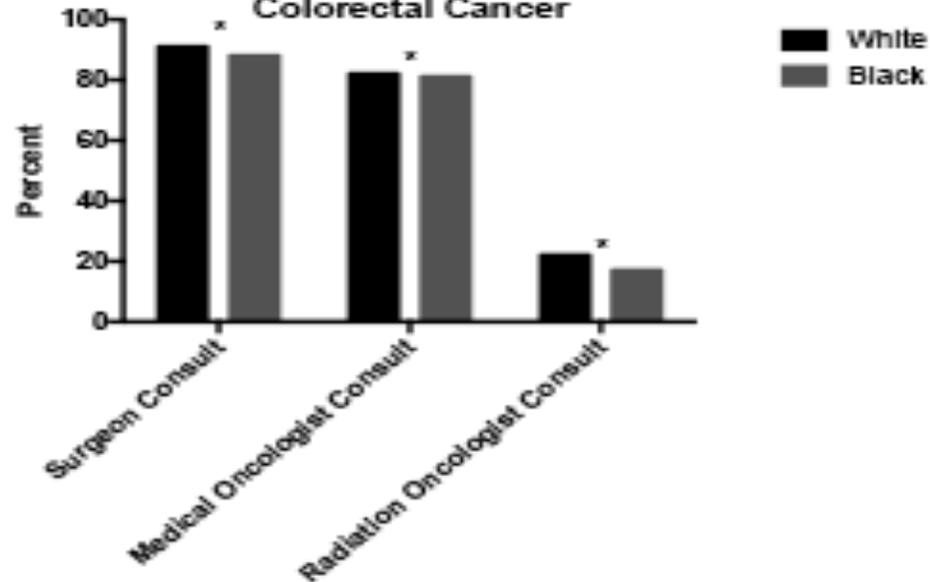
## Similar access to care alone does not equate to equal access to quality care

In a “regular” medical setting, studies show that racial disparity in specialist consultation, as well as subsequent treatment with multimodality therapy for metastatic colorectal cancer, exists.

Racial Differences in Treatment for Stage IV Colorectal Cancer



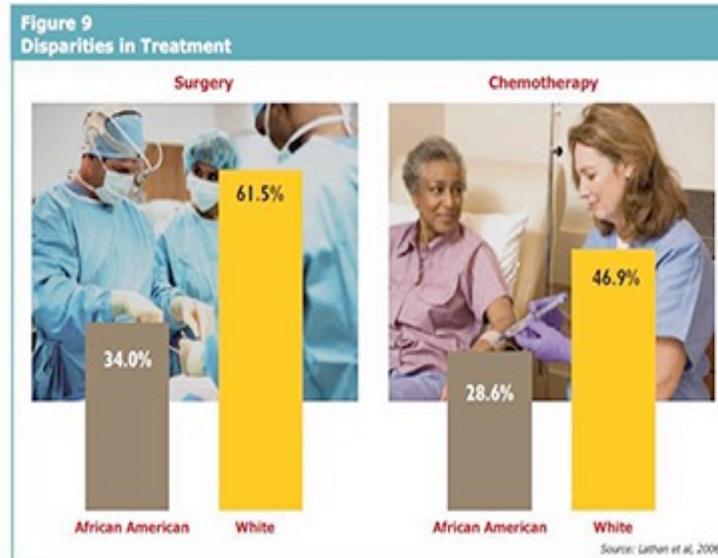
Racial Differences in Treatment for Stage IV Colorectal Cancer



# Uptake of care

## Some of the reasons for disparities in cancer mortality: Access and uptake of care?

- Even among those with medicare, AA are less likely to receive treatment for lung cancer (Cancer 2008 112 900-908)
- African American renal cancer patients are less likely to receive surgical treatment (nephrectomy) and die more often from competing causes than European American patients (*J Clin Oncol* 2007, 25: 3589 – 3595)



ALA – Too Many Cases Too Many Deaths 2010

# Uptake of care

Some of the reasons for disparities in cancer mortality: Access and uptake of care?

**TABLE 4.** Multivariate regression analyses assessing race and the odds of treatment among all of the study subjects and by tumor stage, age, and sex

Parameter	OR <sup>a</sup>	95% CI <sup>a</sup>
Surgery, all subjects	0.75	0.37–1.53
Chemotherapy, all subjects	0.79	0.59–1.04
Tumor stage		
I	2.52	0.64–9.98
II	0.98	0.61–1.60
III	0.55	0.30–1.00
IV	0.80	0.40–1.58
Age at diagnosis, y		
<50	1.10	0.47–2.59
50–64	0.74	0.48–1.15
≥65	0.93	0.60–1.44
Sex		
Men	0.80	0.56–1.14
Women	0.74	0.45–1.22

N = 2560.

<sup>a</sup>ORs and 95% CIs of race (non-Hispanic black versus non-Hispanic white) and treatment after adjusting for race, year of diagnosis, age at diagnosis (continuous), sex, marital status at diagnosis, active duty status at diagnosis, service branch of active duty member/sponsor, colon cancer site, tumor stage, tumor grade, surgery, chemotherapy, recurrence, and comorbidities. Respective treatments and stratified variables were not included in stratified analysis.

In a setting of equal access to care, African Americans with colon cancer are as less likely to receive surgery and chemotherapy as European Americans

*Diseases of the Colon & Rectum Volume 57: 9 (2014)*

➤ **Potential factors that influence uptake of care** Personal beliefs

Fear

Culture

Patient-doctor relationship

Patient bias

Provider bias

Patient-doctor communication

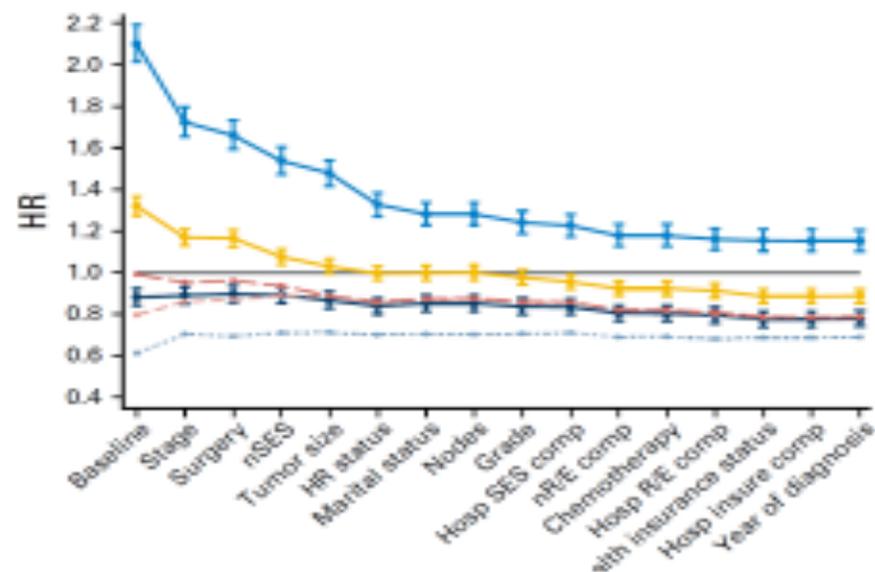
Co-morbid conditions

# Factors affecting survival

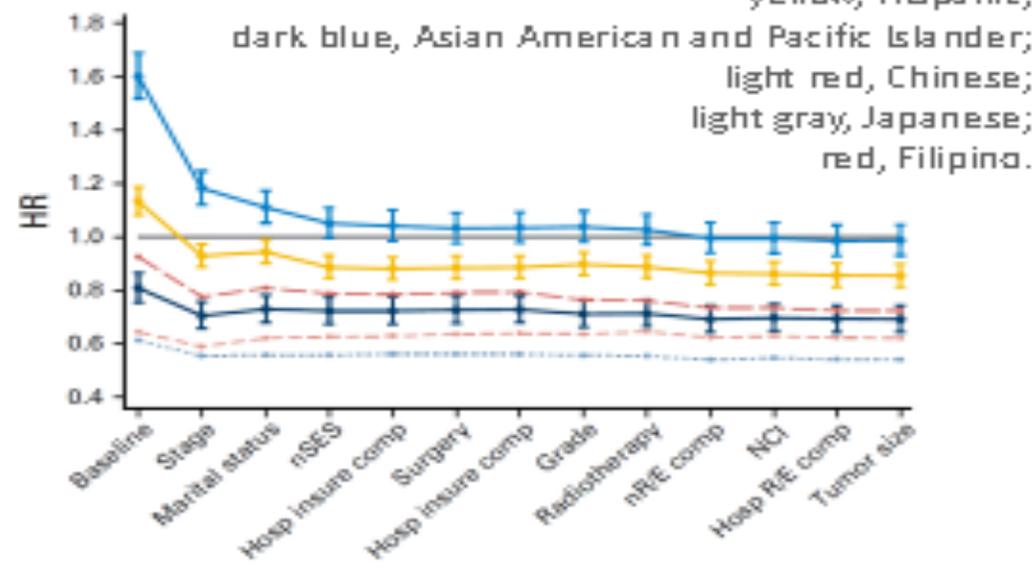
## Factors affecting disparities in cancer survival

*“Stage at diagnosis had the largest effect on racial/ethnic survival disparities, but earlier detection would not entirely eliminate them. The influences of neighborhood socioeconomic status and marital status suggest that social determinants, support mechanisms, and access to health care are important contributing factors.”*

### A Breast Cancer

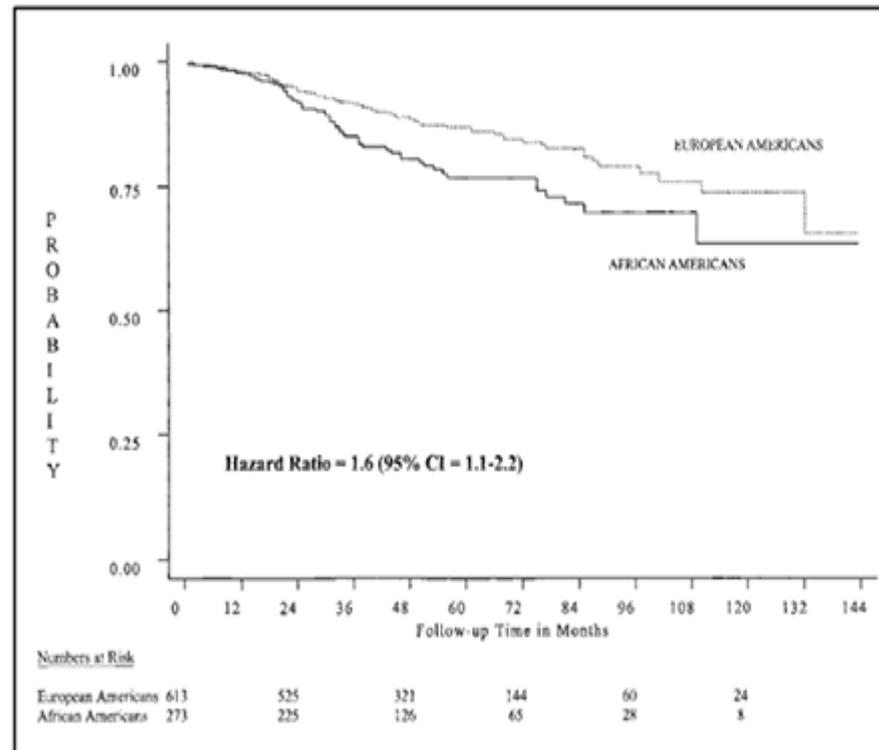


### B Prostate Cancer



# Disparities persist

For some cancers, disparities persist even in equal access to care settings



*Cancer 1998, 82: 1310 - 1318;*

*Cancer 2003, 98: 894 - 899*

*JNCI 91:17, 1999*

*JNCI Monographs, No. 35, 2005*

# Disparities

For some cancers, disparities persist even with *equal access to equal care*

Table 2. Quantile Regression Estimated Racial Difference in Time to Surgery Across Percentiles for Women With a Diagnosis of Breast Cancer in the US Military Health System, 1998-2007

Surgery Type and Time to Surgery, Percentile	Time to Surgery by Race/Ethnicity, (95% CI), d		Model-Estimated Difference (95% CI): Non-Hispanic Black – Non-Hispanic White	
	Non-Hispanic White	Non-Hispanic Black	Unadjusted	Adjusted <sup>a</sup>
<b>Breast conserving or mastectomy (n = 4887)</b>				
25th	7 (5.6 to 8.4)	6 (1.6 to 10.4)	-1.0 (-6.6 to 4.6)	-0.6 (-2.1 to 0.9)
50th	21 (20.6 to 21.4)	22 (20.6 to 23.4)	1.0 (-0.2 to 2.2)	1.3 (-0.2 to 2.9)
75th	35 (34.0 to 36.0)	39.5 (35.7 to 42.3)	4.0 (0.7 to 7.2) <sup>b</sup>	3.6 (1.6 to 5.5) <sup>b</sup>
90th	60 (55.3 to 64.7)	92 (75.9 to 108.0)	32 (12.3 to 51.7) <sup>b</sup>	8.9 (5.1 to 12.6) <sup>b</sup>
<b>Breast conserving (n = 3154)</b>				
25th	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0 (-0.4 to 0.4)
50th	18 (16.9 to 19.1)	19 (16.5 to 21.5)	1.0 (-2.0 to 4.0)	2.0 (0.0 to 4.0)
75th	31 (29.2 to 32.8)	33 (30.1 to 35.9)	2.0 (-1.5 to 5.5)	3.5 (0.9 to 6.1) <sup>a</sup>
90th	48 (45.5 to 50.5)	57 (49.1 to 64.9)	9.0 (-0.7 to 18.7)	7.9 (3.6 to 12.1) <sup>b</sup>
<b>Mastectomy (n = 1733)</b>				
25th	15 (14.2 to 15.8)	14 (12.5 to 15.5)	-1.0 (-2.8 to 0.8)	-0.3 (-3.5 to 2.8)
50th	26 (24.4 to 27.6)	29 (25.7 to 32.3)	3.0 (-0.7 to 6.7)	2.0 (-0.8 to 4.9)
75th	43.5 (40.4 to 47.6)	64 (52.2 to 75.8)	20.0 (5.7 to 34.3) <sup>b</sup>	4.1 (-0.1 to 8.5)
90th	102 (86.5 to 117.5)	149 (125.9 to 172.1)	47.0 (24.2 to 69.8) <sup>b</sup>	9.2 (0.8 to 17.5) <sup>b</sup>

This study's results indicate that time to breast cancer surgery was delayed for NHB compared with NHW women in the Military Health System. However, the racial differences in TTS did not explain the observed racial differences in overall survival among women who received breast-conserving surgery.

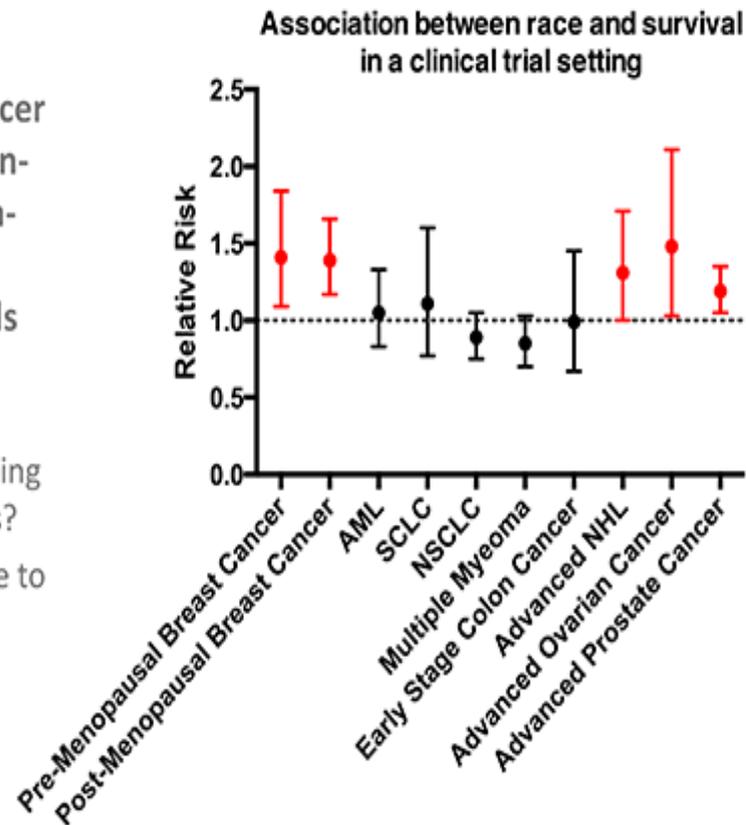
<sup>a</sup> Model adjusted for age, marital status, active duty status, military service/sponsor branch, care source, benefit type, TRICARE region, year of diagnosis, tumor stage, tumor grade, hormone receptor status, preoperative chemotherapy or radiotherapy, and comorbid conditions. (See the Study Variables subsection of the Methods section for a description of the variable levels.)

<sup>b</sup>  $P < .05$ .

# Is biology a contributing factor

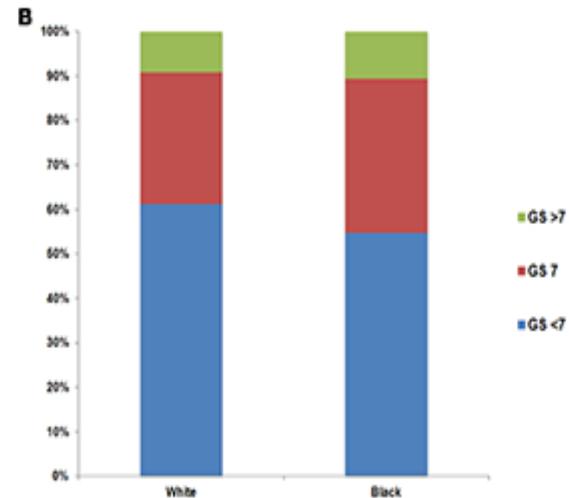
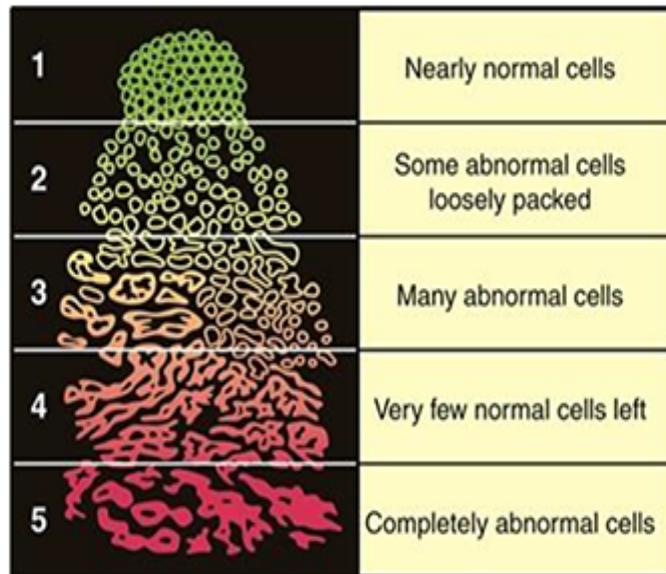
## Is biology a contributing factor?

- Racial disparities in prostate and breast cancer survival between African-American and European-American persist in randomized clinical trials (*JNCI 2009, 101: 984 – 92*)
  - Intrinsic differences in tumor biology influencing disease aggressiveness?
  - Differences in response to therapy?



# Prostate cancer

African Americans are more likely to be diagnosed with Aggressive Prostate Cancer



## Genetic susceptibility

Racial differences in prevalence of 8q24 prostate cancer susceptibility variants (~ 50%)

Admixture mapping identified 8q24 as a locus of increased risk for African-American men when compared to European-American men ([PNAS 2006, 103: 14068-73](#))

Risk alleles are more common among African-American men, leading to the highest population attributable risk conferred by 8q24 in this population ([Nat Genet 2007, 39: 638 – 44 & 954 – 6](#))

Excess of African ancestry at 8q24 ([Hum Genet 2009 Nov;126\(5\):637-42](#))

Risk variants rs114798100 and rs111906923 are only found in men of African descent ([JNCI 2016 108 \(7\)](#))

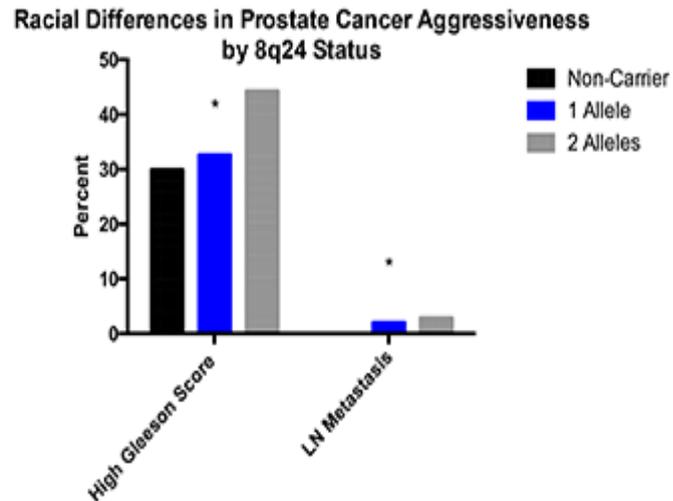
Racial differences in prevalence of 17q21 prostate cancer susceptibility variants (~ 10%)

Risk alleles of a new locus, rs7210100 are more common in populations of African descent ([Nat Gen 2011, 43: 570-573](#))

# Germline genetics

## Germline Genetics

- **8q24 is associated with higher grade, more aggressive prostate cancers**
  - Risk alleles are more common among AA men, (*Powell et al., J Urology 2010, 183: 1792 – 7*)
- **Faster disease progression in AA men (vs. EA men)** (*Powell et al., J Urology 2010, 183: 1792 – 7*)



## ➤ Germline Genetics

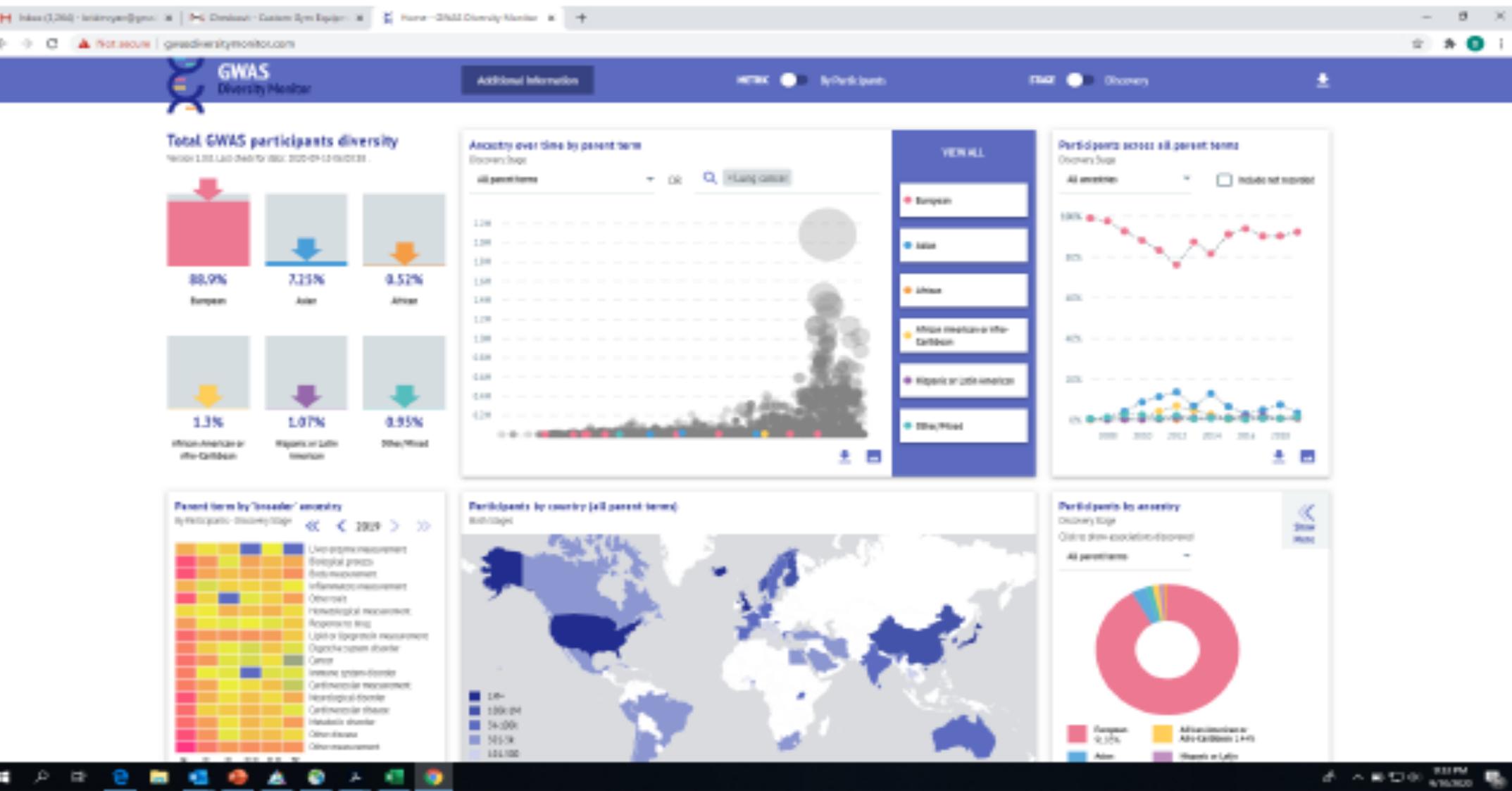
Increased proportion of Native American ancestry is associated with increased risk of childhood acute lymphoblastic leukemia

Screening implications

Also related to treatment—Children with more than 10% Native American ancestry need an additional round of chemotherapy to respond to the treatment (Yang et al., *Nature Genetics* 2011 43(3); 237-241)

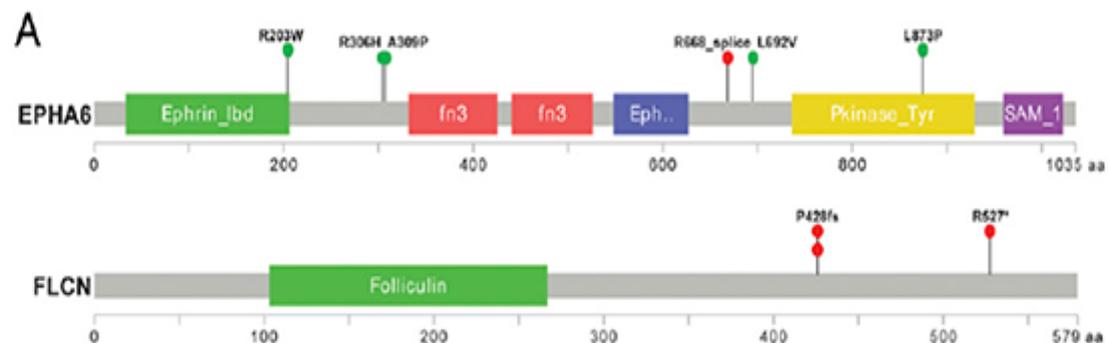
Ancestry informative markers provide a greater granularity to studying race in genetic and genomics studies

# GWAS



# Somatic genetics

## Somatic Genetics



**B**

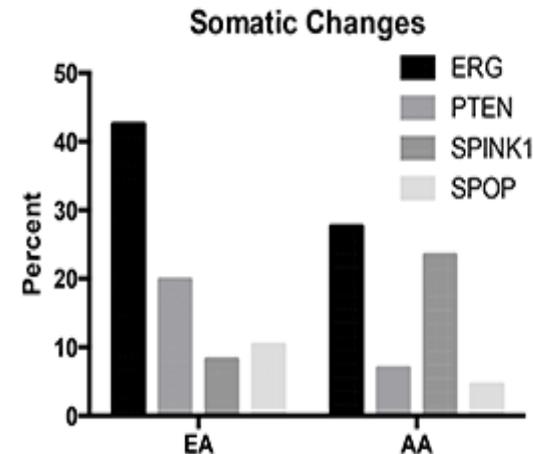
Hugo_Symbol	Tumor ID	Race	Colon cancer Stage	Screen	Variant_Class	Protein_Change	Tumor_Mutant allele frequency	PPH2_Class
<i>EPHA6</i>	11843	AA	Stage IV	Discovery	Missense	R203W	0.20	Deleterious
<i>EPHA6</i>	15873	AA	Stage IV	Discovery	Missense	R306H	0.35	Deleterious
<i>EPHA6</i>	16765	AA	Stage IIIB	Validation	Missense	A309P	0.25	Deleterious
<i>EPHA6</i>	13129	AA	Stage IIB	Validation	Splice	R668_splice	0.47	
<i>EPHA6</i>	16700	AA	Stage IIB	Validation	Missense	L692V	0.21	
<i>EPHA6</i>	16714	AA	Stage IIB	Validation	Missense	L873P	0.10	Deleterious
<i>FLCN</i>	16670	AA	Stage IIA	Validation	FS ins	P428fs	0.66	
<i>FLCN</i>	16518	AA	Stage IIIB	Validation	FS ins	P428fs	0.46	
<i>FLCN</i>	11604	AA	Stage IV	Discovery	Nonsense	R527*	0.80	

# Somatic genetics

## Somatic Genetics

- Global heterogeneity in acquired mutational events in prostate tumors:  
**Evidence of a different disease etiology?**

(*Cancer Res* 2010, 70: 5207 – 12; *Prostate* 2011, 71: 489 – 97; *Urology* 2012, 80: 749 – 53; *Clinical Cancer Res* 2014, 20: 4925 – 34)



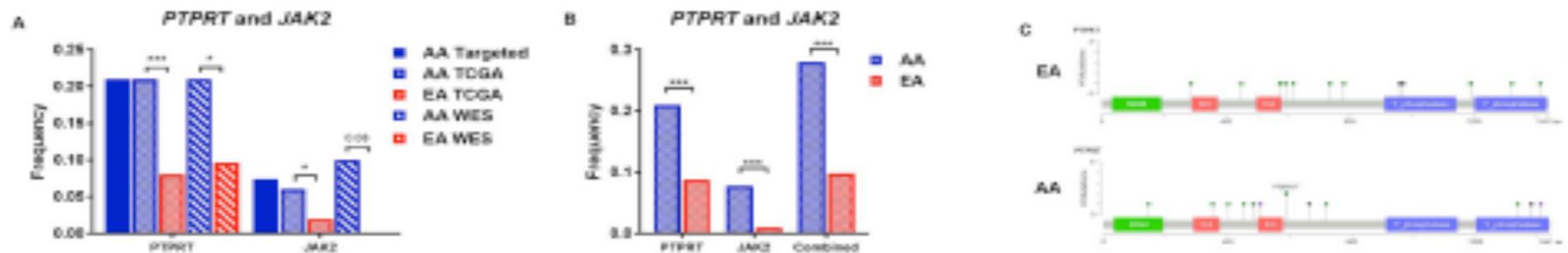
- High frequency of oncogenic TMPRSS2:ERG gene fusion events in European/European-American patients (about 50%), intermediate frequency in African-American patients (24%-31%), but rather uncommon in Asian patients (2%-16% among Chinese, Japanese patients)
- Common PTEN loss in European/European-American patients (30%-50%) but uncommon in Asian and African-American patients (5%-15%)

# Somatic mutation profiling

## Comparative Somatic Mutation Profiling

### • MAIN FINDINGS

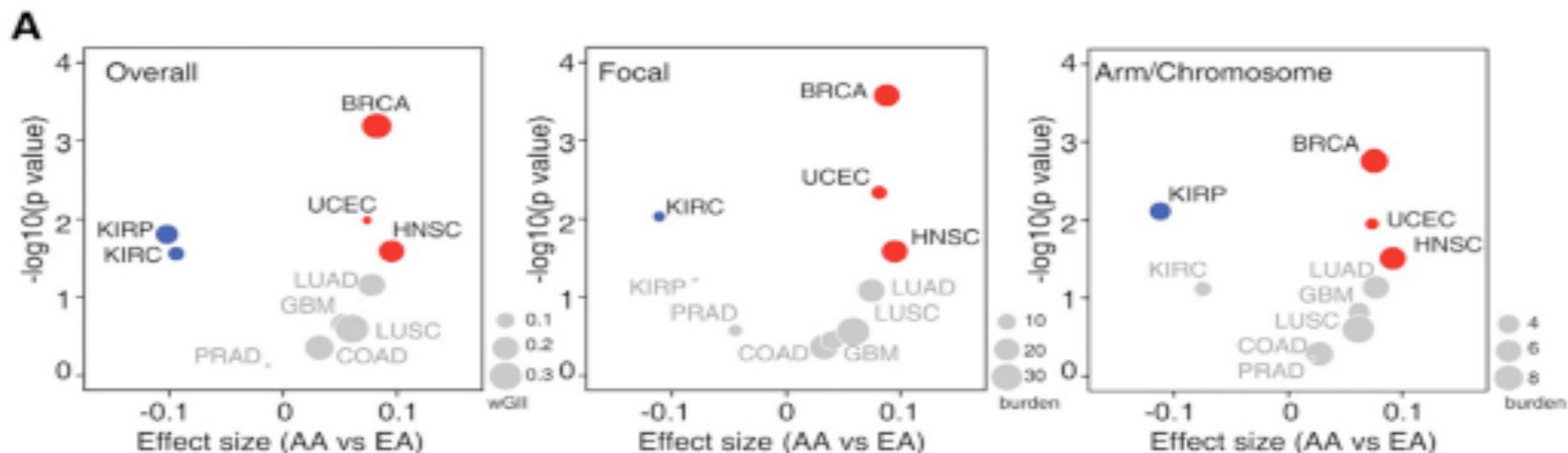
- Frequency of *PTPRT* and *JAK2* mutations are higher among AAs
- Validated in TCGA and by WES sequencing in a separate cohort of samples from NCI-MD
- Combined, mutated in 30% of samples in AAs compared with 10% in EAs



# Somatic genetics

## Somatic Genetics

- Breast, head and neck, and endometrial cancers of African Americans have higher levels of chromosomal instability than those of European Americans
- The frequency of genetic alternations in the PI3K pathway in AA patients is lower

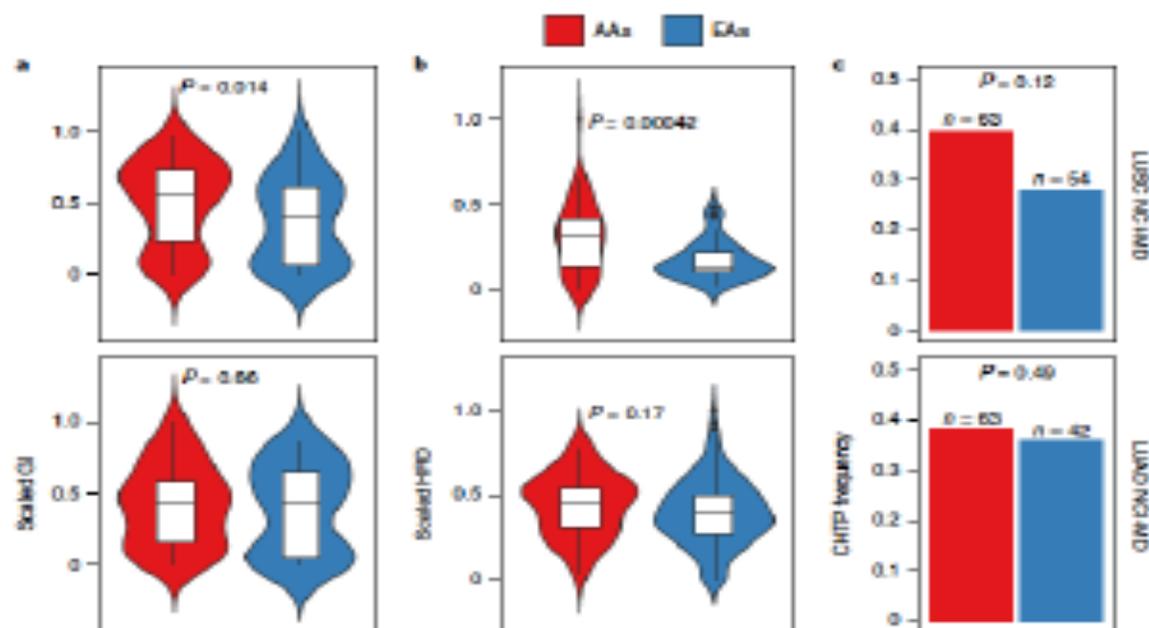


*Cancer Cell* 2018 34(4):549-560

# Somatic genetics

## Somatic Genetics

- Pan-cancer higher levels of genetic instability and homologous recombination repair deficiency in African Americans compared with European Americans



# Transcriptome, molecular subtype

## Transcriptome, molecular subtype

- Population differences in molecular subtypes and disease grade
- Race/ethnic disparity in prevalence of basal-like/triple-negative breast tumors  
(*JAMA* 2006, 295: 2492 – 2502; *J Clin Oncol* 2009, 27: 4514 – 21; *CEBP* 1994, 3: 127-135)

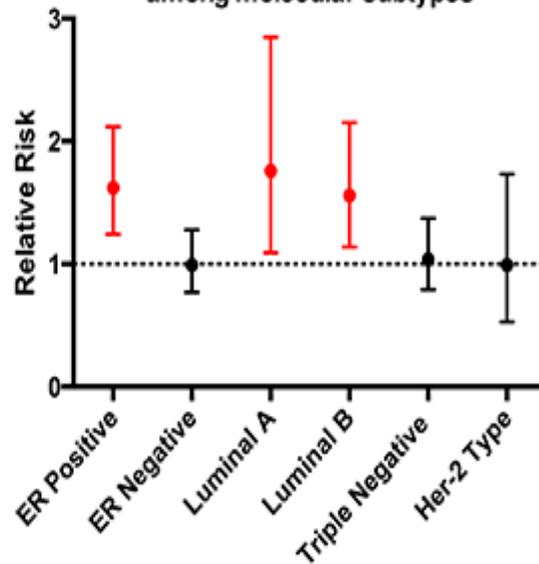
Table 3 Relative odds of specific tumor characteristics among black breast cancer patients compared with whites

Variables	Black		White		Crude		Adjusted*	
	n	%	n	%	OR	95% CI	OR	95% CI
Nuclear atypia								
1	153	30.7	218	47.8	1.00		1.00	
2	263	52.7	187	41.0	2.00	(1.52–2.65)	1.90	(1.42–2.55)
3	83	16.6	51	11.2	2.32	(1.55–3.47)	1.97	(1.27–3.04)
Mitotic activity								
1	249	50.6	291	64.7	1.00		1.00	
2	154	31.3	115	25.6	1.57	(1.17–2.10)	1.47	(1.08–2.00)
3	89	18.1	44	9.8	2.36	(1.59–3.52)	2.05	(1.34–3.14)
Tubular formation <sup>b</sup>								
None or few	377	77.6	266	63.9	1.00		1.00	
Moderate and well	109	22.4	150	36.1	0.51	(0.38–0.69)	0.57	(0.42–0.77)
Grade								
1	109	21.8	129	28.4	1.00		1.00	
2	295	59.0	262	57.7	1.33	(0.98–1.81)	1.19	(0.87–1.64)
3	96	19.2	63	13.9	1.80	(1.20–2.71)	1.58	(1.02–2.45)
Estrogen receptor								
Negative and border	185	44.5	143	36.7	1.00		1.00	
Positive	231	55.5	247	63.3	0.72	(0.55–0.96)	0.78	(0.58–1.05)

# Molecular subtype

## Molecular subtype

Association between race and breast cancer survival among molecular subtypes

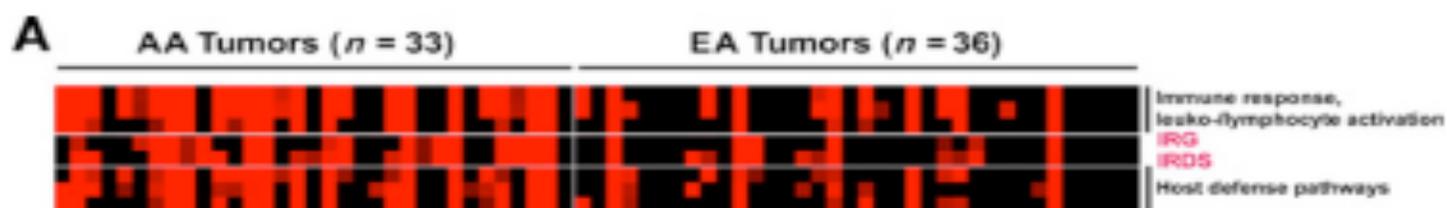


However, breast cancer survival disparity in US is irrespective of some tumor subtypes ([JNCI 2009, 101: 993-1000](#))

# Cell biology

## Cell biology

- Identification of an Interferon signature in prostate cancer tumors from African American men
- The signature is linked with a germline mutation



**Table 1.** *IFNL4* rs368234815- $\Delta$ G allele is associated with occurrence of IRDS in prostate tumors

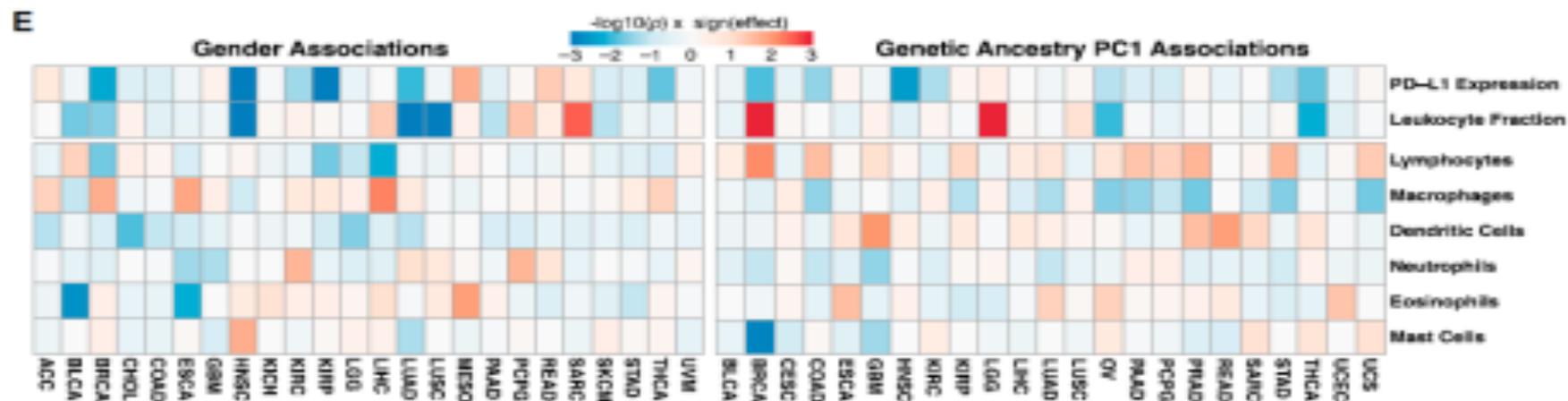
	<i>IFNL4</i> genotype, N (%)		Fisher's exact test	OR
	TT/TT or TT/ $\Delta$ G	$\Delta$ G/ $\Delta$ G	<i>P</i>	Adjusted OR (95% CI) <sup>a</sup>
All tumors, <i>N</i> = 44				
IRDS-negative	23 (92%)	2 (8%)	< 0.001	15.7 (2.7–90.6)
IRDS-positive	8 (42%)	11 (58%)		
Only tumors from AA men, <i>n</i> = 23				
IRDS-negative	6 (75%)	2 (25%)	0.04	8.2 (1.1–60.4)
IRDS-positive	4 (27%)	11 (73%)		

<sup>a</sup>Adjusted for age at diagnosis and pathological stage.

Wallace.... *Ambs, Cancer Res* 2008, 68: 927– 36  
Tang..... *Ambs Clin Cancer Res*. 2018.

# Cell biology-inflammation

## Cell biology-inflammation



**Figure 4. Immune Response and Genome State**

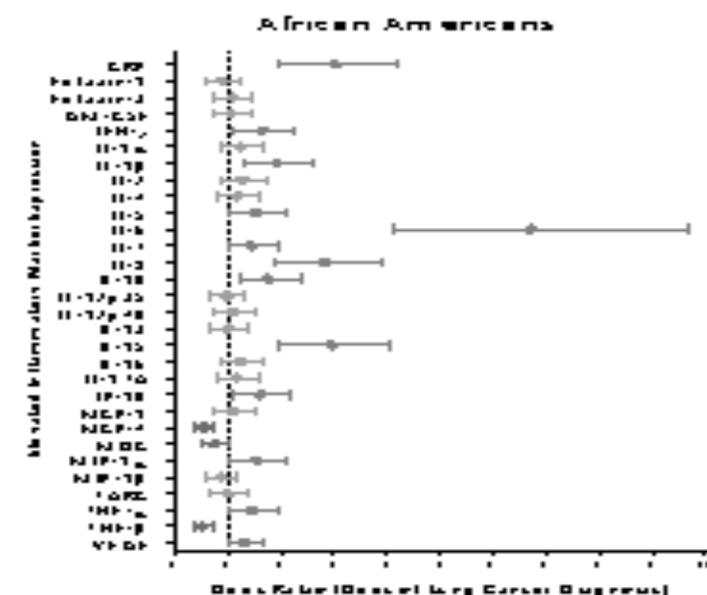
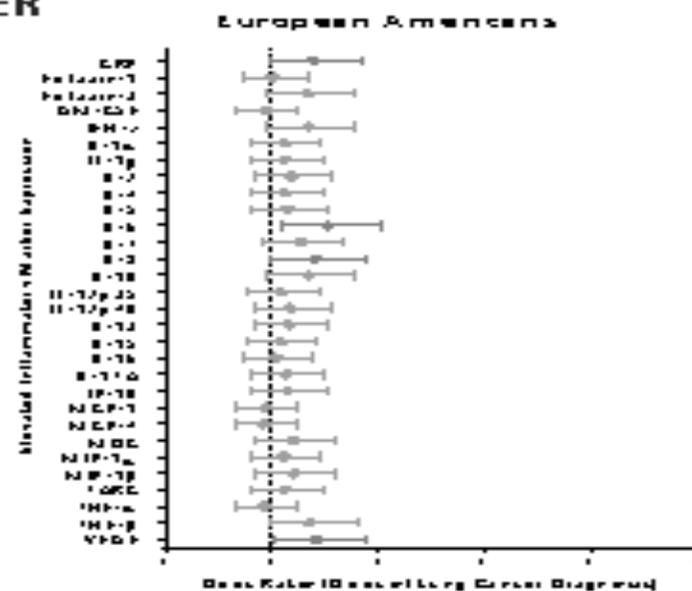
(A) Correlation of DNA damage measures (rows) with LF. From left to right: all TCGA tumors; averaged over tumor type; grouped by immune subtype.

(B) LF association with copy number (CN) alterations. Left: Differences between observed and expected mean LF in tumors with amplifications, by genomic region. Significant (FDR < 0.01) differences in mean LF are marked with black caps on the profiles. Right: Same, for deletions.

# Inflammation and lung cancer

## Inflammation and Lung Cancer

- POPULATION DIFFERENCES IN THE RELATIONSHIP BETWEEN INFLAMMATION AND LUNG CANCER



Red lines denote significant results

Zingone A, Brown D.... *Ryan BM, 2015 (CEBP 28(2):110-115)*  
 Meaney CM Mitchell K.... *Ryan BM, JTD 2019*

# Racial differences

## Racial differences in the response to immunotherapy

PROCEED Trial: Evaluation of sipuleucel-T immunotherapy for asymptomatic/minimally symptomatic metastatic castration-resistant prostate cancer

11.6% were African American

Race was a significant independent predictor of survival

**TABLE 2.** Final Primary Multivariable Analysis of Overall Survival in PROCEED

Baseline Covariate	HR (95% CI)	P*
Log PSA (ng/mL)	1.22 (1.16-1.27)	<.001
Hemoglobin, per g/dL increase	0.87 (0.83-0.91)	<.001
ECOG performance status, >0 vs 0	1.22 (1.05-1.42)	.009
Log ALP (U/L)	1.60 (1.42-1.81)	<.001
Age (y), >median vs ≤median	1.30 (1.12-1.50)	<.001
Race, white vs all others	1.64 (1.30-2.06)	<.001
Time since diagnosis (y), >median vs ≤median	0.72 (0.62-0.83)	<.001
Lymph node only metastases, yes vs no	0.70 (0.63-0.99)	.044
Visceral metastases, any vs none	1.30 (0.95-1.78)	.098
Prior docetaxel/cabazitaxel, yes vs no	1.54 (1.25-1.90)	<.001
Prior abiraterone/enzalutamide, yes vs no	1.53 (1.16-1.27)	<.001

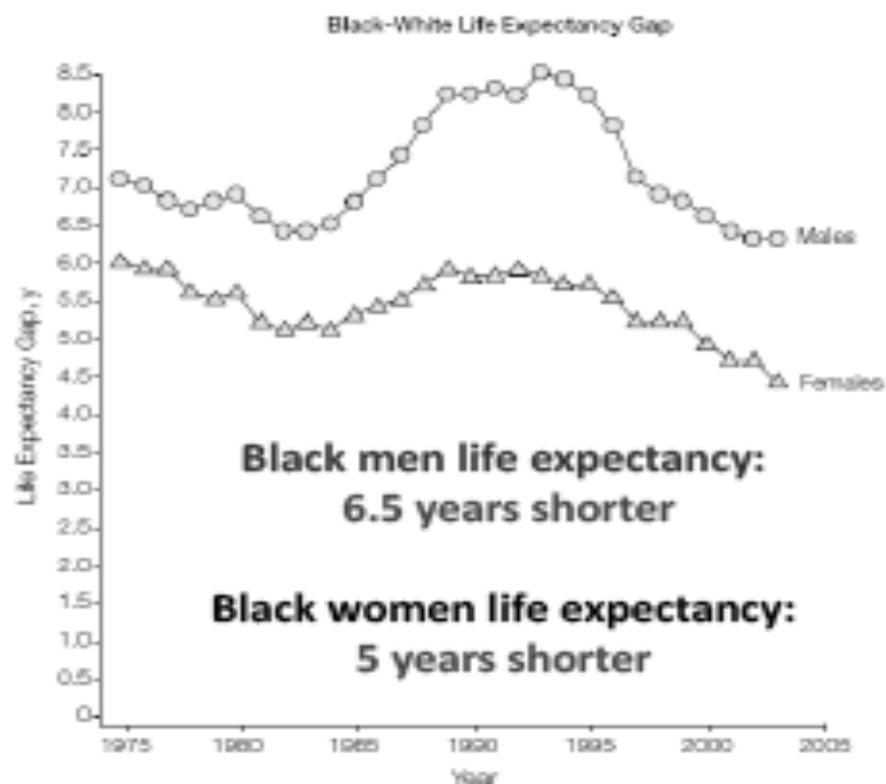
Abbreviations: ALP, alkaline phosphatase; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio; PROCEED, PROVENGE Registry for the Observation, Collection, and Evaluation of Experience Data; PSA, prostate-specific antigen.

\*Multivariable Cox modeling.

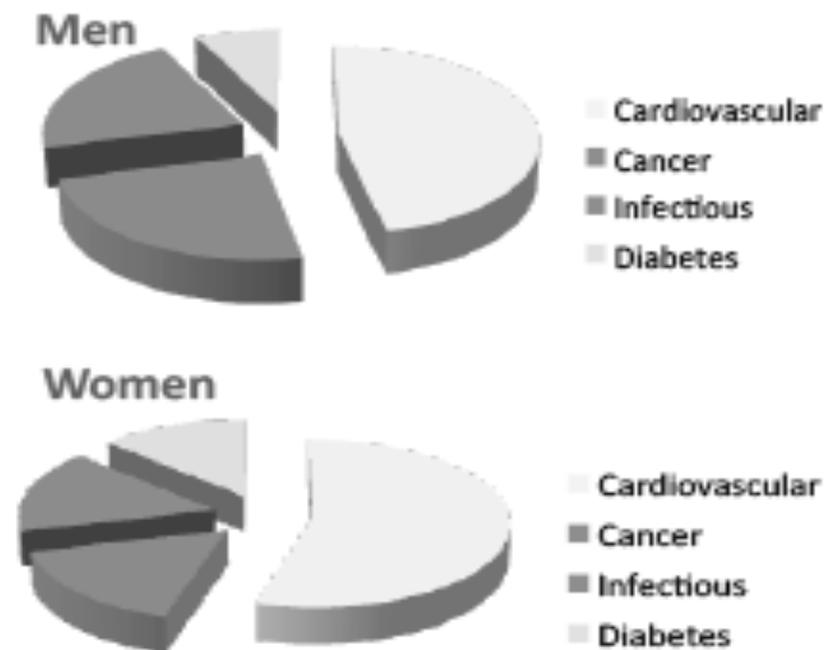
# Health disparities

## Health Disparities in the United States

Racial differences in life expectancy in the United States



Contributing Factors



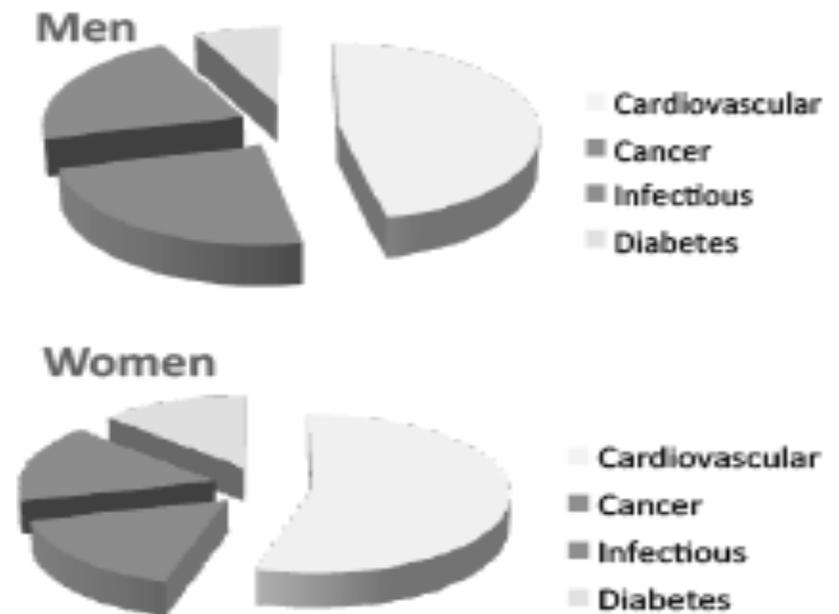
Adapted from JAMA 2007 297:11 1227

# Health disparities in the U.S.

## Health Disparities in the United States

- **Complex web of factors that contribute to disparities in incidence and survival**
  - **Host (biology)**
  - **Environment (SES, geography)**
  - **Behavior (smoking, diet, beliefs)**

### Contributing Factors



Adapted from JAMA 2007 297:11 1227

# Key determinants

## Key determinants of disparities

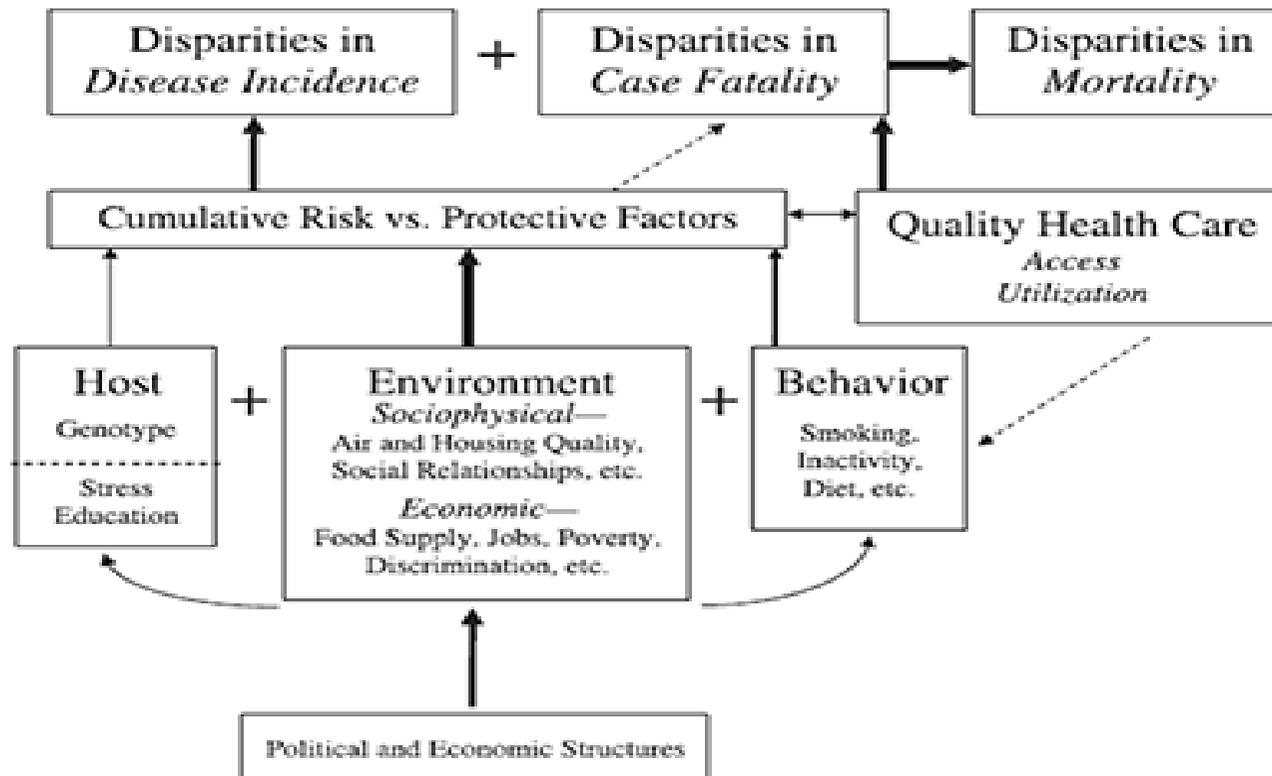


Figure 1. Key determinants of health disparities.