The Causes and Consequences of Cancer Health Disparities

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Outline

• Background

• Disparities in cancer incidence

• Disparities in cancer outcomes
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
USA Health Disparities

Health Disparities in the United States

Race differences in life expectancy in the United States

Black-White Life Expectancy Gap

- Black men life expectancy: 6.5 years shorter
- Black women life expectancy: 5 years shorter

Contributing Factors

Men
- Cardiovascular
- Cancer
- Infectious
- Diabetes

Women
- Cardiovascular
- Cancer
- Infectious
- Diabetes

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

Incidence Rates by Race/Ethnicity and Sex, U.S., 1999–2012
Incidence rates

Incidence Rates by Race/Ethnicity and Sex, U.S., 1999–2012
Breast cancer incidence

Breast cancer incidence is higher in Whites compared with Blacks

Diagnosis age

Younger age at diagnosis for most cancers

Diagnosis age

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

Mortality rates

Mortality Rates by Race/Ethnicity and Sex, U.S., 1999–2012

[Graph showing mortality rates for males and females by race/ethnicity from 1999 to 2012]
Cancer site

Survival Health Disparities by Cancer Site

African Americans have the highest rate of cancer specific mortality
Racial differences are not reducing over time
Breast cancer—might even be getting worse

Survival health disparities between population groups

<table>
<thead>
<tr>
<th>Race</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>1.47</td>
<td>1.43 - 1.61</td>
</tr>
<tr>
<td>1990-1994</td>
<td>1.00</td>
<td>0.91 - 1.10</td>
</tr>
<tr>
<td>1995-1999</td>
<td>1.02</td>
<td>0.97 - 1.05</td>
</tr>
<tr>
<td>2000-2004</td>
<td>1.19</td>
<td>0.86 - 1.46</td>
</tr>
<tr>
<td>2005-2009</td>
<td>1.16</td>
<td>0.87 - 1.35</td>
</tr>
</tbody>
</table>

Prostate cancer

<table>
<thead>
<tr>
<th>Race</th>
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</tbody>
</table>

AA = African-American; EA = European-American

Sources:
Aizer et al., Cancer 2014, 120: 1532-9
Zeng et al., Jama Oncology 2015 1: 88-96
Key determinants of disparities

Disparities in Disease Incidence + Disparities in Case Fatality → Disparities in Mortality

Cumulative Risk vs. Protective Factors

Host
- Genotype
- Stress
- Education

Environment
- Sociophysical—Air and Housing Quality, Social Relationships, etc.
- Economic—Food Supply, Jobs, Poverty, Discrimination, etc.

Behavior
- Smoking, Inactivity, Diet, etc.

Quality Health Care
- Access
- Utilization

Political and Economic Structures

Figure 1. Key determinants of health disparities.
Some of the reasons for disparities in incidence

- Geography

- Genetic? Differential susceptibility?

- Tobacco use

- Nutrition & Physical Activity

- Infection (Hepatitis B, HPV)
Some of the reasons for disparities in mortality

- Lack of early-detection
- Lack of timely and aggressive treatment
- Access to care
- Genetics?
- Biology?
Disparity geography

Some of the reasons for disparities in incidence: Geography?

Incidence Rates by State
The number of people who get cancer is called cancer incidence. In the United States, the rate of getting cancer varies from state to state.

Highest
Kentucky
Rhode Island
Delaware
Louisiana
New Jersey

Lowest
New Mexico
Arizona
Wyoming
Alaska
Virginia
Geography disparity

Some of the reasons for disparities in incidence: Geography?

✓ Regional differences in smoking prevalence may contribute to disparities in lung cancer incidence
✓ Residential migration; Racism; Advertising; Cultural influences; Community structure; Social stress

http://statecancerprofiles.cancer.gov
Geography

Some of the reasons for disparities in incidence: Geography?

- 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
  - Areas with the highest percentage of African Americans have the highest exposure to cancer-associated pollutants \((Environ Health Perspect. 2005 113(6): 693–699)\)
  - Exposure to second-hand tobacco smoke

- Can a deleterious neighborhood-effect early in life affect health outcomes through physiological adaptations to the environment?
  - Similar to the “Barker hypothesis” of the developmental origins of adult diseases including heart disease and diabetes.
  - Mechanism of adaptation may include epigenetic modification of gene expression
Geography

Some of the reasons for disparities in incidence: Geography?

- Rural populations are more likely to experience an unequal burden of pollution:
  - Forego medical care and prescriptions due to cost
  - Report fair/poor health and health-related unemployment
  - Experience psychosocial distress

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Weaver KE et al., Cancer Causes Control, 2013.
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Tobacco use

Some of the reasons for disparities in incidence: Tobacco use?

Lung cancer incidence is highest in African Americans despite having the second to lowest prevalence of high intensity smoking.

Adapted from *N Engl J Med* 2006; 354:333-342
Tobacco use

Some of the reasons for disparities in incidence: Tobacco use?

- Initiate smoking later (average age at onset, 17.4 years for blacks versus 14.7 years for whites; \( p < .05 \))

- Smoke fewer cigarettes (14.1 versus 18.4 cigarettes per day)

- Prevalence as adults similar (Black men, 23.9%; black women, 19.2%; white men, 24.5%; white women, 19.8%)

- Disparities observed in never smokers

- Menthol cigarettes not associated with increased risk of lung cancer relative to non-menthol cigarettes
Some of the reasons for disparities in incidence: Tobacco use?

Figure 1. Predicted Rates of Lung Cancer among Men Who Currently Smoke 10 Cigarettes per Day (Panel A) or 30 Cigarettes per Day (Panel B) and among Women Who Currently Smoke 10 Cigarettes per Day (Panel C) or 30 Cigarettes per Day (Panel D).

Adapted from *N Engl J Med* 2006; 354:333-342
Some of the reasons for disparities in incidence

- Geography
- Genetic? Differential susceptibility?
- Tobacco use
- Nutrition & Physical Activity
- Viruses (Hepatitis B, HPV)
Extrinsic factors

Some of the reasons for disparities in incidence: Extrinsic Factors

- Metformin is one of the most prescribed medications in the United States
- Recent study of VA records finds that metformin use is associated with reduced risk of prostate cancer in Hispanic men only
- Use of metformin and finasteride was associated with a greater prostate cancer incidence reduction in Hispanics and AA compared with NHW

Table 3. HR (95% CI) of prostate cancer incidence associated with metformin use by race/ethnicity: comparison between unadjustment and adjustment of generalizability weights that calibrate between race/ethnic groups

<table>
<thead>
<tr>
<th></th>
<th>NHW</th>
<th>AA</th>
<th>Hispanics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>0.91 (0.82-1.01)</td>
<td>1.10 (0.94-1.27)</td>
<td>0.63 (0.49-0.80)</td>
</tr>
<tr>
<td>Metformin + Statin</td>
<td>0.58 (0.49-0.69)</td>
<td>0.70 (0.58-0.86)</td>
<td>0.50^a,b (0.47-0.52)</td>
</tr>
<tr>
<td>Metformin + Finasteride</td>
<td>0.48 (0.37-0.63)</td>
<td>0.61 (0.44-0.77)</td>
<td>0.32^a,b (0.28-0.35)</td>
</tr>
</tbody>
</table>

Abbreviations: AA, African American; NHW, non Hispanic white.
^Generalizability weights were used to calibrate posttreatment clinical characteristics between comparison groups.
^Significantly different from NHW based on 95% CI of HR.
Lack of early detection

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

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

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

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 (lung, esophagus, etc)
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?

A. Breast cancer ($n = 17,939$)

B. Cervical cancer ($n = 1,832$)

C. Colorectal cancer ($n = 7,445$)

D. Lung cancer ($n = 8,185$)

Cancer Medicine 2013; 2(3): 403–411
Some of the reasons for disparities in cancer mortality: Access to care?
Lung cancer access to care

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

Cancer Epidemiol Biomarkers Prev; 21(10) 2012
Renal cell carcinoma access to care

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

US Department of Defense Cancer Registry Military Health System (MHS)

“The lack of racial difference in survival among RCC patients in the MHS may be related to equal access to health care. Improved access could reduce the survival disparity among RCC patients in the general population.”

Fig. 1 Kaplan–Meier survival curves comparing Black and White clear cell RCC patients diagnosed from 1988 to 2004 in the US Department of Defense Cancer Registry

Cancer Causes Control 2015 26(7):1019-26
Myeloma 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

Waxman et al. Blood 2010
Some of the reasons for disparities in cancer mortality: Access and uptake of care?
Oncologist density

Oncologists per 100,000 residents by hospital service area

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

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

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.
Access and uptake of care

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

Adapted from JNCI 2013 105(23):1814-20
Some of the reasons for disparities in cancer mortality: Access and uptake of care?
Potential factors that influence access and uptake of care:
• Personal beliefs
• Fear
• Culture
• Patient-doctor relationship
• Patient bias
• Provider bias
• Patient-doctor communication
• Co-morbid conditions
Smoking cessation

Some of the reasons for disparities in cancer mortality: Smoking cessation?

- African Americans are at risk for continued smoking and thus poor cessation outcomes
- Lung, pancreatic, bladder, and liver cancer patients at risk of poorer outcomes

Relative Risk of Death and Smoking after Diagnosis

- Never
- Former
- Light (<20)
- Heavy (>20)

CEBP, 2015 24(10)
Smoking cessation

Some of the reasons for disparities in cancer mortality: Smoking cessation?

Racial differences in continued smoking may be attributable to several factors:

- Socioeconomic vulnerabilities (including poverty, stress, and secondhand smoke exposure)

- Although the majority of black smokers express a desire to quit, they are less likely to receive and use evidence-based treatments (e.g., screening for tobacco use and advice to quit, smoking cessation pharmacotherapy, and counseling).

- In addition, black smokers are less likely to enroll in smoking cessation trials.

- Blacks are more likely to smoke mentholated cigarettes, which might be harder to quit than nonmentholated cigarettes, which leads to poorer cessation outcomes.

- Less accurate knowledge about the risks and prevalence of smoking and about the benefits and risks of effective smoking cessation treatments.
Cancer mortality

Some of the reasons for disparities in cancer mortality:

Factors that contribute to racial differences in outcomes:

- Access to screening
  - Less engagement might lead to a later stage of diagnosis

- Access to care
  - Reduced access reduces availability of potentially life saving therapeutic interventions

- Uptake of care
  - Reduced uptake of therapeutic options reduces availability of potentially life saving therapeutic interventions

- Smoking
  - Continued smoking is associated with adverse outcomes

*But..... There are some cancers where, even in an equal access to care setting, disparities in survival persist*
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
Biology

Is biology a contributing factor?

  - Intrinsic differences in tumor biology influencing disease aggressiveness?
  - Differences in response to therapy?
Is Biology a Contributing Factor?

While data suggest that access to quality care is a factor in cancer disparities, other factors also play a major role, including tumor biology and genetics.

Intrinsic differences in tumor biology influencing disease aggressiveness?

Differences in response to therapy?
Is biology a contributing factor?

- Differences in
  - Genetics
  - Somatic mutations
  - Molecular subtype and gene expression
  - Gene expression and methylations profiles
  - Systems biology
  - Inflammation
  - Cell biology

Differences in gene expression, molecular subtypes and molecular signatures will reveal differences in tumor biology between African American and European American patients.
Genetics

Biological determinants of cancer health disparities in outcome: 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)

![Racial Differences in Prostate Cancer Aggressiveness by 8q24 Status](chart.png)
Biological determinants of cancer health disparities in outcome: Genetics

- Duplication event at 14q32.33 encompasses IGHG3 in African American prostate tumors (familial, suggesting inherited predisposition)

- Contribute to the high prevalence and mortality of prostate cancer in African American men?

Prostate 2013 73(6):614-23
Genetics

Biological determinants of cancer health disparities in outcome: Genetics

- Duplication event at 14q32.33 encompasses IGHG3 in African American prostate tumors (familial, suggesting inherited predisposition)
- Contribute to the high prevalence and mortality of prostate cancer in African American men?
- Differences exist in the regions amplified and lost in European American and African American prostate cancers

Prostate 2013 73(6):614-23
Somatic mutations

Biological determinants of cancer health disparities in outcome: Somatic mutations


- 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%)

Molecular subtype

Biological determinants of cancer health disparities in outcome: Molecular subtype

- Population differences in molecular subtypes and disease grade

<p>| Table 2. Prevalence of Breast Cancer Subtypes According to Race and Menopausal Status |
|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|</p>
<table>
<thead>
<tr>
<th>Tumor Status</th>
<th>All Cases</th>
<th>Premenopausal (n = 97)</th>
<th>Postmenopausal (n = 99)</th>
<th>Premenopausal (n = 164)</th>
<th>Postmenopausal (n = 136)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal-like</td>
<td>100</td>
<td>38 (39)</td>
<td>14 (14)</td>
<td>26 (16)</td>
<td>22 (16)</td>
</tr>
<tr>
<td>HER2+/ER−</td>
<td>33</td>
<td>9 (9)</td>
<td>7 (7)</td>
<td>9 (6)</td>
<td>8 (6)</td>
</tr>
<tr>
<td>Luminal A</td>
<td>255</td>
<td>35 (36)</td>
<td>58 (59)</td>
<td>83 (51)</td>
<td>79 (58)</td>
</tr>
<tr>
<td>Luminal B</td>
<td>77</td>
<td>9 (9)</td>
<td>16 (16)</td>
<td>30 (18)</td>
<td>22 (16)</td>
</tr>
<tr>
<td>Unclassified</td>
<td>31</td>
<td>6 (6)</td>
<td>4 (4)</td>
<td>16 (10)</td>
<td>5 (4)</td>
</tr>
</tbody>
</table>

*P < .001, $\chi^2$ test for basal-like vs other tumor types in premenopausal vs postmenopausal African American women.

$\text{†}P = .94$, $\chi^2$ test for basal-like vs other tumor types in premenopausal vs postmenopausal non-African American women.
Molecular subtype

Biological determinants of cancer health disparities in outcome: 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)
Biological determinants of cancer health disparities in outcome: Cell biology

- 162 genes differently expressed by race/ethnicity (FDR ≤ 5%)
  - Several metastasis-related genes, e.g., CXCR4, MMP9, AMFR

- Differently expressed genes were not shared with the published list(s) of marker genes for prostate tumors

**Cell Biology**

**Biological determinants of cancer health disparities in outcome: Cell biology**

- Interferon signature predicts survival and poor outcomes (*PNAS 2008, 105: 18490 – 95; Genome Biol 2007, 8: R191*)

- IRDS is a predictive marker for resistance to chemotherapy and radiation and poor survival. Key signature genes mediate experimental resistance to therapy (*PNAS 2008, 105: 18490 – 95*)

### African-American Tumors (n = 33) vs European-American Tumors (n = 36)

<table>
<thead>
<tr>
<th>Interferon Signature(s)</th>
<th>AA</th>
<th>EA</th>
<th>Permutated P value*</th>
<th>FDR (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epithelial-mesenchymal interaction signature (IRG)</td>
<td>18/33</td>
<td>7/36</td>
<td>1.5x10^{-4}</td>
<td>4.1</td>
</tr>
<tr>
<td>(55%)</td>
<td>(19%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interferon-related DNA damage resistance signature (IRDS)</td>
<td>22/33</td>
<td>12/36</td>
<td>1.6x10^{-4}</td>
<td>3.7</td>
</tr>
<tr>
<td>(67%)</td>
<td>(33%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Ambs, unpublished observations*
Inflammation

Biological determinants of cancer health disparities in outcome: Inflammation

- Increase in some autoimmune/infectious diseases: Lupus and TB (AJPH 2001 91:8 1251-53)

- Increased IL-6 (Am J Hum Genet 2007;80(4):716-26)

- Different allele frequencies (Cytokine 2009;46(2):236-44)

- Cytokine profiles between serum from AA and EA patients are different, some of which are associated with poor outcomes (Pine…. Ryan….. Harris, CEBP 2015)

- Inflammation in non-cancerous prostate biopsies is more prevalent among African American than European American men (JNCI 1998, 90: 756 – 60)

- African Americans more likely to have some co-morbidities, such as COPD
Environmental determinants

Are there environmental determinants of different biological signatures?

- Viral infections
- Germline differences e.g. SNPs by ancestry
- Stress, different inherent responses to stress
- Reactivation of endogenous retroviruses e.g. HERV-K
- Acquired genetic alterations in tumor
- Toxins
- Air pollution
- Carcinogens

Don’t know yet if and how each of these exposures contribute to biological determinants of cancer health disparities
Environmental determinants

Are there environmental determinants of different biological signatures?

AA with head and neck cancer have worse outcome

HPV positive tumors have better outcome


Prevalence of HPV is higher in EA patients, Cullen et al discovered this as one of the key factors leading to improved outcomes in EA patients.
Second cancers

Cancer Health Disparities: Additional perspectives-second cancers

African Americans also have a higher risk of second cancers

European American

African American
Ancestry markers

Cancer Health Disparities: Additional Perspectives-Ancestry Informative Markers

African and European ancestry in self-identified African Americans can vary widely

Frequency Histogram Showing the Percentage of African Ancestry in a Population Living in Cleveland.

Ancestry markers

Cancer Health Disparities: Additional Perspectives—Ancestry Informative Markers

The percentage of European contribution to several African American communities varies 10-fold.

Figure 1 Map showing estimates of the percentage of European contribution to several African American communities throughout the US. The percentage of European contribution to several African American samples within the continental US varies tenfold, from 3.5% in the isolated Gullah-speaking Sea Islanders from South Carolina to 35% in Seattle. Reproduced from Parra [15].

Human Genomics (2015) 9:1
Increased proportion of Native American ancestry is associated with increased risk of childhood acute lymphoblastic leukemic.

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.
Cancer Health Disparities: Additional Perspectives-Screening

Evidence to support the idea that AA are more susceptible to lung cancer at low doses of cigarettes

Implications for lung cancer screening and potential to widen disparities

**Percent of Lung Cancer Diagnosed by Smoking Status (Haiman)**

- African American
- European American

**Cigarettes Smoked Per Day**

- <=10
- 10-20
- 20-30
- > 30

**Lung cancer screening guidelines:**
- Age
- Smoking history
Cancer Health Disparities: Additional Perspectives-Screening

Unintended consequence: Widening of disparities
New Treatments

Some of the reasons for disparities in mortality: Access to care and new treatments?

- We are aware of biological differences between tumors from different ethnic groups
- Key question: will these differences translate to different responses to targeted therapy?
- Key issue: to avoid increasing disparities we need to ensure equal access to new targeted drugs

Figure 2. Age-specific incidence rates of (A) HCC and (B) ICC by ethnicity and gender (SEER, 1996-2000).

Remain vigilant re the use of new drugs in the clinic?
Can we expect similar responses across ethnic groups?

CEBP 2006 15(6):1198-203
J Natl Cancer Inst. 2014 18;106(12)
Some of the reasons for disparities in incidence

✓ Geography
  ▪ Highly possible to play a role but more research needed
  ▪ Is it related to pollution, toxin exposure and air quality?

✓ Genetic? Differential susceptibility?
  ▪ 8q24 may explain up to 60% of prostate cancer differences
  ▪ More research needed on other cancers

✓ Tobacco use
  ▪ Use alone does not explain all disparities
Some of the reasons for disparities in mortality

- **Lack of early-detection**
  - Possibly for some cancers, but not all
  - Still need to work on programs and strategies to ensure that all populations are aware of, and have the opportunity, to avail of screening
  - What are the reasons driving lower use of screening in equal access to care settings/all settings?

- **Access to care**
  - Insurance
  - For some cancers, insurance is the reason for differences in outcomes, for others it isn’t

- **Lack of timely and aggressive treatment**
  - Access to care can drive this, but research also needed on societal, cultural and demographic reasons leading to reduced utility of treatment modalities
Some of the reasons for disparities in mortality

- **Genetics**
  - 8q24 related to prostate cancer aggressiveness
  - Are differences in CNV that are also evident in normal tissue
  - Somatic mutation profiles of some cancer are different as are the molecular subtypes

- **Biology**
  - Gene expression
  - Methylation
  - Less efficient G2M checkpoint
  - Inflammation differences
Determinants

Determinants of cancer health disparities

A multidisciplinary problem that requires a multidisciplinary approach
Determinants of cancer health disparities

• A multidisciplinary problem that requires a multidisciplinary approach including Prevention, Early Detection, Diagnosis, Treatment and Mortality