PUBLIC HEALTH DEMOCRACY:
U.S. and Global Health Disparities in Breast Cancer

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Purpose of Research

- To review health disparity data & to improve the understanding on BC health disparities
- Highlight specific global problem areas in BC
- To stimulate research aimed at reducing breast cancer health disparities in AA women
  - emphasis on AA women who are at disproportionately greater risk of developing ER-negative breast cancer (basal-like)
- To provide possible solutions and policy recommendations for breast cancer challenges
Historical Overview

- 1927 First funding for cancer research
- 1937 Congress established NCI
- 1971 War on Cancer declared
- 1973 SEER Program established
- 1985 Heckler Report on health disparities
- 1990 DHHS Healthy People 2000 report
- 1999, 2002 IOM Reports
- 2000 DHHS Healthy People 2010 report
- 2006 IOM Report on health disparities research
Global Burden of Cancer

10 million new cancer cases (87% outside U.S.)
6 million cancer deaths (90% outside U.S.)
22 million cancer survivors (64% outside U.S.)

Estimated numbers of new cancer cases (incidence) and deaths (mortality) in 2002. Data shown in thousands for developing and developed countries by cancer site for females.  
U.S Cancer Burden

- Estimated Incidence and Mortality, 2008
  - 1,437,180 new cases
  - 565,650 deaths

- Estimated breast cancer cases, 2008
  - Incidence 184,450 (182,460 women)
  - Mortality 40,930 (40,480 women)
  - Mortality for AA women is 34/100,000 vs 25 for NHW
Age at diagnosis of breast cancer by estrogen receptor status: rate per 100,000; percentage age distribution; and hazard ratio for mortality rate after diagnosis.
Breast Cancer Age Specific Incidence by Race
SEER 1992-1997

White: 31.4
AA: 31.5

AA/White ratio (age<35): 1.4
33% of AA Diagnosed Before the Age of 50
Versus 22% of Whites

White: 375
AA: 318

AA/White ratio (age>50): 0.85

Breast Cancer Incidence

Black Rates higher until after ages 40-44

Rate/100,000

Age

Blacks
Whites
Migration and Culture

- Migration patterns and high mortality rates
- Rising incidence in developing countries
  - Changes in demographics, SES, & risk factors
  - Reproductive risk factors
    - early age of first birth
    - high fertility rates and multiparity
    - prolonged lactation
- Cultural values, myths, beliefs, norms, language, and health system access
SES and Environmental Factors

- SES factors in AA women
  - Low family income, education, and occupation
  - Lack of or limited health insurance
- Environmental and genetics
  - Genetic-environment link not well understood
  - BRCA1 gene mutation
  - p53 mutations
  - Polymorphisms and other variants
Breast Cancer Risk Factors

- Age
- Personal and family history of BC
- Atypical hyperplasia
- Early onset of menarche, late menopause
- Age at first live birth
- Parity
- Increased breast density
- Obesity, high fat diet and lack of exercise
Breast Cancer Progression

Genetic Changes

Normal

Hyperplasia

In Situ Cancer

Tumor Aggressiveness

Invasive Cancer

Treatment Response
Influences on Health Disparities in Minorities

- Dietary
- Epigenetic
- Obesity
- Inflammation
- Genetics
- Stress
- Hormonal factors
- Exposure
- Tumor Biology
Breast Tumor Biology

*What is known?*

- Poor differentiation
- High-grade nuclear atypia
- High mitotic activity
- Higher S phase fraction
- ER-negativity/PR-negativity
- p53 mutations
- Younger age at presentation
- Overall poorer survival
Molecular Profile of BC Subtypes

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Magnitude of ER Negative Breast Cancer

- Overall, 20 to 30% of new breast cancer cases are ER-negative
  - Complex heterogeneous disease not responsive to endocrine therapy
  - Higher proportion of ER-negative breast cancer in women under age 50
  - African American women at increased risk of ER-negative breast cancer
  - BRCA1 mutation carriers at increased risk of ER-negative breast cancer
ERN BC Characteristics in AAs

- Larger tumors
- Higher grade histology
- Positive nodes more likely
- Poorer prognosis
  - Triple negative (ER - /PR - /HER2 -)
  - Higher p53 mutations
- Higher risk of recurrence
- Poorer overall survival
Potential ER-negative Correlates

- SES and Cultural Factors
  - Poverty
  - Education
  - Cultural factors

- Lifestyle/Environmental and Host Factors
  - Reproductive factors
  - Obesity/Diet/Physical activity
  - Age of diagnosis
  - Family history
Health disparities in ERN breast cancer

- How much is biological and how much is socio-economic?
- Conflicting evidence from studies of AA and African women
- Powerful evidence from epidemiology in the U. S.
- How many of the 40,480 deaths due to breast cancer each year are attributable to inferior health care, and how many deaths could be prevented by improvements in delivery and elimination of differences in quality of health care to minorities?
Early Detection and Prevention

- Lack of early stage disease relates to lack of optimal screening
- Investment in ER-negative BC prevention
  - Study of potential chemoprevention agents
  - Presurgical model
  - Small biomarker studies
- Need to insure minority populations (especially AAs) are included in clinical trials
Breast Cancer Disparities

What about Treatment?

- AA are less likely to receive standard treatments for cancer even at same insurance & economic status
- Treatment of aggressive breast disease should be guided by tumor biology, not by race or ethnicity
- Primary care Physician education needed on the increased frequency of aggressive breast cancer (ER-negative) in young AA women
- Research needed in areas of treatment and prevention of ER-negative breast cancer
ER-Negative Think Tank

- Evidence-based criteria for identifying BC subtypes
- Research interventions to improve prevention & treatment outcomes
- Differences in tumor microenvironment & normal tissue that contribute to differences in ER-negative cancer between AA and NHWs
- Ensure equal access to cancer care
- Relationship between SES & ER-negative BC
- Collaborative studies to analyze available data for optimization of investment
Health System Barriers

- **Services**
  - Distance to facilities, hours of operation
  - Poor quality of care; inappropriate care
  - Cultural and linguistic differences

- **Customers**
  - Burden of assigned roles
  - Limited awareness and poor understanding of health info

- **Providers/Institutions**
  - Stigma and discrimination in health setting
  - Perceptions and biasness in care provision

- **Insurers**
  - Coverage of effective interventions
  - Cost containment
  - Health budgets
Health System Management

✦ Design effective approach to cancer health disparities
  ● Patient/consumer education and awareness
  ● Health care providers re-education
  ● Health delivery system accessibility for all
  ● Incentivize preventive measures
  ● Legislative solutions

✦ Design a low tech counterpart for every high tech approach to screening, early detection, prevention and treatment
Policy Implications

- Incidence increase from 10M to 20M by 2020
- 70% new cases from developing countries
- Mortality increases from 6M to 12M/year
- What is needed to stem this rise
  - Focus on screening, early detection & prevention
  - Remove race as construct in decision-making
  - Embrace all health aspects to eliminate disparities
  - Adopt new health system management approach
Possible Approaches

<table>
<thead>
<tr>
<th>Barriers to health disparities</th>
<th>Solutions to health disparities</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Poverty-unemployment</td>
<td>● Increase employment options</td>
</tr>
<tr>
<td>● No insurance</td>
<td>● Universal health insurance</td>
</tr>
<tr>
<td>● Clinical trial ineligibility</td>
<td>● Increase research opps</td>
</tr>
<tr>
<td>● Race</td>
<td>● Understand/overcome biases</td>
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<tr>
<td>● Unequal health delivery</td>
<td>● Monitor quality of health delivery</td>
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<tr>
<td>● Co-morbid conditions</td>
<td>● Evaluate comorbid relevance</td>
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<tr>
<td>● Detrimental lifestyles</td>
<td>● Incentivize healthy choices</td>
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<tr>
<td>● Gene-environment</td>
<td>● Evaluate gene-environment</td>
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<tr>
<td>● Differences in tumor biology</td>
<td>● Validate biologic differences</td>
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<tr>
<td>● No effective targeted Rx</td>
<td>● Research targeted Rx</td>
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<tr>
<td>● Inability to use system</td>
<td>● Provide patient navigators</td>
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Economic Impact

- Cancer account for >7M deaths worldwide (’01)
  - Most (3/4) in developing countries
  - Equal to 100M DALYs
- Chronic disease impact in U.S >$1 trillion/yr
- Expected to rise to $6 trillion by 2050
- Economic impact includes
  - Cost of treating disease
  - Decrease in job performance
  - Increases in sick days, and
  - Losses associated with caregiver requirements
Economic Impact

- Chronic disease management cost: ~$277B/yr
- Increases to >$1.3 T for business & govt
- Cancer specific avoidable cost:
  - Direct costs of $37B
  - Indirect cost of $373B
- Even with reported decline in cancer mortality, economic impact remains greater than for other chronic diseases
Economic Impact of Chronic Disease

- Cancers: $48 billion on treatment, $271 billion total
- Hypertension: $33 billion on treatment, $280 billion total
- Mental Disorders: $46 billion on treatment, $171 billion total
- Heart Disease: $65 billion on treatment, $105 billion total
- Pulmonary Conditions: $45 billion on treatment, $94 billion total
- Diabetes: $27 billion on treatment, $105 billion total
- Stroke: $22 billion on treatment, $14 billion lost economic output

Total Treatment Expenditures = $277 billion
Total Lost Economic Output = $1,047 billion

Miliken Institute, 2006
Economic Projections by 2023

- Incidence of 7 leading chronic diseases increase by 43%
  - Cost $231M
  - Treatment & economic output loss $4.2 T

- Shifting to early detection and prevention
  - Possibly eliminate 40 M cases
  - Economic impact reduction by 27% ($1.1T)
  - Increase in GDP by $905B in productivity gains
  - Decrease in treatment cost by $218B/year
Possible Economic Solution

- Institute lifestyle changes,
- Obesity increases BC & several chronic disease risk
  - Decreasing obesity by 15 M cases would –
    - Save $60 B in treatment costs
    - Increase productivity by $254 B
    - Reducing obesity is an achievable goal
Specific Critical Areas of Need

- Breast cancer studies in AAs compared to NHWs and other racial/ethnic groups
- Improved research in ER-negative breast cancer (including triple negative disease)
- ER-negative preclinical breast cancer model
- Prevention and treatment interventions for ER-negative breast cancer especially triple negative disease
- Increase the percentage of AA and other minorities in clinical studies
Health Disparities Conclusion

- Breast cancer is a heterogeneous disease
- Controversy classifying ERN disease (slightly)
  - Previous classification based on morphology
  - New classification based on combination of morphology and molecular markers
- Tumor Biology concerns
  - Differences seen in hypermethylation
  - Other genes also seen in young AA women
  - Timing of exposure during women’s lifetime
- Treatment of aggressive disease should be guided by tumor biology, not by race
Health Disparities Conclusions

- Race matters; SES in combination with other factors important
  - AA are less likely to receive standard treatments for BC even at same insurance & economic status
- Biomarkers of sensitivity/resistance needed
- Preclinical models suggestive but not definitive
- ER, PR, HER2 and grade provide variables in breast cancer description
- Future approaches need more AA specificity
  - Drug selection based on pharmacogenomic studies
  - Appropriate dosing for overweight women based on studies
  - Determine incidence of under-dosing in overweight subjects
Future Directions & Opportunities

- Future studies should focus on race/ethnic-specific gene-exposure interactions to minimize disparities in cancer risk and progression
- Comprehensive evaluation of targeted genes and/or genome-wide association approaches to gain new insight into race/ethnic-specific predictive diagnostic and prognostic profiles
- Ancestry Informative Markers (AIMs) to identify and correct for population stratification and migration
- Lifestyle and behavior change (diet and exercise) – self-motivated cancer prevention approach
- Incentives for insurers, providers, and consumers
Proposed Transdisciplinary Research Framework

Community Input (CBPR)

Biomarker & Animal Model Studies → Preclinical and Clinical Studies → Impact on Patient and Community

- Genetics, Biological Basis of Disparities, Biomarkers for Risk Assessment and Screening
- Etiology, Screening, Prevention, Treatment
- Dissemination of Research, Quality of Life, Access to Care, Policy
We live in an age disturbed, confused, bewildered and afraid of its own forces, in search not merely of its road but even of its direction. There are many voices of counsel, but few voices of vision; there is much excitement and feverish activity, but little concert of thoughtful purpose. We are distressed by our own un gover ned, undirected energies and do many things, but nothing long. It is our duty to find ourselves.

Woodrow Wilson, PhD
Baccalaureate address, June 9, 1907