Disparities in breast cancer: a biology, health services and solutions story

Katherine Reeder-Hayes, MD MBA MS
Stephanie Wheeler, PhD MPH
University of North Carolina-Chapel Hill
April 3, 2018

Objectives

• Review the epidemiology of racial disparities in breast cancer and most affected subtypes
• Discuss how tumor biology impacts racial differences in breast cancer
• Review evidence for disparities in treatment access and costs of treatment as a factor in racial outcome differences
• Highlight potential solutions

Breast Cancer Subtypes… in One Slide

• Defined by two sets of receptors on cell surface: hormone (HR) and HER2
• HR+/HER2-: overall best prognosis, treatment includes endocrine therapy
• HER2+: aggressive, but very responsive to treatment including biologic targeted therapy trastuzumab
• “Triple Negative”: aggressive, no targeted therapies available
The Breast Cancer Survival Gap

Mind the gap: incidence closing, mortality opening

The Perfect Storm: Advanced Stage meets Aggressive Biology and Under-treatment
SEER 2010: Breast Cancer Incidence by Race + Subtype

Where is the disparity?

- The high risk “triple negative” subtype is over-represented among young black women
  **BUT**
- HR+/HER2- subtype is responsible for most breast cancer cases and deaths among black patients

<table>
<thead>
<tr>
<th>Subtype</th>
<th>% of Cases NH White</th>
<th>% of Cases AA/Black</th>
<th>5 year DFS or BCSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triple Negative</td>
<td>10.7%</td>
<td>22.5%</td>
<td>62%-75%</td>
</tr>
</tbody>
</table>
| HR+/HER2-      | 75.5%               | 60.2%               | ~77-86% (AA)
                           |                     | ~84-91% (NHW)      |

Black Women with HR+ Cancer Have Double the Risk of Whites

<table>
<thead>
<tr>
<th>Source*</th>
<th>Adjustment Factors</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carolina Breast Cancer Study 1993-2006</td>
<td>Age, diagnosis year, stage</td>
<td>1.9 (1.3-2.9) for BCSS</td>
</tr>
<tr>
<td>City of Hope 1994-98</td>
<td>Age, stage</td>
<td>1.9 (0.9-3.9) for BCSS</td>
</tr>
<tr>
<td>ECOG 1199 trial participants (stage II-II chemo-treated)</td>
<td>Age, BMI, tumor size, nodes, surgery type, hormonal tx</td>
<td>1.6 (1.2-2.1) for DFS</td>
</tr>
</tbody>
</table>

*In all studies, outcomes for women with triple negative disease were similar between black and white patients

---

From Howlader N et al, US Incidence of Breast Cancer Subtypes Defined by Joint Hormone Receptor and HER2 Status. JNCI 2014; 106(5).

Ma H, Lu Y et al, BMC Cancer 2013 13:225
Historical Disparities in HR+ and HR-/HER2+ Phenotypes

CBCS I-II (1993-2006)
Pre-targeted therapy for adjuvant use
HER2+ patients with ~15% difference in long term breast cancer mortality
HR 2.2, borderline significance

CBCS III RFS by subtype (2008-2013)
• RFS at median 5.5 years: difference of 12% for HER2+ disease, 4% HR+
• Likely static or widening survival gaps

Why does the survival gap grow as targeted therapy improves?
Fundamental cause theory of health disparities (Phelan and Link, 1995):
advantaged group status "embodies an array of resources, such as money, knowledge, prestige, power, and beneficial social connections that protect health no matter what mechanisms are relevant at any given time."
Fundamental Cause Theory and Targeted Therapy

- Few interventional targets → poor overall outcomes but small disparities (e.g., polio prior to vaccination, breast cancer prior to 1950s)
- Development of effective/targeted therapies → disparities widen due to differential resources and access

HR+/HER2- patients, CBCS III (2008-2013)¹

<table>
<thead>
<tr>
<th></th>
<th>Rate Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1</td>
<td>1.03 (1.01, 1.05)</td>
</tr>
<tr>
<td>Model 2</td>
<td>1.02 (1.00, 1.04)</td>
</tr>
<tr>
<td>Model 3</td>
<td>1.05 (1.03, 1.07)</td>
</tr>
</tbody>
</table>

¹ Presentations at SABCS 2017: Reeder Hayes et al., P2-12-05, Sun et al., P6-08-01

Why disparities in HR+ disease?

- A biologic hypothesis: biologically aggressive HR+ disease might be more common in black patients, in ways we don’t identify well in the clinic
- A health services hypothesis: outcome disparities increase as targeted therapy becomes more effective due to fundamental barriers to healthcare access that disproportionately affect minorities
The Biologic Hypothesis

CBCS III Molecular Profile of HR+/HER2- tumors by race

Data from Troester et al, JNCI 2018 Feb 1

Luminal A proportion among HR+/HER2- tumors by race and age

Racial Differences in 21 gene recurrence scores

Gene Expression Profiles Suggest Higher Risk Biology

The Health Services Hypothesis

Endocrine therapy initiation after chemo among high-risk HR+ patients by race (adjusted for clinical factors).

Insurance Data After Initiation (n=1,362)

- Black women under 65 were 29% more likely to be non-adherent
- Race was not a predictor of adherence for women >65
- Young black women more often have “spotty” adherence rather than quitting altogether
Does Adherence Affect Survival?

- Hershman et al analysis of 8,769 women in Kaiser Permanente N California
- early discontinuers: 7% decrement in 10 year overall survival (HR 1.26, 95% CI 1.09–1.46)
- non-adherent but remained on therapy: 4% decrement in 10 year overall survival (HR 1.49, 95% CI 1.23–1.81)


Disparities in Genomic Testing

Proportion of eligible patients receiving gene expression profile testing by race


Disparities in HER2 Targeting

Proportion of HER2+ Medicare patients receiving trastuzumab by race

Disparities in RT after BCS
Proportion of early stage Medicare patients receiving RT after BCS by race

Disparities in Endocrine Therapy (ET)
Proportion of HR+ patients (all ages) taking endocrine therapy at 2 years post-dx

Reasons for ET non-adherence by race

Wheeler et al., BCR&T, 2012

* p<.05
** p<.01
*** p<.001

3% and 6% of responses missing for whites, blacks, respectively (Wheeler et al., 2015, ASCO)
ET-related recurrence risk assessment by race

Perceived Risk of Recurrence if Pills Completed as Prescribed

Perceived Change in Risk if Pills Are Not Completed as Prescribed

ET-related side effect experience by race

Multivariable analysis of ET non-adherence by race

<table>
<thead>
<tr>
<th>Factor</th>
<th>OR</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ET Type (Tamoxifen vs. Aromatase)</td>
<td>1.11</td>
<td>0.77, 1.61</td>
<td>0.34</td>
</tr>
<tr>
<td>Stage (2 vs 1)</td>
<td>0.87</td>
<td>0.58, 1.29</td>
<td>0.51</td>
</tr>
<tr>
<td>Stage (3 vs 1)</td>
<td>0.74</td>
<td>0.43, 1.29</td>
<td>0.27</td>
</tr>
<tr>
<td>Received Herceptin</td>
<td>1.61</td>
<td>1.05, 2.50</td>
<td>0.04</td>
</tr>
<tr>
<td>Followed Chemotherapy</td>
<td>0.89</td>
<td>0.59, 1.35</td>
<td>0.44</td>
</tr>
<tr>
<td>Received Radiation</td>
<td>1.32</td>
<td>0.84, 2.06</td>
<td>0.20</td>
</tr>
<tr>
<td>No Menopause, no Bi-Race Consenting Surgery</td>
<td>0.21</td>
<td>0.06, 0.71</td>
<td>0.08</td>
</tr>
<tr>
<td>Age at Diagnosis</td>
<td>0.98</td>
<td>0.90, 1.07</td>
<td>0.14</td>
</tr>
<tr>
<td>Endocrine Symptoms Subscale</td>
<td>0.90</td>
<td>0.90, 0.99</td>
<td>0.02</td>
</tr>
<tr>
<td>ET Decision Making (ref: Shared Decision Making)</td>
<td>2.15</td>
<td>1.19, 3.87</td>
<td>0.02</td>
</tr>
<tr>
<td>Perceived Recurrence Risk if ET Completed (ref: Low/Very Low)</td>
<td>1.23</td>
<td>0.57, 2.65</td>
<td>0.36</td>
</tr>
<tr>
<td>Perceived Risk if ET Discontinued (ref: Increases a lot)</td>
<td>2.10</td>
<td>1.46, 3.07</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Risk increases a little</td>
<td>2.46</td>
<td>1.62, 3.73</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Risk does not change</td>
<td>3.91</td>
<td>2.67, 5.82</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

OR = Odds Ratio, CI = 95% Confidence Interval, ET = Endocrine Therapy

Results were generated through 50 replications of multiple imputation for missing data.
Cancer care is expensive

Figure: Increase in cancer care and drug costs relative to overall health care costs. SOURCES: Kolodziej presentation, June 9, 2014; 2010 CY claims; commercial and Medicare; all funding; http://www.cancer.gov/newscenter/newsfromnci/2011/CostCancer2020 (accessed August 20, 2014).

The rising cost of cancer care in the U.S. poses real problems to individual patients

- Health behaviors
  - Skipping, foregoing, delaying care
  - Non-adherence to doctor-recommended treatments
- Health-related outcomes
  - Higher stress, anxiety, depression
  - Worse quality of life
- Financial toxicity
  - Debt, inability to acquire loans
  - Medical bankruptcy

Black women with breast cancer are more financially vulnerable than Whites at diagnosis

<table>
<thead>
<tr>
<th></th>
<th>White</th>
<th>Black</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>1256</td>
<td>1205</td>
<td></td>
</tr>
<tr>
<td>Annual Household Income</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;$15,000</td>
<td>78</td>
<td>283</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>($15,000-$24,999)</td>
<td>154</td>
<td>253</td>
<td>(12.0%)</td>
</tr>
<tr>
<td>($25,000-$49,999)</td>
<td>208</td>
<td>236</td>
<td>(17.3%)</td>
</tr>
<tr>
<td>($50,000+)</td>
<td>758</td>
<td>331</td>
<td>(63.5%)</td>
</tr>
<tr>
<td>Insurance status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Private Insurance</td>
<td>1101</td>
<td>734</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Medicare</td>
<td>52</td>
<td>91</td>
<td>(4.2%)</td>
</tr>
<tr>
<td>Medicaid</td>
<td>66</td>
<td>287</td>
<td>(5.5%)</td>
</tr>
<tr>
<td>Uninsured</td>
<td>37</td>
<td>92</td>
<td>(7.5%)</td>
</tr>
</tbody>
</table>

33 Wheeler et al. 2017, under review
Black women with breast cancer report worse financial impact of their cancer at 2yrs post-diagnosis


<table>
<thead>
<tr>
<th></th>
<th>Any Financial Impact</th>
<th>Income Loss</th>
<th>Financial Barrier</th>
<th>Transportation Barrier</th>
<th>Job Loss</th>
<th>Insurance Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Model 1</strong></td>
<td>16.92***</td>
<td>13.25***</td>
<td>13.23***</td>
<td>11.65***</td>
<td>7.13**</td>
<td>3.18***</td>
</tr>
<tr>
<td></td>
<td>(1.99)</td>
<td>(1.99)</td>
<td>(1.78)</td>
<td>(1.12)</td>
<td>(1.28)</td>
<td>(0.82)</td>
</tr>
<tr>
<td><strong>Model 2</strong></td>
<td>14.21***</td>
<td>9.76**</td>
<td>10.34***</td>
<td>9.91***</td>
<td>5.89***</td>
<td>2.71***</td>
</tr>
<tr>
<td></td>
<td>(2.13)</td>
<td>(2.14)</td>
<td>(2.06)</td>
<td>(1.64)</td>
<td>(1.07)</td>
<td>(0.94)</td>
</tr>
<tr>
<td><strong>Model 3</strong></td>
<td>14.21***</td>
<td>9.76**</td>
<td>10.34***</td>
<td>9.91***</td>
<td>5.89***</td>
<td>2.71***</td>
</tr>
<tr>
<td></td>
<td>(2.13)</td>
<td>(2.14)</td>
<td>(2.06)</td>
<td>(1.64)</td>
<td>(1.07)</td>
<td>(0.94)</td>
</tr>
</tbody>
</table>

Results interpreted as average change in probability of outcome relative to the referent category.
Standard errors in parenthesis. Model 2 adjusts for: stage, receipt of mastectomy, chemotherapy, radiation, hormone therapy, and Herceptin, and comorbidities. Model 3 adjusts for all these characteristics and for insurance, household income, education, and marital status.

- Analysis excludes women who had never worked prior to diagnosis or declined to respond (n=2408)
- Analysis is only for women privately insured at the time of the baseline survey (n=1834)

How might we intervene?
Designing multilevel interventions to improve cancer equity, access, outcomes

- Offering motivational interviewing to improve guideline-recommended therapy use (moving away from ‘one-size-fits-all’ strategies)
- Monitoring costs and engaging financial counselors routinely in cancer care
- Engaging settings in treatment (e.g., oncology clinics, workplaces, etc.)
- Using behavioral economics to subtly change the choice architecture in which decisions are made
- Exploring preferences around intervention design in diverse underserved populations
- Developing social support networks
- Leveraging mobile technology

---

GETSET

Workbook and Resource Guide

---

GETSET overview

- Design informed by data collected in study phases 1 & 2
- Elements
  - Introductory Video
  - 5 MI sessions with trained MI counselor
  - Workbook/resource guide
- Evidence-based strategies to support ET use
- Linkage to support groups and other resources

---
How to prevent and mitigate financial burden

**Prevention** - More systematic, early identification of patients at risk for high financial burden
  - Financial distress screening

**Treatment** - Use of navigation to help patients identify resources, understand eligibility, and complete applications.
  - New financial advocate position

**Simplification** - Better coordination of current efforts & reduction in duplicative processes.
  - A ‘universal’ or ‘common’ application for multiple resources

---

[cancer navigators] If you could make one improvement to the system, what would it be?

---

Cancer financial assistance process map
"If you always do what you've always done, you always get what you've always gotten."

-motivational speaker Jessie Potter

"The definition of insanity is doing the same thing over and over again and expecting a different result."

-anonymous (misattributed to Einstein)