Global Trends in Breast Cancer Incidence and Mortality

International Seminar on Breast Cancer: Challenges and Responses
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Although breast cancer continues to be most prevalent in affluent countries, the risks of both breast cancer and related death are increasing worldwide.

1.2 million new cases worldwide each year:
   45% in low/middle resource countries
   55% of deaths in low/middle resource countries
The greatest obstacle to understanding the global risk of breast cancer is the lack of data

- Incidence based on data from small geographic areas—often pooled and extrapolated to large regions.
- Reported rates may reflect only women easiest to reach or with highest standard of living.
- Current global figures cannot truly reflect underlying economic and cultural diversity driving increased incidence and mortality
- GLOBOCAN 2002 is still the source used in almost all reports

### Incidence & Mortality Rates

<table>
<thead>
<tr>
<th>Continent</th>
<th>Incidence</th>
<th>Mortality</th>
<th>MR:IR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Rate</td>
<td>No.</td>
</tr>
<tr>
<td>WORLD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1,152,161</td>
<td>37.5</td>
<td>411,093</td>
</tr>
<tr>
<td>More developed</td>
<td>636,128</td>
<td>67.8</td>
<td>189,765</td>
</tr>
<tr>
<td>Less developed</td>
<td>514,946</td>
<td>23.8</td>
<td>221,028</td>
</tr>
<tr>
<td>CONTINENT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>North America</td>
<td>229,631</td>
<td>99.4</td>
<td>48,239</td>
</tr>
<tr>
<td>Oceania</td>
<td>13,507</td>
<td>84.6</td>
<td>3,338</td>
</tr>
<tr>
<td>Europe</td>
<td>360,746</td>
<td>62.3</td>
<td>129,010</td>
</tr>
<tr>
<td>Central/So America</td>
<td>90,147</td>
<td>41.0</td>
<td>30,361</td>
</tr>
<tr>
<td>Asia</td>
<td>385,853</td>
<td>22.1</td>
<td>152,967</td>
</tr>
<tr>
<td>Africa</td>
<td>65,197</td>
<td>23.4</td>
<td>44,399</td>
</tr>
</tbody>
</table>

*Organization for Economic Co-operation and Development

Country income level & incidence/mortality of breast cancer

*Igene, Breast Journal 2008*
Breast-cancer incidence has been increasing in virtually all regions since 1973, IARC

- **Japan, Singapore, and Korea** have doubled or tripled in the past 40 years
- China’s urban registries document 20 to 30% increases in the past decade
- **India** reports similar trends, with increases concentrated in urban areas
- Local registries in Africa report a doubling of rates over the past 40 years (difficult to assess due to lack of disease tracking and reporting)

Asia: Trends in Breast Cancer Incidence*

*ASR per 100,000 women

Breast Cancer Incidence in Urban and Rural China

Why are breast cancer rates increasing throughout the world?

• Increase in toxic exposures
• Increase in known risk factors
• Changing dietary and exercise patterns
• Genetic or biological predisposition

Long Island (NY) Breast Cancer Study

• Long Island NY reported highest 1988-1992 incidence rates in NY state (137.8 compared with 121.8)
• 1993 study of ~1500 cases and 1500 control women to assess breast cancer risk associated with environmental pollutants
• No added risk for:
  – pesticides e.g. organochlorines (OCs)
  – industrial chemicals polychlorinated biphenyls (PCBs)
  – DDT or its metabolite DDE
• Small increased risk for:
  – air pollutants called polyaromatic hydrocarbons (PAH)

Gammon, et al., CEBP, 2002; Winn, Nature Rev, 2005

Pesticides and PCBs unlikely causes

No large studies have addressed environmental compounds with estrogenic effect
Risk factors for breast cancer

Similar across populations and ethnic groups

- increased age
- early age menarche
- late age first birth
- late age menopause
- nulliparity
- not breastfeeding
- family history
- obesity after menopause
- alcohol consumption
- mammographic density

Sub-Saharan African Women: low incidence

- Reproductive protection
  - Late menarche, early menopause
  - 5-9 live births per woman
  - Median age at first pregnancy=19
  - 96% breast feed average of 16 months

Review: Fregene & Newman, Cancer, 2005
Relationship of fertility rate and incidence by country income

Igene, Breast Journal 2008

The most widely cited reason for the global increase in breast cancer is the “Westernization” of the developing world

- dietary changes
- sedentary workplace and lifestyle
Migration studies indicate breast cancer risk in Asians rises to approach Western levels over two generations


<table>
<thead>
<tr>
<th>Community</th>
<th>Incidence rate*</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States:</td>
<td></td>
</tr>
<tr>
<td>SF, LA, HI</td>
<td></td>
</tr>
<tr>
<td>Whites</td>
<td>91.8</td>
</tr>
<tr>
<td>Chinese</td>
<td>53.7</td>
</tr>
<tr>
<td>Japanese</td>
<td>69.0</td>
</tr>
<tr>
<td>China: Shanghai</td>
<td>27.5</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>37.7</td>
</tr>
<tr>
<td>Japan: Miyagi</td>
<td>40.9</td>
</tr>
<tr>
<td>Japan: Osaka</td>
<td>28.9</td>
</tr>
</tbody>
</table>

*ASR per 100,000

Zeigler, JNCI, 1993

‘Meat/sweet’ diet in Shanghai
~1500 cases and controls

Cui, et al., CEBP, 2007

- Diet patterns
  - Tofu, cauliflower, beans, bean sprouts green leafy vegetables
  - Shrimp, chicken, beef, pork, candy, desserts

- Meat/sweet associated with increased risk in post menopausal women [OR 1.3 (1.0-1.7); p=0.03]
Genetic Differences
BRCA mutation in low/middle income countries

- overall incidence of BRCA-1 and BRCA-2 mutations is still unknown
- spectrum of BRCA-1 and BRCA-2 mutations appears to differ between Asian, African and Caucasian women
- several unique and distinct mutations having been found among African and Asian women
- African and Asian women have a higher incidence of BRCA variants of unknown significance

Global disparities in mortality similar to racial and economic disparities in EEUU

- marginal health care access
- low awareness of breast cancer risk
- cultural barriers to care
- ? genetic and biologic differences that might affect disease outcomes in lower-income countries
American Cancer Society breast cancer mortality rates by race/ethnicity

What contributes to poor survival in African American women?

- Advanced stage at diagnosis
- Treatment disparities
- Biological characteristics of tumor and/or woman
Sub-Saharan African Women: high mortality

- Late stage presentation
  - 70-90% present with Stage III-IV
  - 50% present with matted axillary lymph nodes
  - Mean tumor diameter 10 cm

Review: Fregene & Newman, Cancer, 2005


<table>
<thead>
<tr>
<th>Location</th>
<th>5-year survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harare, Zimbabwe</td>
<td>37.9</td>
</tr>
<tr>
<td>Kampala, Uganda</td>
<td>45.4</td>
</tr>
<tr>
<td>USA AA; SEER</td>
<td>70.1</td>
</tr>
</tbody>
</table>
African American women more likely than whites to have:

- young onset breast cancer
- high grade tumors
- proliferative tumors
- ER- tumors
- ‘triple negative’ (ER/PR/HER2-) tumors

In small studies African women appear to have similar clinical and tumor attributes.

Age specific breast carcinoma incidence for USA and African women
What can be done to address the rising incidence and mortality of breast cancer world wide?

Successful strategies in predominantly white, affluent populations

- early detection through screening
- targeted hormonal therapy
- anti-HER2 therapy
- improvements in chemotherapy
Breast cancer rates will rise--
approaches require

• Guidelines that are evidence-based, economically feasible, and culturally appropriate (BGHI)
• Early detection--metastatic disease is not treated successfully in ANY country
• Improved cancer registries and data collection
• Public advocacy for breast cancer prevention, detection, treatment and research!

Summary

• Breast cancer is highest in affluent countries, Caucasian women and urban women
• Incidence is rising throughout the world--most likely cause is increase in reproductive risk factors
• High mortality rates burden women in low resource countries
• There is an urgent need find and implement country-specific approaches to the detection and treatment for breast cancer
• Advocacy and research are the most powerful forces for advancing breast cancer care