Glass Half Full, Glass Half Empty: Evidence and Perspectives on Overdiagnosis and Cancer Screening:

Breast cancer screening in the context of overdiagnosis

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What is “Overdiagnosis” in Cancer?

- A case of unfortunate semantics?
- A complex conundrum?
- A phenomenon requiring attention?
- An evolution in how we approach disease?
Current Definition

- Overdiagnosis refers to a tumor that's found but that never would have caused harm.
An Expanding Landscape of Messaging
Contributors to “Overdiagnosis” in Cancer

- Advanced imaging technologies
- Imperfect screening tests
- Pathology definitions (e.g. DCIS)
- Public health success of screening
- Knowledge of natural history (e.g. prostate cancer)
“Overdiagnosis” and Breast Cancer Screening

Evidence Base:
1. RCTs
2. Observational studies
3. Modeling

Spectrum of Interpretation
- Too much screening
- About right screening
- Not enough screening
Multiple Interpretations/Recommendations

Questioning The Mammography Debate

The New York Times
Vast Study Casts Doubts on Value of Mammograms
A Brief Look at the Evidence Base

Three ways to show efficacy

1. Earlier detection than without test
2. RCTs must show mortality decrease
3. Population trends with screening onset
A Brief Look at the Evidence Base

Figure 2. Age-Adjusted Incidence Rates of Breast and Prostate Cancer Over Time and by Prescreen and Postscreen Snapshot

Esserman et al.  
JAMA 2009
## A Brief Look at the Evidence Base

**Table 1. Pooled RR for Breast Cancer Mortality From Mammography Screening Trials for All Ages**

<table>
<thead>
<tr>
<th>Age</th>
<th>Trials Included, n</th>
<th>RR for Breast Cancer Mortality (95% Crl)</th>
<th>NNI to Prevent 1 Breast Cancer Death (95% Crl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>39–49 y</td>
<td>8*</td>
<td>0.85 (0.75–0.96)</td>
<td>1904 (929–6378)</td>
</tr>
<tr>
<td>50–59 y</td>
<td>6†</td>
<td>0.86 (0.75–0.99)</td>
<td>1339 (322–7455)</td>
</tr>
<tr>
<td>60–69 y</td>
<td>2‡</td>
<td>0.68 (0.54–0.87)</td>
<td>377 (230–1050)</td>
</tr>
<tr>
<td>70–74 y</td>
<td>1§</td>
<td>1.12 (0.73–1.72)</td>
<td>Not available</td>
</tr>
</tbody>
</table>

Crl = credible interval; NNI = number needed to invite to screening; RR = relative risk.

A Brief Look at the Evidence Base

SEER Observed Incidence, SEER Delay Adjusted Incidence and US Death Rates
Cancer of the Female Breast, by Race

White

Black

SEER Incidence APCs
Delay Adj, 2004-10 = 0.1
Observed, 2004-10 = -0.1

US Mortality APC
1993-10 = -1.5

Delay-Adjusted Incidence
Observed Incidence
Mortality

Rate per 100,000

160
140
120
100
80
60
40
20
0
Year of Diagnosis/Death
A Brief Look at the Evidence Base

<table>
<thead>
<tr>
<th>Recall (%)</th>
<th>Cancer detection rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>UK</strong></td>
</tr>
<tr>
<td><strong>50-54</strong></td>
<td>7.6</td>
</tr>
<tr>
<td><strong>55-59</strong></td>
<td>7.0</td>
</tr>
<tr>
<td><strong>60-64</strong></td>
<td>6.7</td>
</tr>
</tbody>
</table>
A Brief Look at the Evidence Base: DCIS

- DCIS is ~15-20% of cancers dx’d
- 10-15% will become invasive
- Mortality rate in pts. with DCIS is <2%
- ~25% treated with mastectomy

- Is it a case of surveillance, then will be caught if/when it becomes invasive?
- Is it overdiagnosis or overtreatment? Dx is appropriate for surveillance at a minimum
A Brief Look at the Evidence Base

Tipping the balance

-False positives
-Overtreatment

Mortality benefit
Other Ways to Look at the Evidence

False positives over 20 years of screening

Out of 1000 women who have breast screening for 20 years,
412 women experience a false positive result:
they have an abnormal mammogram followed by extra tests but they do not have cancer.

Of these,
• 67 women have a biopsy
and
• 345 women have other extra tests but no biopsy.

Woman who has a false positive with a biopsy
Woman who has a false positive with other tests
Woman who does not have a false positive

SLIDE CREDIT: Jolyn Hersch
Sydney School of Public Health
Other Ways to Look at the Evidence

Over-detection over 20 years of screening

Out of 1000 women who have breast screening for 20 years,
73 women are diagnosed with breast cancer.
Of these,
- 19 women experience over-detection: they are diagnosed and treated for a cancer that would not have caused any trouble and
- 54 women are diagnosed with breast cancer that is not over-detection.

- = extra woman diagnosed with breast cancer due to over-detection
- = woman diagnosed with breast cancer that is not over-detection
= = woman not diagnosed with breast cancer

SLIDE CREDIT: Jolyn Hersch
Other Ways to Look at the Evidence

Breast cancer deaths avoided over 20 years of screening

Out of 1000 women who have breast screening for 20 years,

- 4 women avoid dying from breast cancer because of screening
- 8 women still die from breast cancer
Other Ways to Look at the Evidence

Averted Death
$\frac{4}{1000} = \frac{4000}{1,000,000}$
Over 20 years, so:

200 cancer deaths averted by screening
50,000 women/yr

Follow-up
$\frac{412}{1000} = \frac{412,000}{1,000,000}$
$\frac{67}{1000} = \frac{67,000}{1,000,000}$

Per Year: 20,600 imaging, 3,350/50K/yr biopsy

~93,000,000 age 30+ in 2010 US Census
Here’s the rub...........Populations v. People
Going back to the definition

- Overdiagnosis refers to a tumor that's found but that never would have caused harm
Going back to the definition

- Overdiagnosis refers to a tumor that's found but that never would have caused harm

- Can we find genetic or other biomarkers to help stratify DCIS?
- Are we satisfied with imaging surveillance?
- Can we find new sensitive & specific tests?
Two Sides to the “Diagnosis” Coin

“Overdiagnosis”
Maybe overtreatment and no mortality benefit

“Underdiagnosis”
Not enough treatment and excess mortality
Ultimately – Patient Values & Preferences

- Australian study N=50 of women’s views of ODx

Findings:

Recurring questions/confusions

1. How do you know there are cancers that won’t progress to cause harm?
2. Why isn’t it possible to distinguish the non-threatening cancers?
3. How can you calculate the rate of overdiagnosis?

- Confusion between overdiagnosis and misdiagnosis
  - Consequently we shifted to the term overdetection
Australian study on patient views*

The amount of overdetection mattered to many participants

- 1-10%: Most women considered this negligible & wouldn’t change screening plans
- 30%: Women startled, raised doubts. Ultimately no change in intentions.
- 50%: Perceived as very high, some emotional responses, and change in plans

Kirsten McCaffery, Jolyn Hersch (PhD candidate) Jesse Jansen, Alexandra Barratt, Les Irwig, Nehmat Houssami, Kirsten Howard, Haryana Dhillon
Patient Preferences & Policy

➢ Tension inherent given current structures
➢ Need to align metrics with preferred care
➢ How to reconcile disputes over evidence-
  How can women weigh evidence when we can’t?
➢ Dueling messages in public health?
Key Stakeholders in Breast Cancer Screening

- Patients
- Clinicians
- Researchers
- Policy makers
- Health care systems
- Payers
Thank you!