Rethinking Breast Cancer Screening

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Conflicts of Interest

• Financial: none
• Intellectual: I have been researching and writing on the issue of breast cancer screening for 26 years.
• I am a general internist and clinical epidemiologist. I do not identify myself with either the proponents nor the detractors of screening.
• My allegiance is to the evidence, not to a predefined position.

Underlying Assumptions

• 1. The purpose of breast cancer screening is not just to find cancer; it is to help women live better or longer.
• 2. To propose national screening programs, we need evidence of at least moderate certainty that, in the real world, implementation of the program will lead to benefits that clearly justify harms and costs.

Agenda: 3 Questions

• 1. As mammography has improved over time, is there evidence of at least moderate certainty that its effect on breast cancer mortality has increased?
• 2. Are further enhancements to current mammography likely to lead to an increase in benefits that clearly outweighs any change in harms and costs?
• 3. Where should we go from here?
10 RCTs of Screening
(depending on how you count)

- Oldest (HIP) started in 1963: 23% relative risk reduction for breast cancer mortality (RRR) for ages 40-64.
- Most recent (AGE) reported results in 2006: 17% RRR for ages 39-41.
- Range of studies in between: 0% (CNBSS – 1980 and 2014) to 32% for ages 40 to 74 (Kopparberg, 1977).

Observational Studies
(over 20 ecologic and cohort studies, 1960s to 2014)

- Review shows many methodological problems. Most did not adjust for important potential confounders or changes in treatment.
- No clear trend toward increased or decreased relative risk reduction over time.
- Range from 0 to 43%.

Observational Study of Medicare Patients
Killelea BK et al. 2014, JNCI

- This was a period of evolution toward digital and CAD advances in mammography.
- Average screening-related costs per capita increased from $76 to $112 (constant dollars).
- No change in cancer detection rate.

Netherlands Observational Study
de Glas NA et al. BMJ 2014

- In Netherlands, upper age of breast cancer screening was increased from 69 to 75 in 1998.
- Incidence rate of early stage invasive or DCIS breast cancer increased by 46% between 1995 and 2011; incidence of late stage (III and IV) breast cancer at diagnosis decreased by 12%.
Question 1

- Is there reasonable evidence of a trend toward decreased breast cancer mortality as a result of improved screening?

- Answer: No

- There is, in fact, concern that, as treatment for breast cancer has improved, the effect of mammography screening on breast cancer mortality may be diminishing.

Question 2

- Are further enhancements to current mammography likely to lead to an increase in benefits that clearly outweighs any increase in harms and costs?

Costs of Breast Cancer Screening

- Conservative estimate of cost of mammography screening in US in 2010 was $7.8 billion. Using digital and CAD for all would add $1.2 billion more. (O’Donoghue et al, Annals of Int Med 2014)
Harms of Breast Cancer Screening
(Harris R et al JAMA Int Med 2014)

• More sensitive screening tests often increase overdiagnosis and false positives. (Note: HIP study found no overdiagnosis.)

• Harms occur immediately while benefits are delayed. Harms occur on multiple levels in screening cascade. Overdiagnosis is most likely about 20% of screen-detected invasive cancers, higher % when DCIS included.

Question 2

• Enhancements in mammography have been working to improve the sensitivity of screening (i.e., cancer detection) by better detecting the same “signals”.

• To date, the enhancements have increased costs without any clear evidence that they have led to reduced mortality.

• Is it likely that further improving our ability to detect the same signals will lead to an increase in benefits that clearly outweigh increasing harms and costs?

Question 3: Where Do We Go From Here?

• Possible directions:
  – Chemoprevention: may be difficult to do
  – Further improving current mammography (color me skeptical)
  – Entirely different screening signal – (I would be interested, but would take an RCT)
  – Lifestyle: post-menopausal weight gain, physical activity, excessive alcohol

• RH: We should push lifestyle and think about the others
Thank You