Evidence Summary Title:
Screening for breast cancer with mammography: Evidence and implications for public health

Quality Assessment Rating: 8 (strong)

Review on which this evidence summary is based:

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This is an evidence summary written to condense the work of the authors of this systematic review, referenced above. The intent of this summary is to provide an overview of the findings and implications of the full review. For more information on individual studies included in the review, please see the review itself.

Note: The Cochrane review that this evidence summary is based on has been updated. This evidence summary summarizes the above-cited version of this review, not the updated version. An updated evidence summary will be provided as soon as possible.

Review content summary
This meta-analysis of 8 randomized controlled trials (600,000 participants) was conducted to determine the effectiveness of mammography screening for breast cancer in decreasing mortality and morbidity. Findings conclude that the use of mammography to screen for breast cancer is likely effective in reducing mortality. Based on the evidence presented in the highest quality trials, the relative risk reduction was estimated at 15% and the absolute risk reduction was 0.05%. This means that for every 2000 women invited for screening throughout 10 years, one will have her life prolonged and 10 healthy women, who would not have been diagnosed if there had not been screening, will be treated unnecessarily. The review also revealed that screening might lead to overdiagnosis and overtreatment. Given this evidence, the authors conclude that it is not clear whether screening does more harm than good and assert that women invited to screening should be informed of both the benefits and harms.

Comments on this review’s methodology
This is a methodologically strong meta-analysis. A focused clinical question was clearly identified. Appropriate inclusion criteria were used to guide the search. A comprehensive search was not employed, as only one health databases was searched, although reference lists of primary studies were reviewed, grey literature sources were searched, and key informants were contacted. The search was not limited by language. Primary studies were assessed for methodological quality using the following quality criteria: research design; study sample; participation rates; source of bias (confounders, respondent bias); follow up/attrition rates; and data analysis, but only the sufficiency of allocation concealment was reported by review authors. Review methods were described in sufficient detail so as to allow replication and two independent reviewers were involved in quality appraisal, with discrepancies resolved through discussion. Results were clearly presented in graphical form so as to allow for comparisons across studies. Heterogeneity was assessed and a fixed effects model, with 95% confidence intervals, was employed to enable the synthesis of study results.

Why this issue is of interest to public health
Breast cancer is the most common cancer diagnosed among Canadian women, and the second leading cancer cause of death in women. Despite a recent decline in mortality rates, 1 in 9 Canadian women will develop breast cancer in her lifetime, while 1 in 25 Canadian women will die from this disease. An estimated 22,400 women will be diagnosed with breast cancer and 5,400 women will die from the disease in 2008. The Canadian Breast Cancer Initiative launched in 1993 to support research, care and treatment, professional education, programs for early detection, and access to information for women became the responsibility of the Public Health Agency of Canada (PHAC) in 2004. Organized breast cancer screening programs now exist in all provinces, and the Northwest and Yukon Territories for women between 50 and 69 years of age, without a previous breast cancer diagnosis. Mammography is considered the optimal screening tool for breast cancer, given that early detection allows for better and broader treatment options and, ultimately, a greater chance for a successful recovery. Moreover, mammography is an effective means of determining that women do not have breast cancer. Mammography is the only technique proven to be safe and effective in screening for breast cancer, and mammography equipment is the only imaging technique licensed by Health Canada for breast cancer screening. Although the numbers...
appear high, the targeted program participation rate of 70% among women 50 to 69 years for biennial screening is far from being reached through organized programs. In 2003 and 2004, only 36.5% of the target population received a screening mammogram through an organized program. A 2003-2004 report of organized mammography screening programs authored by PHAC noted that a total of, 6,900 cancers (invasive, in situ and unclassified types combined) were detected among women aged 50 to 69 during 2003 and 2004 by organized screening programs. This is significant, particularly given that efforts aimed at the primary prevention of breast cancer have been limited. Until modifiable risk factors are addressed more rigorously, screening appears to be the best tool for the reduction of breast cancer-related morbidity and mortality.

Evidence and implications

Evidence points identified in the table below are not presented in order of the strength of the evidence. Absolute Risk Reductions (ARR) are included for adequately randomized trials, along with ARR for adequately- plus suboptimally randomized trials. ARR from suboptimally randomized trials alone were not included as inadequate randomization may overestimate the intervention’s effect.

<table>
<thead>
<tr>
<th>What’s the evidence?</th>
<th>Implications for practice and policy:</th>
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<tbody>
<tr>
<td><strong>1. Mammography and death from breast cancer (8 trials; 3 adequately randomized; 4 sub-optimally randomized; 1 trial provided insufficient data)</strong></td>
<td><strong>1. Mammography and death from breast cancer</strong></td>
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<tr>
<td>1.1. In 4 high quality, adequately randomized controlled trials, participants who had mammography screening were no less likely to die from breast cancer compared to non-screened participants.</td>
<td>1.1. Evidence from the highest quality studies suggests that mammography screening is not recommended to reduce breast cancer deaths in women at 7 and 13 years follow-up.</td>
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<tr>
<td>1.1.1. The true risk ranged from 21% less likely to 9% more likely to die from breast cancer (RR 0.93, 95% CI 0.79 - 1.09) at 7 years follow-up; absolute risk reduction of 0.02%</td>
<td>1.2. When less rigorous studies are included in the analysis, mammography screening is recommended to reduce breast cancer deaths among all women, and among those aged 50 and over, but not in those under age 50.</td>
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<td>1.1.2. This result was consistent at 13 years follow-up (RR 0.90, 95% CI 0.79 – 1.02); absolute risk increase 0.007%</td>
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<td>1.2. In 7 studies without adequate randomization participants who had mammography screening were 29% less likely to die from breast cancer compared to controls (this finding is statistically significant).</td>
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<td>1.2.1. The true risk ranged from 39% less likely to 17% less likely to die from breast cancer (RR 0.71, 95% CI 0.61 - 0.83) after 7 years follow-up</td>
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<td>1.2.2. This result was consistent at 13 years follow up (RR 0.75, 95% CI 0.67 to 0.83) [5 studies],</td>
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<td>1.2.3. These results must be interpreted with caution as inadequate randomization may over estimate the effect.</td>
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<td>1.3. Pooled results of both suboptimally and adequately randomized trials found that participants who had mammography screening were 19% less likely to die from breast cancer compared to controls (this finding is statistically significant) at 7 years follow-up.</td>
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<td>1.3.1. The true risk ranged from 28% less likely to 10% less likely to die from breast cancer (RR 0.81, 95% CI 0.72 - 0.90) after 7 years follow-up; absolute risk reduction 0.047%</td>
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<td>1.3.2. This result was consistent at 13 years follow up (RR 0.81, 95% CI 0.74 to 0.87); absolute risk reduction 0.068%</td>
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<td><strong>Mammography and death in young women (under 50 at randomization)</strong></td>
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<td>1.4. In the 3 adequately randomized controlled trials, mammography participants were no less likely to die from breast cancer compared to non-screened participants at 7 years follow-up.</td>
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<td>1.4.1. The true risk ranged from 22% less likely to 14% more likely to die from breast cancer (RR 0.94, 95% CI 0.78-1.14) at 7 years follow-up; absolute risk reduction 0.019%</td>
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1.4.2. This result was consistent at 13 years follow-up (RR 0.87, 95% CI 0.73 – 1.03); absolute risk reduction 0.013%.

1.5. In 6 studies without adequate randomization participants who had mammography screening were 19% less likely to die from breast cancer compared to controls.
   1.5.1. The true risk ranged from 37% less likely to 5% more likely to die from breast cancer (RR 0.81, 95% CI 0.63 - 1.05) after 7 years follow-up.
   1.5.2. This result was consistent at 13 years follow-up (RR 0.80, 95% CI 0.64 to 0.98) [5 studies].
   1.5.3. These results must be interpreted with caution as inadequate randomization may over estimate the effect.

1.6. Pooled results of both suboptimally and adequately randomized trials found that women younger than 50 years of age who had mammography screening were 11% less likely to die from breast cancer compared to controls at 7 years follow-up (this is not statistically significant).
   1.6.1. The true risk ranged from 23% less likely to 4% more likely to die from breast cancer (RR 0.89, 95% CI 0.77 – 1.04) after 7 years follow-up; absolute risk reduction 0.029%.
   1.6.2. This result was consistent at 13 years follow-up (RR 0.84, 95% CI 0.73 – 0.96); absolute risk reduction 0.03%.

Mammography and death in older women (over 50 years at randomization)

1.7. In the 2 adequately randomized controlled trials, mammography participants were no less likely to die from breast cancer compared to non-screened participants.
   1.7.1. The true risk ranged from 36% less likely to 20% more likely to die from breast cancer (RR 0.88, 95% CI 0.64-1.20) at 7 years follow-up; absolute risk reduction 0.03%.
   1.7.2. This result was consistent at 13 years follow-up (RR 0.94, 95% CI 0.77 – 1.15); absolute risk reduction 0.03%.

1.8. In 5 studies without adequate randomization participants who had mammography screening were 33% less likely to die from breast cancer compared to controls. This finding is statistically significant.
   1.8.1. The true risk ranged from 44% less likely to 19% less likely to die from breast cancer (RR 0.67, 95% CI 0.56 – 0.81) after 7 years follow-up.
   1.8.2. The result was consistent at 13 years follow-up (RR 0.70, 95% CI 0.62 to 0.80).
   1.8.3. These results must be interpreted with caution as inadequate randomization may over estimate the effect.

1.9. Pooled results of both suboptimally and adequately randomized trials found that women over 50 years of age who had mammography screening were 28% less likely to die from breast cancer compared to controls at 7 years follow-up.
   1.9.1. The true risk ranged from 38% less likely to 15% less likely to die from breast cancer (RR 0.72, 95% CI 0.62 – 0.85) after 7 years follow-up; absolute risk reduction 0.08%.
   1.9.2. This result at 13 years follow-up (RR 0.77, 95% CI 0.69 – 0.86) showed an absolute risk reduction of 0.16%.

2. Mammography and death from any cancer (6 studies)
   2.1. In 3 adequately randomized controlled trials, participants who had mammography screening were no less likely to die from any cancer.

2. Mammography and death from any cancer
   2.1. Mammography screening is not recommended to reduce cancer deaths in women.
from any cancer compared to non-screened participants at 10.5 and 9 years follow-up.

2.1.1. The true effect ranged from 5% less likely to 10% more likely die from any cancer compared to non-screened participants (RR 1.02, 95% CI 0.95 -1.10).

2.1.2. The absolute risk *increase* of death from any cancer in those receiving mammography screening 0.04%.

2.2. In 3 suboptimally randomized trials participants who had mammography screening were no less likely to die from any cancer compared to non-screened participants.

2.2.1. The true effect ranged from 7% less likely to 6% more likely to die from any cancer compared to non-screened participants (RR 0.99, 95% CI 0.93 0.106).

2.3. Unreliable data from the suboptimally randomized trials prevented the pooling of both suboptimally randomized and adequately randomized trials.

3. **Mammography and death from all causes (11 studies)**

3.1. In the 4 adequately randomized controlled trials, participants who had mammography screening were no less likely to die from any cause compared to non-screened participants at 7 years follow-up.

3.1.1. The true effect ranged from 6% less likely to 3% more likely to die from any cause compared to non-screened participants (RR 0.98, 95% CI 0.94 -1.03); absolute risk *increase* 0.2%.

3.1.2. This result was consistent at 13 years follow-up (RR 0.99, 95% CI 0.95 – 1.03); absolute risk *increase* 0.6%.

3.2. The sub-optimally randomized trials (n = 7) did not provide reliable estimates to assess risk of death from any cause, or to calculate a pooled absolute risk reduction.

3.3. In 2 high quality, adequately randomized controlled trials, participants under 50 years of age who had mammography screening were no less likely to die from any cause compared to non-screened participants at 7 years follow up.

3.3.1. The true effect ranged from 10% less likely to 4% more likely to die from any cause compared to non-screened participants (RR 0.97, 95% CI 0.90 – 1.04); absolute risk reduction 0.2%.

3.3.2. This result was consistent at 13 years follow-up (RR 0.98, 95% CI 0.92 – 1.04); absolute risk reduction 0.02%.

3.4. In one high quality, adequately randomized controlled trial, participants over 50 years of age who had mammography screening were no less likely to die from any cause compared to non-screened participants at 7 years follow up.

3.4.1. The true effect ranged from 15% less likely to 20% more likely to die from any cause compared to non-screened participants (RR 1.01, 95% CI 0.85 – 1.20); absolute risk *increase* 0.01%.

3.4.2. This result was consistent at 13 years follow-up (2 studies; RR 1.00, 95% CI 0.95 – 1.04); absolute risk reduction 0.04%.

4. **Mammography and potential harms**

4.1. Participants who had mammography screening were more likely to undergo surgery compared to non-screened participants.

4.2. **Mastectomy plus lumpectomy (5 studies)**

4.2.1. In 3 adequately randomized controlled trials, participants who had mammography screening were 31% more likely to undergo mastectomy plus lumpectomy compared to non-screened participants. This finding is statistically significant.

4.2.1.1. The true effect ranged from 22% to 42% more likely to undergo surgery (RR 1.31, 95% CI 1.22 -1.42).

4.2.1.2. The absolute risk *increase* of undergoing mastectomy plus lumpectomy is statistically significant.

4.2.2. Women considering mammography screening should be advised that mammography is associated with a 20% greater risk of undergoing unnecessary mastectomy.

4.3. Women considering mammography screening should be advised that mammography is associated with a 32% greater risk of receiving potentially harmful radiotherapy.
4.2. In 2 studies without adequate randomization participants who had mammography screening were 42% more likely to undergo mastectomy plus lumpectomy compared to non-screened participants.
4.2.1. The true effect ranged from 26% to 61% more likely to undergo mastectomy plus lumpectomy (RR 1.42, 95% CI 1.26 – 1.61).
4.2.2. Pooled results of both suboptimally and adequately randomized trials found that participants who had mammography screening were 35% more likely to undergo mastectomy plus lumpectomy compared to non-screened participants.
4.2.3. The true effect ranged from 26% to 44% more likely to undergo mastectomy plus lumpectomy compared to non-screened participants (RR 1.35, 95% CI 1.26 – 1.44); absolute risk increase 0.3%.

4.3. Mastectomy (5 studies)
4.3.1. In 3 studies with adequate randomization participants who had mammography screening were 20% more likely to undergo mastectomy compared to non-screened participants. This finding is statistically significant.
4.3.1.1. The true effect ranged from 8% to 32% more likely to undergo mastectomy (RR 1.20, 95% CI 1.08-1.32).
4.3.1.2. The absolute risk increase for mastectomy in those receiving mammography was 0.2%.
4.3.2. In 2 studies without adequate randomization participants who had mammography screening were 21% more likely to undergo compared to non-screened participants.
4.3.2.1. The true effect ranged from 6% to 38% more likely to undergo mastectomy plus lumpectomy (RR 1.21, 95% CI 1.06 – 1.38).
4.3.3. Pooled results of both suboptimally and adequately randomized trials found that participants who had mammography screening were 20% more likely to undergo mastectomy compared to non-screened participants.
4.3.3.1. The true effect ranged from 11% to 30% more likely to undergo mastectomy compared to non-screened participants (RR 1.20, 95% CI 1.11 – 1.30); absolute risk increase 0.14%.

4.4. Radiotherapy (2 studies)
4.4.1. Participants who had mammography screening were significantly more likely to undergo radiotherapy compared to non-screened participants.
4.4.1.1. In one adequately randomized study, participants were 24% more likely to undergo radiotherapy (RR 1.24, 95% CI 1.04-1.49) after 9 years follow up; and in a suboptimally randomized study, 40% more likely (RR 1.40, 95% CI 1.17-1.69).
4.4.1.2. The absolute risk increase with radiotherapy based on the adequately randomized trial is 0.24%.
4.4.2. Pooled results of both the suboptimally and adequately randomized trials found that participants who had mammography screening were 32% more likely to receive radiotherapy compared to non-screened participants.
4.4.2.1. The true effect ranged from 16% to 50% more likely to receive radiotherapy.
compared to non-screened participants (RR 1.32, 95% CI 1.16 – 1.50); absolute risk increase 0.26%.

5. Methodological Issues
5.1. In 6 of the 8 included trials, randomization was inadequate and age was not adequately adjusted for.

5. Program Evaluation and Research
5.1. Future research should assess long term effects, including breast cancer mortality and all cause mortality, of women who receive mammography.
5.2. Rigorous research should assess the psychological and adverse outcomes related to mammography screening.

6. Cost Benefit or Cost-effectiveness information
6.1. No cost related information was included in the review.

6. Cost Benefit or Cost-effectiveness information
6.1. Future research should include cost effectiveness of interventions.

General Implications
- This review suggests that for every 2000 women who participate in regular screening over 10 years, one will have her life prolonged. As such, mammography screening is not recommended to reduce breast cancer deaths in women.
- Women who receive mammography should be advised of the risk of overtreatment (e.g. surgery and radiotherapy), as this review demonstrates that mammography screening led to approximately 30% overdiagnosis and overtreatment (or an absolute risk increase of 0.5%). In other words, 10 healthy women, who would not have been diagnosed if there had not been screening, will be treated unnecessarily.
- Rigorous program evaluations and high quality research studies should be conducted to determine the effectiveness of mammography screening on morbidity and mortality as well as adverse outcomes such as overtreatment.

Legend:
CI – Confidence Interval; OR – Odds Ratio; RR – Relative Risk
**For definitions see the healthevidence.org glossary http://www.healthevidence.org/glossary.aspx

References used to outline issue

Other quality reviews on this topic

Related links
- Canadian Cancer Society http://www.cancer.ca/
- Cancer Control PLANET http://cancercontrolplanet.cancer.gov
- Canadian Breast Cancer Foundation http://www.cbcf.org/
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