Summary Statement Title:
Magnetic resonance imaging (MRI) as an addition to mammography and ultrasound in screening young women at high risk of breast cancer: Evidence and implications for public health

Review Quality Rating: 6 (moderate)

Review on which this summary statement is based:

Review author contact information:
S.J. Lord, National Health and Medical Research Council Clinical Trials Centre, The University of Sydney. Level 5, Bldg. F, 88 Mallett Street, Locked Bag 77, Camperdown, NSW 2050, Australia; Tel: +61295635322; Fax: +61295651863; E-mail: slord@ctc.usyd.edu.au.

This is a summary statement 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.

Review content summary
This systematic review of five prospective studies (2059 participants) aimed to determine the effectiveness of adding MRI to mammography with or without breast ultrasound and clinical breast examination (CBE). Participants studied were: women under 50 years of age at high risk of developing breast cancer. To be included, studies were: comparative studies of the addition of MRI to mammography reporting on prognostic tumour characteristics, interval cancer rates, or relevant patient outcomes. Interventions described in this review included: MRI and mammography alone, or MRI and mammography plus ultrasound +/- CBE. Outcomes measured include: screening accuracy. Authors report that no studies assessed whether adding MRI reduces patient mortality, interval or advanced breast cancer rates, and there was no strong evidence to demonstrate that MRI leads to the detection of earlier stage disease.

Comments on this review's methodology
This is a methodologically moderate systematic review. A focused clinical question was clearly identified. Appropriate inclusion criteria were used to guide the search. A comprehensive search was not employed using only health databases and not utilizing other resources. The search was limited by language (English). Primary studies were not adequately assessed for methodological quality using only research design and source of bias for assessment. The methods were not described in sufficient detail so as to allow replication although two reviewers were involved in quality appraisal. Any discrepancies in appraisal results were not indicated in the review. The results of this review were transparent. Results were clearly presented in narrative form so as to allow for comparisons across studies. Heterogeneity was assessed. Appropriate analytical methods (fixed effects, random effects) were not employed to enable the synthesis of study results. A limitation of this review was the failure to weigh study results in estimating overall effects. Therefore the results should be interpreted with some caution.

Why this issue is of interest to public health
Women between the ages of 20-49 account for over 20% of breast cancer diagnoses; in addition, breast cancer is the leading cause of cancer death in women under 40. About 50,000 new cases and 13,000 deaths will occur between ages 20 and 59 typically the most productive years for employment and raising families. More specifically, it is estimated that about 1% of women carry the BRCA1 or BRCA2 gene for breast cancer believed to be responsible for 3-8% of all breast cancers. This translates to approximately 1/200 Canadian women developing breast cancer due to the presence of a high-risk gene. Women with a strong family history of breast cancer or a high-risk gene have a cumulative lifetime risk of developing breast cancer of 21–65% with a substantial proportion of these cancers diagnosed before the age of 50 years. Although mammography is a sensitive test for screening postmenopausal women, it is less sensitive in younger women and those with a genetic predisposition to breast cancer. As such, the UK, the US and Australia have adopted a policy of using MRI for screening very high risk women. In Canada, because the majority of breast cancer is detected in women aged 49-69, and because of the limited effectiveness of screening mammography for younger women, organized screening programs exclude women under the age of 49 who are asymptomatic and are not considered part of a high risk group. Digital mammography, MRI, and Ultrasound (Sonography) are proving to be more effective as diagnostic tools for younger women due to their greater sensitivity, but come with a higher price tag, and higher false-positive rates. The role of MRI in screening high-risk women or very high-risk women remains uncertain, and warrants further research, particularly given the asymptomatic nature of breast cancer, the absence of rigorous interventions targeting modifiable risk factors, and the tendency for improved outcomes with early detection.
**Evidence and implications**

**Evidence points are not in order of the strength of evidence**

### What’s the evidence?

<table>
<thead>
<tr>
<th>1. Mammography plus MRI to detect breast cancer in high risk women under age 50 (5 studies)</th>
<th>Implications for practice and policy:</th>
</tr>
</thead>
</table>
| 1.1. MRI plus conventional tests correctly detected breast cancer between 86% and 100% of the time compared to 25%- 59% for mammography alone and 49% - 67% for mammography and ultrasound with or without CBE.  
1.1.1. The results of the meta-analysis for three of the 5 studies evaluating mammography plus MRI compared to mammography alone demonstrated that breast cancer was correctly detected 94% of the time with the true rate ranging from 86% to 98% of the time. The absolute benefit increase of MRI was 41%, in comparison to mammography alone, and the 95% confidence interval for the absolute benefit increase was 16%-66%.  
1.1.1.1. The added benefit (incremental sensitivity) of MRI in correctly detecting breast cancer versus mammography alone was the detection of breast cancer an additional 58% of the time, with the true effect ranging from an additional 47% to 70% of the time.  
1.1.1.2. The added benefit of MRI in correctly detecting breast cancer versus mammography plus ultrasound was slightly less effective at 44%, with the true effect ranging from 27% to 61% correct identification of breast cancer.  
1.1.1.3. The added benefit of MRI in correctly detecting breast cancer versus mammography, ultrasound and CBE was the least effective at 31% – 33% of the time. | 1. Mammography plus MRI to detect breast cancer in high risk women under age 50  
1.1. MRI should be added to conventional testing for breast cancer screening in high risk women under age 50, particularly in areas where mammograms only are the standard practice.  
1.2. In areas where standard practice with high risk women under age 50 consists of mammogram plus ultrasound, the added benefit of MRI is less than it is for mammogram only, but MRI is still recommended based on the data presented in this review.  
1.3. MRI provides the least added benefit in areas where standard practice with high risk women under age 50 consists of mammogram plus ultrasound plus CBE, although an added detection rate of 31%-33% is still an important improvement, and therefore is recommended at this time.  
1.4. There is some evidence to suggest that MRI should be included with all the other traditional diagnostic tests for breast cancer in high risk women, as MRI detects cancers where other test do not, but also, other tests detect cancer when MRI does not. |
| 1.2. MRI plus conventional testing correctly ruled out breast cancer between 77% and 96% of the time compared to conventional testing.  
1.2.1. Meta-analysis across all 5 studies was not possible due to the wide variability in the results in the 5 studies. | |
| 1.3. The addition of MRI to screening for women with negative results from conventional testing resulted in an additional 10 to 24 cancers detected per 1000 screening rounds.  
1.3.1. In 2 studies of women with different risk levels, the added benefit of MRI in correctly detecting breast cancer versus mammography alone was an additional 50% – 54%. The greatest benefit was observed among women with the highest risk and prevalence of breast cancer.  
1.4. 4 studies found that mammography detected cancers not visible on MRI and that MRI detected cancers not visible through other screening modalities. | |
| 2. Test recall following MRI plus mammography (3 studies) | 2. Test recall following MRI plus mammography |
| 2.1. Women who underwent MRI plus mammography were 3 to 5 times more likely to be recalled for further investigation with eventual benign results compared to women who underwent mammography alone.  
2.1.1. The true effect ranged from 3.43 times more likely to 4.86 times more likely to be recalled (95% CI 3.43 - 4.86); or an additional 71-74 false positive recalls per 1000 screens.  
2.1.2. Women who underwent MRI plus mammography were 1.2 to 9.5 times more likely to undergo a benign biopsy compared to women who underwent mammography alone (95% CI 1.22 – 9.50); or an additional 7- 46 benign biopsies per 1000 screens. | 2.1. Screening should include MRI, mammography and ultrasound to improve screening effectiveness and minimize unnecessary recall.  
2.2. Women should be advised of the risk of false positive results and recall leading to additional biopsies. |
2.1.3. In one study women who underwent MRI plus mammography were twice as likely to undergo surgical biopsy with benign results compared to women who underwent mammography alone. However the results were not statistically significant.

3. Early Detection and MRI plus mammography (4 studies)

3.1. Among invasive cancers detected by MRI plus mammography compared to those detected through mammography alone or mammography and ultrasound (with and without CBE) there was no difference in tumour size or lymph node involvement.

3.1.1. One study found that cancers detected by MRI alone were statistically significantly smaller and less invasive than those detected by mammography and ultrasound; although a second, larger study did not report similar findings.

3. Early Detection with MRI plus mammography

3.1. The data at this point do not suggest that the inclusion of MRI with mammography results in earlier detection of breast cancer as measured by tumour size or lymph node involvement.

3.2. There is limited data suggesting MRI alone identifies smaller and less invasive tumours than is detected by mammography and ultrasound, however, additional research is needed to recommend MRI for the purpose of promoting earlier detection.

4. Methodological Issues with the Primary Studies in the Review

4.1. No significant methodological issues were identified

5. Implications for Future Research

4.1. Additional rigorous research should be conducted to determine the relative effectiveness of breast screening modalities in high risk women under 50 years of age.

4.2. Additional rigorous research should assess breast cancer mortality outcomes for different screening modalities.

4.3. Additional rigorous research should assess the relationship between MRI use in addition to traditional tests and earlier detection of disease.

5. Cost Benefit or Cost-effectiveness Information

5.1. Screening women at very high risk for breast cancer who are younger than 50 – 54 years of age with MRI plus mammography is cost effective compared to mammography alone. MRI plus mammography is less cost effective for wider risk or older-aged populations.

5.1. High risk women for breast cancer under 50 years of age should be screened with MRI and mammography since it is more cost-effective than mammography alone.

General Implications

- Breast cancer screening for high risk women under 50 years should include MRI, mammography, and ultrasound
- Rigorous research should be conducted to determine the relative effectiveness of breast screening modalities in high risk women under 50 years of age
- Rigorous research should assess breast cancer mortality outcomes in high risk women under 50 years for different screening modalities, as well as the ability to detect the disease at an earlier stage

Legend: CI – Confidence Interval; OR – Odds Ratio; RR – Relative Risk

**For definitions see the healthevidence.org glossary [http://www.healthevidence.org/glossary.aspx](http://www.healthevidence.org/glossary.aspx)

References used to outline issue


Other quality reviews on this topic


Related links

- Canadian Breast Cancer Foundation http://www.cbcf.org/
- Canadian Breast Cancer Research Alliance www.breast.cancer.ca
- Canadian Cancer Society Research Institute http://www.cancer.ca/research/

Suggested citation


The opinion and ideas contained in this document are those of the summary statement author(s) and healthevidence.org. They do not necessarily reflect or represent the views of the author's employer or other contracting organizations. Links from this site to other sites are presented as a convenience to healthevidence.org internet users. Healthevidence.org does not endorse nor accept any responsibility for the content found at these sites.