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[Intervention Review]

Mammography in combination with breast ultrasonography versus mammography for breast cancer screening in women at average risk

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ABSTRACT

Background

Breast cancer is the most common malignant disease diagnosed in women worldwide. Screening with mammography has the ability to detect breast cancer at an early stage. The diagnostic accuracy of mammography screening largely depends on the radiographic density of the imaged breasts. In radiographically dense breasts, non-calcified breast cancers are more likely to be missed than in fatty breasts. As a consequence, some cancers are not detected by mammography screening. Supporters of adjunct ultrasonography to the screening regimen for breast cancer argue that it might be a safe and inexpensive approach to reduce the false negative rates of the screening process. Critics, however, are concerned that performing supplemental ultrasonography on women at average risk will also increase the rate of false positive findings and can lead to unnecessary biopsies and treatments.

Objectives

To assess the comparative effectiveness and safety of mammography in combination with breast ultrasonography versus mammography for breast cancer screening for women at average risk of breast cancer.

Search methods

We searched the Cochrane Breast Cancer Group's Specialised Register, MEDLINE (via OvidSP) and EMBASE up until February 2012.

To detect ongoing or unpublished studies, we searched the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP), ClinicalTrials.gov and the National Cancer Institute's clinical trial database until June 2012. In addition, we conducted grey literature searches using the following sources: OpenGrey; National Institute of Health RePORTER; Health Services Research Projects in Progress (HSRPROJ); Hayes, Inc. Health Technology Assessment; The New York Academy of Medicine's Grey Literature Index and Conference Papers Index.

Selection criteria

For efficacy, we considered randomised controlled trials (RCTs), with either individual or cluster randomisation, and prospective, controlled non-randomised studies with a low risk of bias and a sample size of at least 500 participants.

In addition to studies eligible for efficacy, we considered any controlled, non-randomised study with a low risk of bias and a study size of at least 500 participants for the assessment of harms.

Our population of interest were women between the ages of 40 and 75 years who were at average risk for breast cancer.

Data collection and analysis

Two review authors screened abstracts and full-text publications against the inclusion criteria. None of the studies met our inclusion criteria.

Main results

Our review did not detect any controlled studies on the use of adjunct ultrasonography for screening in women at average risk for breast cancer. One ongoing randomised controlled trial was identified (J-START, Japan).

Authors' conclusions

Presently, there is no methodologically sound evidence available justifying the routine use of ultrasonography as an adjunct screening tool in women at average risk for breast cancer.

PLAIN LANGUAGE SUMMARY

Mammography followed by ultrasonography compared to mammography alone for breast cancer screening in women at average risk of breast cancer

Worldwide, breast cancer is the most common malignancy in women. Evidence shows that mammography in healthy women 50 to 70 years of age can detect breast cancer early and reduce the risk of dying from breast cancer. Mammography, however, is not a perfect tool to detect breast cancer and misses some tumours in some women, particularly in women who have dense breasts. In women with dense breasts, the normal breast tissue and the tumour are difficult to distinguish from each other on the mammogram. Because of this, some supporters feel that the addition of ultrasonography screening of these women in addition to the mammography screening will detect those tumours that are missed by mammography alone. Others feel that this will increase the rate of false positive tumours and increase the number of biopsies and unnecessary treatment.

The benefit of ultrasound as an additional examination for women who do not have especially dense breasts and who have normal mammographies is uncertain. This review sought to examine the evidence for and against adding ultrasonography screening to mammograms for women at average risk for breast cancer. It is important to weigh positive and negative sides of screening because the detection of more tumours by screening does not necessarily mean that more women will have their lives saved. We need to assess whether the few additional cancers that may be detected by ultrasonography lead to a real decrease in mortality from breast cancer and then balance any benefit against the harm caused by many women being incorrectly alarmed or diagnosed.

We did not find any trials that addressed our review question. One randomised controlled trial is currently underway in Japan (called J-START). Because it is unclear whether ultrasonography in women with normal mammographies can reduce the risk of dying from breast cancer, they should not be used on a routine basis. If screening with ultrasonography is performed it should be as part of a clinical trial designed to test the effect of additional screening on mortality and the harms experienced by women who have a positive ultrasonography screening test.

BACKGROUND

Description of the condition

Breast cancer is the most common malignant disease diagnosed in women worldwide, comprising 16% of all female cancers (World Health Organization 2011). The risk of developing breast cancer increases with age and certain risk factors such as dense breasts, family history of breast or ovarian cancer, or familial breast cancer gene mutations of BRCA1 (BReast CAncer 1, early onset) and BRCA2 (BReast CAncer 2, susceptibility protein).

Screening with mammography has the ability to detect breast cancer at an early stage. Subsequent effective diagnostic pathways and treatment regimens can reduce the burden of disease of breast cancer, most importantly mortality in women aged 50 to 70 years (USPSTF). A Cochrane review estimated a relative reduction of mortality from breast cancer of 15%, corresponding to an absolute risk reduction of 0.05 per cent in women aged 50 and older (Gøtzsche 2011). In addition to a reduction in mortality, studies evaluating the efficacy of mammographic screening have repeatedly reported a reduction in breast cancer morbidity (Griffin 2010). The sensitivity of mammography ranges between 77% and 95% and the specificity ranges between 94% and 97% (Nelson 2009). The diagnostic accuracy of mammography screening largely depends on the radiographic density of the imaged breasts (Carney 2003). In radiographically dense breasts, non-calcified breast cancers are more likely to be missed than in fatty breasts. As a consequence, some cancers are not detected by mammography screening.

Ultrasonography of the breast is currently not recommended in screening of women at average risk for breast cancer (Elmore 2005; Griffin 2010). Most clinical practice guidelines specify ultrasonography of the breast as a supplementary examination for further clarification of ambiguous findings (Albert 2009). The *European Guidelines on Quality Assurance in Breast Cancer Screening and Diagnosis* state that ultrasonography should be carried out in the presence of a discrete clinical mass even if negative on mammography (Perry 2008).

Supporters of supplemental ultrasonography to the screening regimen for breast cancer argue that it might be a safe and inexpensive approach to reduce the false negative rates of the screening process. Critics, however, are concerned that performing supplemental ultrasonography on women at average risk will also increase the rate of false positive findings and can lead to unnecessary biopsies and treatments. Authors of a 2009 systematic review of six observational studies in ultrasonography noted the increased biopsy rate in women at intermediate risk, finding a mean positive predictive value of 15% (range 2% to 28%) from four of the six studies, that is, the percentage of positively classified findings for which no carcinoma was subsequently found ranged from 72% to 98% (Nothacker 2009).

Description of the intervention

The intervention entails any form of mammography screening (for example one view, two views, digital, etc) that meets the technical standards of the *European Guidelines for Quality Assurance in Breast Cancer Screening and Diagnosis* (Perry 2008) with adjunct breast ultrasonography used as a sequential screening test (that is breast ultrasonography that is conducted in women with negative screening mammograms). Breast ultrasonography as a diagnostic test following a positive mammogram is not of interest for this systematic review. We draw this distinction because only ultrasonographies conducted in women with negative mammograms are true screening tests because their goal is to increase the sensitivity of the screening procedure.

To be eligible for this report, ultrasonography needs to be performed with a high-frequency transducer of 7.5 MHz or higher.

How the intervention might work

To increase either sensitivity or specificity, two or more screening tests may be applied in the same individuals. These tests can be used sequentially or simultaneously. Sequential screening tests are applied in a proportion of the population with a specific result of the first screening test. In sequential screening the post-test probability of the first screening test becomes the pre-test probability of the second screening test. The goal of sequential screening is usually to increase sensitivity. By contrast, simultaneous screening applies two (or more) tests to the screened individuals without knowledge of the results of each individual test. Therefore, the pre-test probability remains the same for all tests.

Breast ultrasonography is used routinely as a diagnostic measure to distinguish benign from malignant lesions because it can differentiate between cysts and solid tumours and thus lowers the number of indeterminate mammographical findings. A 2008 study found an increase in diagnostic accuracy when using breast ultrasonography in addition to mammography (accuracy of 0.78 (95% confidence interval (CI) 0.67 to 0.87) for mammography alone compared with 0.91 (95% CI 0.84 to 0.96) when mammography is combined with ultrasonography) (Berg 2008). Thus, breast ultrasonography as an adjunct screening tool to mammography might also be able to detect cancer lesions that mammography screening misses. We consider adjunct breast ultrasonography a sequential screening test because it is administered as an add-on test in women with a negative mammogram. Women with a positive mammogram will also receive breast ultrasonography, but for this population ultrasonography is a diagnostic test.

In women at increased risk for breast cancer, defined by high breast density or other risk factors, several studies have demonstrated that supplemental screening with ultrasonography can increase the detection rates of cancer, particularly in women with dense breasts (Berg 2008; Nothacker 2009). Mammographically dense breast tissue is an independent risk factor for breast cancer and is as-

sociated with a high risk of interval cancers, that is cancers that become clinically apparent between screening tests (Boyd 2007). Ultrasonography, therefore, has the potential to detect mammographically occult cancers at an earlier stage and to improve surrogate outcomes such as tumour size and lymph node status, which have been linked to a poor prognosis of breast cancer (Michaelson 2002; Michaelson 2003).

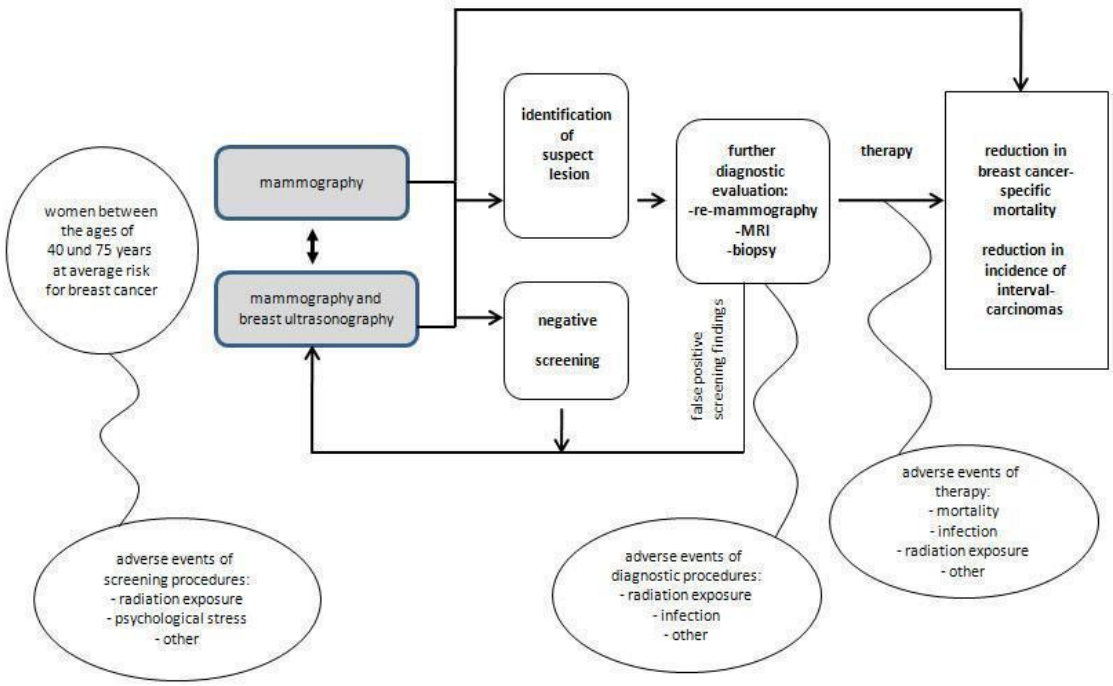
Why it is important to do this review

In women at increased risk for breast cancer, adjunct ultrasonography can improve the diagnostic yield of breast cancer screening (Berg 2008). Based on these findings, ultrasonography is sometimes used routinely as an adjunct screening tool in women at average risk. It is unclear whether the use of ultrasonography as an adjunct screening tool in women at average risk corresponds to a reduction in mortality and morbidity (the ultimate goal of any screening programme) or to an increase in screening-related harms.

OBJECTIVES

To assess the comparative effectiveness and safety of mammography in combination with breast ultrasonography versus mammography for breast cancer screening for women at average risk of breast cancer. Figure 1 depicts the analytic pathway of the research question.

Figure 1. Analytic pathway of the comparative efficacy and risk of harms of mammography screening with and without supplemental ultrasonography



METHODS

Criteria for considering studies for this review

Types of studies

For efficacy we considered RCTs with either individual or cluster randomisation and prospective, controlled non-randomised studies with a low risk of bias and a sample size of at least 500 participants.

In addition to studies eligible for efficacy, we considered any controlled, non-randomised study with a low risk of bias and a study size of at least 500 participants for the assessment of harms. Studies needed to have a follow-up period of at least one year and had to include at least one relevant outcome.

Types of participants

Women between the age of 40 and 75 years who are at average risk for breast cancer, have not previously had breast cancer, and who participate in a breast cancer screening program or undergo mammography screening.

We define women at average risk as those who have a lifetime risk of less than 15% or who have dense breasts without any additional risk factors for breast cancer.

Types of interventions

Any form of mammography screening (for example one view, two views, digital, etc) that meets the technical standards of the *European Guidelines for Quality Assurance in Breast Cancer Screening and Diagnosis* (Perry 2008) with additional breast ultrasonography compared with mammography screening without breast ultrasonography.

Types of outcome measures

Primary outcomes

- Breast cancer mortality

Secondary outcomes

- All-cause mortality
- Incremental cancer detection rate
- Incremental detection rate of invasive cancers
- Rate of interval cancers
- Lymph node status
- Size of detected cancers
- Health-related quality of life
- False positive rate
- False negative rate
- Rate of biopsies
- Screening associated harm (psychological distress, adverse effects caused by subsequent diagnostic or therapeutic interventions, others)

Search methods for identification of studies

Electronic searches

We searched the following databases:

1. The Cochrane Breast Cancer Group (CBCG) searched their Specialised Register. Details of the search strategies used by the Group for the identification of studies and the procedure used to code references are outlined in the Group's module: http://www.mrw.interscience.wiley.com/cochrane/clabout/articles/BREASTCA/frame.html.
2. MEDLINE (via OvidSP) (from July 2008 to February 2012). See Appendix 1 for the full search strategy.
3. EMBASE (via Embase.com) (2008 to February 2012). See Appendix 2 for the full search strategy.
4. The WHO International Clinical Trials Registry Platform (ICTRP) search portal (http://apps.who.int/trialsearch/AdvSearch.aspx) for all prospectively registered and ongoing trials to January 2012. See Appendix 3 for the search strategy.

Searching other resources

We manually searched reference lists of pertinent reviews and relevant background articles on this topic to look for any relevant citations that our searches might have missed.

We searched for grey literature (through June 2012) in the following databases:

1. OpenGrey;
2. ClinicalTrials.gov;
3. National Cancer Institute's clinical trial database;
4. National Institute of Health RePORTER;
5. Health Services Research Projects in Progress (HSRPROJ);
6. Hayes Inc. Health Technology Assessment;
7. The New York Academy of Medicine's Grey Literature Index; and
8. Conference Papers Index.

Data collection and analysis

Selection of studies

We developed and pilot-tested literature review forms for abstract and full-text reviews. Two authors (AC, AK, DB, GG, KT, THH, MvN) independently reviewed abstracts. We retrieved full-text copies of all studies that potentially met the inclusion criteria based on the abstract review. Studies marked for possible inclusion by either review author underwent a full-text review. For studies that lacked adequate information to determine inclusion or exclusion, we retrieved the full text and then made the determination. If the necessary information in the full-text articles was unclear or missing, we contacted authors of the publications. Two trained members of the research team (GG, KT) independently reviewed each full-text article for inclusion or exclusion based on the eligibility criteria described above. If both review authors agreed that a study did not meet the eligibility criteria, we excluded it. If the

review authors disagreed, they resolved conflicts by discussion and consensus or by consulting a third member of the review team. All results were tracked in an EndNote X5 database.

Data extraction and management

We designed, pilot-tested and used structured data extraction forms to gather pertinent information from relevant articles; this included characteristics of study populations, settings, interventions, comparators, study designs, methods and results.

Assessment of risk of bias in included studies

We planned to assess the risk of bias of included randomised trials using the Cochrane 'Risk of bias' tool as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). The tool includes assessment of: sequence generation; allocation sequence concealment; blinding of participants, personnel and outcome assessors; incomplete outcome data; selective outcome reporting and other potential threats to validity. In addition, we planned to assess whether all relevant outcomes for the trial were reported in the published articles. We intended to rate each domain as high risk of bias, low risk of bias or unclear risk of bias.
For non-randomised studies, we planned to use criteria involving selection of cases or cohorts and controls, adjustment for confounders, methods of outcomes assessment, length of follow-up and statistical analysis (Higgins 2011).

Measures of treatment effect

We planned to use extracted data from the original studies to construct 2 x 2 tables. Where multiple studies would have allowed for quantitative analysis, we planned to calculate the risk ratio or odds ratio with 95% confidence intervals for each outcome. In addition, we planned to pool continuous data using the mean difference or standardised mean difference. For time-to-event data, we planned to calculate a pooled hazard ratio where this was available or to dichotomise data at multiple time points into response/no response (e.g. at one week, two weeks, four weeks, etc).

Unit of analysis issues

The unit of our analyses was intended to include women (not cancer lesions).

Dealing with missing data

We intended to use intention-to-treat analysis where data were missing from participants who dropped out of trials before completion. Where data regarding an outcome of interest were not reported, we planned to contact authors of publications to obtain missing results.

Assessment of heterogeneity

We planned to use the Cochran Chi^2 test (Q-test) to assess heterogeneity. We intended to use the I^2 statistic to estimate the degree of heterogeneity. This measure describes the percentage of total variation across studies that results from heterogeneity rather than chance. We would have interpreted the importance of any heterogeneity in terms of its magnitude and the direction of effects. We would not have used thresholds; instead we would have adopted the overlapping bands suggested in the *Cochrane Handbook*. For example, we planned to consider an I^2 of between 0% and 40% as probably not important, between 30% and 60% as representing moderate heterogeneity, between 50% and 90% as substantial heterogeneity, and between 75% and 100% as considerable heterogeneity (Higgins 2011).

Assessment of reporting biases

We checked trial registries (for example WHO ICTRP and www.clinicaltrials.gov) to detect completed but unpublished trials.

Data synthesis

We planned to analyse data using Review Manager 5.1 (RevMan 5.1). We would have pooled data for meta-analysis where the participant groups were similar and the studies assessed the same treatments with the same comparator and had similar definitions of outcome measures over a similar duration of treatment. We planned to use a fixed-effect model where heterogeneity was low and a random-effects model where the presence of heterogeneity resulted in a higher I^2 unless too few studies were included in the analysis. We planned to rate the strength of the evidence based on the system developed by the GRADE Working Group.

Subgroup analysis and investigation of heterogeneity

We planned to perform subgroup analyses based on breast density.

Sensitivity analysis

We had planned to conduct sensitivity analyses excluding small studies, studies with a high risk of bias and studies published in abstract form.

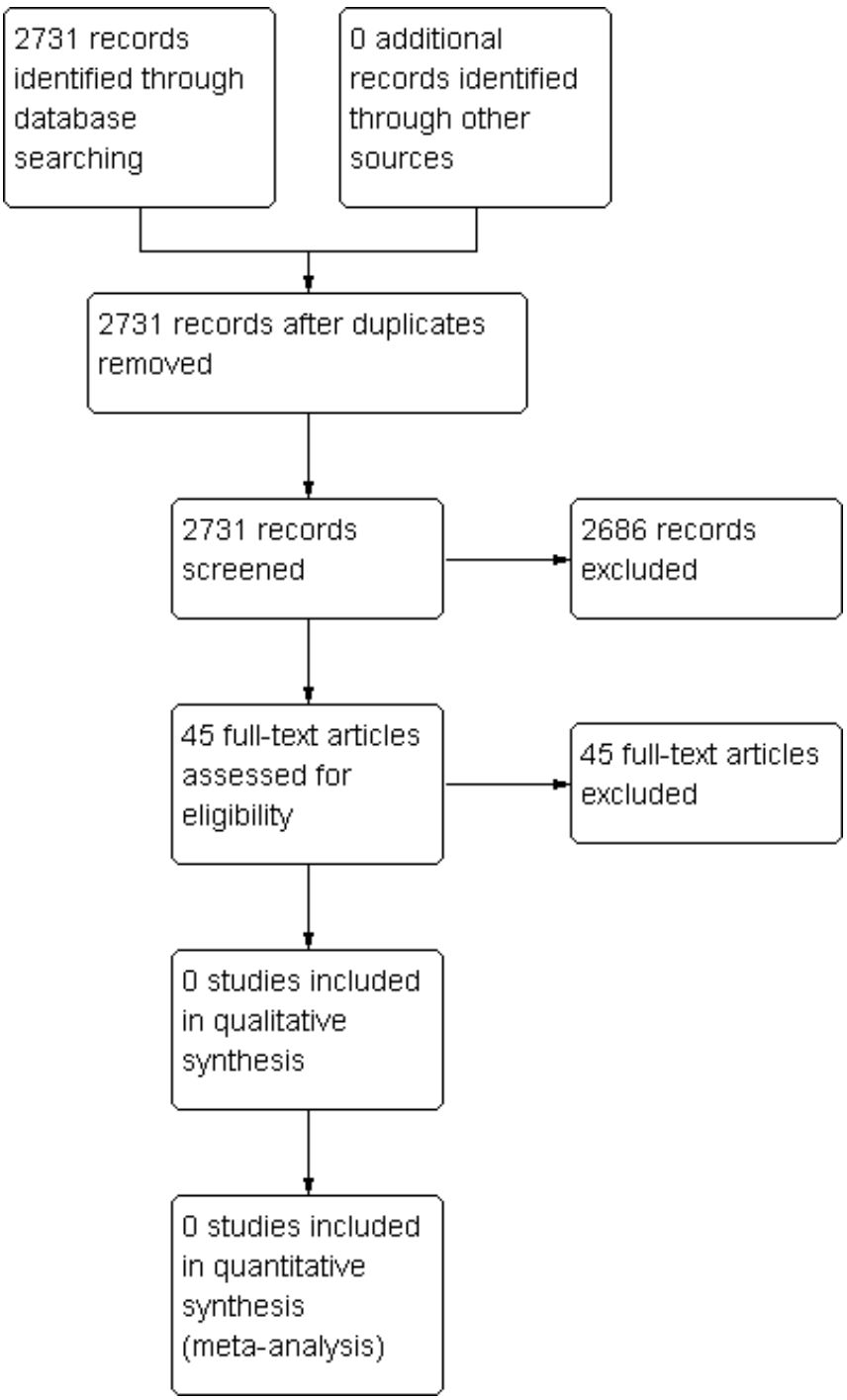
RESULTS

Description of studies

Results of the search

We identified 2731 citations from searches and reviews of reference lists. Overall, we did not find any completed studies that met our eligibility criteria. Figure 2 depicts the numbers of search results and the flow of the literature for this report.

Figure 2. Study flow diagram.



Included studies

We did not find any controlled studies assessing the incremental benefits and harms of adjunct screening ultrasonography in women at average risk for breast cancer. Our searches in clinical trial registries detected one ongoing RCT in Japan that is potentially relevant. This trial, termed J-START (Japan-Strategic Anticancer Randomized Trial), is a large-scale study that will randomly assign 100,000 Japanese women aged 40 to 49 years to either mammography or mammography with adjunct ultrasonography (Ohuchi 2011). The primary endpoints of this trial are sensitivity and specificity; the secondary endpoint is the accumulated incidence rate of advanced cancers during the four-year follow-up period.

Excluded studies

Overall, we excluded 45 studies. The main reasons for exclusion were study populations that did not meet the eligibility criteria (e.g. women with high risk of breast cancer) or study designs that ascertained only the diagnostic yield of adjunct ultrasonography without taking screening-relevant health outcomes into consideration. Reasons for excluding studies after full-text review are summarised under Characteristics of excluded studies.

Risk of bias in included studies

We did not include any studies.

Allocation

We did not include any studies.

Blinding

We did not include any studies.

Incomplete outcome data

We did not include any studies.

Selective reporting

We did not include any studies.

Other potential sources of bias

We did not include any studies.

Effects of interventions

We did not include any studies.

DISCUSSION

Summary of main results

Overall, our review did not detect any controlled studies that provided evidence for (or against) the use of adjunct ultrasonography for screening in women at average risk for breast cancer. The only available evidence regarding adjunct breast ultrasonography in women at average risk is limited to one uncontrolled observational study of women with normal screening mammograms who received sequential ultrasonography screening (Buchberger 2000). This study, conducted in Tyrol, Austria, reported an incremental diagnostic yield of 2.6 cancers per 1000 women without a personal history of breast cancer. Although this study provides some information regarding the performance of adjunct ultrasonography as a sequential screening test, i.e. how well it diagnoses illness, it cannot provide information on the overall usefulness as a screening test, i.e. whether adjunct ultrasonography results in a reduction of morbidity and mortality. Simply diagnosing more cases of illness does not necessarily result in lower mortality or less morbidity. Screening for neuroblastoma in children in Japan in the late 1990s provides a dramatic historical example of how inferences on the usefulness of cancer screening, when based solely on incremental cancer detection rates, can result in a screening programme that causes more harm than benefits (Soderstrom 2005).

Overall completeness and applicability of evidence

Despite extensive searches of the grey literature, we did not find any eligible studies. A separate publication will extrapolate findings of results from women at elevated risk for breast cancer to estimate the false positive rates in women at average risk who were recalled because of positive ultrasonographies (Gartlehner 2013).

Quality of the evidence

We did not include any studies.

Potential biases in the review process

Publication bias is a threat for any systematic review. Although we have conducted extensive searches of grey literature, we cannot be sure that we have detected each study conducted in this field. We have identified one study that has been registered but has not yet been published (Ohuchi 2011).

Agreements and disagreements with other studies or reviews

We did not find any other studies that addressed the research question. A systematic review of adjunct ultrasonography in women at high risk for breast cancer, defined by increased breast density or other risk factors, demonstrated that supplemental screening with ultrasonography can increase the detection rates of cancer at the cost of a high false positive rate (Nothacker 2009).

AUTHORS' CONCLUSIONS

Implications for practice

The majority of women undergoing breast cancer screening do not have dense breasts and are at average risk. Presently, no methodologically sound evidence is available justifying the routine use of ultrasonography as an adjunct screening tool in such a population. The prevalence (pre-test risk) of breast cancer in a population with radiographic BI-RADS (Breast Imaging Reporting and Data System) breast density grades 1 or 2 is low (1.0/1000 women in an Italian cohort) (Corsetti 2011). Even if only a small proportion of screened women will be recalled because of positive ultrasonography findings, the rate of false positive results and unnecessary harm caused by subsequent investigations may be unacceptably high given the lack of evidence supporting a gain in health benefits. The conclusion that adjunct ultrasonography should not be used in women at average risk for breast cancer is in line with the World Health Organization's recommendation that no screening programme should be implemented without sound evidence of a reduction in morbidity and mortality (Wilson 1968).

Implications for research

The lack of evidence clearly indicates the need for well-conducted, controlled studies. Ideally, a methodologically sound RCT of screening would assess the comparative benefits and risks of mammography only and mammography with adjunct ultrasonography. The outcomes of such a study have to look beyond the incremental diagnostic yield and assess interval cancer rates, morbidity, screening-related harms and mortality, although for mortality to be included this would require a long follow-up period.

ACKNOWLEDGEMENTS

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REFERENCES

References to studies excluded from this review

Benson 2004 *{published data only}*
Benson SRC, Blue J, Judd K, Harman JE. Ultrasound is now better than mammography for the detection of invasive breast cancer. *American Journal of Surgery* 2004;**188**(4): 381–5.

Berg 2008 *{published data only}*
Berg WA, Blume JD, Cormack JB, Mendelson EB, Lehrer D, Bohm-Velez M, et al. Combined screening with ultrasound and mammography vs mammography alone in women at elevated risk of breast cancer. *JAMA* 2008;**299** (18):2151–63.

Brancato 2007 *{published data only}*
Brancato B, Bonardi R, Catarzi S, Iacconi C, Risso G, Taschini R, et al. Negligible advantages and excess costs of routine addition of breast ultrasonography to mammography in dense breasts. *Tumori* 2007;**93**(6):562–6.

Buchberger 1999 *{published data only}*
Buchberger W, DeKoekkoek-Doll P, Springer P, Obrist P, Dunser M. Incidental findings on sonography of the breast: clinical significance and diagnostic workup. *American Journal of Roentgenology* 1999;**173**(4):921–7.

Buchberger 2000 *{published data only}*
Buchberger W, Niehoff A, Obrist P, DeKoekkoek-Doll P, Dünser M. Clinically and mammographically occult breast lesions: detection and classification with high-resolution sonography. *Seminars in ultrasound, CT, and MR* 2000;**21** (4):325–36.

Chan 2008 *{published data only}*
Chan SW, Cheung PS, Chan S, Lau SS, Wong TT, Ma M, et al. Benefit of ultrasonography in the detection of clinically and mammographically occult breast cancer. *World Journal of Surgery* 2008;**32**(12):2593–8.

Cho 2010 *{published data only}*
Cho N, Moon WK, Chang JM, Yi A, Koo HR, Han BK. Sonographic characteristics of breast cancers detected by supplemental screening US: Comparison with breast cancers seen on screening mammography. *Acta Radiologica* 2010;**51**(9):969–76.

Corsetti 2006 *{published data only}*
Corsetti V, Ferrari A, Ghirardi M, Bergonzini R, Bellarosa S, Angelini O, et al. Role of ultrasonography in detecting mammographically occult breast carcinoma in women with dense breasts. *La Radiologia Medica* 2006;**111**(3):440–8.

Corsetti 2008 *{published data only}*
Corsetti V, Houssami N, Ferrari A, Ghirardi M, Bellarosa S, Angelini O, et al. Breast screening with ultrasound in women with mammography-negative dense breasts: evidence on incremental cancer detection and false positives, and associated cost. *European Journal of Cancer* 2008;**44**(4): 539–44.

Corsetti 2011 *{published data only}*
Corsetti V, Houssami N, Ghirardi M, Ferrari A, Speziani M, Bellarosa S, et al. Evidence of the effect of adjunct ultrasound screening in women with mammography-negative dense breasts: Interval breast cancers at 1 year follow-up. *European Journal of Cancer* 2011;**47**(7):1021–6.

Crystal 2003 *{published data only}*
Crystal P, Strano SD, Shcharynski S, Koretz MJ. Using sonography to screen women with mammographically dense breasts. *American Journal of Roentgenology* 2003;**181** (1):177–82.

De Felice 2007 *{published data only}*
De Felice C, Savelli S, Angeletti M, Ballesio L, Manganaro L, Meggiorini ML, et al. Diagnostic utility of combined ultrasonography and mammography in the evaluation of women with mammographically dense breasts. *Journal of Ultrasound* 2007;**10**(3):143–51.

Dilhuydy 2008 *{published data only}*
Dilhuydy MH. Assessment of the dense breast within the French screening program: the role of ultrasonography. *Journal de Radiologie* 2008;**89**(9 Pt 2):1180–6.

Duijm 1997 *{published data only}*
Duijm L, Guit G, Zaat J, Koomen A, Willebrand D. Sensitivity, specificity and predictive values of breast imaging in the detection of cancer. *British Journal of Cancer* 1997;**76** (3):377–81.

Flobbe 2003 *{published data only}*
Flobbe K, Bosch AM, Kessels AG, Beets GL, Nelemans PJ, von Meyenfeldt MF, et al. The additional diagnostic value of ultrasonography in the diagnosis of breast cancer. *Archives of Internal Medicine* 2003;**163**(10):1194–9.

Grady 2011 *{published data only}*
Grady I, Gorsuch-Rafferty H, Hadley P. Improved cancer diagnostic outcomes obtained through surgeon-performed ultrasound screening. Scientific session abstracts, official proceedings. The American Society of Breast Surgeons 12th Annual Meeting; 2011 April 27 - 7 May; Washington DC. 2011; Vol. 18:No. 1741, page S169.

Hellquist 2011 *{published data only}*
Hellquist BN, Duffy SW, Abdsaleh S, Björneld L, Bordás P, Tabár L, et al. Effectiveness of population-based service screening with mammography for women ages 40 to 49 years: evaluation of the Swedish Mammography Screening in Young Women (SCRY) cohort. *Cancer* 2011;**117**(4): 714–22.

Honjo 2007 *{published data only}*
Honjo S, Ando J, Tsukioka T, Morikubo H, Ichimura M, Sunagawa M, et al. Relative and combined performance of mammography and ultrasonography for breast cancer screening in the general population: a pilot study in Tochigi Prefecture, Japan. *Japanese Journal of Clinical Oncology* 2007;**37**(9):715–20.

Hou 2002 *{published data only}*
Hou MF, Chuang HY, Ou-Yang F, Wang CY, Huang CL, Fan HM, et al. Comparison of breast mammography, sonography and physical examination for screening women at high risk of breast cancer in Taiwan. *Ultrasound in Medicine & Biology* 2002;**28**(4):415–20.

Kaplan 2001 *{published data only}*
Kaplan SS. Clinical utility of bilateral whole-breast US in the evaluation of women with dense breast tissue. *Radiology* 2001;**221**(3):641–9.

Kelly 2010a *{published data only}*
Kelly KM, Dean J, Comulada WS, Lee SJ. Breast cancer detection using automated whole breast ultrasound and mammography in radiographically dense breasts. *European Radiology* 2010;**20**(3):734–42.

Kelly 2010b *{published data only}*
Kelly KM, Dean J, Lee SJ, Comulada WS. Breast cancer detection: radiologists' performance using mammography with and without automated whole-breast ultrasound. *European Radiology* 2010;**20**(11):2557–64.

Kolb 1998 *{published data only}*
Kolb TM, Lichy J, Newhouse JH. Occult cancer in women with dense breasts: detection with screening US--diagnostic yield and tumor characteristics. *Radiology* 1998;**207**(1): 191–9.

Kolb 2002 *{published data only}*
Kolb TM, Lichy J, Newhouse JH. Comparison of the performance of screening mammography, physical examination, and breast US and evaluation of factors that influence them: an analysis of 27,825 patient evaluations. *Radiology* 2002;**225**(1):165–75.

Leconte 2003 *{published data only}*
Leconte I, Feger C, Galant C, Berliere M, Berg BV, D'Hoore W, et al. Mammography and subsequent whole-breast sonography of nonpalpable breast cancers: the importance of radiologic breast density. *American Journal of Roentgenology* 2003;**180**(6):1675–9.

Madjar 1994 *{published data only}*
Madjar H, Makowiec U, Mundinger A, Du Bois A, Kommoss F, Schillinger H. Value of high resolution sonography in breast cancer screening. *Ultraschall in der Medizin* 1994;**15**(1):20–3.

Madjar 2010 *{published data only}*
Madjar H, Becker S, Doubek K, Horchler T, Mendoza M, Moisidis-Tesch C, et al. Impact of breast ultrasound

screening in gynecological practice. *Ultraschall in der Medizin* 2010;**31**(3):289–95.

Maestro 1998 ***{published data only}***
Maestro C, Cazenave F, Marcy PY, Bruneton JN, Chauvel C, Bleuse A. Systematic ultrasonography in asymptomatic dense breasts. *European Journal of Radiology* 1998;**26**(3): 254–6.

Marini 2003 ***{published data only}***
Marini C, Traino C, Cilotti A, Roncella M, Campori G, Bartolozzi C. Differentiation of benign and malignant breast microcalcifications: mammography versus mammography-sonography combination. *La Radiologia Medica* 2003;**105** (1-2):17–26.

McCavert 2009 ***{published data only}***
McCavert M, O'Donnell ME, Aroori S, Badger SA, Sharif MA, Crothers JG, et al. Ultrasound is a useful adjunct to mammography in the assessment of breast tumours in all patients. *International Journal of Clinical Practice* 2009;**63** (11):1589–94.

Meden 1995 ***{published data only}***
Meden H, Neues KP, Röben-Kämpken S, Kuhn W. A clinical, mammographic, sonographic and histologic evaluation of breast cancer. *International Journal of Gynaecology and Obstetrics* 1995;**48**(2):193–9.

Moon 2000 ***{published data only}***
Moon WK, Im JG, Koh YH, Noh DY, Park IA. US of mammographically detected clustered microcalcifications. *Radiology* 2000;**217**(3):849–54.

Moss 1999 ***{published data only}***
Moss HA, Britton PD, Flower CD, Freeman AH, Lomas DJ, Warren RM. How reliable is modern breast imaging in differentiating benign from malignant breast lesions in the symptomatic population?. *Clinical Radiology* 1999;**54**(10): 676–82.

Najafi 2010 ***{published data only}***
Najafi M, Hashemi E, Kaviani A, Beheshtian T, Alavi N, Fonooni L, et al. The additional value of whole-breast ultrasonography in the evaluation of women with mammography-negative dense breast. *European Journal of Cancer Supplements* 2010;**8**(3):235.

Ohlinger 2006 ***{published data only}***
Ohlinger R, Heyer H, Thomas A, Paepke S, Warm H, Klug U, et al. Non-palpable breast lesions in asymptomatic women: diagnostic value of initial ultrasonography and comparison with mammography. *Anticancer Research* 2006; **26**(5B):3943–55.

Rahbar 1999 ***{published data only}***
Rahbar G, Sie AC, Hansen GC, Prince JS, Melany ML, Reynolds HE, et al. Benign versus malignant solid breast masses: US differentiation. *Radiology* 1999;**213**(3):889–94.

Richter 1997 ***{published data only}***
Richter K, Heywang-Kobrunner SH, Winzer KJ, Schmitt KJ, Prihoda H, Frohberg HD, et al. Detection of malignant and benign breast lesions with an automated US system: results in 120 cases. *Radiology* 1997;**205**(3):823–30.

Richter 1998 ***{published data only}***
Richter K, Hamm B, Heywang-Kobrunner SH, Fobbe F, Prihoda H, Schmitt KJ, et al. Automated mammary sonography and mammography: the differentiation of benign and malignant breast lesions. *RöFo : Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin* 1998;**169**(3):245–52.

Tohno 2009 ***{published data only}***
Tohno E, Ueno E, Watanabe H. Ultrasound screening of breast cancer. *Breast Cancer* 2009;**16**(1):18–22.

Uchida 2008 ***{published data only}***
Uchida K, Yamashita A, Kawase K, Kamiya K. Screening ultrasonography revealed 15% of mammographically occult breast cancers. *Breast Cancer* 2008;**15**(2):165–8.

Vercauteren 2008 ***{published data only}***
Vercauteren LD, Kessels AG, van der Weijden T, Koster D, Severens JL, van Engelshoven JM, et al. Clinical impact of the use of additional ultrasonography in diagnostic breast imaging. *European Radiology* 2008;**18**(10):2076–84.

Weining 2005 ***{published data only}***
Weining C, Weining-Klemm O, Barth V. One-view mammography combined with ultrasound mammography versus two-view mammography for examination of the female breast. A new concept for early detection of breast cancer. *Geburtshilfe und Frauenheilkunde* 2005;**65**(3): 289–96.

Youk 2011 ***{published data only}***
Youk JH, Kim EK, Kim MJ, Kwak JY, Son EJ. Performance of hand-held whole-breast ultrasound based on BI-RADS in women with mammographically negative dense breast. *European Radiology* 2011;**21**(4):667–75.

Zanello 2011 ***{published data only}***
Zanello PA, Robim AF, Oliveira TM, Elias Junior J, Andrade JM, Monteiro CR, et al. Breast ultrasound diagnostic performance and outcomes for mass lesions using Breast Imaging Reporting and Data System category 0 mammogram. *Clinics (Sao Paulo)* 2011;**66**(3):443–8.

Zonderland 1999 ***{published data only}***
Zonderland HM, Coerkamp EG, Hermans J, van de Vijver MJ, van Voorthuisen AE. Diagnosis of breast cancer: Contribution of US as an adjunct to mammography. *Radiology* 1999;**213**(2):413–22.

References to ongoing studies

Ohuchi 2011 ***{published data only}***
Ohuchi N, Ishida T, Kawai M, Narikawa Y, Yamamoto S, Sobue T. Randomized controlled trial on effectiveness of ultrasonography screening for breast cancer in women aged 40-49 (J-START): research design. *Japanese Journal of Clinical Oncology* 2011;**41**(2):275–7.

Additional references

Albert 2009
Albert US, Altland H, Duda V, Engel J, Geraedts M, Heywang-Kobrunner S, et al. 2008 update of the guideline:

early detection of breast cancer in Germany. *Journal of Cancer Research and Clinical Oncology* 2009;**135**(3):339–54.

Boyd 2007
Boyd NF, Guo H, Martin LJ, Sun L, Stone J, Fishell E, et al. Mammographic density and the risk and detection of breast cancer. *New England Journal of Medicine* 2007;**356**(3):227–36.

Carney 2003
Carney PA, Miglioretti DL, Yankaskas BC, Kerlikowske K, Rosenberg R, Rutter CM, et al. Individual and combined effects of age, breast density, and hormone replacement therapy use on the accuracy of screening mammography. *Annals of Internal Medicine* 2003;**138**(3):168–75.

Elmore 2005
Elmore JG, Armstrong K, Lehman CD, Fletcher SW. Screening for breast cancer. *JAMA* 2005;**293**(10):1245–56.

Gartlehner 2013
Gartlehner G, Thaler K, Chapman A, Kaminski A, Berzaczy D, VanNoord MG, et al. Adjunct ultrasonography for breast cancer screening in women at average risk: a systematic review. Submitted for publication.

Griffin 2010
Griffin JL, Pearlman MD. Breast cancer screening in women at average risk and high risk. *Obstetrics and Gynecology* 2010;**116**(6):1410–21.

Gøtzsche 2011
Gøtzsche PC, Nielsen M. Screening for breast cancer with mammography. *Cochrane Database of Systematic Reviews* 2011, Issue 4. [DOI: 10.1002/14651858.CD001877.pub2]

Higgins 2011
Higgins JPT, Green S, editors. Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.1 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Michaelson 2002
Michaelson JS, Silverstein M, Wyatt J, Weber G, Moore R, Halpern E, et al. Predicting the survival of patients with breast carcinoma using tumor size. *Cancer* 2002;**95**(4):713–23.

Michaelson 2003
Michaelson JS, Silverstein M, Sgroi D, Cheongsiatmoy JA, Taghian A, Powell S, et al. The effect of tumor size and lymph node status on breast carcinoma lethality. *Cancer* 2003;**98**(10):2133–43.

Nelson 2009
Nelson HD, Tyne K, Naik A, Bougatsos C, Chan BK, Humphrey L, U.S. Preventive Services Task Force. Screening for breast cancer: an update for the U.S. Preventive Services Task Force. *Annals of Internal Medicine* 2009;**151**(10):727-37, W237-42.

Nothacker 2009
Nothacker M, Duda V, Hahn M, Warm M, Degenhardt F, Madjar H, et al. Early detection of breast cancer: benefits and risks of supplemental breast ultrasound in asymptomatic women with mammographically dense breast tissue: A systematic review. *BMC Cancer* 2009;**9**:335.

Perry 2008
Perry N, Broeders M, de Wolf C, Tornberg S, Holland R, von Karsa L. European guidelines for quality assurance in breast cancer screening and diagnosis. Fourth edition--summary document. *Annals of Oncology* 2008;**19**(4):614–22. [PUBMED: 18024988]

RevMan 5.1 [Computer program]
The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). Version 5.1. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2011.

Soderstrom 2005
Soderstrom L, Woods WG, Bernstein M, Robison LL, Tuchman M, Lemieux B. Health and economic benefits of well-designed evaluations: some lessons from evaluating neuroblastoma screening. *Journal of the National Cancer Institute* 2005;**97**(15):1118–24. [PUBMED: 16077069]

USPSTF
United States Preventive Services Task Force. Preventive Services Task Force recommendation statement. *Annals of Internal Medicine* 2009;**151**(10):716-26, W-236. [USPSTF]

Wilson 1968
Wilson JMG, Jungner YG. Principles and practice of mass screening for disease (WHO Public Health Paper 34). Boletin de la Ofina Sanitaria Panamericana, World Health Organization. Geneva: WHO, 1968; Vol. 65, issue 4: 281–393.

World Health Organization 2011
World Health Organization. Breast cancer: prevention and control. Available at: http://www.who.int/cancer/detection/breastcancer/en/index.html 2011 (accessed 15 July 2011).

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Benson 2004	Ineligible population (women with breast cancer)
Berg 2008	Ineligible population (women with elevated risk)
Brancato 2007	Ineligible study design (retrospective cohort study)
Buchberger 1999	Ineligible study design, ineligible outcome (uncontrolled prospective cohort study assessing diagnostic yield)
Buchberger 2000	Ineligible study design, ineligible outcome (uncontrolled prospective cohort study assessing diagnostic yield)
Chan 2008	Ineligible population (women with breast cancer)
Cho 2010	Ineligible population (women with breast cancer)
Corsetti 2006	Ineligible study design (retrospective cohort study)
Corsetti 2008	Ineligible study design (retrospective cohort study)
Corsetti 2011	Ineligible study design (retrospective cohort study)
Crystal 2003	Ineligible population (high-risk women)
De Felice 2007	Ineligible study design (uncontrolled prospective cohort study)
Dilhuydy 2008	Ineligible study design (retrospective analysis of data of the Women's Health Initiative)
Duijm 1997	Ineligible population (symptomatic patients)
Flobbe 2003	Ineligible population (symptomatic patients)
Grady 2011	Ineligible population (high-risk women)
Hellquist 2011	No sonography screening
Honjo 2007	Ineligible study design (uncontrolled cohort study)
Hou 2002	Ineligible population (high-risk women)
Kaplan 2001	Ineligible study design (retrospective cohort study)
Kelly 2010a	Ineligible study design (uncontrolled cohort study)

(*Continued*)

Kelly 2010b	Ineligible study design (uncontrolled cohort study)
Kolb 1998	Ineligible study design (uncontrolled retrospective cohort study)
Kolb 2002	Ineligible study design (uncontrolled cohort study)
Leconte 2003	Ineligible population (symptomatic patients)
Madjar 1994	Ineligible study design (uncontrolled prospective cohort study)
Madjar 2010	Ineligible study design (uncontrolled retrospective cohort study)
Maestro 1998	Ineligible study design (uncontrolled prospective cohort study)
Marini 2003	Ineligible population (women with microcalcifications)
McCavert 2009	Ineligible population (symptomatic patients)
Meden 1995	Ineligible population (symptomatic patients)
Moon 2000	Ineligible population (women with microcalcifications)
Moss 1999	Ineligible population (symptomatic patients)
Najafi 2010	Published as abstract only
Ohlinger 2006	Ineligible outcome (diagnostic yield)
Rahbar 1999	Ineligible population (symptomatic patients)
Richter 1997	Ineligible population (symptomatic patients)
Richter 1998	Ineligible population (symptomatic patients)
Tohno 2009	Ineligible study design (uncontrolled retrospective cohort study)
Uchida 2008	Ineligible study design, ineligible outcome (uncontrolled, retrospective cohort study comparing the diagnostic yield of mammography, ultrasonography and physical examination)
Vercauteren 2008	Ineligible population (symptomatic patients)
Weining 2005	Ineligible population (symptomatic patients)
Youk 2011	Ineligible population (symptomatic patients)
Zanello 2011	Ineligible population (symptomatic patients)

(*Continued*)

Zonderland 1999	Ineligible population (symptomatic patients)

Characteristics of ongoing studies *[ordered by study ID]*

Ohuchi 2011

Trial name or title	Randomized controlled trial on effectiveness of ultrasonography screening for breast cancer in women aged 40-49 (J-START)
Methods	RCT
Participants	Women ages 40 to 49 years
Interventions	Mammography versus mammography plus ultrasonography
Outcomes	Sensitivity, specificity, false positive rates
Starting date	2011
Contact information	Yoko Narikawa at narikawayoko@gmail.com
Notes	Trial information: http://apps.who.int/trialsearch/Trial.aspx?TrialID=JPRN-UMIN000000757

RCT: randomised controlled trial

DATA AND ANALYSES

This review has no analyses.

APPENDICES

Appendix 1. MEDLINE (via OVID) search strategy February 2012

#	Searches
1	exp Breast Neoplasms/
2	breast cancer.mp.
3	1 or 2
4	exp Diagnosis/
5	diagnosis.ab,ti,tw.
6	screening.ab,ti,tw.
7	exp Mass Screening/
8	mass screening.ab,ti,tw.
9	exp "Early Detection of Cancer"/
10	4 or 5 or 6 or 7 or 8 or 9
11	3 and 10
12	exp Mammography/
13	mammograph*.ab,ti,tw.
14	mammogram.ab,ti,tw.
15	12 or 13 or 14
16	exp Ultrasonography/
17	exp Ultrasonography, Mammary/
18	breast ultrasonography.mp.

(*Continued*)

19	mammary ultrasonography.mp.
20	16 or 17 or 18 or 19
21	mammary.ab,ti,tw.
22	breast.ab,ti,tw.
23	21 or 22
24	20 and 23
25	11 and 15 and 24
26	limit 25 to humans
27	limit 26 to (clinical trial, all or clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or clinical trial or comparative study or controlled clinical trial or evaluation studies or meta analysis or multicenter study or randomized controlled trial or "review" or validation studies)
28	("Single Blind Method" or "Double Blind Method" or "Case Control Study" or "Cohort Study" or "Epidemiologic Study" or "Cross Sectional Study" or "Cross Over Study" or "Follow Up Study" or "Longitudinal Study" or "Prospective Study" or "observational study").mp. [mp=title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
29	26 and 28
30	**27 or 29**

Appendix 2. EMBASE (via Embase.com) search strategy

#25 #24 AND [humans]/lim AND [embase]/lim AND [2008-2012]/py
#24 #8 AND #12 AND #23
#23 #21 AND #22
#22 'breast cancer screening'
#21 #18 OR #20

(*Continued*)

#20 #18 AND #19
#19 #15 OR #16 OR #17
#18 #13 OR #14
#17 'breast'/de OR breast AND ultrasonograph*
#16 'breast ultrasonography'/exp OR 'breast ultrasonography'
#15 'ultrasonography'/exp OR ultrasonography
#14 mammograph*
#13 'mammography'/exp OR mammography
#12 #9 OR #10 OR #11
#11 'breast cancer risks'
#10 'breast cancer risk'
#9 'breast neoplasm'
#8 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7
#7 groups:ab
#6 trial:ab
#5 randomly:ab

(*Continued*)

#4 placebo:ab
#3 randomi*ed:ab
#2 controlled AND clinical AND trial
#1 randomised AND controlled AND trial

Appendix 3. WHO ICTRP search strategy

Advanced search:
1. Title: mammography in combination with breast ultrasonography versus mammography for breast cancer screening
Recruitment Status: ALL
2. Condition: breast AND (cancer% OR carcinoma% OR neoplas% OR tumour% OR tumor%)
Intervention: (breast mammograph% OR breast ultrasonograph%) AND breast screening
Recruitment Status: ALL

CONTRIBUTIONS OF AUTHORS

1. Draft the protocol: GG, KT
2. Study selection: GG, KT, AC, AK, TH, DB, MvN
3. Extract data from studies: GG, KT, AC, AK
4. Enter data into RevMan: AC, MvN
5. Carry out the analysis: GG, KT
6. Interpret the analysis: GG, KT, TH
7. Draft the final review: GG, KT
8. Disagreement resolution: TH
9. Update the review: GG, KT

DECLARATIONS OF INTEREST

None known.

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Internal sources

- No sources of support, Not specified.

External sources

- Ministry of Health, Austria.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

None.

INDEX TERMS

Medical Subject Headings (MeSH)

Breast Neoplasms [*radiography; *ultrasonography]; Early Detection of Cancer [*methods]; Mammography [*methods]; Ultrasonography, Mammary [*methods]

MeSH check words

Female; Humans