Breast Cancer Screening

PHAC Scientific Officer:
S. Connor Gorber

D. Ciliska & P. Raina
McMaster Evidence Review and Synthesis Centre

Consultant: N. Hodgson

Project Staff: M. Gauld, D. Fitzpatrick-Lewis, M Rice
McMaster University
Hamilton Ontario Canada

CFTPC Leads:
M. Tonelli and R. Birtwhistle,

April 5, 2010

Work Plan

Contents:

1. Purpose and Background

Purpose

The purpose of this review is to provide an update of the 2001 Canadian Task Force recommendations on breast cancer screening (Baxter with the Canadian Task Force on Preventive Health Care, 2001; Ringash with the Canadian Task Force on Preventive Health Care, 2001). Previous reviews found fair evidence for mammography every 1-2 years for women 40 years of age and olde; with benefits increasing and harms decreasing with age. Identified gaps included estimates of proportion of benefits due to screening and cost-effectiveness of screening before age 50 and after age 69 (Ringash et al., 2001; Nelson, Tyne, Nalk et al, 2009a). The goal is to determine the effectiveness of mammography screening in decreasing breast cancer mortality among average-risk women aged 40 to 49 years and 70 years or older, the effectiveness of clinical breast examination and breast self-examination, and the harms of screening. Comparison data from women aged 50-69 will be included.

The US Preventive Service Task Force (USPSTF) updated their 2002 guidelines in 2009 (Nelson, et al., 2009a). The 2009 update had key differences compared to the 2002 guidelines in terms of the populations recommended to receive mammography. The absence of current Canadian recommendations and the differences between the 2002 and 2009 USPSTF recommendations were the basis for selecting this topic for an update by the revitalized Canadian Task Force in 2010.

Condition Background

1. Definition

Breast cancer is a proliferation of malignant cells that arise in breast tissue and represents a continuum of conditions ranging from noninvasive to invasive carcinoma (Simpson & Wilkinson, 2004). The most common form is ductal carcinoma; there are a number of other subtypes of noninvasive and invasive lesions.

Noninvasive carcinomas are epithelial proliferation of the mammary duct (ductal carcinoma in situ [DCIS], or of the lobule (lobular carcinoma in situ [LCIS]). Noninvasive lesions do not metastasize; however, DCIS is considered to be a precursor lesion for invasive ductal carcinoma, while LCIS is not a precursor lesion (a bystander lesion found incidentally on biopsies), but considered to be a marker of increased risk of invasive ductal or lobular breast cancer. DCIS has several subtypes including cribriform, comedo, micropapillary, papillary and solid (Page & Langios, 2004).

Invasive lesions have metastatic potential as they invade the basement membrane into the adjacent stroma. The most common sites of metastasis include adjacent lymph nodes, bone, liver, lung, and brain. Approximately 80-90% of invasive breast cancers are invasive ductal and 10% are invasive lobular carcinoma, the are remainder special types (i.e mucinous, tubular, adenoid cystic etc) (Simpson & Wilkinson, 2004).

2. Prevalence and burden of disease

In Canada in 2009, there were an estimated 22,700 new cases of breast cancer and 5,400 deaths from breast cancer (Canadian Cancer Society's Steering Committee, 2009). For women aged 20-59 years, breast cancer was the most common form of cancer and most common cause of cancer death. Twenty-nine percent of new breast cancer cases diagnosed in Canadian women were for those over age 69, and 20% were in women under 50 years of age. There is little variation by province. Since 1986, age-standardized mortality rates have fallen 30% (from 32 to 22 per 100,000) likely due to higher rates of screening and use of more effective therapies following breast cancer surgery (Canadian Cancer Society's Steering Committee, 2009).

3. Etiology and natural history

Breast cancer development is attributed to dysfunction in cell cycle regulation. Inherited and acquired mutations may influence the cycle. The majority of breast cancers are sporadic (over 95%) About 5% of breast cancers can be attributed to mutations in the genes *BRCA1* and *BRCA2,* but other genes have also been studied.

Environmental exposures to hormones, diet, and viruses may play a role, but no single factor has been isolated (Amarante, & Watanabe, 2009; Cade, Taylor, Burley, & Greenwood, 2010; Collins, Blake, & Crosignani, 2005). The precise role these factors play in tumor development is not clear, but each factor may be responsible for different steps of a series required to create malignant cells (Amarante, & Watanabe, 2009).

Information about the natural history of DCIS is lacking because it historically was treated by mastectomy (Allegra, Aberle, Ganschow, et al. (2009). DCIS can recur or progress to invasive breast cancer, which has led to two conflicting models to explain the relationship between DCIS and invasive cancer: *parallel disease* and *linear progression*. The relationship is probably more complex, and both models may occur simultaneously.

This co-occurrence is supported by different studies, including immunohistochemical analysis and gene expression profiling (Wiechmann, & Kuerer, 2008).

4. Consequences if left untreated

Different types of breast cancer have different growth rates, dependent on tumor biology. There are few reports of untreated patients; however, poor survival is characteristic of locally advanced breast cancer. Erbas and colleagues (2006), reviewed studies where DCIS was initially misdiagnosed as benign and treated by biopsy alone; 14-53% of patients with DCIS progressed to a diagnosis of invasive cancer over a period of 10 or more years.

5. Risk factors

The most important risk factors for breast cancer are sex and age. Past history of noninvasive breast cancer or previous abnormal biopsy containing LCIS or atypical ductal hyperplasia (ADH) increase the risk of invasive cancer (Li et al, 2006). Strength of family history as a risk factor for breast cancer is related to number of relatives affected, degree of the relationship and age at diagnosis of family members (Nelson, Huffman, Fu, et al., 2005).

Endogenous estrogen exposure is related to risk; early age at menarche, older age at menopause, postmenopausal HRT, and postmenopausal obesity are all associated with increased risk. Other risk factors such as environmental exposures to radiation, therapeutic radiation commonly given for lymphoma) and excess alcohol intake have been documented (Nelson, Tyne, Nalk, et al, 2009b).

6. Rationale for screening

There is widespread acceptance of the value of regular breast cancer screening as the single most important public health strategy to reduce breast cancer mortality. Mammography, clinical breast exam and self-breast exam can all identify tumors. Mammography can identify asymptomatic breast cancer. Breast cancer can be more effectively treated at the asymptomatic stage. A recent systematic review concluded that screening is likely to reduce breast cancer mortality by an estimated 15% reduction, corresponding with an absolute risk reduction of 0.05% (Gøtzsche, & Nielsen, 2009). However, other outcomes such as disease free survival and quality of life are important.

7. Screening strategies

The screening strategies considered in this review are mammography, self-exam (BSE) and clinical exam (CBE). Mammography screening is sensitive (77-95%), but with lower

sensitivity for women under age 50 (58-85%); it is specific (94-97%) and acceptable to most women (Nelson at al, 2009b). Mammography is in the process of shifting from plain film to digital technologies.

BSE and CBE have been promoted as inexpensive screening strategies. Breast self-exam has been suggested as a monthly examination of the woman's breasts. There are varying estimates of the sensitivity (12-41%) (Nelson et al., 2009b); specificity has been estimated between 66%–81% (Vahabi, 2003). Baxter (2001) found that in women who regularly performed BSE, many tumors were found incidentally, not upon self-examination; only 7.6% of women with tumors, who were regularly practicing BSE, actually detected their tumors.

Clinical breast exam is examination of the breasts by a health professional. Effectiveness of examination of the breasts by clinicians is highly influenced by the training and skills of the practitioner, age of the woman and tumor size. CBE sensitivity ranges from 40-69%, specificity from 88-99%, and positive predictive value at 4-50% (Nelson et al, 2009b).

Outcomes of breast cancer screening such as tumor detection and mortality must be put into context of costs to the individual and to the health care system, as well as the individual and health care system costs of over-diagnosis and over-treatment. Consideration of benefits, harms and costs, is complicated by variations in risk factors, type and stage of cancer. Any positive finding of screening has emotional costs such as anxiety and worry for patients and their families, and financial costs to the individual and health care system as a result of additional diagnostic tests. One review found that screening led up to 30% over-diagnosis and overtreatment (Gøtzsche, & Nielsen, 2009). One of two large trials comparing BSE with no intervention found increased detection of tumors, but neither study found differences in breast cancer mortality (Kösters, & Gøtzsche 2003). Few studies have assessed clinical breast exam and those that exist have found no difference in mortality (Nelson et al, 2009a).

Mammography screening is widely available in urban areas in Canada, with some mobile clinics for more rural areas. Cost calculations must consider the overall program cost, cost per screening exam, cost per cancer detected and, ultimately, overall cost-effectiveness, as measured by the cost per year of life gained. In 1996/97 costs in British Columbia; the cost per screening exam was $45.94, the cost per cancer detected was $15,211, and the total provincial costs for mammography screening were approximately $14 million (Olivotto, Kan, Mates, & King, 1999).

Ahern and Shen (2009) compared cost-effectiveness of mammography with CBE. The US Preventive Services Task Force recommendation (mammography and clinical breast exam in alternating years from ages 40 to 79 years) was a cost-effective strategy, costing $35,500 per quality adjusted life year (QALY) saved compared with no screening. The American Cancer Society guideline (yearly mammography and yearly CBE) was the most effective and the most expensive, costing over $680,000 for an added QALY compared with no screening.

8. Interventions/treatments

Women with positives finding on BSE, CBE or mammography will be recommended to undergo additional diagnostic tests, which may include further mammography, ultrasound, MRI, and/or tissue sampling via needle core biopsy. Tissue testing includes identification of tumor type and preliminary grade, as well as examination of cellular receptors (Nelson et al, 2009b).

The goal of therapy is to improve survival, reduce recurrence, delay disease progression, maximize the patient's quality of life, and to support the patient and family. Treatment usually requires combinations of therapy, including surgery, chemotherapy, hormonal therapy, and radiation, depending on type and stage of cancer (Nelson et al, 2009b).

9. Current clinical practice.

In Canada, several guidelines exist recommending that women aged 50 and older have a screening mammogram every two years, and that women 40-49 talk to their health care provider to make a personal decision about mammography (Public Health Agency of Canada, 2005; Toward Optimized Practice; 2007). However, only 33.9% of eligible women accessed organized screening nationally, leaving unmet the target of at least 70% participation among women aged 50 to 69 (Public Health Agency of Canada, 2005).

Abdel-Malek and colleagues (2008) conducted a cross-sectional study of Ontario active general and family physicians. Adherence to screening was defined as recommending screening to women aged 50-69 every two years. Only 38.9% of physicians followed recommended breast screening guidelines. After adjusting for physician sex and age, predictors of screening adherence included physicians working in academic or research centers (OR 8.3, 95% CI 1.7-39.7), and those reporting that over 31% of their patients were of low-income (OR 1.6, 95% CI 1.1-2.4). Those physicians located in a large city (>100 000 people) versus a rural/town (<10 000 people), were less likely to adhere to screening guidelines (OR 0.5, 95% CI 0.3-0.7). The two reports are consistent in estimating that about one third of women in Canada between the ages of 50-69 received the breast screening as recommended.

2. Previous Review and CTFPHC Recommendations

In 1994, the Canadian Task Force on the Periodic Health Exam published a guideline on breast cancer screening (Morison, 1994). In 2001, it was updated in two separate publications: screening mammography among women age 40-49 years at average risk of breast cancer (Ringash, 2001), and routine teaching of breast self-examination for breast cancer (Baxter, 2001). The first concluded that the evidence did not support inclusion or exclusion of screening mammography for women 40-49 years of age at average risk of breast cancer (Grade C recommendation). With regard to teaching breast self-examination (BSE) to screen for breast cancer, the recommendations were that:

1) women 40-49 and 50-59 years – routine teaching of BSE be excluded from the periodic health exam (grade D recommendation)
2) women <40 years and >69 years – insufficient evidence to make a recommendation

In 2002, The USPSTF recommended mammography screening, with or without clinical breast examination every 1-2 years for women aged 40 or older, and concluded that evidence was insufficient to recommend for or against routine clinical breast examination (CBE) alone and for or against teaching or performing routine BSE. The 2009 update found:

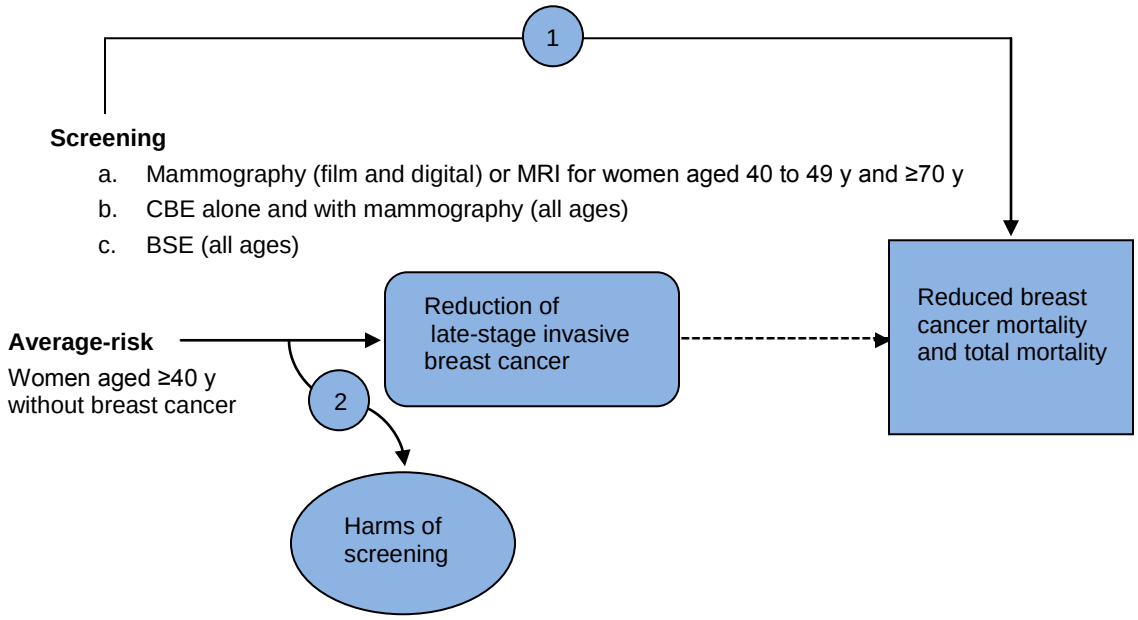
- mammography screening reduces breast cancer mortality by 15% for women aged 39-49 years (RR 0.85, 95% credible interval 0.75 to 0.96); data are lacking for women 70 years and older;
- radiation exposure from mammography is low;
- adverse experiences are common and transient;
- estimates of over diagnosis vary from 1% to 10%
- younger women have more false-positive results and additional imaging but fewer biopsies than older women (Nelson et al, 2009a).

The absence of current Canadian recommendations and the differences between the 2002 and 2009 USPSTF recommendations were the basis for selecting this topic for an update by the revitalized Canadian Task Force in 2010.

3. Analytic framework

Screening for Breast Cancer

Appendix Figure 1. Analytic framework and key questions.



4. Key Questions

1a. Does screening with mammography (film and digital) or MRI decrease breast cancer mortality among women aged 40 to 49 y and >70 y?

1b. Does CBE screening decrease breast cancer mortality? Alone or with mammography?

1c. Does BSE practice decrease breast cancer mortality?

2a. What are the harms associated with screening with mammography (film and digital) and MRI?

2b. What are the harms associated with CBE?

2c. What are the harms associated with BSE?

Also cost-effectiveness of screening will be explored as a contextual question.

5. Literature search and review

USPSTF (Nelson et al, 2009a) searched The Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews (through the fourth quarter of

2008), MEDLINE® (January 2001 to December1, 2008), reference lists, and Web of Science searches for published studies and Breast Cancer Surveillance Consortium for screening mammography data. There were separate searches for screening, digital mammography, MRI, ductal carcinoma in situ (DCIS), adverse effects, and costs. The same search terms and databases will be used, and all searches will be updated to March 10, 2010. Only one search strategy will be altered and that was that the limits on study methods will be removed in Medline, allowing for randomized controlled trials, meta-analyses, and systematic reviews to be left in the search. As an update, we will accept that EMBASE will not be searched, and will acknowledge that in the limitations of this review.

6. Inclusion/ Exclusion Criteria

The following inclusion criteria were established:

Methods -Randomized controlled trials, meta-analyses with breast cancer mortality outcomes for screening effectiveness
- studies of various designs and multiple data sources for harms.

Population - women, age 40-49 or >70 years, without preexisting breast cancer and not considered to be at high risk for breast cancer on the basis of extensive family history of breast or ovarian cancer or other personal risk factors, such as abnormal breast pathology or deleterious genetic mutations.

Harms - radiation exposure, pain during procedures, patient anxiety and other psychological responses, consequences of false-positive and false-negative test results, and over diagnosis (women receiving a diagnosis of invasive or noninvasive breast cancer who had abnormal lesions that were unlikely to become clinically evident during their lifetimes in the absence of screening).

Screening methods – MRI, clinical breast examination, self breast examination, mammography

Follow-up - minimum 10 years

Outcome ascertainment >90% complete

Language - English, French

7. Quality and strength of evidence criteria

The retrieved included studies will be reviewed according to the criteria set out in the CTFPHC Procedure Manual (Feightner, 2009), Appendices VII and VIII.

References

Abdel-Malek, N, Chiarelli, A.M., Sloan, M., Stewart, D.E., Mai, V., Howlett, R.I. (2008) Influence of physician and patient characteristics on adherence to breast cancer screening recommendations. *European Journal of Cancer Prevention, 17*(1), 48-53.

Ahern, C.H., & Shen, Y. (2009). Cost-Effectiveness Analysis of Mammography and Clinical Breast Examination Strategies: A Comparison with Current Guidelines. *Cancer Epidemiology, Biomarkers and Prevention, 18*(3), 8–25.

Allegra, C.J., Aberle, D.R., Ganschow, P., Hahn, S.M., Lee, C.N., et al. (2009). National Institutes of Health State-of-the-Science Conference statement: Diagnosis and Management of Ductal Carcinoma In Situ September 22-24, 2009. *Journal of the National Cancer Institute, 102*(3),161-169.

Amarante, M.K., & Watanabe, M.A.E. (2009). The possible involvement of virus in breast cancer. *Journal of Cancer Research and Clinical Oncology, 135*, 329–337.

Baxter, N. with the Canadian Task Force on Preventive Health Care (2001). Preventive health care, 2001 update: Should women be routinely taught breast self-examination to screen for breast cancer? *Canadian Medical Association Journal, 164* (13), 1837-1846.

Cade, J.E., Taylor, E.F., Burley, V.J., & Greenwood, D.C. (2010). Common Dietary Patterns and Risk of Breast Cancer: Analysis From the United Kingdom Women's Cohort Study. *Nutrition and Cancer, 62*(3), 300-6.

Canadian Cancer Society's Steering Committee (2009). *Canadian Cancer Statistics 2009.* Toronto: Canadian Cancer Society, 2009. Retrieved March 2010 from http://www.cancer.ca/canada-wide/about%20cancer/cancer%20statistics.aspx?sc_lang=en

Collins, J.A., Blake, J.M., & Crosignani, P.G. (2005). Breast cancer risk with postmenopausal hormonal treatment. *Human Reproduction Update, 11*(6), 545-560.

Erbas, B., Provenzano, E., Armes, J., & Gertig D. (2006). The natural history of ductal carcinoma in situ of the breast: a review. *Breast Cancer Research and Treatment, 97*(2), 135-144.

Feightner, J.W. (2009). *Procedure Manual*. Ottawa: Canadian Task Force on Preventive Health Care.

Gøtzsche, P.C., & Nielsen, M. (2009). Screening for breast cancer with mammography. *Cochrane Database of Systematic Reviews, 4,* Art. No.: CD001877. DOI: 10.1002/14651858.CD001877.

Kösters JP, & Gøtzsche PC. (2003). Regular self-examination or clinical examination for early detection of breast cancer. *Cochrane Database of Systematic Reviews, 2,* Art. No.: CD003373. DOI: 10.1002/14651858.CD003373.

Li, C.I., Malone, K.E., Saltzman, B.S., & Daling, J.R. (2006). Risk of invasive breast carcinoma among women diagnosed with ductal carcinoma in situ and lobular carcinoma in situ, 1988-2001. *Cancer, 106*(10), 2104-2112.

Morison, B. (1994). Breast cancer screening. In: Canadian Task Force on Preventive Health Care. *The Canadian Guide to Clinical Preventive Health Care.* Ottawa: Canada Communication Group, 787-795.

Nelson, H.D., Huffman, L.H., Fu, R., et al. (2005). Genetic risk assessment nad BRCA mutation testing for breast and ovarian cancer susceptibility: a systematic evidence review for the US Preventive Services Task Force. *Annals of Internal Medicine, 143*(5), 362-379.

Nelson, H.D., Tyne, K., Nalk, A., Bougatsos, C., Chan, B., & Humphrey, L, (2009a). Screening for breast cancer: an update for the U.S. Preventive Services Task Force. *Annals of Internal Medicine, 151*(10), 727-737.

Nelson, H.D., Tyne, K., Nalk, A., Bougatsos, C., Chan, B., & Humphrey, L, (2009b). *Screening for breast cancer: Systematic evidence review update for the U.S. Preventive Services Task Force*. Evidence review Update No. 74. AHRQ Publication No. 10-05142-EF-1. Rochville, Maryland: Agency for Healthcare Research and Quality.

Olivotto, I.A., Kan, L. Mates, D., & King, S. (1999). Screening Mammography Program of British Columbia: pattern of use and health care system costs. *CMAJ, 160* (3), 337-341.

Page, D.L., & Langios, M.D. (2004). In situ carcinomas of the breast: Ductal carcinoma in situ, Piaget's disease, lobular carcinoma in situ. In K.I. Bland, J.F. Simpson & E.J. Wilkinson (Eds.). *The Breast: Comprehensive Management of Benign and Malignant Disorders. St*. Louis: Saunders.

Public Health Agency of Canada, (2005). *Organized Breast Cancer Screening Programs in Canada: Report on program performance in 2001 and 2002*. Ottawa: Public Health Agency of Canada. Retrieved march 2010 from: http://www.phac-aspc.gc.ca/publicat/obcsp-podcs01/pdf/Breast-En_2001-2002.pdf

Ringash, J. with the Canadian Task Force on Preventive Health Care (2001). Preventive health care, 2001 update: screening mammography among women aged 40-49 years at average risk of breast cancer. *Canadian Medical Association Journal, 164* (4), 469-476.

Saslo, D., Boetes, C., Burke, W., et al, (2007). American Cancer Society guidelines for breast screein gwith MRI as an adjunct to mammography. *CA: A Cancer Journal for Clinicians, 57*(2), 75-89.

Simpson, J.F. & Wilkinson, E.J. (2004). Malingant neoplasia of the breast: infiltrating carcinomas. In K.I. Bland, J.F. Simpson & E.J. Wilkinson (Eds.). *The Breast: Comprehensive Management of Benign and Malignant Disorders.* St. Louis: Saunders.

Toward Optimized Practice (2007). Guideline for Early Detection of Breast Cancer. Alberta Medical Association. Retrieved March 2010 from http://www.topalbertadoctors.org/informed_practice/clinical_practice_guidelines/complete%20set/Breast%20Cancer/breast_cancer_guideline.pdf

Vahabi, M. (2003). Breast cancer screening methods: a review of the evidence. *Health Care for Women International, 24(*9), 773-793.

Wiechmann, L, & Kuerer, H.M. (2008).The molecular journey from ductal carcinoma in situ to invasive breast cancer. *Cancer, 112*(10), 2130-42.

Appendix 1: Search Terms

Screening:

Medline
March 2 2010
1. exp breast neoplasms/
2. exp neoplasms/di
3. exp breast/
4. 2 and 3
5. 1 or 4
6. exp mass screening/
7. (screen$ or (rountine$ adj3 (test$ or check$ or diagnos$ or detect$))).mp.
8. 6 or 7
9. 5 and 8
10. exp physical examination/
11. exp breast/
12. exp breast neoplasms/
13. 11 or 12
14. 10 and 13
15. exp mammography/
16. 9 and 14
17. 9 and 15
18. exp mortality/
19. mo.fs.
20. 18 or 19
21. 16 and 20
22. 17 and 20
23. 21 or 22
24. limit 23 to (english language and humans)
25. limit 24 to (meta analysis or practice guideline or randomized controlled trial)
26. (random$ or rct).mp.
27. 24 and 26
28. (meta-analy$ or metaanaly$ or (systematic$ adj10 review$)).mp.
29. 24 and 28
30. 25 or 27 or 29
31. 24 not 30
32. limit 31 to ed=20081101-20100302
33. limit 30 to ed=20081101-20100302

Cochrane Central
March 3 2010
1. ((breast$ or mammary) adj3 (neoplas$ or tumor$ or cancer$ or carcinom$)).mp.
2. (screen$ or (rountine$ adj3 (test$ or check$ or diagnos$ or detect$))).mp.
3. ((clinical$ or physical$) adj3 (exam$ or detect$ or diagnos$)).mp.

4. 2 or 3
5. 1 and 4
6. limit 5 to yr="2008 -Current"

Cochrane Database of Systematic Reviews
March 3 2010
1. ((breast$ or mammary) adj3 (neoplas$ or tumor$ or cancer$ or carcinom$)).mp.
2. (screen$ or (rountine$ adj3 (test$ or check$ or diagnos$ or detect$))).mp.
3. ((clinical$ or physical$) adj3 (exam$ or detect$ or diagnos$)).mp.
4. 2 or 3
5. 1 and 4
6. limit 5 to last 2 years
7. ((breast$ or mammary) adj3 (neoplas$ or tumor$ or cancer$ or carcinom$)).kw.
8. 1 not 7
9. 4 and 7
10. limit 9 to last 2 years

Digital Mammography:

MERSC_DigitalBreastScreening_medline
March 2 2010
1. exp breast neoplasms/
2. exp neoplasms/di
3. exp breast/
4. 2 and 3
5. 1 or 4
6. exp mass screening/
7. (screen$ or (rountine$ adj3 (test$ or check$ or diagnos$ or detect$))).mp.
8. 6 or 7
9. 5 and 8
10. exp physical examination/
11. exp breast/
12. exp breast neoplasms/
13. 11 or 12
14. 10 and 13
15. exp mammography/
16. 9 and 14
17. 9 and 15
18. 16 or 17
19. (digital$ adj7 mammogra$).mp.
20. exp image processing, computer-assisted/
21. exp mammography/
22. 20 and 21
23. 19 or 22

24. 8 and 23
25. limit 24 to english language
26. limit 25 to ed=20081101-20100302

Cochrane Central
March 3 2010
1. ((digital$ or computer$) adj7 mammogra$).mp.
2. limit 1 to yr="2008 -Current"

Cochrane Database of Systematic Reviews
March 3 2010
1. ((digital$ or computer$) adj7 mammogra$).mp.
2. limit 1 to yr="2008 -Current"

MRI
Medline
March 2 2010
1. exp breast neoplasms/
2. exp neoplasms/di
3. exp breast/
4. 2 and 3
5. 1 or 4
6. exp mass screening/
7. (screen$ or (rountine$ adj3 (test$ or check$ or diagnos$ or detect$))).mp.
8. 6 or 7
9. 5 and 8
10. exp physical examination/
11. exp breast/
12. exp breast neoplasms/
13. 11 or 12
14. 10 and 13
15. exp mammography/
16. 9 and 14
17. 9 and 15
18. 16 or 17
19. exp magnetic resonance imaging/
20. 5 and 19
21. 8 and 20
22. limit 21 to ed=20081101-20100302

Cochrane Central
March 3 2010
1. ((breast$ or mammary) adj3 (neoplas$ or tumor$ or cancer$ or carcinom$)).mp.
2. (mri or magnetic resonance imag$).mp.

3. 1 and 2
4. limit 3 to yr="2008 -Current"

Cochrane Database of Systematic Reviews
March 3 2010
1. ((breast$ or mammary) adj3 (neoplas$ or tumor$ or cancer$ or carcinom$)).mp.
2. (mri or magnetic resonance imag$).mp.
3. 1 and 2
4. limit 3 to yr="2008 -Current"

DCIS

Medline
March 2 2010
1. exp carcinoma, intraductal, noninfiltrating/
2. exp breast neoplasms/
3. 1 and 2
4. overdiagnos$.mp.
5. over-diagnos$.mp.
6. (overtreat$ or over-treat$).mp.
7. exp Diagnostic errors/
8. exp mass screening/
9. exp mammography/
10. 8 or 9
11. 3 and 7 and 10
12. 4 or 5 or 6
13. 3 and 12
14. limit 13 to ed=20081101-20100302

Adverse Effects

Medline
March 2 2010
1. exp mammography/
2. exp physical examination/
3. exp mass screening/
4. 1 or 2 or 3
5. exp breast/
6. exp breast diseases/di, ep
7. 5 or 6
8. 4 and 7
9. exp mammography/ae, ct

10. exp physical examination/ae, ct
11. exp mass screening/ae, ct
12. 9 or 10 or 11
13. 7 and 12
14. exp diagnostic errors/
15. (overtest$ or overdiagnos$ or over-test$ or over-diagnos$).mp.
16. misdiagnos$.mp.
17. (false$ adj (positiv$ or negativ$)).mp.
18. ((incorrect$ or false$ or wrong$ or bias$ or mistake$ or error$ or erroneous$) adj3 (result$ or finding$ or test$ or diagnos$)).mp.
19. ((inappropriat$ or unnecess$ or unneed$) adj3 (treat$ or Surg$ or therap$ or regimen$)).mp.
20. (observ$ adj3 bias$).mp.
21. or/14-20
22. 8 and 21
23. exp "wounds and Injuries"/ci, et
24. exp stress, psychological/
25. exp prejudice/
26. exp stereotyping/
27. or/23-26
28. 8 and 27
29. 13 or 22 or 28
30. limit 29 to english language
31. limit 30 to (meta analysis or randomized controlled trial)
32. exp evaluation studies/
33. comparative study.pt.
34. exp epidemiologic studies/
35. 32 or 33 or 34
36. 30 and 35
37. 31 or 36
38. limit 37 to ed=20081101-20100302

Cochrane Central
March 4 2010
1. exp mammography/
2. mammogra$.mp.
3. exp physical examination/
4. ((physical$ or clinical$ or manual$) adj3 exam$).mp.
5. exp mass screening/
6. screen$.mp.
7. or/1-6
8. exp breast/
9. exp breast diseases/di, ep
10. (breast$ or mammar$).mp.
11. or/8-10
12. 7 and 11

13. ((advers$ adj3 effect$) or harm$ or contraindicat$).mp.
14. ae.fs.
15. or/13-14
16. 12 and 15
17. exp mammography/ae, ct
18. exp physical examination/ae, ct
19. exp mass screening/ae, ct
20. or/17-19
21. 11 and 20
22. exp diagnostic errors/
23. (overtest$ or overdiagnos$ or over-test$ or over-diagnos$).mp.
24. (false$ adj (result$ or positiv$ or negativ$)).mp.
25. (observ$ adj3 bias$).mp.
26. (diagnos$ adj3 (error$ or mistak$ or incorrect$)).mp.
27. or/22-26
28. 12 and 27
29. exp "wounds and Injuries"/ci, et
30. exp stress, psychological/
31. exp prejudice/
32. exp stereotyping/
33. (anxiet$ or anxious$ or fear$ or discriminat$ or unfair$ or prejudic$ or stigma$ or stereotyp$).mp.
34. or/29-33
35. 12 and 34
36. 16 or 21 or 28 or 35
37. limit 36 to yr="2008 -Current"

Cost
Medline
March 2 2010
1. exp breast neoplasms/
2. exp neoplasms/di
3. exp breast/
4. 2 and 3
5. 1 or 4
6. exp mass screening/
7. (screen$ or (rountine$ adj3 (test$ or check$ or diagnos$ or detect$))).mp.
8. 6 or 7
9. 5 and 8
10. exp physical examination/
11. exp breast/
12. exp breast neoplasms/
13. 11 or 12
14. 10 and 13
15. exp mammography/
16. 9 and 14

17. 9 and 15
18. 16 or 17
19. exp "Costs and Cost Analysis"/
20. 18 and 19
21. limit 20 to english language
22. limit 21 to ed=20081101-20100302

Cochrane Central
March 5 2010
1. ((breast$ or mammary) adj3 (neoplas$ or tumor$ or cancer$ or carcinom$)).mp.
2. (screen$ or (rountine$ adj3 (test$ or check$ or diagnos$ or detect$))).mp.
3. ((clinical$ or physical$) adj3 (exam$ or detect$ or diagnos$)).mp.
4. (cost or costs or costing or economic$ or financial$).mp.
5. 1 and (2 or 3) and 4
6. limit 5 to yr="2008 -Current"

Cochrane Database of Systematic Reviews
March 5 2010
1. ((breast$ or mammary) adj3 (neoplas$ or tumor$ or cancer$ or carcinom$)).mp.
2. (screen$ or (rountine$ adj3 (test$ or check$ or diagnos$ or detect$))).mp.
3. ((clinical$ or physical$) adj3 (exam$ or detect$ or diagnos$)).mp.
4. (cost or costs or costing or economic$ or financial$).mp.
5. 1 and (2 or 3) and 4
6. limit 5 to yr="2008 -Current"