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Screening for Breast Cancer With Digital Breast Tomosynthesis

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Chapter 1. Introduction

Purpose

Digital breast tomosynthesis (DBT) has rapidly been adopted by many providers of mammography screening in the United States. This report summarizes the evidence published through October 2015 regarding the diagnostic test characteristics of tomosynthesis in screening populations.

Background

DBT, also known as 3D mammography, uses a computer algorithm to reconstruct multiple low-dose digital images of the breast into thin "slices" spanning the entire breast. These images can be displayed individually or in cine mode. Tomosynthesis is typically performed as a supplement to standard two-view digital screening mammography, which more than doubles the total radiation exposure compared to a standard digital mammography screening examination.[1-5] In 2013, the U.S. Food and Drug Administration (FDA) approved the use of synthetic 2D images to take place of the standard 2-D, two-view digital mammograms. While this technology eliminates the additional radiation of a digital mammogram, it is currently not known how frequently synthetic views are used.[1] A General Electric tomosynthesis system was approved by the FDA in September 2014,[6] and a single 3D view from this system is reported to have a similar radiation dose as a standard two-view digital mammography examination.[7] However, it is not yet clear how this system will be used in practice.

Chapter 2. Methods

Key Question

Using the USPSTF's methods[8] (detailed in **Appendix A**), we addressed the following key question:

1. What are the test performance characteristics of DBT as a primary screening modality for breast cancer, performed either alone or simultaneously with 2D digital mammography? How do these performance characteristics differ by age and risk factors?

Data Sources and Searches

We searched MEDLINE, PubMed, Embase, and the Cochrane library from January 2000 through October 2015. To ensure the comprehensiveness of our retrieval strategy, we reviewed the reference lists of included studies and relevant systematic reviews to identify relevant articles. We also supplemented our database searches with suggestions from experts, searched the grey literature for relevant reports and reviewed their references, and searched Clinicaltrials.gov to identify relevant ongoing trials (**Appendix B**).

Study Selection

Two reviewers independently screened titles and abstracts for relevance. For inclusion, we required studies to: 1) be conducted in screening populations (asymptomatic women aged 40 years and older), and 2) evaluate test performance characteristics with a comprehensive reference standard applied to both negative and positive tests. For breast cancer screening, this requires further imaging and/or biopsy of positive results, and a minimum of 1 year of clinical followup for negative results to ascertain interval breast cancers not identified by screening.

Quality Assessment and Data Abstraction

Two reviewers independently assessed the full text of each study to assess whether it met our predefined inclusion criteria. Two reviewers independently assessed the methodological quality of each study using predefined criteria developed by the USPSTF[9] and supplemented with the National Institute for Health and Clinical Excellence methodology checklists[10] and the QAREL tool[11] for assessing diagnostic reliability. Disagreements in quality were resolved by discussion. Each study was given a final quality rating of good, fair, or poor. To illustrate the state of available research addressing this key question, results from screening population studies were abstracted into a standard evidence table. A second reviewer checked the data for accuracy. Elements abstracted included population characteristics (e.g., baseline demographics, family or personal history of breast cancer), study design (e.g., inclusion/exclusion criteria, followup, screening rounds), screening environment (e.g., number of readers), and test performance

characteristics (e.g., sensitivity, specificity, positive predictive value). When available, we also abstracted proximate health outcomes (e.g., breast cancer detection rates, invasive breast cancer detection rates, recall rates, and biopsy rates).

Chapter 3. Results

Literature Search

Our literature search yielded 1,024 unique citations. From these, we identified 18 articles for full-text review based on titles and abstract, including a systematic review of the use of DBT for breast cancer screening or diagnosis performed by the Technology Evaluation Center.[12] This review identified one additional study we had not previously located.[13] After screening the full-text articles, we identified one study meeting inclusion criteria of reporting test performance characteristics of DBT in a screening population.

Summary of Results

The evidence available on test performance characteristics of DBT was limited to a single study conducted in Italy. This study met inclusion criteria since it reported results on a screening population and employed a comprehensive reference standard. We found no studies that described the difference in test performance characteristics of DBT by age or risk factor.

We excluded nine studies from this review.[1, 12, 14-20] One small study from Sweden included both symptomatic and asymptomatic women.[18] This study also applied a comprehensive reference standard, including 1 year of clinical followup. However, of 185 total women, 89 (48%) were diagnosed with breast cancer, so the study sample was not representative of a screening population. Five studies utilized test sets of mammograms with known diagnoses, with and without DBT images, to evaluate radiologist diagnostic performance.[1, 15-17, 20] All of these test sets were enriched with images of known breast cancers, ranging from 16 percent[16] to 41 percent[1] of the total images. Two studies recruited women with abnormal mammograms.[14, 19]

To illustrate the state of available research addressing the proximate health outcomes of DBT screening, the characteristics of the additional studies identified are briefly summarized in this report.

Test Performance of DBT

The single good-quality study meeting inclusion criteria (the Screening with Tomosynthesis OR standard Mammography [STORM] trial) assembled a prospective, single cohort of 7,292 women aged 48 years or older from population-based screening programs from two towns in Northern Italy.[5, 21] Women were recruited from August 2011 to June 2012, and underwent both digital mammography and DBT. Mammograms were interpreted sequentially by eight trained radiologists. Initially the 2D mammogram was read, and then the 2D and DBT images were interpreted together by the same radiologist during the same session. The study utilized independent double reading but reports results from the initial single reader; these results, which more closely resemble U.S. practice, are reported here. Median followup was 19.7 months. The study was rated as good quality based on the screening population, application of a reference

standard to those with both positive and negative results, and adequate followup time. Overall, 63 women were diagnosed with 65 breast cancers over the course of the study. Sensitivity for a single reading with digital mammography was 0.54 (95% CI, 0.42 to 0.65) compared with 0.85 (95% CI, 0.74 to 0.92) for DBT. Specificity for digital mammography was 0.96 (95% CI, 0.95 to 0.98) and 0.97 (95% CI, 0.96 to 0.98) for DBT with mammography (**Table 1**). The overall cancer detection rates were 4.8 per 1,000 women with digital mammography and 7.4 per 1,000 women with DBT with mammography. Recall rates were 4.2 % for digital mammography and 3.6% for DBT with mammography (**Table 1**).

Proximate Health Outcomes of DBT

Due to the limited literature on test performance characteristics of DBT, we also summarized studies reporting cancer detection outcomes, recall rates, and biopsy rates of DBT.

After excluding the previously discussed studies,[1, 15-18] eight screening cohort studies reported on recall rates and cancer detection rates for digital mammography with or without DBT, including the STORM trial described previously (**Table 2**).[4, 5, 13, 21-27] These studies compared findings within a single cohort of women undergoing both studies[4, 5, 21] or compared two screening cohorts, one undergoing digital mammography only compared to a cohort undergoing mammography and DBT.[13, 22-25] In most of these studies, DBT was associated with an increase in the breast cancer detection rates compared to digital mammography alone. The proportions of invasive cancers with and without the use of DBT were somewhat higher with tomosynthesis in some studies[4, 23-25] and similar to digital mammography in others.[5, 13, 22] In most studies, compared to digital mammography, DBT was associated with reduced immediate recall rate and higher positive predictive value for an initial positive result.[4, 13, 22-25] In two of four studies reporting biopsy rates, the biopsy rate was slightly higher with DBT compared to digital mammography alone.[22-25]

Chapter 4. Discussion

Only one study from Italy provided information on diagnostic test characteristics of tomosynthesis for breast cancer screening, and suggested markedly higher sensitivity for the combination of DBT with digital mammography. However, the sensitivity of digital mammography in this study (54%) was much lower than that found in a recent large population-based U.S. study (87%).[28] Other studies did not report on a comprehensive reference standard or interval cancer rates. There is a pressing need for rigorous U.S.-based studies to define the test performance characteristics and long-term clinical outcomes of this rapidly diffusing breast imaging technology.

Several retrospective cohort studies suggested DBT with digital mammography is associated with reduced overall recall rates with similar or higher biopsy rates compared to digital mammography alone. One factor that may reduce immediate recall rates with tomosynthesis is that the technology obtains additional breast images at the time of initial screening. These additional images obtained at screening may obviate the need to recall many women for further imaging after 2D mammography screening. Depending on the screening technology, the additional images acquired during DBT screening, however, may double the breast radiation dose associated with screening. Technology approved by the FDA in 2013 for synthetic 2D mammography reduces the radiation dose to that of the tomosynthesis examination alone.[1]

In most cohort studies, cancer detection rates were somewhat higher with DBT as compared to digital mammography alone, and the proportion of invasive cancers detected was similar to or higher than the proportion detected with digital mammography alone. Ongoing studies registered with ClinicalTrials.gov are listed in **Appendix B** and descriptions of these studies suggest that results of the application of a comprehensive reference standard to a screening population may become available within a few years. Studies are needed that employ the standard approach to breast imaging interpretation in the United States (single reading), and that report on both interval cancers identified by a comprehensive reference standard and longer-term outcomes, including effects of the addition of DBT to digital mammography on the stage distribution of detected cancers, breast cancer recurrence or second (contralateral) breast cancers, and mortality rates.

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Table 1. Screening for Breast Cancer Using Digital Breast Tomosynthesis: Study Details and Test Performance Characteristics

Author, Year (Location) USPSTF Quality Rating	Study Design and Setting	Study N	Radiologist/ Population Characteristics	Breast Cancer Type	Sensitivity (95% CI)	Specificity (95% CI)
Houssami, 2014[21] *STORM Trial* (Italy) Good quality	Prospective cohort (1 arm) Population screening program from 2 cities	7,292 women DM+DBT images interpreted independently from DM only	8 radiologists Median age: 58 y Screen positive if either reader interpreted DM or DBT as abnormal	All breast cancer	DBT+ DM: 0.85 (0.74 to 0.92) DM only: 0.54 (0.42 to 0.65)	DBT + DM: 0.97 (0.96 to 0.98) DM only: 0.96 (0.95 to 0.97)

Abbreviations: CI=confidence interval; DBT=digital breast tomosynthesis; DM=digital mammography; USPSTF=U.S. Preventive Services Task Force.

Table 2. Screening for Breast Cancer Using Digital Breast Tomosynthesis: Study Details and Proximate Health Outcomes

Author, Year (Location)	Study Design and Setting	Study N	Radiologist/ Population Characteristics	Breast Cancer Prevalence	Cancer Detection Rate (% Invasive)	Recall/ Biopsy Rate	Positive Predictive Value
Lang, 2015[26] *Mälmo Trial* (Sweden)	Prospective cohort (1 arm) Organized screening programs	7,500 women DM+DBT images interpreted independently from DM only images	6 radiologists	DBT only: 20/7500 women DM only: 46/7500 women	DBT only: 2.8 per 1,000 women (85.0%) DM only: 6.3 per 1,000 women (89.0%)	*Recall:* DBT only: 3.2% DM only: 2.6%	NR
Destounis, 2014[27] (New York)	Retrospective cohort (2 arm) Community breast clinic	DBT+DM: 524 women DM only: 524 women DM+DBT images interpreted independently from DM only	6 radiologists Mean age: DBT+DM: 59 y DM only: 59 y	DBT+DM: 3/524 women DM only: 2/524 women	DBT+DM: 5.4 per 1,000 women (33.3%) DM only: 3.8 per 1,000 women (50.0%)	*Recall:* DBT+DM: 4.2% DM only: 11.4% *Biopsy:* DBT+DM: 1.1% DM only: 2.3%	NR
Greenberg, 2014[24] (Washington, DC area)	Retrospective cohort (2 arm) Community-based multi-site radiology practice	DBT+DM: 20,943 exams DM only: 38,674 exams	14 radiologists	DBT+DM: 131/20,943 exams DM only: 190/38,674 exams	DBT+DM: 6.3 per 1,000 exams (73.6%) DM only: 4.9 per 1,000 exams (62.1%)	*Recall* DBT+DM: 13.6% DM only: 16.2% *Biopsy* DBT+DM: 2.6% DM only: 2.2%	DBT+DM: 4.6% DM only: 3.0%
Friedewald, 2014*[25] (Multi-state)	Retrospective cohort (2 arm) 13 academic health centers and community breast diagnostic/screening centers	DBT+DM: 173,663 exams DM only: 281,187 exams	139 radiologists Mean age: DBT+DM: 56.2 y DM only: 57.0 y Limited to screening exams and subsequent follow-ups	DBT+DM: 950/173,663 exams DM only: 1207/281,187 exams	DBT+DM: 5.5 per 1,000 exams (74.5%) DM only: 4.3 per 1,000 (67.4%)	*Recall* DBT+DM: 8.9% DM only: 10.6% *Biopsy* DBT+DM: 1.9% DM only: 1.8%	DBT+DM: 6.1% DM only: 4.1%

Table 2. Screening for Breast Cancer Using Digital Breast Tomosynthesis: Study Details and Proximate Health Outcomes

Author, Year (Location)	Study Design and Setting	Study N	Radiologist/ Population Characteristics	Breast Cancer Prevalence	Cancer Detection Rate (% Invasive)	Recall/ Biopsy Rate	Positive Predictive Value
Houssami, 2014[5, 21] *STORM Trial* (Italy)	Prospective cohort (1 arm) Population screening program from 2 cities	7,292 women DM+DBT images interpreted independently from DM only	8 radiologists Median age: 58 y Screen positive if either reader interpreted DM or DBT as abnormal	DBT+DM: 55/7292 women DM only: 35/7292 women	DBT+DM: 7.4 per 1,000 women DM only: 4.8 per 1,000 women	*Recall* DBT+DM: 3.6% DM only: 4.2%	DBT+DM: 21% DM only: 11%
McCarthy, 2014[22] (Pennsylvania)	Cohort (2 arm) One academic medical center	DBT+DM: 15,571 exams DM only: 10,728 exams	6 radiologists Mean age DBT+DM: 56.7 y DM only: 56.9 y	DBT+DM: 85/15,571 exams DM only: 49/10728 exams	DBT+DM: 5.5 per 1,000 exams (71%) DM only: 4.6 per 1,000 exams (69%)	*Recall*: DBT+DM: 8.8% DM only: 10.4% *Biopsy*: DBT+DM: 2.0% DM only: 1.8%	DBT+DM: 6.2% DM only: 4.4%
Haas, 2013[13] (Connecticut)	Retrospective cohort (2 arm) Multi-site (1 academic medical center, 2 outpatient radiology clinics, 1 mobile mammography van)	DBT+DM: 6,100 women DM only: 7,058 women	8 radiologists Mean age: DBT+DM: 55.8 y DM 57.5 y Personal hx of BC: DBT+DM: 5.5% DM only: 2.8%	DBT+DM: 35/6,100 women DM only: 37/7,058 women	DBT+DM: 5.7 per 1,000 women (69%) DM only: 5.2 per 1,000 women (68%)	*Recall* DBT+DM: 8.4% DM: 12.0% *Biopsy*: NR	DBT+DM: 6.8% DM only: 4.3%
Rose, 2013[23] (Texas)	Cohort (2 arm) Multisite community-based comprehensive breast cancer center	DBT+DM: 9,499 exams DM only: 13,856 exams	6 radiologists Asymptomatic women	DBT+DM: 51/9,499 exams DM only: 56/13,856 exams	DBT+DM: 5.4 per 1,000 exams (80%) DM only: 4.0 per 1,000 exams (70%)	*Recall*: DBT+DM: 5.5% DM only: 8.7% *Biopsy*: DBT+DM: 1.4% DM only: 1.5%	DBT+DM: 10.1% DM only: 4.1%
Skaane, 2013[4] (Norway)	Prospective cohort (1 arm) City-wide (Oslo) breast cancer screening program	12,621 exams DM+DBT images interpreted independently from DM only images	8 radiologists Median age: 58 y Screen positive if either reader interpreted DM or DBT as abnormal	DBT+DM: 101/12,621 exams DM only: 77/12,621 exams	DBT+DM: 8.0 per 1,000 exams (80.2%) DM: 6.1 per 1,000 exams (72.7%)	*Recall*: DBT+DM: 6.1% DM only: 6.7% *Biopsy*: NR	DBT+DM: 13.1% DM only: 9.1%

*Possible inclusion of data from Rose (2013) and Greenberg (2014).

Abbreviations: BC=breast cancer; DBT=digital breast tomosynthesis; DM=digital mammography; hx=history; NR=not reported; PPV=positive predictive value.

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Key Question Literature Search Strategy

Note: The literature search strategy for this supplemental review overlapped with our main evidence review, *Adjunctive Screening for Breast Cancer in Women with Dense Breasts*, and is therefore not limited to only DBT.

Database: Cochrane
Search Strategy:

'*mammogra* AND screen* AND (breast density OR dense breast OR parenchym*) in Title, Abstract, Keywords*

Database: Ovid MEDLINE(R)
Search Strategy:
---
1. "breast densit*".ti,ab.
2. parenchym*.ti,ab.
3. mammo* pattern.ti,ab.
4. mammo* patterns.ti,ab.
5. radiological pattern*.ti,ab.
6. wolfe*.ti,ab.
7. tabar*.ti,ab.
8. mammo* feature*.ti,ab.
9. breast pattern*.ti,ab.
10. mammo* densit*.ti,ab.
11. tissue densit*.ti,ab.
12. or/1-11
13. (negative test result* or false negative).mp. or exp False Negative Reactions/
14. "sensitivity and specificity"/ or "limit of detection"/ or roc curve/ or signal-to-noise ratio/
15. "sensitivity and specificity"/ or "limit of detection"/ or roc curve/ or signal-to-noise ratio/
16. or/13-15
17. ((negative adj4 mammogra*) or negative screen).mp.
18. 16 or 17
19. (supplementa* adj3 screen*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
20. (breast or mammogra*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
21. 12 and 16 and 18
22. 20 and 21
23. 12 and 19
24. (((supplementa* adj5 ultraso*) or supplementa*) adj5 imag*).mp.
25. 12 and 24
26. 20 and 25
27. 22 or 26

28. 23 or 27
29. limit 28 to ((abstracts or english language) and yr="2000 -Current")

Database: Ovid MEDLINE(R)
Search Strategy:
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1. exp "Sensitivity and Specificity"/
2. sensitivity.tw.
3. specificity.tw.
4. ((pre-test or pretest) adj probability).tw.
5. post-test probability.tw.
6. post-test probability.tw.
7. likelihood ratio$.tw.
8. or/1-7
9. Breast Neoplasms/
10. (breast adj (neoplasm or neoplasms or tumour or tumor or tumors or tumours or cancer or carcinoma or carcinomas or oncologic or oncology)).mp.
11. 9 or 10
12. exp Mammography/
13. Mammograph$.ti,ab.
14. 12 or 13
15. 8 and 14
16. "breast densit*".ti,ab.
17. parenchym*.ti,ab.
18. mammo* pattern.ti,ab.
19. mammo* patterns.ti,ab.
20. radiological pattern*.ti,ab.
21. wolfe*.ti,ab.
22. tabar*.ti,ab.
23. (birad* or bi-rad*).ti,ab.
24. mammo* feature*.ti,ab.
25. breast pattern*.ti,ab.
26. mammo* densit*.ti,ab.
27. tissue densit*.ti,ab.
28. "breast imaging reporting and data system".ti,ab.
29. or/16-28
30. 8 and 11 and 14 and 29
31. limit 30 to english language

1. 65. Image Processing, Computer-Assisted/ or Radiographic Image Interpretation, Computer-Assisted/ or Tomography, X-Ray Computed/ or Radiographic Image Enhancement/ or Tomography, X-Ray/ or tomosynthesis.mp. or Imaging, Three-Dimensional/
2. 66. 64 and 65
3. 67. Ultrasonography, Mammary/ or automated ultrasound.mp.
4. 68. whole breast ultrasound.mp.
5. 69. hand help ultrasound.mp.
6. 70. magnetic resonance imaging.mp. or Magnetic Resonance Imaging/

7. 71. mri.mp.
8. 72. Technetium Tc 99m Sestamibi/ or scintimammography.mp.
9. 73. or/67-72
10. 74. 31 and 73
11. 75. limit 74 to (english language and yr="2000 -Current")
12. 79. or/76-78
13. 80. 62 and 79
14. 81. limit 80 to (english language and yr="2000 -Current")
15. 82. 81 not 75
16. 83. 65 or 73
17. 84. 82 and 83

Database: Embase
Search Strategy:
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1. 'mammography'/exp OR 'mammography' OR 'mammography system'/exp OR 'mammography system' OR mammograph*:ab,ti AND [2000-2014]/py
2. 'dosimetry'/exp OR 'dosimetry' OR 'radiation protection'/exp OR 'radiation protection' OR 'radiation measurement'/exp OR 'radiation measurement' AND [2000-2014]/py
4. 'radiation exposure'/exp OR 'radiation exposure' OR 'radiation induced neoplasm'/exp OR 'radiation induced neoplasm' OR 'radiation injury'/exp OR 'radiation injury' AND [2000-2014]/py
5. 'morbidity'/exp OR 'morbidity' OR 'mortality'/exp OR 'mortality' OR 'adverse effect':ab,ti OR 'adverse effects':ab,ti OR harm:ab,ti OR harms:ab,ti OR contraindic*:ab,ti AND [2000-2014]/py
6. #2 OR #4
7. #1 AND #5 AND #6

8.1 'breast tumor'/exp/dm_pc,dm_di
8.2 (breast NEXT/5 (neoplasm* OR tumour* OR tumor* OR cancer* OR carcinom* OR oncolog*)):ab,ti
8.3 #8.1 OR #8.2
8.4 'mass screening'/exp OR 'mass radiography'/exp
8.5 'neoplasm'/exp/dm_pc,dm_di
8.6 'mammography'/exp OR 'mammography system'/exp OR mammograph*:ab,ti
8.7 screen*:ab,ti
8.8 #8.4 OR #8.5 OR #8.6 OR #8.7
8.9 #8.3 AND #8.8
8.10 'sensitivity and specificity'/exp OR sensitivity:ab,ti OR specificity:ab,ti
8.11 (('pre test' OR pretest) NEAR/5 probability):ab,ti
8.12 (('pre test' OR pretest) NEAR/5 probability):ab,ti
8.13 'likelihood ratio':ab,ti OR 'likelihood ratios':ab,ti
8.14 #8.10 OR #8.11 OR #8.12 OR #8.13
8.15 #8.9 AND #8.14
8.16 'breast density':ab,ti OR 'dense breasts':ab,ti OR 'dense breast':ab,ti OR parenchym*:ab,ti OR 'mammographic feature':ab,ti OR 'mammographic features':ab,ti OR (mammography

NEAR/2 feature*):ab,ti OR 'breast pattern':ab,ti OR 'breast patterns':ab,ti OR (breast NEAR/3 pattern):ab,ti OR 'mammographic density':ab,ti OR (mammography NEAR/3 density):ab,ti OR 'mammographic pattern':ab,ti OR 'mammographic patterns':ab,ti OR (mammography NEAR/2 patterns):ab,ti OR 'radiological pattern':ab,ti OR 'radiological patterns':ab,ti OR wolfe*:ab,ti OR tabar*:ab,ti OR birad*:ab,ti OR 'bi rad':ab,ti OR 'breast imaging reporting and data system':ab,ti OR 'tissue density':ab,ti OR (tissue NEAR/3 density):ab,ti
8.17 #8.15 AND #8.16
8.18 #8.17 AND [english]/lim AND [2000-2014]/py

Appendix A Table 1. Inclusion and Exclusion Criteria

Category	Inclusion	Exclusion
Populations	Women primarily aged 40 years and older receiving tomosynthesis screening	Women with: • Pre-existing breast cancer • Clinically significant BRCA 1/2 mutations • Li-Fraumeni syndrome • Cowden syndrome • Hereditary diffuse gastric syndrome • Other familial breast cancer syndromes • High-risk breast lesions (DCIS, LCIS, ADH, ALH) • Previous doses of chest radiation (>20Gy) before age 30 • Undergoing diagnostic or surveillance mammography
Setting	Conducted in primary care or other setting with primary care-comparable population	Settings not generalizable to primary care
Intervention or Exposure	Digital breast tomosynthesis	Digital or full-film mammography alone; other new technologies, such as MRI or ultrasound; use for diagnostic or surveillance purposes; use in a diagnostic or surveillance setting only
Comparisons or Nonexposue	Digital or film mammography	
Outcomes	Test performance characteristics (sensitivity, specificity, positive predictive value, negative predictive value, likelihood ratios for invasive breast cancers, breast lesions [DCIS], total breast cancers, breast cancers by stage); biopsy rates, recall rates	
Study Designs	Diagnostic accuracy studies with reference standard and more than one radiologist/reader, RCTs, cohort studies with more than one radiologist/reader, and meta-analyses	
Language	English only	Non-English languages
Publication Date	Studies published from January 2000 to present	Studies published before January 2000
Study Quality	Fair- and good-quality studies	Poor-quality studies

Appendix B. Ongoing Studies and Trials Pending Assessment

Investigator (Location) Study Title/Name	Number of Participants/ Estimated Enrollment	Intervention	Outcomes	2014 Status
Sophia Zackrisson (Sweden) *Malmö Breast Tomosynthesis Screening Trial*	15,000	Screening with tomosynthesis compared to digital mammography	Cancer detection; sensitivity; specificity	Study Period: March 2010 – March 2016 Recruiting
Emily Conant (United States) *Comparison of Full-Field Digital Mammography With Digital Breast Tomosynthesis Image Acquisition in Relation to Screening Call-Back Rate*	550	Screening with digital mammography compared to a combination of 2D and 3D tomosynthesis	Recall rates; sensitivity; specificity; lesion characterization; radiation dose	Study Period: December 2012 – June 2012 Status unknown
Jules Sumkin (United States) *Assessment of Digital Breast Tomosynthesis (DBT) in the Screening Environment*	1,080	Screening with digital mammography and tomosynthesis (images interpreted independently)	Recall rates; specificity	Study Period: May 2010 – May 2014 Recruiting
Per Skaane (Norway) *Tomosynthesis in the Oslo Breast Cancer Screening Program (DBT)*	25,000	Screening with digital mammography and tomosynthesis	Screening performance indicators; interval cancer rates	Study Period: November 2010 – September 2015 Ongoing, but not recruiting
Thomas Moritz (Austria) *Digital Breast Tomosynthesis vs. Digital Mammography: A National Multicenter Trial*	600	Screening with digital mammography and tomosynthesis	Specificity; sensitivity	Study Period: January 2012 – December 2012 Status unknown