Health Technology Assessment of Breast Cancer Screening Techniques in India

ABBREVIATIONS

ANMs	Auxillary Nurse and Midwifery
ASHA	Accredited Social Health Activist
BRCA 1 & 2	Breast Cancer 1 & 2
BMI	Body Mass Index
CBE	Clinical Breast Examination
CDSR	Cochrane Database of Systematic Reviews
CI	Confidence Interval
CVD	Cardiovascular Disease
DALYs	Disability Adjusted Life Years
DDTs	Dichlorodiphenyltrichloroethane
EEDs	Environment Endocrine Disruptors
FN	False Negative
FP	False Positive
HTA	Health Technology Assessment
HWCs	Health and Wellness Centres
IARC	International Agency on Research on Cancer
ICER	Incremental Cost Effectiveness Ratio
LMICs	Low Middle Income Countries
LYS	Life Years Saved
OOP	Out of Pocket
QALYs	Quality Adjusted Life Years
MMG	Mammography
MRI	Magnetic Resonance Imaging
NFHS	National Family Health Survey
NICE	The National Institute for Health and Care Excellence
NPCDCS	National Programme for Prevention and Control of Cancer, Diabetes, CVD and Stroke
PAHs	Polycyclic Aromatic Hydrocarbons
PEF	Piezoelectric finger
PHC	Primary Healthcare Centre
PHFI	Public Health Foundation of India
PRISMA	Preferred Reporting Items for Systematic Reviews
RCTs	Randomized Controlled Trials
TN	True Negative
TNM	Tumour Node Metastasis
TP	True Positive
USG	Ultrasonography
PICO	Population, Intervention, Comparator and Outcome
PSA	Probability Sensitivity Analysis
+	Followed

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Executive Summary

A Health Technology Assessment (HTA) was carried out to study clinical effectiveness and the cost-effectiveness of various breast cancer screening strategies in Indian women with healthcare system perspective. Six screening strategies included in Cost effectiveness analysis (CEA) were Clinical Breast Examination (CBE) only , CBE followed by Ultrasonography (USG), CBE paralleled with USG, Mammography only (MMG), MMG followed by USG (MMG+USG) and piezoelectric finger followed by USG (Piezo+USG).

For clinical effectiveness diagnostic accuracy of Breast cancer screening modalities were estimated from the Meta-analysis done by NHSRC 2018. CBE was found to show a sensitivity of 0.73 and specificity of 0.94, MMG had sensitivity value of 0.71 and specificity value of 0.95, USG had sensitivity value of 0.73 and specificity value of 0.94, Piezoelectric finger had sensitivity of 0.83 and specificity of 0.88. In combination CBE followed by USG pooled sensitivity and specificity were 0.61 and 1, CBE paralleled with USG sensitivity and specificity were 0.91 and 0.99, MMG followed by USG sensitivity and specificity were 0.67 and 1 respectively. No evidence were found on the diagnoctic accuracy of Piezoelectric finger followed by Ultrasonography. Biopsy was taken as a gold standard with 100 % sensitivity and specificity.

A Cost-effectiveness analysis (CEA) was done to study the cost-effectiveness of these six breast cancer screening strategies in Indian women compared to no screening with healthcare system perspective. The CEA included screening cost of each screening strategy and life time treatment cost for diagnosed breast cancers and the effectiveness was measured as the Quality Adjusted Life Years (QALYs) gained per unit cost incurred.

A decision tree using probabilistic Markov model was developed to study the natural history of developing breast cancer in a hypothetical cohort of 1,00,000 women aged 35-40 years, 40-45 years, 45-50 years, 50-55 years and 55-60 years with life time horizon of annual cycle. Seven health states viz. healthy; breast cancer with stages 1, 2, 3, 4; death due to breast cancer and death due to all causes were used in the Markov model.

Age-specific incidence rates of breast cancer were considered from Indian population based cancer registry data, probability of natural deaths and stage distribution of clinically detected breast cancers were referred using Indian data. Breast cancer prevalence rates, transition

probabilities, annual mortality rate of breast cancers, utility weights were used from international studies. Pooled Sensitivity and specificity of various screening tests were aken from the meta-analysis undertaken separately.

In the cohort of 1,00,000 women, estimated annual breast cancer incidence was highest in women aged 35-40 years and lowest in women aged 55-60 years. Breast cancer incidence also declined from youngest to the oldest age-groups in 3 years and 5 years screening. Three years screening by six screening strategies reduced the likelihood of breast cancer cases by 39% to 45% and Breast Cancer deaths by 47% to 52% as compared to the annual screening. Five years screening reduced the likelihood of breast cancer cases and deaths by more than 75% as compared to the annual screening.

In annual screening, estimated lifetime cost in CBE was $172.62 per woman and estimated effect was highest i.e. 22.8328 per woman aged 35-40 years in screening by CBE solo, CBE parallel with USG showed a lifetime cost of $ 372.91 and effect size of 22.8387. For the 3 year screening interval CBE solo had a lifetime cost of $78.56 with effect of 11.4313 and CBE paralleled with USG had a lifetime cost of $197.30, effect size 11.4324, 5 year screening interval showed CBE solo $47.66, effect size 8.1575 and CBE paralleled with USG had lifetime cost of $ 136.41, with effect size of 8.1579. Estimated lifetime cost and QALYs gained per woman were decreased with the increasing age of the woman suggested that early screening is helpful to reduce the cost of treatment and gain more QALYs.

Incremental Net Monetary Benefit for screening by CBE alone and CBE paralleled with USG was higher for screening at 3 years than the screening at 5 years suggested that CBE alone and CBE paralleled with USG screening is the most cost-effective strategy for conducting screening at triennial i.e. 3 years interval in Indian women aged 35-60 years.

The MOHFW operational framework for the management of common cancers recommends screening by Nurse/ANM by CBE at the HWC/sub-centre level followed by an evaluation of those suspected positive by an Ultrasound scan in age group of 30 and above (71). As our study has a modality CBE paralleled with USG that has shown to be clinically effective as well as cost effective in the screening interval of 3 and 5 years that can be considered as an alternative screening modality in the Public Health care facilities.

A. INTRODUCTION

Breast Cancer

Excessive growth of cells in the breast leads to Breast cancer. This excessive growth of cells form a tumour. The tumour is regarded as Malignant (cancerous) if the cells can grow (invade) surrounding tissues or spread (metastasize) to distant areas of the body. Breast cancer start to occur from different parts of the breast. Majority of the breast cancer arise in the ducts or lobules and also in glands that make breast milk those are referred to as lobular cancers. Breast cancer can spread outside the breast through blood and lymph vessels. The most common kinds of breast cancer are Invasive ductal carcinoma and Invasive lobular carcinoma *(1)*.

Disease burden

Breast cancer is the most commonly occurring cancer among females in the world, with an estimated 1.67 million cases diagnosed in 2012 *(2)*. Estimated 627,000 women died from breast cancer in the year 2018 accounting for 15% of all cancer deaths *(2)*. The annual incidence of breast cancer is approximately 1, 44,000 new cases making it the most commonly occurring cancer in females in India *(2)*. Effective screening techniques serve as the basis for the prevention of breast cancer among females.

Breast cancer has ranked number one cancer among Indian females with age-adjusted rate as high as 25.8 per 100,000 women and mortality 12.7 per 100,000 women (30). As per available literature, the age-adjusted incidence rate of breast cancer was found as high as 41 per 100,000 women for Delhi, followed by Chennai (37.9), Bangalore (34.4) and Thiruvananthapuram district (33.7). Mumbai, Bangalore, Chennai, Thiruvananthapuram, Dibrugarh and New Delhi hold first rank and Barshi rural with the second rank. Chennai and Thiruvananthapuram reported the highest crude rate of 40.6 and 43.9, and Barshi rural having the lowest crude rate of 13.2. Mumbai and New Delhi have a crude rate of 33.6 and 34.8 respectively *(3)*.

In 2008, the National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Disease and Stroke (NPCDCS) was begun. Cancer wasn't a part of this programme and was later included only in 2009. The advent of Operational Framework for Management of Common Cancers by Ministry of Health & Family Welfare (MOHFW) in 2016, serves as strengthening the cancer screening programme.

Risk classification

The risk for breast cancer can be divided into three categories General Population risk, Moderate risk and High risk.

General population risk

Women have about an 11 % chance of developing breast cancer having the risk as same as the general population. For this level of risk, 110 women in every 1000 will develop breast cancer. Majority of the women in the general population develop the cancer after the age of 50.

Moderate risk

Women belonging to the moderate risk of population have a lifetime risk of developing breast cancer greater than 17 % but less than 30 %, among them 3 to 8 % of women have a chance of developing breast cancer between the ages of 40 and 50.

High risk

High-risk population of women belong to the 30 % of the population. 300 women in every 1000 will develop breast cancer. Age group of these women is 40 – 50. High-risk females have much higher chance of developing breast cancer at young ages than women in the general population *(4)*.

Early diagnosis and Screening for breast cancer

Early diagnosis of breast cancer involves timely access to effective diagnosis services. Screening of breast cancer involves various screening tools such as Mammography, Clinical Breast Examination, Breast self-examination and Ultrasonography etc.

Screening modalities

Clinical Breast Examination

Clinical breast examination (CBE) is the clinical examination of the breast by a trained healthcare professional to detect any lumps or warning signs of breast cancer. The goal for CBE is the early detection of breast cancer.

Mammography

Mammography is an x-ray technique that captures the image of the breast on an x-ray film. It is an imaging modality that uses low energy x rays for imaging of breast tissue.

Mammography is used as a screening technique involving two or more x-ray pictures. The x-ray film helps in detecting the tumours. Screening mammography is used to detect early cancer in asymptomatic women *(2)*.

Breast ultrasound

Breast ultrasound uses sound waves to produce images of the breast. The images produced are referred to as sonograms. Breast USG is an imaging test that uses sound waves to detect signs of breast cancer. The technique uses a transducer over the skin to make the images of the breasts. The transducer sends out sound waves that bounce off the breast tissue, the transducer then picks up the bounced sound waves and make the pictures of the inside of the breast *(2)*.

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is an imaging technique in radiology. MRI is used to visualize internal structures in detail by using magnetic radiation. It provides real-time 3 D view of the organs. In the case of breast cancer screening, it is used as a supplemental tool to Mammography and Ultrasound. A breast MRI is mainly used for women who have been diagnosed with breast cancer, to further measure the size of a tumour, looking for more tumours. It is found useful for women at high risk *(5)*.

Piezoelectric finger

The iBreast exam device was developed as a pre-screening tool to identify women in need of further breast imaging. This handheld device uses the technique of piezoelectric palpation to enhance the Clinical breast examination (CBE) for detection of the breast masses requiring further investigations. This device is built on the principle of the piezoelectric finger (PEF) detector. This device can be used to detect signs of breast cancer and any abnormality in the breast, without requiring radiologist for interpretation. *(6)*.

B. Health Technology Assessment

Background

Health Technology Assessment refers to the systematic evaluation of properties, effects, and/or impacts of Healthcare technology. It also takes into consideration to address the direct, intended consequences of technologies as well as their indirect, unintended consequences. The primary purpose is to generate evidence for technology-related policymaking in Healthcare. That shall improve the uptake of the novel and more cost-effective technologies

in the Healthcare system. HTA also serves the purpose of finding gaps in the presently existing technologies and devising ideas for the development of new technologies thus promoting innovation in the sphere of Healthcare.

HTA has a dimension of economic analysis as a major component to it. That includes different types of Economic analysis namely cost-benefit analysis, Cost-utility analysis, Cost-effectiveness analysis, Cost – minimization analysis, and also Budget impact analysis. Quality-adjusted life years (QALYs) and Disability-adjusted life years (DALYs) are outcomes in Health Technology Assessment. The domains of Health Technology Assessment are Clinical effectiveness, Ethics, Social and Organizational issues. HTA aims to address important questions pertaining to implementation, need and working of a new technology in the sphere of Healthcare *(7)*.

Rationale for conducting HTA

Breast cancer is a majorly occurring cancer among females in India; it is the major cause of morbidity and mortality among females in the metropolitan cities of India namely Delhi, Kolkata, Pune, Thiruvananthapuram, Bangalore and Mumbai. As per data presented by the available literature that shows high cancer incidence in India, reflecting an urgent need for strengthening and improving the existing diagnostic/treatment facilities for breast cancer *(3)* in relation to lack of nation-wide breast cancer screening program.

Aim

The aim of this Health Technology Assessment is to compare the clinical and cost effectiveness of early detection of multiple breast cancer screening techniques. This will help in systematically implementing different breast cancer screening strategies.

It is clear that the treatment of breast cancer in its advanced stage, demands a huge proportion of Healthcare resources in a resource constrain situation such as India it is beyond the reach of the average patient, making early cancer detection a priority.

This Health Technology Assessment (HTA) aims to assess the clinical effectiveness and cost-effectiveness of various technologies in the screening of breast cancer. In cost-effectiveness analysis, we are taking into account the costs included during the treatment of breast cancer along with the costs incurred in the screening process. This HTA would provide evidence to

policymakers to draw upon national or regional guidelines to suggest appropriate breast cancer screening techniques based on their clinical and cost-effectiveness.

Objectives

The objectives of the following Health Technology Assessment are:

1. To assess the clinical effectiveness, safety and diagnostic accuracy of different screening modalities in women at low and high risk of breast cancer.

2. To determine the age at which screening should be offered e.g. the minimum and maximum age for screening will be determined.

3. To determine the optimal screening interval and to assess the most cost-effective option regarding time duration for conducting periodic screening of 3 and 5 years.

4. To evaluate the cost-effectiveness of various technologies available for breast cancer screening.

This HTA report is divided into the following sections

1. Clinical Effectiveness Review
2. Economic Evaluation Review
3. Modelling Cost-Effectiveness Analysis
4. Health Equity

I. CLINICAL EFFECTIVENESS REVIEW

Aim

To assess the diagnostic accuracy of different breast cancer screening methods in women at low and high risk of breast cancer.

Objective

To assess clinical effectiveness, safety and diagnostic accuracy of different screening methods in women at low and high risk of breast cancer.

Methods
Sources:

A literature search was performed using a database like PubMed, Cochrane and EBSCO for studies published from January 1, 2000, to Feb 28, 2018.

Screening of the literature:

Two reviewers reviewed the abstracts. For abstracts meeting the eligibility criteria full – text articles were obtained. Reference lists for any additional relevant studies not identified through the search were also examined.

We used this search strategy (appendix) to identify titles and abstracts of relevant trials. Reviewer screened these titles and abstracts and discarded non – relevant or duplicate publications. For studies where the classification of risk was unclear, the issue was resolved in discussion with the third reviewer. Articles included were limited to those available only in the English language. Any disagreement was resolved by discussion and consensus with other authors. The results of the selection process were summarized and were depicted in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow diagram and document reasons for exclusion.

Inclusion criteria

The following criteria were used:
- Population: Females

- Intervention: CBE, Mammography, MRI, USG, and Piezoelectric finger

- Comparator: No screening

- Outcome: Diagnostic Accuracy (Accuracy for detection of breast cancer – Sensitivity and Specificity

Outcome of Interest

Diagnostic Accuracy:

- Sensitivity (true – positive rate)

- Specificity (true – negative rate)

- False – negative rate

- False – positive rate

- Positive predictive value (the proportion of all positive results that were true – positives) among women who tested positive for the disease and among women who received a follow – up biopsy

Study Design:

- Randomized controlled trials and prospective, comparative studies; paired study designs were considered the ideal design for observational studies

- Prospective, comparative studies (including studies of ultrasound among women with negative mammography) and retrospective, comparative studies

- Retrospective, comparative studies

Diagnostic performance:

For similar studies with minimal clinical heterogeneity, we pooled outcomes using Review Manager 5.3. To assess the diagnostic accuracy of each test, we constructed 2×2 tables (true – positives, false – positives, true – negatives and false – negatives). We reported calculations of sensitivity, specificity, positive predicted value, biopsy rates, and recall rates as provided in the research articles. When the study did not report results of interest, we calculated outcomes for each intervention based on data provided in the articles.

Sensitivity and specificity for each test within each paired study were plotted using Review Manager 5.3, in the receiver operating characteristic space as well as on forest plots to explore to study variations and heterogeneity, where sufficient clinical and methodological homogeneity was found. Meta disc 1.4 was used to pool studies and calculate the pooled

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sensitivity and specificity and their 95 % confidence intervals, and generating Summary Receiver Operating Curve.

Results

The databases search yielded 496 citations published between January 1, 2000, and Feb 28, 2018. Articles were excluded based on information available in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment.

The figure below presents the flow diagram for the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

PRISMA – Flow Chart
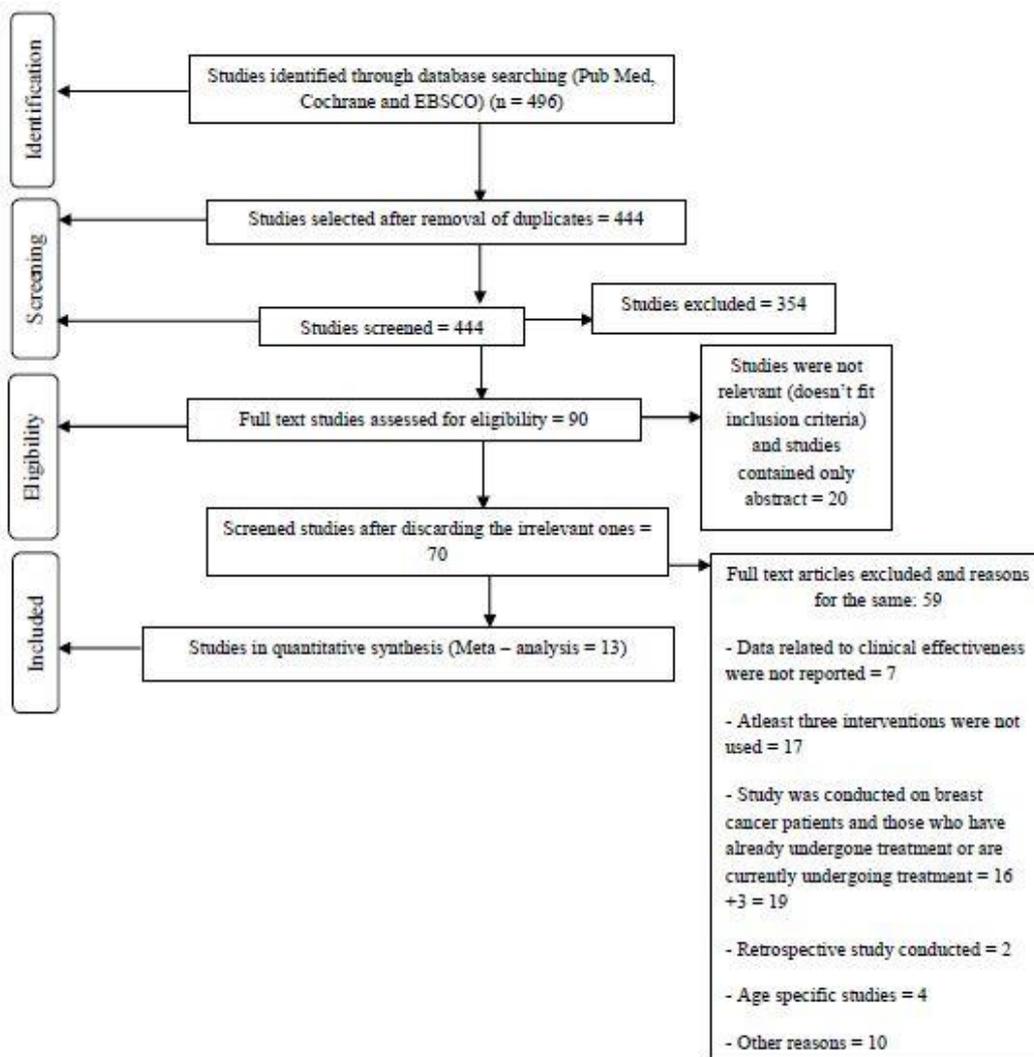
Fig 1: PRISMA Flowchart of Clinical Effectiveness of Breast cancer screening modalities)

Table No. 1: Summary of characteristics of the included studies of clinical effectiveness of different breast cancer screening modalities

S.No	Author, Year	Country, No. of sites	Women (completed screens)	Mean Age, Years (Range)	Study design	Population of interest
1.	Broach, 2016 (6)	USA	78	42 (21 – 79)	Prospective cohort study	Adult patients presenting for diagnostic work up
2.	Kuhl, 2005 (8)	Germany	529	41.7 (27 – 59)	Prospective observational cohort study	Lifetime risk > 20 % based on family history
3.	Ozulker, 2010 (9)	Turkey	46	46.1 ±13.31 (22 – 82)	Prospective cohort study	Women with suspicious lesions detected in their breasts by palpitation, imaging modalities or clinically
4.	Pediconi, 2009 (10)	Italy	238	47.5 ± 9.3 (16 – 77)	Retrospective cohort study	Women with dense breast parenchyma who were suspicious for breast cancer
5.	Riedl, 2016 (11)	Austria	559	Median 44 (22 – 83)	Prospective non-randomized comparison study	*BRCA1 or BRCA2 mutation *Lifetime risk >20 %
6.	Schwarz, 2010 (12)	Germany	99	Median 50 (30 – 66)	Prospective multicentre trial	Patients underwent one or more breast imaging modalities before surgery in addition to clinical examination
7.	Somashekhar, 2016 (13)	India	916	Women above 40 and under 40	Prospective three arm triple blinded comparative study	Asymptomatic women
8.	Vassiou, 2008 (14)	Greece	69	53 (39 – 68)	Prospective comparative study	Women with focal breast lesions
9.	Warner, 2004 (15)	Canada	236	46.6 (26.4 – 64.8)	Prospective observational study	Women with BRCA1 or BRCA2 mutations who underwent 1 to 3 annual screening examination
10.	Weinstein, 2009 (16)	USA	609	Median 49	Prospective multi-modality	Asymptomatic high-risk

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			(27 – 81)	cohort study	women
11.	Malur, 2000 (17)	Germany	413	58 (19 – 85)	Prospective cohort study	Abnormal breast findings
12.	Huang, 2012 (18)	China	3028	25 years or older	Randomized controlled trial	Females seeking organized and opportunistic screening, women with existing untreated malignancies, known metastatic disease or psychiatric condition
13.	Sankarnarayan,2011 (19)	India	50366	30 – 69 years	Cluster randomized controlled trial	Healthy women aged 30 – 69 years with no history of breast cancer

c) Methodological quality of the included studies
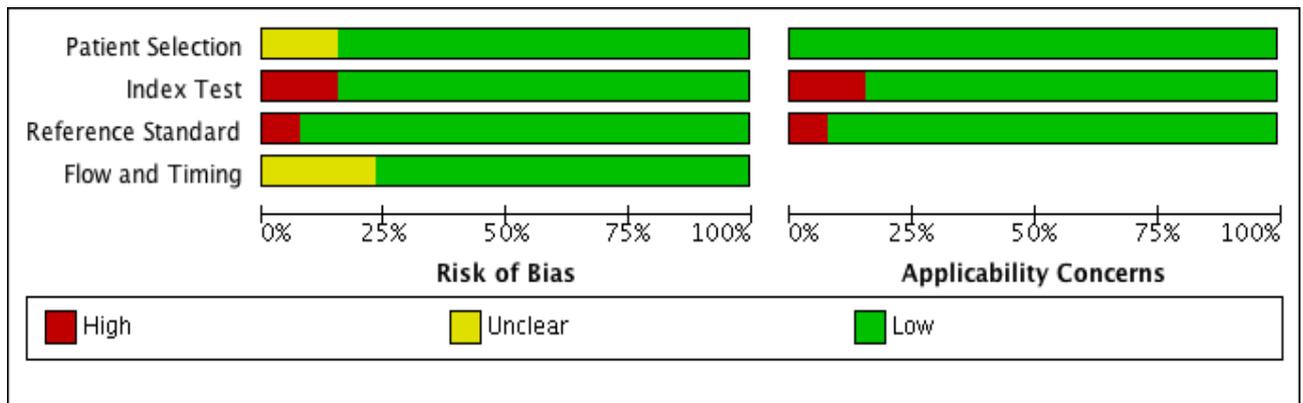
Fig 2: Risk of bias and applicability concerns graph: review authors judgments about each domain presented as percentages across included studies

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Fig 3: Risk of bias and applicability concerns summary: review authors judgments about each domain for each included study.

Assessment for the risk of bias of included studies was performed. Only two studies (*Broach_2016 & Somashekar_2016*) had limitations associated with the patient selection. In the case of the index test, these two studies had a high risk of bias. Only one study *(Somashekhar_2016)* had a high risk of bias in case of the reference standard. In flow and timings criteria, three studies *(Schwarz_2010, Somashekhar_2016 and Warner_2004)* had an unclear risk of bias.

Overall, there were low applicability concerns in all the studies in terms of the selection of the patient samples. Two studies (*Broach_2016 & Somashekhar_2016*) had high applicability concerns in terms of index test. Only one study (*Somashekhar_2016)* had high applicability concern in terms of the reference standard used in that study.

i) Mammography:

Total of 10 studies reported the sensitivity and specificity on Mammography. The lowest sensitivity of 0.33 reported by Kuhl_2005 and highest sensitivity of 0.93 was reported by Schwarz_2010. In terms of specificity highest specificity value of 1.00 was reported by Warner_2004 and lowest value of 0.15 was reported by Ozulker_2010. The pooled sensitivity was 0.71 and specificity was 0.95.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Huang_2012	28	48	5	2947	0.85 [0.68, 0.95]	0.98 [0.98, 0.99]
Kuhl_2005	14	45	29	1364	0.33 [0.19, 0.49]	0.97 [0.96, 0.98]
Malur_2000	155	76	30	157	0.84 [0.78, 0.89]	0.67 [0.61, 0.73]
Ozulker_2010	13	11	3	2	0.81 [0.54, 0.96]	0.15 [0.02, 0.45]
Pediconi_2009	40	23	15	19	0.73 [0.59, 0.84]	0.45 [0.30, 0.61]
Riedl_2015	15	38	25	1287	0.38 [0.23, 0.54]	0.97 [0.96, 0.98]
Schwarz_2010	37	3	3	4	0.93 [0.80, 0.98]	0.57 [0.18, 0.90]
Vassiou_2008	44	15	9	10	0.83 [0.70, 0.92]	0.40 [0.21, 0.61]
Warner_2004	8	1	14	434	0.36 [0.17, 0.59]	1.00 [0.99, 1.00]
Weinsten_2009	7	13	11	131	0.39 [0.17, 0.64]	0.91 [0.85, 0.95]

Fig 4: Forest plots of Mammography as an intervention for breast cancer. The square represents the sensitivity and specificity of one study and the black line represents the CI. TP = True positive; FP = False positive; FN = False negative; TN = True negative.
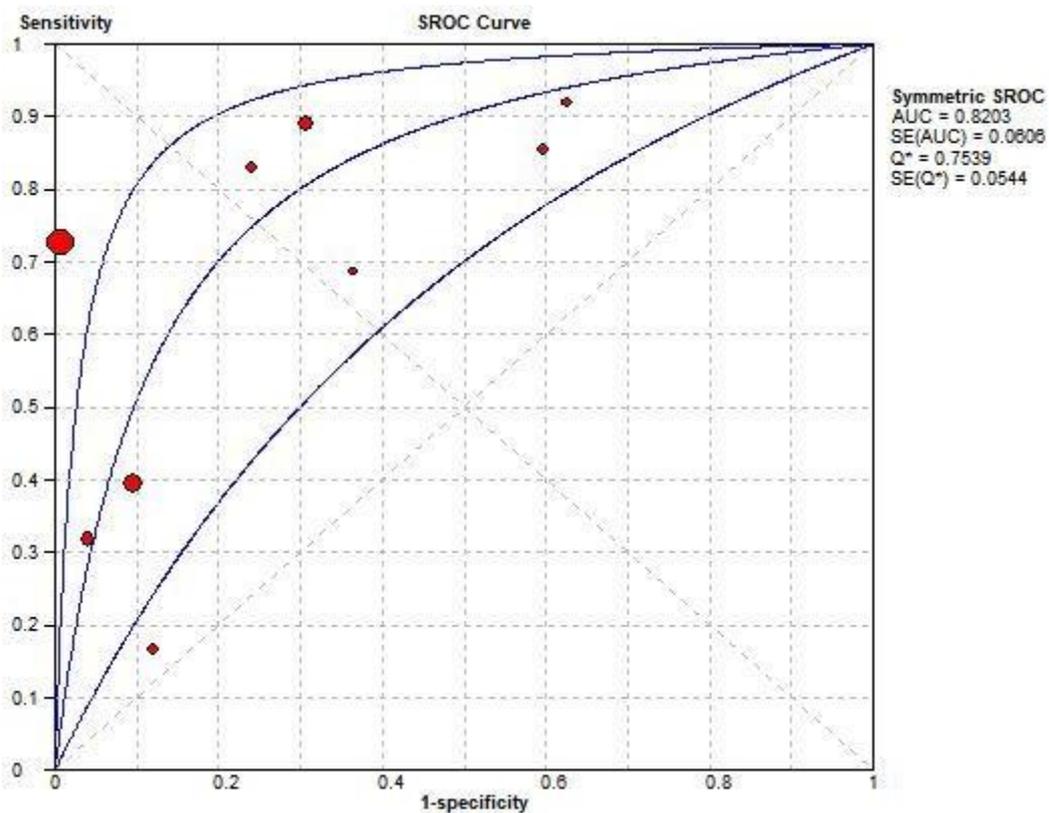
Fig 5: SROC – Mammography

ii) Ultrasonography:

For ultrasonography highest value of sensitivity of 0.92 was reported by Schwarz_2010 and lowest value of 0.17 by Weinsten_2009. Highest specificity of 0.99 was reported by Huang_2012 and lowest value of 0.40 by Pediconi_2009. The pooled sensitivity value was 0.73 and specificity of 0.94.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Huang_2012	24	19	9	2976	0.73 [0.54, 0.87]	0.99 [0.99, 1.00]
Kuhl_2005	17	134	26	1275	0.40 [0.25, 0.56]	0.90 [0.89, 0.92]
Malur_2000	165	89	20	202	0.89 [0.84, 0.93]	0.69 [0.64, 0.75]
Ozulker_2010	11	4	5	7	0.69 [0.41, 0.89]	0.64 [0.31, 0.89]
Pediconi_2009	47	25	8	17	0.85 [0.73, 0.94]	0.40 [0.26, 0.57]
Riedl_2015	15	41	25	1284	0.38 [0.23, 0.54]	0.97 [0.96, 0.98]
Schwarz_2010	46	5	4	3	0.92 [0.81, 0.98]	0.38 [0.09, 0.76]
Vassiou_2008	44	6	9	19	0.83 [0.70, 0.92]	0.76 [0.55, 0.91]
Warner_2004	7	17	15	412	0.32 [0.14, 0.55]	0.96 [0.94, 0.98]
Weinsten_2009	3	17	15	125	0.17 [0.04, 0.41]	0.88 [0.82, 0.93]

Fig 6: Forest plots of ultrasonography as an intervention for breast cancer screening. The square represents the sensitivity and specificity of one study and the black line represents its CI. TP = true positive; FP = False positive; FN = False negative; TN = True negative
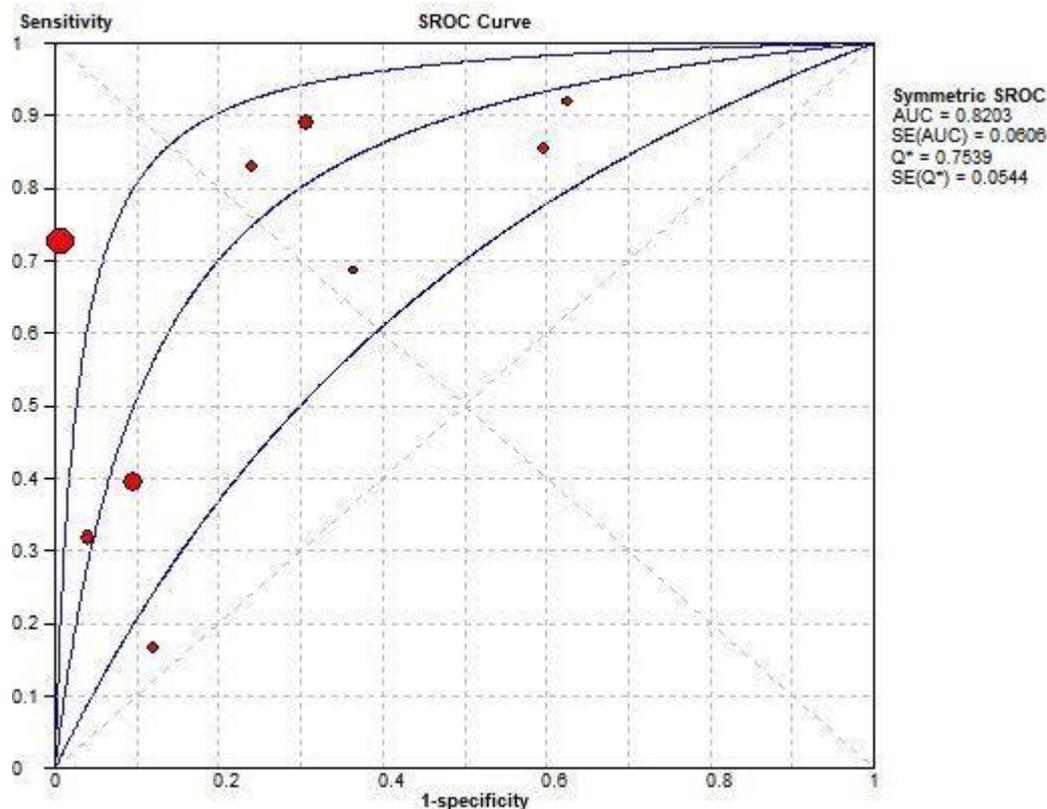
Fig 7: SROC - Ultrasonography

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iii) Clinical breast examination (CBE):

As per the meta-analysis results, 3 studies had the sensitivity and specificity value for Clinical breast examination as a screening modality. The study by Huang_2012 reported sensitivity value of 0.67 and specificity value of 0.99. A study by Sankarnarayan_2011 reported the sensitivity of 0.51 and specificity of 0.94. The study was conducted in Trivandrum district (Kerela, India). A total of 275 clusters that included 115652 healthy women, aged 30 – 69 years, randomly allocated to intervention CBE. The study by Schwarz_2010 reported the highest sensitivity of 0.91 among all the three studies and a specificity value of 0.53. The pooled sensitivity calculated was 0.73 and specificity value of 0.94. Positive predictive value of CBE was 0.04 and the Negative predictive value was 0.99.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Huang_2012	22	23	11	2972	0.67 [0.48, 0.82]	0.99 [0.99, 1.00]
Sankarnarayan_2011	30	2850	29	47457	0.51 [0.37, 0.64]	0.94 [0.94, 0.95]
Schwarz_2010	75	8	7	9	0.91 [0.83, 0.96]	0.53 [0.28, 0.77]
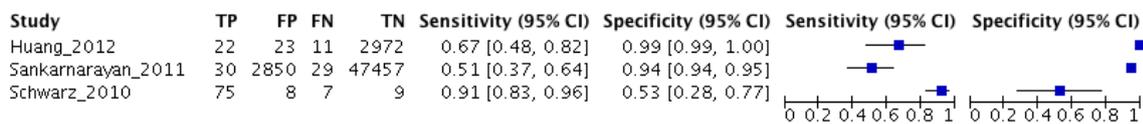
Fig 8: Forest plots of clinical breast examination as an intervention for breast cancer screening. The square represents the sensitivity and specificity of one study and the black line represents its CI. TP = true positive; FP = False positive; FN = False negative; TN = True negative
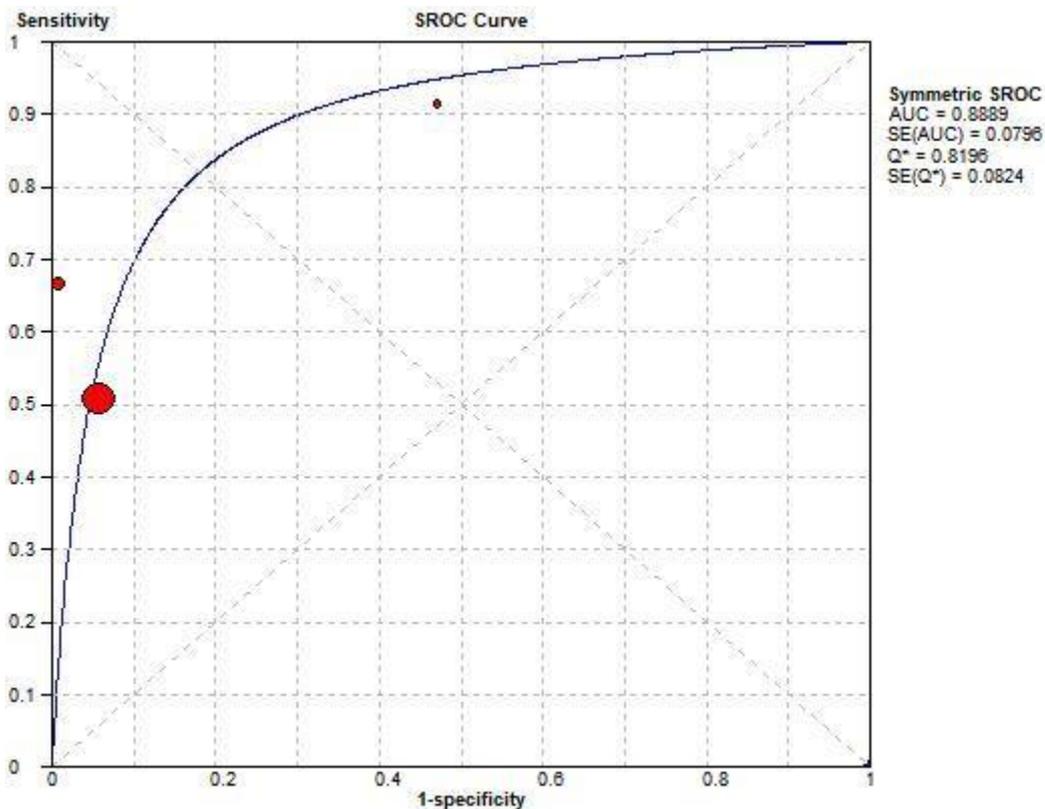
Fig 9: SROC – Clinical Breast Examination

iv) MRI

For magnetic resonance imaging (MRI) total of 9 studies were included reporting the sensitivity and specificity value for MRI as a screening modality. 5 studies reported high sensitivity ranging from 0.90 to 0.98. Schwarz_2010, Pediconi_2009, and Vassiou_2008 reported the sensitivity value of 0.98. The lowest sensitivity value of 0.64 was reported by Kuhl_2005, followed by 0.71 value reported by Weinsten_2009 and Warner_2004 with a value of 0.77. Kuhl_2005, followed by Warner_2004 with a specificity of 0.95, reported highest specificity value of 0.97. Two studies reported the lowest specificity value. 0.40 by Schwarz_2010 and 0.44 by Vassiou_2008. Pooled sensitivity calculated was 0.89 and pooled specificity was 0.90 with a positive predictive value of 0.55 and negative predictive value of 0.98.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Kuhl_2005	39	39	22	1370	0.64 [0.51, 0.76]	0.97 [0.96, 0.98]
Malur_2000	175	82	10	157	0.95 [0.90, 0.97]	0.66 [0.59, 0.72]
Ozulker_2010	13	3	3	5	0.81 [0.54, 0.96]	0.63 [0.24, 0.91]
Pediconi_2009	54	2	1	40	0.98 [0.90, 1.00]	0.95 [0.84, 0.99]
Riedl_2015	36	147	4	1178	0.90 [0.76, 0.97]	0.89 [0.87, 0.91]
Schwarz_2010	40	3	1	2	0.98 [0.87, 1.00]	0.40 [0.05, 0.85]
Vassiou_2008	52	14	1	11	0.98 [0.90, 1.00]	0.44 [0.24, 0.65]
Warner_2004	17	20	5	415	0.77 [0.55, 0.92]	0.95 [0.93, 0.97]
Weinsten_2009	12	36	5	135	0.71 [0.44, 0.90]	0.79 [0.72, 0.85]

Fig 10: Forest plots of MRI as an intervention for breast cancer screening. The square represents the sensitivity and specificity of one study and the black line represents its CI. TP = true positive; FP = False positive; FN = False negative; TN = True negative

Fig 11: SROC - MRI

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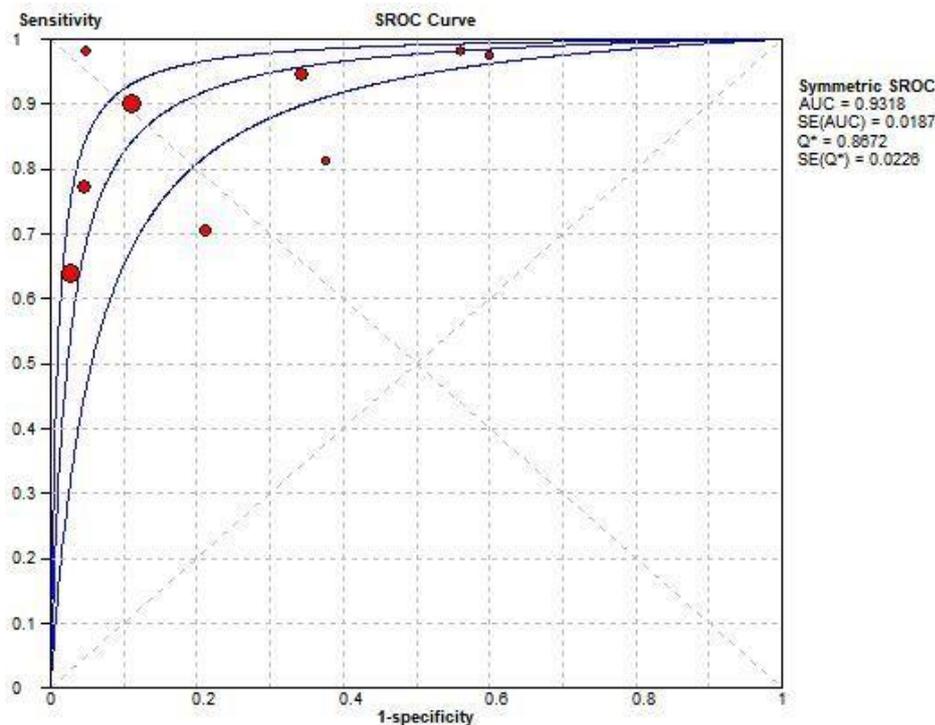
v) Piezoelectric finger:

Two studies (Broach_2016 and Somashekhar_2016) were found to contain data on the sensitivity and specificity of a Piezoelectric finger used for breast cancer screening. The pooled sensitivity was found to be 0.83 and specificity 0.88 with a positive predictive value of 0.62 and a negative predictive value of 0.96.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Broach_2016	78	63	16	185	0.83 [0.74, 0.90]	0.75 [0.69, 0.80]		
Somashekhar_2016	105	56	19	748	0.85 [0.77, 0.91]	0.93 [0.91, 0.95]		

Fig 12: Forest plots of the Piezoelectric finger as an intervention for breast cancer screening. The square represents the sensitivity and specificity of one study and the black line represents its CI. TP = true positive; FP = False positive; FN = False negative; TN = True negative

The SROC could not be generated because of two data points as a limitation of Meta disc software.

vi) Mammography paralleled with MRI:

All three studies included reported high sensitivity and specificity of Mammography paralleled with MRI. Vassiou_2008, followed by 0.95 for Riedl_2015, reported highest sensitivity of 0.98 the study by Kuhl reported the sensitivity of 0.93. Highest sensitivity was of 0.96 reported by Kuhl_2005 study, and by Riedl_2015 with specificity value of 0.88. Least specificity was 0.44 reported by the study Vassiou_2008. The positive predictive value was found to be 0.36 and negative predictive value 0.99.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Kuhl_2005	40	55	3	1354	0.93 [0.81, 0.99]	0.96 [0.95, 0.97]		
Riedl_2015	38	157	2	1168	0.95 [0.83, 0.99]	0.88 [0.86, 0.90]		
Vassiou_2008	52	14	1	11	0.98 [0.90, 1.00]	0.44 [0.24, 0.65]		
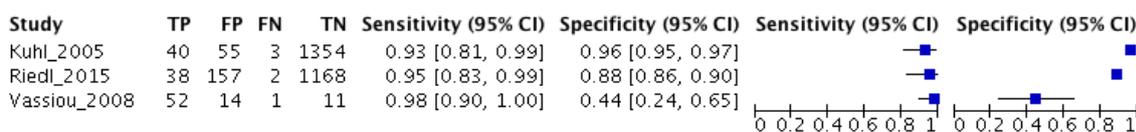
Fig 13: Forest plots of Mammography paralleled with MRI as an intervention for breast cancer screening. The square represents the sensitivity and specificity of one study and the black line represents its CI. TP = true positive; FP = False positive; FN = False negative; TN = True negative
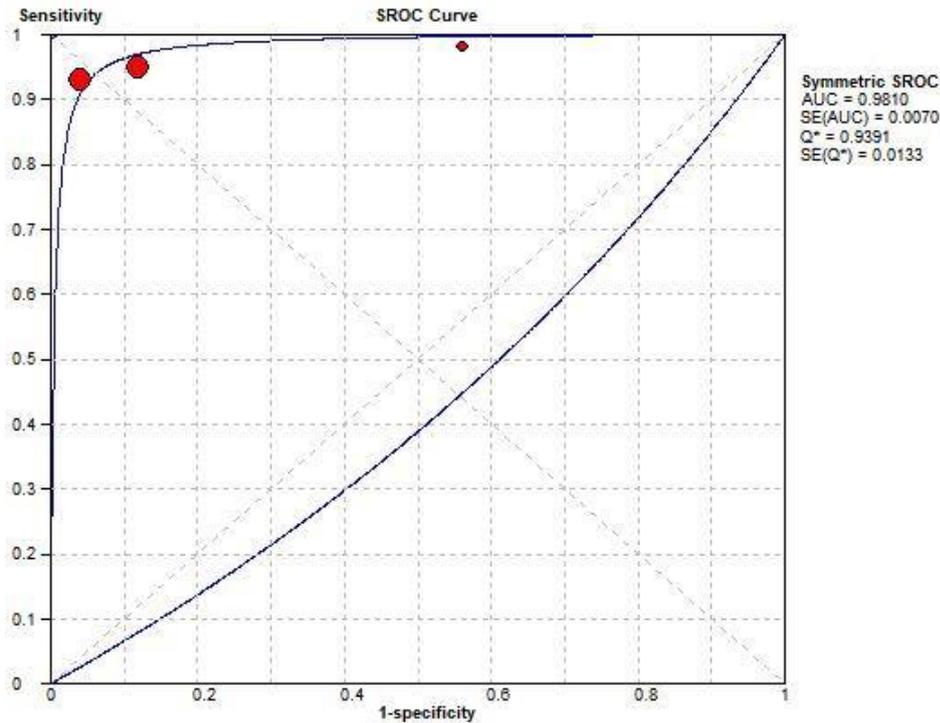
Fig 14: SROC - MMG paralleled with MRI

vii) Mammography paralleled with Ultrasonography:

Out of the total 4 studies, only two studies reported high sensitivity. Hunag_2012 reported a sensitivity of 0.94 and 0.89 by Vassiou_2008. Kuhl_2005 reported low sensitivity with a value of 0.49 and Riedl_2015 with a value of 0.50. Huang_2012 reported highest specificity with a value of 0.98; the Riedl_2015 study reported specificity of 0.96. Least specificity among the included study was found to be 0.44 by the Vassiou_2008 study. The positive predictive value was found to be 0.29 and Negative predictive value 0.99.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Huang_2012	31	59	2	2936	0.94 [0.80, 0.99]	0.98 [0.97, 0.98]
Kuhl_2005	21	155	22	1250	0.49 [0.33, 0.65]	0.89 [0.87, 0.91]
Riedl_2015	20	57	20	1268	0.50 [0.34, 0.66]	0.96 [0.94, 0.97]
Vassiou_2008	47	14	6	11	0.89 [0.77, 0.96]	0.44 [0.24, 0.65]

Fig 15: Forest plots of Mammography paralleled with Ultrasonography as an intervention for breast cancer screening. The square represents the sensitivity and specificity of one study and the black line represents its CI. TP = true positive; FP = False positive; FN = False negative; TN = True negative

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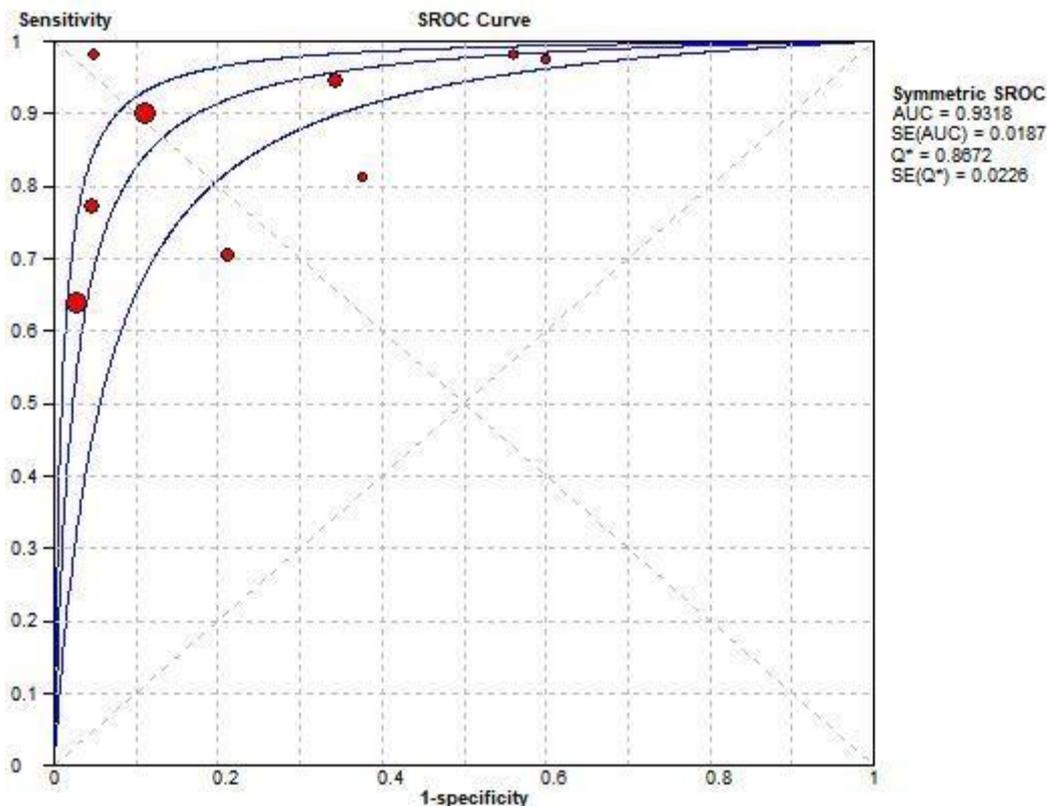
Fig 16: SROC – MMG paralleled USG

viii) MRI paralleled with Ultrasonography:

Only one study by Riedl_2015 was included for MRI paralleled with Ultrasonography as a screening modality with a sensitivity value of 0.90 and specificity value of 0.88. The positive predictive value was found to be 0.18 and the Negative predictive value was found to be 0.99.

Fig 17: Forest plots of MRI paralleled with Ultrasonography as an intervention for breast cancer screening. The square represents the sensitivity and specificity of one study and the black line represents its CI. TP = true positive; FP = False positive; FN = False negative; TN = True negative

The SROC could not be generated because of single data points as a limitation of Meta disc software.

ix) Clinical Breast Examination followed by Ultrasonography:

The study by Huang_2012 reported a sensitivity of 0.61 and specificity of 1.00, with a positive predictive value of 0.66 and Negative predictive value of 0.99.

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Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Huang_2012	20	10	13	2985	0.61 [0.42, 0.77]	1.00 [0.99, 1.00]		
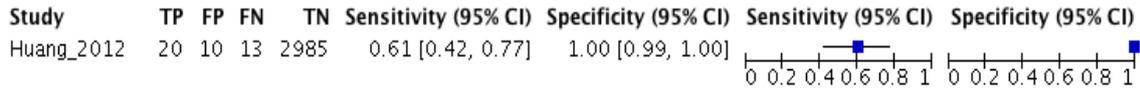
Fig 18: Forest plots of Clinical Breast Examination followed by Ultrasonography as an intervention for breast cancer screening. The square represents the sensitivity and specificity of one study and the black line represents its CI. TP = true positive; FP = False positive; FN = False negative; TN = True negative

The SROC could not be generated because of single data points as a limitation of Meta disc software.

x) Clinical Breast Examination followed by Mammography:

The sensitivity of 0.70 and specificity of 0.99 was reported by Huang_2012 study with a positive predictive value of 0.57 and Negative predictive value of 1.03.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Huang_2012	23	17	10	2978	0.70 [0.51, 0.84]	0.99 [0.99, 1.00]		
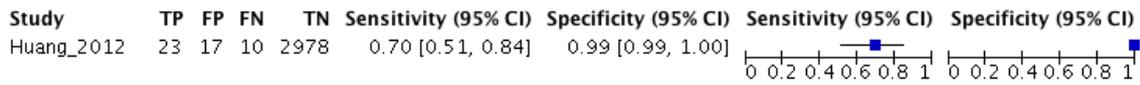
Fig 19: Forest plots of Clinical Breast Examination followed by Mammography as an intervention for breast cancer screening. The square represents the sensitivity and specificity of one study and the black line represents its CI. TP = true positive; FP = False positive; FN = False negative; TN = True negative

The SROC could not be generated because of single data points as a limitation of Meta disc software.

xi) Clinical Breast Examination paralleled with Ultrasonography:

The high sensitivity of 0.91 and specificity of 0.99 was reported by Huang_2012 with a positive predictive value of 0.90 and negative predictive value of 0.99.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Huang_2012	30	36	3	2959	0.91 [0.76, 0.98]	0.99 [0.98, 0.99]		
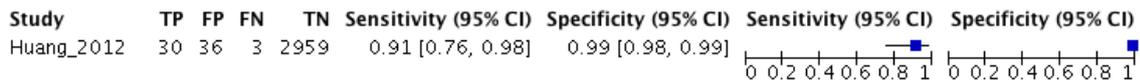
Fig 20: Forest plots of Ultrasonography paralleled with Clinical Breast Examination as an intervention for breast cancer screening. The square represents the sensitivity and specificity of one study and the black line represents its CI. TP = true positive; FP = False positive; FN = False negative; TN = True negative

The SROC could not be generated because of single data points as a limitation of Meta disc software.

xii) Mammography followed by Ultrasonography:

The high sensitivity of 0.667 and specificity of 0.997 was reported by Huang_2012.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Huang_2012	22	9	11	2986	0.67 [0.48, 0.82]	1.00 [0.99, 1.00]		
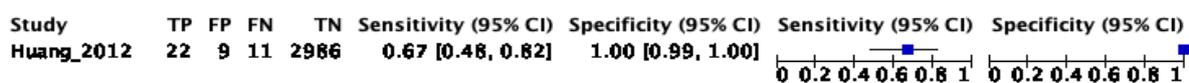
Fig 20: Forest plots of Mammography folloed by Ultrasonography as an intervention for breast cancer screening. The square represents the sensitivity and specificity of one study and

the black line represents its CI. TP = true positive; FP = False positive; FN = False negative; TN = True negative

The SROC could not be generated because of single data points as a limitation of Meta disc software.

xiii) Mammography paralleled with Clinical Breast Examination:

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Huang_2012	28	60	5	2935	0.85 [0.68, 0.95]	0.98 [0.97, 0.98]		
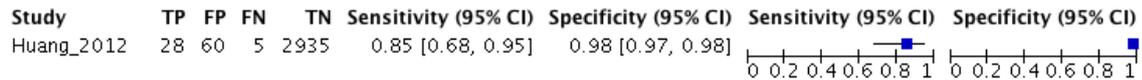
Fig 21: Forest plots of Mammography paralleled with Clinical Breast Examination as an intervention for breast cancer screening. The square represents the sensitivity and specificity of one study and the black line represents its CI. TP = true positive; FP = False positive; FN = False negative; TN = True negative

The SROC could not be generated because of single data points as a limitation of Meta disc software.

Table 2: Diagnostic accuracy of single and combined screening modalities obtained from meta-analysis results:

Screening modalities	Positives		Negatives		Sensitivity (95 % CI)	Specificity (95 % CI)	Predictive value	
	True (n)	False (n)	True (n)	False (n)			Positive (95 % CI)	Negative (95 % CI)
Clinical Breast Examination	127	2881	50438	47	0.730 (0.657 – 0.794)	0.946 (0.948 – 0.944)	0.04	0.99
Ultrasonography	379	357	6320	136	0.730 (0.657 - 0.794)	0.946 (0.948 – 0.944)	0.51	0.97
Mammography	361	273	6356	144	0.715 (0.673 – 0.754)	0.959 (0.954 – 0.963)	0.56	0.97
MRI	438	346	3313	52	0.894 (0.863 – 0.920)	0.905 (0.895 – 0.915)	0.55	0.98
Piezoelectric finger	183	119	933	35	0.839 (0.784 – 0.886)	0.887 (0.866 – 0.905)	0.62	0.96
Clinical Breast Examination followed by Ultrasonography	20	10	2985	13	0.61 (0.42 – 0.77)	1.00 (0.99 – 1.00)	0.66	0.99
Clinical Breast Examination paralleled with Ultrasonography	30	36	2959	3	0.91 (0.76 – 0.98)	0.99 (0.98 – 0.99)	0.90	0.99
Mammography followed by Ultrasonography	22	9	2986	11	0.67 (0.48-0.82)	1.00 (0.99-1.00)	0.710 (0.520 to 0.858)	0.996 (0.993 to 0.998)
Mammography	119	285	5465	50	0.704	0.950	0.29	0.99

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paralleled with Ultrasonography					(0.629-0.772)	(0.945-0.956)		
MRI paralleled with Ultrasonography	36	162	1163	4	0.90 (0.76 – 0.97)	0.88 (0.86 – 0.89)	0.18	0.99
Mammography paralleled with MRI	130	226	2533	6	0.956 (0.906 – 0.984)	0.918 (0.907 – 0.928)	0.36	0.99
Clinical Breast Examination followed by Mammography	23	17	2978	10	0.70 (0.51 – 0.84)	0.99 (0.99 – 1.00)	0.57	1.03
Mammography paralleled with Clinical Breast Examination	28	60	5	2935	0.85 (0.68 – 0.95)	0.98 (0.97 – 0.98)	0.84	0.99

Discussion:

The present systematic review and meta-analysis have been summarized and presented according to diagnostic accuracy of different breast cancer screening modalities (Table No.2) across various age groups of women. The diagnostic accuracy that has been presented i.e. sensitivity and specificity is a result of an exhaustive literature search for modalities both single and in combination.

Our systematic review and meta-analysis results have provided the sensitivity and specificity values of the modalities used as single and in combination, namely Clinical Breast Examination, Mammography, Ultrasonography, Piezoelectric finger and Magnetic Resonance Imaging. The paired combination of modalities are as follows: MMG paralleled with MRI, MMG paralleled with USG, MRI paralleled with USG, CBE followed by USG, CBE followed by MMG, USG paralleled with CBE and MMG paralleled with CBE.

From the results of the meta-analysis performed. MMG and CBE had the least sensitivity of 71 % and 73 % respectively, making it relatively less clinical effective among all the modalities. USG alone had 73 % sensitivity. Piezoelectric finger had a sensitivity of 83 % and MRI with the highest sensitivity value of 89 %. In the case of specificity, CBE had a specificity of 94 %, MMG with 95 % specificity, USG with 94 % specificity and Piezoelectric finger with the lowest specificity value of 88%. The meta-analysis results also suggest that screening modalities in combination prove to be robust in there diagnostic accuracy when used alone that may prove to be effective in confirming the results of the

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screening done as from our review, CBE paralleled with USG had a sensitivity of 91 % and Specificity of 99 %.

For the sensitivity values of modalities obtained in combination the highest sensitivity was demonstrated by MMG paralleled with MRI having a sensitivity value of 95 %. USG paralleled with CBE had sensitivity value of 91 % and MMG paralleled with CBE had a sensitivity of 85 %. Highest specificity in combination was shown by CBE followed by USG with a specificity value of 100 %. MRI paralleled with USG was found to be least specific with a specificity value of 0.88. For a diagnostic modality to be clinically more effective the sensitivity and specificity both needs to be high. From our meta-analysis, MRI is the only modality to have high sensitivity and specificity value making it clinically superior among rest of the modalities in solo performance.

As per the values obtained for sensitivity and specificity for different breast cancer screening modalities MRI and Piezoelectric finger as a new technology has a higher clinical effectiveness as compared to the rest of the screening techniques. CBE and MMG offer higher specificity but low sensitivity reducing clinical effectiveness. MRI among all the screening modalities offers the highest sensitivity of (89 %) and Specificity of (90 %) in solo. Higher nuber of RCTs need to be conducted on the usage of breast cancer screening on the respective modalities mentioned. This will lead to the generation of evidence, to facilitate in decision of breast cancer and screening. Clinical effectiveness values obtained provide a rational basis for its implementation in the public health care system.

Limitations:

Due to the scarcity of peer reviewed literature on determining the clinical effectiveness of various breast cancer screening techniques singly and in combination, it is difficult to reach a consensus in terms of determining the clinical effectiveness of various breast cancer screening techniques, in asymptomatic women to have sufficient evidence available to come to a conclusion that will help in deciding the current uptake of breast cancer screening modalities in relation to their clinical effectiveness in the screening of breast cancer. Age group included in most of studies were above 40, only two study were included which has included with age group between 25 to 30 year (18,19). Most of the studies Fewer studies were found in use of breast cancer screening modalities in solo and in combination with each other determining the clinical effectiveness of the respective modalities in comparison to the gold standard and same for recently developed techniques like a Piezoelectric finger.

II. ECONOMIC EVALUATION REVIEW

Background:

Breast cancer is the most commonly occurring cancer among females in the world, with an estimated 1.67 million cases diagnosed in 2012 *(WHO, 2012)*. The annual incidence of breast cancer is approximately 1, 44,000 new cases making it the most commonly occurring cancer in females in India *(WHO, 2012)*. Effective screening techniques serve as the basis for early screening and prevention of breast cancer among females. The overall effectiveness of different screening modalities depends on two aspects i.e. clinical and cost-effectiveness under the purview of Health Technology Assessment in the context of Health Systems Strengthening.

Introduction:

Cost-effectiveness analysis s a central components of any Health Technology Assessment and helps the policymakers to make evidence-based decisions on the usage and uptake of new Healthcare technologies, assessment under the purview of Health Systems Strengthening. With regard to Breast cancer screening techniques, different screening techniques are available namely CBE, USG, MMG and Piezoelectric finger. Each of the techniques has its' own demonstrated Clinical effectiveness that differs from one another. Uptake of any screening modality majorly depends on two factors i.e. clinical effectiveness (sensitivity and specificity) and cost of the technique. The technique that offers the highest clinical effectiveness at the lowest cost in relation to other techniques is considered to be the most cost-effective.

Cost-effectiveness analysis (ICER) is analysed in terms of Incremental Cost Effectiveness Ratio (ICER), calculation of ICER is based on two outcomes i.e. Quality – Adjusted life years (QALY) gained and per life years saved. The incremental cost-effectiveness ratio (ICER) is calculated using the baseline comparator and intervention.

ICER is computed using the formula:

ICER = (C2 – C1)/ (E2 – E1)

Where

C1 = Cost of No screening

C2 = Cost of Intervention

E1 = No. of QALYs gained/Life-years saved with no screening

E2 = No. of QALYs gained/Life yeas saved with intervention

This systematic review has been conducted for different modalities of breast cancer screening Clinical Breast Examination, Mammography, Ultrasonography and Piezoelectric finger. The systematic review has been done for these modalities alone and in combination with each other. The purpose of this review is to assess and compare the cost effectiveness of different modalities of breast cancer screening when used for screening at an interval of 3 and 5 years in females of different age groups.

Economic evaluation of Healthcare technologies involves principles of Economics applied to new and existing Healthcare modalities such as cost-effectiveness, modelling, and clinical trials. The cost-effective analysis specifically aims to compare and analyse cost and health-related consequences of different modalities/interventions together. It serves as a tool for assessment of the value of new and existing medical technologies, their Healthcare benefits in relation to their incremental costs. Cost-effective analysis paves the way for priority setting and the necessary allocation of Healthcare interventions.

The outcome of interest in cost-effectiveness analysis is measured in terms of QALYs that reflects both the quality and quantity of life associated with different Health states. The utilities/interventions are on the scale from 0 to 1, 0 representing death and 1 representing perfect Health (NICE). The comparison of the intervention is made on the basis of low ICER obtained for Clinical Breast Examination.

Aim
To conduct a systematic review of economic evaluation of different breast cancer screening modalities namely Mammography, Clinical Breast Examination, Ultrasonography and Piezoelectric finger in the female population.

Objective
To review the cost-effectiveness of different breast cancer screening modalities namely Mammography, Clinical Breast Examination, Ultrasonography and Piezoelectric finger in the Indian and international female population.

Methods

I) Study design: Cost-effectiveness studies/Economic evaluations/Health technology assessments

ii) Inclusion criteria: The inclusion criterion of the studies were done based on the following criteria:

- Population-Women who have undergone screening for breast cancer by Mammography, CBE, Piezoelectric finger followed by USG once in 3 years or once in 5years (triennial/quinquennial).

- Interventions/Modalities-Mammography, CBE, Piezoelectric finger, MMG+USG, CBE+USG, Piezo+USG

- Comparator- No screening

- Outcome-Cost per QALY gained, Cost per Life year saved, Cost per DALY averted, ICER

iii) Exclusion Criteria: The following criteria were used for exclusion of studies.

- Studies focused on diagnostic modality.

- Screening interval other than 3 and 5 years.

- Different set of interventions.

- Studies not focused on cost-effectiveness

- Studies not having paired combination screening

iv) Process followed for inclusion of studies: One reviewer assessed the different studies and then these were verified independently by another reviewer. Any disagreement was resolved by involving a third reviewer.

v) Literature search

Electronic database searching was done in PubMed, Cochrane and Embase having studies dated from 2008 – 2018. Search filters were applied as per the inclusion criteria.

vi) Studies selection

The two-stage PRISMA screening guidelines were followed to select the potential studies for the review. After removing the duplicates, the closely matching studies fulfilling the inclusion criteria as per methodology were selected.

Critical Appraisal: Included studies were appraised for reporting quality using Drummond 2015 checklist.

Review 1: Cost-effectiveness of Clinical Breast Examination as a screening modality for 3 and 5-year screening interval
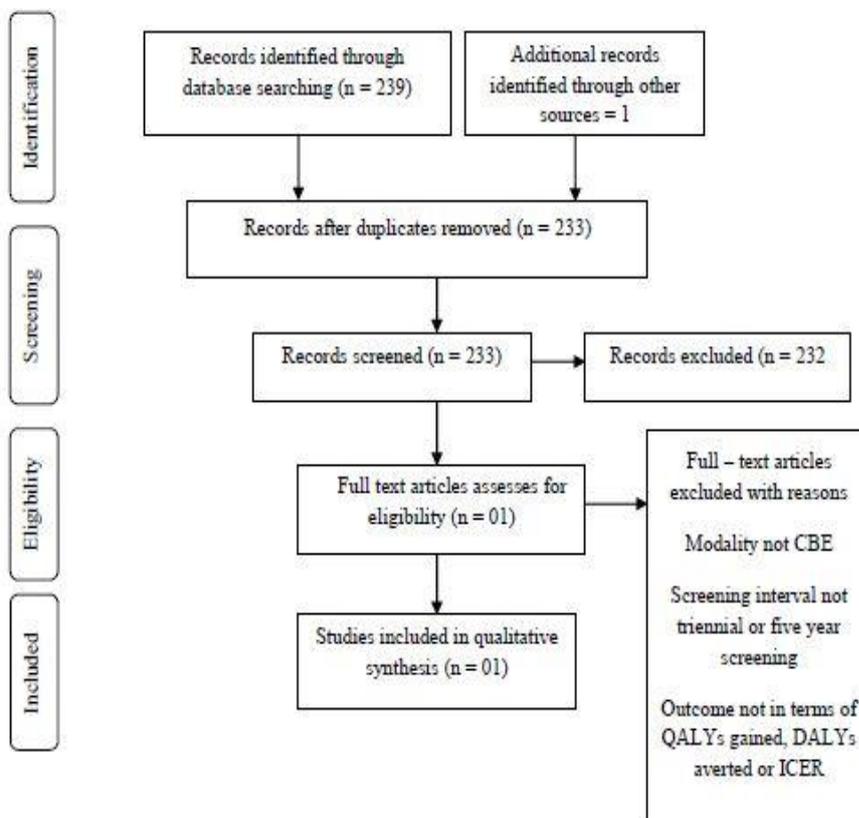
Fig 22: PRISMA model of the cost-effectiveness of clinical breast examination as a screening modality for 3 and 5 year

b) Results and discussion:

Table No. 3: Data extraction table for 5-year screening interval by Clinical Breast Examination for females:

Study ID	Country	Target Population	Study type	Perspective	Outcome measures	ICER	Modality	Comparator
Quinquennial Screening (5-year screening)								
Okonkwo_ 2008 (20)	India	Females (age 50 – 70)	Microsimu lation modelling study	Societal	Cost per death prevented Int $ - 13532 Cost per life gained Int $ - 1218	Dominated	CBE	No screening
Okonkwo_ 2008 (20)	India	Females (age 40 – 60)	Microsimu lation modelling study	Societal	Cost per life year gained Int $ - 15152 Cost per life year gained Int $ - 1634	1251 *(ICER mentioned is compared to screening program of one lifetime CBE at age 50, that has a cost per death prevented Int $ 11054 and Cost per year life gained Int $, 793).*	CBE	No screening
Laxminara yan_2006 (21)	India	Females (age 40 – 60)	-	Societal	7125 – 9907 per death prevented (India): 522 – 722 per LYS	N/A	CBE	No screening

As per the findings from the study Okonkwo_2008 (20) the breast cancer screening program for clinical breast examination conducted for the age group 50 – 70 the Incremental cost-effectiveness ratio was found to be dominated i.e. the program was not cost-effective.

The cost per death prevented in $ for the CBE for the age group 50 – 70 was 13532 $ (621254.12 Rs in 2008 and 395,244.47 Rs in 2018) and for 40 – 60 it was 15152 $ (695628.32 Rs in 2008 and 1,562,619 Rs in 2018). Cost per life year gained for the age group

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50 – 70 was 1218 $ (55918.38 Rs in 2008 and 125,611.04 Rs in 2018) and for age group 40 – 60 was 1634 $ (75016.94 Rs in 2008 and 168,513.96 Rs in 2018) (20).

For the age group, 40 – 60 the ICER mentioned was 1251 in comparison to the screening program of one lifetime CBE at the age of 50, the cost per death prevented Int $ was 11054 (507489.14 Rs in 2008 and 1139994.69 Rs in 2018) and cost per life year gained Int $ was 793.

The available literature suggests that CBE conducted in every 5 years from age group 40 – 60 (five screens) was estimated to reduce steady-state mortality by 8 % and prevents the loss of 2462 life years at a cost of Int $2.8 million (128548000 Rs in 2008 and 288762981.84 Rs in 2018), the ICER relative to a single CBE at age 50 was Int $1251 per life year gained (20).

As per the study Okonkwo et al, 2008 (20), Breast cancer screening policies in developing countries: A cost-effectiveness analysis for India. Screening every 5 years, biennial, and annual CBE for women aged 40-60 lead to considerable reductions in mortality and high numbers of life years gained, literature also says that main factors affecting cost-effectiveness were breast cancer incidence, stage distribution, and cost savings on prevented palliative care.

Review 2: **Cost-Effectiveness of Breast Cancer Screening Using Mammography (Triennial and Quinquennial screening)**

a) PRISMA Model:
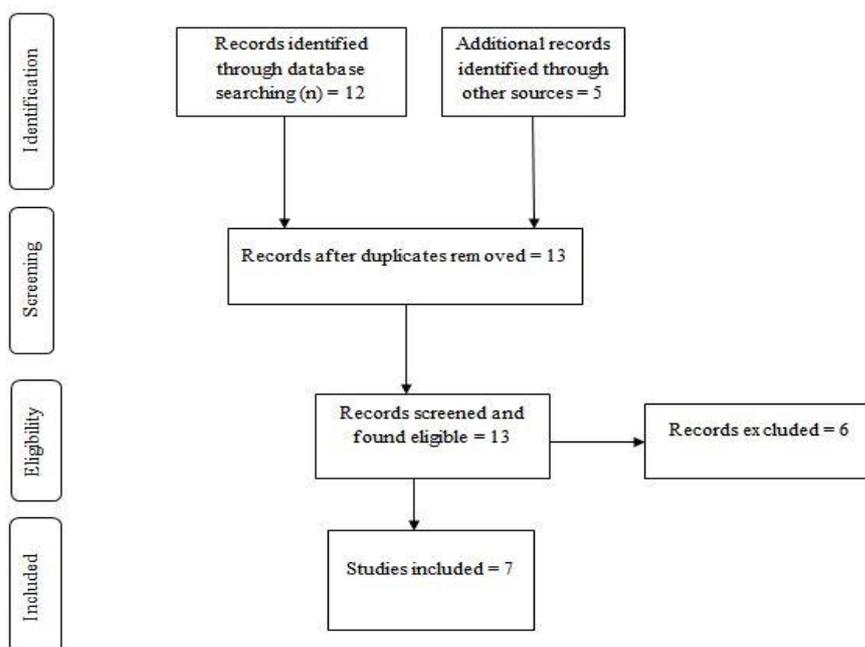
Fig 23: PRISMA Model for Breast cancer screening for Mammography as a modality

b) Results and discussions:

Table no. 4: Data extraction table for Mammography as a breast cancer screening modality
(3 and 5-year screening interval)

Study ID	Country	Target population	Study type	Perspective	Outcome measures	ICER	Modality	Comparator
Triennial Screening (3 year screening)								
Rashidian_ 2013 (22)	Global	Women (General population)	Systematic review	Societal & health system	LYG, QALY, DALY	Varied based on the age of the screened population.	Mammography	No screening
Rojnik_ 2008 (23)	Slovenia	50-65 yrs	Modelling (Markov Model)	Health care sector	QALY	$9801(Rs. 450846 in 2008) (Rs.962253 in 2018) per QALY gained	Mammography	No screening
Madan_ 2010 (24)	U.K.	47-49 yrs	Model based simulation study of a cohort of 10,000 women	Health system	QALY	$44,692(Rs.2055832 in 2010) (Rs.3479100in 2018) per QALY gained	Mammography	No screening
Lee_ 2009 (25)	Korea	45-65 yrs	Stochastic model	Health System	Per cancer detected	$100007 (Rs.5000350 in 2009) (Rs.9728572in 2018) per cancer detected	Mammography	No screening
Mittmann_ 2015 (Undiscounted) (26)	Canada	50-69 yrs	Wisconsin Breast cancer Epidemiology simulation model	Societal	QALY	$94,762 (Rs.4453814in 2012) (Rs.6465944in 2018) per QALY gained	Mammography	No screening
Mittmann_ 2018 (Discount= 1.5%) (per 1000 women) (27)	Canada	50-69 yrs	Wisconsin Breast car Epidemiology simulation model modified to fit in Canadian perspective	Health system	Life year gained & QALYs	$30,536 (Rs.1435192 in 2012) (Rs.2083578in 2018) per life year gained $36981(Rs.1738107 in 2012)(Rs.2523343 in	Mammography	No screening

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						2018) per QALY gained		
Quinquennial Screening (5 year screening)								
Sun_ 2018 (28)	China	40 – 69 yrs	Modelling (Markov)	Societal	QALY	6917 (5157 to 9416)	Mammography	No screening

The study by **Klemen Rojnik** (23) aims to determine at what age screening for breast cancer will be the most cost-effective. Here, a simplified TNM stage of breast cancer was modelled in a time-dependent Markov model. As per the findings of this study, the optimal screening policy is a triennial screening one. Using the commonly quoted threshold of $50,000 (approximately €38,500., Rs.23,00,000 in 2008 and Rs.4,908,956 in 2018) per QALY (35), the optimal screening policy would be screening women aged from 40 to 80 years every 3 years (screening policy 28). However, screening policy 33 (screening from ages 50 to 65 years every 3 years) has the lowest cost per QALY (€173,Rs 11004 in 2008 and Rs.23486 in 2018 for approximately 2 quality-adjusted life-weeks) incrementally to no screening.

Among the studies considered by **Rashidian et al** (22), in **Carter et al (1993)** (29) they have done a MISCAN modelling of triennial breast cancer screening for **50-69 years** old in Australia from a health system perspective. As per Carter et al, the cost per life year gained was found to be $13081(Rs. 405511 in 1993)(Rs.2201850 in 2018).

Similarly, in the study by **Boer et al** (1998) (30) as per the MISCAN model developed for triennial screening of women in U.K. Aged **50-64 years and 50-69 years**, the cost per life year gained was $4195(Rs.176190 in 1998) (Rs.624927 in 2018) and $4343 (Rs 182406 in 1998)(Rs.646975 in 2018) respectively. The cost per death averted was found to be $41824(Rs 1756608 in 1998) (Rs.6230507 in 2018) and $40265(Rs.1691130 in 1998) (Rs.5998264 in 2018) respectively.

Madan et al (24). simulated the experience of a hypothetical cohort of 10,000 women aged **47 to 49** years attending a single breast cancer screening appointment. A portion of the women who have turned up for screening received diagnosis too. As a comparator the proportion of screen-detected breast cancer cases had the screening not been done was also

estimated. Using data on the treatment costs and 10-year survival (a proxy for a cure) for each group, the model estimates the impact of the screening program on treatment costs and mortality for the cohort.

The base-case PSA (24) (suggests that there is a moderate possibility that the intervention is cost-effective for the 47- to 49-year cohort. At a willingness-to-pay threshold of £20,000 (Rs 14,20,000 in 2010)(Rs.2403077 in 2018) per QALY, there is an estimated 29% probability that the additional screening round is cost-effective, rising to 52% if the threshold is set to £30,000(Rs 2130000 in 2010) (Rs.3604615 in 2018) per QALY gained. The probabilistic mean was £23,700 (Rs 1682700 in 2010)(Rs.2847646 in 2018) per QALY gained. It would also cost $44692(Rs.1993263 in 2010) (Rs.3373214 in 2018) to gain 1 QALY in case of triennial screening for 47-49 years old.

Based on the above studies (refer to, mammography screening doesn't seem to be cost-effective in age groups under 50 or above 70 years (24). A study published by Lee et al. in 2009 (25), to determine the most cost-effective screening interval and the target age range for Korean women from the perspective of the national healthcare system. In its' case the cost per cancer detected amounted to $100007 (Rs.9728572) per cancer detected

Mittmann et al. (2015) (26) in his study titled " **Total Cost-effectiveness of mammography screening strategies" mentions** that triennial screening at ages 50 to 69 was the most cost-effective at $94,762 (Rs 4548576 in 2012)(Rs.6603517 in 2018) per QALY. The framework for this analysis is the Canadianized University of Wisconsin Breast Cancer Epidemiology Simulation Model.

The cost-effectiveness ratio of various screening strategies: for no screening, triennial screening for women aged 50 to 69 years and triennial screening for 50 to 74 years is mentioned as follows.

Table 5: Cost of screening strategies – Mammography (26)

Screening strategy	Total cost per 1000 women ($)	Total Quality-adjusted life years (QALYs)per 1000 women	Incremental cost per QALY($)	Average cost per QALY relative to No Screening ($)
No screening (26)	1,387,948 (Rs 66621504 in 2012) (Rs.96719557 in 2018)	14,059	....	Base case
Triennial (3 year)	2,511,486	14,071	94762 (Rs	94,762

50 to 69 years (26)	(Rs 120551328 in 2012) (Rs.175013627 in 2018)		4548576 in 2012) (Rs.6603517 in 2018)	(Rs 4548576 in 2012) (Rs.6603517 in 2018)
Triennial (3 year) 50 to 74 yrs (26)	2,652,005 (Rs 127296240 in 2012) (Rs.184805734 in 2018)	14,072	Dominated	99,670 (Rs 4784160 in 2012) (Rs.6945532 in 2018)

Incremental cost-effectiveness analysis showed that triennial screening at ages 50 to 69 was the most cost-effective at $94,762(Rs 4548576 in 2012)(Rs.6603517 in 2018).

Mittmann et al. (2018) (27) in his study titled **"Cost-effectiveness of mammography from a publicly funded health care system perspective"** mentions that Life time costs for triennial screening per 1000 women (aged 50-74 years) cost was about $5.3million(Rs 254400000 in 2012)(Rs.369332030 in 2018). The incremental cost-utility ratio was $36 981 in (Rs.1775088 in 2012) (Rs.2577031 in 2018)/QALY for triennial screening in women aged 50–69.

Table 6: Cost-Effectiveness scenario – Mammography (27)

Scenario	Modelled overall healthcare system cost, $	Modelled life-years	Modelled QALYs	Marginal cost effectiveness ratio, $/life-year gained	Marginal cost–utility ratio, $/QALY
No screening (27)	1965899 (Rs.94363152 in 2012) (Rs 136994239 in 2018.)	30 602	24 998	-	-
Triennial (3 year) age 50–69 yr (27)	3368225 (Rs.161674800 in 2012) (Rs. 234715731 in 2018)	30 648	25 036	30 536 (Rs.1465728 in 2012) (Rs. 2,127,909 in 2018)	36 981 (Rs.1775088 in 2012) (Rs. 2,577,031 in 2018)
Triennial (3 year) age 50–74 yr (27)	3642494 (Rs.174839712 in 2012) (Rs. 253,828,246 in 2018)	30 653	25 039	33026 (Rs.1585248 in 2012) (Rs. 2,301,426 in 2018)	40 193 (Rs.1929264 in 2012) (Rs. 2,800,860 on 2018)

In a study by **Sun et al** (2018) (28), the comparison among triennial screening and quinquennial screening in case of urban China was modelled.

Table 7: Review 3 - Mammography only versus mammography and ultrasound (28):

Comparators	Lifetime costs per case (US$)	QALY	Incremental costs(US$)	Difference in QALY	ICER (95% CI)
Screening every 3 years (28)	172.94 (Rs. 13140)	22.9960	-11.73 (Rs. 891)	-0.0011	11 000 (-73 330 to 99 983)
Screening every 5 years (28)	145.37 (Rs11045.)	22.9912	-6.72 (Rs. 509)	-0.0007	9 366 (-114 804 to 98 149)

It indicates that compared to no - screening, the risk-based cancer screening programme is more cost effective. It shows that for high-risk women aged 45-69 years, the benefit of ultrasound in addition to mammography is uncertain. The findings suggest mammography screening alone for high-risk women aged 45-69 years is a better alternative compared to both ultrasound and mammography. Also, screening triennially is the most cost-effective screening strategy. This reduces the costs significantly while no major difference is observed in the effects.

Note: All the costs have been adjusted taking into account the conversion rate of the currency for the particular year in which the study was carried out and then adjusted with the inflation rate.

Review 4: Cost-Effectiveness of Breast Cancer Screening Using Piezoelectric finger (triennial and quinquennial screening)

No studies were found assessing the cost-effectiveness of the piezo-electric finger as a breast cancer screening modality with respect to triennial and quinquennial breast cancer screening.

Review 5: Cost-Effectiveness of Breast Cancer Screening of CBE and Ultrasonography as a paired modality for triennial and quinquennial screening

No studies were found assessing the cost-effectiveness of CBE and Ultrasonography as a paired modality.

Review 6: Cost-Effectiveness of Breast Cancer Screening of Piezoelectric finger and Ultrasonography as a paired modality for triennial and quinquennial screening

Limitations and gaps: Less no. of publications is present with respect to the eligibility/inclusion criteria of the cost-effectiveness of triennial (3 years) and quinquennial (5 years) screening for different breast cancer screening modalities in different age groups of females. Among the different breast cancer screening modalities Mammography, Clinical Breast Examination, Ultrasonography and Piezoelectric finger in relation to their solo performance and in combination. For only Clinical Breast Examination publications were found citing their cost-effectiveness only for quinquennial screening (5 years) and not for triennial screening (3 years). No studies were found for cost-effectiveness of the respective

modalities in solo and in the combination namely Piezoelectric finger, Clinical Breast Examination and Ultrasonography, Piezoelectric finger and Ultrasonography as a screening modality for both triennial and quinquennial screening.

In solo performance Mammography had studies citing cost-effectiveness when used in triennial and quinquennial screening mode and Clinical Breast Examination had only 2 studies for 5-year screening interval. The study of Okonkwo_2008 (20) did not report clearly the ICER status (whether dominated or dominant) of CBE 5 year screening program for female's age group 40-60 years. The study by Laxminarayan_2006 (21) had not reported ICER for the 5 year CBE screening program for female's age group (40-60).

III. MODELLING COST-EFFECTIVENESS ANALYSIS

Background

A systematic review was conducted on economic evaluation of different breast cancer screening modalities in female population. Various breast cancer-screening techniques available for screening are clinical breast examination (CBE), mammography (MMG), ultrasonography (USG), piezoelectric finger (Piezo) and biopsy. However, studies done earlier (22 to 27) on cost-effectiveness analysis of breast cancer screening were included mammography verses no screening. Only one study done by Sun et al (28) compared cost-effectiveness of MMG only verses MMG followed by USG strategies. In systematic review, it was also observed that the cost-effectiveness of CBE followed by USG, Piezo followed by USG was not studied in women population across the globe as well as in India. Limited research was done in cost-effectiveness of breast cancer screening techniques in Indian women. There was also a gap in the previously done studies such as which screening will be cost-effective in Indian women, at what age screening should be offered in public healthcare facilities, what could be the optimum screening interval. To address these gaps, a cost-effectiveness analysis was planned with the following objectives.

Objectives

- To develop a model for natural history of breast cancer in Indian women
- To study cost-effectiveness of breast cancer screening with no screening in Indian women
- To identify most cost-effective screening strategy from various screening techniques for Indian women
- To determine the age at which screening should be offered e.g. the minimum and maximum age for screening will be determined.
- To determine the optimal screening interval and to assess the most cost-effective option regarding time duration for conducting periodic screening ie. 3 years or 5 years.

Methodology

A Cost-effectiveness analysis (CEA) was done to study the cost-effectiveness of four-breast cancer screening strategies in Indian women compared to no screening with healthcare system perspective.

Breast cancer screening strategies

Six breast cancer-screening strategies are considered for screening of breast cancer and the comparator was no screening. A clinical breast examination followed by ultrasonography (CBE+USG screening) is used as a standard breast cancer screening strategy as per MOHFW operational guidelines in every 5 years of interval in the age group of 30 to 65 years (32). Other screening strategies used are CBE only, CBE paralleled with USG screening, MMG alone, MMG followed by USG (MMG+USG) and piezoelectric finger followed by USG (Piezo+USG screening). If first screening test is positive, then the women will be screened by the second screening test (except CBE only, CBE parallel with USG and MMG only strategy). Biopsy is used as confirmatory test for diagnosis of breast cancer in the positive cases screened by these six screening methods i.e. CBE only, CBE parallel with USG, CBE+USG, MMG only, MMG+USG and Piezo+USG. Each of these six screening strategies compared with no screening. A clinical pathway is shown in the Fig 24.
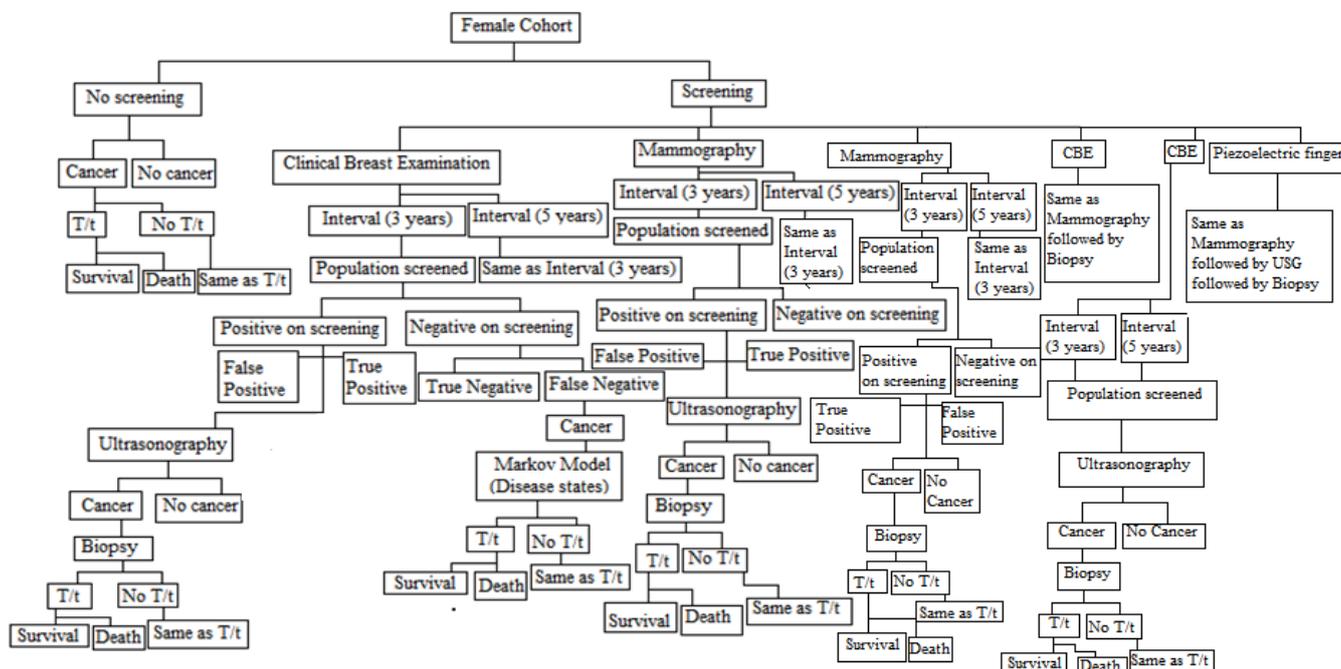
Fig 24: Clinical Pathway to assess the cost-effectiveness of various technological interventions

It was assumed that CBE and piezoelectric finger screening can be conducted at sub-centre/ health and wellness centre and above level by the auxiliary nurse midwives (ANM),

supervised or supported by the physician. Mammography, ultrasonography and biopsy can be conducted at district hospital by trained radiologist and pathologist.

The CEA included screening cost of each screening strategy and life time treatment cost for diagnosed breast cancers and the effectiveness was measured as the Quality Adjusted Life Years (QALYs) gained per unit cost incurred. A decision tree using probabilistic Markov model was developed using TreeAgePro 2018 software version R2.1 (TreeAge software Inc. Williamstown, United States of America) (31).

Modeling natural history of breast cancer

A probabilistic Markov model was developed to study the natural history of developing breast cancer in a hypothetical cohort of 1,00,000 women aged 35-40 years, 40-45 years, 45-50 years, 50-55 years and 55-60 years with life time horizon of annual cycle. Seven health states viz. healthy; breast cancer with stages 1, 2, 3, 4; death due to breast cancer and death due to all causes were used in the Markov model.
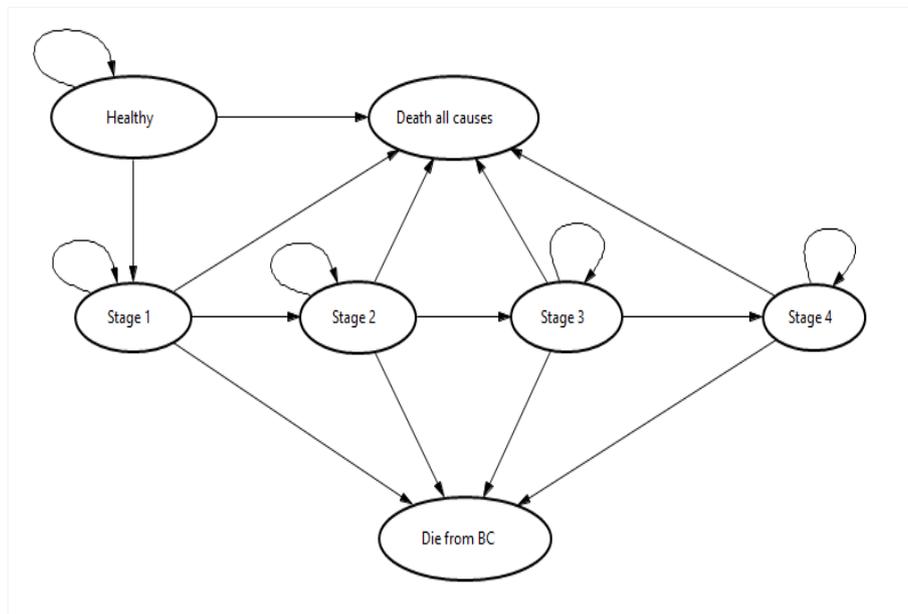
Figure 25: Markov model for natural history of breast cancer

Figure 25 shows the Markov model for natural history of breast cancer. Ovals show 7 health states, straight arrows show the likelihood of movement from one health state to another, circular arrows starting and ending in the same state show the likelihood of remaining in the same state. A healthy woman may remain healthy, or may get a stage 1 breast cancer in the

next cycle or may die naturally. In each stage of breast cancer, woman may remain in the same stage; or progress to the next stage; or die due to breast cancer or naturally in the next cycle.

Age-specific breast cancer incidence rates were used for healthy women to diagnose with breast cancer through various screening strategies and for no screening, age-specific breast cancer prevalence rates were used for the clinical diagnosis of breast cancer in the women. Annual transition probabilities were used for movement through breast cancer stages and also for breast cancer deaths after the treatment. Age-specific probabilities of deaths were used for all cause deaths in the Markov model. Details of variables used in the model are given in Table 8.

Clinical variables

A secondary data on age-specific breast cancer incidence from the population based cancer registry database of Cancer Samiksha National Centre for Disease Informatics and Research (ICMR) was used in the model (33). The mean incidence rate was calculated using age-specific incidence rates of 27 districts for the latest year. The probability of the incidence was calculated by dividing mean value by 1,00,000 since the incidence rates were available per 1,00,000 population.

Age-specific breast cancer prevalence rates, proportion of patients in different breast cancer stages, annual mortality rate of breast cancer were referred from Ginsberg *et al*, 2012 (34). Annual transition probabilities of breast cancer from stage 1 to 2, stage 2 to 3 and stage 3 to 4 were considered from the study conducted by Toskos et al. (35) while transition probability of stage 4 to death was considered from the study conducted by Wong et al, 2007 (36). Proportion of breast cancer patients diagnosed clinically in different stages was considered from Gogai *et al*, 2018 (37) studies respectively. Annual probability of death due to all causes was considered from SRS 2012-2016 life tables for India (38).

Table 8: Parameters used for Cost-Effectiveness modeling of tests, India, 2018

Variables	Base value	Distribution	Reference/ Source
Incidence rate of breast cancer in Indian women			
Age 35-39 years	0.0002233		
Age 40-44 years	0.0003969		
Age 45-49 years	0.0005209		Cancer Samiksha (33)
Age 50-54 years	0.0006759		
Age 55-59 years	0.0007145		
Prevalence of breast cancer			
Age 30-44 years	0.0024		Ginsberg et al, 2012 (34)
Age 45-59 years	0.0034		
Stage distribution of breast cancer: Screened			
Stage 1	0.490		
Stage 2	0.374		Ginsberg et al, 2012 (34)
Stage 3	0.086		
Stage 4	0.050		
Stage distribution of breast cancer: non-screened/ clinical			
Stage 1	0.04		
Stage 2	0.33		Gogai et al, 2018 (37)
Stage 3	0.45		
Stage 4	0.18		
Annual progression rate			
Stage 1 to Stage 2	0.06		
Stage 2 to Stage 3	0.11		Toskos et al, 1987 (35)
Stage 3 to Stage 4	0.15		
Stage 4 to Death	0.23		Wong et al, 2007 (37)
Annual mortality rate after treatment			
Stage 1	0.006		
Stage 2	0.042		Ginsberg et al, 2012 (34)
Stage 3	0.093		
Annual all cause mortality			
Age 35-40 years	0.00980		
Age 40-45 years	0.01376		
Age 45-50 years	0.01879		SRS 2012-2016 life tables (38)
Age 50-55 years	0.03609		
Age 55-60 years	0.04957		
Utility scores			
Perfect health	1	Log-normal	
Stage 1	0.79	Log-normal	
Stage 2	0.79	Log-normal	Shi et al, 2016 (43)
Stage 3	0.77	Log-normal	
Stage 4	0.69	Log-normal	

Table 8: Parameters used for Cost-Effectiveness modeling of tests, India, 2018 (continued...)

Variables	Base value	Distribution	Reference/ Source
Sensitivity of tests			
Clinical Breast Examination (CBE)	0.73	Beta	
Mammography (MMG)	0.71	Beta	
Ultrasonography (USG)	0.73	Beta	Meta-analysis of studies done by NHSRC, 2018
Piezoelectric finger	0.83	Beta	
CBE parallel with USG	0.91	Beta	
Biopsy	1		
Specificity of tests			
Clinical Breast Examination (CBE)	0.94	Beta	
Mammography (MMG)	0.95	Beta	
Ultrasonography (USG)	0.94	Beta	Meta-analysis of studies done by NHSRC, 2018
Piezoelectric finger	0.88	Beta	
CBE parallel with USG	0.99	Beta	
Biopsy	1		
Screening costs (in US $) (US $1 = INR 70/-)			
Clinical Breast Examination (CBE)	0.27	Gamma	Estimated cost (as per CGHS rates, 2014) (39)
Mammography (MMG)	5.00	Gamma	as per CGHS rates, 2014 (39)
Ultrasonography (USG)	5.31	Gamma	as per CGHS rates, 2014 (39)
Piezoelectric finger	1.09	Gamma	Estimated cost
Biopsy	6.57	Gamma	as per CGHS rates, 2015 (42)
OPD visit for non-screened patients	3.93	Gamma	as per ECHS rates, 2011 (40)
Treatment costs (in US $) (US $1 = INR 70/-) (Public health sector)			
Stage 1	2887.83	Gamma	
Stage 2	2887.83	Gamma	Estimated cost (as per CGHS 2015, ECHS 2011 and CGHS drug list) (39,40,41)
Stage 3	2890.11	Gamma	
Stage 4	2775.83	Gamma	
GDP per capita, India (in US $) (US $1 = INR 70/-)			
Willingness to pay for Screening and treatment	1963.55		https://tradingeconomics.com/india/gdp-growth-annual, 2017 (44)

Diagnostic accuracy of screening tests

Sensitivity and specificity of the screening test were used to measure diagnostic accuracy of the screening. The sensitivity and specificity of the screening tests were calculated as pooled estimates on the basis of the results obtained from the meta-analysis of the studies for the clinical effectiveness of different breast cancer screening strategies. The sensitivity and specificity were calculated on the basis of True Positive, False Positive, False Negative and True Negative as obtained from each study as per the meta-analysis performed using Rev Man 5.3 and biopsy was taken as a gold standard. Hence the sensitivity and specificity of biopsy was considered as 1.

Costs of screening and treatment

Cost of screening clinical breast examination was estimated using monthly salary and working hours of ANM; time require for 1 screening test; and number of screenings per day. Cost of piezoelectric finger screening test was estimated using cost of device, cost of scans and cost of cartridge. Details of cost of CBE and Piezoelectric finger screening tests are given in Appendix 3. Costs of mammography, ultrasonography and biopsy were used from CGHS 2014 rate list (39).

Stage wise types and frequency of treatment regimens, drugs, number of hospital days, number of follow-up visits etc. were discussed with the expert oncologist. The treatment regimens for stage 1 and 2 are Lumpectomy with axillary dissection, Adjuvant Chemotherapy (6-8 cycles), Radiotherapy course (Linear Accelerator Radical Therapy), Targeted Therapy (17 injections), Endocrine therapy. The treatment regimens for stage 3 are Modified Radical Mastectomy, New-Adjuvant Chemotherapy (4 cycles), Radiotherapy course (Linear Accelerator Radical Therapy), Targeted Therapy (17 injections), Endocrine therapy. The treatment regimens for stage 4 are Simple Mastectomy, Palliative Chemotherapy (4 cycles), Radiotherapy course (Linear Accelerator Radical Therapy), Targeted Therapy (17 injections), Endocrine therapy. All the stages require follow-up visit and hospital stay of 2 days. Stage wise treatment cost was estimated using cost from CGHS 2015 (42), ECHS 2011 (40) and CGHS drug list (41) as advised by expert oncologist. Detailed stage wise treatment regimens and costs are given in Appendix 4.

For no screening, it was assumed that the woman, who suffers from breast cancer symptoms, would visit the provider in the public health facility. Women will be screened using standard CBE+USG+Biopsy protocol for breast cancer screening. Women will be treated if diagnosed with breast cancer as per the treatment regimen given in Appendix 4. Hence cost of Out Patient Department (OPD) visit, costs of CBE+USG+Biopsy, along with the cost of stage wise treatment were considered for the analysis. Costs were converted to US $ using rate US $1 = INR 70/- (47). Costs were not inflated since the rates of CGHS and ECHS are same in 2018 and there is no change in all the rates.

It was considered that all the women who detected with breast cancer would be treated as per the stage of the breast cancer protocol.

Quality Adjusted Life Years (QALYs)

Quality adjusted life years (QALYs) is a measure of effectiveness of the screening strategy which was calculated using length of life and the quality of health i.e. utility scores of each health state. Utility score for healthy was considered as 1 and 0 for death. Breast cancer stage wise health utility scores are not available for Indian women. Hence secondary data on utility scores for stage 1, 2, 3 and 4 were considered from the study conducted by Shi *et al*, 2016 (43).

Cost-effectiveness analysis and screening scenarios

Base CEA decision tree was developed using markov-modeling approach for annual screening by four different screening strategies and no screening as comparator. Costs, QALYs, cost-effectiveness (CE) ratio were estimated for each screening strategy and the no screening. Incremental cost and effectiveness were calculated as the difference between the screening strategy and the no screening. Incremental cost-effectiveness ratio (ICER) was calculated as the division of incremental cost and the incremental effect.

Using base model, CEA with two different scenarios of screening once in 3 years and 5 years were done for the Indian women of these 5 age groups. In all 15 models were developed to study the cost-effectiveness of different screening strategies 3 models in each age group namely, age group 35-40 years (annual screening, screening interval 3 years, screening interval 5 years), age group 40-45 years (annual screening, screening interval 3 years, screening interval 5 years), age group 45-50 years (annual screening, screening interval 3 years, screening interval 5 years), age group 50-55 years (annual screening, screening interval 3 years, screening interval 5 years) and, age group 55-60 years (annual screening, screening interval 3 years, screening interval 5 years).

Discount rate of 3% was applied to both cost and QALYs. Gross Domestic Product (GDP) per capita of India was used as the willingness to pay (WTP) for both screening and treatment cost threshold in the CEA (44).

One-way sensitivity analysis was done to study the uncertainty of the CEA was by using minimum and maximum values of costs, sensitivity, utility scores of various health states, sensitivity and specificity of the screening tests. As per Briggs, 2005, costs follow Gamma distribution, sensitivity and specificity follow beta distribution and health utility scores follow log-normal distribution (45). Parameters of these distributions were estimated and used

simultaneously in the probabilistic sensitivity analysis to study the uncertainty. A Monte Carlo Simulation with 1,00,000 iterations was used to estimate the incidence and relative risk of breast cancer, costs, effects, cost-effectiveness ratio, incremental cost-effectiveness ratio (ICER), net monetary benefit and probability of accepting the screening strategy which is most cost-effective in each of 15 models. Net Monetary Benefit (NMB) was calculated as (incremental effect x threshold) – incremental cost. Incremental Net Monetary Benefit (INMB) was calculated as the difference between NMB of screening strategy and no screening. A screening strategy considered as cost-effective if the INMB is positive i.e. INMB > 0 (35).

Results:

A probabilistic Markov model estimated breast cancer (BC) incident cases per 1,00,000 women for four different screening strategies of 5 age groups of women.
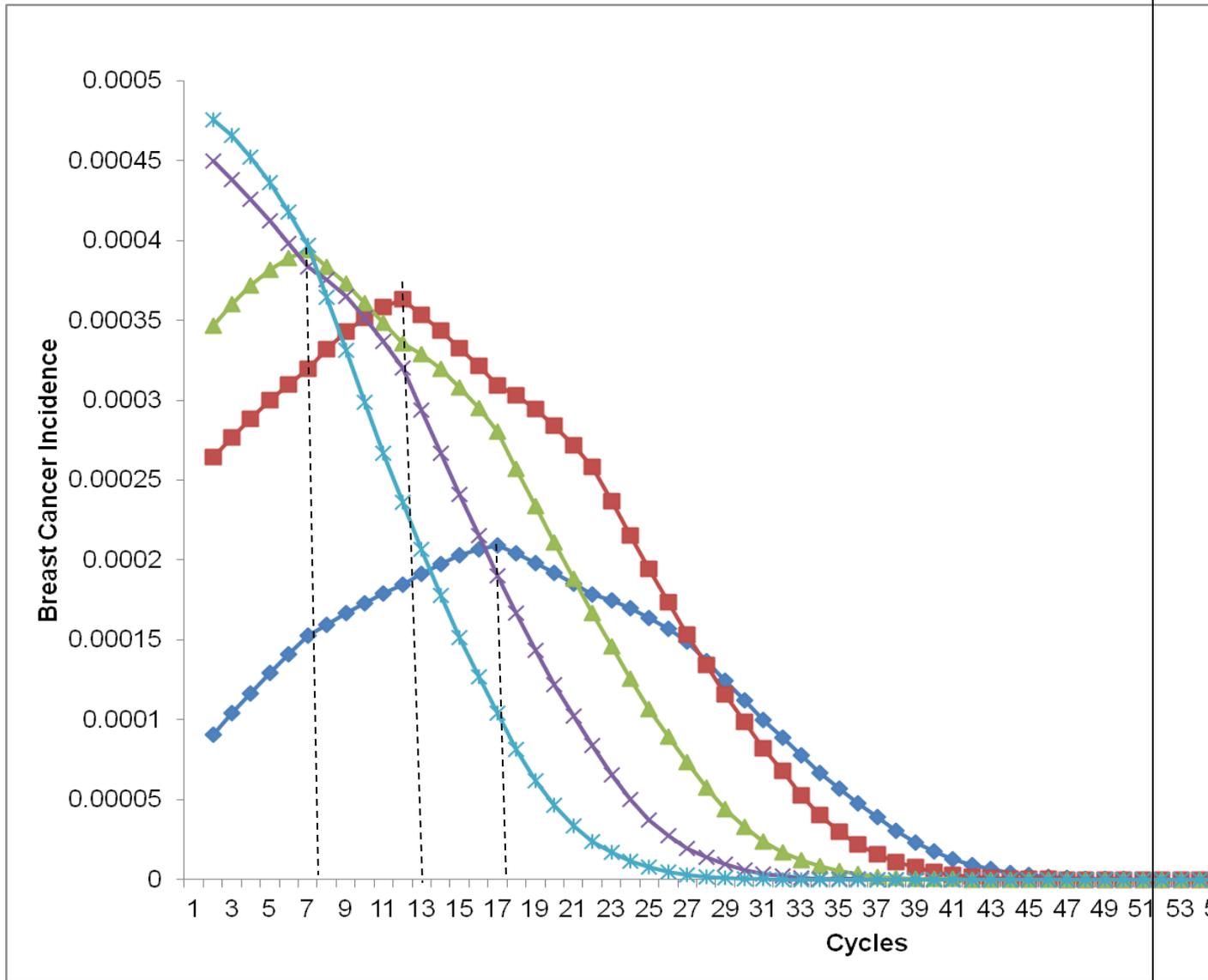
Fig 26: Annual incidence of breast cancer in screened women, India, 2018

Figure 26 shows the incidence probabilities in the different age group of women over lifetime horizon. Incidence of breast cancer would likely to increase till age 53 and then it will start decreasing. It was observed that if screening were started at younger age 35-40 years, then it would take 17 years for incidence to reach at its peak. If screening is started at age 40-45 years and 45-50 years, then it will take 13 and 8 years respectively for the incidence to reach at its peak. After 50 years, there will be decrease in the incidence. Hence if the screening is offered in the younger age i.e. 35-40 years, it will be effective to detect cancer cases earlier and improve quality of women's life.

In base case analysis i.e. annual screening, total 53 breast cancer cases per 1,00,000 women were detected through CBE only screening, 68 cases through CBE parallel with USG

screening, 62 cases through MMG screening, 43 cases through CBE+USG screening, 52 cases through Piezo+USG screening, 49 cases through MMG+USG screening, and 369 cases were detected clinically in the absence of screening. Figure 27 shows age-specific incidence probabilities with 95% confidence interval error bars (95% CI).
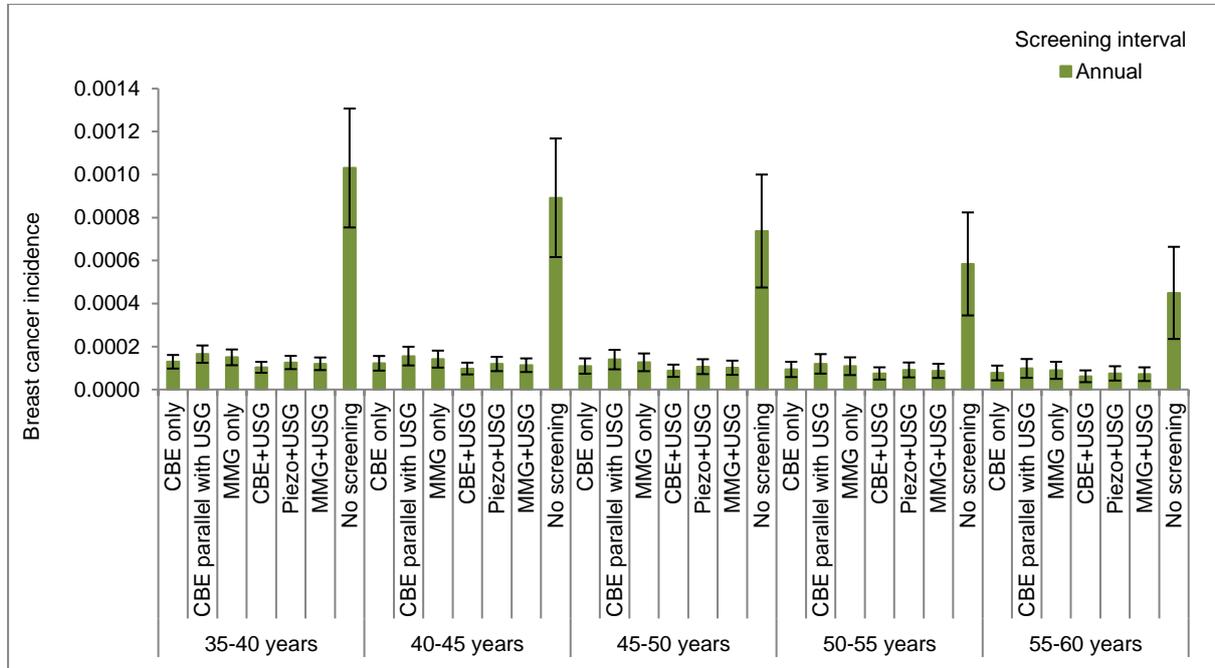
Fig 27: Annual incidence of breast cancer in screened and non-screened women, India, 2018
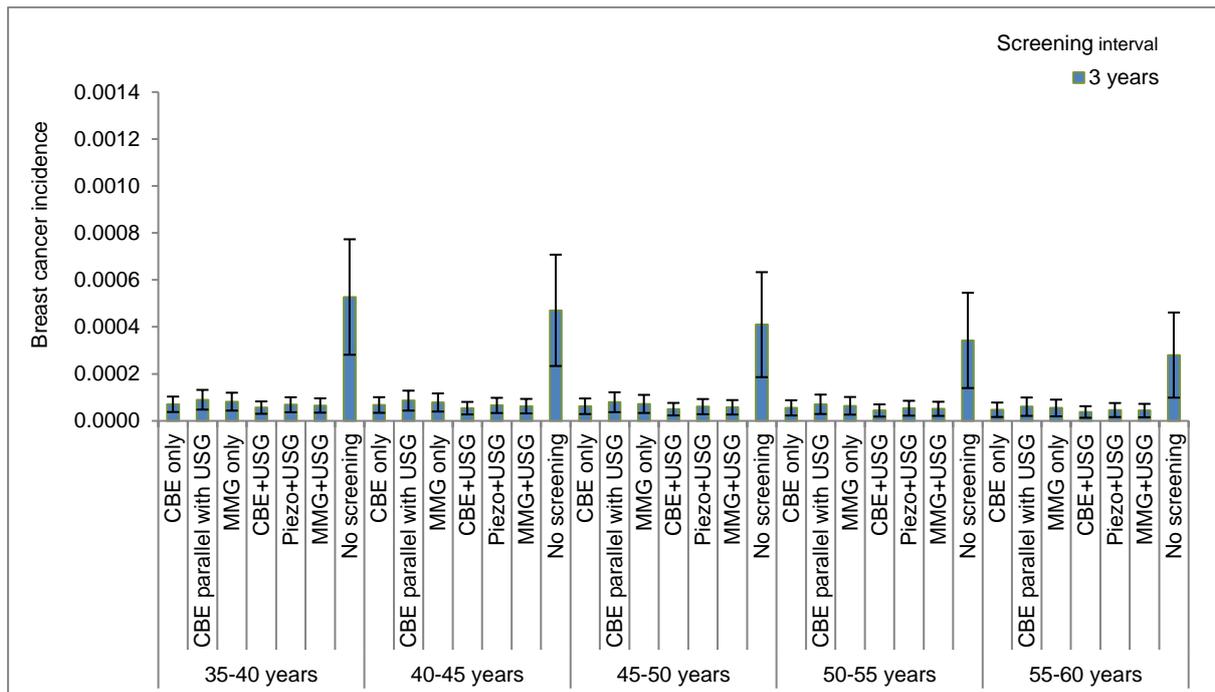
Fig 28: Three years incidence of breast cancer in screened and non-screened women, India, 2018

In triennial screening (once in 3 years), total 30 incident breast cancer cases per 1,00,000 women were detected through CBE only screening, 39 cases through CBE parallel with USG screening, 35 cases through MMG screening, 24 cases through CBE+USG screening, 30 cases through Piezo+USG screening, 28 cases through MMG+USG screening, and 203 cases were detected clinically in the absence of screening (Fig 28).

Similarly, **i**n quinquennial screening (once in 5 years), total 22 incident BC cases per 1,00,000 women were detected through CBE only screening, 29 cases through CBE parallel with USG screening, 26 cases through MMG screening, 18 cases through CBE+USG screening, 22 cases through Piezo+USG screening, 21 cases through MMG+USG screening, and 152 cases were detected clinically in the absence of screening (Fig 29).
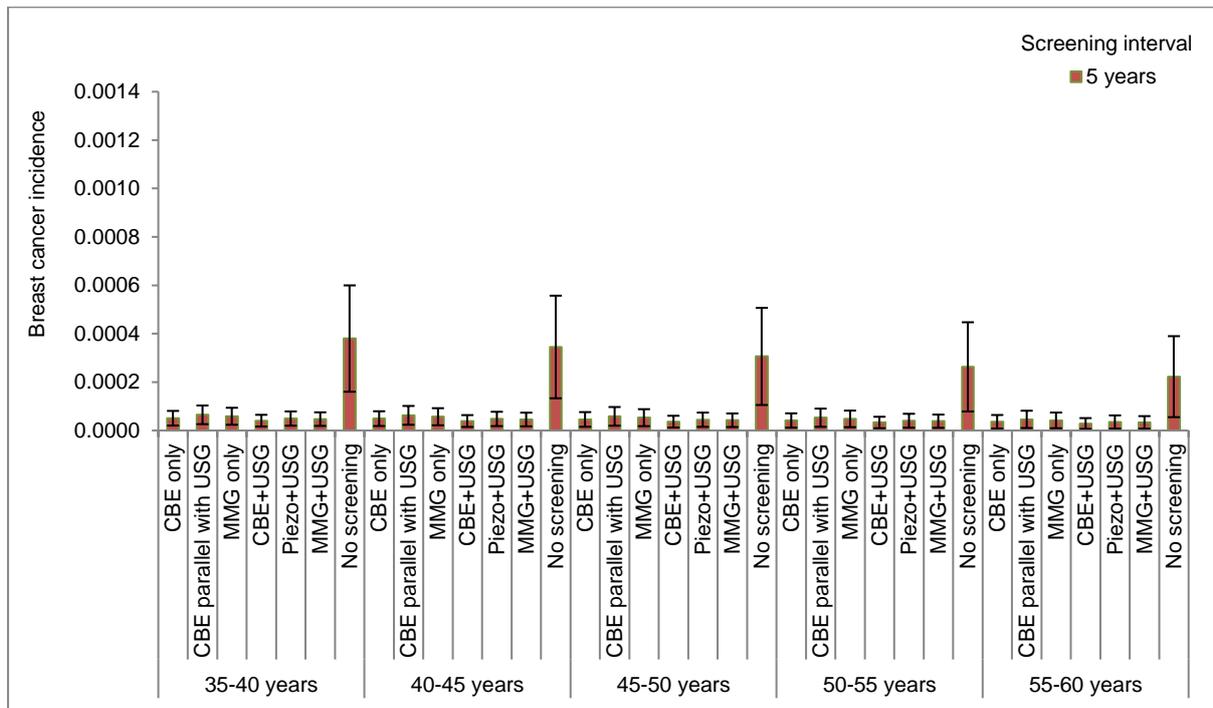
Fig 29: Five years incidence of breast cancer in screened and non-screened women, India, 2018

Sensitivity and specificity of CBE parallel with USG screening is higher than other screening tests resulted in more number of estimated incident cases as compared to other screening strategies.

In the cohort of women aged 35-40 years, annual BC incidence was highest as 79 cases per 1,00,000 women, and lowest incidence was 47 cases in women aged 55-60 years. Similar declining trend of BC incidence from youngest to the oldest age-groups was observed in 3 years and 5 years screening (Fig 27, 28, 29).

Table 9 to 13 shows the BC incidence, incidence ratio (screen/no screen). It was observed on an average 65 cases were detected through annual screening, and BC incidence was decreased in 3 years screening as an average 37 BC cases and further it decreased in 5 years screening as an average 27 BC cases.

Total 10,527 cancer cases were detected through CBE parallel with USG screening in the cohort of 1,00,000 women aged 35-40 years annually and 44,320 cases were detected clinically in the absence of screening. Total 544 BC deaths were estimated annually through CBE parallel with USG screening and 4,781 BC deaths in absence of screening in the age-group 35-40 years.

Table 9: Incidence and relative risk of breast cancer by screening strategies in women aged 35-40 years, India, 2018

Age group	Screening interval	Strategy	Breast cancer incidence	Breast cancer incidence ratio (screen/no screen)	Cancer cases detected and treated (per 1 lakh women)	Cancer deaths after treatment (per 1 lakh women)
35-40 years	Annual	CBE only	0.0001291	0.1253	9885	599
		CBE parallel with USG	0.0001647	0.1598	10527	544
		MMG only	0.0001497	0.1453	10257	567
		CBE+USG	0.0001033	0.1002	9419	639
		Piezo+USG	0.0001258	0.1220	9824	605
		MMG+USG	0.0001198	0.1162	9716	614
		No screening	0.0010307	Reference	44320	4781
35-40 years	3 years	CBE only	0.0000705	0.1337	3337	175
		CBE parallel with USG	0.0000899	0.1705	3458	150
		MMG only	0.0000818	0.1550	3407	160
		CBE+USG	0.0000564	0.1070	3248	194
		Piezo+USG	0.0000687	0.1302	3325	178
		MMG+USG	0.0000654	0.1240	3305	182
		No screening	0.0005273	Reference	16252	1560
35-40 years	5 years	CBE only	0.0000508	0.1336	1836	86
		CBE parallel with USG	0.0000648	0.1704	1882	71
		MMG only	0.0000589	0.1549	1862	78
		CBE+USG	0.0000406	0.1069	1802	96
		Piezo+USG	0.0000495	0.1302	1831	87
		MMG+USG	0.0000471	0.1240	1824	90
		No screening	0.0003800	Reference	9356	808

Further in 3 years screening, 3458 BC cases and 150 deaths were estimated through CBE parallel with USG screening, i.e. in 3 years screening. In 5 years screening, 1882 BC cases and 71 deaths were estimated through CBE parallel with USG screening (Table 9). Thus highest numbers of BC cases were detected through CBE parallel with USG screening which resulted in reducing the cancer deaths as compared to the other 5 screening strategies.
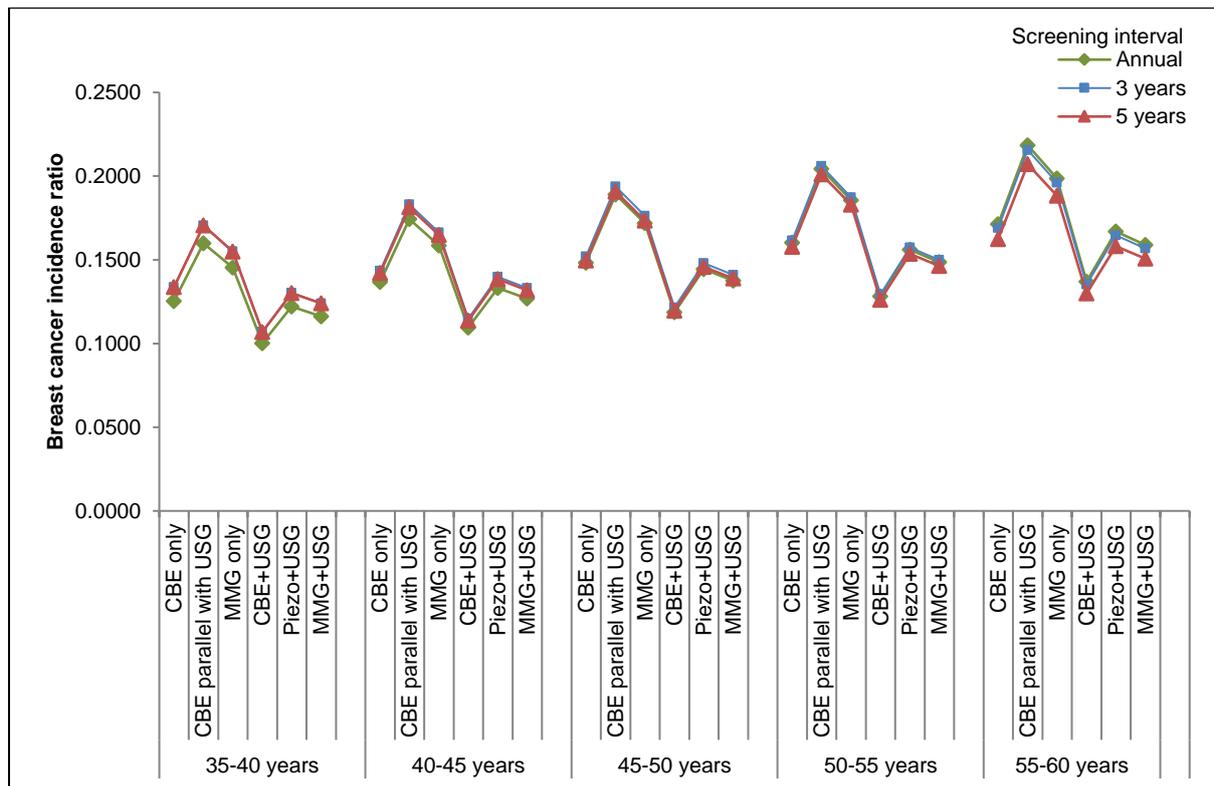
Fig 30: Screening interval wise incidence ratio of breast cancer in women, India, 2018

Breast cancer incidence ratio of CBE parallel with USG screening to no screening was 0.1705 in 3 years screening and 0.1704 in 5 years screening. There was no statistically significant difference in the incidence ratio of 3 years and 5 years screening (p=0.998). Similar trend was observed in other screening strategies and other age groups suggested that 3 years screening would be effective in early detection of more cancer cases and avert more cancer deaths in the women (Fig.30, Table 9 to 13).

Table 10: Incidence and relative risk of breast cancer by screening strategies in women aged 40-45 years, India, 2018

Age group	Screening interval	Strategy	Breast cancer incidence	Breast cancer incidence ratio (screen/no screen)	Cancer cases detected and treated (per 1 lakh women)	Cancer deaths after treatment (per 1 lakh women)
40-45 years	Annual	CBE only	0.0001220	0.1368	8869	531
		CBE parallel with USG	0.0001556	0.1744	9414	479
		MMG only	0.0001415	0.1586	9185	501
		CBE+USG	0.0000976	0.1094	8473	569
		Piezo+USG	0.0001188	0.1332	8817	536
		MMG+USG	0.0001132	0.1268	8726	545
		No screening	0.0008922	Reference	36461	3876
40-45 years	3 years	CBE only	0.0000675	0.1435	3064	531
		CBE parallel with USG	0.0000861	0.1830	3169	479
		MMG only	0.0000783	0.1664	3125	501
		CBE+USG	0.0000540	0.1148	2987	569
		Piezo+USG	0.0000658	0.1398	3054	536
		MMG+USG	0.0000626	0.1331	3036	545
		No screening	0.0004706	Reference	13680	3876
40-45 years	5 years	CBE only	0.0000491	0.1422	1715	531
		CBE parallel with USG	0.0000626	0.1813	1756	479
		MMG only	0.0000569	0.1649	1739	501
		CBE+USG	0.0000393	0.1137	1686	569
		Piezo+USG	0.0000478	0.1385	1711	536
		MMG+USG	0.0000455	0.1319	1704	545
		No screening	0.0003451	Reference	8013	3876

Table 11: Incidence and relative risk of breast cancer by screening strategies in women aged 45-50 years, India, 2018

Age group	Screening interval	Strategy	Breast cancer incidence	Breast cancer incidence ratio (screen/no screen)	Cancer cases detected and treated (per 1 lakh women)	Cancer deaths after treatment (per 1 lakh women)
45-50 years	Annual	CBE only	0.0001093	0.1482	7351	432
		CBE parallel with USG	0.0001394	0.1890	7767	385
		MMG only	0.0001267	0.1718	7592	405
		CBE+USG	0.0000874	0.1186	7048	466
		Piezo+USG	0.0001064	0.1443	7311	436
		MMG+USG	0.0001014	0.1375	7241	444
		No screening	0.0007374	Reference	28175	2934
45-50 years	3 years	CBE only	0.0000622	0.1520	2648	432
		CBE parallel with USG	0.0000794	0.1938	2731	385
		MMG only	0.0000722	0.1762	2696	405
		CBE+USG	0.0000498	0.1216	2587	466
		Piezo+USG	0.0000606	0.1480	2640	436
		MMG+USG	0.0000577	0.1409	2626	444
		No screening	0.0004096	Reference	11066	2934
45-50 years	5 years	CBE only	0.0000458	0.1496	1514	432
		CBE parallel with USG	0.0000584	0.1908	1547	385
		MMG only	0.0000531	0.1735	1533	405
		CBE+USG	0.0000366	0.1197	1490	466
		Piezo+USG	0.0000446	0.1457	1511	436
		MMG+USG	0.0000425	0.1388	1506	444
		No screening	0.0003062	Reference	6626	2934

Table 12: Incidence and relative risk of breast cancer by screening strategies in women aged 50-55 years, India, 2018

Age group	Screening interval	Strategy	Breast cancer incidence	Breast cancer incidence ratio (screen/no screen)	Cancer cases detected and treated (per 1 lakh women)	Cancer deaths after treatment (per 1 lakh women)
50-55 years	Annual	CBE only	0.0000936	0.1601	5689	325
		CBE parallel with USG	0.0001193	0.2042	5978	286
		MMG only	0.0001085	0.1857	5856	303
		CBE+USG	0.0000749	0.1281	5479	353
		Piezo+USG	0.0000911	0.1560	5661	329
		MMG+USG	0.0000868	0.1485	5613	335
		No screening	0.0005843	Reference	20518	2076
50-55 years	3 years	CBE only	0.0000553	0.1615	2165	325
		CBE parallel with USG	0.0000706	0.2060	2226	286
		MMG only	0.0000641	0.1873	2200	303
		CBE+USG	0.0000443	0.1292	2121	353
		Piezo+USG	0.0000539	0.1573	2159	329
		MMG+USG	0.0000513	0.1498	2149	335
		No screening	0.0003424	Reference	8451	2076
50-55 years	5 years	CBE only	0.0000415	0.1577	1279	325
		CBE parallel with USG	0.0000529	0.2011	1304	286
		MMG only	0.0000481	0.1828	1293	303
		CBE+USG	0.0000332	0.1262	1260	353
		Piezo+USG	0.0000404	0.1536	1276	329
		MMG+USG	0.0000385	0.1463	1272	335
		No screening	0.0002630	Reference	5227	2076

Table 13: Incidence and relative risk of breast cancer by screening strategies in women aged 55-60 years, India, 2018

Age group	Screening interval	Strategy	Breast cancer incidence	Breast cancer incidence ratio (screen/no screen)	Cancer cases detected and treated (per 1 lakh women)	Cancer deaths after treatment (per 1 lakh women)
55-60 years	Annual	CBE only	0.0000770	0.1713	4112	226
		CBE parallel with USG	0.0000982	0.2185	4292	196
		MMG only	0.0000893	0.1986	4216	209
		CBE+USG	0.0000616	0.1370	3980	247
		Piezo+USG	0.0000750	0.1668	4094	229
		MMG+USG	0.0000714	0.1589	4064	234
		No screening	0.0004496	Reference	14200	1381
55-60 years	3 years	CBE only	0.0000473	0.1691	1666	226
		CBE parallel with USG	0.0000604	0.2156	1707	196
		MMG only	0.0000549	0.1960	1690	209
		CBE+USG	0.0000379	0.1352	1637	247
		Piezo+USG	0.0000461	0.1646	1662	229
		MMG+USG	0.0000439	0.1568	1656	234
		No screening	0.0002801	Reference	6227	1381
55-60 years	5 years	CBE only	0.0000361	0.1624	1017	226
		CBE parallel with USG	0.0000461	0.2071	1034	196
		MMG only	0.0000419	0.1883	1027	209
		CBE+USG	0.0000289	0.1299	1004	247
		Piezo+USG	0.0000352	0.1582	1015	229
		MMG+USG	0.0000335	0.1506	1012	234
		No screening	0.0002225	Reference	4014	1381

Cost-effectiveness of screening strategies

Tables 14 to 18 show costs, QALYs, cost-effectiveness (C/E) ratio, incremental costs and effects, incremental cost-effectiveness ratio (ICER), net monetary benefits (NMB) and incremental net monetary benefits (INMB).

In the presence of annual screening, total estimated lifetime screening and treatment cost of BC was US\$ 344,02,254.11 and in the absence of the screening, total lifetime cost was US\$ 793,13,088.90 for 1,00,000 women of aged 35-40 years. So the estimated lifetime cost for early detection of BC was US\$ 344.02 (INR 24,081/-) per woman and US\$ 793.13 (INR 55,519/-) per woman aged 35-40 years in late detection of BC.

Similar trend was observed in the estimates of life-time costs in early and late detection of BC cases in 3 years and 5 years. Estimated life-time cost was US\$ 182.60 (INR 12,782/-) and US\$ 143.06 (INR 10,014/-) per woman in the presence of 3 years and 5 years screening respectively. Estimated life-time cost was US\$ 365.85 (INR 25,610/-) and US\$ 225.74 (INR 15,802/-) in the absence of screening at 3 and 5 years respectively. Thus late detection of BC resulted in likelihood of increasing life-time cost twice as compared to the early detection of BC in the women aged 35-40 years (Table 14).

For annual screening, estimated average 22.83 QALYs were gained per woman as compared to the 22.32 QALYs gained per women aged 35-40 years. In early detection of BC, estimated QALYs gained were 11.43 and 8.16 per woman in the 3 years and 5 years screening respectively. In late detection of BC, in absence of screening estimated QALYs gained were 11.35 and 8.13 per woman in the 3 years and 5 years respectively (Table 14).

Thus incremental cost was reduced by US\$ 449.11 (INR 31,438/-) and incremental effect of 0.52 QALYs were gained per woman aged 35-40 years through annual screening. So the NMB was US\$ 44,490.19 (INR 31,14,313/-) per woman, US\$ 22,263.43 (INR 15,58,440/-) per woman and US\$ 15,891.63 (INR 11,12,414/-) per woman aged 35-40 years in the presence of annual, 3 years and 5 years screening respectively (Table 14).

In annual screening, estimated life-time cost was lowest US\$ 172.62 (INR 12,083/-) per woman aged 35-40 years in the CBE screening. Second cost-effective screening strategy was

CBE parallel with USG resulting in estimated life-time cost of US$ 372.91 (INR 26,104/-) per woman. Also estimated effect was highest i.e. 22.8362 QALYs and 22.8387 QALYs gained per woman aged 35-40 years in the CBE only and CBE parallel with USG screening respectively.

Similar trend was observed in 3 years and 5 years screening, life-time estimated cost was US$ 78.56 (INR 5,499/-) per woman and US$ 47.66 (INR 3,336/-) per women; estimated QALYs gained were 11.43 and 8.16 women aged 35-40 years screened through CBE only screening at interval of 3 years and 5 years respectively. Apart from CBE only screening strategy, another cost-effective strategy was CBE parallel with USG with life-time cost of US$ 197.30 (INR 13,811/-) per woman and US$ 136.41 (INR 9,549/-) per women; estimated QALYs gained were 11.43 and 8.16 women aged 35-40 years screened at an interval of 3 years and 5 years respectively (Table 14).

Similar trend was observed in other age-groups. CBE parallel with USG screening and CBE only screening were most cost-effective than other screening strategies in all the screening intervals annual; 3 years; and 5 years. Estimated life-time cost and QALYs gained per woman were decreased with the increasing age of the woman. (Table 15 to 18).

Thus in CEA, it was observed that both CBE only and CBE parallel with USG were Undominated and cost-effective screening strategies in all age groups and all screening intervals.

In one-way sensitivity analysis, a small effect of variation in cost of MMG, biopsy, cost of treatment at stage 2, 3, 4; sensitivity of MMG and utility scores was observed on ICERs of MMG screening verses no screening in all the age-groups. ICERs were lower than the willingness to pay threshold US$ 1963.55.

In probabilistic sensitivity analysis, estimated probability of cost-effective screening at various willingness to pay US$ 550, US$ 1100 and US$ 2200 was 100% for CBE only screening across all 5 age-groups and all screening intervals 3 years and 5 years including base model i.e. annual screening (Table 19).
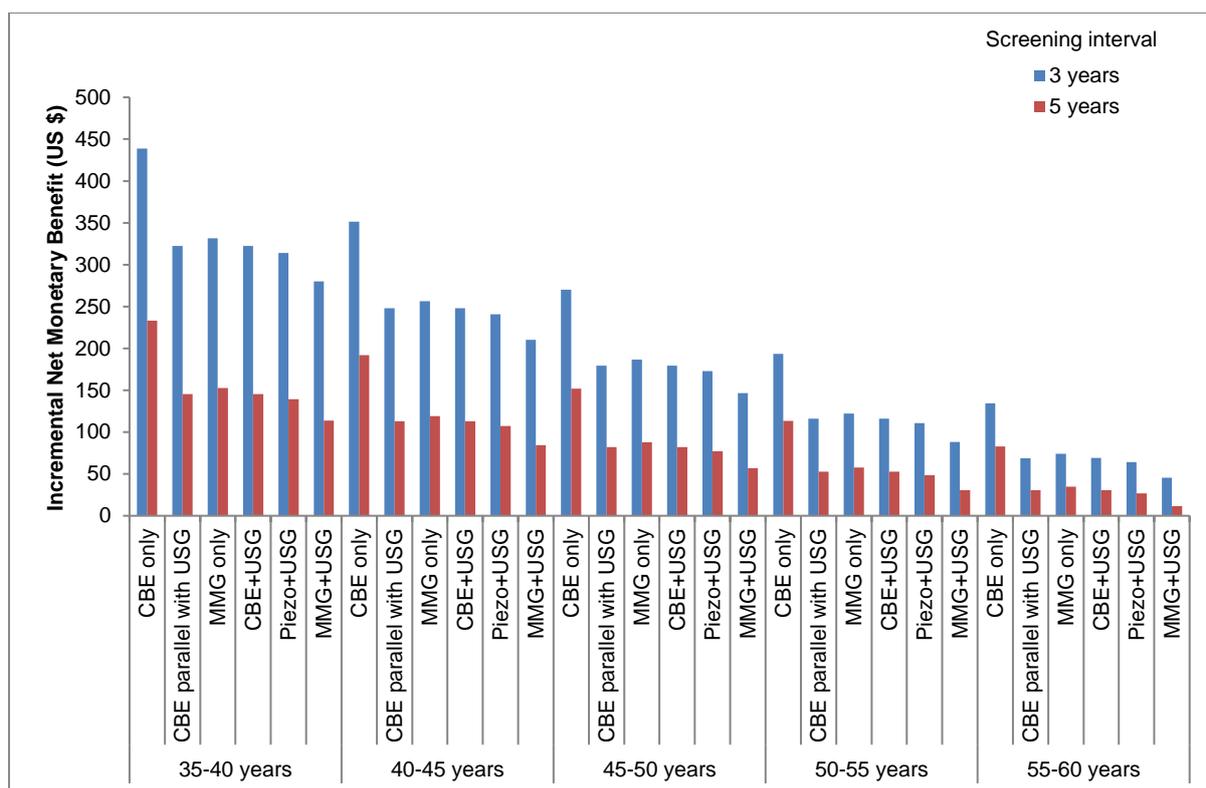
Fig 30: Incremental Net Monetary Benefit (INMB) of breast cancer screening strategies, India, 2018

Incremental NMB was positive across all the 5 age-groups for all screening strategies as compared to the no screening in screening intervals annual, 3 years and 5 years. INMB was highest as US$ 438.78 (INR 30,715/-) and US$ 233.21 (INR 16,325/-) for the CBE only screening in the age-group 35-40 years as compared to the other screening strategies in 3 years and 5 years screening respectively. Similar trend was observed in other 4 age-groups, where INMB was highest for CBE only screening as compared to the other screening strategies. INMB decreased with an increasing age for all the screening strategies in 3 and 5 years screening intervals; still INMB for CBE screening was higher than the other screening strategies. INMB for CBE screening was higher for screening at 3 years than the screening at 5 years suggested that CBE screening is the most cost-effective strategy for conducting screening at triennial i.e. 3 years interval (Fig 30).

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Table 14: Cost effectiveness of breast cancer screening strategies in women aged 35-40 years, India, 2018

Age group	Screening interval	Strategy	Life time cost per woman (US $)	Effect (QALY)	Cost Effectiveness ratio (CE)	Incremental Cost (US $)	Incremental Effect (QALY)	ICER (US $)	NMB (US $)	INMB (US $)	Dominance
35-40 years	Annual	CBE only	172.62	22.8328	7.56	-620.51	0.5147	-1205.51	44660.63	1631.21	**Undominated**
		CBE parallel with USG	372.91	22.8387	16.33	-420.22	0.5207	-807.06	44472.00	1442.58	**Undominated**
		MMG only	353.28	22.8362	15.47	-439.85	0.5182	-848.85	44486.72	1457.30	Ext. dominated
		CBE+USG	357.09	22.8284	15.64	-436.04	0.5104	-854.29	44467.69	1438.27	Abs. dominated
		Piezo+USG	376.59	22.8322	16.49	-416.54	0.5142	-810.13	44455.56	1426.14	Abs. dominated
		MMG+USG	431.65	22.8312	18.91	-361.48	0.5132	-704.42	44398.53	1369.12	Abs. dominated
		No screening	793.13	22.3180	35.54				43029.42		Abs. dominated
35-40 years	3 years	CBE only	78.56	11.4313	6.87	-287.29	0.0771	-3726.43	22367.28	438.68	**Undominated**
		CBE parallel with USG	197.30	11.4324	17.26	-168.56	0.0783	-2153.98	22250.82	322.21	**Undominated**
		MMG only	186.85	11.4319	16.34	-179.00	0.0778	-2301.78	22260.30	331.70	Ext. dominated
		CBE+USG	193.29	11.4304	16.91	-172.56	0.0763	-2262.96	22250.90	322.29	Abs. dominated
		Piezo+USG	202.94	11.4311	17.75	-162.91	0.0770	-2116.13	22242.68	314.08	Abs. dominated
		MMG+USG	236.66	11.4310	20.70	-129.19	0.0768	-1682.35	22208.58	279.97	Abs. dominated
		No screening	365.85	11.3542	32.22				21928.60		Abs. dominated
35-40 years	5 years	CBE only	47.66	8.1575	5.84	-178.08	0.0281	-6342.08	15969.95	233.21	**Undominated**
		CBE parallel with USG	136.41	8.1579	16.72	-89.33	0.0285	-3131.00	15882.08	145.35	**Undominated**
		MMG only	128.92	8.1577	15.80	-96.82	0.0283	-3416.44	15889.20	152.47	Ext. dominated
		CBE+USG	134.79	8.1571	16.52	-90.94	0.0278	-3277.06	15882.17	145.44	Abs. dominated
		Piezo+USG	141.51	8.1574	17.35	-84.23	0.0280	-3004.35	15876.01	139.28	Abs. dominated
		MMG+USG	167.01	8.1574	20.47	-58.73	0.0280	-2100.30	15850.36	113.63	Abs. dominated
		No screening	225.74	8.1294	27.77				15736.73		Abs. dominated

Note: Negative ICER indicates reduction in life-time screening and treatment cost of breast cancer through respective screening strategy as compared to No screening

Table 15: Cost effectiveness of breast cancer screening strategies in women aged 40-45 years, India, 2018

Age group	Screening interval	Strategy	Life time cost per woman (US $)	Effect (QALY)	Cost Effectiveness ratio (CE)	Incremental Cost (US $)	Incremental Effect (QALY)	ICER (US $)	NMB (US $)	INMB (US $)	Dominance
40-45 years	Annual	CBE only	167.73	19.0407	8.81	-526.99	0.3555	-1482.36	37219.61	1225.04	**Undominated**
		CBE parallel with USG	344.26	19.0457	18.08	-350.46	0.3606	-971.99	37053.01	1058.44	**Undominated**
		MMG only	326.84	19.0436	17.16	-367.89	0.3584	-1026.37	37066.26	1071.69	Ext. dominated
		CBE+USG	329.64	19.0370	17.32	-365.09	0.3518	-1037.67	37050.50	1055.93	Abs. dominated
		Piezo+USG	347.05	19.0402	18.23	-347.67	0.3550	-979.29	37039.36	1044.79	Abs. dominated
		MMG+USG	395.24	19.0394	20.76	-299.48	0.3542	-845.57	36989.49	994.92	Abs. dominated
		No screening	694.72	18.6852	37.18				35994.57		Abs. dominated
40-45 years	3 years	CBE only	74.32	9.9627	7.46	-241.95	0.0558	-4334.16	19487.89	351.56	**Undominated**
		CBE parallel with USG	180.01	9.9637	18.07	-136.26	0.0568	-2397.61	19384.18	247.85	**Undominated**
		MMG only	170.71	9.9633	17.13	-145.56	0.0564	-2580.46	19392.65	256.32	Ext. dominated
		CBE+USG	176.43	9.9619	17.71	-139.84	0.0551	-2538.34	19384.35	248.02	Abs. dominated
		Piezo+USG	185.02	9.9626	18.57	-131.25	0.0557	-2355.13	19377.00	240.67	Abs. dominated
		MMG+USG	215.00	9.9624	21.58	-101.26	0.0556	-1822.65	19346.69	210.35	Abs. dominated
		No screening	316.27	9.9069	31.92				19136.33		Abs. dominated
40-45 years	5 years	CBE only	45.28	7.2337	6.26	-151.42	0.0206	-7362.29	14158.53	191.80	**Undominated**
		CBE parallel with USG	125.04	7.2341	17.29	-71.66	0.0210	-3417.36	14079.56	112.83	**Undominated**
		MMG only	118.31	7.2340	16.35	-78.39	0.0208	-3768.99	14085.96	119.23	Ext. dominated
		CBE+USG	123.58	7.2334	17.08	-73.11	0.0203	-3606.15	14079.66	112.93	Abs. dominated
		Piezo+USG	129.62	7.2337	17.92	-67.08	0.0205	-3267.62	14074.12	107.39	Abs. dominated
		MMG+USG	152.52	7.2336	21.09	-44.17	0.0205	-2158.90	14051.08	84.35	Abs. dominated
		No screening	196.70	7.2132	27.27				13966.73		Abs. dominated

Note: Negative ICER indicates reduction in life-time screening and treatment cost of breast cancer through respective screening strategy as compared to No screening

Table 16: Cost effectiveness of breast cancer screening strategies in women aged 45-50 years, India, 2018

Age group	Screening interval	Strategy	Life time cost per woman (US $)	Effect (QALY)	Cost Effectiveness ratio (CE)	Incremental Cost (US $)	Incremental Effect (QALY)	ICER (US $)	NMB (US $)	INMB (US $)	Dominance
45-50 years	Annual	CBE only	149.06	15.4208	9.67	-419.41	0.2244	-1868.90	30130.52	860.05	**Undominated**
		CBE parallel with USG	299.18	15.4247	19.40	-269.28	0.2283	-1179.56	29988.00	717.53	**Undominated**
		MMG only	284.47	15.4231	18.44	-283.99	0.2267	-1252.94	29999.51	729.04	Ext. dominated
		CBE+USG	287.19	15.4180	18.63	-281.27	0.2216	-1269.26	29986.86	716.39	Abs. dominated
		Piezo+USG	301.84	15.4205	19.57	-266.62	0.2240	-1190.02	29977.01	706.54	Abs. dominated
		MMG+USG	342.84	15.4198	22.23	-225.62	0.2234	-1009.99	29934.74	664.27	Abs. dominated
		No screening	568.46	15.1964	37.41				29270.47		Abs. dominated
45-50 years	3 years	CBE only	66.09	8.5331	7.74	-196.10	0.0376	-5213.62	16689.03	269.96	**Undominated**
		CBE parallel with USG	158.34	8.5339	18.55	-103.84	0.0384	-2703.06	16598.35	179.28	**Undominated**
		MMG only	150.28	8.5335	17.61	-111.91	0.0381	-2938.91	16605.75	186.68	Ext. dominated
		CBE+USG	155.43	8.5325	18.22	-106.75	0.0370	-2882.96	16598.53	179.46	Abs. dominated
		Piezo+USG	162.86	8.5330	19.09	-99.33	0.0375	-2646.16	16592.11	173.03	Abs. dominated
		MMG+USG	189.06	8.5329	22.16	-73.12	0.0374	-1955.09	16565.63	146.56	Abs. dominated
		No screening	262.19	8.4955	30.86				16419.07		Abs. dominated
45-50 years	5 years	CBE only	40.70	6.3284	6.43	-124.58	0.0140	-8920.22	12385.40	152.00	**Undominated**
		CBE parallel with USG	111.33	6.3287	17.59	-53.94	0.0143	-3773.57	12315.41	82.01	**Undominated**
		MMG only	105.39	6.3286	16.65	-59.88	0.0142	-4230.31	12321.09	87.68	Ext. dominated
		CBE+USG	110.13	6.3281	17.40	-55.14	0.0137	-4016.95	12315.50	82.09	Abs. dominated
		Piezo+USG	115.44	6.3284	18.24	-49.83	0.0139	-3576.00	12310.60	77.19	Abs. dominated
		MMG+USG	135.74	6.3283	21.45	-29.53	0.0139	-2127.76	12290.19	56.78	Abs. dominated
		No screening	165.27	6.3144	26.17				12233.41		Abs. dominated

Note: Negative ICER indicates reduction in life-time screening and treatment cost of breast cancer through respective screening strategy as compared to No screening

Table 17: Cost effectiveness of breast cancer screening strategies in women aged 50-55 years, India, 2018

Age group	Screening interval	Strategy	Life time cost per woman (US $)	Effect (QALY)	Cost Effectiveness ratio (CE)	Incremental Cost (US $)	Incremental Effect (QALY)	ICER (US $)	NMB (US $)	INMB (US $)	Dominance
50-55 years	Annual	CBE only	122.93	12.2068	10.07	-313.02	0.1287	-2431.49	23845.77	565.79	**Undominated**
		CBE parallel with USG	246.83	12.2095	20.22	-189.11	0.1314	-1438.77	23727.17	447.19	**Undominated**
		MMG only	234.92	12.2084	19.24	-201.02	0.1303	-1542.74	23736.85	456.87	Ext. dominated
		CBE+USG	237.98	12.2049	19.50	-197.96	0.1268	-1561.55	23726.86	446.88	Abs. dominated
		Piezo+USG	249.71	12.2066	20.46	-186.23	0.1285	-1449.55	23718.49	438.51	Abs. dominated
		MMG+USG	283.74	12.2061	23.25	-152.20	0.1280	-1188.89	23683.56	403.58	Abs. dominated
		No screening	435.94	12.0781	36.09				23279.98		Abs. dominated
50-55 years	3 years	CBE only	55.60	7.1534	7.77	-149.25	0.0225	-6622.03	13990.52	193.51	**Undominated**
		CBE parallel with USG	134.30	7.1540	18.77	-70.56	0.0231	-3050.08	13912.98	115.98	**Undominated**
		MMG only	127.49	7.1538	17.82	-77.37	0.0229	-3381.03	13919.31	122.30	Ext. dominated
		CBE+USG	132.12	7.1530	18.47	-72.73	0.0221	-3289.79	13913.15	116.14	Abs. dominated
		Piezo+USG	138.35	7.1534	19.34	-66.51	0.0225	-2958.15	13907.66	110.65	Abs. dominated
		MMG+USG	160.76	7.1533	22.47	-44.09	0.0224	-1969.92	13885.05	88.04	Abs. dominated
		No screening	204.85	7.1309	28.73				13797.01		Abs. dominated
50-55 years	5 years	CBE only	35.01	5.4407	6.43	-97.29	0.0083	-11763.56	10648.12	113.53	**Undominated**
		CBE parallel with USG	96.43	5.4410	17.72	-35.86	0.0085	-4207.81	10587.19	52.60	**Undominated**
		MMG only	91.29	5.4409	16.78	-41.00	0.0084	-4871.69	10592.12	57.53	Ext. dominated
		CBE+USG	95.51	5.4405	17.55	-36.79	0.0081	-4548.91	10587.25	52.66	Abs. dominated
		Piezo+USG	100.08	5.4407	18.39	-32.21	0.0082	-3906.26	10582.99	48.40	Abs. dominated
		MMG+USG	117.75	5.4407	21.64	-14.54	0.0082	-1772.24	10565.24	30.65	Abs. dominated
		No screening	132.29	5.4324	24.35				10534.59		Abs. dominated

Note: Negative ICER indicates reduction in life-time screening and treatment cost of breast cancer through respective screening strategy as compared to No screening

Table 18: Cost effectiveness of breast cancer screening strategies in women aged 55-60 years, India, 2018

Age group	Screening interval	Strategy	Life time cost per woman (US $)	Effect (QALY)	Cost Effectiveness ratio (CE)	Incremental Cost (US $)	Incremental Effect (QALY)	ICER (US $)	NMB (US $)	INMB (US $)	Dominance
55-60 years	Annual	CBE only	94.17	9.5019	9.91	-222.94	0.0676	-3295.53	18563.33	355.77	**Undominated**
		CBE parallel with USG	194.13	9.5036	20.43	-122.98	0.0694	-1773.19	18466.73	259.16	**Undominated**
		MMG only	184.81	9.5029	19.45	-132.30	0.0686	-1927.60	18474.64	267.07	Ext. dominated
		CBE+USG	188.29	9.5007	19.82	-128.82	0.0664	-1939.77	18466.78	259.22	Abs. dominated
		Piezo+USG	197.29	9.5018	20.76	-119.82	0.0675	-1775.45	18459.90	252.33	Abs. dominated
		MMG+USG	225.03	9.5015	23.68	-92.08	0.0672	-1370.26	18431.60	224.03	Abs. dominated
		No screening	317.11	9.4343	33.61				18207.57		Abs. dominated
55-60 years	3 years	CBE only	44.03	5.9235	7.43	-110.19	0.0122	-9006.31	11587.10	134.21	**Undominated**
		CBE parallel with USG	110.20	5.9239	18.60	-44.01	0.0126	-3483.00	11521.71	68.82	**Undominated**
		MMG only	104.56	5.9238	17.65	-49.66	0.0125	-3983.15	11527.03	74.13	Ext. dominated
		CBE+USG	108.73	5.9232	18.36	-45.48	0.0119	-3808.38	11521.83	68.94	Abs. dominated
		Piezo+USG	113.83	5.9235	19.22	-40.38	0.0122	-3310.80	11517.22	64.33	Abs. dominated
		MMG+USG	132.76	5.9234	22.41	-21.45	0.0121	-1768.78	11498.16	45.27	Abs. dominated
		No screening	154.21	5.9113	26.09				11452.89		Abs. dominated
55-60 years	5 years	CBE only	28.42	4.6264	6.14	-74.60	0.0042	-17732.72	9055.74	82.86	**Undominated**
		CBE parallel with USG	81.19	4.6266	17.55	-21.83	0.0044	-4977.47	9003.31	30.44	**Undominated**
		MMG only	76.81	4.6265	16.60	-26.21	0.0043	-6080.45	9007.55	34.67	Ext. dominated
		CBE+USG	80.55	4.6263	17.41	-22.47	0.0041	-5510.59	9003.35	30.48	Abs. dominated
		Piezo+USG	84.42	4.6264	18.25	-18.60	0.0042	-4438.28	8999.70	26.82	Abs. dominated
		MMG+USG	99.64	4.6263	21.54	-3.38	0.0042	-812.79	8984.43	11.55	Abs. dominated
		No screening	103.02	4.6222	22.29				8972.88		Abs. dominated

Note: Negative ICER indicates reduction in life-time screening and treatment cost of breast cancer through respective screening strategy as compared to No screening

Table 19: Probabilistic sensitivity analysis of breast cancer screening strategies in women, India, 2018

Age group	Screening interval	Probability of cost-effective screening at willingness to pay (US $/QALY)																	
		550						1100						2200					
		CBE only	CBE parallel with USG	CBE+ USG	MMG only	MMG+ USG	Piezo+ USG	CBE only	CBE parallel with USG	CBE+ USG	MMG only	MMG+ USG	Piezo+ USG	CBE only	CBE parallel with USG	CBE+ USG	MMG only	MMG+ USG	Piezo+ USG
35-40 years	Annual	1	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0
	3 years	1	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0
	5 years	1	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0
40-45 years	Annual	1	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0
	3 years	1	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0
	5 years	1	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0
45-50 years	Annual	1	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0
	3 years	1	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0
	5 years	1	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0
50-55 years	Annual	1	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0
	3 years	1	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0
	5 years	1	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0
55-60 years	Annual	1	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0
	3 years	1	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0
	5 years	1	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0

Discussion

It was observed from the CEA results that screening at intervals 3 years and 5 years was cost-effective strategy as compared to the no screening. CBE only and CBE parallel with USG screening strategies were the most cost-effective screening strategy as compared to the other screening strategies CBE+USG, Piezo+USG and MMG+USG. It was also observed that MMG only screening was also cost-effective as compared to CBE+USG, Piezo+USG and MMG+USG screening in all age group.

Our study findings differ than the other studies in terms of CBE only and CBE parallel with USG screening strategies. However, findings were similar to the previous studies done by Sun *et al*, 2018 (47) in China and Nguyen *et al*, 2018 (48) in Vietnam, which reported that MMG screening is most cost-effective screening strategy. As per Sun *et al* (2018) (47), MMG screening was most cost-effective with US$ 184.37 per QALY gained with screening 3 years interval in Chinese women aged 35-60 years. Our findings were different from the study done by Haghighat *et al* (2016) in Iranian women, where MMG screening was not cost-effective (49).

Conclusion

CBE only and CBE parallel with USG screening strategies with screening at triennial (i.e. once in three years) interval are the most cost-effective screening strategies in Indian women aged 35-60 years.

IV. HEALTH EQUITY

Background:

Indian health system has witnessed remarkable achievements since independence in various key health indicators (50). But there exists huge disparity on the basis of caste, gender, geography, etc. To address this disparity, public healthcare services need to be provided equitably and effectively. The high out of pocket health expenditure (OOPE) push already poor patients into the trap of poverty and impoverishment. As per National Health Accounts, Out of Pocket Expenditure (OOPE) on health by households is Rs. 3,02,425 crores (62.6% of THE, 2.4% of GDP, Rs. 2,394 per capita) for the year 2014-15. Private Health Insurance expenditure is Rs. 17,755 crores (3.7% of THE) for the year 2014-15 (51). The delivery of affordable and equitable cancer care is one of India's greatest public health challenges (52). Rajpal et al found that out of pocket expenditure on cancer treatment is among the highest for any ailment (53). Despite long-standing national programmes, such as the National Cancer Control Programme launched in 1975, under the National Programme for Cardiovascular Disease, Diabetes, Cancer and Stroke (NPCDCS) launched under the 12th five year Plan from 2012 to 2017) (52) to increase awareness and early detection behaviours, the mortality rates for breast cancer continue to rank the highest in the country (55) . The OOPE as a major mode of financing can push 25% of the breast cancer affected households below the poverty line (63) In order to reduce the prevailing inequities, we need to identify and address the challenges faced in the uptake of breast cancer screening.

Aim:

To identify potential equity issues in the uptake of breast cancer screening and treatment services among Indian women. We aim to summarise the data and identify the gaps in access and equity based on the components mentioned in **PROGRESS Plus.** These components include place of residence, race/culture, occupation, gender/sex, religion, education and socio-economic status. Plus components included age, disability, excluded from school, etc.

Literature Review

Methodology: We conducted a literature search through online databases (the Cochrane Library including the Cochrane Database of Systematic Reviews (CDSR), PubMed, and

Google Scholar). These articles were screened on the basis of titles and abstracts as per the inclusion and exclusion criteria. Full-length papers were screened after initial inclusion.

Inclusion Criteria The studies were included based on the following PICO criteria:
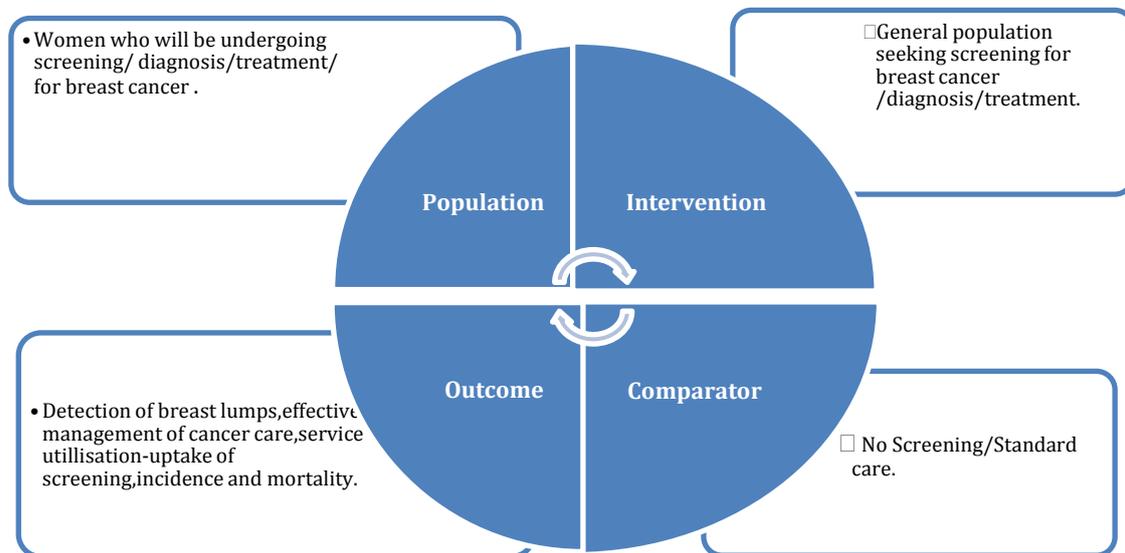
Fig 30: PICO framework for Health Equity systematic review

Exclusion Criteria
- Equity studies performed in countries other than Low Middle-Income Countries (LMICS).
- Language other than English.
- Equity studies related to cancer screening by MRI and Self-breast examination.

PRISMA Model
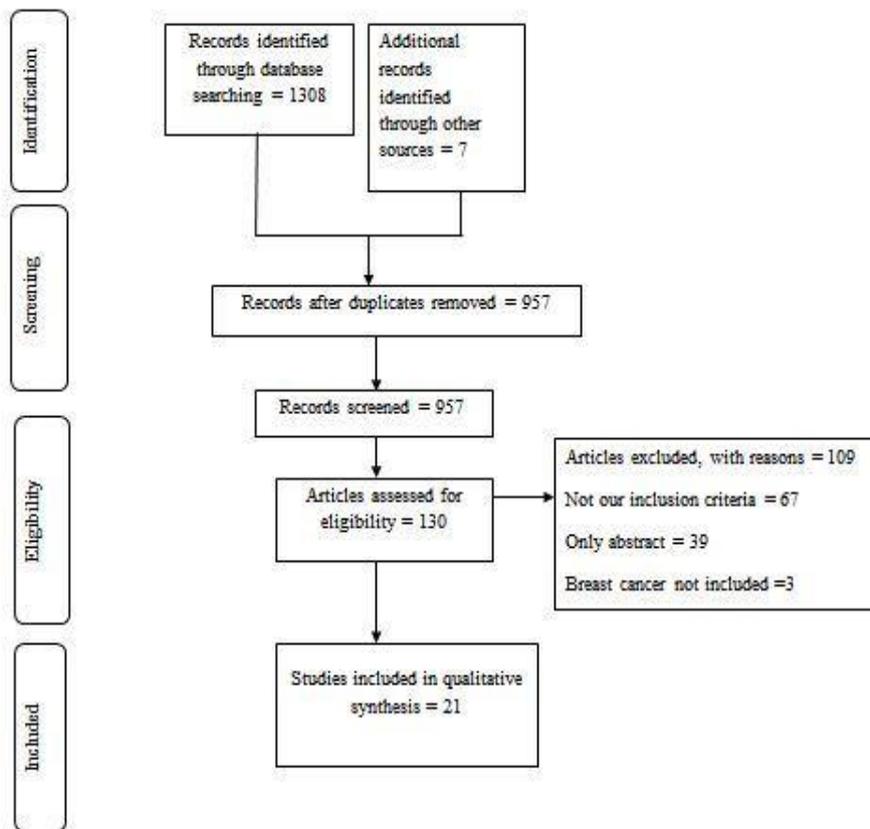
Fig 31: PRISMA Model for Health Equity

Search strategy:

Last search was done on October 9, 2018.

Data Extraction & Synthesis:

One reviewer extracted the data while the other reviewer cross-checked it. Any discrepancies were resolved by discussing it with a third reviewer.

Quality Assessment:

The methodological quality of the included studies was assessed using the R-AMSTAR tool.

Results:

Literature Search:

The search yielded a total of 1308 through database searching and 7 from additional sources out of which 21 were selected for final analysis after removing duplicates which were related to breast cancer.

Systematic review of studies analysing equity in the access to breast cancer screening among women in India and other LMIC countries (Arranged as PROGRESS-Plus)

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1. **Place of Residence**:

Despite rising burden of Breast cancer in urban areas, majority of the patients discover their cancer status only in advanced stage due to lack of awareness regarding the disease coupled with non-affordability and non-availability of facilities for early detection and treatment (65) Breast cancer among Indian women accounts for the second most common cause of cancer. Although the incidence in urban areas is increasing. Among the cases found in rural India, 50-70% of the cases present in late stages (56) As per NFHS IV data 11.7% of the urban residents responded that they have undergone breast examination while only 8.8% of the respondents in rural area responded in favour of it (58)

Women in rural regions were less likely to be provided with adequate health services (screening or diagnosis). Hence, this difference in screening and diagnosis facilities can or cannot be attributed to higher cancer incidence recorded in urban regions rather in rural ones. Moreover, the influence of unhealthy lifestyle resulted in higher BMI values and increasing alcohol consumption among the population, increasing accessibility to hormone replacement therapy and oral contraceptive, and higher exposure to xenoestrogens and other environment endocrine disruptors (EEDs), which also has the potential related to higher breast cancer incidence in urban regions (56).

Rajpal *et al.* emphasiz community-based educational intervention which they suggest to be very productive. Clinical breast examination by trained personnel in the rural areas like female health workers has been suggested as a viable screening option considering the socio-economic condition and the unavailability of facilities at the remote places (53).

2. **Race/ethnicity/culture/language:**

Findings from studies have suggested that in the case of the migrated population the uptake of screening is less compared to that in the general population. In the context of India which is witnessing an increase in migration to cities, this section of the population also need to be made aware so as to participate in the screening process. Also, the migrants face another hurdle of a language barrier which prevents them from participating in the screening process. Similarly, minority groups also are less likely to participate in the screening process as compared to the general population. Poverty and lack of education act as a barrier to gaining knowledge of breast cancer. Nomads are more vulnerable as they keep on moving from one place to another and thus it is difficult for the community health workers to reach out to them.

The NFHS IV data provides an overview of the percentage of the caste/tribe of the respondents who have undergone breast examination.

Table 20: Breast cancer screening as per caste and tribe

Caste/Tribe	Percentage of that caste/tribe who have undergone a breast examination
Scheduled Caste	9.2
Scheduled tribe	8.6
Other backward class	9.8
Other	10.7
Don't know	7.7

3. **Occupation:**

Exposure to night-shift work represents the most significant occupational risk associated with breast cancer and it has been classified as a carcinogen by the IARC. The IARC also established a strong association that exposure to ionizing radiation can increase the risk of breast cancer. Similarly, chemical substances such as ethylene oxide, polycyclic aromatic hydrocarbons (PAHs), perfluorooctanoic acid and different pesticides are investigated as carcinogenic factors for breast cancer in occupational settings (56, 60). The rural population of agricultural workers and their families who may be exposed to higher doses of OCPs, such as DDT, compared to the general population, have been reported to have a higher incidence of breast cancer compared to the non-exposed populations (57).

4. **Gender awareness:**

While breast cancer is the most common cancer among Indian female (with age-adjusted rate as high as 25.8 per 100,000 women and mortality 12.7 per 100,000 in Indian women) (3), breast cancer in male is a rare malignancy with an estimated incidence rate of 0.5–1 % of all breast cancer cases (59). As compared to the number of studies regarding breast cancer in females, there are very few studies regarding breast cancer in males, the reason being the rarity of the disease in males.

In a study conducted among women in Villupuram, Tamil Nadu in 2013, it was found out that only 18% women were aware of breast cancer screening and only 24% were aware of the symptoms of breast cancer. Only 35% of the women were willing to undergo screening (Clinical breast examination in PHC) for breast cancer and out of these women, 16% did not undergo screening due to personal work or overcrowding in the PHCs. This clearly shows

that women need to be first made aware about the need for undergoing CBE. Any screening programme about breast cancer won't succeed without the willingness of the women to undergo screening (62). Also, as breast cancer is common only among females, awareness drive should also be done for males so as to sensitise them regarding the disease.

5. **Education:**

Tomi et al conducted a study among a total of 22 283 women residing in five countries namely India, Mexico, China, South Africa and Russia. The authors pointed out that almost half of women had at least a secondary school education (43%); a third of women had no formal education (34%) ranging from 58% in India, 28% in Mexico, 25% in China, 23% in South Africa to 1.3% in Russia. The authors found that breast cancer screening increased with increasing education, ranging from 10% among those with no formal education to 56% among those with a college education. It can be observed that Breast cancer screening was low (<10%) regardless of education among women in India while screening increased markedly with increasing education among women in China, Mexico and Russia. The table below depicts the relation of education with Breast cancer screening:

Table 22: Relation of female education with Breast cancer screening

Educational status		China (n=4946)	India (n=3640)	Mexico (n=755)	South Africa (n=1472)	Russia (n=1320)
Own Education	No Formal Education	27.40%	0.75%	52.40%	7.60%	6.40%
	Primary School	31.50%	0.70%	56.70%	19.40%	14.10%
	Secondary/ High School	43.70%	0.60%	52.80%	37.10%	52.10%
	College/ University/ PG	83.70%	0.20%	66.30%	7.80%	54.50%
Mother's Education	No Formal Education	35.10%	0.80%	53.60%	21.00%	43.00%
	Primary School	57.20%	0.30%	64.50%	16.00%	48.90%
	Secondary/ High School	69.60%	1.50%	81.40%	54.10%	53.80%
	College/ University/ PG	48.60%	0.00%	63.80%	6.30%	65.30%
Father's Education	No Formal Education	32.80%	0.70%	52.40%	23.50%	43.50%
	Primary School	47.80%	1.60%	74.10%	12.80%	39.90%
	Secondary/ High School	61.50%	0.70%	62.20%	37.20%	56.00%
	College/ University/ PG	49.80%	0.00%	63.20%	7.60%	54.70%

Source: Akinyemiju T et al, 2016, Life course socioeconomic status and breast and cervical cancer screening: analysis of the WHO's study on Global Ageing and Adult Health (SAGE)

Tomi et al found that having a college degree or higher (OR 4.18; 95% CI 2.36 to 7.40) or secondary school education (OR 1.86; 95% CI 1.27 to 2.78) was associated with higher odds of breast cancer screening compared with those with no formal education. The authors also pointed out that having a parent with a secondary school education (mother OR 2.50; 95% CI

1.60 to 3.92; father OR 2.48; 95% CI 1.73 to 3.55) or higher increased the odds of breast cancer screening (66).

The above findings are in tune to the data published by NFHS-IV. As per the NFHS 4 data, for the year 2015-16, the interview schedule has captured data for the women undergoing breast examination and their schooling (58).

Table 23: Women undergoing breast examination and schooling

Schooling	Breast Examination
No Schooling	8.6
<5 years complete	10.0
5-7 years complete	10.7
8-9 years complete	9.1
10-11 years complete	10.2
12 or more years complete	10.8

6. **Socio-economic status:**

Socio-economic status be it any form like caste, class or gender affects the willingness of women to participate in the screening process. Among the women unwilling to undergo screening, many women feels that it might affect their societal status. Even though they were willing to share the information with their husband, they perceived it may cause marital conflict and thus wanted to keep their cancer status confidential. It is clearly evident that there is a stigma associated with breast cancer and the society as a whole needs to be sensitised about it. Low levels of breast cancer awareness is considered as an important risk factor for delay in presentation by the patient (54). Gupta et al plotted multiple studies and found that there is no increase in the cancer literacy over time (50). However, among those who are aware, studies have pointed out that among women who had at least heard of breast cancer the major sources of information were friends, relatives and other women from neighbourhood followed by Television (62,51).

After adjusting for age, health status, rural/urban residence and marital status, Tomi et al (66) found that women who were themselves employed in public sectors, had either of their parents employed in the public sector were significantly more likely to receive screening but this trend was less observed in India. The authors also observed that in India, Breast cancer screening is reported to be highest among women with maternal self-employment (19%), while screening increased markedly with increasing education among women in China,

Mexico and Russia (66). The figure below depicts the relation of employment with Breast cancer screening.
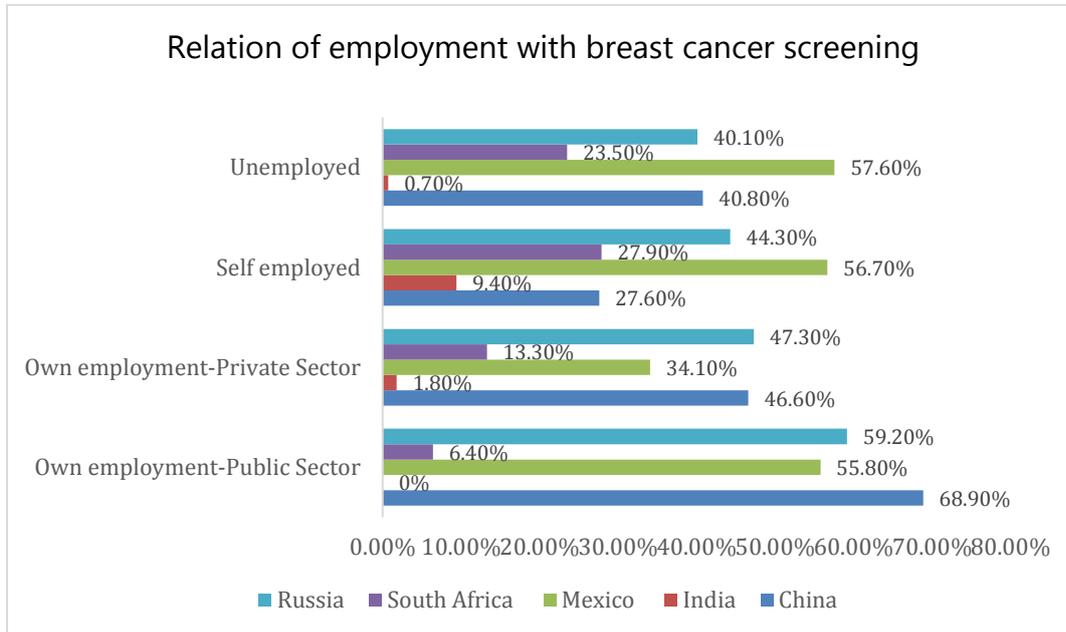
Relation of employment with breast cancer screening

Employment	Russia	South Africa	Mexico	India	China
Unemployed	40.10%	23.50%	57.60%	0.70%	40.80%
Self employed	44.30%	27.90%	56.70%	9.40%	27.60%
Own employment-Private Sector	47.30%	13.30%	34.10%	1.80%	46.60%
Own employment-Public Sector	59.20%	6.40%	55.80%	0%	68.90%

Source: Akinyemiju T et al, 2016, Life course socioeconomic status and breast and cervical cancer screening: analysis of the WHO's study on Global Ageing and Adult Health (SAGE)

Fig 32: Relation of employment with breast cancer screening

7. **Age:**

Xufeng fei et al (69) et al pointed out that cancer incidence increases with age. In particular, for female breast cancer incidence, the peak appeared in the 50–54 age groups. Breast cancer risk declines in the case of individuals older than 55 years. Also, breast cancer risk is strongly influenced by oestrogen concentration, and most women enter the menopause stage after the age of 55 years (experiencing a declined concentration of body oestrogens), the diminishing levels of circulating oestrogen may result in the decreased breast cancer risk too (69). Madhu et al conducted a cross-sectional study and observed a definite association between knowledge of breast cancer screening procedures; as age advanced, there was a significant increase in knowledge of the procedures. It was found that there was a definite association between the practice of breast cancer screening procedures and age; women greater than forty-six years of age practised the breast cancer screening procedures more than the women in the younger age groups (63).

It was found that disease incidence in rural regions showed a decrease after the age of 65 years. It was suggested that two elements might contribute to this decrease: Firstly, rural

women, especially older women, have a significantly smaller chance to get educated. A large percentage of them are illiterate, which leads to lower income, lower awareness of health state and lack of health insurance, directly or indirectly. These older rural women can't afford or are unwilling to seek treatment, resulting to a decreased disease incidence. Secondly, due to the tough living conditions in rural areas, the women, particularly those of earlier generations, have a shorter life expectancy.

Evidence from multiple studies suggests that women with chronic disabling conditions are less likely to participate in breast cancer screening due to the multiple barriers they face. These Barriers include those related to finances, environment, physical limitations, health care providers' attitudes and lack of knowledge, and psychosocial issues (68). So there needs to be a focus on making disabled women aware about breast cancer screening.

8. **Accesss to technology:**

In Indian Public Healthcare scenario the accessibility of breast cancer screening techniques is of prime importance for the effective Healthcare service delivery in the context of Health systems Strengthening. As per the available data (70) presented in the table below it is reflected that Mammography is present in 31 out of 36 states in India (refer to Appendix 5), at the district Healthcare facilities and are not present at PHC and CHC level making it practically less accessible (71). As per the current HR data available presently in India there are total 195 posts of Radiologist in India sanctioned under National Health Mission (NHM) (72) which indicates a shortage of manpower.

Table 24: Existing Human resource & MMG Machine

Total No. of Districts	No. of radiologists posts sanctioned	No. of MMG at District Hospital Level (Appendix 5)
763	195	55

Discussion:

1. Most of the studies have pointed to the lack of awareness among both men and women regarding screening procedures for breast cancer resulting in ignorance and lack of support. Both women and men need to be made aware about the screening procedures for breast cancer. Sensitisation among men is also necessary as they should provide social support for their family members and their wives.

2. Studies have pointed out that community based awareness should be provided by "Anganwadi workers, ANMs, ASHAs" and other community health workers. They should be made aware about the risks, symptoms and screening procedures related to breast cancer and they further need to reach out to the women in the community and share their knowledge.

3. As evident from the study carried out in Villupuram, it was noticed that there is stigma associated with breast cancer and the women are shy about sharing their cancer status, this needs to be addressed.

4. International Agency for Research on Cancer (IARC) pointed out that exposure to hazardous chemicals and other carcinogens among families of agricultural workers poses a risk factor for breast cancer. The use of these chemicals should be avoided.

5. The awareness among educated women also seems to be low with regard to the symptoms and screening for breast cancer as pointed out in a study conducted in different countries including India. Awareness about the symtoms and screening for breast cancer is also low among nomads, urban poor and the migrants.

6. Perceived fear of pain in the screening process and embarrassment in cases of screening due to a male physician has also been reported in various studies. Preconceived notion regarding pain during the screening process needs to be done away with by awareness drive being carried out. In cases of women who are reluctant to undergo CBE by a male physician, ANMs or female physicians need to be involved for community sensitization and mobilization.

7. Studies have also pointed out to the long waiting duration due to higher population density and limited screening devices in public health facilities posing an impediment in up-taking of the screening process in urban areas

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C. Research Gaps:

Lack of sufficient studies on the comparison of clinical effectiveness of different breast cancer screening modalities in solo performance and in combination in Indian context along with less literature and data on screening of breast cancer in females for the respective modality used with respect to 3 and 5 year screening interval in India and in South East Asia Region. Few cost effectiveness studies are present of different breast cancer screening modalities being used in India. Limited data exists on the proportion of Indian women screened and not screened in both urban and rural settings in India especially in age group below 30 years. These areas need to be explored for future research.

D. Policy Recommendations:

(i) With increasing burden of breast cancer among females in India (3), early detection and prevention are key to preventing cancer-related deaths. Diagnostic accuracy of screening, cost-effectiveness, accessibility and equity are the three major factors essential for uptake and implementation of a screening technique in the Public Health System.

(ii) Current policy recommends once in five year screening for all women over 30 years of age, using CBE at the Health and Wellness Centres/Sub-Health Centre level by Mid level Health Providers or /ANM followed by an Ultrasound scan for suspected (mass, nipple discharge, skin or nipple retraction, edema, erythema, peau d'orange, or ulcers) cases. (71).

(iii) This Health Technology Assessment assessed the clinical and cost-effectiveness of various breast cancer screening modalities in women in the age groups of 35 – 40, 40-45, 45-50, 50-55, 55-60, 60-65 years, at screening intervals of 3 and 5 years. The modalities were *CBE alone, CBE paralleled with USG, MMG alone, CBE followed by USG, Piezoelectric finger followed by USG, MMG followed by USG*. Clinical effectiveness of each of the modalities was determined from the meta-analysis of the studies done (Table No.2). The cost-effective analysis included several parameters such as lifetime cost per woman (US $), Effect (QALY), Cost-Effectiveness ratio, incremental effect (QALY), ICER (US $), and Net monetary benefit to arrive at the dominance status of each screening strategy.

(iv) The HTA findings show that CBE paralleled with USG was found to be the most clinically effective (Sensitivity: 91% & Specificity: 99 %) and cost effective technique compared to the rest of the methods across all age groups and screening intervals. This technique may optimise breast cancer detection in India. Whereas, CBE alone follwoed by USG has a sensitivity 61% and a specificity 100%. However, between these two methods there is not much difference in Incremental Net Monetary Benefit. Moreover, the pooled sensitivity of CBE alone is 73%, this means that there is a risk of missing out the true positive cases of breast cancer patient by 27 %.

(v) However, as per studies conducted (19) it is not yet clear whether early detection by CBE alone decreases breast cancer specific mortality. The efficacy of CBE alone in reducing breast cancer mortality has not been shown by well-designed

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clinical trials (74). Subsequently, many organizational guidelines (those from the Canadian Task Force on Preventive Health Care (75), the U.S. Preventive Services Task Force (74, 76), the American Cancer Society(77), the U.K. National Health Services(78), and the World Health Organization(79)) removed CBE from their recommendations. However, some still include it (specifically, those from the U.S. National Comprehensive Cancer Network (80), the American College of Obstetricians and Gynecologists (81), and Memorial Sloan Kettering Cancer Center(82)).

(vi)   For new technologies such as Piezoelectric finger diagnostic accuracy, practical applicability, accessibility, is yet to be explored along with surrounding factors such training of existing manpower to use the technique, large-scale procurement for its implementation in the Public Healthcare system in India.

(vii)   From the equity point of view, National Operational Guidelines do emphasize the role of screening as an important tool. Breast Health awareness is necessary to spread awareness regarding breast cancer and screening as a preventive measure in the community. Frontline Health workers are important source of dissemination of breast cancer knowledge to women. Studies from India showed high acceptance of healthcare workers as educators for breast cancer (83).

(viii)   CBE as the first line screening method, offers frontline workers, nurses and medical officers an opportunity to educate women about the risks of breast cancer, the importance of early detection and breast awareness. However Healthcare workers need to be highly proficient in CBE, for which quality training, consistent monitoring and refresher of skills and competency is needed.

(ix)   Currently, availability of USG at facilities below DH/CHC in most states are low. Also, the probe needed for breast cancer through Ultrasonography should be of frequency 7.7-10 MHz(as per WHO) which is much higher than the one used for pregnant women acting as a limitation presently. Therefore, the existing ultrasound machine in these facilities needs to be upgraded in order to conduct the Breast cancer screening through CBE paralleled or followed by Ultrasonography.

(x)   Access is a key barrier to breast cancer screening, although universal screening does make effort to address this. While CBE alone could serve as an equity measure to improve access to breast cancer screening. The policy will need to evolve to strengthen USG as a followed method and ensure wide availability of USG machine and probe for CBE paralleled with USG.

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APPENDIX

Appendix 1: Search Strategy: PubMed

Systematic review – Clinical Effectiveness of different breast cancer screening modalities

PubMed Search Strategy (from June 2017 to March 2018)			
Search	**Query**	**Items found**	**Time**
#39	Search (((((((((("Breast Neoplasms"[Mesh] OR "Breast Cancer Lymphedema"[Mesh]) OR "Unilateral Breast Neoplasms"[Mesh]) OR "BRCA1 Protein"[Mesh]) OR "BRCA2 Protein"[Mesh]) OR "BCAR4 non-coding RNA, human"[Supplementary Concept]) OR "BRCA2 protein, human"[Supplementary Concept]) AND ("Ultrasonography, Mammary"[Mesh] OR "Mammography"[Mesh])) AND (((("Ultrasonography"[Mesh] OR "Ultrasonics"[Mesh]) OR "Diagnostic Imaging"[Mesh]) OR "diagnostic imaging"[Subheading])) AND ("Magnetic Resonance Imaging"[Mesh] OR "Magnetic Resonance Imaging, Interventional"[Mesh] OR "Magnetic Resonance Imaging, Cine"[Mesh])) AND (("diagnosis"[MeSH Terms] OR "diagnosis"[All Fields] OR "diagnostic"[All Fields]) AND Accuracy[All Fields])	242	23:48:26
#38	Search ((((((((((("Breast Neoplasms"[Mesh]) OR "Breast Cancer Lymphedema"[Mesh]) OR "Unilateral Breast Neoplasms"[Mesh]) OR "BRCA1 Protein"[Mesh]) OR "BRCA2 Protein"[Mesh]) OR "BCAR4 non-coding RNA, human" [Supplementary Concept]) OR "BRCA2 protein, human" [Supplementary Concept]) AND ((("Ultrasonography, Mammary"[Mesh]) OR "Mammography"[Mesh])) AND	242	23:48:07

	(((("Ultrasonography"[Mesh]) OR "Ultrasonics"[Mesh]) OR "Diagnostic Imaging"[Mesh]) OR "diagnostic imaging" [Subheading])) AND ("Magnetic Resonance Imaging"[Mesh] OR "Magnetic Resonance Imaging, Interventional"[Mesh] OR "Magnetic Resonance Imaging, Cine"[Mesh])) AND Diagnostic Accuracy		
#35	Search "Magnetic Resonance Imaging"[Mesh] OR "Magnetic Resonance Imaging, Interventional"[Mesh] OR "Magnetic Resonance Imaging, Cine"[Mesh]	387529	23:45:50
#32	Search (((("Ultrasonography"[Mesh]) OR "Ultrasonics"[Mesh]) OR "Diagnostic Imaging"[Mesh]) OR "diagnostic imaging" [Subheading]	2441599	23:44:56
#30	Search ("Ultrasonography, Mammary"[Mesh]) OR "Mammography"[Mesh]	30181	23:43:29
#28	Search (((((("Breast Neoplasms"[Mesh]) OR "Breast Cancer Lymphedema"[Mesh]) OR "Unilateral Breast Neoplasms"[Mesh]) OR "BRCA1 Protein"[Mesh]) OR "BRCA2 Protein"[Mesh]) OR "BCAR4 non-coding RNA, human" [Supplementary Concept]) OR "BRCA2 protein, human" [Supplementary Concept]	263908	23:41:31
#26	Search ((((Diagnostic accuracy) AND exp Breast cancer) AND exp magnetic resonance imaging) AND exp ultrasonography) AND exp mammography	1	23:38:47
#25	Search ((("diagnosis"[MeSH Terms] OR "diagnosis"[All Fields] OR "diagnostic"[All Fields]) AND accuracy[All Fields]) AND (exp[All Fields] AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR	5	23:38:17

	("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]))) AND (exp[All Fields] AND ("mammography"[MeSH Terms] OR "mammography"[All Fields]))		
#24	Search ((Diagnostic accuracy) AND exp Breast cancer) AND exp mammography	5	23:38:11
#23	Search ((("diagnosis"[MeSH Terms] OR "diagnosis"[All Fields] OR "diagnostic"[All Fields]) AND Accuracy[All Fields]) AND (exp[All Fields] AND ("diagnostic imaging"[Subheading] OR ("diagnostic"[All Fields] AND "imaging"[All Fields]) OR "diagnostic imaging"[All Fields] OR "ultrasonography"[All Fields] OR "ultrasonography"[MeSH Terms]))) AND (exp[All Fields] AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]))	15	23:37:36
#22	Search ((Diagnostic Accuracy) AND exp ultrasonography) AND exp Breast cancer	15	23:37:20
#21	Search ((("diagnosis"[MeSH Terms] OR "diagnosis"[All Fields] OR "diagnostic"[All Fields]) AND accuracy[All Fields]) AND (exp[All Fields] AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]))) AND (exp[All Fields] AND ("magnetic resonance imaging"[MeSH Terms] OR ("magnetic"[All Fields] AND "resonance"[All Fields] AND "imaging"[All Fields]) OR "magnetic resonance imaging"[All Fields]))	7	23:36:49

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#20	Search ((diagnostic accuracy) AND exp breast cancer) AND exp magnetic resonance imaging	7	23:36:38
#19	Search ((Diagnostic Accuracy) AND exp Breast cancer) AND exp Magnatic resonance imaging	0	23:36:38
#18	Search (((("sensitivity and specificity"[MeSH Terms] OR ("sensitivity"[All Fields] AND "specificity"[All Fields]) OR "sensitivity and specificity"[All Fields] OR "sensitivity"[All Fields]) AND ("sensitivity and specificity"[MeSH Terms] OR ("sensitivity"[All Fields] AND "specificity"[All Fields]) OR "sensitivity and specificity"[All Fields] OR "specificity"[All Fields])) AND (exp[All Fields] AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]))) AND (exp[All Fields] AND ("mammography"[MeSH Terms] OR "mammography"[All Fields]))	9	23:35:57
#17	Search (((Sensitivity) AND Specificity) AND exp Breast cancer) AND exp mammography	9	23:35:44
#16	Search (((("sensitivity and specificity"[MeSH Terms] OR ("sensitivity"[All Fields] AND "specificity"[All Fields]) OR "sensitivity and specificity"[All Fields] OR "sensitivity"[All Fields]) AND ("sensitivity and specificity"[MeSH Terms] OR ("sensitivity"[All Fields] AND "specificity"[All Fields]) OR "sensitivity and specificity"[All Fields] OR "specificity"[All Fields])) AND (exp[All Fields] AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND	21	23:35:04

	"cancer"[All Fields]) OR "breast cancer"[All Fields]))) AND (exp[All Fields] AND ("diagnostic imaging"[Subheading] OR ("diagnostic"[All Fields] AND "imaging"[All Fields]) OR "diagnostic imaging"[All Fields] OR "ultrasonography"[All Fields] OR "ultrasonography"[MeSH Terms]))		
#15	Search (((Sensitivity) AND Specificity) AND exp Breast cancer) AND exp ultrasonography	21	23:34:57
#14	Search (((("sensitivity and specificity"[MeSH Terms] OR ("sensitivity"[All Fields] AND "specificity"[All Fields]) OR "sensitivity and specificity"[All Fields] OR "sensitivity"[All Fields]) AND ("sensitivity and specificity"[MeSH Terms] OR ("sensitivity"[All Fields] AND "specificity"[All Fields]) OR "sensitivity and specificity"[All Fields] OR "specificity"[All Fields])) AND (exp[All Fields] AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]))) AND (exp[All Fields] AND ("magnetic resonance imaging"[MeSH Terms] OR ("magnetic"[All Fields] AND "resonance"[All Fields] AND "imaging"[All Fields]) OR "magnetic resonance imaging"[All Fields]))	14	23:34:10
#13	Search (((Sensitivity) AND Specificity) AND exp Breast cancer) AND exp magnetic resonance imaging	14	23:33:46
#12	Search ((("sensitivity and specificity"[MeSH Terms] OR ("sensitivity"[All Fields] AND "specificity"[All Fields]) OR "sensitivity and specificity"[All Fields] OR "sensitivity"[All	241	23:33:11

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	Fields]) AND ("sensitivity and specificity"[MeSH Terms] OR ("sensitivity"[All Fields] AND "specificity"[All Fields]) OR "sensitivity and specificity"[All Fields] OR "specificity"[All Fields])) AND (exp[All Fields] AND ("magnetic resonance imaging"[MeSH Terms] OR ("magnetic"[All Fields] AND "resonance"[All Fields] AND "imaging"[All Fields]) OR "magnetic resonance imaging"[All Fields]))		
#11	Search ((Sensitivity) AND Specificity) AND exp magnetic resonance imaging	241	23:32:59
#10	Search exp[All Fields] AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields])	4155	23:31:36
#9	Search exp Breast cancer	4155	23:31:18
#8	Search er breast cancer	18307	23:31:12
#7	Search expBreast cancer	3633187	23:31:12
#6	Search exp magnetic resonance imaging	3681	23:29:39
#5	Search exp magnetic resonance imaging	0	23:29:39
#4	Search exp ultrasonography	6894	23:28:53
#3	Search exp mammography	62	23:28:10

ID	Search
Cochrane database – Search strategy (June 2017 to March 2018)	
#1	Breast cancer:ti,ab,kw (word variations have been searched)
#2	Screening in other reviews, trials, method studies, technology assessments and economic evaluations
#3	Magnetic resonance imaging:ti, ab, kw (word variations have been searched)
#4	Diagnostic accuracy: ti,ab,kw (word variations have been searched)
#5	"sensitivity and specificity":ti,ab,kw(word variations have been searched)
#6	"ultrasonography": ti,ab,kw (word variations have been searched)
#7	"magnetic resonance imaging": ti,ab,kw (word variations have been searched)
#8	"mammography": ti,ab,kw (word variations have been searched)
#9	# 1 and # 2and # 3and # 4and #5
#10	# 1 and #2 and #4 and #5
#11	#1 and #2 and #4 and #5 and #6
#12	#1 and #2 and #4 and #5 and #7
#13	#1 and #2 and #4 and #5 and #8
#14	#1 and #2 and #3 and #4 and #5 and #6 and #7 and #8

Search strategy:

Systematic review – Cost effectiveness of breast cancer screening using Mammography as a screening modality: A systematic review

1. ((Economic evaluation) AND Triennial breast cancer screening AND Mammography-5 results

("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("economic"[All Fields] AND "evaluation"[All Fields]) OR "economic evaluation"[All Fields]) AND (Triennial[All Fields] AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields])) AND ("mammography"[MeSH Terms] OR "mammography"[All Fields]).

2. **((Cost-effectiveness) AND mammography screening AND Triennial breast cancer screening-6 results**

("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields]) AND ("mammography"[MeSH Terms] OR "mammography"[All Fields]) AND (Triennial[All Fields] AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))

3. **((Health technology assessment) AND Triennial breast cancer screening) AND mammography-1 result**

(("technology assessment, biomedical"[MeSH Terms] OR ("technology"[All Fields] AND "assessment"[All Fields] AND "biomedical"[All Fields]) OR "biomedical technology assessment"[All Fields] OR ("health"[All Fields] AND "technology"[All Fields] AND "assessment"[All Fields]) OR "health technology assessment"[All Fields]) AND (triennial[All Fields] AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND ("mammography"[MeSH Terms] OR "mammography"[All Fields]).

4. **((Cost-effectiveness) AND triennial breast cancer screening) AND mammogram with adjunct ultrasound-0 results**

(("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields]) AND (triennial[All Fields] AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All

Fields]))) AND (("mammography"[MeSH Terms] OR "mammography"[All Fields] OR "mammogram"[All Fields]) AND adjunct[All Fields] AND ("diagnostic imaging"[Subheading] OR ("diagnostic"[All Fields] AND "imaging"[All Fields]) OR "diagnostic imaging"[All Fields] OR "ultrasound"[All Fields] OR "ultrasonography"[MeSH Terms] OR "ultrasonography"[All Fields] OR "ultrasound"[All Fields] OR "ultrasonics"[MeSH Terms] OR "ultrasonics"[All Fields]))

5. ((Cost-effectiveness) AND triennial breast cancer screening) AND mammogram with supplemental ultrasound-0 results

(("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields]) AND (triennial[All Fields] AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND (("mammography"[MeSH Terms] OR "mammography"[All Fields] OR "mammogram"[All Fields]) AND supplemental[All Fields] AND ("diagnostic imaging"[Subheading] OR ("diagnostic"[All Fields] AND "imaging"[All Fields]) OR "diagnostic imaging"[All Fields] OR "ultrasound"[All Fields] OR "ultrasonography"[MeSH Terms] OR "ultrasonography"[All Fields] OR "ultrasound"[All Fields] OR "ultrasonics"[MeSH Terms] OR "ultrasonics"[All Fields]))

6. ((Economic evaluation) AND triennial breast cancer screening) AND mammogram with supplemental ultrasound-0 results

(("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("economic"[All Fields] AND "evaluation"[All Fields]) OR "economic evaluation"[All Fields]) AND (triennial[All Fields] AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND (("mammography"[MeSH Terms] OR "mammography"[All Fields] OR "mammogram"[All Fields]) AND supplemental[All Fields] AND results[All Fields])

7. ((**Health technology assessment) AND triennial breast cancer screening) AND mammogram with supplemental ultrasound-0 results**

(("technology assessment, biomedical"[MeSH Terms] OR ("technology"[All Fields] AND "assessment"[All Fields] AND "biomedical"[All Fields]) OR "biomedical technology assessment"[All Fields] OR ("health"[All Fields] AND "technology"[All Fields] AND "assessment"[All Fields]) OR "health technology assessment"[All Fields]) AND (triennial[All Fields] AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND (("mammography"[MeSH Terms] OR "mammography"[All Fields] OR "mammogram"[All Fields]) AND supplemental [All Fields] AND results [All Fields])

8. **((Health technology assessment) AND triennial breast cancer screening) AND mammogram with adjunct ultrasound-0 results**

(("technology assessment, biomedical"[MeSH Terms] OR ("technology"[All Fields] AND "assessment"[All Fields] AND "biomedical"[All Fields]) OR "biomedical technology assessment"[All Fields] OR ("health"[All Fields] AND "technology"[All Fields] AND "assessment"[All Fields]) OR "health technology assessment"[All Fields]) AND (triennial[All Fields] AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND (("mammography"[MeSH Terms] OR "mammography"[All Fields] OR "mammogram"[All Fields]) AND adjunct[All Fields] AND results[All Fields])

9. **((Economic evaluation) AND triennial breast cancer screening) AND mammogram with adjunct ultrasound-0 results**

(("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("economic"[All Fields] AND "evaluation"[All Fields]) OR "economic evaluation"[All Fields]) AND (triennial[All Fields] AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All

Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND (("mammography"[MeSH Terms] OR "mammography"[All Fields] OR "mammogram"[All Fields]) AND adjunct[All Fields] AND results[All Fields])

10. ((Economic evaluation) AND quinquennial breast cancer screening) AND mammogram with adjunct ultrasound-0 results

(("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("economic"[All Fields] AND "evaluation"[All Fields]) OR "economic evaluation"[All Fields]) AND (quinquennial[All Fields] AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND (("mammography"[MeSH Terms] OR "mammography"[All Fields] OR "mammogram"[All Fields]) AND adjunct[All Fields] AND results[All Fields])

11. ((Health technology assessment) AND quinquennial breast cancer screening) AND mammogram with adjunct ultrasound-0 results

(("technology assessment, biomedical"[MeSH Terms] OR ("technology"[All Fields] AND "assessment"[All Fields] AND "biomedical"[All Fields]) OR "biomedical technology assessment"[All Fields] OR ("health"[All Fields] AND "technology"[All Fields] AND "assessment"[All Fields]) OR "health technology assessment"[All Fields]) AND (quinquennial[All Fields] AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND (("mammography"[MeSH Terms] OR "mammography"[All Fields] OR "mammogram"[All Fields]) AND adjunct[All Fields] AND results[All Fields])

12. ((Cost-effectiveness) AND quinquennial breast cancer screening) AND mammogram with adjunct ultrasound-0 results

(("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields]) AND (quinquennial[All Fields] AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND

"cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND (("mammography"[MeSH Terms] OR "mammography"[All Fields] OR "mammogram"[All Fields]) AND adjunct[All Fields] AND results[All Fields])

13. **((Cost-effectiveness) AND quinquennial breast cancer screening) AND mammogram-0 results**

(("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields]) AND (quinquennial[All Fields] AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND ("mammography"[MeSH Terms] OR "mammography"[All Fields] OR "mammogram"[All Fields])

15. **((Economic evaluation) AND quinquennial breast cancer screening) AND mammogram-0 results**

(("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("economic"[All Fields] AND "evaluation"[All Fields]) OR "economic evaluation"[All Fields]) AND (quinquennial[All Fields] AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND ("mammography"[MeSH Terms] OR "mammography"[All Fields] OR "mammogram"[All Fields]).

16. **((Health technology assessment) AND quinquennial breast cancer screening) AND mammogram-0 results**

(("technology assessment, biomedical"[MeSH Terms] OR ("technology"[All Fields] AND "assessment"[All Fields] AND "biomedical"[All Fields]) OR "biomedical technology assessment"[All Fields] OR ("health"[All Fields] AND "technology"[All Fields] AND

"assessment"[All Fields]) OR "health technology assessment"[All Fields]) AND (quinquennial[All Fields] AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields])) AND ("mammography"[MeSH Terms] OR "mammography"[All Fields] OR "mammogram"[All Fields])

17. ((Cost effectiveness) AND mammogram) AND screening once in five years-0 results

(("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields]) AND ("mammography"[MeSH Terms] OR "mammography"[All Fields] OR "mammogram"[All Fields])) AND (("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]) AND once[All Fields] AND five[All Fields] AND years[All Fields])

18. ((Economic evaluation) AND mammogram) AND screening once in five years-0 results

(("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("economic"[All Fields] AND "evaluation"[All Fields]) OR "economic evaluation"[All Fields]) AND ("mammography"[MeSH Terms] OR "mammography"[All Fields] OR "mammogram"[All Fields])) AND (("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]) AND once[All Fields] AND five[All Fields] AND years[All Fields])

19. ((Cost-effectiveness) AND) Triennial mammography screening AND breast cancer-0 results

("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields]) AND (Triennial[All Fields] AND ("mammography"[MeSH Terms] OR "mammography"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass

screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields])) AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields])

Systematic review of Cost effectiveness of Clinical Breast Examination as a breast cancer screening modality:

Search Terms:

1. **Clinical Breast Examination and three year screening and cost effectiveness**
Total items - 7

((clinical[All Fields] AND ("breast"[MeSH Terms] OR "breast"[All Fields]) AND ("physical examination"[MeSH Terms] OR ("physical"[All Fields] AND "examination"[All Fields]) OR "physical examination"[All Fields] OR "examination"[All Fields])) AND (three[All Fields] AND year[All Fields] AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields])) AND ("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields])

2. **Breast cancer screening techniques and quinquennial screening and cost effectiveness**
Total items – 1

(((("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]) AND ("methods"[Subheading] OR "methods"[All Fields] OR "techniques"[All Fields] OR "methods"[MeSH Terms] OR "techniques"[All Fields])) AND (quinquennial[All Fields] AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND ("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR

"cost-benefit analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields])

3. Clinical breast examination and quinquennial screening and cost effectiveness

Total items – 0

((clinical[All Fields] AND ("breast"[MeSH Terms] OR "breast"[All Fields]) AND ("physical examination"[MeSH Terms] OR ("physical"[All Fields] AND "examination"[All Fields]) OR "physical examination"[All Fields] OR "examination"[All Fields])) AND (quinquennial[All Fields] AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND ("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields])

4. Quinquennial breast cancer screening and cost effectiveness

Total items – 1

(quinquennial[All Fields] AND ("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields])) AND ("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields])

5. Quinquennial CBE screening and cost effectiveness

Total items – 0

(quinquennial[All Fields] AND ("Cell Biol Educ"[Journal] OR "CBE Life Sci Educ"[Journal] OR "cbe"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields])) AND ("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields])

6. Breast cancer screening techniques and triennial screening and cost effectiveness

Total items – 8

(((("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]) AND ("methods"[Subheading] OR "methods"[All Fields] OR "techniques"[All Fields] OR "methods"[MeSH Terms] OR "techniques"[All Fields])) AND (triennial[All Fields] AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND ("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields])

7. Breast cancer mixed screening technique and triennial screening and cost effectiveness

Total items – 0

(((("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND mixed[All Fields] AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]) AND technique[All Fields]) AND (triennial[All Fields] AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND ("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields])

8. Cost effectiveness and CBE and QALYs

Total items – 5

(("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields]) AND ("Cell Biol Educ"[Journal] OR "CBE Life Sci Educ"[Journal] OR "cbe"[All Fields])) AND ("quality-adjusted life years"[MeSH Terms] OR ("quality-adjusted"[All Fields] AND "life"[All Fields] AND "years"[All Fields]) OR "quality-adjusted life years"[All Fields] OR "qalys"[All Fields])

9. Clinical Breast Examination and Cost Effectiveness and females

Total items – 109

((clinical[All Fields] AND ("breast"[MeSH Terms] OR "breast"[All Fields]) AND ("physical examination"[MeSH Terms] OR ("physical"[All Fields] AND "examination"[All Fields]) OR "physical examination"[All Fields] OR "examination"[All Fields])) AND ("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields])) AND ("female"[MeSH Terms] OR "female"[All Fields] OR "females"[All Fields])

10. Breast cancer screening techniques and cost effectiveness and QALYs

Total items – 106

(((("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]) AND ("methods"[Subheading] OR "methods"[All Fields] OR "techniques"[All Fields] OR "methods"[MeSH Terms] OR "techniques"[All Fields])) AND ("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields])) AND ("quality-adjusted life years"[MeSH Terms] OR ("quality-adjusted"[All Fields] AND "life"[All Fields] AND "years"[All Fields]) OR "quality-adjusted life years"[All Fields] OR "qalys"[All Fields])

11. Clinical Breast Examination and Cost effectiveness analysis and QALYs gained and females and high risk

Total items – 1

(((((clinical[All Fields] AND ("breast"[MeSH Terms] OR "breast"[All Fields]) AND ("physical examination"[MeSH Terms] OR ("physical"[All Fields] AND "examination"[All

Fields]) OR "physical examination"[All Fields] OR "examination"[All Fields])) AND ("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields] AND "analysis"[All Fields]) OR "cost effectiveness analysis"[All Fields])) AND (("quality-adjusted life years"[MeSH Terms] OR ("quality-adjusted"[All Fields] AND "life"[All Fields] AND "years"[All Fields]) OR "quality-adjusted life years"[All Fields] OR "qalys"[All Fields]) AND gained[All Fields])) AND ("female"[MeSH Terms] OR "female"[All Fields] OR "females"[All Fields])) AND (high[All Fields] AND ("risk"[MeSH Terms] OR "risk"[All Fields]))

12. Clinical breast examination and screening interval and 3 years and cost effectiveness

Total items – 0

((((clinical[All Fields] AND ("breast"[MeSH Terms] OR "breast"[All Fields]) AND ("physical examination"[MeSH Terms] OR ("physical"[All Fields] AND "examination"[All Fields]) OR "physical examination"[All Fields] OR "examination"[All Fields])) AND (("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]) AND interval[All Fields])) AND (3[All Fields] AND years[All Fields])) AND ("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields])

13. Clinical breast examination and QALYs gained and screening intervals and cost effectiveness

Total items – 0

((((clinical[All Fields] AND ("breast"[MeSH Terms] OR "breast"[All Fields]) AND ("physical examination"[MeSH Terms] OR ("physical"[All Fields] AND "examination"[All Fields]) OR "physical examination"[All Fields] OR "examination"[All Fields])) AND (("quality-adjusted life years"[MeSH Terms] OR ("quality-adjusted"[All Fields] AND "life"[All Fields] AND "years"[All Fields]) OR "quality-adjusted life years"[All Fields] OR "qalys"[All Fields]) AND gained[All Fields])) AND (("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]) AND intervals[All Fields])) AND ("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields])

14. Clinical breast examination and QALYs gained and cost effectiveness and females

Total items – 1

((((clinical[All Fields] AND ("breast"[MeSH Terms] OR "breast"[All Fields]) AND ("physical examination"[MeSH Terms] OR ("physical"[All Fields] AND "examination"[All Fields]) OR "physical examination"[All Fields] OR "examination"[All Fields])) AND (("quality-adjusted life years"[MeSH Terms] OR ("quality-adjusted"[All Fields] AND "life"[All Fields] AND "years"[All Fields]) OR "quality-adjusted life years"[All Fields] OR "qalys"[All Fields]) AND gained[All Fields])) AND ("cost-benefit analysis"[MeSH Terms] OR ("cost-benefit"[All Fields] AND "analysis"[All Fields]) OR "cost-benefit analysis"[All Fields] OR ("cost"[All Fields] AND "effectiveness"[All Fields]) OR "cost effectiveness"[All Fields])) AND ("female"[MeSH Terms] OR "female"[All Fields] OR "females"[All Fields])

15. Clinical breast examination and screening interval and 5 years and QALYs gained

Total items – 0

((((clinical[All Fields] AND ("breast"[MeSH Terms] OR "breast"[All Fields]) AND ("physical examination"[MeSH Terms] OR ("physical"[All Fields] AND "examination"[All Fields]) OR "physical examination"[All Fields] OR "examination"[All Fields])) AND (("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]) AND interval[All Fields])) AND (5[All Fields] AND years[All Fields])) AND (("quality-adjusted life years"[MeSH Terms] OR ("quality-adjusted"[All Fields] AND "life"[All Fields] AND "years"[All Fields]) OR "quality-adjusted life years"[All Fields] OR "qalys"[All Fields]) AND gained [All Fields])

Systematic review on Health Equity:

1.   ((Equity) AND breast cancer screening) AND India - 4 results

(equity[All Fields] AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND ("india"[MeSH Terms] OR "india"[All Fields])

2.   ((Place of residence) AND breast cancer screening) AND India - 5 results

((place[All Fields] AND residence[All Fields]) AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR

("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields])) AND ("india"[MeSH Terms] OR "india"[All Fields])

3. ((Race) AND breast cancer screening) AND India - 23 results

(("continental population groups"[MeSH Terms] OR ("continental"[All Fields] AND "population"[All Fields] AND "groups"[All Fields]) OR "continental population groups"[All Fields] OR "race"[All Fields]) AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields])) AND ("india"[MeSH Terms] OR "india"[All Fields])

4. ((Culture) AND breast cancer screening) AND India - 60 results

(("ethnology"[Subheading] OR "ethnology"[All Fields] OR "culture"[All Fields] OR "culture"[MeSH Terms]) AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields])) AND ("india"[MeSH Terms] OR "india"[All Fields])

5. ((Ethnicity) AND breast cancer screening) AND India - 45 results

(("ethnology"[Subheading] OR "ethnology"[All Fields] OR "ethnicity"[All Fields] OR "ethnology"[MeSH Terms] OR "ethnicity"[All Fields] OR "ethnic groups"[MeSH Terms] OR ("ethnic"[All Fields] AND "groups"[All Fields]) OR "ethnic groups"[All Fields]) AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All

Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND ("india"[MeSH Terms] OR "india"[All Fields])

6. ((Language) AND breast cancer screening) AND India -12 results

(("programming languages"[MeSH Terms] OR ("programming"[All Fields] AND "languages"[All Fields]) OR "programming languages"[All Fields] OR "language"[All Fields] OR "language"[MeSH Terms]) AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND ("india"[MeSH Terms] OR "india"[All Fields])

7. ((Occupation) AND breast cancer screening) AND India - 9 results

(("occupations"[MeSH Terms] OR "occupations"[All Fields] OR "occupation"[All Fields]) AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND ("india"[MeSH Terms] OR "india"[All Fields])

8. ((Gender) AND breast cancer screening) AND India - 45 results

(("sex"[MeSH Terms] OR "sex"[All Fields] OR "gender"[All Fields] OR "gender identity"[MeSH Terms] OR ("gender"[All Fields] AND "identity"[All Fields]) OR "gender identity"[All Fields]) AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND ("india"[MeSH Terms] OR "india"[All Fields])

9. ((Sex) AND breast cancer screening) AND India - 33 results

(("sex"[MeSH Terms] OR "sex"[All Fields]) AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND

("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields])) AND ("india"[MeSH Terms] OR "india"[All Fields])

10. ((Religion) AND breast cancer screening) AND India - 11 results

(("religion"[MeSH Terms] OR "religion"[All Fields]) AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields])) AND ("india"[MeSH Terms] OR "india"[All Fields])

11. ((Education) AND breast cancer screening) AND India - 196 results

(("education"[Subheading] OR "education"[All Fields] OR "educational status"[MeSH Terms] OR ("educational"[All Fields] AND "status"[All Fields]) OR "educational status"[All Fields] OR "education"[All Fields] OR "education"[MeSH Terms]) AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields])) AND ("india"[MeSH Terms] OR "india"[All Fields])

12. ((Schooling) AND breast cancer screening) AND India - 196 results

(("educational status"[MeSH Terms] OR ("educational"[All Fields] AND "status"[All Fields]) OR "educational status"[All Fields] OR "schooling"[All Fields] OR "education"[MeSH Terms] OR "education"[All Fields]) AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields])) AND ("india"[MeSH Terms] OR "india"[All Fields])

13. ((Socio-economic status) AND breast cancer screening) AND India - 15 results

(("social class"[MeSH Terms] OR ("social"[All Fields] AND "class"[All Fields]) OR "social class"[All Fields] OR ("socio"[All Fields] AND "economic"[All Fields] AND "status"[All Fields]) OR "socio economic status"[All Fields]) AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields])) AND ("india"[MeSH Terms] OR "india"[All Fields])

14. ((Disability) AND breast cancer screening) AND India - 7

(Disability[All Fields] AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields])) AND ("india"[MeSH Terms] OR "india"[All Fields])

15. ((Age) AND breast cancer screening) AND India - 291 results

(("Age"[Journal] OR "Age (Omaha)"[Journal] OR "Age (Dordr)"[Journal] OR "Adv Genet Eng"[Journal] OR "age"[All Fields]) AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields])) AND ("india"[MeSH Terms] OR "india"[All Fields])

16. ((Strategies) AND breast cancer screening) AND India - 52 results

(Strategies[All Fields] AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields]

AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND ("india"[MeSH Terms] OR "india"[All Fields])

17. ((Equity) AND breast cancer screening) AND Low middle income countries - 7 results

(equity[All Fields] AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND (low[All Fields] AND middle[All Fields] AND ("income"[MeSH Terms] OR "income"[All Fields]) AND countries[All Fields])

18. ((Place of residence) AND breast cancer screening) AND Low middle income countries - 0 results

((Place[All Fields] AND residence[All Fields]) AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND (Low[All Fields] AND middle[All Fields] AND ("income"[MeSH Terms] OR "income"[All Fields]) AND countries[All Fields])

19. ((Race AND breast cancer screening) AND Low middle income countries - 3 results

(("continental population groups"[MeSH Terms] OR ("continental"[All Fields] AND "population"[All Fields] AND "groups"[All Fields]) OR "continental population groups"[All Fields] OR "race"[All Fields]) AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND (Low[All Fields] AND middle[All Fields] AND ("income"[MeSH Terms] OR "income"[All Fields]) AND countries[All Fields])

20. ((Ethnicity AND breast cancer screening) AND Low middle income countries - 13 countries

(("ethnology"[Subheading] OR "ethnology"[All Fields] OR "ethnicity"[All Fields] OR "ethnology"[MeSH Terms] OR "ethnicity"[All Fields] OR "ethnic groups"[MeSH Terms] OR ("ethnic"[All Fields] AND "groups"[All Fields]) OR "ethnic groups"[All Fields]) AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields])) AND (Low[All Fields] AND middle[All Fields] AND ("income"[MeSH Terms] OR "income"[All Fields]) AND countries[All Fields])

21. ((Culture AND breast cancer screening) AND Low middle income countries – 12 results

(("ethnology"[Subheading] OR "ethnology"[All Fields] OR "culture"[All Fields] OR "culture"[MeSH Terms]) AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND (Low[All Fields] AND middle[All Fields] AND ("income"[MeSH Terms] OR "income"[All Fields]) AND countries[All Fields])

22. ((Language AND breast cancer screening) AND Low middle income countries - 6 results
(("programming languages"[MeSH Terms] OR ("programming"[All Fields] AND "languages"[All Fields]) OR "programming languages"[All Fields] OR "language"[All Fields] OR "language"[MeSH Terms]) AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND (Low[All Fields] AND middle[All Fields] AND ("income"[MeSH Terms] OR "income"[All Fields]) AND countries[All Fields])

23. ((Occupation AND breast cancer screening) AND Low middle income countries - 2 results

(("occupations"[MeSH Terms] OR "occupations"[All Fields] OR "occupation"[All Fields]) AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND (Low[All Fields] AND middle[All Fields] AND ("income"[MeSH Terms] OR "income"[All Fields]) AND countries[All Fields])

24. ((Gender AND breast cancer screening) AND Low middle income countries -5 results

(("sex"[MeSH Terms] OR "sex"[All Fields] OR "gender"[All Fields] OR "gender identity"[MeSH Terms] OR ("gender"[All Fields] AND "identity"[All Fields]) OR "gender identity"[All Fields]) AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND (Low[All Fields] AND middle[All Fields] AND ("income"[MeSH Terms] OR "income"[All Fields]) AND countries[All Fields]).

25. ((Religion AND breast cancer screening) AND Low middle income countries - 191 results

(("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields])) AND (Low[All Fields] AND middle[All Fields] AND ("income"[MeSH Terms] OR "income"[All Fields]) AND countries[All Fields])

26. ((Education AND breast cancer screening) AND Low middle income countries - 51 results

(("education"[Subheading] OR "education"[All Fields] OR "educational status"[MeSH Terms] OR ("educational"[All Fields] AND "status"[All Fields]) OR "educational status"[All Fields] OR "education"[All Fields] OR "education"[MeSH Terms]) AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields])) AND (Low[All Fields] AND middle[All Fields] AND ("income"[MeSH Terms] OR "income"[All Fields]) AND countries[All Fields])

27. ((Socio -economic status AND breast cancer screening) AND Low middle income countries - 11 results

(("social class"[MeSH Terms] OR ("social"[All Fields] AND "class"[All Fields]) OR "social class"[All Fields] OR ("socio"[All Fields] AND "economic"[All Fields] AND "status"[All Fields]) OR "socio economic status"[All Fields]) AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields])) AND (Low[All Fields] AND middle[All Fields] AND ("income"[MeSH Terms] OR "income"[All Fields]) AND countries[All Fields])

28. ((Disability AND breast cancer screening) AND Low middle income countries – 3 results

(Disability[All Fields] AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields])) AND (Low[All Fields] AND middle[All Fields] AND ("income"[MeSH Terms] OR "income"[All Fields]) AND countries[All Fields])

29. ((Age AND breast cancer screening) AND Low middle income countries - 56 results

(("Age"[Journal] OR "Age (Omaha)"[Journal] OR "Age (Dordr)"[Journal] OR "Adv Genet Eng"[Journal] OR "age"[All Fields]) AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND (Low[All Fields] AND middle[All Fields] AND ("income"[MeSH Terms] OR "income"[All Fields]) AND countries[All Fields])

30. ((Strategies AND breast cancer screening) AND Low middle income countries - 38 results

(Strategies[All Fields] AND (("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields] OR "screening"[All Fields] OR "early detection of cancer"[MeSH Terms] OR ("early"[All Fields] AND "detection"[All Fields] AND "cancer"[All Fields]) OR "early detection of cancer"[All Fields]))) AND (low[All Fields] AND middle[All Fields] AND ("income"[MeSH Terms] OR "income"[All Fields]) AND countries[All Fields])

Drummonds Checklist:

Is the Economic Evaluation likely to be usable?

	Yes	Can't tell	No
1. Was a well – defined question posed in an answerable form? Consider: • Is it clear what the authors were trying to do?			
2. Was a comprehensive description of the competing alternatives			

given (i.e. can you tell who did what to whom, where and how often)?			
3. Was there evidence that the programme's effectiveness had been established? Consider: • Was the study attached to the economic evaluation an RCT? • How valid was the study design used? (N.B. You may want to appraise it using an appropriate checklist).			

How were outcomes and costs assessed and compared?

	Yes	Can't tell	No
4. Were all the important and relevant outcomes and costs for each alternative identified? Consider: • What perspective (s) was/were taken, e.g. health service, patient, society			
5. Were outcomes and costs measured accurately in			

appropriate units (e.g. hours of nursing time, number of physician visits, years – of – life gained) prior to evaluation?			
6. Were the outcomes and costs valued credibly? Consider: • Were opportunity costs considered?			
7. Were outcomes and costs adjusted for different times at which they occurred (discounting)?			
8. Was an incremental analysis of the outcomes and costs of alternatives performed?			
9. Was a sensitivity analysis performed? Consider: • Were all the main areas of uncertainty considered?			

Will the results help in purchasing for local people?

	Yes	Can't tell	No
10. Did the presentation			

and discussion of the results include all, or enough, of the issues that are of concern to purchasers?			
11. Were the conclusions of the evaluation justified by the evidence presented?			
12. Can the results be applied to the local population? Consider: • Are the patients similar enough to your population? • Is your local setting similar to that in the study?			

Appendix 3: *Estimated cost of CBE and Piezoelectric finger screening tests*

Details	Amount (INR)	Time	Number
Clinical Breast Examination			
Human Resources*			
Salary of ANM	12,000		
Total working days for ANM in a month		26days	
Working hours for ANM per day		6hours	
Total working hours for ANM in a month		156hours	
Total earnings of ANM per hour	77		
Women over 30 years in a 5000(sub centre) level population			910
Time taken to conduct screening of 1 woman		15minutes	
Time taken to conduct screening of 910 women		13,650 minutes/227hours	
Amount the ANM gets for conducting screening of 910 women	17,479		
Amount the ANM gets for conducting 1 screening	**19**		
Piezoelctric finger test			
Piezoelctric finger device			
Cost of the device which can do 8000 scans	4,00,000		
Cost of the cartridge which can do 2000 scans	1,00,000		
Cost per test	**50**		
Human Resources**			
Salary of ANM	12,000		
Total working days for ANM in a month		26days	
Working hours for ANM per day		6hours	
Total working hours for ANM in a month		156hours	
Total earnings of ANM per hour	77		
Women over 30 years in a 5000(sub centre) level population			910
Time taken to conduct screening of 1 woman		20 minutes	
Time taken to conduct screening of 910 women		18,200 min or 303 hrs	
Amount the ANM gets for 910 screening	23331		
Amount the ANM gets for 1 screening	**26**		

*Only Sunday is a holiday for the ANM. It excludes the cost on training of ANMs

This cost excludes any tax on the device as well as the cost incurred for training the ANMs to use this device. Only Sunday is a holiday for the ANM.) *Only Sunday is a holiday for the ANM. It excludes the cost on training of ANMs. The operational Guidelines on **"Prevention, screening and control of NCDs" mentions that in a Sub Centre with a catchment area of 5000 population level, the number of women above 30 years of age is 910.Basically this is the target population for the breast cancer screening to be conducted.

**This cost excludes any tax on the device as well as the cost incurred for training the ANMs to use this device. Only Sunday is a holiday for the ANM.). Regarding Piezo-electric, the costing which we had done was taken based on the email which their team had communicated to NHSRC that they can provide their device at a price of Rs.4, 00,000 to public health setups.Approx.8000 scans can be done using this device. So the cost turns out to Rs.50 per scan. Similarly the cartridge can be replaced and will cost Rs.1, 00,000 for 2000 scans.

Appendix 4: *Estimated stage wise treatment cost*

	Treatment	Resource use per patient	CGHS Cost (INR)	Total cost per patient (INR)	Reference
Stage 1					
1	Lumpectomy with axillary dissection**	1	45,000	45,000	CGHS, 2015
2	Adjuvant Chemotherapy (6-8 cycles)	8	1,960	15,680	ECHS, 2011 *(https://echs.gov.in/img/Policy/Medical/Policy/Rates/Med6.pdf)*
3	Radiotherapy course (Linear Accelerator Radical Therapy)	1	95,000	95,000	ECHS, 2011 *(https://echs.gov.in/img/Policy/Medical/Policy/Rates/Med6.pdf)*
4	Targeted Therapy (17 injections)	17	1,310	22,270	ECHS, 2011 *(https://echs.gov.in/img/Policy/Medical/Policy/Rates/Med6.pdf)*
5	Endocrine therapy	1	9,198	9,198	https://cghs.nic.in/ls_online.jsp
6	Hospital bed days (Rs.2000/- per day)	2	2,000	4,000	CGHS, 2015
7	Outpatient visit - follow-up	40	275	11,000	ECHS, 2011 *(https://echs.gov.in/img/Policy/Medical/Policy/Rates/Med6.pdf)*
	Total cost			**2,02,148**	
Stage 2					
1	Lumpectomy with axillary dissection**	1	45,000	45,000	CGHS, 2015
2	Adjuvant Chemotherapy (6-8 cycles)	8	1,960	15,680	ECHS, 2011 *(https://echs.gov.in/img/Policy/Medical/Policy/Rates/Med6.pdf)*
3	Radiotherapy course (Linear Accelerator Radical Therapy)	1	95,000	95,000	ECHS, 2011 *(https://echs.gov.in/img/Policy/Medical/Policy/Rates/Med6.pdf)*
4	Targeted Therapy (17 injections)	17	1,310	22,270	ECHS, 2011 *(https://echs.gov.in/img/Policy/Medical/Policy/Rates/Med6.pdf)*
5	Endocrine therapy*	1	9,198	9,198	https://cghs.nic.in/ls_online.jsp CGHS, 2015
6	Hospital bed days (Rs.2000/- per day)	2	2,000	4,000	CGHS, 2015
7	Outpatient visit - follow-up	40	275	11,000	ECHS, 2011 *(https://echs.gov.in/img/Policy/Medical/Policy/Rates/Med6.pdf)*
	Total cost			**2,02,148**	
Stage 3					
1	Modified Radical Mastectomy**	1	45,000	45,000	CGHS, 2015
2	Neo-Adjuvant Chemotherapy (4 cycles)	4	1,960	7,840	ECHS, 2011 *(https://echs.gov.in/img/Policy/Medical/Policy/Rates/Med6.pdf)*
3	Radiotherapy course	1	95,000	95,000	ECHS, 2011

	(Linear Accelerator Radical Therapy)				*(https://echs.gov.in/img/Policy/Medical/Policy/Rates/Med6.pdf)*
4	Targeted Therapy (17 injections)	17	1,310	22,270	ECHS, 2011 *(https://echs.gov.in/img/Policy/Medical/Policy/Rates/Med6.pdf)*
5	Endocrine therapy	1	9,198	9,198	https://cghs.nic.in/ls_online.jsp
6	Hospital bed days (Rs.2000/- per day)	6	2,000	12,000	CGHS, 2015
7	Outpatient visit - follow-up	40	275	11,000	ECHS, 2011 *(https://echs.gov.in/img/Policy/Medical/Policy/Rates/Med6.pdf)*
	Total cost			**2,02,308**	
Stage 4					
1	Simple Mastectomy**	1	45,000	45,000	CGHS, 2015
2	Palliative Chemotherapy (4 cycles)	4	1,960	7,840	ECHS, 2011 *(https://echs.gov.in/img/Policy/Medical/Policy/Rates/Med6.pdf)*
3	Radiotherapy course (Linear Accelerator Radical Therapy)	1	95,000	95,000	ECHS, 2011 *(https://echs.gov.in/img/Policy/Medical/Policy/Rates/Med6.pdf)*
4	Targeted Therapy (17 injections)	17	1,310	22,270	ECHS, 2011 *(https://echs.gov.in/img/Policy/Medical/Policy/Rates/Med6.pdf)*
5	Endocrine therapy	1	9,198	9,198	https://cghs.nic.in/ls_online.jsp
6	Hospital bed days (Rs.2000/- per day)	2	2,000	4,000	CGHS, 2015
7	Outpatient visit - follow-up	40	275	11,000	ECHS, 2011 *(https://echs.gov.in/img/Policy/Medical/Policy/Rates/Med6.pdf)*
	Total cost			**1,94,308**	

*In CGHS cost of endocrine was not given so taken cost from CGHS drug list. Cost of Tamoxifen 2.5 mg is INR 31.5/- . Dose is of 20 mg per day, so 8 tablets per day. Per year cost comes to INR 9198/-.

** Includes Surgery charges=INR 25,000/-, Operation theatre charges=INR 10,000/- and Anesthesia charges=INR 10,000/-. Total cost of surgery is INR 45,000/-

Appendix 5: Mammography availability status in India:

S.No	States/UT	Mammography present (Nos) at District level Hospitals	Total no. of districts in state	No. of districts having MMG at District level Hospitals
1	Andaman and Nicobar Island	Data not available	3	Data not available
2	Andhra Pradesh	3	13	3
3	Arunachal Pradesh	0	21	0
4	Assam	2	33	2
5	Bihar	0	38	0
6	Chandigarh	1	1	1
7	Chhattisgarh	1	27	1
8	Dadar and Nagar Haveli	Data not available	1	Data not available
9	Daman and Diu	1	1	1
10	Delhi	Data not available	11	Data not available
11	Goa	1	2	1
12	Gujarat	Data not available	33	Data not available
13	Haryana	4	22	4
14	Himachal Pradesh	3	12	3
15	Jammu and Kashmir	0	22	0
16	Jharkhand	1	24	1
17	Karnataka	5	30	5
18	Kerela	1	14	1
19	Lakshadweep	0	1	0
20	Madhya Pradesh	0	51	0
21	Maharashtra	0	36	0
22	Manipur	Data not available	16	Data not available
23	Meghalaya	0	11	0
24	Mizoram	1	8	1
25	Nagaland	1	11	1
26	Odisha	2	30	1
27	Puducherry	1	4	1
28	Punjab	4	22	4
29	Rajasthan	4	33	3
30	Sikkim	0	4	0
31	Tamilnadu	0	32	0
32	Telangana	3	31	2
33	Tripura	0	8	0
34	Uttarakhand	7	13	5
35	Uttar Pradesh	2	75	1
36	West Bengal	7	23	4

Source: *State wise mapping data of Mammography, HCT Division, NHSRC, 2018 (70)*