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Systematic review on women's values and preferences concerning breast cancer screening and diagnostic services

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Abstract

Background: There is still lack of consensus on the benefit-harm balance of breast cancer screening. In this scenario women's values and preferences are crucial for developing health related recommendations. In the context of the European Commission Initiative on Breast Cancer, we conducted a systematic review to inform *the European Breast Guidelines*.

Methods: We searched Medline and included primary studies assessing women's values and preferences regarding breast cancer screening and diagnosis decision making. We used a thematic approach to synthesise relevant data. The quality of evidence was determined with GRADE, including GRADE CERQual for qualitative research.

Results: We included 22 individual studies. Women were willing to accept the psychological and physical burden of breast cancer screening and a significant risk of overdiagnosis and false-positive mammography findings, in return for the benefit of earlier diagnosis. The anxiety engendered by the delay in getting results of diagnostic tests was highlighted as a significant burden, emphasising the need for rapid and efficient screening services, and clear and efficient communication. The confidence in the findings was low to moderate for screening and moderate for diagnosis, predominantly due to methodological limitations, lack of adequate understanding of the outcomes by participants, and indirectness.

Conclusions: Women value more the possibility of an earlier diagnosis over the risks of a false positive result or overdiagnosis. Concerns remain that women may not understand the concept of overdiagnosis. Women highly value time efficient screening processes and rapid result delivery, and will accept some discomfort for the peace of mind screening may provide.

Key words: breast cancer, diagnostic services, patient-centered care, patient preference, practice guideline, screening, cancer, oncology.

Introduction

Breast cancer is the most common cancer in women and one of the leading causes of all cancer deaths both in Europe and worldwide[1]. Breast cancer screening with mammography, the only population-based method for the early detection of breast cancer currently used, has been shown to reduce breast cancer mortality in women aged 50–74 years[2] and is widely implemented in most European countries[3]. However, mammography screening is also associated with potential important undesirable effects, including overdiagnosis, and hence overtreatment, and false positive mammography results[4]. False-positive mammography findings may cause psychological distress[5]. The balance between benefits and harms of screening becomes less favourable after 74 years of age and at 90, harms are considered to outweigh benefits, largely as a consequence of overdiagnosis[6]. There is still a lack of consensus on the benefit-harm balance of breast cancer screening thus underlining the need for women to receive balanced and adequate information in order to make informed decisions concerning their participation in screening programmes.

The European Commission Initiative on Breast Cancer (ECIBC) (http://ecibc.jrc.ec.europa.eu/) uses the GRADE approach when formulating recommendations for breast cancer screening and diagnosis. This includes the use of Evidence to Decision (EtD) frameworks when moving from evidence to recommendations[7]. The EtD frameworks provide an explicit and transparent system for decision making that can help ensure all important criteria, informed by the best available research evidence, needed to make a decision are considered. One of these criteria is how those affected by a recommendation value the main desirable and undesirable outcomes of the interventions considered. In the case of recommendations on breast cancer screening, this means considering women's values and preferences regarding potential consequences of participating in screening.

Women's values and preferences refer to the relative weight those affected by a recommendation place on the different outcomes, such as the potential benefits, harms, costs, limitations, and inconveniences of the available interventions or management options[8]. Inclusion of women's values in the screening decision making process has been proposed for decades now[9], but its implementation is still suboptimal. GRADE's EtD frameworks provide guidance on how to incorporate women's values and preferences while drafting clinical recommendations. This systematic review was thus conducted to inform ECIBC's clinical recommendations' development process.

Methods

Design

A systematic literature review, following standard Cochrane Collaboration methodology[10], was performed to address the following question: What are the values and preferences of women regarding decision making on breast cancer screening and diagnosis. The review protocol is registered in PROSPERO (https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=41487).

Search strategy and Selection criteria

Medline (assessed through Ovid) was searched using terms regarding breast neoplasm/cancer; screening; diagnosis; different screening and diagnosis outcomes; values, and preferences (complete search strategy in **Appendix 1**). As a source for individual studies, systematic reviews with no time restrictions were searched. For primary studies, publications from 2006 until the end of June 2018 were included. Only studies in English were included.

Only studies examining women's preferences for breast cancer screening versus no screening or about the potentially available breast cancer diagnostic alternatives, studies evaluating how women value breast cancer screening and diagnosis outcomes, and those examining the choices women facing a breast cancer screening or diagnostic decision make, when informed about the expected desirable and undesirable outcomes, were included. We excluded studies restricted to women´s knowledge, views, behaviours, perceptions, attitudes and expectations regarding breast cancer screening and diagnosis. We also excluded those conducted in countries outside the Organisation for Economic Co-operation and Development (OECD), or those focusing exclusively on minorities from geographic regions outside Europe.

Screening and data collection

One reviewer screened the search results based on title and abstract. Two reviewers independently confirmed eligibility of relevant articles based on the full text, and disagreement between researchers was solved by a third reviewer. One reviewer extracted the main characteristics and main findings of the included studies in a tabular format. Another reviewer checked the extracted data for accuracy. The synthesis of the results is described narratively, and is based on the identification and grouping of themes reported in the included studies.

Risk of bias assessment was carried out using the domains suggested in the GRADE approach for quantitative studies[11], and the Critical Appraisal Skills Programme (CASP) checklist[12] for qualitative studies. The confidence (quality or certainty) of the evidence was rated from high to very low considering the standard GRADE domains for quantitative data[10]. For qualitative studies, the CERQual (Confidence in the Evidence from Reviews of Qualitative Research) approach was used[13]. The results of the systematic review

were reported according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement[14].

Results

The search yielded 5,063 unique references, of which 96 were deemed potentially eligible for inclusion, based on initial screening of titles and abstracts. After full text appraisal, 22 individual studies (15 on screening and seven on diagnosis) involving 12,174 women were included. The PRISMA flowchart is presented in **Figure 1**. A tabular summary of the findings and rating of certainty of evidence is presented in **Table 1**. Evidence profiles including main findings and certainty of evidence, for both screening and diagnosis are included in **Appendix 2**.

Screening

We identified the following main themes that contribute to how women value the main outcomes of screening: risk of overdiagnosis and false positive screening results, burden of breast cancer screening, and challenges elderly women face when making a decision to participate in screening programmes.

Overdiagnosis

Five studies, four conducted in Europe[15,16,17,18] and one in Australia[19], evaluated women's knowledge and acceptability of the risk of overdiagnosis. Results revealed limited awareness of the risk of overdiagnosis among women. Only 29% and 53% of participants in two population-based surveys, conducted in the UK, were aware of the concept of overdiagnosis[16,18]. In a study from Spain, only 10% of women had adequate knowledge about the implications of being overdiagnosed[15].

Four studies[15,17,18,19] assessed the impact exposure to information concerning overdiagnosis has on women of screening age. Information about overdiagnosis and its implications triggered different immediate reactions among participants. These included surprise and concern regarding the undesirable psychological and physical consequences, as well as defensive reactions and mistrust of the investigators' motives. On the one hand, women considered it would be appropriate and fair to provide adequate information regarding overdiagnosis to women invited for screening but, on the other, they were concerned this information may cause confusion and deter women from participating.

Two studies evaluated the impact information concerning overdiagnosis had on women's intention to participate in screening[17,18]. Ninety per cent of participants answered they would probably or definitely attend screening in the future. Only seven per cent, especially women below the recommended screening age, actually showed a decrease in screening intention[18].

Two studies evaluated the rate of overdiagnosis that women were willing to accept[16,19]. On the one hand, a survey showed they were willing to accept 15% and 31% overdiagnosis for an expected benefit of 10% and 50% reduction in cancer specific mortality, respectively[16]. On the other hand, a focus group study, showed that a rate of 1-10% of overdiagnosis was perceived as completely acceptable, 30% was perceived as still acceptable by most women, but 50% was considered to be extremely high[19].

The willingness to accept overdiagnosis was related to socio-demographic factors: those with a higher educational status accepted significantly higher levels of overdiagnosis than those with a lower educational status. Furthermore, women over 50 accepted significantly less overdiagnosis than younger women[16]. However, in another study, younger participants interpreted overdiagnosis as a distinctly negative factor, discouraging them from participating in screening[19].

The confidence in the evidence regarding overdiagnosis was considered low. There were significant concerns regarding some studies about whether women were adequately informed in order to fully understand the extent of the risks and benefits associated with breast cancer screening, and specifically the implications of overdiagnosis. This can be seen, for example, in a cross-sectional study evaluating 510 British females, 15% of the participants declared that they were prepared to accept overdiagnosis in the complete population, strongly suggesting that they may have not comprehended the aims of screening and the concept of overdiagnosis[16]. Indirectness was an additional limitation in some of the studies, as some studies included adult women of any age, rather than women at screening age.

False positive screening results

The burden and acceptability of false positive mammography screening results was evaluated in seven studies[20,21,22,23,24,25,26]. A European cross-sectional study involving 1,018 women from the general population used an online discrete choice experiment survey to elicit patients' preferences regarding false positive results[26]. Respondents highly valued the possibility of early diagnosis and were prepared to accept unnecessary follow-up appointments as a result of a false positive screening result. In fact, over 60% of participants were prepared to accept a 20% false positive rate for a 3% probability of detecting cancer.

Two longitudinal European studies[21,22] included a pooled population of 671 patients with false positive screening results, 174 patients diagnosed with breast cancer and 1,363 matched women with negative results. Here, a false positive mammography screening result was associated with consistently greater negative psychosocial consequences compared to a negative result, even three years after final diagnosis. However, a study conducted in the United States[25], found only a transient increase in personal anxiety after false positive results, which did not persist at one year after final negative diagnosis was made.

Four studies assessed women's attitudes and beliefs on the effects of false positive mammograms towards future screening behaviour. Ganott and colleagues[23] reported that, prior to mammography examination, 97% of women believed a false positive result would not deter them from screening. Tosteson et al[25] reported that among women with a previous false positive mammography finding, the future screening intention was significantly increased compared to those with a negative mammogram. These findings were confirmed by two qualitative studies including women with false positive mammography results[20,24]. A significant proportion of women would accept the inconvenience and anxiety associated with a higher recall rate if this implied the possibility to detect breast cancer earlier[23].

The confidence in the evidence from the cross-sectional studies regarding false positive findings was moderate due to methodological limitations (significant concerns regarding inadequacy of information provided to participants that led to poor understanding of benefits and risks of breast cancer screening). The confidence in the evidence from qualitative studies was low, as there were similar methodological limitations, but also these studies mostly evaluated preferences of women who had already received a false positive result and their preferences may not be representative of the general population of women at screening age. Based on all available evidence, the confidence in the evidence was moderate.

Burden

A metasynthesis[27] including 21 qualitative studies, assessed barriers for breast cancer screening from the women's perspective. The authors reported several aspects of breast cancer screening that may be burdensome for women including: logistical implications, such as investing time and money to reach the screening site, psychological distress associated with the screening process itself, derived from fear of a positive result, embarrassment, and from not receiving services in line with their cultural and religious beliefs. The confidence in the evidence was moderate being limited by the insufficiency of data and methodological limitations.

Screening decisions among elderly women

Two studies in the United States assessed factors that influence the decision of elderly women (aged 80 and over) to participate in screening programmes[28,29]. A qualitative study highlighted a more pronounced variability in elderly women's preferences[28]. Factors influencing more their decision to be screened included women's perceived individual risk of BC, physician's advice, previous screening habits and experiences with mammography, as well as social and family influences. The most important reasons for declining screening were the decision not to undergo a possible operation given their age, and the discomfort associated with an additional clinical visit[28]. In a cross-sectional study, women aged 80 and older

who decided not to undergo breast cancer screening, ranked their age and doctor's counselling as the factors mostly influencing their decision[29].

Diagnosis

Anxiety

One of the main themes concerning diagnostic procedures in breast cancer is the avoidable anxiety, mostly due to inadequacy of the information regarding procedures, and the delay in receiving test results. This theme was reported in four cross-sectional studies[30,31,32,33], one qualitative study[34], and one systematic review[35].

Women highly valued receiving diagnostic results in a timely manner. Twelve per cent of women, who underwent image-guided breast biopsies in the US, were not even satisfied with a one-day waiting time for their results. However, 90% of them found receiving the test results over the phone to be acceptable if that accelerated the process[30]. A cross-sectional study including women who had previously undergone sentinel node biopsy with intraoperative diagnosis found similar results; ninety-five per cent of participants would choose to undergo the procedure again in the future, in order to have the results earlier[31]. Another cross-sectional study showed that better communication with the radiologist performing the biopsies was associated with lower post-biopsy anxiety[32].

A systematic review showed that the needs for supportive care concerning diagnosis touch upon many domains, which cluster around psychological and information needs. These needs are influenced by individual clinical, demographic, emotional, psychological, or psychosocial characteristics of subjects[35]. Finally, one study, including only women aged 60 and over, provided information on the benefits of a decision aid[33]. The authors did not find any significant differences in decisional support needs based on age at diagnosis, education level, ethnicity, or presence of co-morbidities. Approximately 90% of women indicated they had received a high level of support during their cancer diagnosis. However, the desire for additional educational resources such as worksheets, consultation summaries, or workbooks to assist treatment decisions was highlighted. The overall confidence in these findings concerning anxiety is moderate because of inadequacy of data.

Inconvenience

As part of a trial in Australia, a cross-sectional study with 49 women assessed their experience with contrast enhanced spectral mammography (CESM) compared with contrast enhanced MRI (CEMRI) during preoperative breast cancer staging[36]. Significantly higher overall preference towards CESM was shown, with faster procedure time, greater comfort and lower noise level cited as the commonest reasons. Participants

also reported significantly lower rates of anxiety during CESM compared with CEMRI. The overall confidence in these findings is moderate because of inadequacy of data.

Discussion and Conclusions

Main findings

Our review shows that women place a low value on the psychosocial and physical effects of overdiagnosis and false positive mammography screening results, as well on the inconvenience and burden associated with it. Women generally consider these undesirable effects acceptable, recognising the potential benefits of breast cancer screening. However, the confidence in the evidence supporting these findings is low to moderate, due to methodological limitations. Regarding diagnosis, women highly appreciate avoiding anxiety caused by delays in the receipt of results or suboptimal communication with healthcare professionals. They also appear to value faster procedures over the inconvenience associated with them.

Our results in the context of previous results

Overdiagnosis

The level of overdiagnosis that women were willing to accept was relatively high; up to 30%[16,19]. The most commonly reported estimates of overdiagnosis from screening programmes are around 10% and vary widely[4]. Thus the level of overdiagnosis women were willing to accept was on the high end of the estimated average figures. The high rates of overdiagnosis women were willing to accept could put into question whether the concept was really understood by study participants. According to our review, women's knowledge and understanding concerning overdiagnosis was variable, and in general limited, with only about 30-50% of women being aware of the concept, and only 10% having adequate knowledge about its implications. Results from a recently published study from the UK revealed that almost one third of participants reported having previously encountered the term overdiagnosis, but responses often indicated they had very limited knowledge about its implications[37].

Women appear to overestimate the benefits of mammography screening. Up to 70% of women overestimated the possibility of having breast cancer detected during screening[23]. The fear of getting breast cancer may also lead women to be willing to accept a high**er** level of overdiagnosis. Population-based studies have consistently shown that between a quarter to a half of the general population worry to some extent about getting some type of cancer, and 5%-10% experience extreme worry[38]. Altogether these findings may partially explain the high levels of overdiagnosis women were willing to accept, and also

underlines the importance of providing women with balanced information concerning the benefits and harms of breast cancer screening.

False positive findings

European studies show that false positive screening results were associated with long-term negative psychosocial consequences[20,21,22], whereas a US study showed only a transient increase in anxiety[25]. These conflicting results may be related to the different instruments used to measure anxiety. European studies used a screening-specific validated questionnaire 'Consequences of Breast Cancer Screening' specifically developed to assess the long term psychosocial consequences of false-positive mammography screening, while the US study used the 6 question short-form (STAI-6) of the Spielberger State-Trait Anxiety Inventory (STAI) instrument focusing on measurement of general anxiety. Previous studies have shown inconsistent results concerning psychosocial consequences of false positive results, with some women showing persistent and others only transient anxiety[39]. A systematic review focusing on the UK population reported that receiving a false positive screening mammogram caused breast cancer-specific psychological distress that may endure up to 3 years, and the degree of distress appears to be related to the level of invasiveness of the assessment procedure[34]. False positive results may have substantial other impacts on women's health behaviour and well-being. Women with false positive findings have been shown to make a greater use of healthcare services, and have reported lower quality of life than those without false positive findings[40].

Healthy women at screening age were prepared to accept a high risk of false positive screening results in order to detect breast cancer early. Irrespective of false positive findings, the screening intention remained high, and was even higher among those with a false positive result compared to those with a negative result. Despite significant psychosocial burden caused by false positive screening results, women acknowledge the value of mammography screening. Our results are consistent with another recent systematic review and meta-synthesis by Health Care Ontario, assessing the burden of false-positive and false-negative results and their impact on women's screening intentions[41].

Screening decision among elderly women

Elderly women's preferences regarding breast cancer screening were more heterogeneous. This is consistent with the decreased benefit to risk ratio that these women face[42]. For these reasons, screening of elderly women is not recommended by the majority of available guidelines[42].

Diagnostic procedures

The importance of the quick receipt of diagnostic results has been previously emphasised in several studies[43,44]. A very high number of women would choose to undergo the diagnostic procedure again in the future in order to have the results earlier[31]. A substantial proportion of women are also willing to accept the inconvenience and anxiety associated with a higher recall rate if it results in earlier breast cancer detection[23]. Altogether these findings show that women appear to value more the possibility of an earlier and accurate detection of cancer over the inconvenience and anxiety associated with the diagnostic process itself.

Our results are in agreement with Pahade and coworkers[45] who have shown that most patients showed decreased anxiety after receiving the examination results from the radiologist. Although it is generally assumed in clinical practice that the best way for patients to receive diagnostic results is to personally discuss them with a qualified professional, Brandon and colleagues reported that most women (90%) found it acceptable to receive the results even over the phone[29]. This finding can also partially explain the higher value women place on fast delivery of test results over the method chosen to communicate them.

Study limitations

Our review has several strengths. To the best of our knowledge, this is the first systematic review focusing specifically on women´s values and preferences about breast cancer screening and diagnostic services. In our evaluation we applied rigorous methods, including the GRADE approach and CERQual methodology for evidence synthesis and quality evaluation of qualitative results.

The main limitation of our findings relates to the methodological limitations of the included studies. More specifically, we are not confident that the participants of several of the included studies received balanced information in order to understand complex concepts, such as overdiagnosis. Our study is also limited by the relatively small number of studies and small sample size in some of them. Another limitation is that we only included studies published in English. However, the included studies evaluated a wide variety of populations and countries so we do not believe this limits the generalisation of our findings. The restriction of the search to the last 10 years for primary studies may have also limited our findings, but we are confident that the most important outcomes, such as overdiagnosis, have been mostly studied within this period. The inclusion of previous systematic reviews also limits these concerns. In addition, more recent studies are likely to be more relevant because diagnostic and therapeutic options and outcomes of breast cancer have significantly changed over the last decade.

Clinical implications

The low-to-moderate quality of the evidence for breast cancer screening and moderate quality evidence for breast cancer diagnosis underlines the need to carry out more well-designed studies on women´s values and preferences, including also minorities, women with disabilities, with different cultural, religious, educational and economic backgrounds. Such studies would provide valuable data to panels developing clinical or public health recommendations, as well as to policy-makers when making coverage or public health decisions.

Healthcare community should focus on providing clear, adequate and balanced information on the benefits and risks of breast cancer screening to ensure informed participation. In this context, the use of decision aids could be helpful[46]. A particular emphasis should be made on the communication of overdiagnosis, which was poorly understood based on our findings. Clinicians should also be encouraged to improve their communication skills, and healthcare systems to provide adequate and timely information about test results.

Ethical background

The European Commission Initiative on Breast Cancer (ECIBC) (http://ecibc.jrc.ec.europa.eu/) uses the GRADE approach when formulating recommendations for breast cancer screening and diagnosis. This includes the use of Evidence to Decision (EtD) frameworks that provide an explicit and transparent system for decision making to ensure all important criteria needed to make a decision are considered. One of these criteria is how those affected by a recommendation value the main desirable and undesirable outcomes of the interventions considered. This systematic review was thus conducted to inform ECIBC's clinical recommendations' development process.

Neither patient consent nor ethical committee approval was necessary as, due to the type of work presented (a systematic review of the literature), this is not needed.

Conflict of interests

AM, HPH, IS and PAC were working at the time this work was carried out for Iberoamerican Cochrane Collaboration which received payments from the European Commission to develop the systematic reviews informing the ECIBC recommendations.

LP, ZSP, AB, SD, DL and LN were working, or are working, for the European Commission, JRC.

No other interests are declared.

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Authors' contributions

Alexander Mathioudakis, Ivan Solà and Pablo Alonso-Coello were responsible for conducting the systematic review, including the interpretation of the results and the drafting of the full report of the systematic review (available upon request). Alexander Mathioudakis and Hector Pardo-Hernandez conducted the search and data extraction. Liisa Pylkkanen, Silvia Deandrea, and Donata Lerda contributed to the definition of the research protocol, and provided comments to the preliminary results. Alexander Mathioudakis, Pablo Alonso-Coello, Minna Salakari and Liisa Pylkkänen drafted the first version of the article. All authors contributed to the interpretation and reporting of the results and provided comments on subsequent versions of the article. All authors read and approved the final manuscript prior submission.

Table 1. Tabulated summary of findings and rating of the confidence in the evidence about screening

Review Finding	Confidence in the Evidence	Explanation	Studies Contributing to the Review Finding
False positives Women significantly place a low value on the psychosocial and physical effects of false positive results. However, women consider false positive results an acceptable consequence of mammographic breast cancer screening.	Moderate confidence	There are significant concerns regarding women's lack of understanding about breast cancer screening, especially the undesirable effects. In addition, the adequacy of the information provided to the breast cancer participants, which would help them take an informed decision, seems to be inadequate.	Bolejko 2014, Bolejko 2015, Ganott 2006, Brodersen 2013, Thompson 2015, Tosteson 2014, Vass 2018
Overdiagnosis Women significantly place a low value on the psychosocial and physical effects of overdiagnosis. However, women generally seem to consider	Low confidence	There are significant concerns regarding women's lack of understanding about breast cancer screening, especially the undesirable effects. For instance, Van den Bruel et al reported that 10-14% of the participants accepted overdetection	Baena-Cañada 2014, Hersch 2013, Van den Bruel 2015, Waller 2013, Waller

these undesirable effects acceptable given their knowledge about the potential desirable consequences of breast cancer screening.		in the overall population, implying that they did not comprehend the aims of screening and the concept of overdiagnosis. In addition, the information provided to breast cancer participants, which would help them take an informed decision, seems to be inadequate. Also, indirectness is a limitation of some of the included studies, which assessed adult women of any age, rather than women of screening age.	2014

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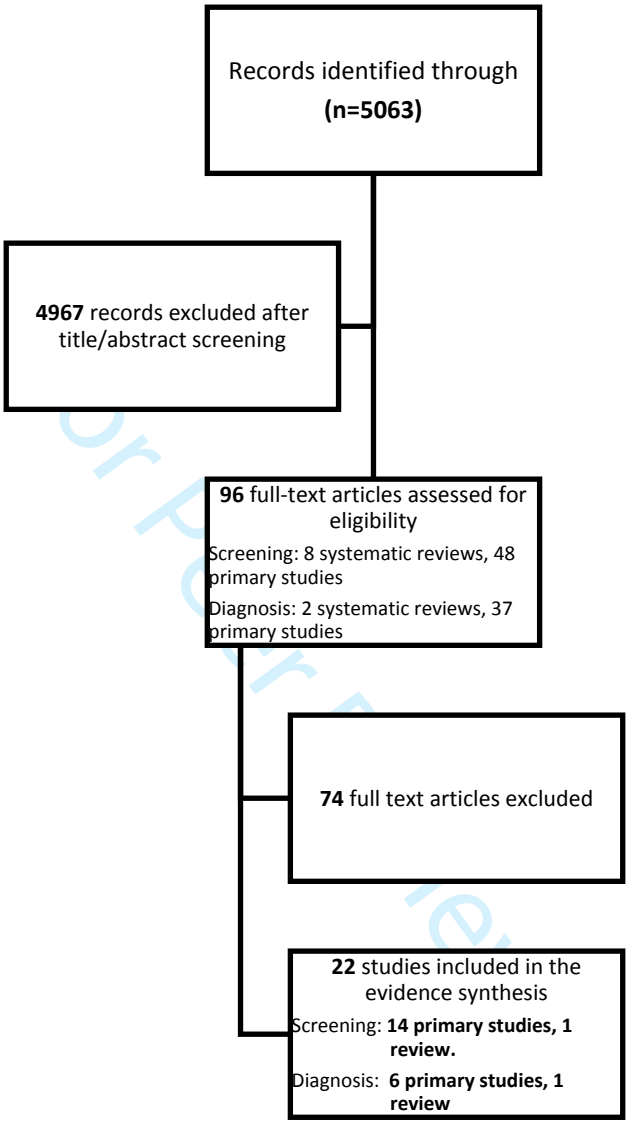
Figure 1. PRISMA Flowchart for inclusion and exclusion of the studies



Appendix 1. Search algorithm and references retrieved

Database and date	
MEDLINE Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present> 09.12.2015	1 *Breast Neoplasms/di (17240) 2 *Breast Neoplasms/ra (6704) 3 breast.ti. (212016) 4 1 or 2 or 3 (218134) 5 *Mass Screening/ (46220) 6 Early Detection of Cancer/ (11933) 7 screen*.ti,ab. (534189) 8 5 or 6 or 7 (546404) 9 4 and 8 (17898) 10 *Mammography/ (15268) 11 mammogra*.ti,ab. (26732) 12 9 or 10 or 11 (38342) 13 diagnos*.ti,ab. (1857062) 14 overdiagnos*.ti,ab. (2622) 15 over diagnos*.ti,ab. (885) 16 overdetection.ti,ab. (75) 17 over detection.ti,ab. (67)

	18 13 or 14 or 15 or 16 or 17 (1858213) 19 3 and 18 (37972) 20 12 or 19 (66766) 21 *Choice Behavior/ (11911) 22 *Decision Making/ (31408) 23 *Attitude to Health/ (38689) 24 understanding.ti,ab. (554994) 25 perception*.ti,ab. (171098) 26 preference*.ti,ab. (106827) 27 attitude*.ti,ab. (108337) 28 expectation*.ti,ab. (62344) 29 (value or values).ti,ab. (1410329) 30 (view or views).ti,ab. (280091) 31 informed choice*.ti,ab. (1813) 32 informed decision*.ti,ab. (4662) 33 (women* adj5 decision*).ti,ab. (3170) 34 (screening adj5 decision*).ti,ab. (1777) 35 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 (2569146) 36 20 and 35 (13444)

	37 Qualitative Research/ (25350) 38 Focus Groups/ (19437) 39 qualitative.ti,ab. (142495) 40 interview*.ab. (231234) 41 focus group*.ti,ab. (26987) 42 purposive.ab. (4779) 43 theory.ab. (206388) 44 grounded theory.ab. (7063) 45 (mixed adj3 method*).ti,ab. (9327) 46 meta-ethnograph*.ti,ab. (227) 47 meta-synthe*.ti,ab. (337) 48 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 (547218) 49 36 and 48 (1316) 50 limit 49 to "systematic reviews" (28) 51 limit 49 to "reviews (best balance of sensitivity and specificity)" (75) 52 50 or 51 (85) 53 49 not 52 (1231) 54 36 not 49 (12128) 55 exp Decision Support Techniques/ (66253) 56 (health adj3 utilit*).ti,ab. (2466)

	57 gamble*.ti,ab. (3318) 58 prospect theor*.ti,ab. (174) 59 preference score*.ti,ab. (373) 60 (preference* adj5 elicitat*).ti,ab. (165) 61 health utilit*.ti,ab. (1362) 62 (utilit* adj3 (value* or score* or estimate*)).ti,ab. (3224) 63 (state adj5 utilit*).ti,ab. (773) 64 health state.ti,ab. (2958) 65 feeling thermometer*.ti,ab. (54) 66 best-worst scaling.ti,ab. (63) 67 standard gamble.ti,ab. (740) 68 time trade-off.ti,ab. (889) 69 TTO.ti,ab. (721) 70 probability trade-off.ti,ab. (16) 71 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 (77125) 72 54 and 71 (154) 73 54 not 72 (11974) 74 *Questionnaires/ (33072) 75 Cross-Sectional Studies/ (209337)

	76 (survey or questionnair* or cross-sectional).ti,ab. (784271) 77 74 or 75 or 76 (858049) 78 73 and 77 (1486) 79 limit 78 to "systematic reviews" (29) 80 limit 78 to "reviews (best balance of sensitivity and specificity)" (50) 81 79 or 80 (64) 82 78 not 81 (1422) 83 73 not 82 (10552) 84 review.pt. (2087807) 85 83 and 84 (1226) 86 52 or 53 or 72 or 81 or 82 or 85 (4144)

Appendix 2. Evidence Profiles.

Screening decisions

Quality assessment							Study population and characteristics	Findings	Quality	Studies Contributing to the Review Finding
No. of studies	Study design	Risk of bias/Methodological limitations	Inconsistency/Coherence	Indirectness/Relevance	Imprecision/Adequacy of data	Other considerations				
Overdiagnosis										
3	Cross-sectional studies	serious[1]	none	non serious[2]	none	none	3216 adult women	The disutility of overdiagnos was high among women in the included studies. However, they consider it an acceptable risk of mammographic breast cancer screening.	⊕⊕◯◯ LOW	Baena-Cañada 2014, Van den Bruel 2015, Waller 2014
2	Qualitative studies	serious[1]	none	none	serious[3]	none	90 women of breast screening age		⊕⊕◯◯ LOW	Hersch 2013, Waller 2013
False positives										
4	Cross-sectional studies	non serious[3]	none	none	none	none	1173 women with a false positive mammographic result versus 1424 women with a negative mammographic result.	The disutility of false positive mammographic results was high among women in the included studies. However they	⊕⊕⊕◯ MODERATE	Bolejko 2015, Brodersen 2013, Ganott 2006, Tosteson 2014, Vass 2018

2	Qualitative studies	serious[1]	none	Serious[5]	none	none	53 women who have received a false positive mammographic result.	consider it an acceptable risk of mammographic breast cancer screening.	⊕⊕◯◯ LOW	Bolejko 2014, Thompson 2013
Burden associated with breast cancer screening programmes										
1	Systematic review of 21 qualitative studies	non serious[5]	none	non serious	non serious[6]	none	1084 women of different ethnicities. USA (8), Iran (3), Jordan (1), Black minority ethnic groups in the UK, Greece (1), Western Cape (1), Malaysia (1), Turkey (1), Spain (1), Chile (1), United Arab Emirates (1).	Logistical implications of breast cancer screening, including time and money expenditure, may be burdensome for women who participate in these screening programs.	⊕⊕⊕◯ MODERATE	Azami-Aghdash 2015

[1] Concerns regarding adequacy of information given to participants in order to take an informed decision.

[2] Questionnaires were distributed among adult women in general, rather than women of screening age.

[3] Only limited data are available.

[4] Values of patients who have already received a false positive result were assessed.

[5] The included studies were subject to minor methodological limitations. Authors do not link findings and the studies they were derived from.

[6] Only three of the included studies were conducted in Europe. Authors also acknowledge that some of the review findings were highlighted in <25% of the included studies.

Diagnostic decisions

Quality assessment							Study population and characteristics	Findings	Quality	Studies Contributing to the Review Finding
No. of studies	Study design	Risk of bias/Methodological limitations	Inconsistency/Coherence	Indirectness/Relevance	Imprecision/Adequacy of data	Other considerations				
Anxiety										
1 4	SR of cross sectional studies Cross sectional studies	None	none	none	serious[1]	none	3056 breast cancer patients.	Patients highly disvalue avoidable anxiety.	⊕⊕⊕◯ MODERATE	Fiszer 2014, Brandon 2011, Chicken 2007, Miller 2013, Presutti 2014
Inconvenience										
1	Cross sectional study	None	none	none	serious[1]	none	49 women who underwent both CESM and CEMRI as part of a trial in Australia.	Women highly value comfortable and fast procedure.	⊕⊕⊕◯ MODERATE	Hobbs 2015

[1] Inadequate data.

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	P. 1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	P. 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	P. 3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	P. 3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	P. 3
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	P. 4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	P. 4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	P. 4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	P. 4
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Table 1 P. 15
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	P. 4
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	N/A
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	P. 4

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	P. 4
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	P. 5
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1 p. 15
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	N/A
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Appendix 2
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Appendix 2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	P. 9
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	P. 11
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	P. 9-12
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	P. 13

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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