Cost-effectiveness of digital mammography compared to film mammography in screening of breast cancer: a systematic review

Aziz Rezapour, Hossein Bouzarjomehri, Akhtar Shah-Savandi, Emad Karimianrad, Narges Pirani, Jalal Arabloo, Samira Soleimanpoor, Yasaman Herandi

Health Management and Economics Research Center, Iran University of Medical Sciences, Tehran, Iran

Abstract

Background: Mammography as the best method of diagnosing breast cancer in its early stages has been accepted in many countries. Digital mammography is in development and is used in breast cancer screening in countries such as the United States, however, cost-effectiveness of digital mammography screening (DMS) compared to film mammography screening (FMS) is debatable. This study is designed to systematically review the available evidence in this regard.

Methods: This study is designed as a systematic review using PRISMA guidelines. The search was conducted on October 2019 on the PubMed, Web of Science core collection, Embase, Scopus, Cochrane library and ProQuest databases. All full economic evaluation studies (cost-effectiveness analysis (CEA), cost-utility analysis (CUA), and cost-benefit analysis (CBA)) that assessed DMS compared to FMS are included. The quality of final articles were evaluated by CHEERS checklist and data was collected using a data extraction form. Finally, the data was analyzed by a meta-synthesis method.

Results: Five studies were included. Three of them were conducted in the U.S., one in the Australia, and one the Brazil. Studies show that despite the slight difference in the effectiveness of DMS, its costs increased more. Three studies concluded that age-targeted DMS and FMS might be cost-effective and two concluded biennial DMS might be cost-effective digital strategy, however one study concluded that biennial FMS is still cost-effective.

Conclusion: There is currently little evidence on the cost-effectiveness of DMS over FMS and more evidence is needed, especially in developing countries. While the cost-effectiveness of DMS has not been fully confirmed, manufacturers are developing digital mammography; on the other hand, film mammography is obsoleting. Therefore, the move towards digital mammography, especially in developing countries, should be gradual and targeted.

Keywords: digital mammography, screening, breast cancer, economic evaluation, systematic review

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Introduction

Due to social and industrial changes and epidemiological transition, the pattern of diseases has changed, shifting from infectious diseases to chronic diseases such as cancers¹⁾. Among the cancers, breast cancer is the most common cancer in women and is the leading cause of death in women aged 40 to 45 years. Breast cancer accounts for 32% of all cancers, and in general, 19% of women die from cancer²⁾. The incidence rate of breast cancer is one in nine women in United States, one in twelve in the United Kingdom and one in thirteen in Australia²⁾. According to the Global Burden of Disease study in 2016, annually breast cancer had the highest incidence rate of all cancers in women (1.7 million), accounting for 535,000 deaths and about 15 million

disability-adjusted life years (DALYs). Also, for adults (20 to 39 years old), the most common cancer in the world is breast cancer, and in total, it was the third most common cancer among all cancers³⁾. According to the World Health Organization report, 508,000 women died of breast cancer in 2011, and the number of annually new cases is expected to increase from 10 million to 15 million by 2020⁴⁾.

One of the most effective ways to reduce the risk of breast cancer and increase the life expectancy of patients is early detection of the disease by screening methods. Studies show that early detection will increase the life expectancy of more than 90 percent of cancer patients⁵⁾. Breast cancer can be detected early by regular self-examination or physical examination by a doctor or mid-wife⁶⁾, however, the mammography is considered the best method for screening and diagnosing of breast cancer in early stages in most countries around the world⁷⁾ due to its 80 to 85% sensitivity for diagnosis of breast masses⁸⁾.

As new technologies are changing from analog to digital, mammography is no exception. Digital mam-

Corresponding author: Hossein Bouzarjomehri, Ph.D. Health Management and Economics Research Center, School of Health Management and Information Sciences, Yasemi St, Valiasr St, Vanaq Sq, Tehran, Iran. P.O.Box: 1996713883, E-mail: H.Bouzarjomehri@gmail.com

mography, as an alternative choice to film mammography, has the innate advantage of digital technologies, however its cost-effectiveness for breast cancer screening is still controversial. Different results were observed in studies comparing effectiveness of film mammography with digital mammography. Some studies expressed relatively equal effectiveness for both technologies while some studies have considered digital mammography to be more effective in certain age groups⁹. In Carney and Kerlikowske's study, the sensitivity of digital mammography was significantly higher in women under 50 years old, women with extremely dense breast, women with entirely fatty breast density and pre- or peri-menopausal women, however film mammography had a higher sensitivity in women upper 50 years old^{10, 11}. Similarly, in Pisano study, the sensitivity of digital mammography in screening and diagnosis of breast cancer was significantly higher in women under 50 (78 vs. 51) and had a similar advantage in premenopausal women and women with dense breasts¹². These findings have been confirmed in other studies¹³⁻¹⁵.

Modern technologies have introduced digital mammography devices to global market, which their higher accuracy in diagnosis comes with higher costs. Although there are studies comparing effectiveness or cost-effectiveness of digital mammography versus film mammography in screening of breast cancer, there is no systematic review of cost-effectiveness studies. Therefore, this study is designed to review the evidence on cost-effectiveness of digital mammography screening (DMS) compared to film mammography screening (FMS).

Methods

This systematic review and meta-synthesis assessed the existing evidences until October 2019 using PRISMA guidelines¹⁶. Its protocol is registered at the PROSPERO system under the code number of CRD42019139131¹⁷ and ethical clearance is obtained from the authors institute research ethics committee under the code number of IR.IUMS.REC.1398.388. In order to conduct the systematic review, the structured components of PICOS defined as women prone to breast cancer (population), DMS (intervention), FMS (control), incremental cost-effectiveness (ICER) (outcome) and economic evaluation studies (cost-effectiveness, cost-utility and cost-benefit) (study design).

Search strategy

To find appropriate keywords for search strategy, the basic literatures were reviewed and with help of MeSH database, search strategies were determined. Search strategy components were selected using PICOS. These components for PubMed were contained (A) economic evaluation keywords ("cost-benefit"[Mesh] OR "cost-effectiveness"[TIAB]), (B) mammogra-

phy keywords ("mammography"[Mesh] OR "digital mammograph*"[TIAB]), and (C) breast cancer keywords ("breast neoplasms"[Mesh] OR "breast cancer"[TIAB]). The full search strategy is available at appendix 1.

Five main scientific databases were searched including Web of Sciences, PubMed, Scopus, Embase, Cochrane, and ProQuest. Search results were extracted into EndNote software and duplications were excluded, resulted in 1739 articles.

Inclusion and exclusion criteria

We included all full economic evaluation studies (cost-effectiveness analysis (CEA), cost-utility analysis (CUA), and cost-benefit analysis (CBA)) that assessed digital mammography compared to film mammography in screening of breast cancer. Outcomes were cost per life-years gained or cost per quality-adjusted life years (QALYs) gained or in monetary units or incremental cost-effectiveness ratio (ICER). Exclusion criteria contained studies that report micro economic evaluation (e.g. evaluation of only effectiveness or costs or QALY) and studies in non-English language.

Screening

At this step, according to PRISMA checklist, two researchers screened the studies separately. firstly based on the title of the studies and then based on the abstracts. At this point 51 articles were selected for full text review by two researchers and finally 5 articles were included (Fig. 1).

Quality assessment

In order to evaluate the studies' quality, CHEERS checklist was used which consists of 24 questions for evaluating economic evaluation studies design¹⁸.

Data extraction

In order to prepare data extraction tool, the instrument that introduced in the study of Wijnen et al was used¹⁹. For each included study a sheet was created in Microsoft Excel software containing the studies' information such as first author name, publication year, country, reference year, population, effectiveness criteria, study perspective, type of used model, costs and expenses, cost-effectiveness results, sensitivity analysis methods and results, and final conclusion. Two researchers were responsible for extracting data.

Data analyzing

The final data was analyzed through meta-synthesis methods. In order to prevent bias, the whole process of search to data analysis was carried out by two researchers independently under the supervision of an advisor.

Fig. 1 PRISMA chart

Results

Five papers were selected (Table 1, 2). Three of which were conducted in the U.S.²⁰⁻²², one in Australia¹³, and one in Brazil²³. Quality assessment with CHEERS checklist shows scores of about or over 80% for all of studies and they are of fine quality. Two studies were from the perspective of Society^{13,20}, two from the federal payer^{20,21}, and two from health system^{22,23}. Studies have been published from 2008 to 2015 (Table 1).

Modeling

Three of studies which were conducted in the U.S. had used models from the Cancer Intervention and Surveillance Modeling Network (CISNET)²⁰⁻²². Tosteson et al. employed a discrete-event simulation model as a CISNET²⁴. Stout et al. have used five CISNET models²⁴⁻²⁸. Ravesteyn et al. used two models of MISCANFadia (MIcrosimulation SCreening Analysis—Fatal Diameter) and SPECTRUM (Simulating Population Effects of Cancer Control inTerventions—Race and Understanding Mortality) which were developed independently within the CISNET^{27,28}. Wang et al. used a study based model¹³ and Souza and Polanczyk used the Markov model²³.

Costs and outcomes measures

Studies included fixed, variable and semi-variable costs of DMS and FMS into the analysis for the base year of 2005²⁰, 2007¹³, 2010²², 2011²³, and 2012²¹. For outcomes, three studies used quality adjusted life years gained (QALY)^{20,21,23}, two of them used life years gained (LYG) and death averted or mortality reduction^{21,22}, and one only used the number of additional cancers detected which is an intermediate output¹³.

Compared strategies

Studies compared different strategies and had up to ten strategies for comparison. Three of them compared annual and biennial DMS with FMS²¹⁻²³, three evaluated DMS for populations with dense breast^{13,20,21}, all studies examined age-targeted strategies and one study examined strategies for different American races (black, white and Hispanic)²².

Cost-effectiveness

Studies have reported their results in different ways that makes it hard to aggregate them. Three studies concluded that age-targeted DMS and FMS for older population might be cost-effective^{13,20,22} and two concluded biennial DMS might be cost-effective digital strategy^{21,22}, however one study that conducted in the Brazil conclud-

Table 1 Included Studies

Title	First author	Year	Journal	Country	Perspective	Target population	Study type	Conflict of interests	CHEERS quality assessment score (%)
Transition from film to digital mammography: Impact for breast cancer screening through the national breast and cervical cancer early detection program	Nicolien T. van Ravesteijn	2015	American Journal of Preventive Medicine	U.S	Not mentioned - but it seems to be health system	Women aged 40–64 in 2010	CEA	No	79.54
Benefits, harms, and costs for breast cancer screening after US implementation of digital mammography	Natasha K. Stout	2014	Journal of the National Cancer Institute	U.S	Federal payer	Woman 50–47 y in 2001–2008	CEA, CUA	No	89.13
Is Age-targeted full-field digital mammography screening cost-effective in emerging countries? A micro simulation model	Fabiano Hahn Souza	2013	SpringerPlus	Brazil	Health system	Woman between 40 to 49 years in 2010	CUA	No	93.5
Cost and cost-effectiveness of digital mammography compared with film-screenmammography in Australia	Shuhong Wang	2009	Australian and New Zealand Journal of Public Health	Australia	Society	Woman <50 y Pre- or peri-menopausal women, Women with heterogeneously or extremely dense breasts in 2007	CEA	No	95.65
Cost-effectiveness of digital mammography breast cancer screening	Anna N.A. Tosteson	2008	Annals of internal medicine	U.S	Society and Medicare	Women age 40 years or older in 2000	CUA	No	100

Table 2 Extracted data from studies

First aut., yr (ref.)	Analytic models	Discount rate	Interventions / Strategies	Cost per outcome	Uncertainty/ Sensitivity analysis
Ravesteijn, 2015 (22)	1. MISCAN 2. SPECTRUM	Not mentioned, 2010 US\$	Annual FMS vs 1. Annual DMS with fixed no. of mmg 2. Annual DMS with fixed budget 3. Biennial DMS with fixed budget 4. Biennial DMS for age ≥ 50 with fixed budget	Cost per LYG, US\$: 1. 182,558 to 415,000 (LYG 2%-4% increases and costs 34.0% -34.7% increases) 2. LYG 22%-24% decreases 3. LYG 8%-13% increase 4. LYG 16%-17% increase	Multiple sensitivity analyses
Stout, 2014 (21)	Five CISNET models	3%, 2012 US\$	1. No screening 2. FMS biennial 50 to 74 years 3. DMS biennial 50 to 74 years 4. DMS biennial from ages 40 to 74 years, 5. DMS annual from ages 50 to 74 years, 6. DMS annual from ages 40 to 74 years, 7. DMS annual from ages 40 to 49 years followed by biennial from ages 50 to 74 years, 8. DMS annual from ages 40 to 74 years for those with dense breast tissue and biennial screening otherwise	Cost per QALY's, US\$: 3. 175000 Efficient Digital Strategies: 4. 33 200 to 113 300 8. 59 300 to 264 700 6. 74 400 to 582 000	One-way sensitivity analyses
Souza, 2013 (23)	Markov model	5%, 2010 Brazilian Real (R\$)	1. Usual care 2. Annual FMS 3. Biennial FMS 4. Annual DMS 5. Biennial DMS 6. Annual DMS (<50) and FMS (50–69) 7. Annual DMS (<50) and biennial FMS (50–69)	Cost per QALY's, R\$: 3. 1,509; 2. 13,131; 6. 30,520;	One-way sensitivity analysis
Wang, 2009 (13)	Study base	5%, 2007 Australian Dollars (AU\$)	DMS vs FMS in 1. Woman under the age of 50 years 2. Pre- or peri-menopausal women 3. Women with radiographically dense breasts	Cost per extra cancer detected, AU\$: 1. 10,364 [6,333, 28,500] 2. 8,143 [5,182, 19,000] 3. 10,364 [6,000, 57,000]	One-way sensitivity analyses
Tosteson, 2008 (20)	Validated, discrete-event simulation model as a CISNET	3%, 2005 US\$	Women age >40 y: base case 1. All-film 2. Age-targeted digital 3. Age- and density-targeted digital 4. All-digital Women age >65 y: base case 5. All-film 6. Density-targeted digital 7. All-digital Women age >65 y: alternative case 8. All-film 9. Density-targeted digital 10. All-digital	Cost per QALY, US\$: 1. – 2. 26 500 (21 000–33 000) 3. 84 500 (75 000–93 000) 4. Dominated 5. – 6. 97 000 (77 000–131 000) 7. Dominated 8. – 9. 253 000 (91 000–536 000) 10. Dominated	One-way sensitivity analyses

ed that biennial FMS is still cost-effective²³⁾.

The study of Tosteson et al. shows that lowest ICER level yield from age-targeted DMS which is US\$26500. Based on that, age-targeted DMS is recommended, however the rest of DMS strategies considered not cost-effective²⁰⁾.

Wang et al. concluded that the ICER of DMS compared to FMS in women under the age of 50 and women with heterogeneous breasts was AU\$10,364, and in pre- or postmenopausal women was AU\$8143; however, they recommended DMS for women under the age of 50, and FMS for older women¹³⁾.

Souza and Polanczyk showed that the biennial FMS with ICER of R\$1509 is still cost-effective especially in developing countries. However, due to geographical differences in large countries, the use of DMS as an age-target in areas with a higher incidence of breast cancer (such as southern Brazil) may be recommended²³⁾.

The study of Stout et al. found that biennial DMS was slightly more effective than film (average 1% reduction in mortality and 7% more QALY (equivalent to 2 years)) but also had higher costs (about 11% increase in costs) and its ICER will be US\$175,000. Among the most effective DMS strategies were biennial DMS for 40–74 years old women and DMS for 40–74 years old women with dense breast tissue and biennial DMS for others. The ICER of these strategies varied between the five used models (Table 2). This study shows that changes from film to digital mammography increased costs but have little effects, especially for women aged 40–49²¹⁾.

The findings of study of Ravesteyn et al. estimate that 32,9721 film mammograms were performed in 2010 to prevent 106–136 deaths, and that 1948–2305 years of life were gained. If this number of mammograms were done digitally, it would prevented 111–138 deaths and gained 2034–2345 years of life, which means a 2–4% increase in effectiveness but also higher costs (34–35%). Assuming a fixed budget, by shifting from FMS to DMS, 25–26% less women can receive mammograms. This leads to a 23–24% increase in breast cancer mortality and a 22–24% decrease in LYG. The use of fixed-budget DMS on a biennial basis continues to provide fewer mammography services to women, but the benefits of each mammogram for biennial screening outweigh the annual screening to 8–13% increase. In addition, if biennial screening is restricted to women over the age of 50, LYG is increased by 17–16%. The study concludes that with a fixed budget, fewer women with less LYG may be less likely to be served. Changes in the screening program, including only having biennial screening, increase LYG/screening rates, and can compensate for the potential reduction in LYG when transferring to digital mammography²²⁾.

Sensitivity analysis

Four studies used one-way sensitivity analysis and one

study, used multiple sensitivity analysis^{13, 20-23)}. The results were most sensitive to the costs of DMS²⁰⁻²²⁾, the prevalence of dense breast²⁰⁾, throughput of a mammography system¹³⁾, and opportunistic screening coverage²³⁾. If the cost of DMS is equivalent to FMS, the development of digital mammography will be more cost-effective^{21, 22)}.

Discussion

In Western countries, mammography screening has been set as a standard for early detection of breast cancer. Some studies presented the cost-effectiveness of FMS in Western countries^{20, 29, 30)}, however, its benefits in developing countries remains under question^{31, 32)}. In addition, due to diagnostic value of digital mammography, especially for women of young age and women with high dense breasts³³⁾, it is being developed day by day and is used for breast cancer screening in developed countries such as the U.S.²¹⁾. Zegordi et al carried out a systematic review comparing effectiveness of DMS with FMS, claiming that DMS is more effective, therefore suggested DMS even for developing countries⁹⁾. However, the effectiveness studies did not consider the extra costs of DMS. While digital mammography devices, have proven to be more accurate in diagnosis, they come at higher costs.

Although there are few and heterogeneous studies on cost-effectiveness of DMS compared to FMS, and there is a lack of sufficient data for decision making in many countries, especially developing countries, as a general conclusion from the available studies, the results of this systematic review similarly indicates that like other studies, DMS is more effective; However, despite the slight difference in effectiveness, the additional costs of DMS significantly increase²¹⁾. Still, DMS may be cost-effective in certain cases such as women aged 40–49 years (age-targeted strategies)^{13, 20)}, regions where breast cancer is more common²³⁾, biennial strategies and women with extremely dense breasts²²⁾. Although, the increase of false positive diagnoses in DMS results in reduced effectiveness and subsequently DMS may not be cost effective anymore²¹⁾. In case of misdiagnosis, failing to account the QALY lost and future additional costs, is one of the limitations of found studies and making more accurate judgments is not possible. These unwanted and hidden costs must be considered before using new technologies.

Digital mammography as an alternative to film mammography, despite having hidden costs, also has the innate advantages of digital technologies, hence its overt and covert advantages must be taken into account. In addition, the film mammography devices are no longer technically developed by manufacturers and will become obsolete over time³⁴⁾. Many of the digital mammography advantages cannot be measured in economic evaluation studies. First, due to reduced supports for film mammography equipment, the costs of film mammography may

increase over time in the near future. Second, although the average time spend in digital mammography process is longer than film mammography, the access to digital images through the PACS system in different medical centers will increase, which leads to minimization of traveling time; therefore, flexibility and efficiency will increase. In addition, by development of tele-mammography, the cost of film transferring to diagnostic centers is reduced. Third, technological advances and post-process imaging ability of digital mammography may be able to reduce the plausible need for repeating the mammography³⁵⁾. This can lead to economic savings especially for rural women and people who are distant from imaging center. Finally, digital mammography may reduce absorbed dose for patients. This matter can even benefit the health and safety of healthcare staff by making their job easier and less exposed to hazardous chemicals.

At last, it should be mentioned that four out of five studies have been conducted in developed countries, which three of them have been in the United States. However, these studies have not confirmed the cost-effectiveness of annual DMS for all age groups, rather they considered DMS to be cost-effective for extremely dense breasts, for specific age groups or for biennial strategies and the cost-effectiveness of DMS is still questionable for developed countries like the United States. The only study conducted in developing countries, concluded that DMS is not cost-effective. Therefore, although developed countries are moving towards digital mammography, developing countries should be more careful in this transition. Developing countries, due to their weak regulations, may be more vulnerable to the marketing of medical equipment companies and they should be more careful in applying new technologies, as due to the inevitable risk of induced demand, limiting access for new technologies to certain age groups or certain physical conditions (such as breast density) could be struggling²¹⁾. Accordingly, the whole costs and advantages of digital mammography should also be considered, especially since the costs of digital mammography will decrease over time³⁶⁻³⁸⁾. Therefore, moving towards digital mammography, particularly in developing countries, should be gradual.

Conclusion

In regard to making an evidence-based decision on breast cancer screening by mammography, there is a need for more specific studies especially for developing countries. Existing studies show that DMS might be cost-effective under certain conditions such as biennial or age-targeted DMS or DMS for women with dense breast or in regions with high incidence of breast cancer. In other conditions such as annual screening and older women the FMS might be more cost-effective. It is considerable that four out of five studies were from developed coun-

tries and the only study that evaluated DMS in a developing country concluded that FMS is more cost-effective. Whilst this study did not confirm the DMS for all conditions, it shows that moving towards digital technologies may be inevitable in future, therefore it is recommended to apply digital mammography gradually.

Limitations:

Although the reviewed studies were of high quality, it must be noted that this study confronted with number of limitations including lack of studies particularly in developing countries. Existing studies did not covered all the costs and advantages of digital mammography. Therefore, further studies in this field seems to be necessary in developing countries.

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Conflict of interest:

The Authors declare that they have no conflict of interest.

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