RESEARCH ARTICLE

Is Mammography for Breast Cancer Screening Cost-Effective in Both Western and Asian Countries?: Results of a Systematic Review

Ki-Bong Yoo[1,2], Jeoung A Kwon[1,2], Eun Cho[3], Moon Hae Kang[1,2], Jung-Mo Nam[4], Kui Son Choi[5], Eun Kyung Kim[6], Yun Jeong Choi[7], Eun-Cheol Park[2,4]**

Abstract

<u>Background</u>: Mammography is considered the gold standard of breast cancer mass screening and many countries have implemented this as an established breast cancer screening strategy. However, although the incidence of breast cancer and racial characteristics are different between Western and Asian countries, many Asian countries adopted mammography for mass screening. Therefore, the objective of this research was to determine whether mammography mass screening is cost-effective for both Western and Asian countries. <u>Materials and Methods</u>: A systematic review was performed of 17 national mammography cost-effectiveness data sets. Per capita gross domestic product (GDP), breast cancer incidence rate, and the most optimal cost-effectiveness results [cost per life year saved (LYS)] of a mammography screening strategy for each data set were extracted. The CE/per capita GDP ratio is used to compare the cost-effectiveness of mammography by countries. Non-parametric regression was used to find a cut-off point which indicated the breast cancer incidence rate boundary line determining whether mammography screening is cost-effective or not. <u>Results:</u> We found that the cost-effective cut-off point of breast cancer incidence rate was 45.04; it exactly divided countries into Western and Asian countries (p<0.0014). <u>Conclusions:</u> Mammography screening is cost-effective in most of Western countries, but not in Asian countries. The reason for this result may be the issues of incidence rate or racial characteristics, such as dense breast tissue. The results indicate that mammography screening should be adopted prudently in Asian countries and other countries with low incidence rates.

Keywords: Breast cancer - cost-effectiveness - mammography - mass screening - systematic review - Asia

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Introduction

Breast cancer is not only the most common cancer among women throughout the world in developing and developed regions, but is also the most frequent cause of cancer death in women in developing and developed regions (Ferlay et al., 2010). A key determinant of breast cancer outcome is to detect breast cancer at the early stages (Yip et al., 2008). Early detection leads to a lower breast cancer mortality rate. Thus, many countries – at least 22 – have established population-based breast screening programs using mammography (Shapiro et al., 1998).

Many research publications demonstrate that mammography lowers breast cancer mortality by 25-30% (Shapiro et al., 1998). Currently, mammography is the gold standard for early screening of breast cancer (Yip et al., 2008) because mammography has proven successful in early detection and good prognosis for breast cancers across the range of ages and mutation status (Maurice et al., 2012). As such, some Asian countries, including Korea (Kim et al., 2011), Japan (Kikuchi et al., 2012), China (Huang et al., 2001; Ma et al., 2012), and Taiwan (Huang et al., 2001; Leong et al., 2010), as well as many Western countries, including the US (White et al., 1990; USPSTF, 2009), Canada (Tonelli et al., 2011), the UK (Parkin et al., 2005; Evans et al., 2012), Norway (Lynge et al., 2011; Hofvind et al., 2012; Olsen et al., 2013), and The Netherlands (de Koning et al., 1995; Fracheboud et al., 1998), are implementing mammography for breast cancer screening and they expect lower mortality as well as cost-effectiveness, but the cost-effectiveness was unclear (Kikuchi et al., 2012).

The factors of age, breast tissue density, history of breast biopsy, family history of breast cancer, and

*[1]Department of Public Health, Graduate School, [7]School of Economics, Yonsei University, [2]Institute of Health Services Research, [4]Department of Preventive Medicine, [6]Department of Radiology, Research Institute of Radiological Science, Yonsei University College of Medicine, [3]College of Pharmacy, Sookmyung Women's University, [5]National Cancer Control Institute, National Cancer Center, Republic of Korea *For correspondence: ecpark@yuhs.ac*

screening interval must be considered for a mammography screening strategy (Schousboe et al., 2011). However, Mammography for breast cancer mass screening has been applied around the world even though there is much variability between Asian and Western countries. An Asian mammography screening program should consider cultural, and educational barriers prior to developing a screening program for breast cancer (Green and Raina, 2008).

The incidence rates of breast cancer in women with age-adjusted as reported by the OECD in 2008 showed a wide range, with The Netherlands having the highest rate at 98.5 per 100,000 people and China having the lowest at 21.6 per 100,000 people (Ferlay et al., 2010). While the incidence rates of breast cancer in North America and the European Union are 76 and 77.1 per 100,000 people, respectively, incidence rates in Asian countries is 26 per 100,000 people (Ferlay et al., 2010). In addition, because a larger proportion of Asian women have dense breast tissue compared to Western women (El-Bastawissi et al., 2001), the accuracy of mammography could be reduced. The risk for breast cancer is four to six times higher in women with dense breasts. Breast density may also decrease the sensitivity, specificity and increase both false-positive and false-negative mammography. Radiographically dense breast tissue may also obscure tumors, which increases the difficulty of detecting breast cancer. In addition, dense breast tissue may mimic breast cancer on mammography, which increases recall rates, reduces specificity, and compromises the benefit of screening in women with dense breasts such as women who use HRT or who are premenopausal (Carney et al., 2003).

Because the incidence rates of breast cancer and dense breast rate are different for each country, especially Western and Asian countries, there is a need to review the cost-effectiveness of mammography screening for breast cancer. Therefore, this study aims to compare the cost-effectiveness of mammography screening in different incidence rate of Western and Asian countries by systematic review. The CE/per capita GDP ratio is used to compare the cost-effectiveness of mammography by countries. It is calculated by (Cost per LYS of each of the screening strategies/per capita GDP of the corresponding country). The CE/per capita GDP ratio is proposed by the WHO Commission on Macroeconomics and Health (WHO, 2001).

Materials and Methods

Search strategy

This study is a systematic review. Ovid-Medline, Ovid-Embase, and Cochrane Library database from 1974 to June 25, 2012 were used.

Advanced search and "Exploding" a search term for retrieving all records with not only the exact term, but also those in the hierarchy of the medical subject headings (MESH) were used. The search formula was: (breast cancer.mp. OR exp breast cancer/OR exp breast neoplasms OR mass screening.mp. OR exp mass screening/) AND (exp mammography/OR exp digital mammography/OR mammography.mp.) AND (cost-effectiveness.mp. OR exp cost-effectiveness analysis/). Additionally, references of articles were searched and a hand search was conducted.

Selection criteria

Original articles published in English regarding breast cancer, mammography screening, and cost-effectiveness analysis of a screening strategy compared with no screening are included. Cost per life year saved (LYS), cost per quality adjusted life year (QALY), and cost per disability adjusted life year (DALY) averted were included in the scope of cost-effectiveness analysis. Additionally, this research included a result from a national report which is supported by the National R&D Program for Cancer Control, Ministry of Health and Welfare, Republic of Korea, which also supports the research presented here.

Extracted information

Two researchers reviewed the abstract first in accordance with the inclusion criteria independently and reviewed the full selected articles. Extracted information was study objective, type of model, cost inclusion, country, study period, reference year of incidence, reference year of cost, screening strategy (age, interval), and cost per LYS. If the cost per LYS was not used, cost per DALY averted or cost per QALY were included. Cost-effectiveness analysis between mammography and no screening was selected. If the results of the cost-effectiveness analysis were divided into sub-groups for each screening interval and age group, the most optimal cost-effectiveness result of the article was selected for statistical analysis.

Cost per LYS was converted into US dollars on the reference year of cost of each article. Per capita gross domestic product (GDP) corresponded with the study country, and the cost reference year of each article was retrieved from the World Bank to adjust for each countries characteristics (The World Bank, 2013). In the guidelines proposed by the WHO Commission on Macroeconomics and Health (WHO, 2001), the CE (cost-effectiveness)/per capita GDP ratio is defined as the ratio of cost per LYS and per capita GDP. This ratio was computed to determine cost-effectiveness of mammography and to compare this value with each country's cost effectiveness result while also considering time-period effects. The discount rate was not considered in calculating the cost effectiveness, because this study calculated each country's cost effectiveness with the ratio.

Breast cancer incidence rates were retrieved from GLOBOCAN 2008 and IARC CI5 plus, which includes data up to the year 2002 (Ferlay et al., 2010; IARC, 2011). Each article's incidence rate was selected by reference year of incidence and mean of incidence rate during the study period was used as an incidence rate. For the period of 2003-2007, for which there is no data in GLOBOCAN or CI5 plus, the incidence rate was projected by simple interpolation.

Quality criteria

For assessment of article quality, two researchers independently used the Quality of Health Economic Studies (QHES) instrument and came to an agreement after having assessed the tool (Ofman et al., 2003) (Table

1). The QHES tool was composed of a total of 16 criteria, with each of the criteria to be answered with either "yes" or "no." Points ranging from 1 to 9 were allocated for each of the items. Full points were given for each item if the answer was "yes" and 0 points were given if the answer was "no." Total score was 100 points.

Statistical analysis

After collecting the cost per LYS data from selected articles, statistical analyses were conducted to find out the cut-off point of incidence to divide countries based on whether the mammography mass screening is cost-effective or not.

The analysis was determined with the weighted value of the quality assessment on the CE/per capita GDP ratio as the dependent variable. The QHES results by each study were various, so the weighted ratio was used to adjust for the quality of each study. We have included both the unweighted CE/per capita GDP ratio and the weighted one in the analysis model. Non-parametric statistical methods were used because the CE/per capita GDP ratio data are skewed and the number of articles is small.

Non-parametric regression (GAM procedure) that fits generalized additive models was used to determine incidence rate cut-off points, which indicate the CE/per capita GDP ratio is 1. This is similar to normal regression but can be used when the dependent variable is not normally distributed or the data is not the assumed linear (Hardle, 1990). The dependent variable is the logged CE/per capita GDP and the independent variable is the incidence rate.

Differences in the CE/per capita GDP ratios between the two groups were confirmed through Wilcoxon Rank Sum Test by dividing the subject into two groups on the basis of the deduced cut-off point by non-parametric regression. In the case of district, differences in the CE/per capita GDP ratios were confirmed through Kruskal-Wallis analysis by dividing the district into three groups, namely, Asia, Europe, and the US. The statistical test was performed using SAS, version 9.2.

Results

Search results

A total of 907 papers were searched, and among these, abstracts of 677 papers, after having excluded 230 repetitive papers based on a selective withdrawal standard, were reviewed independently by two researchers. Three overseas papers were additionally selected through a hand-search, along with one article from Korea that was funded by the National R&D Program for Cancer Control, Ministry of Health and Welfare in the Republic of Korea. A total of 16 papers were selected and 17 national data sets extracted from the selected papers (Figure 1). Full articles of the selected studies were independently reviewed by two researchers. The reasons for excluding the remaining articles were: study type other than a cost-effectiveness study, no comparison with a no-screening test, and duplicate publication.

Mammography cost-effectiveness literature review

Results of the literature review on mammography cost-effectiveness are summarized in Table 2. The total number of selected studies was 16 with a total of 17 national data sets deduced from the studies, including 5 from the US, 7 from Asian countries, and 6 from the European Union.

Each study period among each study was defined as the duration of simulation or data used. The reference year of incidence indicates the year of incidence data in each study. The reference year of cost indicates the year of cost data in each study.

Among 16 studies, 11 studies (de Koning et al., 1991; Garuz et al., 1997; Van der Maas et al., 1989; Rosenquist and Lindfors, 1998; Stout et al., 2006; Woo et al., 2007; Okonkwo et al., 2008; de Gelder et al., 2009; Wong et al., 2010; Carles et al., 2011; Schousboe et al., 2011)

Table 1. The Quality of Health Economic Studies (QHES) Instrument

Questions	Points	Yes	No
1. Was the study objective presented in a clear, specific, and measurable manner?	7		
2. Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4		
3. Were variable estimates used in the analysis from the best available source (i.e., randomized control trial - best, expert opinion - worst)?	8		
4. If estimates came from a subgroup analysis, were the groups prespecified at the beginning of the study?	1		
5. Was uncertainty handled by (1) statistical analysis to address random events, (2) sensitivity analysis to cover a range of assumptions?	9		
6. Was incremental analysis performed between alternatives for resources and costs?	6		
7. Was the methodology for data abstraction (including the value of health states and other benefits) stated?	5		
8. Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3% to 5%) and justification given for the discount rate?	7		
9. Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8		
10. Were the primary outcome measure(s) for the economic evaluation clearly stated and did they include the major short-term was justification given for the measures/scales used?	6		
11. Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7		
12. Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear, transparent manner?	8		
13. Were the choice of economic model, main assumptions, and limitations of the study stated and justified?	7		
14. Did the author(s) explicitly discuss direction and magnitude of potential biases?	6		
15. Were the conclusions/recommendations of the study justified and based on the study results?	8		
16. Was there a statement disclosing the source of funding for the study?	3		
Total Points	100		

Table 2. Characteristics of All Identified Studies and Data of Mammography Cost-Effectiveness Analysis

Author, publication year	Objective	Type of model	Cost inclusion	Study period	Reference year of incidence†	Reference year of cost	Age/ interval (y)	Cost (US$) per LYS‡ or QALY§	QHES¶
US Rosenquist & Lindfors, 1998	To re-appraise the cost-effectiveness of mammography screening including a 40-49 years of age group.	Markov	Direct	1975-1988	1975-1988	1984	40-79/1 40-79/1,50-79/1,40-49/2 40-64/1,65-79/2 40-49/1,50-79/2	18800 18200 17700 16100	63
US Stout et al., 2006	To compare the cost-effectiveness of current national breast cancer screening and alternatives.	Discrete event simulation	Direct	1990-2000	1975-2000	2000	55-70/5,55-70/3,50-75/3, 45-75/3,50-75/2,45-75/2 40-80/2,45-75/1,45-80/1, 40-80/1	27000, 28000, 31000, 31000, 34000, 34000 47000, 49000, 53000, 58000	82
China Woo et al., 2007	To estimate the cost-effectiveness of mammography by age, breast tissue density, history of breast biopsy, family history of breast cancer, and screening interval.	Markov	Direct	1995-2006 Following lifetime	1975-2005	2008	40-49/3-4,50-59/3-4 60-69/3-4,70-79/3-4	130771, 37101 17062, 10603	94
China Woo et al., 2007	To develop a policy- relevant generalized cost-effectiveness model of population-based cancer screening for Chinese women.	Decision analysis	Direct and indirect	2003/2004	2003-2004	2001	50-74/2,40-74/2 50-74/1,40-74/1	90771, 107310 321608, 385092	93
Chin Wong et al., 2010	To assess the cost-effectiveness of mammography screening between Hong Kong and the US.	Markov	Direct and indirect	2005-2007	2005-2007	2005	50-69/2,50-79/2 40-69/2,40-79/2	Dominated,Dominated 64400,206300	84
US Wong et al., 2010				2005-2007	2005-2007	2005	50-69/2,50-79/2,40-69/2,40-79/2	37000, Dominated, 47800, 80400	
UK Knox, 1988	To estimate the cost-effectiveness of national mammography screening.	Computer modeling process	Direct and indirect	1975	1975	1985-1986	50-65/3	3730	78
The Netherlands Van der Maas et al., 1989	To compare the cost-effectiveness of breast cancer screening strategies.	MISCAN	Direct	1988-2015	1986	1986	52-68/4,51-69/2 50-69/4/3,50-69/1	4050, 4850 5900, 6840	84
Japan Okubo et al., 1991	To compare the cost-effectiveness of breast cancer screening with mammography or physical examination.	Mathematical	Direct	1989, Target on 30 years old, following 50 years.	1987	1986	30-80/1	14300	90
Spain Garuz et al., 1997	To estimate the cost-effectiveness of national mammography screening.	Decision analysis	Direct	1991-2015	1991	1993	50-65/2,45-65/2	8833, 11374	93
Spain Carles et al., 2011	To compare and analyze the cost-effectiveness of different mammographic screening strategies.	Lee and Zelen stochastic	Direct	1975-2005	1980-2002	2005	50-69/2,45-65/2,45-69/1, 40-69/1,40-74/1,40-79/1	4691, 9555, 16041, 22020, 33256, 614811	88
Finland Leivo et al., 1999	To estimate the cost-effectiveness of national mammography screening.	Decision analysis	Direct and indirect	1987-2020	1992	1995	50-84/2	18955	78
Norway Norum, 1999	To estimate the cost-effectiveness of national mammography screening.	Decision analysis	Direct and indirect	1996	1996	1996	50-69/2	14554	79
Switzerland de Gelder et al., 2009	To compare the cost-effectiveness of various mammography screening strategies in Switzerland.	MISCAN	Direct	1999-2020	1974-1985	2007.6	50-69/2,50-69/2,50-69/2, 50-69/2,50-69/2/1	31638, 31732, 15468, 19492, 34375	87
The Netherlands de Koning et al., 1991	To estimate the cost-effectiveness of national mammography screening.	MISCAN	Direct and indirect	1990-2017	1989	1985-1990	50-70/2, 40-70/2,50-70/1.3, 50-75/2,50-65/3	3825, 5385, 4670, 4100, 3235	77
South Korea Kang et al., 2013	To estimate the cost-effectiveness of national mammography screening.	Decision analysis	Direct and indirect	2002	2008	2009	40-/2	29964	80
India Okonkwo et al., 2008	Estimates of the cost-effectiveness of feasible breast cancer screening policies in India.	MISCAN	Direct	2000	2000	2001	40/Once, 50/Once 50-70/2,40-60/2	1634, 6496 3308, 3468	82

†Mean of incidence during reference year

analyzed the various range of the age groups and intervals of scenarios. The other 5 studies (Knox, 1988; Okubo et al., 1991; Leivo et al., 1999; Norum, 1999; Kang et al., 2013) analyzed a single screening strategy. Research on the cost-effectiveness of a single screening strategy, with the exception of Japan (Okubo et al., 1991), analyzed the mammography screening strategy that was being implemented in the corresponding country at that time.

In Schousboe et al.'s (2011) study, the cost per LYS was reduced even further as age increased under the same intervals. According to Stout et al. (2006), the cost per LYS decreased as the screening interval increased when compared with the cost per LYS of screening intervals of 1, 2, and 3 years for the age group of 45-75 years. Woo et al. (2007) illustrated that the cost per LYS decreased when the screening interval was increased. The same phenomenon was found in other studies (Van der Maas et al., 1989; de Koning et al., 1991; Carles et al., 2011). In addition, the cost per LYS decreased when the screening age group was reduced from 40~74 to 50~74 under the same screening interval. This was found to be the case in Garuz et al. (1997), de Koning et al. (1991), and Okonkwo et al. (2008) studies. In the research by Wong et al. (2010), when the US was compared with China, there were differences in the cost-effectiveness under the same screening interval and screening age group.

Research by de Gelder et al. (2009) sought to find an appropriate mammography screening strategy by combining the opportunistic screening and organized screening of mammography. In Switzerland, opportunistic screening and organized screening are being combined for application on mammography for each of the cantons. Rosenquist et al. (1998) sought to re-appraise the cost-effectiveness of mammography screening in the 40-49 years of age group.

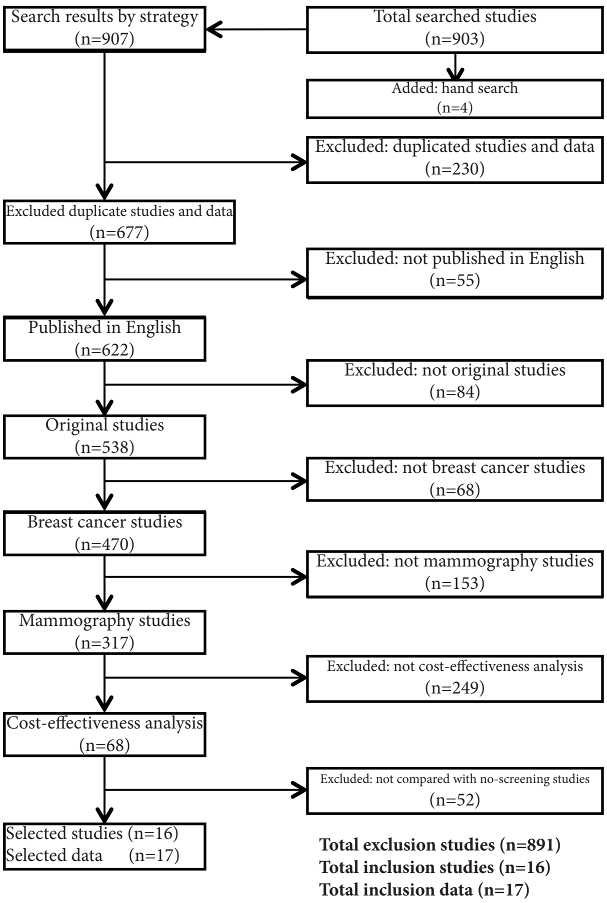

Figure 1. Summary of the Literature Search

Quality criteria

Overall average quality assessment score was 82.1. For questions 1, 8, 10, and 15, the proportion of "yes" as the answer was 100% in all studies. The question with the lowest proportion of "yes" answers was question 11, at 11.8%. In the majority of the literature, it was found that aspects on the health outcome following mammography are insufficient. Questions 6 and 7 had the second lowest "yes" answers, at 58.8%. Question 6 was on the incremental analysis performed between alternatives for resources, while 7 studies did not carry out studies on these aspects and 7 studies did not mention data abstraction, which is question 7.

Incidence rate cut-off point to determine cost-effectiveness of mammography

Incidence rates and mortality rate of breast cancer for each study were retrieved from CI5 plus and GLOBOCAN

Table 3. Incidence Rate, Mortality Rate of Breast Cancer and Per-Capita GDP for Each Study

Country	References	Incidence rate*	Mortality rate*	Per-capita GDP (US$) (a)	Cost (US$) per LYS or QALY (b)	CE/per capita GDP ratio (b/a)	Logged CE/per capita GDP ratio predictions**
India	Okonkwo et al., 2008	26.1	11.1	460	3,308	7.19	0.46
Japan	Okubo et al., 1991	26.2	6	16,882	14,300	0.85	0.50
China	Wong et al., 2010	28.5	5.8	1,731	64,400	37.20	1.42
China	Woo et al., 2007	35.8	5.9	1,042	90,771	87.10	1.69
South Korea	Kang et al., 2013	38.9	5	16,959	29,964	1.77	0.50
Spain	Carles et al., 2011	53.6	15.8	26,056	4,691	0.18	-0.69
UK	Knox, 1988	55.4	27.4	10,064	3,730	0.37	-0.51
Spain	Garuz et al., 1997	62	17.3	13,009	8,833	0.68	-0.15
Finland	Leivo et al., 1999	70.8	16.6	25,609	18,955	0.74	-0.29
The Netherlands	Van der Maas et al., 1989	72.1	26.4	12,768	4,050	0.32	-0.41
Norway	Norum, 1999	72.6	19.7	36,555	14,554	0.40	-0.45
The Netherlands	de Koning et al., 1991	74.2	27.1	16,116	3,235	0.20	-0.51
Switzerland	de Gelder et al., 2009	75.7	24.6	57,490	15,468	0.27	-0.43
US	Rosenquist and Lindfors, 1998	77.4	22	16,539	16,100	0.97	-0.25
US	Woo et al., 2007	81.2	15.3	42,516	37,000	0.87	-0.05
US	Stout et al., 2006	84	21	35,082	27,000	0.77	-0.04
US	Schousboe et al., 2011	84.1	20.1	46,760	48,884	1.05	-0.04

*Age-standardized rates per 100,000 females. **Results from nonparametric regression test. Model significance : p<0.001, DF=7.0

based on the each study's reference year (Table 3). Per capita GDP was found through the World Bank on the basis of the reference year of cost of each study. The most cost-effective values in each of the studies were selected as the representative values for cost per LYS or QALY. In addition, the CE/per capita GDP ratio was computed by dividing cost per LYS or QALY by per capita GDP. In the case of research by Schousboe et al. (2011), average cost per LYS of all screening strategies was used as a representative value, because the result was for the same screening strategy.

We displayed the result of execution of non-parametric regression to find the cut-off points of incidence rate in Table 3. Logged CE/per capita GDP ratio predictions were generated by non-parametric regression. The value over 0 means that the CE/per capita GDP ratio is more than 1, it is inefficient. The predicted values were changed from positive to negative number between South Korea to Spain. As our calculation, incidence rate cut-off was 45.04 per 100,000 women with age-adjusted at the point where the CE/per capita GDP ratio=1.

The difference between the two groups divided by the calculated cut-off=45.04 was analyzed by Wilcoxon Rank Sum Test. With a p-value of 0.0003, statistically significant results were obtained (Table 4). The average CE/per capita GDP ratios of the two groups were 8.10 and 0.51, thereby indicating a difference between the two groups. The countries that were on the borderline were Korea and Spain, which were categorized into Asian and Western countries, respectively (Figure 2). There were the same statistical results between the weighted p values and non-weighted p values. When the countries were divided into three groups, namely, Asia, the US, and Europe, the differences between the Europe-Asia, Europe-US, and Asia-US groups were significant.

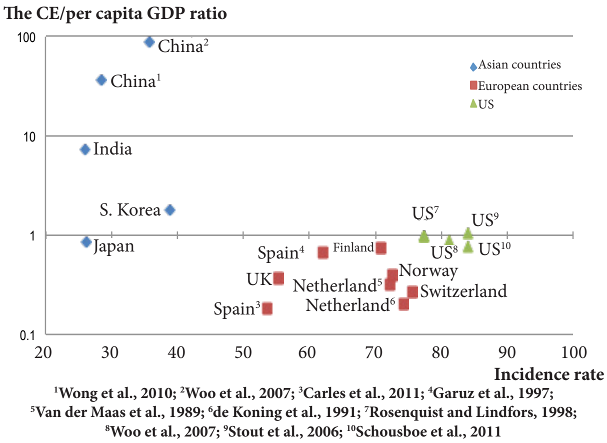

Figure 2. The CE Per Capita GDP Ratio by Incidence Rate

Table 4. Influence Factors of Cost-Effectiveness Cut-Off Point by Groups

	No. of studies	Incidence rate‡	Average CE/per capita GDP ratio†	p value (weighted)
Incidence rate†				0.001 (<0.001)
<45.04	5	30.7	8.1	
≥45.04	12	71.2	0.48	
Countries				<0.001 (<0.001)
Asia	5	30.5	8.1	Europe-Asia*
Europe	8	66.5	0.35	Europe-US*
US	4	81.6	0.91	Asia-US*

* $p<0.05$. †Cut-off point by non-parametric regression. ‡Geometric average

Discussion

In this study, studies on the cost-effectiveness of mammography screening for the general population were reviewed systematically, and the differences in the cost-effectiveness of mammography screening between Western and Asian countries were also examined.

Sixteen studies were selected and the number of countries included in the analysis was 11. The quality of the study was assessed using QHES. QHES is useful for this study because it was developed to evaluate three main types of health economic analysis; cost-minimization, cost-effectiveness, and cost-utility. The QHES tool has been formally validated and shown to be simple, consistent, and valid for measuring cost-effectiveness studies (Peterson et al., 2009). In general, a score of more than 70 is determined to be the cut-off for a "good-quality study" (Peterson et al., 2009). In this study, the average QHES of the literature was 82.1, and most of the studies can be considered good quality with QHES scores of more than 70.

To examine the differences in cost-effectiveness, a comparison was made using the CE/per capita GDP ratio. If the CE/per capita GDP ratio is more than 1, then mammography screening can be deemed to be inefficient because the cost per LYS exceeds the per capita GDP (WHO, 2001; Okonkwo et al., 2008). That is, it can be said to be inefficient if the cost of saving one person for a period of 1 year is more than the total value a person generates in a year. The advantage of this method is that the differences for each year and the cost of goods can be adjusted because the computation is made in the form of a CE/per capita GDP ratio between per capita GDP and cost per LYS for the corresponding year, regardless of the diversity year for per capita GDP and cost per LYS.

Table 3 illustrates that it is not cost-effective in most Asian countries (Korea, China, and India) with the CE/per capita GDP ratio of more than 1. In contrast, it is cost-effective in Western countries (the US, Spain, Switzerland, The Netherlands, the UK, Norway, and Finland), with the CE/per capita GDP ratio of less than 1. As an exception, Japan had the CE/per capita GDP ratio of approximately 0.85 in contrast to the other Asian countries. The incidence rate of breast cancer in Japan is rapidly increasing and already has the highest incidence rate among all female cancers (Yip et al., 2008). It can be presumed that Japan is in a situation similar to Western countries such as the US, Norway, and the Netherlands. In the case of the US (Schousboe et al., 2011), the CE/per capita GDP ratio was computed to be 1.05 in a 2011 study. It can be interpreted that the cost per LYS of mammography in the US in comparison to the per capita GDP is higher than other countries. This is because the US population is consisted of more complex races; therefore, dense breast rate can be higher than other western countries. Also, the total medical cost of population in the US is relatively higher than other western countries.

As illustrated in Table 4, when the countries are divided into two groups, one including India (Okonkwo et al., 2008), Japan (Okubo et al., 1991), China (Woo et al., 2007; Wong et al., 2010), and Korea (Kang et al., 2013), and the other including the UK (Knox, 1988), Spain (Garuz et al., 1997; Carles et al., 2011), Finland (Leivo et al., 1999), The Netherlands (Leivo et al., 1999), Norway (Norum, 1999), Switzerland (de Gelder et al., 2009), and the US (Lindfors and Rosenquist, 1995; Rosenquist and Lindfors, 1998; Stout et al., 2006; Wong et al., 2010; Schousboe et al., 2011) on the basis of the cut-off point of 45.04 for the incidence rates, there was a statistically significant difference in the CE/per capita GDP ratios, and the two groups are definitely divided into Asian and Western countries. This illustrates that there is difference in the cost-effectiveness of breast cancer mammography screening between Asian countries such as India, Japan, China, and Korea with low incidence rates, and Western countries such as the UK, Spain, Finland, The Netherlands, Norway, Switzerland, and the US with relatively higher incidence rates. These differences emphasize the need for consideration of the incidence rate at the time of application of mammography screening. When the incidence rate of breast cancer is high, breast cancer is more likely to be detected by mammography; therefore, the more people can save life years compared to low incidence rates of breast cancer. If the cost of the mammography is the same, the cost per LYS decreases in countries with a high incidence rate of breast cancer.

Such difference in the CE/per capita GDP ratios between Western and Asian countries can be deemed to be the result in the differences in incidence rates and breast tissue density. Although there is an increasing trend of incidence rates of breast cancer in both Asian and Western countries, incidence rates in Western countries are fundamentally higher than those of Asian countries (Leong et al., 2010). There may be a difference in the appearance of incidences of breast cancer between Western and Asian countries due to racial characteristics, geographic variation, racial/ethnic background, genetic variation, lifestyle, environmental factors, socioeconomic status, the presence of known risk factors, use of screening mammography, stage of disease at diagnosis, and the availability of appropriate care (Hortobagyi et al., 2005). For example, breast cancer in China showed more aggressive behavior than in Western countries – more invasive ductal carcinoma with larger tumor size, later stage, lower estrogen receptor and progesterone receptor expression, and higher human epidermal growth factor receptor 2 over expression than in Western countries (Zheng et al., 2012).

Differences of cost-effectiveness of breast cancer mammography between Asian and Western countries include the issue of dense breast tissue. The probability that Asian women have dense breast tissue is 2.1 times that of Caucasian women, and, when compared with other races, the ratio of dense breast tissue in Asian women was the highest (El-Bastawissi et al., 2001). Breast density may also decrease the sensitivity and, thus, the accuracy of mammography. The dense breast tissue appears white on a mammogram. So it can be difficult to recognize whether the white shadow is tumor or not. It increases the difficulty of detecting breast cancer (Graham-Rowe, 2012). The risk for breast cancer is four to six times higher in women with dense breasts. Therefore, dense breast tissue may increase recall rates, reduce specificity and compromises the benefits of screening in women with dense breasts such as women who use HRT or who are premenopausal (Carney et al., 2003). As a result, the decreased accuracy of mammography leads to an increase in the risk of a false-positive result of breast cancer (Ohuchi et al., 2009; Graham-Rowe, 2012). Therefore, there was an opinion in preceding research that the application of magnetic resonance imaging or ultrasonography should be recommended for Asians even though it is not yet included in the guidelines for all Asia countries (Ohuchi et al., 2009; Leung et al., 2010).

Some limitations are in this study. The total number of selected studies was 16 with a total of 17 national data sets deduced from the studies. The result should be interpreted carefully, because the small number of studies is included in final analysis. There is the measurement limitation. The used cost-effectiveness results were diverse. When the cost per LYS was not available, cost per QALY or cost per DALY averted were included. We could consider more confounders such as adjusting the various intervals, age groups and cost-effectiveness model. Even though the data source is the same, the results can vary by each simulation model (Mandelblatt et al., 2009). In addition, even if policymakers measure the value of human life in dollars to simplify the situation, there are moral and ethical issues around measuring the value of human life in dollars. The quality of mammography can also vary by country. However, the sensitivity and specificity of each study's mammography were not adjusted because of a lack of this information.

This study compared the cost-effectiveness of mammography in Western and Asian countries for breast cancer screening by incidence rates. The results show that mammography mass screening is not cost-effective in Asian countries, unlike Western countries, due to breast cancer incidence rate and racial characteristics issues. The countries that have a low breast cancer incidence rate, such as Asian countries, should act prudently when implementing mammography as the reference test targeting the general population. Other screening methods such as clinical breast examination could be a possible alternative.

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