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Cost-Effectiveness Analysis of a Quality-Controlled Mammography Screening Program from the Swiss Statutory Health-Care Perspective: Quantitative Assessment of the Most Influential Factors

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ABSTRACT

Objectives: Quality-controlled mammography screening programs (MSP) have led to a reduction in breast cancer mortality. The purpose of this economic analysis was to assess the cost-effectiveness of MSP compared with an established opportunistic screening strategy (OS) in Switzerland, to identify the major factors influencing the economic outcome.

Methods: Using cancer registries and clinical data, a Markov-based decision model was designed to compare MSP with OS in the Swiss female population, considering the main screening-specific performance parameters.

Results: The discounted incremental life expectancy amounted to 0.022 life-years gained in favor of MSP when screening started at age 40 years and decreased to 0.008 years at the age of 70 years (number needed to screen to avoid one death over 10 years ranged from 10,000 to 2439 women depending on the baseline age). The total discounted life-time cost for screening, treatment at the baseline age of 40 years amounted in MSP to $4366 (OS: $2802) and decreased with the baseline age of 70 years to $2412 (OS: $1446). The discounted incremental cost-effectiveness ratio comparing MSP versus OS ranged from $73,018 (age 40 years) to $118,193 (age 70 years) per life-year gained. Testing all model variables confirmed that both incidence and mortality of breast cancer play the most important role in the health economic outcome, whereas cost and performances (sensitivity, specificity) of screening had a minor impact on the efficiency.

Conclusion: This analysis, performed under conservative assumptions, supports that MSP in Switzerland enables a relevant reduction of breast cancer mortality, at moderate additional cost, compared with OS.

Keywords: cost-effectiveness, health economics, quality-controlled mammography Screening, Switzenland.

Introduction

The main objective of screening is to reduce the burden of a disease by detecting it in an early stage where an effective treatment enhances the chance of survival. A screening test separates apparently healthy, asymptomatic individuals into those with a high versus a low probability of the disease. The World Health Organization (WHO) pioneered the development of criteria for mass screening [1], and the WHO guidelines have been widely used for implementing organized screening programs. According to these guidelines, a screening test should have a high sensitivity, detecting as many cases as possible with the disease, and a high specificity, preventing further diagnostic tests and unwarranted treatment in disease-free individuals. Additionally, the disease should preferably be highly prevalent in the population because, for a given sensitivity, the chance that a positive screening test will give a correct result (positive predictive value) increases with the prevalence of the disease.

Breast cancer is the most frequent cancer among women in both developing and developed countries, with 1.1 million new cases being diagnosed each year [2]. Overall, the incidence increases with age modified by environmental factors [3], genetic predisposition [4], lifestyle [5,6], and use of exogenous hormones [3,7–9]. Despite being curable when detected at an early stage, breast cancer is responsible for the deaths of about 411,000 women worldwide every year [2].

Mammography screening trials have been shown to significantly reduce breast cancer mortality by 21% to 26% in women more than 50 years of age [10,11]. The mechanism by which mammography screening reduces

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breast cancer mortality is directly related to the increased chance of detecting a malignant growth at an earlier, curable stage [12].

Based on clinical practice with an established opportunistic screening strategy (OS), the achievable reduction of mortality by a mammography screening program (MSP) in a setting with OS may range from 5% to 20% [13,14].

The impact of MSP on breast cancer mortality is strongest for women more than 50 years old. The evidence is weaker for younger women because 1) the incidence of breast cancer is substantially lower among women in their 40s, although their cancer is more often diagnosed as aggressive; 2) the mammography test is less performing in younger women with denser breast tissue; and 3) the delay in breast cancer mortality is difficult to allocate to the beginning of screening at the age of 40 years rather than at the age of 50 years [15–17]. Because of the increase in comorbidities, a decreasing benefit of MSP is assumed at age more than 70 years, even though the sensitivity and specificity of MSP improve with increasing age [18,19].

Motivated by positive results obtained in randomized screening trials and meta-analyses evaluating MSP, breast cancer screening programs have been introduced in several countries since the mid-1980s [20,21].

In Switzerland, approximately 5000 breast cancers are diagnosed each year and about 1350 deaths from breast cancer are reported [22]. Breast cancer mortality in Switzerland has been decreasing since the early 1990s, whereas the incidence of breast cancer is increasing. Reasons underpinning these temporal changes are multiple, such as better systematic treatment and widespread screening, but also alteration in risk exposures and lifestyle [23–25].

The feasibility and acceptability within the Swiss health-care setting of quality assessed MSP have been demonstrated in a pilot study [21,26]. Since 1999, a Swiss government edict has been in place to finance quality-controlled breast cancer screening programs as part of the service catalog of statutory health insurances. A Swiss MSP quality standard recommendation comprises a two-view mammography, with a blinded double reading performed by two specially trained radiologists, with a third arbitration reading if necessary, and the screening administration (organization, invitation, quality assessment, evaluation) [21,27]. Three regional quality-controlled MSP have been established since 1999 [28].

The efficacy of mammography screening trials was questioned in a meta-analysis that revealed imbalances in the characteristics of the screening and control groups, as well as a discrepancy in the number of randomized women, and concluded that randomized screening trials yielded no protective effect [29,30]. Most arguments against mass screening and criticisms based on randomized screening trials have been rebutted and disproved by scientific reinvestigations confirming that mammography is effective at least in women older than 50 years [11,31–33]. Despite this, some debate persists in Switzerland about the pros and cons of mammography screening, and the medical and economic benefits of MSP versus OS remain uncertain [34]. This cost-effectiveness study was performed to assess the specific Swiss situation, but because of the limited and controversial information regarding indirect costs, only direct costs were implemented.

Objective

The purposes of this study were to evaluate the cost-effectiveness of a quality-controlled MSP compared with an established OS, and to identify factors influencing the clinical and economic outcomes with respect to the benefits, harms, and costs of the technique from the Swiss third-party payer perspective.

Methods

A comprehensive literature search of English and German-language publications (studies, meta-analysis, and reviews) from January 1970 to September 2004 was performed, using the MEDLINE and PubMed databases and the following terms in different combinations: "breast neoplasm," "mortality," "mammography," "mass screening," "female," "economic," and "cost."

Model

A Markov model was implemented in the Data Pro software (TreeAge Inc., Boston, MA) to compare the health economic effect of a national quality-controlled MSP with an OS strategy in the Swiss female population (Fig. 1). The Markov model is based on a set of health states linked via transition probabilities, which were derived from the most relevant sources for the Swiss context (see Tables 1 and 2). During a simulation run the primary cohort (population at breast cancer risk, see Fig. 1) can split into distinct disease states determined by the transition probabilities. This process is repeated for a defined number of cycles, where the transition from one state to another is calculated over time in 1-year-cycle lengths. The simulation ends when the number of predefined cycles or the terminal state (e.g., death) is reached.

The model starts with a cohort of women being in a predefined baseline age (40, 50, 60, or 70 years) and simulates the annual occurrence of malignant (defined as ductal carcinoma in situ, invasive ductal carcinoma, or invasive lobular carcinoma) and benign breast tumors, the detection rate of mammography, the further assessment induced by a positive test result, the recall rate because of false positive test results, and the

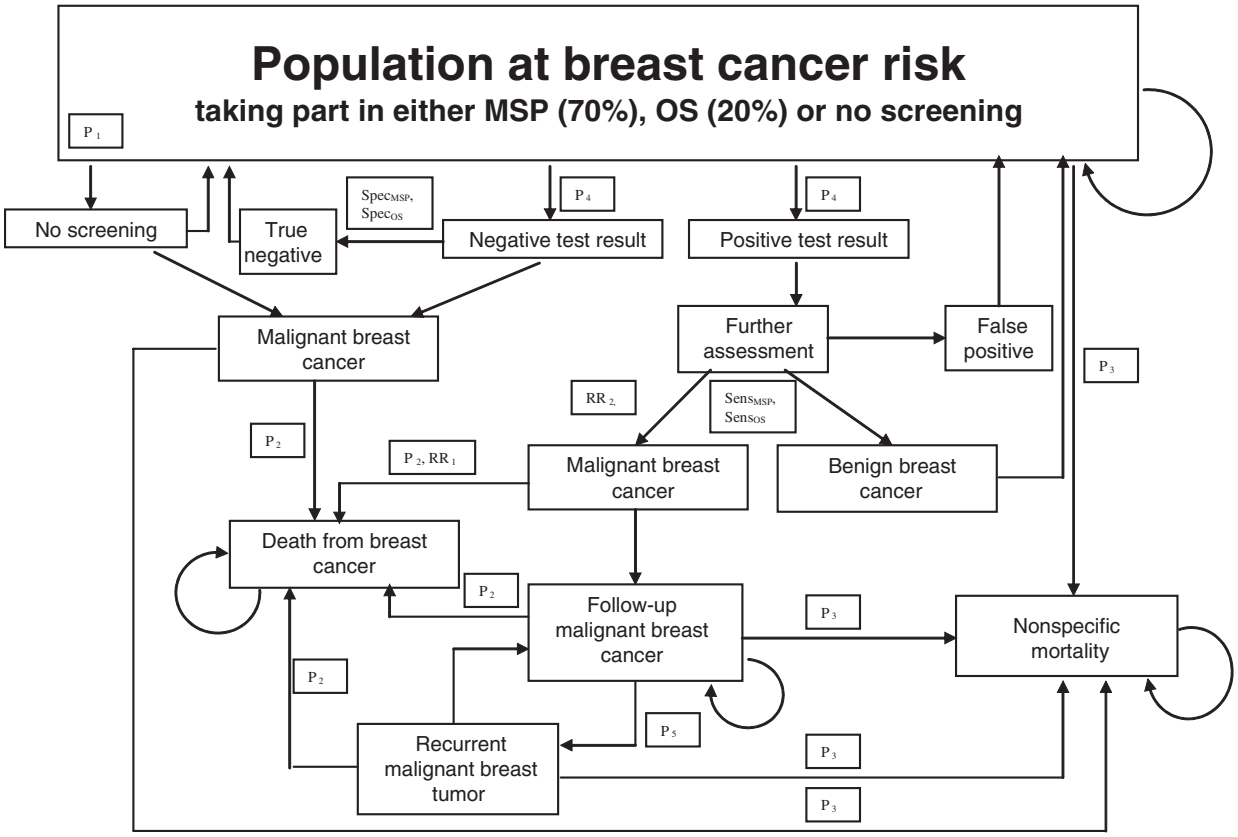

Figure 1 Schema of the Markov model used in the health economic analysis. MSP, mammography screening program; OS, opportunistic screening; P, probability; RR, relative risk; Sens, sensitivity; Spec, specificity.

progression of detected and nondetected malignant breast cancers.

During the simulation the mortality (breast cancer-related fatality, age-related general mortality), as well as the screening and treatment costs, was accumulated over time.

The model compares two scenarios. Scenario 1 assumes that at the beginning of the simulation 70% of the target population takes part in a biennial quality-assured MSP whereas the remaining 30% are not screened (a diagnostic method in a rare disease reaches the best benefit only if the participation is next to 100%. In a voluntary program this high participation rate will not be attainable. Therefore, a plausible baseline participation rate of 70% was specified. This participation rate of 70% corresponds to the European Guidelines for MSP. This value seems to be the threshold necessary to obtain a MSP-attributable reduction in breast cancer mortality within a 10-year period). Nonparticipants will have no benefit from screening.

Because experience from OS in Switzerland is available for several years [21], scenario 2 assumes a biennial participation rate in OS of 20% at the beginning of the simulation. In contrast, the residual 80% receives no screening.

Although OS is not necessarily quality-ensured [35] and data for its evaluation are limited, this procedure is likely to impact on breast cancer detection and achieves some reduction of breast cancer mortality. The economic impact of different participation rates was tested within the scope of a sensitivity analysis.

Because of the high reattendance rate and the low screening uptake among initial nonparticipants observed in the Swiss pilot study, the proportion of women switching between MSP and OS was considered negligible in this analysis [28].

A quality-of-life analysis was not performed because the related utilities were not available for every health state in the model (e.g., false positive screening results).

Mortality

The overall mortality of the study cohorts was calculated by combining age- and female-specific all-cause mortality rates [36,37] with breast cancer-related fatality rates of the Swiss female population. These were derived from mortality associated with ICD-10 (International Classification of Diseases) code C50 and published breast cancer survival rates [37–40] The model-based outcomes were total mortality (%) and

Table 1 Event rates, transition rates, and relative risks used in the model

Model parameter	Baseline		Range*	Source
Annual incidence of breast cancer in Swiss female population (P_1)	Age (year)	Incidence	±10%	[22]
	40–44	0.0011		
	45–49	0.0018		
	50–54	0.0024		
	55–59	0.0028		
	60–64	0.0029		
	65–69	0.0030		
	70–74	0.0032		
	75–79	0.0035		
	80–84	0.0037		
	85+	0.0032		
Annual fatality rate from breast cancer (i.e., mortality rate in females with breast cancer; P_2)	Age (year)	Mortality	±10%	[22,39,40]
	40–44	0.038		
	45–49	0.041		
	50–54	0.046		
	55–59	0.051		
	60–64	0.058		
	65–69	0.068		
	70–74	0.094		
	75–79	0.143		
	80–84	0.192		
	85+	0.220		
Corrected annual all-cause female mortality† (P_3)	Age (year)	Mortality		[36,37]
	40–44	0.0009		
	45–49	0.0015		
	50–54	0.0026		
	55–59	0.0042		
	60–64	0.0070		
	65–69	0.0116		
	70–74	0.0192		
	75–79	0.0317		
	80–84	0.0524		
	85+	0.2319		

*Applied range in one-way sensitivity analysis and probabilistic sensitivity analysis.
†To avoid double counting of fatal events, all-cause Swiss mortality rates were corrected for breast cancer-related mortality.

remaining life time (years, discounted by 0 and 1.5% p.a.).

Costs and Perspective

The perspective of the statutory health-care insurance in Switzerland was adopted. The costs of detecting and treating breast cancer were separated into three categories (Table 3). First, there is the cost of mammography examination; second, there are the costs of diagnostic evaluation for mammograms interpreted as positive (abnormal); and third, there is the cost of treatment for detected malignant breast cancers.

The cost per mammography varies in MSP between $104 and $198, of which up to $144 are paid by the statutory health insurances. About 25% of the total cost is covered by additional public copayments [27,41]. Because of this cost sharing, the fee of this service ranges from $0 to $11 per participant and screening examination.

The cost of OS has to be paid partly by the individual herself (copayment). An economic analysis carried out in western Switzerland estimated the total cost of OS (including further investigation) at $240 per screening [42]. Within the scope of the present

Table 2 Mammography screening parameters used in the model and their range of variability applied for the sensitivity analysis

Model parameter	Baseline (%)	Range(%)*	Source
Reduction of breast cancer mortality due to MSP in a setting with established OS (RR_1)	15	13.5–16.5	[13,14]
Proportion of malignant tumor if screening positive (PPV) (RR_2)	20	18–22	[21]
Sensitivity of MSP (mean value)† ($Sens_{MSP}$)	70	65–86	[21]
Specificity of MSP (mean value)† ($Spec_{MSP}$)	96.5	90–98	[21]
Sensitivity of OS (mean value)† ($Sens_{OS}$)	70	63–77	assumption derived from [21]
Specificity of OS (mean value)† ($Spec_{OS}$)	90	81–99	assumption derived from [21]
Biennial participation rate in MSP (P_4)	70	63–77	[21]
Annual recurrence rate of breast cancer (P_5)	5	4.5–5.5	[53]

*Applied range in one-way sensitivity analysis and probabilistic sensitivity analysis.
†The performance values of mammography screening improves with higher age. Because of the lack of information in the Swiss setting the mean values were adapted from Carney et al. [18].
MSP, mammography screening program; OS, opportunistic screening; P, probability; PPV, positive predictive value; RR, relative risk; Sens, sensitivity; Spec, specificity.

Table 3 Cost of screening, diagnostic measurement, treatment, and range of variability used for the sensitivity analysis

Model parameter	Baseline ($)	Range ($)*	Source
Cost per screening (two-view) including quality assessment program	120	104–198	[27,41]
Cost per screening in opportunistic screening program (assumption)	160	144–176	[42]†
Cost of complementary examinations for positive screening result‡	607	546–668	[42]
Cost of initial breast cancer treatment	24,095	21,689–26,505	[43,44]
Cost of recurrent breast cancer treatment	24,095	21,689–26,505	[43,44]
Annual follow-up cost after treated breast cancer (assumption 10% of breast cancer treatment)	2,410	2,169–2,651	[43]

*Applied range in one-way sensitivity analysis and probabilistic sensitivity analysis.
†Personal communication, Dr. de Landtsheer, 2005.
‡Weighted cost of complementary examinations, including echography and biopsy.

economic analysis an estimated amount of $160 is covered by the statutory health insurances (Personal communication, Dr. de Landtsheer, 2005).

In absence of detailed treatment and follow-up costs for diagnosed malignant breast cancer in Switzerland, data from an international cost analysis were used [43,44]. As a conservative assumption, the follow-up costs per diagnosed cancer were considered equal in both screening methods (MSP, OS) and the nonscreening group. It could, however, be assumed that the lesser severity of a tumor diagnosed at an earlier stage is likely to be associated with a lower treatment cost than that of cases detected at a more advanced stage.

Swiss cost parameters were converted to 2004 values by an annual inflation rate of 1.4% (corresponding to the average cost increase in the inpatient medical service in Switzerland over the last 7 years [45]) and an exchange rate of US$1 = CHF 1.25.

Primary Outcome Measures and Economic Evaluation

The total mortality and the number needed to screen (NNS) to avoid one death over 10 years as well as life expectancy were derived from annual breast cancer- and age-related general mortality. Screening and treatment costs were cumulated over the simulation period. Life expectancy was discounted at the rates of 0% and 1.5%, and costs at the rates of 0% and 3%, respectively [46].

To compare the cost-effectiveness of MSP versus OS, the incremental cost-effectiveness ratios (ICER) in terms of costs per life-year gained (CLYG) were calculated [47] and defined as

$$(C_{MSP} - C_{OS})/(LE_{MSP} - LE_{OS})$$

where C_{MSP} is the total cost with MSP; C_{OS} is the total cost with OS; LE_{MSP} is the life expectancy with MSP; and LE_{OS} is the life expectancy with OS.

Sensitivity Analyses/Probabilistic Sensitivity Analysis

Univariate sensitivity analyses were performed to determine key factors that influenced incremental CLYG, the main outcome measure. The probabilistic sensitivity analysis relied on randomly sampled values from probability distributions (rather than from a range defined by upper and lower bounds) to quantify the total impact of uncertainty on the model outcomes. In this analysis all model parameters (event rates and costs listed in Tables 1–3) were varied by the most probable range and tested for their impact on CLYG.

Results

Mortality and NNS

The MSP reduced the 10-year mortality rate by 0.2% (baseline age 70 years) to 0.7% (40 years) more than OS. With regard to the 10-year mortality rate, the NNS was 10,000 in MSP compared with OS at the baseline age of 40 years and 2439 at the baseline age of 70 years (Table 4). In a population of 100,000

Table 4 Ten-year all-cause mortality and the number needed to screen (NNS) under the baseline assumption of a participation rate of 70% in MSP and 20% in OS, respectively

Baseline age (year)	All-cause mortality over 10 years (%)		NNS over 10 years to prevent one death*	Number of extra deaths prevented with MSP over OS per 100,000 women over 10 years†
	MSP	OS		
40	1.448	1.458	10,000	10
50	3.875	3.899	4,167	24
60	9.719	9.754	2,857	35
70	23.782	23.823	2,439	41

*100/(% all-cause mortality $_{OS}$ − % all-cause mortality $_{MSP}$).
†(% all-cause mortality $_{OS}$ − % all-cause mortality $_{MSP}$)/100 × 100,000.
MSP, mammography screening program; OS, opportunistic screening.

Table 5 Results when MSP is performed in 70% of the population compared with OS in 20% of the population (discount rates: cost 3.0%, life expectancy 1.5%)

Baseline age at start of screening (year)	Total life time cost ($)		Incremental life time cost ($)	Life expectancy (year)		Incremental life expectancy (years)	CLYG ($/LYG)
	MSP	OS		MSP	OS		MSP vs. OS
40	4366	2802	1564	30.674	30.652	0.022	73,018
50	4149	2676	1473	25.322	25.302	0.02	75,602
60	3356	2103	1253	19.663	19.649	0.014	90,635
70	2412	1446	966	13.924	13.916	0.008	118,193

MSP, mammography screening program; OS, opportunistic screening.

women, 10 (40 years) to 41 extra deaths (70 years) were prevented with MSP over OS.

Costs and Life Expectancy

The total discounted life-time cost (discount rate: 3%) related to breast cancer, and screening for a 40-year-old woman amounted in the MSP to $4366 (OS: $2802) and decreased with age to $2412 (OS: $1446) at the age of 70 years (Table 5). The discounted incremental life expectancy (discount rates: cost 3%, life expectancy 1.5%) amounted to 0.022 life-years gained in favor of MSP when starting screening at age 40 years (0.008 years when starting screening at age 70 years). An alternative scenario, applying a discount rate of 0%, amounted to a gain in life expectancy of 0.035 with the baseline age of 40 years (0.01 years at the age of 70 years) (Table 6).

Cost-Effectiveness

Discounted (costs 3%, life expectancy 1.5%) ICER comparing MSP with OS ranged from $73,018 per life-year gained (LYG) when screening starts at the age of 40 years, to $118,193 per LYG (baseline age 70 years) (Table 5). Considering no discount rate in life expectancy reduced the ICER to $44,005 per LYG (age 40 years) and $94,353 per LYG (age 70 years), respectively (Table 6).

Sensitivity and Scenario Analyses

Sensitivity analyses were performed to test the robustness of the outcomes by varying all input parameters one at a time.

By decreasing order of importance, the most influential factors for the CLYG-based economic outcome were breast cancer mortality, the incidence of breast cancer, the cost of initial tumor treatment, the cost of biopsy, the cost of MSP, and the sensitivity of MSP (Fig. 2). The specificity of OS, the annual recurrence rate of breast cancer, the annual follow-up cost of tumor treatment, the expected reduction of breast cancer mortality, and the cost of OS showed a marginal influence on the CE outcome.

Figure 3 shows that a lower specificity and/or sensitivity of MSP reduces the economic benefit per LYG from $75,602 (specificity 96.5%, sensitivity 70%) to $507,000 (specificity 50%, sensitivity 50%).

The result of the probabilistic sensitivity analysis, which is based on a random assignment of all input parameter distributions as listed in Tables 1–3, represents the range and uncertainty of the possible outcome (Fig. 4). The distribution of ICER ranged from $45,000 per LYG to $135,000 per LYG with the highest probability of occurrence by about $75,000 per LYG (based on a woman aged 50 years).

An additional analysis indicated that the economic impact of MSP is also a function of the participation rates, both in MSP and in OS, in so far as a higher participation rate in MSP—for a given participation rate in OS—reduced the economic benefit, whereas a rise in OS participation improved the efficiency (Fig. 5).

Discussion

This economic modeling analysis of breast cancer screening combined long-term results from randomized trials with those available from Swiss regional screening programs to compare the cost-effectiveness

Table 6 Results when MSP is performed in 70% of the population compared with OS in 20% of the population (discount rates: cost 3.0%, life expectancy undiscounted)

Baseline age at start of screening (year)	Total life time cost ($)		Incremental lifetime cost ($)	Life expectancy (year)		Incremental life expectancy (year)	CLYG ($/LYG)
	MSP	OS		MSP	OS		MSP vs. OS
40	4366	2802	1564	41.697	41.662	0.035	44,005
50	4149	2676	1473	32.444	32.415	0.029	50,898
60	3356	2103	1253	23.790	23.771	0.019	66,720
70	2412	1446	966	15.956	15.946	0.01	94,353

CLYG, costs per life-year gained; MSP, mammography screening program; OSP, opportunistic screening.

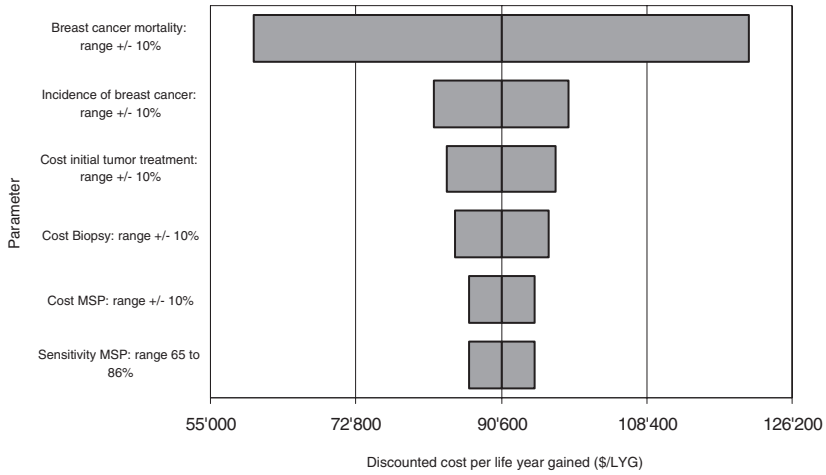

Figure 2 Ranking of the input parameters in a univariate sensitivity analysis influencing the cost per life-year gained. The age at the start of the mammography screening program (MSP) was not considered because of the predominant effect on life expectancy. The parameters with the highest impact on the cost per life-year gained are the annual breast cancer mortality, the incidence of breast cancer, the cost of initial tumor treatment, the cost of biopsy, the cost of MSP, and the sensitivity of MSP.

of MSP and OS within the liberal Swiss health-care setting. In this particular context, where significant health expenditures arise, the results indicate that MSP is cost-effective compared with OS. Interestingly, incidence and mortality from breast cancer were the main influential factors of the economic outcome, whereas cost and performances of mammography screening played a less prominent role.

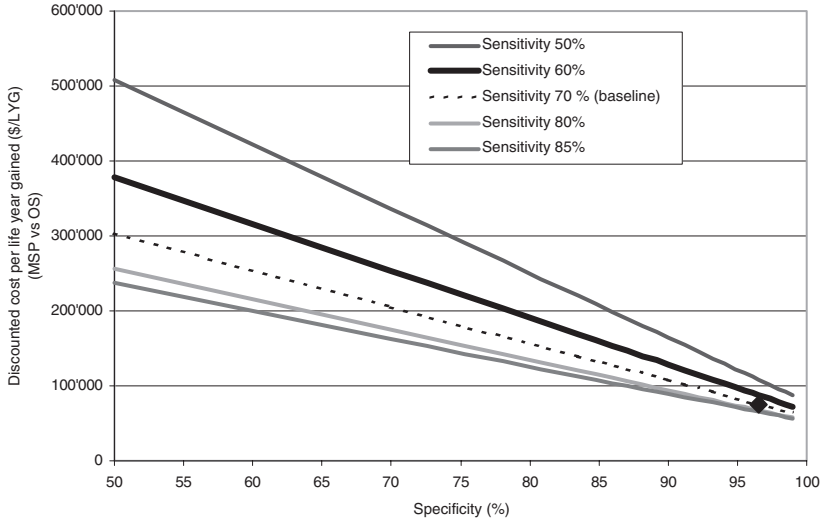

Figure 3 Influence of test sensitivity and specificity on the discounted cost-effectiveness ratio ($/LYG). ◆ = MSP baseline value of sensitivity (70%) and specificity (96.5%). LYG, life-year gained; MSP, mammography screening program; OS, opportunistic screening.

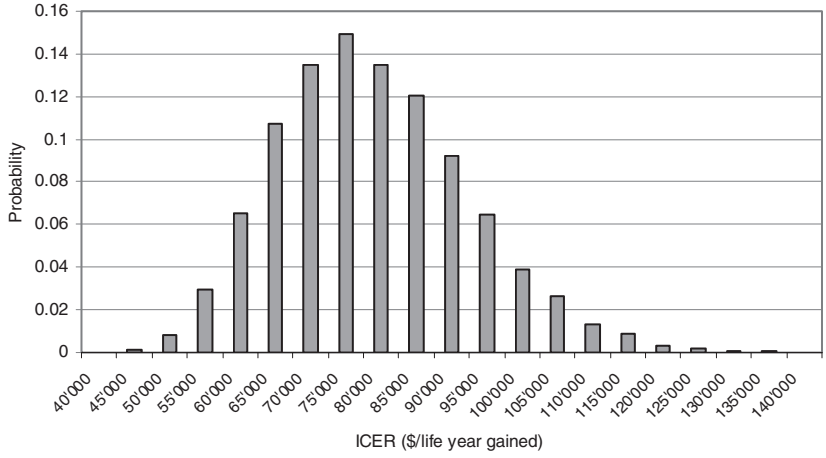

Figure 4 Distribution of discounted cost-effectiveness ratio derived by a Monte Carlo (probabilistic sensitivity analysis) simulation. Baseline age 50 years.

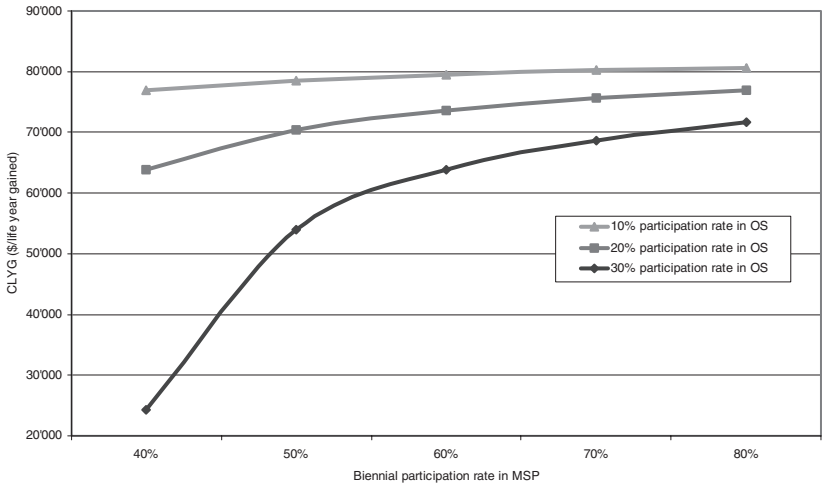

Figure 5 Impact of MSP and OS participation rate on cost-effectiveness ratio. MS, mammography screening program; OS, opportunistic screening.

Although the association between mammography screening and breast cancer mortality is complex, several studies have shown that early detection can significantly reduce breast cancer mortality [10,16]. Most studies, however, have compared a "screening" versus a "no screening" scenario. In several countries, including Switzerland, mammography screening is delivered either through an organized public health program (MSP) or on an individual (private) basis (OS). Because both screening methods are likely to yield favorable health benefits to the population, a comparison in relative terms of both strategies is most relevant for public health decision-makers in these countries.

Methods to compare the efficacy of a new health technology with a given strategy, i.e., screening method, present the results either as relative risk differences or, more appropriately, the overall clinical benefit, expressed as the number needed to screen (NNS) to avoid one complication, or as the number of extra deaths prevented [48,49]. The NNS in the current analysis of mammography screening was comparable with figures found in analogous mammography screening analyses [10] and in other secondary prevention techniques, e.g., hemoccult testing (NNS to prevent one colon cancer death: 1300 individuals for 5 years [48]) or osteoporosis screening (NNS to prevent one hip fracture in women aged 50–54 years: 7446 women for 5 years [50]). A recent Australian study predicted an approximately five to eight times greater number of prevented deaths using mammography screening than was revealed in the analysis presented here [49]. This deviation can be mainly attributed to the proportion of screened and non-screened women (i.e., 100% and 0% vs. 70% and 30%, respectively) and to a higher reduction of breast cancer mortality due to screening (i.e., 23–37% vs. 15%, respectively). This finding shows that the effectiveness of a screening program strongly depends on the existing health-care system (i.e., well-established OS).

The number of symptom-free individuals necessary to detect one case highlights the importance of the reliability of the screening method. Although MSP is not discussed without criticism, current evidence emphasizes that this strategy yields a clear medical benefit for the female population [10].

Translating these findings into monetary units reveals that the additional life-time costs of MSP over OS are related to the higher life expectancy and the tumor treatment costs rather than to the cost of screening itself.

The results are presented in terms of incremental CLYG values because this is a widely accepted method in health economic evaluations, which can assist with the decision-making process. The upper willingness-to-pay threshold was fixed at a value of $50,000, which represents "good value for money" for a lifesaving intervention, according to the international literature and health economic guidelines [47,51]. The discounted cost-effectiveness ratios of an exhaustive MSP relative to OS have been found to be on the upper acceptable threshold value [52].

This result is partly supported by other studies, especially in analyses performed in older age groups, which have shown a cost-effectiveness ratio (ICER) ranging from $34,000 to $88,000 per LYG [53,54]. Other available cost-effectiveness analyses in MSP present a more favorable ICER within a range from $3400 to $12,000 per LYG [55–57]. There are several aspects influencing the outcome of a cost-effectiveness analysis, e.g., the decreasing breast cancer mortality over time and a well-established OS in Switzerland, as well as the baseline health-care perspective, which is fundamental in the assessment of different study outcomes.

The average age in the observed Swiss female population (range 50–95 years) is about 65 years. Applying this age distribution, one can expect a weighted and discounted ICER of about $104,000 per LYG (undiscounted $80,500 per LYG).

Because of the following two conservative assumptions in this analysis, there is a trend to overestimate the cost and underestimate the clinical benefit:

1. considering the competing risk, i.e., evaluating the screening benefit as a reduction in all-cause mortality rather than breast cancer mortality alone; and
2. postponing the benefit of MSP and OS in lowering breast cancer mortality to the subsequent years whereas the cost of treatment was allocated to the year of detection.

Our extensive sensitivity analysis of all variables in the model confirms that both breast cancer incidence and mortality play a major role in the health economic outcome, whereas the cost and the performance (sensitivity, specificity) of screening have a minor impact on the efficiency. From an economic perspective, the small effect of the screening cost points out the limited influence that different regional health-care systems in Switzerland, which regulate the public copayments of MSP, have on the cost-effectiveness of mammography screening.

The model validation performed by the authors (see Appendix) provides some statistical confidence about the adequacy of the disease model. Some limitations, however, are inherent to any modeling approach:

1. A model can only consider the most relevant aspects of a disease. The resulting picture is less complex than the reality but adequate enough to provide the answers to questions asked (e.g., reduction of the sensitivity due to hormone replacement therapy not considered).
2. The applied transition probabilities may vary over time. Whether this shift is illustrated correctly in the disease model remains open. Marked fluctuations of breast cancer mortality have been observed in the last decade, but to what extent these downward trends are related to screening activity is difficult to assess [25].
3. Scarce clinical and economic data available for Switzerland resulted in the inclusion of international data, particularly for OS, which leads to questions regarding the transfer of evidence between different health-care systems.
4. A nationwide screening program has to take into account all levels of medical care. It can well be that relevant differences between different medical institutions, such as doctors' offices and outpatient clinics, exist. This could not be taken into account for this modeling study (e.g., regional differences in the health-care system of Switzerland).
5. A further limitation in this analysis are the missing health-related quality of life (HRQL) outcomes. For a comprehensive, population-based consideration of HRQL, health-related utilities are needed for different circumstances (e.g., false positive screening result, true negative screening result). Unfortunately, these kind of HRQL data are incomplete, and including them would have likely created a bias in our result.

The development of new technologies (e.g., digital mammography) could improve various aspects of breast cancer screening. Whether a new method also fulfill economical claims will decisively depend on the quality improvement and the prevailing epidemiological conditions.

Conclusion

Based on the present decision analysis with its underlying assumptions, mammography screening has been shown to be effective in terms of reducing mortality and to be worthwhile from an economic perspective. These findings are supported by analyses in other countries. Because these results are derived from a modeling study, future attention should be paid to the results of ongoing structured MSP in Switzerland and the model should be adapted as new evidence arises.

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Appendix

Model Validation

The current mammography model underwent a comprehensive validation process. The intention was to compare the model outcomes with published epidemiological data.

In the first step, the difference between the calculated and the predicted remaining age-specific life expectancy was assessed (Table A), using the published age distribution of women in Switzerland: The maximum absolute deviation of the calculated remaining life-years amounts to –0.8 years (–1.9%) in the age group of 40-year-old women. The deviation between the calculated and the predicted remaining life-years is a result of the assessment method in the underlying data sources: The annual mortality rates used in the model are based on the 1999 statistics [36,37]. The model's predicted remaining life expectancy is derived from the annual increase in the further life expectancy and represents therefore a continuous changing parameter.

In the next step, the difference between the expected and calculated number of breast cancer cases was assessed (Table B): The main absolute deviation between the observed and calculated number of breast cancer cases per year was –9 cases (–0.9%) in the age group of 45 to 54 years. The explanation for this deviation can be found in the regression formula, which was derived from the raw data.

The comparison of expected and calculated number of annual breast cancer deaths revealed a main absolute deviation of –15 death cases (–5.6%) in the age group of 65 to 74 years (Table C): The most important reason for this deviation is defined in the method of data collection. To complete the age-specific annual breast cancer incidence, data from different sources were used to perform a regression analysis.

Table A Comparison of predicted and model-based remaining life expectancy for different baseline ages

	Age at baseline (year)			
	40	50	60	70
Remaining life time				
Predicted [36]	42.5	33.0	24.0	15.6
Calculated by the model	41.7	32.4	23.8	15.9
Difference: years (%)	–0.8	–0.6	–0.2	+0.3
	(–1.9)	(–1.8)	(–0.8)	(–1.9)

Chi-square test of goodness-of-fit: $P = 1.00$.

Table B Comparison of observed and model-based annual number of breast cancer cases in different age ranges

	Age range (year)		
	45–54	55–64	65–74
Annual breast cancer cases			
Observed [22]	1074	1258	1023
Calculated by the model	1065	1251	1029
Difference: cases (%)	–9	–6	+6
	(–0.9)	(–0.5)	(–0.6)

Chi-square test of goodness-of-fit: $P = 0.97$.

Table C Comparison of observed and model-based annual number of breast cancer deaths in different age ranges

	Age range (year)		
	45–54	55–64	65–74
Annual breast cancer mortality			
Observed [37]	159	225	267
Calculated by the model	157	225	252
Difference: cases (%)	–2	0	–15
	(–1.3)	(0)	(–5.6)

Chi-square test of goodness-of-fit: $P = 0.90$.