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Cost-effectiveness of opportunistic versus organised mammography screening in Switzerland

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ARTICLE INFO

Article history:
Received 9 July 2008
Received in revised form
17 September 2008
Accepted 25 September 2008
Available online 27 November 2008

Keywords:
Breast cancer
Mammography
Mass screening
Opportunistic screening
Cost-benefit analysis
Cost-effectiveness
Breast cancer mortality
Computer simulation
Computer models

ABSTRACT

Background: Various centralised mammography screening programmes have shown to reduce breast cancer mortality at reasonable costs. However, mammography screening is not necessarily cost-effective in every situation. Opportunistic screening, the predominant screening modality in several European countries, may under certain circumstances be a cost-effective alternative. In this study, we compared the cost-effectiveness of both screening modalities in Switzerland.

Methods: Using micro-simulation modelling, we predicted the effects and costs of biennial mammography screening for 50–69 years old women between 1999 and 2020, in the Swiss female population aged 30–70 in 1999. A sensitivity analysis on the test sensitivity of opportunistic screening was performed.

Results: Organised mammography screening with an 80% participation rate yielded a breast cancer mortality reduction of 13%. Twenty years after the start of screening, the predicted annual breast cancer mortality was 25% lower than in a situation without screening. The 3% discounted cost-effectiveness ratio of organised mammography screening was €11,512 per life year gained. Opportunistic screening with a similar participation rate was comparably effective, but at twice the costs: €22,671–24,707 per life year gained. This was mainly related to the high costs of opportunistic mammography and frequent use of imaging diagnostics in combination with an opportunistic mammogram.

Conclusion: Although data on the performance of opportunistic screening are limited, both opportunistic and organised mammography screening seem effective in reducing breast cancer mortality in Switzerland. However, for opportunistic screening to become equally cost-effective as organised screening, costs and use of additional diagnostics should be reduced.

1. Introduction

Breast cancer mortality has decreased in several countries in the last decade. Mammography screening is one of the factors contributing to this decline.[1–3] Various organised mammography screening programmes have shown to be effective in reducing breast cancer mortality[4–6] at costs well below the WHO threshold[7] of cost-effectiveness.[8–10] However,

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doi:10.1016/j.ejca.2008.09.015

mammography screening is not necessarily cost-effective in every situation. Cost-effectiveness depends on country-specific demographic and epidemiologic characteristics, breast cancer incidence, tumour stage distribution and breast cancer mortality before the initiation of screening, and the characteristics of screening, such as attendance, targeted screening ages and screening interval. The organisation of a health care system, and the costs of screening, diagnostics and treatment also determine whether mammography screening is cost-effective.

Under certain circumstances, 'opportunistic' mammography screening in asymptomatic women, the predominant form of screening in several European countries, may be a cost-effective alternative to programme-based mammography screening. The objective of the current study is to compare the cost-effectiveness of both screening modalities in Switzerland. Six French-speaking Swiss cantons have a biennial organised mammography screening programme (MSP), which coexists with opportunistic screening (OS). While OS is assumed to have started around the mid-eighties, programme screening in these areas started between 1999 and 2007, currently inviting approximately 25% of the 50–69 years old Swiss female population.[11] Other, mainly German-speaking, cantons only screen opportunistically, to a smaller or larger extent.

A previous analysis of the incremental cost-effectiveness of MSP relative to OS estimated that in Switzerland, MSP would yield a relevant reduction of breast cancer mortality at moderate additional costs.[12] In that study, however, cost-effectiveness was predicted using a single-cohort model, based on a conservative screening-associated breast cancer mortality reduction of 15% (randomised controlled trials showed reductions of 21–31%).[4–6,13,14] Cost savings related to a decreased use of palliative care were not included. In the present analysis, the effects and costs of MSP and OS were predicted at population level, using the internationally validated micro-simulation model 'MISCAN'.[15–18] Trial-based screening effects, specific Swiss demographic and epidemiologic data and MSP- and OS- specific screening characteristics were taken into account. To account for regional variations, five OS and MSP scenarios with varying screening participation rates were studied. Because data on the performance of OS are scarce, a sensitivity analysis on the test sensitivity of OS was performed.

2. Methods

2.1. The 'MISCAN' model

With the micro-simulation screening analysis model 'MISCAN', the consequences of introducing a screening programme on individual life histories were assessed. In MISCAN, the natural history of breast cancer starts with a transition from 'no breast cancer' into pre-clinical screen-detectable breast cancer, in a certain percentage of the modelled population. Tumour development is modelled as a progression through the successive invasive disease stages T1A, T1B, T1C and T2+ (diameter $\leqslant$ 5 mm, 6–10 mm, 11–20 mm and >20 mm, respectively). Invasive cancer may or may not be preceded by pre-clinical DCIS. In each pre-clinical stage, a tumour may be clinically diagnosed or may grow into the next pre-clinical stage. If women are screened, the pre-clinical tumour may also be detected by screening (Fig. 1). Screening ages, interval and attendance and the type of screening ('opportunistic' or 'organised'), as well as the sensitivity and specificity of mammography are defined in the model.

MISCAN parameters are mean dwelling times, transition probabilities between pre-clinical stages and survival after clinical diagnosis or screen detection. These age- and stage-dependent parameters were estimated using breast cancer incidence and stage distribution of screened and unscreened populations. Transition probabilities, stage durations and survival after diagnosis were based on the outcomes of the Dutch nation-wide breast cancer screening programme[19] and the Dutch pilot studies in Nijmegen and Utrecht.[15,20–22] The survival after clinical diagnosis or screen detection was modelled using several international sources.[23–27] The improvement of prognosis after detection by screening (defined as 1 minus the ratio of the risk of dying of screen-detected cancer divided by the risk of dying when the cancer had been diagnosed in the absence of screening) was based on experience from the Swedish randomised trials.[14,24,28,29]

2.2. Model calibration

To adjust MISCAN for the Swiss situation, the model was calibrated with observed breast cancer data in the canton of Vaud, where a long-standing cancer registry including pre-screening years and the largest Swiss centrally organised screening programme operate.[30,31] For this purpose, we modelled the Vaud female population between 1974 and 2005. The Swiss life table of 1999 was used to model mortality from other causes than breast cancer. Breast cancer incidence before the introduction of screening was then modelled, using data from the Vaud Cancer Registry between 1974 and 1985. The mean duration of the pre-clinical tumour stages was estimated by fitting the model predictions to the stage distribution in the years before screening, and to the detection rates and interval cancer rates after the introduction of the screening programme. As data on the tumour stage distribution in pre-screening years were unavailable in Vaud, data from the Geneva Cancer Registry between 1980 and 1984 were used. The breast cancer mortality was calibrated with data from the Vaud Cancer Registry between 1974 and 1985. The test sensitivity of screening was estimated by modelling screening characteristics of the Vaud screening programme[32] and calibrating the model to replicate the observed rates of interval cancers and screen-detected tumours by age, stage and screening round (first/subsequent). For the tumour stages DCIS, T1A, T1B, T1C and T2+, the test sensitivity was accordingly estimated to be 80%, 70%, 75%, 80% and 100%, respectively. The breast cancer survival in the basic MISCAN model was slightly decreased to replicate the breast cancer mortality in Vaud. A χ^2 test applied to the deviance was used as a test of goodness-of-fit. The model parameters are shown in Appendix 1.

2.3. Screening assumptions

By comparing a screening scenario to a scenario without screening, cost-effectiveness was calculated. In the current analysis, we predicted the effects and costs of screening

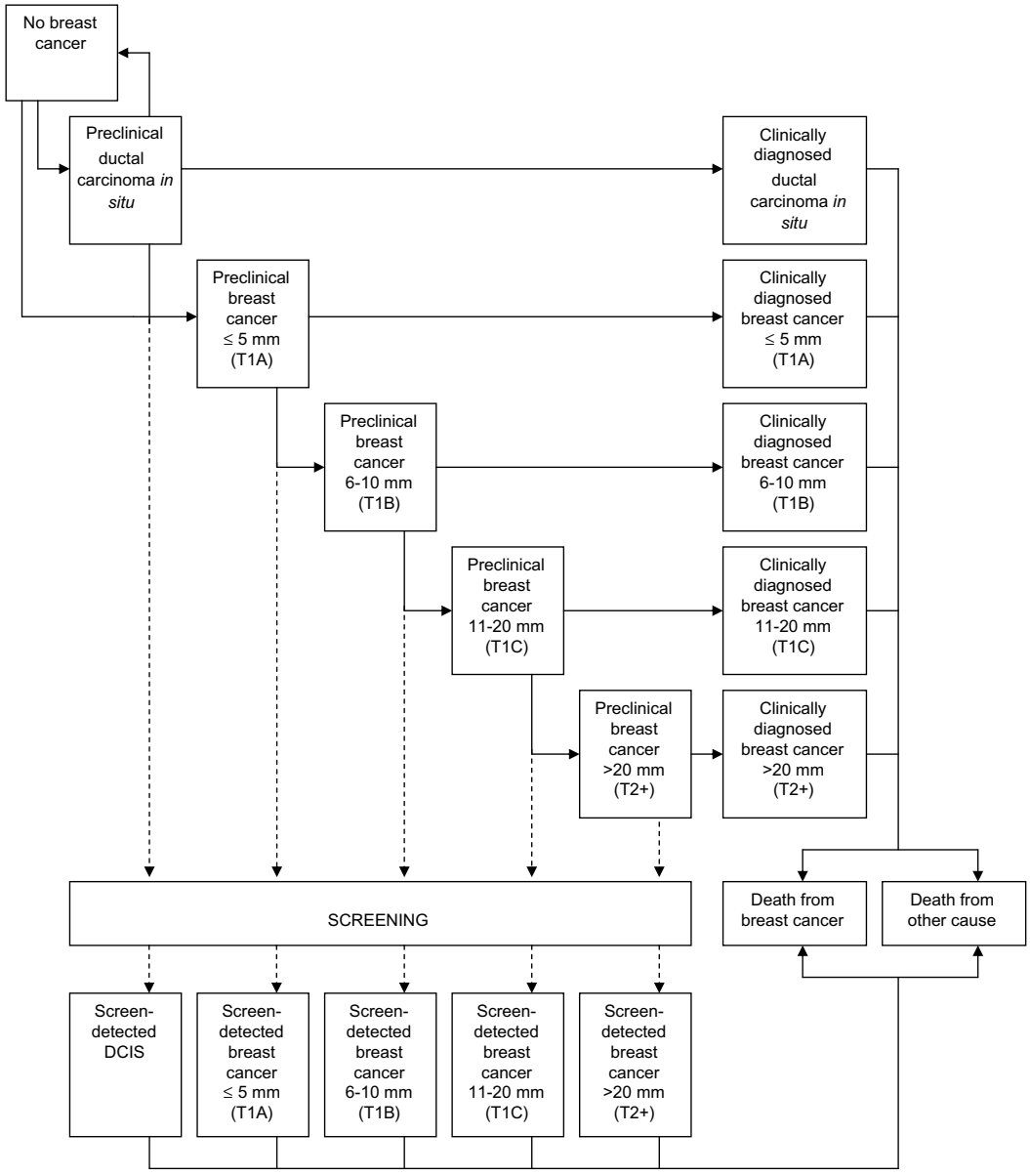

Fig. 1 – Transitions in the MISCAN model.

50–69 years old Swiss women between 1999 and 2020, by MSP and/or OS. Computed effects were the number of breast cancer deaths prevented, life years gained and quality-adjusted life years gained per 1,000,000 women; the latter was calculated using utilities reported by de Haes et al.[33] Effects were calculated for the Swiss female population aged 30–70 in 1999, during the whole lifespan of this population. The breast cancer mortality reduction was also calculated for women aged 55–74, where the most relevant breast cancer mortality reduction was expected to be observed.[6] Additionally, the maximum reduction of the annual breast cancer mortality rate was computed. The modelled population had the same age distribution as observed in Vaud between 1999 and 2005.

Costs included all expenses on screening, (over)diagnosis, (over)treatment, follow-up and palliative care. Costs incurred during and after the screening period were included. Five hypothetical screening scenarios (Sc 1–5) were analysed:

(Sc 1) 40% biennial OS (40% of the target population has an opportunistic mammogram every other year),
(Sc 2) 80% biennial OS (80% of the target population has an opportunistic mammogram every other year),
(Sc 3) 80% biennial MSP (all women in the target population are biennially invited to participate in an organised screening programme, and 80% participates),
(Sc 4) 60% biennial MSP and 20% biennial OS (all women in the target population are biennially invited to participate in an organised screening programme, and 60% participates. Another 20% of the target population has an opportunistic mammogram every other year),

(Sc 5) 40% biennial MSP and 40% annual OS (all women in the target population are biennially invited to participate in an organised screening programme, and 40% participates. Another 40% of the target population has an opportunistic mammogram every year).

We assumed that women who participated in a MSP were not screened opportunistically, and *vice versa*. Once a woman is screened, opportunistically or in a programme, she is assumed to have biennial (Sc 1–4 and Sc 5, MSP) or annual (Sc 5, OS) mammograms until age 70. Women who are not screened were assumed never to have a mammogram. The 'intervals' for annual and biennial OS were assumed to be 0.75–1.25 years and 1.75–2.25 years, respectively. Scenarios 1, 4 and 5 represent mammography screening practice in parts of Switzerland; scenarios 2 and 3 were not regarded to be realistic representations of current or future mammography screening practice. However, scenario 3 approaches a screening situation such as observed in the North-European countries, where attendance rates around 80% have been observed.[34] Scenarios 2 and 3 enable a direct comparison of OS and MSP. As little is known about the performance of OS and the sensitivity of mammography may vary across Switzerland, a sensitivity analysis was performed, with three model variants of varying false-negative rates for OS compared to MSP:

A. An 'optimistic' variant (A), with a 25% lower false-negative rate of OS compared to MSP.
B. A 'baseline' variant (B), with similar false-negative rates of OS and MSP.
C. A 'pessimistic' variant (C), with a 25% higher false-negative rate of OS compared to MSP.

2.4. Costs and cost-effectiveness

The costs of diagnostics and treatment were calculated as the resource use multiplied with costs per unit. The number of diagnostic examinations done after a positive programme-based mammogram was estimated from referral rates in the Vaud screening programme.[32] The number of diagnostics used after an opportunistic mammogram was estimated with data from the largest Swiss health insurance company CSS, which provided individualised records on the use of health care services of women who had a mammogram between 2004 and 2006. The health insurance, however, did not register opportunistic mammography as a separate procedure, since it was reimbursed similarly as diagnostic mammography. Because the majority of these mammograms correspond to OS, all reimbursed mammograms were regarded as opportunistic mammograms. The number of clinical breast examinations performed for each mammogram was estimated by calculating the ratio between reimbursed clinical breast examinations and mammograms, using aggregated data on the use of breast cancer diagnostics from the health insurance organisation Santé Suisse. The number of diagnostic examinations needed to clinically diagnose 1 tumour outside the MSP and OS was, in absence of Swiss data, based on the results from the Dutch COBRA study.[35] The treatment use after the detection of a tumour in a MSP was derived from registrations in the Vaud screening programme.[32] Reliable data on the treatment of tumours detected by opportunistic screening and clinically diagnosed breast cancer were unavailable. Considering the Swiss health care structure, we assumed that a tumour detected by OS was treated similarly as a MSP-detected tumour. The probability of a specific treatment for a clinically diagnosed tumour was calculated as the same probability for a screen-detected tumour (as observed in Vaud) multiplied with the ratio of these probabilities between a screen-detected tumour and a clinically diagnosed cancer, as observed in the Netherlands.[35] The probability that a specific treatment is used depends on tumour stage.

The costs of an opportunistic mammogram were calculated as the costs of a programme-based mammogram (€138[11]) multiplied by the ratio of CSS-reimbursed costs between a programme-based mammogram and an opportunistic mammogram. The costs of imaging and minimal invasive diagnostics were directly derived from CSS. Costs in Swiss Francs (CHF) were converted to Euro (€), using a currency exchange rate of 1.66 (June 2007). Since no reliable data were available on the costs of treatment in Switzerland, Dutch cost estimates were used.[36] A health care specific purchasing power parity (PPP) of 1.21 was applied to those costs, to account for the relatively higher health care costs in Switzerland[37] compared to the Netherlands. The costs of sentinel node procedures were estimated based on an analysis in the USA.[38] To account for time preference, both effects and costs were discounted at 3% per year,[39] from 1999 onwards.

3. Results

3.1. Calibration

The calibrated model resembled the incidence and stage distribution of clinically diagnosed breast cancer, screen-detected breast cancer, interval cancers and the mortality due to breast cancer in Vaud reasonably well (Table 1). However, MISCAN predictions were optimistic with regard to the detection of T2+ tumours at subsequent screening examinations ($p < 0.01$).

3.2. Effects

Effects are shown in Table 2. Biennial organised screening of 80% of the 50–69 years old female population ('Sc 3') was predicted to increase the total number of diagnosed breast cancers by 1.4%, compared to a situation without screening (80% MSP: 94,376 tumours; no screening: 93,036 tumours). Without screening, 42% of the tumours in the total simulated population were smaller than 20 mm or non-invasive, versus 51% with screening (data not shown). For each screen-detected tumour, 222 screen-mammograms were performed, and for each prevented breast cancer death, 798 screen-mammograms were needed (data not shown). Opportunistic screening had similar outcomes.

Both MSP and OS were predicted to reduce breast cancer mortality. Biennial 80% MSP prevented 4921 breast cancer deaths per 1,000,000 women aged 30–70 in 1999, which is a

Table 1 – Breast cancer incidence, mortality, detection rates and interval cancer rates as observed in the canton of Vaud, compared with MISCAN predictions

Parameter		Observed	MISCAN-predicted	*p*-Value
Clinical breast cancer incidence in pre-screening years, 1974–1985 (per 100,000 women years)	Age 0–100	104.5	106.4	0.3
Stage distribution of tumours in pre-screening years, 1980–1984 (%)				
DCIS	Age 0–100	3.9	4.1	0.9
T1A	Age 0–100	3.2	1.5	0.2
T1B	Age 0–100	10.4	6.5	0.2
T1C	Age 0–100	36.9	32.3	0.4
T2+	Age 0–100	45.6	55.6	0.2
Breast cancer mortality in pre-screening years, 1974–1985 (per 100,000 women years)	Age 0–100	39.1	37.8	0.3
Detection rates 1999–2005 (per 100,000 examinations)				
DCIS, first screening examinations	Age 50–69	130.4	155.3	0.2
DCIS, subsequent screening examinations	Age 50–69	85.8	85.8	1.0
T1A, first screening examinations	Age 50–69	78.3	66.4	0.4
T1A, subsequent screening examinations	Age 50–69	76.8	88.2	0.4
T1B, first screening examinations	Age 50–69	164.4	133.8	0.1
T1B, subsequent screening examinations	Age 50–69	135.5	131.2	0.8
T1C, first screening examinations	Age 50–69	255.7	283.8	0.3
T1C, subsequent screening examinations	Age 50–69	173.9	154.0	0.3
T2+, first screening examinations	Age 50–69	91.3	112.5	0.2
T2+, subsequent screening examinations	Age 50–69	74.5	35.4	<0.01
Interval cancers 1999–2004 (per 100,000 examinations)				
After first screening examinations	Age 50–69	144.5	165.5	0.3
After subsequent screening examinations	Age 50–69	135.1	102.2	0.1

Abbreviations: ductal carcinoma *in situ* (DCIS), diameter ⩽ 5 mm (T1A), diameter 6–10 mm (T1B), diameter 11–20 mm (T1C), diameter > 20 mm (T2+).

breast cancer mortality reduction of 13% during the lifespan of this population, and a gain of 81,000 life years. Biennial 80% OS ('Sc 2', baseline variant) resulted in a breast cancer mortality reduction of 13%, a prevention of 4876 breast cancer deaths and a gain of 80,400 life years. In the optimistic and pessimistic variant, the reductions were 14% and 13%, respectively (data not shown). Between the ages 55 and 74, the predicted breast cancer mortality reduction was 20% (80% MSP and 80% OS). We predicted that in 2018, 20 years after its start, MSP would reduce the breast cancer mortality rate by 25% (at population level) and 32% (age 55–74). For OS, these reductions were 23% (at population level) and 30% (age 55–74) (Table 2, Fig. 2). The screening effects decreased proportionally with the fraction of women screened: 40% OS ('Sc 1') was predicted to reduce the breast cancer mortality over the whole lifespan of the population by 7%, and the annual breast cancer mortality rate in 2018 by 12% (at population level). The 40% biennial MSP/40% annual OS scenario ('Sc 5') was most effective, with a 15% breast cancer mortality reduction during the lifespan of the population, and a reduction of the breast cancer mortality rate in 2018 of 27% (at population level).

3.3. Costs

The unit costs for a programme-based mammogram were €138 and the costs for an opportunistic/diagnostic mammogram were €171. The costs of breast cancer diagnostics and treatment are shown in Table 3. For each opportunistic mammogram, 2.9 clinical breast examinations were performed. In 53% of the opportunistic mammograms, an additional ultrasound or MRI was performed. In a MSP, on the contrary, only 4.3% of the mammograms were followed by an imaging examination, and no additional clinical breast examinations were done (Table 4). Consequently, the costs of diagnostics other than mammography in the baseline 80% OS scenario were predicted to be 305 million euros higher than in a scenario without screening, while in the 80% MSP scenario, the costs were 5 million euros lower (Table 5, scenarios 2 and 3 versus scenario 0, 3% discounted). Related to the higher costs of an opportunistic mammogram (Table 3), the costs of screening were higher for OS than for MSP (€500 million versus €406 million, Table 5). For both the 80% MSP and 80% OS scenarios, the relative costs of primary treatment increased compared to a situation without screening, by 34 million euros (without screening: €421 million). This was related to the improved stage distribution and to the fact that screen-detected cancers and smaller tumours were more commonly treated by (the more expensive) tumorectomy, while clinically diagnosed cancers and larger-sized tumours were more frequently treated by (the cheaper) mastectomy. Related to the increased cancer incidence and improved survival, the costs of follow-up also increased, by €15 million, in both the 80% OS and 80% MSP scenarios (without screening €113 million). Cost savings were predicted in palliative care: the more breast cancer deaths prevented, the lower the costs (up to a reduction of €57 million in the 80% OS and 80% MSP scenarios). The total costs increased proportionally with the fraction of screened women. Costs rose only slightly with an improved

Table 2 – Predicted effects of opportunistic screening (OS) and mammography screening programme- (MSP) scenarios with varying participation rates, compared to a no-screening scenario, no discounting

	Sc 0 No screening	Sc 1 40% OS	Sc 2 80% OS	Sc 3 80 % MSP	Sc 4 60 % MSP 20 % OS	Sc 5 40 % MSP 40 % annual OS
Effects (no discounting)						
Breast cancers diagnosed during lifespan of population, population level (N, %)	93,036	+670 (+0.7)	+1,319 (+1.4)	+1,340 (+1.4)	+1,335(+1.4)	+1,430(+1.5)
Breast cancer deaths during lifespan of population, population level (N, %)	36,519	−2,446 (-7)	−4,876 (−13)	−4,921 (−13)	−4,909 (−13)	−5,482 (−15)
Breast cancer deaths during lifespan of population, age 55-74 (N, %)	16,568	−1,652 (−10)	−3,298 (−20)	−3,342 (−20)	−3,331 (−20)	−3,733 (−23)
Reduction of the breast cancer mortality rate in 2018 ,population level (%)	-	−12	−23	−25	−24	−27
Reduction of the breast cancer mortality rate in 2018, age 55-74 (%)	-	−15	−30	−32	−32	−35
Life years, during lifespan of population, population level (N)	36,390,700	+40,200	+80,400	+81,000	+80,825	+90,400
Quality adjusted life years, during lifespan of cohort, population level (N)	36,287,649	+38,305	+76,603	+77,176	+77,008	+86,174
Mammograms (N), population level	0	1,965,490	3,928,610	3,928,490	3,928,520	5,731,380

All effects and costs were rescaled to a population of 1,000,000 women. The results of the opportunistic screening scenarios were presented for the baseline model variant only. The maximal reduction of the annual breast cancer mortality rate was reached in 2018, 20 years after the start of screening.
Abbreviations: opportunistic screening (OS), mammography screening programme (MSP).

test performance: in the optimistic 80% OS variant, the total costs were €793 million higher than in a situation without screening, while in the pessimistic variant, the costs were €798 million higher (without screening: €1239 million, 3% discounted, Table 6).

3.4. *Cost-effectiveness*

Each life year gained (LYG) in the 80% MSP scenario is predicted to cost €11,512 (Table 5, 3% discounting). In the 80% OS scenario, the costs per LYG would increase to €22,671 in the optimistic model variant, and to €24,707 in the pessimistic variant (Table 6). A 5% discount rate raised the cost-effectiveness ratio (CER) of 80% MSP to €17,141 per LYG, and that of 80% OS to €34,318 per LYG (data not shown). Costs per life year gained increased proportionally with the fraction of women screened opportunistically. Participation rates did not strongly influence the CER. Quality-adjustment of gained life years resulted in less favourable CERs: €12,424 in the 80% MSP scenario and €25,541 in the 80% OS scenario (Table 5, 3% discounted).

4. Discussion

This study showed that mammography screening in Switzerland is likely to be effective in reducing breast cancer mortality. A biennial organised mammography screening programme, covering 80% of the 50–69 years old Swiss female population, was predicted to reduce the breast cancer mortality by 13% at the population level and by 20% among women aged 55–74. Opportunistic screening with a similar participation rate was predicted to reach comparable results. The costs of OS per life year gained, however, were twice that of MSP.

The predicted breast cancer mortality reduction in this study seems somewhat lower than the reductions of 20–31% observed in randomised controlled trials and nation-wide mammography screening programmes.[4–6,13,14,40] Several programme evaluations predicted reductions of 17–19% at the population level.[17,41,42] OS has been estimated to reduce breast cancer mortality by 8–23% in the USA population[43] (participation 70%[44]). Because screening effects were measured over the whole period that the simulated population is alive, rather than during the screening period only, and because a breast cancer mortality reduction among screened women gradually decreases once screening has ended, our predicted reduction is lower than in the above-mentioned studies. However, an analysis over the whole lifespan enables all potential effects and costs to be accounted for. A shorter period of analysis would increase the predicted breast cancer mortality reduction, up to a maximal reduction of 25% at the population level, and 32% among 55–74 years old women (80% MSP) in 2018, 20 years after the start of screening.

We predicted the breast cancer mortality reduction for women aged 30–70 years in 1999, because these women will at least once be targeted for screening. Including younger and older women would lower the predicted mortality reduction. Breast cancer mortality reduction may also have been overestimated by the fact that the predicted stage distribution at subsequent screening examinations was more favourable than actually observed. Because this was counteracted with a less favourably modelled stage distribution at first screening examinations, the inaccuracies in the mortality predictions

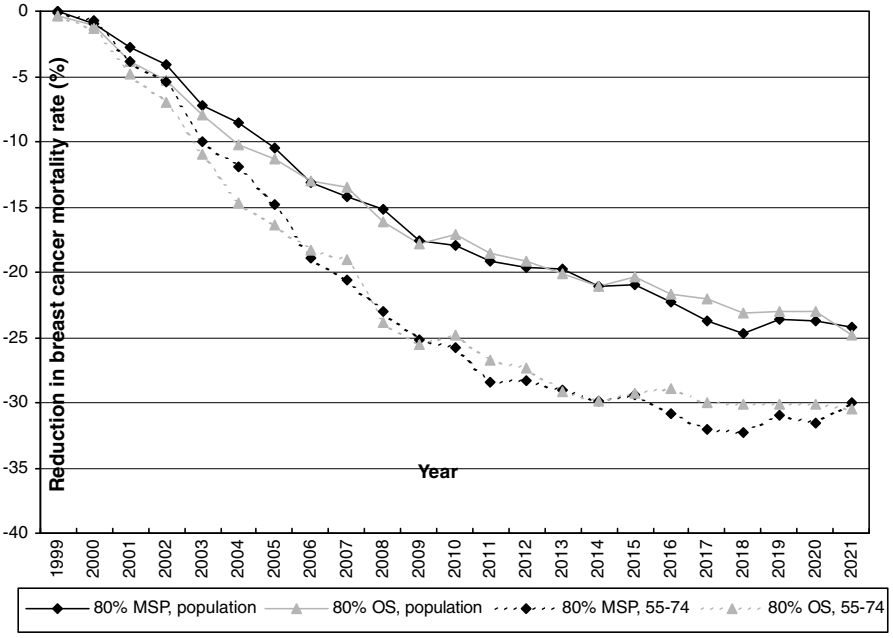

Fig. 2 – Annual reduction in the breast cancer mortality rate, relative to a situation without screening.

Table 3 – Costs of diagnostics and treatment per unit (€)

Screen invitation	1.2
Screen mammography	138
Diagnostic mammography	171
Opportunistic mammography	171
Imaging diagnostics	114
Minimal invasive diagnostics	653
Clinical breast examination	19
Sentinel node procedure	3313
Tumorectomy without radiotherapy	7126
Tumorectomy with radiotherapy	9791
Mastectomy without radiotherapy	3684
Mastectomy with radiotherapy	6410
Excision axillary lymph nodes	4904
Chemotherapy	1796
Hormonal therapy	989
Follow-up, first year	220
Follow-up, other years	156
Palliative treatment	21,417

Costs in Swiss Francs (CHF) were recalculated in Euro (€), using a currency exchange rate of 1.66 (June 2007).

Table 4 – Number of diagnostics associated with 1 mammogram, per screening modality

1 mammogram, MSP	0 clinical breast examinations 0.04 imaging diagnostics (MRI, ultrasound) 0.02 minimal invasive diagnostic examinations
1 mammogram, OS	2.9 clinical breast examinations 0.5 imaging diagnostics (MRI, ultrasound) 0.004 minimal invasive diagnostic examinations
1 diagnostic mammogram, outside screening	5.0 clinical breast examinations 0.2 imaging diagnostics (MRI, ultrasound) 0.1 minimal invasive diagnostic examinations

Abbreviations: mammography screening programme (MSP), magnetic resonance imaging (MRI), opportunistic screening (OS).

due to lack of fit between modelled and observed breast cancer were likely to be small.

Our study supports the findings of Neeser et al.[12] that in Switzerland, MSP is cost-effective compared to OS. By assuming a larger screening-related breast cancer mortality reduction than Neeser et al. (25% annually, instead of 15%), and by taking into account cost-savings related to palliative care, we expect that the incremental cost-effectiveness of MSP opposed to OS would be substantially more favourable than €53,677 per LYG[e] (starting screening at age 50), as predicted in the above-mentioned study.

Nevertheless, the cost-effectiveness ratio (CER) of breast cancer screening in Switzerland was high compared to other countries. The 3% discounted CER of programme-based screening, targeting women aged 50–69 years, varied between €2207 per life year gained (LYG) in the Netherlands[9] and €13,458 per LYG in Finland.[e,8] The predicted 3% discounted CER in Switzerland of €11,512 was in line with the Finnish estimate. The 5% discounted CERs of MSPs in various European countries and Australia ranged from €2650 to €8300 per LYG.[45] The corresponding Swiss prediction of €17,141 was higher than these estimates, even after correction of these estimates for inflation with

[e] Costs in US dollars were recalculated in Euro using a currency exchange rate of 0.71 (October 2007).

Table 5 – Predicted effects, costs and cost-effectiveness of opportunistic (OS) and mammography screening programme (MSP) scenarios with varying participation rates, compared to a no-screening scenario, 3% discounted

	Sc 0 No screening	Sc 1 40% OS	Sc 2 80% OS	Sc 3 80% MSP	Sc 4 60% MSP 20% OS	Sc 5 40% MSP 40% annual OS
Effects						
Life years (N)	21,290,900	+16,900	+33,700	+34,000	+33,925	+37,950
QALYs (N)	21,239,159	+15,656	+31,161	+31,506	+31,547	+35,179
Costs (x € 10^6)						
Screening	0	+250	+500	+406	+430	+680
Diagnostics	269	+153	+305	−5	+72	+304
Primary treatment	421	+17	+34	+34	+34	+36
Adjuvant treatment	41	−1	−2	−2	−2	−2
Follow-up	113	+7	+15	+15	+15	+16
Palliative care	395	−29	−57	−57	−57	−64
Total costs (x € 10^6)	1,239	+398	+796	+391	+492	+971
Cost-effectiveness (€)						
Costs per life year gained	-	23,547	23,617	11,512	14,507	25,584
Costs per QALY gained	-	25,418	25,541	12,424	15601	27,599

To calculate cost-effectiveness, the difference in costs between the scenario without screening (scenario 0) and the scenarios with screening (1–5) were divided by the difference in effects. All effects and costs were rescaled to a population of 1,000,000 women, and calculated over the whole lifespan of the simulated cohort. The results of the opportunistic screening scenarios were presented for the baseline model variant only.

Abbreviations: opportunistic screening (OS), mammography screening programme (MSP), quality-adjusted life year (QALY).

(harmonised) consumer price indices[46,47] (corrected CERs: between €3557 and €11,962 per LYG). Opportunistic breast cancer screening in Switzerland was comparably cost-effective as decentralised breast cancer screening in the USA: €23,617 per LYG in Switzerland versus €24,140 per LYG[44] in the USA (the latter was quality-adjusted and based on screening women in the age of 50–75 years; both 3% discounted).

The relatively unfavourable cost-effectiveness ratio of mammography screening is related to the health care costs in Switzerland, which are among the highest in Europe. The estimated costs of a programme-mammogram, which were in line with the previous Swiss estimates,[12] were circa 2.5 times higher than, for instance, in the Netherlands. Reducing these costs to Dutch cost-levels (€50[19] instead of €138) improved the 3% discounted CER of MSP to €3967 per LYG, which is on the same level as the CER of mammography screening in other western countries. A 50% reduction in the use of imaging examinations that are done in combination with an opportunistic mammogram could lower the CER of OS from €23,617 to €20,971 per LYG. A further 50% reduction of the costs of an opportunistic mammogram would decrease the CER to €13,550 per LYG.

Without data on breast cancer treatment and with limited data on OS, the assessment of the cost-effectiveness of screening in Switzerland includes uncertainties. The costs of clinical breast examinations related to OS may have been overestimated, because we used the ratio between all reimbursed breast examinations and mammograms to estimate resource use, regardless whether the clinical breast examination was indeed related to the mammogram. Costs of diagnostics may have been underestimated, because only health insurance-reimbursed costs could be included. Screening-related examinations done without seeking reimbursement and investigations performed in an in-patient setting could not be accounted for. The costs of treatment were based on Dutch data from 1991,[36] which likely have increased in later years. Indirect costs of screening, such as the additional health care costs made if a woman is saved by mammography, costs that would be necessary to increase screening participation and personal time costs were not included in the analysis.

As the model was calibrated with breast cancer and screening data from Vaud, the extrapolation of the results to the whole of Switzerland may involve some uncertainties. Mammography screening practice and quality, and possibly, breast cancer treatment varies across the country.[48] Nevertheless, it is unlikely that the natural history of breast cancer differs much between cantons, because such differences were also small between the Swiss model and, for instance, the Dutch screening evaluation model.[35] The baseline, optimistic and pessimistic scenarios for test sensitivity of OS reflected variations in opportunistic screening 'quality'. It might be argued that the performance of OS will be lower than MSP, related to less 'mammographic experience' of radiologists who work outside a programme, less possibility of discussion and feedback between screening, diagnostic and treatment disciplines, less (specific) training of radiologists and technicians, a lower number of readings and lower technical quality control.[16,49] A recent Danish study showed that programme-mammograms were considerably more sensitive than those performed opportunistically.[50] Improved performance of OS may be plausible as well, in particular when other imaging

Table 6 – Predicted effects, costs and cost-effectiveness for an optimistic, baseline and pessimistic model variant of OS, assuming a 25% lower, similar and a 25% higher false-negative rate of OS compared to MSP, participation rate 80%, 3% discounted

Model Variant	No screening	80% OS Optimistic	80% OS Baseline	80% OS Pessimistic
Effects				
Breast cancer deaths (N)	18,421	−2,762	−2,658	−2,542
Life years (N)	21,290,900	+35,000	+33,700	+32,300
Quality-adjusted life years (N)	21,239,159	+32,430	+31,161	+29,889
Total costs (x € 10^6)	1,239	+793	+796	+798
Cost-effectiveness (€)				
Costs per life year gained	-	22,671	23,617	24,707
Costs per quality-adjusted life years gained	-	24,467	25,541	26,700

To calculate cost-effectiveness, the difference in costs between the scenario without screening and the scenarios with screening (the optimistic, baseline and pessimistic model variant) were divided by the difference in effects. All effects and costs were rescaled to a population of 1,000,000 women, and calculated over the whole lifespan of the simulated cohort.
Abbreviations: opportunistic screening (OS), mammography screening programme (MSP).

diagnostics are used in combination with mammography. For instance, a review of breast cancer cases detected by opportunistic screening in Austria showed a favourable tumour stage distribution, with T2+ tumours only comprising 10% of all breast cancer cases.[51] This could be related to the fact that women aged 35 and older are screened and to the average screening interval of 16 months, but also to additional diagnostics, such as breast ultrasound, that are performed in combination with mammography in 64% of the cases. Studies comparing the performance of mammography between countries with organised screening and countries with opportunistic screening showed no differences between the two screening modalities in the detection of larger-sized tumours[49] or in the prognostic characteristics of invasive screen-detected and interval tumours.[52] A comparison between centralised and decentralised screening projects with in the European Breast Cancer Network neither showed differences in performance indicators.[53] These studies, however, did not account for specific breast cancer and screening characteristics (e.g. screening interval and screening age) between the various countries. Within Switzerland, cantonal differences in screening outcomes indicate that the performance of mammography varies regionally. For example, in Valais, OS resulted in a slightly more favourable prognostic profile than MSP, which might indicate that the test sensitivity of OS was better than that of MSP.[32] On the contrary, in Vaud, no differences in prognostic profile were observed between MSP and OS, which might indicate that the two screening modalities have a similar test sensitivity in this canton.[32] Although the hypothetical model variants of a 25% lower, similar and a 25% higher false-negative rate of OS compared to MSP are chosen rather arbitrarily, these scenarios do reflect likely variations in screening performance across Switzerland and the way they influence screening effects. Higher or lower false-negative rates of OS might be possible, but the true performance of opportunistic screening is difficult to assess. Several screening scenarios with varying participation rates and screening intervals were analysed to account for differences in screening practice across Switzerland. An 80% population coverage by OS was not considered a likely representation of current or future screening practice, in particular in a decentralised health care setting.[53] Several organised programmes, however, reach participation rates around 80%.[34] The actual breast cancer mortality reduction in the population, to be obtained by OS, is therefore likely to be smaller than that of MSP, and lower than the 13% (80% OS) predicted in our study.

Although the analysed scenarios were less cost-effective than breast cancer screening in other European countries, they were cost-effective according to WHO guidelines, which defined a CER smaller than the GDP per capita as 'very cost-effective' and a CER that is one to three times the GDP per capita as 'cost-effective'[7] (GDP per capita in Switzerland approximately €35,000[54]). However, strong improvements can be obtained if the use of imaging diagnostics would be diminished and costs were decreased. A centralised screening centre would enhance the possibilities of multiple readings, discussion and feedback, which should increase the screening volume and performance. It would also enable a more effective use of equipment and a faster acquisition of work-up diagnostics. Furthermore, continuous quality control and evaluation of screening could ensure that maximum benefits are obtained at reasonable costs.

5. Conclusion

Both organised and opportunistic screening are predicted to be effective in reducing breast cancer mortality in Switzerland. However, the costs of opportunistic screening per life year gained were twice those of organised screening: € 23,617 versus € 11,512. For opportunistic screening to become equally cost-effective as organised screening, costs and use of additional diagnostics should be reduced.

Conflict of interest statement

None declared.

Table A1 – Model parameters on natural history of breast cancer and screening

Mean duration (years) of screen-detectable preclinical stage by age	Age+			
Stage	40	50	60	70
Preclinical DCIS	5.2	5.2	5.2	5.2
Preclinical T1A (diameter ⩽ 5 mm)	0.2	0.3	0.4	0.5
Preclinical T1B (diameter 6–10 mm)	0.4	0.6	0.9	1.1
Preclinical T1C (diameter 11–20 mm)	1.1	1.4	2.1	2.6
Preclinical T2+ (diameter > 20 mm)	0.6	0.8	1.2	1.5

Long-term relative survival by clinical stage and age	*Stage*								
Age	DCIS	T1AN–	T1AN+	T1BN–	T1BN+	T1CN–	T1CN+	T2+N–	T2+N+
40	1.000	0.853	0.676	0.809	0.595	0.712	0.435	0.508	0.195
50	1.000	0.866	0.701	0.826	0.623	0.734	0.467	0.540	0.220
60	1.000	0.851	0.671	0.807	0.588	0.707	0.425	0.500	0.181
70	1.000	0.854	0.676	0.810	0.594	0.712	0.432	0.507	0.187

Sensitivity of mammography by stage, age ⩾ 50 years	Study variant			
Stage	MSP	OS, optimistic model variant A	OS, baseline model variant B	OS, pessimistic model variant C
Preclinical DCIS	80%	85%	80%	75%
Preclinical T1A (diameter ⩽ 5 mm)	70%	77.5%	70%	62.5%
Preclinical T1B (diameter 6–10 mm)	75%	81.25%	75%	68.75%
Preclinical T1C (diameter 11–20 mm)	80%	85%	80%	75%
Preclinical T2+ (diameter > 20 mm)	100%	100%	100%	100%

Reduction in risk of dying of breast cancer by stage at age 50		
Stage	Reduction in risk, N–	Reduction in risk, N+
Preclinical DCIS	100%	100%
Preclinical T1A (diameter ⩽ 5 mm)	86.6%	70.1%
Preclinical T1B (diameter 6–10 mm)	82.6%	62.3%
Preclinical T1C (diameter 11–20 mm)	73.4%	46.7%
Preclinical T2+ (diameter > 20 mm)	54.0%	22.0%

Quality of life; durations and utilities		
Health stage	Duration[30]	Utility[30]
Terminal illness	1 month	0.712
Palliative therapy + chemotherapy	4 months	0.469
Palliative therapy + radiotherapy	1 month	0.419
Palliative therapy + surgical therapy	5 weeks	0.383
Palliative therapy + hormonal therapy	14 months	0.337
Initial chemotherapy	6 months	0.283
Initial radiotherapy	2 months	0.197
Initial surgery	2 months	0.133
Initial hormonal therapy	2 years	0.180
Excision lymph nodes	1 month	0.100
Sentinel node procedure	1 month	0.100
Disease-free 2 months – 1 year after mastectomy	10 months	0.156
Disease-free 2 months – 1 year after breast saving theraphy	10 months	0.086
Disease-free > 1 1year after mastectomy	1 year	0.053
Disease-free > 1 1year after breast saving theraphy	1 year	0.040
Screening attendance	1 week	0.006

Abbreviations: ductal carcinoma *in situ* (DCIS), diameter ⩽ 5 mm lymph node negative (T1AN–), diameter 6–10 mm lymph node negative (T1BN–), diameter 11–20 nm lymph node negative (T1CN–), diameter > 20 mm lymph node negative (T2+N–), diameter ⩽ 5 mm lymph node positive (T1AN+), diameter 6–10 mm lymph node positive (T1BN+), diameter 11–20 mm lymph node positive (T1CN+), diameter > 20 mm lymph node positive (T2+N+).

Acknowledgements

This study was funded by the Swiss Cancer League and Onco-Suisse. The authors are grateful to Prof. Levi (Vaud Tumour Registry) for providing pre-screening cancer registry data and for his contribution to the study design, and to Dr. Bouchardy (Geneva Tumour Registry), for pre-screening cancer registry data. Dr. Beck, Mr. von Rotz (CSS Health Insurance Company) and Dr. Guetg (SantéSuisse) are also acknowledged for their most helpful advice and provision of health insurance data.

Appendix 1

See Table A1.

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