

Mammography screening in Switzerland: limited evidence from limited data

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Summary

Questions under study: In Switzerland controversy exists on how to summarise the evidence on the efficacy and effectiveness, as well as adverse effects, of mammography screening, and breast cancer mortality trends are often discussed in the context of the impact of mammography.

Principles/methods: Single-study publications, meta-analyses, and reports by international expert groups on mammography screening are reviewed. Breast cancer mortality trends from 1970–2000 are reported and discussed in the context of the Swiss screening situation.

Results: In Switzerland breast cancer mortality rates for female Swiss nationals aged 50–79 years fell between 1990 and 2000 by some 25% in all language regions. The data from randomised studies in large populations in several countries with well organised mammography programmes prompt the conclusion that participation in organised screening programmes with rigorous quality standards reduces breast cancer mortality. The achievable long-term reduction in breast cancer mortality ranges from 5–20% in the target population provided that appropriate diagnostic investigation and treatment are available. To achieve this in Switzerland 830 to 3300 women need to be invited to screening for ten years to prevent one death

from breast cancer. The risk-benefit profile of mammography screening is likely to be less favourable if mammographies are performed outside the context of organised screening programmes. In Switzerland we are now confronted with growing regional disparities in access to screening mammography which is under systematic quality control.

Conclusions: The decrease in breast cancer mortality in Switzerland is most probably due to treatment developments and changes in cause-of-death coding. Public health measures in Switzerland should aim at regulating quality control for screening mammography, monitoring mammography use and improving the information on mammography available to women. For an evidence-based decision regarding health insurance coverage of screening mammography in 2007, large gaps need to be filled. The current coexistence of systematic screening programmes and opportunistic screening, with distinct regional differences, provides a unique opportunity for research into the merits and drawbacks of the two approaches.

Key words: *mammography; breast cancer; screening; public health*

Introduction

Breast cancer is a significant public health problem worldwide [1] and, with about 1500 deaths annually in the years 1990 to 1999 [2], it is the most common cause of cancer mortality among women in Switzerland. In the absence of effective prevention or curative treatment regardless of the diagnostic stage, early detection remains an essential option in reducing the physical and psychological burden of breast cancer.

Since 1990 and despite rising trends in breast cancer incidence, breast cancer mortality rates have started to decline in the US and other indus-

trialised countries [1, 3–5]. In January 2000, the review by Gøtzsche and Olsen in the *Lancet* triggered intense debate on the effectiveness of mammography screening [6]. They dismissed the results of the majority of the randomised trials of mammography screening and claimed that mammography is ineffective. This affected impending decisions in Switzerland on systematic mammography. Since then a number of authors and organisations have re-evaluated the studies and summarised the evidence on the efficacy of mammography screening (table 5) [7–15].

In this article we attempt to clarify the definitions used in discussing mammography screening, review the evidence on efficacy and effectiveness, discuss adverse effects and discuss the Swiss situation with regard to breast cancer mortality and access to mammography screening. In this way we hope to shed light on key issues relevant to the dis-

cussion of screening mammography and to clarify what the public health community, especially in Switzerland, should and should not expect from screening mammography in general and from organised mammography screening programmes specifically.

What is meant by mammography screening?

As this review discusses screening mammography only, a clear-cut distinction is necessary between screening and diagnostic mammography according to the following definitions.

Screening mammography

A) Mammography screening programme or systematic early detection of breast cancer using mammography

Systematic early detection of breast cancer using mammography means a quality-assured programme with systematic periodic invitation of all women in a particular age group (in the target group) to mammography examination that is cost-free at the point of delivery. Subsequently, the terms “systematic mammography”, “mammography screening programme” and “organised mammography programmes” will be used interchangeably. Here one should note that organised screening programmes comprise six specific characteristics (table 1) ([9], p. 47).

B) Opportunistic mammography screening

This means individually chosen access by asymptomatic women to a mammography examination that is not a response to an invitation in the

context of a mammography screening programme. Accordingly, quality assurance aspects (that are part of a mammography screening programme) are not uniformly regulated or documented. Also, comprehensive and cost-free access for all women – regardless of social or economic background – to mammography is not guaranteed.

Diagnostic mammography

By diagnostic mammography we mean the use of mammography x-ray examinations to determine whether a breast tumour is present in a woman having symptoms of, or a predisposition for, breast cancer.

Other breast cancer screening methods

Systematic mammography for early detection of breast cancer has been investigated for over 30 years. Screening mammography has clearly documented limits of sensitivity and specificity (table 3) [10, 16–19]. More reliable technologies and methods for the early detection of breast cancer are the subject of intensive research efforts, but so far no alternative method has been sufficiently well evaluated to justify a systematic population-based application [16, 20].

Table 1

Features of organised screening programmes (adapted from [9] p. 47).

Existence of an explicit policy, with specified age categories, method and interval for screening
Definition of a target population
Definition and existence of a clear responsibility (e.g. management team) for implementation
Definition and existence of a health care team for decisions and care
Definition and existence of a quality assurance structure
Existence of a method for identifying cancer occurrence in the target population (e.g. cancer registries)

Efficacy of screening mammography from randomised trials

The need for randomised trials

To establish the efficacy of any cancer screening programme we cannot rely on observational studies, as they are affected by a variety of biases and confounding factors that may distort comparisons [21–24]. The randomised controlled trial with mortality as the outcome is the only study design in which these biases can be eliminated [25]. The studies conducted so far have been designed to detect a reduction in cancer-specific mortality. Whether population-based early detection of can-

cer should prove its efficacy by a reduction in total mortality or by a reduction in cancer-specific mortality is a matter of ongoing debate [11, 12, 26, 27]. The study design implications of assessing the effect on all-cause mortality would be enormous. Starting in 1994, a large randomised trial to investigate several cancer screening options simultaneously will include more than 140 000 participants and rely on cancer-specific mortality after an expected follow-up period of 15 years [25].

Table 2

Definitions. Distinguishing efficacy, programme efficacy and population effectiveness (adapted from [79]).

Term	Definition
Efficacy	The extent to which a specific intervention, procedure, regimen or service produces a beneficial result under ideal conditions. Ideally, the determination of efficacy is based on the results of a randomised trial.
Programme efficacy	The extent to which a specific and specified series of multiple measures and procedures produces a beneficial result under ideal conditions. Ideally, the determination of programme efficacy is based on the results of a randomised trial.
Effectiveness	The extent to which a specific intervention, procedure, regimen, or service, when deployed in the field in routine circumstances, does what it is intended to do for a specified population.
Programme effectiveness	The extent to which a specific and specified algorithm of measures and procedures, when deployed in the field in routine circumstances, does what it is intended to do for a specified population.

Efficacy versus programme efficacy

Efficacy is commonly used to designate the effect, usually beneficial, estimated in well conducted randomised trials by comparing the outcome rates of the group receiving the new intervention with the rates in the group receiving the standard or no intervention. However, in the case of screening, efficacy reflects the combined effect of a sequence of procedures designed to achieve a reduction in mortality [23]: invitation to screening, screening procedure according to defined quality standards, follow-up examinations to confirm or refute a cancer diagnosis, and initiation and completion of adequate treatment. In contrast to results of randomised studies comparing different drugs, the efficacy achieved in randomised trials of screening procedures should be considered in the context of a specific health care system and of the treatment options available at the time when the trial was conducted.

To highlight this we might choose to call this “programme efficacy”, reflecting what might be achieved under ideal conditions in a specific health care environment (table 2).

Programme efficacy versus effectiveness

In addition, one needs to distinguish effectiveness from efficacy (table 2). Effectiveness refers to the benefits achieved in real-life implementation rather than in the context of a randomised trial, and can be estimated only from observational studies. It is commonly expected that the benefits in real life implementation will tend to be less than those achieved in randomised trials where conditions tend to maximise the effect of the intervention [28].

Estimates of the programme efficacy of mammography screening

In the last 4 decades, 8 large population-based and randomised studies on the efficacy of screening mammography have been conducted in several

countries, most notably the USA, Canada, Sweden and the United Kingdom, and a series of systematic reviews have been conducted to obtain a summary of the efficacy of screening mammography (table 5) [6, 10–12, 14, 23, 29, 30]. Unsurprisingly, the estimated relative risk for breast cancer mortality – comparing the trial groups systematically invited to mammography screening with the group not systematically invited – was influenced by the rationale and decision about which trials to include in calculating the summary relative risk. Reviews including most of the trials estimate a relative risk of death from breast cancer of between 0.71 and 0.79, corresponding to a mortality reduction of 21–29%. Solid evidence has therefore accumulated from randomised studies that systematic and regular invitation of women aged 50–69 to mammography examinations reduces breast cancer mortality. The best estimate of the magnitude of the reduction achieved in randomised studies is 25%, as summarised in 2002 by different expert meetings and the International Agency for Research on Cancer [23, 31]. This represents programme efficacy based on a comparison of women systematically invited to mammography with those not systematically invited. This is likely to be an underestimate of the mortality reduction achieved for women who actually participate in mammography screening, since not all those invited will undergo mammography and not all those not invited will not undergo mammography [32].

These beneficial results were achieved in programmes incorporating tight quality controls. The challenge today is to evaluate the effectiveness of population-based breast cancer screening programmes in the routine health care environment. The impact on breast cancer mortality is a crucial indicator of effectiveness. In addition, early indicators of performance are needed to ascertain whether adjustments are required to a screening programme in the early stages or during continuous operation of the programme.

Effectiveness of population-based mammography screening programmes

Screening in Europe and other countries

In Europe the first organised screening programmes were begun between 1986 and 1989 in the Nordic countries and the United Kingdom [33]. These programmes were expanded to nationwide programmes in 1997 and 1996 in Sweden and the United Kingdom respectively. Additional nationwide programmes currently exist in Australia, Canada, Finland, France, Iceland, Israel, Luxembourg and the Netherlands. In most European countries regional programmes or pilot projects were implemented in the late 80s and 90s ([9] p. 49). Breast cancer screening in the USA is opportunistic, except for some programmes organised within health care plans. The majority of these programmes target women between the ages of 50 and 69 for screening [34].

Indicators of performance

Several indicators of performance can be used to predict the final reduction in breast cancer mortality that is likely to be achieved with the current level of screening performance. They also serve to keep to a minimum the rate of false-positive mammograms and the rate of unnecessary biopsies. Performance indicators include parameters such as participation rate, age-specific or age-standardised cancer detection rate, interval cancer rate, stage of distribution of screen-detected cancers, rate of advanced cancers, and the benign:malignant biopsy ratio. The European guidelines for performance give operational definitions and target values for various performance indicators and are the standard against which European mammography screening programmes, including the Swiss programmes, must be assessed [35, 36]. It is essential that mammography screening be conducted in a programmatic context to allow systematic assessment and continuous evaluation of performance indicators, and the availability of population-based cancer registry data for assessment of the rates of interval and advanced cancers is crucial.

Breast cancer mortality

A reduction in breast cancer mortality due to a population-based screening programme takes many years to evolve and is difficult to estimate. First, screening programmes usually take a long time to cover the whole target population. Second, programme effectiveness increases with the learning process among the staff involved. Third, national statistical data are diluted by deaths related to cancer diagnosed before the introduction of

screening and cancers diagnosed among women undergoing opportunistic screening. If record linkage to a cancer registry is available, "refined breast cancer mortality" can be calculated which excludes deaths among women in whom cancer was diagnosed before the start of screening or, depending on the registry's data collection, among women not actually screened. Fourth, even in the absence of screening effects breast cancer mortality trends may be affected by changes in the prevalence of breast cancer risk factors and hence in breast cancer incidence, by improvements in treatment, and by changes in coding of death certificates [37, 38]. A further complicating factor is that screening and treatment may not independently affect breast cancer mortality.

National breast cancer incidence and mortality trends have recently been analysed in 16 European countries [5]. Decreases in breast cancer mortality were observed in countries with national screening programmes implemented at an early stage, i.e. the UK, Sweden and the Netherlands. In some countries with screening programmes, decreases in mortality started before screening was introduced, and decreases also occurred in non-screened age groups and in some countries without national screening programmes. Nevertheless, more refined analyses have been conducted for individual countries and regions, in an attempt to differentiate between screening and other factors influencing mortality and to assess the impact on women invited to screening or actually screened. These analyses indicate a decrease in recent breast cancer mortality rates that is at least in part attributable to screening (see appendix on results in European countries).

What to expect from population-based screening programmes?

Studies on the effectiveness of population-based mammography screening programmes, including those based on modelling of breast cancer mortality from performance indicators, have so far resulted in estimates of 5–10% reductions in breast cancer mortality in the target population due to screening ([9] p. 134). The effects are expected to increase with the time elapsed since initiation of various national and regional programmes. The size of the maximum attainable reduction in breast cancer mortality will obviously not only depend on programme performance but also on factors such as the rate and quality of opportunistic screening before the programme started.

Adverse effects of mammography screening and cost-effectiveness

The vast majority of women undergoing mammography screening are healthy and therefore cannot derive a direct health benefit from screening. The major categories of possible adverse effects are, on the one hand, false-positive results and over-diagnosis, and, on the other, false-negative results and delayed diagnosis and treatment of breast cancer due to a false reassurance after negative or false-negative mammograms. These adverse effects relate to the limits of sensitivity and specificity for two-view mammography, which vary considerably in population-based settings with ranges for two-view mammography of 70–95% for sensitivity and 90–97% for specificity [17] (see table 3). Both test characteristics vary with the round of screening and characteristics of the women screened, and are lower in younger women. Additionally, reader characteristics [39, 40] also modify sensitivity and specificity, with volume being one aspect that is regulated in mammography quality control guidelines ([36] p. 153) and double-reading being recommended to increase both sensitivity and specificity.

False-positive results

The harm of false-positive mammograms relates to additional testing and invasive procedures which cause psychosocial stress as well as generating health care costs which would not have arisen in the absence of screening [41, 42]. Depending on the specificity achieved in screening mammographies in different settings and countries, a woman has on average a 3–10% likelihood of a false-positive result with each mammogram [17]. Because women are screened repeatedly, a woman's risk of having a false-positive mammogram increases over time, and one US study estimated that about half of the women screened annually in certain US settings will have a false-positive result after 10 mammograms [18, 43]. If we apply an estimate of 4–6% for the likelihood of a false-positive result of screening mammograms to a biennial screening schedule, we can expect that after 10 years (five rounds) of screening 18.5–26.5% of women screened will have had a false-positive mammogram necessitating further evaluation and 2.4–3.4% will have had a biopsy with a benign diagnosis (table 4). The potential for reducing recall and biopsy rates was shown in a recent comparison of mammography screening programmes in the United States and the United Kingdom [44]. The recall and open biopsy rates after screening mammograms were twice as high in the US as in the UK, but cancer detection rates were similar.

European research into strategies to decrease false-positive rates is ongoing and includes alteration of hormone use before the mammogram, screening during the luteal phase of the menstrual cycle, the establishment of explicit goals for recall

Table 3
Sensitivity and specificity of screening mammography for early detection of breast cancer in women aged 50–69 years estimated from randomised trials (based on three systematic reviews [10, 16, 17]).

Characteristic	Sensitivity	Specificity
Overall	70%–95%	90%–97%
Screening round		
First	somewhat higher	lower
Subsequent	somewhat lower	higher
Age		
younger (40–49)	lower	lower
older (50–69)	higher	higher

Table 4
Estimated outcomes among 10 000 women starting at age 50–55 to undergo mammography screening every two years for 10 years.

	biennial (5 mammographies)
Women with 1 or more mammograms needing additional evaluation ¹	1850–2650
Women with 1 or more benign biopsies (needle or open) ¹	240–340
Women who would have developed breast cancer regardless of screening ²	200
Women who are diagnosed with ductal carcinoma in situ ³	50
Women who die of breast cancer when no screening is performed ²	60
Women who will not die of breast cancer due to mammography screening ⁴	3–12
Number needed to invite to screen for ten years to prevent one death due to breast cancer	833–3333

The following assumptions were used where indicated:

- ¹ For the occurrence of positive mammograms and of performed biopsies we assumed a false-positivity of screening mammography of 4–6% and a biopsy rate of 0.8–1% (first round) and 0.4–0.6% (subsequent rounds) [19, 35]. The estimates of the number of women with a positive mammogram were rounded to the nearest 50.
- ² In the 50–55 age group an age-specific breast cancer incidence of 200 per 100 000 women and an agespecific breast cancer mortality rate of 60 per 100 000 were assumed based on weighted averages of the 45–54, and 55–64 age-specific rates available from the International Agency for the Research on Cancer (in Globocan [www.iarc.fr]).
- ³ This is based on Fletcher's review [52], and assuming that ductal carcinoma in situ detected in mammography screening is of the order of 25% of the breast cancers that would have developed regardless of screening.
- ⁴ Based on a reduction of breast cancer deaths due to mammography screening for real-life implementations estimated to be between 5 and 20% [67].

Table 5

Systematic reviews of randomised trials of screening mammography among women over 50 and efficacy estimates for follow-up of at least 10 years.

Author of study and year of publication	Included trials	Methods for meta-analysis	Relative risk of breast cancer mortality (95% confidence interval)
Nystrom et al. 1993 [29]	All trials conducted in Sweden	Analysis of pooled individual participant data	0.71 (0.57–0.89)
Kerlikowske et al. 1995 [30]	Summary of 8 trials ¹⁾	Fixed effects	0.74 (0.66–0.83)
Gøtzsche & Olson 2000 [6]	Malmö and Canada (all other excluded)	Fixed effects	1.04 (0.84–1.27) *
Gøtzsche & Olson 2001 [11, 12]	Malmö and Canada (all other excluded)	Fixed effects	0.94 (0.77–1.15) **
Nystrom et al. 2002 [14]	All trials conducted in Sweden	Analysis of pooled individual participant data	0.79 (0.70–0.89)
Humphrey et al. 2002 [10]	Summary of 8 trials ¹⁾	Bayesian random-effects model	0.78 (0.70–0.87)
IARC review [23]	All 8 trials plus the Finnish national programme are described ([23] p. 93) but quantitative summaries are based on the Swedish trials and the Finnish programme	Presumably fixed effects	0.75 (0.67–0.85)

* Results only reported for all age groups combined: Malmö study recruited women aged 45–49, and the Canadian trials women aged 40–59.

** Results for women age 50 or over.

¹⁾ The 8 trials include: Health insurance plan study in New York, Canada 1 and Canada 2 study, Edinburgh study, Göteborg study, Stockholm study, the two-county study in Kopparberg and Ostergötland, the Malmö study (Malmö I).

rates in a programmatic context, the availability of a baseline mammogram and the training of radiologists in the interpretation of screening mammograms ([9] p. 144, and [18]).

Overdiagnosis

Overdiagnosis refers to the detection of cancers that would never have been found were it not for the screening test. These cancers cause unnecessary anxiety (associated with a diagnosis of potentially fatal disease) and unnecessary treatment. Estimates range from 5–25% of cancers detected at mammography representing an overdiagnosis ([9] p. 176, and [15]). Evidence supporting the concept of overdiagnosis stems from randomised trials where an elevated breast cancer incidence persists in the screened group, as well as from national breast cancer incidence data. Results from the Canadian National Breast Screening Study and incidence data from populations in which breast cancer screening has been implemented provide no evidence that the rising incidence rates of DCIS have been accompanied by a decrease in the incidence of invasive cancer. This is what would be expected if a substantial proportion of cases of DCIS were destined to progress to invasive breast cancer ([45], and [9] p. 149). Furthermore, many more breast cancers are found in autopsy studies than will ultimately matter to women ([9] p. 146, and [18]). Ductal carcinoma in situ, which accounts for about 9–21% of cancers detected by screening in Europe, has an uncertain natural course but triggers invasive treatment including mastectomy [18, 46]. This is the likely explanation for the higher rate of mastectomies in the screened groups reported by Olsen and Gøtzsche [11, 12]. While detection of DCIS is probably one of the benefits derived from breast cancer screening, it remains unclear what proportion of DCIS actually exhibit

the potential to progress to invasive cancer. In the future, genomic analysis of breast lesions may improve the identification of subgroups with different potential for progression and allow targeted intervention.

Psychosocial consequences

Women who do or do not want to participate in mammography programmes may also experience adverse psychological, social, and financial consequences, and these must also be considered side effects [41, 42, 47, 48].

Earlier diagnosis means that women must live longer knowing that they have a potentially life-threatening disease. This is balanced only for some women by less intensive surgery and improved survival or cure. Thus the immediate negative impact on quality of life should be weighed against any prolongation of life [9, 10, 43, 49].

Necessity of adequate information

Ultimately decisions about screening should be made by the women themselves in consultation with their physician [50–52]. To make this decision, women need to be well informed concerning both the benefits and the potential adverse effects of screening mammography. Information must be offered in an understandable fashion [46, 52, 53]. Information pamphlets on mammography screening [54] often report the benefits of mammography screening chiefly in terms of relative risk reduction instead of absolute risk reduction and rarely explicitly state the limitations of mammograms; misconceptions about the likely results and benefits of mammography are therefore widespread [55, 56]. In a recent survey among women in four countries, including Switzerland, we found that a majority of women believed that screening prevents or reduces the risk of contracting breast

cancer, that screening at least halves breast cancer mortality, and that 10 years of regular screening will prevent 10 or more breast cancer deaths per 1000 women [56]. The contribution of high participation rates to the success of population-based mammography screening programmes must not bias the information that women are provided with [57].

Cost-effectiveness

Questions need to be answered regarding the efficient use of resources in comparison with other population-based measures in primary and secondary prevention [58, 59]. The estimated costs per year of life gained depend on the incidence of the disease, the quality of the screening programme, the participation rate achieved, and the form and cost structure of the healthcare system [59, 60]. If cost estimates for Germany are appli-

cable to Switzerland, then long-term mammography screening programmes are associated with costs of CHF 15,000 to 20,000 per year of life gained [59, 61]. For the USA the estimated costs are somewhat higher [58]. This is plausible, given that in the US annual mammography screening is recommended [62]. Even if the absolute cost estimates are not applicable to Switzerland, the US study by Coffield contains a useful comparison with other population-based healthcare measures. Colon cancer screening appeared to be more cost-efficient than mammography screening, but costs per quality-adjusted year of life gained in mammography screening were of the same order of magnitude as for cervical carcinoma screening [58]. For Switzerland, cost-effectiveness data on opportunistic mammography screening, which is at least in part paid by health insurance, are lacking.

The Swiss situation

Breast cancer mortality in Switzerland

As in other countries with and without established mammography screening programmes [1, 4, 5], breast cancer mortality rates in Switzerland in the 50-79 age group decreased by some 25% between 1990 and 2000 (figure 1). This decline began in all language regions well before the launch of systematic mammography screening programmes in the cantons of Vaud, Geneva and Valais in 1999 (figure 2). Several factors may have contributed to this decline.

First, part of the decline is attributable to changes in cause-of-death coding introduced by the switch from International Classification of Diseases (ICD)-8 (up to 1994) to ICD-10 (starting 1995) by the Swiss Federal Office of Statistics [38, 63]. The change to ICD-10 classification rules meant that reported cancer diagnoses on the death certificate less frequently resulted in attributing death to cancer as the primary cause, especially when other likely causes of death were recorded. The effect of this is obvious in the 80-and-over age group, with a fall of 15% from 273 per 100000 in 1994 to 232 per 100000 in 1995. If all the diagnostic information on the death certificates is included then the time trends before 1990 appear more steady and the decline since the early 1990s is less impressive (figure 1).

Second, treatment developments have reduced the risk of recurrence and improved outcomes in metastatic disease. Breast cancer mortality has decreased in women aged 35-49 as well as in all age groups combined. This is indicative of improved survival due to advances in treatment of the disease [5, 37], as Swiss oncologists rapidly adopted the conclusions of the Early Breast Cancer Trialists' Collaborative Group on prescribing tamoxifen in breast cancer treatment [64] (personal communication Monica Castiglione).

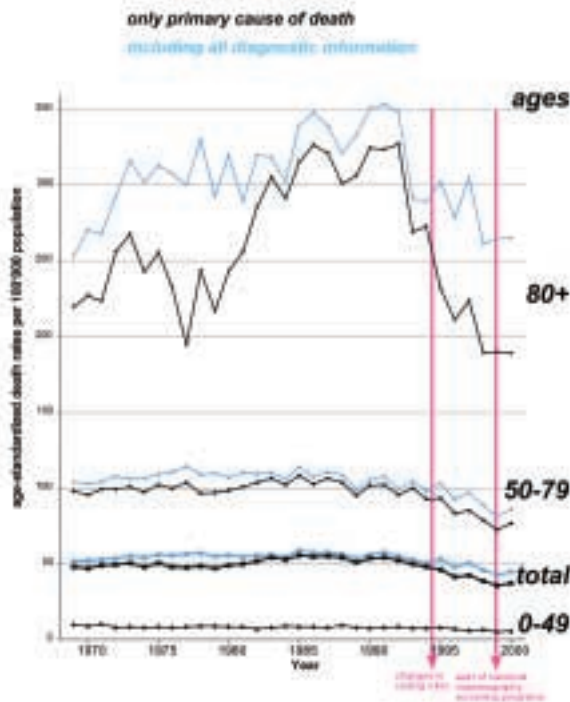
Third, opportunistic screening mammography in Switzerland has become more common. According to the 1997 national health survey, 47% (95% CI: 45-48%) of Swiss women over 40 had undergone at least one mammography examination. Although these proportions were comparable between urban and rural areas, wide differences were observed between age groups and linguistic areas [65]. While the figures represent an overestimation for screening mammography (approximately 25% of these mammograms were probably performed for diagnostic purposes), the differences between linguistic areas, most prominent for the 40-79 age group, are very probably influenced by prescription and attitudes of physicians to screening mammography [66]. The differences existed before the onset of the cantonal screening programmes in the cantons of Vaud, Geneva and Valais in 1999.

The first Swiss mammography pilot programme was established in 1993 and operated until 1998 in three districts of the French-speaking canton of Vaud for women aged 50-69 [35]. When it started the canton of Vaud had one of the highest self-reported mammography screening rates in Switzerland, with approximately 60% of ever-users and nearly 20% of annual users among 50-69-year-old women. The results from this first Swiss pilot programme supported the feasibility and acceptability of an organised mammography screening programme in the liberal Swiss healthcare system, where routine opportunistic screening exists. In view of the results of the pilot project the programme was expanded to the whole canton of Vaud and screening programmes were implemented in two additional Swiss cantons, Geneva and Valais, in 1999 [35].

The higher prevalence of mammography use in western Switzerland and the introduction of

Figure 1

Breast cancer mortality rates (per 100 000 female population) in Switzerland by age group and calendar year for Swiss nationals versus rates with mention of breast cancer irrespective of primary cause of death. Rates within age groups are age-standardised to the Swiss female population at the end of 1990. Arrow "changes in ICD coding rules" indicates the change from cause-of-death coding according to the International Classification of Diseases (ICD)-8 (up to 1994) to ICD-10 (starting 1995) and a simultaneous change in prioritising the primary cause of death by the Swiss Federal Office of Statistics. Arrow "start of cantonal mammography screening programmes" indicates the start of the mammography screening programmes in the cantons of Geneva, Vaud and Valais in the period 1998–2000.



Conclusions

After forty years in the conduct and interpretation of clinical trials, various international expert teams recently concluded that high quality mammography screening programmes offered to women aged 50 and over reduced breast cancer mortality by about 20–30%, the effect being dependent on compliance, coverage, prevalence of opportunistic screening, the quality of mammography and other factors [9, 14, 31, 62]. At the Milan Global Summit on Mammographic Screening in 2002 the international experts concluded that doctors and women can be confident that participation in organised screening programmes with rigorous quality assurance standards is of benefit with regard to breast cancer mortality, provided appropriate diagnostic investigation and treatment are available [31].

Evidence is accumulating from several countries that organised mammography programmes (implemented outside randomised studies) may reduce breast cancer mortality in the target age group. Experience in European countries suggests that, in the long term, a reduction of about 20% can be achieved in the target population, but achieved reductions may vary substantially from country to country, resulting in a wide range of programme effectiveness estimates of 5–20% [67, 68]. It is likely and plausible that long-term achievable effectiveness is lower than if mammography screening is opportunistic rather than anchored within an organised programme.

Crude analysis of trends in overall national breast cancer mortality is an inadequate tool for estimating the risk-benefit profile of mammography

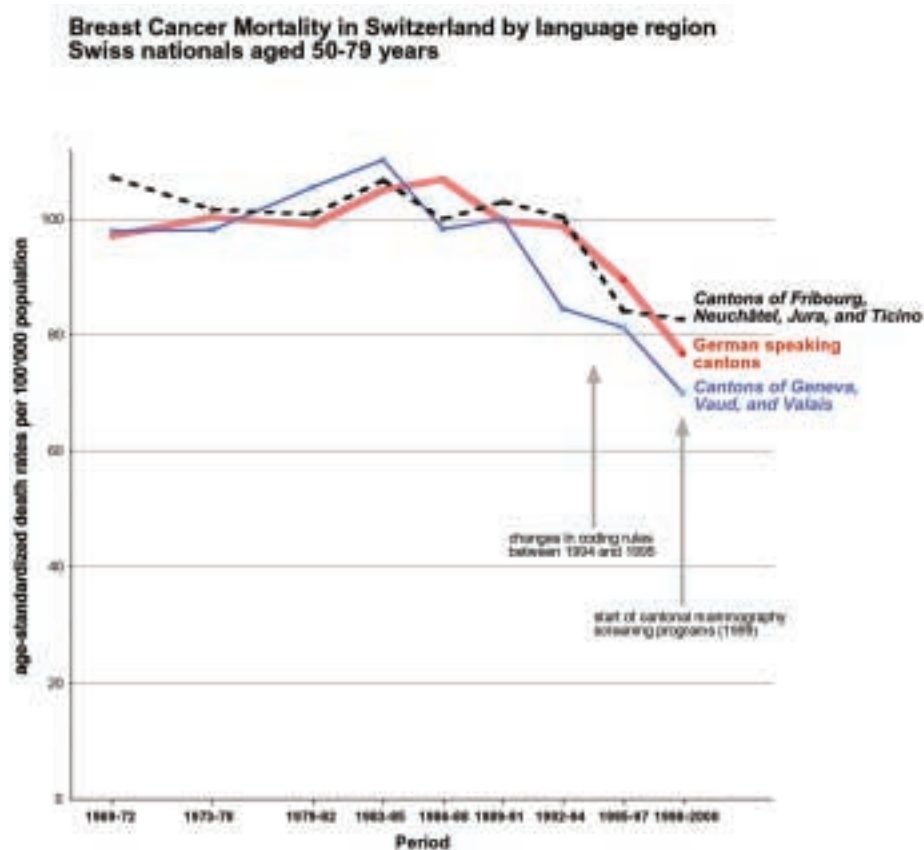
screening programmes in the cantons of Vaud, Geneva and Valais coincides with a somewhat earlier decrease and a lower breast cancer mortality rate in these three cantons in the years before the start of the programmes (figure 2). It may be speculated that the standard of care, including secondary prevention, for breast cancer is generally higher in cantons that were able to set up a population-based screening programme.

Finally, it is difficult to estimate precisely by how much cause-of-death coding, treatment developments and use of screening mammography have contributed to the observed decline in breast cancer mortality in Switzerland. We believe, however, that increased mammography since 1990 may have contributed only marginally and that the main factors were treatment developments and changes in cause-of-death coding.

Country-specific estimates regarding the benefit of screening mammography depend on the availability of data from organised screening programmes and cancer registries, in addition to national mortality statistics. Such data are not currently available for most of Switzerland where organised screening programmes exist in only three cantons – all in the French-speaking part of the country – and where nine cancer registries cover only 13 of the 26 cantons. The balance of beneficial and adverse effects of mammography screening is considered favourable in countries that have established tightly organised mammography programmes (e.g. the Netherlands) but is likely to be less favourable where mammography screening is opportunistic within a fragmented health care setup without a systematic quality control mechanism. In Switzerland we are now confronted with growing regional disparities in access to screening mammography under systematic quality control. These disparities are very likely to lead to growing differences in the net balance of beneficial and adverse effects of screening mammography in Switzerland. To correct these developments appropriate public health measures are needed and should aim at, first, regulating quality control for screening mammography, second, monitoring mammography use, and third, improving the information on mammography available to women from health organizations and physicians. Finally, health insurance cover for screening mammography will be re-evaluated by the Federal authorities in 2007, and we are likely, as in 1996, to be faced with a similar body of inadequate evidence on

Figure 2

Breast cancer mortality rates (per 100 000 female population) in Switzerland by language region and calendar time periods for Swiss nationals aged 50-79. Rates are age-standardised to the Swiss female population at the end of 1990. Calendar years were grouped in the following periods: 1969-72, 1973-78, 1979-82, 1983-85, 1986-88, 1989-91, 1992-94, 1995-97, 1998-2000; grouping before 1983 was restricted by availability of denominator (population) data. Arrow "changes in ICD coding rules" indicates the change from cause-of-death coding according to the International Classification of Diseases (ICD)-8 (up to 1994) to ICD-10 (starting 1995) and a simultaneous change in prioritising the primary cause of death by the Swiss Federal Office of Statistics. Arrow "start of cantonal mammography screening programmes" indicates the start of the mammography screening programmes in the cantons of Geneva, Vaud and Valais in the period 1998-2000.



which to decide for or against health insurance cover for screening mammography in Switzerland.

Important gaps in the evidence base should thus be filled by a coordinated research effort. The current situation, involving the co-existence of systematic screening programmes and opportunistic screening and distinct regional differences, provides a unique opportunity for research into the merits and drawbacks of the two approaches. Parallel to evaluation of the three organised screening programmes in the French-speaking parts of Switzerland, the same indicators of performance should be collected from cohorts of women undergoing opportunistic mammography screening in these cantons as well as in cantons that are not covered by organised programmes but operate population-based cancer registries. Indicators to be compared between the two situations include: (1) the percentage of false-positive mammograms and thus additional diagnostic procedures, (2) the percentage of cancers occurring among women within two years of a negative mammogram (interval cancers), (3) average costs of mammography

and additional diagnostic procedures, (4) specialisation and annual volume of mammography screening by physicians, and (5) women's knowledge of and satisfaction with mammography screening. A concerted and open-minded effort by physicians, radiology units, health insurances and other health institutions could thus lay the foundation for an evidence-based policy decision in 2007 in favour of an optimum mammography screening programme in the Swiss context. In the meantime, non-programmatic approaches to improve the risk-benefit profile of opportunistic mammography screening should be implemented in cantons without programmes, most importantly double-reading of mammograms and development and distribution of objective and comprehensible information material for women. These measures of quality assurance not only seem justified but are necessary in a country with a seemingly high rate of opportunistic screening on the one hand, and limited access to mammography screening programmes for over half the country.

Appendix: Results in European countries

United Kingdom

In the United Kingdom National Health Service a breast screening programme was introduced in England and Wales in 1988 for women aged 50-64, with mammography screening every three

years. The first round was not completed until 1995. Blanks et al. [69] compared observed national breast cancer mortality rates in England and Wales from 1990 to 1998 with those predicted from an age-cohort model based on mortality data

from 1971–1989, 6% (range 5.4–11.8%) of the observed 21% reduction in breast cancer mortality among women aged 55–69 was attributed to the first screening round, although this estimate is based on the assumption that treatment effects do not vary by age group. However, in the UK the benefit of tamoxifen has been reported to be greater for women aged 55–69 than for those aged 50–54 [15]. McCann and colleagues, using data from the East Anglian mammography screening programme, compared the distribution of prognostic factors in two groups of cancers: one diagnosed before, and one after the first invitation for screening [70]. They predicted that – by 2004 – the second round of screening in East Anglia should reduce breast cancer mortality by around 7% in women under 55 at diagnosis, and by around 19% in those aged 55–64, as a result of the more favourable tumour size, grade and node status of cancers in the invited study group.

Sweden

More refined data on changes in breast cancer mortality are available from the Swedish studies. No mammography or other breast-cancer screening took place in Östergötland and Dalarma (formerly called Kopparberg) before late 1977, but by 1988 the entire female population aged 40–69 had been invited to screening [71]. Comparisons of deaths from breast cancer diagnosed in the 20 years before (1958–1977) and in the 20 years after (1978–1997) the introduction of screening (1978–1997), between women aged 20–39 and 40–69, and between women undergoing screening and non-participants, allowed estimation of the direct screening effect and calculation of breast cancer mortality reduction restricted to screened women. There was a significant 44% reduction in breast cancer mortality in women aged 40–69 exposed to screening. Only 18% of the reduction in breast cancer mortality was attributed to non-screening factors, with a large percentage of the mortality reduction attributed to the screening programme itself. Jonsson et al. [72] compared counties from all of Sweden and estimated a refined 20% reduction in breast cancer mortality due to screening in women aged ≥ 50 after a mean follow up time of 10.6 years. By 1997, screening having been introduced nationwide, the effect on overall breast cancer mortality – not restricted to breast cancers diagnosed after the introduction of screening – was estimated to be 5–6%, close to the observed decrease in breast cancer mortality in the UK study [69].

The Netherlands

Breast cancer mortality is also in decline in the Netherlands. A national screening programme was first introduced in 1988/1989 in Nijmegen/Utrecht and gradually recruited women aged 50–69, and by 1997 all eligible women had been invited at least once [73, 74]. Broeders et al. [75] compared breast cancer mortality in Nijmegen,

where a screening pilot programme for breast cancer was introduced in 1975, to rates in the control city of Arnhem and in the Netherlands as a whole over a 20-year period. The results suggested a statistically non-significant 6–16% reduction in breast cancer mortality due to screening 20 years after the start of the programme in Nijmegen. Otto et al. [74] were able to link mortality to the specific initiation (month and year) of screening in more than 500 municipalities across the Netherlands in order to analyse screening-related changes in breast cancer mortality in the Netherlands as a whole. They observed a decline in non-refined breast-cancer mortality in the 55–74 age group which was significantly different from 1997 onwards, reaching a 20% reduction in 2001 which they attributed at least in part to the mammography screening programme.

Finland

The Finnish mammography screening programme was implemented in 1986. No obvious change in national trends in mortality from breast cancer corresponding to the screening programme was seen in the crude data, but a more refined analysis allowing identification of individual women by invitation-to-screening status and by date of invitation to screening demonstrated that the refined breast cancer mortality rate by 1992 was 24% lower among women invited to screening than among those not invited to screening [76, 77]. The data are supported by another, more recent Finnish investigation in Helsinki (population 0.5 million) where the breast cancer screening programme started in 1986. Antilla et al. [76] observed a 19% decrease in refined mortality in the screened cohort compared with the death rate in women of comparable ages in the non-screened reference cohort.

Florence Region

Paci et al. [78] linked data from the Tuscany tumour registry and the databank from the Florence City screening programme which invited female residents aged 50–69 over the period from 1990–1996 to undergo 2-view, high quality mammography every 2 years. All cases were followed up for vital status until the end of 1999, resulting in an average follow-up of 8 years after the start of the programme. The cumulative number of breast cancer deaths among cases was divided by screening and invitation status. The calculated incidence-based mortality ratio, comparing the mortality rate for two periods (1985–1986, 1990–1996; pre- and during screening), was 0.50 (95% CI: 0.38–0.66); the reduction was 41% among non-invited women and 55% among women invited for screening. The reduction from the reference period of –3.9 deaths per 10000 in the invited women (and the –4.4 per 10000 fewer deaths among women actually screened) indicates, when compared with the –2.8 death reduction in the non-invited, that about one third of the reduction in

women exposed to screening is due to the screening rounds and the other two thirds to other causes, including therapeutic advances.

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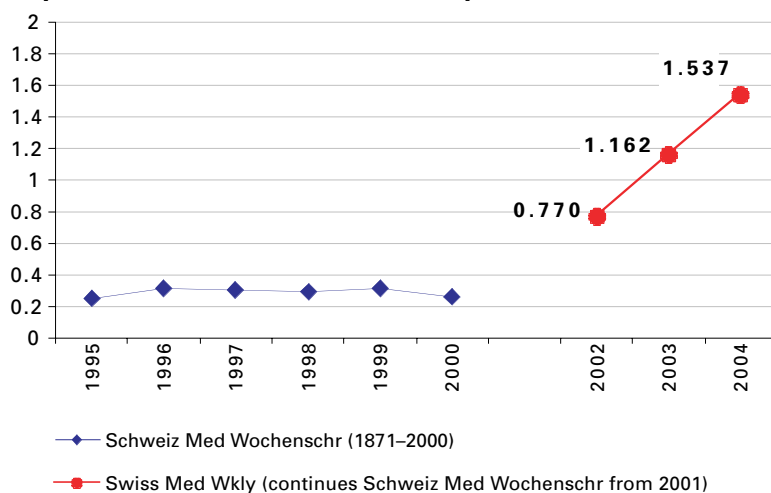
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