Original Article

Effectiveness of Population-Based Service Screening With Mammography for Women Ages 40 to 49 Years

Evaluation of the Swedish Mammography Screening in Young Women (SCRY) Cohort

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BACKGROUND: The effectiveness of mammography screening for women ages 40 to 49 years still is questioned, and few studies of the effectiveness of service screening for this age group have been conducted. **METHODS:** Breast cancer mortality was compared between women who were invited to service screening at ages 40 to 49 years (study group) and women in the same age group who were not invited during 1986 to 2005 (control group). Together, these women comprise the Mammography Screening of Young Women (SCRY) cohort, which includes all Swedish counties. A prescreening period was defined to facilitate a comparison of mortality in the absence of screening. The outcome measure was refined mortality, ie, breast cancer death for women who were diagnosed during follow-up at ages 40 to 49 years. Relative risks (RRs) with 95% confidence intervals (CIs) were estimated. **RESULTS:** There was no significant difference in breast cancer mortality during the prescreening period. During the study period, there were 803 breast cancer deaths in the study group (7.3 million person-years) and 1238 breast cancer deaths in the control group (8.8 million person-years). The average follow-up was 16 years. The estimated RR for women who were invited to screening was 0.74 (95% CI, 0.66-0.83), and the RR for women who attended screening was 0.71 (95% CI, 0.62-0.80). **CONCLUSIONS:** In this comprehensive study, mammography screening for women ages 40 to 49 years was efficient for reducing breast cancer mortality. ***Cancer*** **2011;117:714–22.** *© 2010 American Cancer Society.*

KEYWORDS: mammography, screening, breast cancer, mortality.

Consensus has been reached that mammography screening is efficient for women ages 50 to 69 years; however, the effectiveness of such screening for women ages 40 to 49 years still is questioned. Randomized controlled trials (RCTs) have revealed a significant effect for women aged ≥40 years.[1-4] Recommendations to invite women from age 40 years to screening based on these RCTs later were contested when meta-analyses and overviews that focused on women ages 40 to 49 years revealed no statistically significant effect (throughout this report, results are considered statistically significant at the 5% level).[5,6] However, both the Gothenburg trial and the Malmö trial reported significant mortality reductions among women aged <50 years at randomization.[7,8] A few studies have focused on screening for the group ages 40 to 49

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years. The Canadian National Breast Screening Study randomized women ages 40 to 49 years and invited them to 4 or 5 annual screens, but that study demonstrated no significant effect on breast cancer mortality.[9] In the Age trial, which is the only RCT that was designed to study this age group, women were randomized at ages 39 to 41 years,[10] and the results indicated a statistically nonsignificant 17% reduction in mortality. Few studies have investigated the effectiveness of service screening for the group ages 40 to 49 years. A study comparing breast cancer mortality in Swedish counties in which women ages 40 to 49 years were invited to screening versus breast cancer mortality among women in counties in which the same age group was not invited to screening indicated a statistically nonsignificant 14% reduction in mortality for the women who were invited to screening and were followed for 10 years.[11] A study in northern Sweden indicated a statistically significant 36% reduction in mortality for this age group.[12]

The European guidelines for quality assurance in breast cancer screening and diagnosis recommend offering service screening to women ages 50 to 69 years.[13] In the United States, the US Preventive Services Task Force (USPSTF) recently changed its guidelines and no longer recommends screening for women ages 40 to 49 years; instead, the USPSTF argues that screening for women in this age group should be an individual choice.[14] The objective of the current study was to estimate the effectiveness of service screening with mammography for the group ages 40 to 49 years on breast cancer mortality.

MATERIALS AND METHODS

Breast Cancer Screening Programs in Sweden

As early as 1974, the county council in Gävleborg decided to initiate a service-screening program with mammography. Between 1976 and 1983, RCTs on mammography screening were initiated in the cities of Stockholm, Malmö, and Gothenburg and in the counties of Östergötland and Dalarna (the WE trial). After publishing of the first results from the WE trial, the National Board of Health and Welfare in 1986 issued their guidelines recommending that the county councils invite women ages 40 to 54 years to screening every 18 months and women ages 55 to 74 years every second year. Thus, national service screening with mammography was initiated between 1986 and 1997. In 1987 and 1988, the guidelines were modified recommending that, in case of a lack of resources, county councils should focus on the group ages 50 to 74 years. Consequently, approximately 50% of the Swedish counties invited women aged $\geq$40 years, and the remaining counties invited women aged $\geq$50 years. Screening programs mostly included whole counties but included only parts of counties in some instances (referred to below as areas; in total, there were 34 areas).

Study Group and Control Group

The primary objective of the current study was to compare breast cancer mortality between areas that did and did not invite women ages 40 to 49 years to attend mammography screening. The study group included women who were living in areas that had service-screening programs for the group ages 40 to 49 years for at least 6 years during the study period between 1986 and 2005. The control group included women who were living in areas in which women ages 40 to 49 were not invited to attend service screening during the study period (Table 1). The study group and the control group constitute the Mammography Screening of Young Women (SCRY) cohort, which includes all Swedish counties. In 1990, there were 620,620 women in the group ages 40 to 49 years in Sweden.

Service-screening programs that invited women ages 40 to 49 years started between 1974 (Gävleborg) and 1997 (Gotland). Blekinge County only invited women aged $\geq$45 years; thus, women ages 40 to 44 years from that area were not included. In Gävleborg County, where service screening started early, women were included in the study group from the year when the service-screening program was adjusted to the Swedish guidelines, ie, 1997. In several programs, the age group that was invited changed over time (Table 1). Figure 1 provides a map of the areas for the control group and the study group.

Swedish Breast Cancer Screening Programs for Ages 40 to 49 Years in 1986 Through 2005

One-view or 2-view mammography was practiced, depending on the breast density of the individual woman. Some areas practiced 2-view mammography regardless of breast density, but 1-view mammography regardless of breast density was rare. Double reading of the mammograms was more common than single reading. The screening intervals varied between 18 months and 24 months and increased in most areas over the study period. Attendance rates varied between 80% and 90% but decreased over the study period in most areas. The recall rates varied between 2% and 4% with no obvious time trend.

Table 1. Composition of the Study Group and the Control Group: Period of Inclusion in the Control Group (No Screening of Women Ages 40-49 Years) and the Study Group (Screening of Women ages 40-49 Years)

Area	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Part of SG for ages 40-49 y																				
Dalarna	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG
Jönköping (Höglandet)	n/SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG
Kalmar	n/SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG
Västmanland	n/SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG
Jönköping (Jönköping)		SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG
Skåne (SoW)		SG	SG	SG	SG	SG	SG	SG	SG	SG	SG									
Örebro (SoE)		n/SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG
Skåne (SoE)		n/SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG								
Uppsala			n/SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG
Östergötland				SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG
Södermanland				n/SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG
Skåne (middle)				n/SG	SG	SG	SG	SG	SG											
Västernorrland					SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG
Norrbotten					SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG
Skåne (NW)						n/SG	SG	SG	SG	SG	SG									
Örebro (all other)							SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG	SG
Gävleborg												SG	SG	SG	SG	SG	SG	SG	SG	SG
Part of SG ages 45-49 y																				
Blekinge			n/s45	s45	s45	s45	s45	s45	s45	s45	s45	s45	s45	s45	s45	s45	s45	s45	s45	s45
Part of CG and then of SG																				
Gotland	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	SG	SG	SG	SG	SG	SG	SG	SG	SG
Jönköping (Habo, Mullsjö)	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	SG	SG	SG	SG	SG	SG	SG
Kronoberg	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG/SG	SG	SG	SG	SG	SG	SG
Part of CG																				
Vasterbotten	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG					
Västra Götaland (N Bohuslän)	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG				
Västra Götaland (So Bohuslän)	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG				
Halland	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG				
Västra Götaland (Skaraborg)		CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG			
Västra Götaland (N Älvsborg)			CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG		
Västra Götaland (So Älvsborg)				CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG
Värmland				CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG
Skåne (NE, Kristianstad)				CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG
Stockholm				CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	
Skåne (Malmö)					CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG
Jämtland					CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG
Västra Götaland (Göteborg)										CG	CG	CG	CG	CG	CG	CG	CG	CG	CG	CG

SG indicates study group; n/SG, not part of the SG at the beginning of the year; SoW, southwestern; SoE; southeastern; NW, northwestern; s45, part of the SG for ages 45-49 years only; CG, control group; N, northern; So, southern; NE, northeastern.

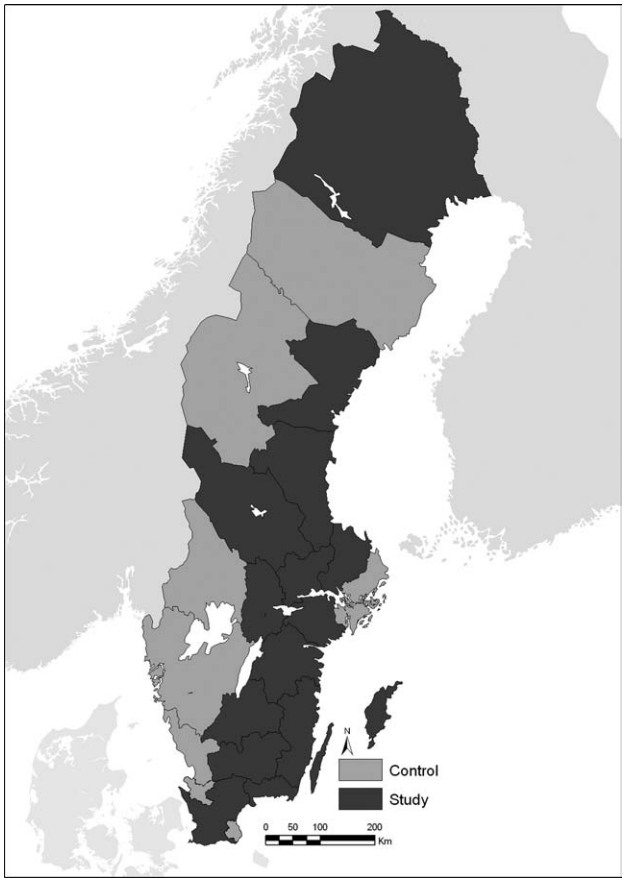

Figure 1. This is a simplified map of the areas that were included in the study group and the control group.

Refined Mortality, Follow-Up, and Definition of Breast Cancer

In every area, there was a cohort of women between ages 40 years (in 1 area, 45 years) and 49 years at the time of cohort entry. Women in the study group entered the cohort either at the time screening started or when they reached the lower invitation age (ie, 40 years except in 1 area). In the control group, women entered the cohort at a corresponding starting point or when they reached age 40 years.

The women were followed until the occurrence of an event (death from breast cancer), death from a cause other than breast cancer, or the end of follow-up (December 31, 2005). Person-years were calculated using a method similar to that used normally for cohort studies; however, because individual data were available only for women with breast cancer, person-years were calculated using aggregated population data. In some areas where the screening program changed during the study period, an earlier end of follow-up was chosen (Table 1). For the control group, follow-up periods were chosen so that both the average follow-up time and the average mid-calendar year of follow-up were similar in the control group and the study group (16 years and 1996, respectively). In both instances the average was weighed using population sizes as weights. The mortality measure used was refined mortality, which means that the events were breast cancer deaths among women who had a breast cancer diagnosis at ages 40 to 49 years. Thus, there was no upper age limit for an event except for that determined by the end of follow-up. A breast cancer death was defined as a death with breast cancer as the underlying cause according to the Swedish Cause of Death Register (International Classification of Diseases for Oncology Ninth Edition [ICD9] code 174 or ICD10 code C50). Only first primary breast cancers were included in the study. Relative risks (RR) were estimated based on breast cancer as the underlying cause of death.

Data Sources and Computer Program

Data on diagnosis and death were retrieved from the national Swedish Cancer Registry. Population data that were used in the calculation of person-years were supplied by Statistics Sweden. Information on the 34 area service-screening programs, including initiation of the program, invited age groups, and changes during the study period, was collected through a questionnaire. Individual screening information on invitation to and participation in the service-screening program preceding the breast cancer diagnosis were supplied by the screening centers for all breast cancer deaths. The software program R was used for statistical analyses (R Foundation for Statistical Computing, Vienna, Austria).[15]

Studied Exposures

In most studies, the exposure of interest has been *invitation* to screening. In the current study, 2 exposures were studied; *invitation* to screening and *attendance* to screening. Only invitation and attendance before diagnosis were of interest. During the first screening round, several women ages 40 to 49 years in the study group received a breast cancer diagnosis before the invitation to screening. Furthermore, not all women who were diagnosed at ages 40 to 42 years had been invited to screening. For the exposure *invitation*, an adjustment was made for those women. Similarly, the exposure of *attendance* was studied by adjusting for women who did not attend screening. The method described by Cuzick et al[16] was used for adjustment but was modified for application to a Poisson

distribution. This method also was used to adjust for contamination caused by short periods of screening of women aged <50 years in a few of the control areas. Without these adjustments, a bias toward no effect was expected.

Reference Period

A prerequisite for an unbiased comparison between a control group and study group is similar baseline mortality. We checked this by estimating RR for death from breast cancer during the period from 1970 to 1985, when screening had not begun. Five areas that covered 18% of the population could not be included in this calculation because of screening activities (eg, RCTs on mammography screening[5]) that took place before the start of their service-screening programs in 1986.

Lead Time Adjustment

Lead time may cause a bias, because women in the study group who would have been diagnosed after age 50 years without screening may have been diagnosed before age 50 years. This possible bias against screening was adjusted for by *adding* person-years to the study group. Screening activities before the start of follow-up, such as RCTs, also may cause lead time bias in the opposite direction because of an earlier diagnosis before the start of follow-up. We adjusted for this possibility by *subtracting* person-years from the study group.

The person-years that were added or subtracted corresponded to the number in the continuous age interval (50 − LT, 50) and in the time interval (S, S + LT), respectively, where LT is the estimated lead time, and S the start point. However, only the lead time for women who actually died from breast cancer can cause a bias. Therefore, the lead time was estimated for this group. The lead time for women ages 40 to 49 years who died from breast cancer reportedly was much shorter than the usual lead time for all women who are targeted or who have disease detected in a screening program.[11,12,17] In the current study, the lead time for women who died of breast cancer, which we estimated as the difference in the mean time from diagnosis to breast cancer death between the study group and the control group, was approximately 1 month. An alternative estimate based on 49 women from the RCT WE[4] was approximately 1 year.

Ages 40 to 44 Years and 45 to 49 Years

One area (Blekinge) that comprised 11% of the person-years in the study group invited only women aged ≥45 years. This may have caused a bias against screening, because breast cancer mortality increases with age. RR estimates were made for 2 age strata, women ages 40 to 44 years and ages 45 to 49 years, at diagnosis to avoid the influence of such bias. These RR estimates were weighted together to an unbiased RR estimate for women ages 40 to 49 years using the number of deaths in each age group as weights.

Stockholm County

Stockholm County contributed with 38% of the person-years to the control group and may differ from other control areas in terms of its big-city characteristics, eg, later childbirth and contamination from private screening.[18] Therefore, the RR estimates were calculated both including and excluding Stockholm. The average length of follow-up in years in the control group did not change when Stockholm was excluded, nor did the average mid-calendar year of follow-up.

Excess Mortality

Excess mortality-based RR estimates were made to validate the results based on breast cancer as the underlying cause of death.[12] The excess number of deaths was calculated at the group level (year and attained age) as the difference between the number of observed and expected deaths (all-cause mortality) among the women with breast cancer. The expected number of deaths was calculated as the product of the number of person-years among the women with breast cancer and the population total mortality. Thus, this measure is independent of the individual cause-of-death determination.

Number Needed to Screen

The number of women needed to invite to screening (NNS) between ages 40 years and 49 years to save 1 life was estimated by dividing the number of women invited by the number of lives saved. The number of lives saved (LS) was calculated as the difference between the observed number (O) of breast cancer deaths in the absence of screening and the expected number of breast cancer deaths in the presence of screening using the estimated RR for invitation to screening in women ages 40 to 49 years, so that LS = O−O*RR. Assume O is the observed number of breast cancer deaths in the control group during follow-up with a breast cancer diagnosis at ages 40 to 49 years during the first year, and let P be the number of women ages 40 to 49 years during that year. O also can be an approximation of the number of deaths from breast cancer diagnosed between ages 40 years and 49 years in the same

Table 2. Summary per Mammography Screening Area in the Study Group: Year Service-Screening Started Among Women Aged ≥40 Years at Invitation, Year Follow-Up Started, Number of Follow-Up Years, Number of Person-Years, and Cumulative Numbers of Breast Cancer Deaths (Total Number, Number Not Invited to Screening, and Number Not Attending Screening)

	Start of		No. of		Cumulative No. of Deaths		
Study Group	Service-Screening for Women Aged ≥40 y	Year of Follow-Up	Follow-Up, y	Person-Years	Total	Noninvited	Nonattending
Östergötland	1986[a]	1989	17	824,700	117	6	14
Dalarna	1986[a]	1986	20	715,223	69	5	9
Uppsala	1988	1988	18	669,237	74	20	10
Västmanland	1986	1986	20	635,196	71	14	9
Kalmar	1986	1986	20	599,819	64	16	10
Södermanland	1989	1989	17	543,979	61	16	9
Norrbotten	1990	1990	16	493,071	52	6	5
Västernorrland	1990	1990	16	477,759	46	8	7
Jönköping (Jönköping)	1987	1987	19	450,384	58	15	3
Örebro (SoE)	1987	1987	19	384,703	39	6	1
Jönköping (Höglandet)	1986	1986	20	266,994	29	NA	NA
Blekinge	1988[b]	1988	18	247,274	34	9	3
Gavleborg	1974	1997	9	235,425	23	4	7
Örebro (all other)	1992	1992	14	174,117	20	11	5
Skåne (middle)	1989	1989	6	148,550	10	7	0
Kronoberg	1999	1999	7	103,411	4	2	1
Skåne (SoW)	1987	1987	10	91,653	12	5	0
Skåne (NW)	1991	1991	6	79,728	7	2	1
Skåne (SoE)	1987	1987	11	59,446	8	3	1
Gotland	1997	1997	9	50,495	5	0	1
Jönköping (Habo, Mullsjö)	1999	1999	7	10,251	0	0	0
Total				7,261,415	803	155	96
Weighted mean			15.8				

SoE indicates southeast; NA, not available; SoW, southwest; NW, northwest.
[a] A randomised, controlled trial that included individuals aged ≥40 years preceded the start of screening.
[b] In Blekinge, the lower age of invitation was 45 years.

women, but then the corresponding population will be P/10, and the estimation will be NNS = (P/10)/LS. However, to reduce the standard error, instead, O was calculated for breast cancers diagnosed during the first 5 years of follow-up, resulting in the estimate NNS = (P/10)/(LS/5). These women were followed until the end of follow-up in the study (12-16 years), which resulted in 14 years on average. Because breast cancer death also can occur later, NNS may be somewhat overestimated.

RESULTS

By using the definition of refined mortality, there were 607 breast cancer deaths during 4.8 million person-years in the study group and 846 breast cancer deaths during 6.3 million person-years in the control group during the reference period (from 1970 to 1985; ie, before the start of service screening), resulting in an RR of 0.94 (95% confidence interval [CI], 0.85-1.05). For the study period (from 1986 to 2005), there were 803 breast cancer deaths during 7.3 million person-years in the study group (Table 2) and 1238 breast cancer deaths during 8.8 million person-years in the control group (Table 3), resulting in an estimated crude RR of 0.79 (95% CI, 0.72-0.86), (Table 4). The crude cumulative breast cancer mortality per 100,000 person-years is illustrated in Figure 2. The curves start to diverge after 3 years and continue to diverge throughout follow-up.

The RR estimate for the exposure invitation to screening, adjusted for women who were not invited to screening in the study group (Table 2) and for contamination in the control group (Table 3), was 0.74 (95% CI, 0.66-0.83). The RR estimate for the exposure attendance in screening, adjusted for nonattendance, was 0.71 (95% CI, 0.62-0.80). When Stockholm was excluded from the control group, the corresponding RR estimates were 3 or 4 percentage points lower. For the group ages 40 to 44, the corresponding RR estimates were 0.83 (95% CI, 0.70-1.00) and 0.82 (95% CI, 0.67-1.00) adjusted for women who were not invited and who did not attend, respectively; and, for the group ages 45 to 49 years, the RR estimates were 0.68 (95% CI, 0.59-0.78) and 0.63

Table 3. Summary per Mammography Screening Area in the Control Group: Year Service-Screening Started Among Women Aged ≥50 Years, Start of Follow-Up, Number of Follow-Up Years, Number of Person-Years, and Cumulative Number of Breast Cancer Deaths (Total and Contamination [Possibly Attended Screening])

	Start of		No. of		Cumulative No. of Deaths	
Control G roup	Service-Screening Among Women [AQ 13]Aged ≥50 y	Year of Follow-Up	Follow-Up, y	Person-Years	Total	Contamination
Stockholm	1989[a]	1989	16	3,384,107	453	
Skåne (NE, Kristianstad)	1989	1989	17	591,262	100	
Värmland	1993	1989	17	564,078	53	
Västra Götaland (So Älvsborg)	1991	1989	17	558,178	76	9
Västra Götaland (Göteborg)	1995[a]	1995	11	490,495	70	
Halland	1989	1986	16	480,948	80	
Västra Götaland (Skaraborg)	1989	1987	16	463,772	54	
Skåne (Malmö)	1990[a]	1990	16	434,767	59	5
Västerbotten	1995	1986	15	407,331	57	
Västra Götaland (So Bohuslän)	1986	1986	16	371,916	65	12
Västra Götaland (N Älvsborg)	1993	1988	16	320,267	45	
Jämtland	1996	1990	16	243,399	32	
Kronoberg	1990	1986	13	235,714	54	
Västra Götaland (N Bohuslän)	1986	1986	16	213,195	29	7
Gotland	—[b]	1986	11	60,638	8	
Jönköping	1989	1986	13	23,785	3	
Total				8,843,852	1238	33
Weighted mean			15.7			

NE indicates northeastern; So, southern; N, northern.
[a] A randomized, controlled trial that included women aged ≥40 years preceded the start of screening.
[b] In Gotland, the lower invitation age was never 50 years; instead, Gotland began screening in 1997 with a lower invitation age of 40 years.

Table 4. Summary of Results by Exposure and Age Group: Excluded Areas, Numbers of Breast Cancer Deaths, Person-Years in the Study Group and the Control Group, Relative Risks and 95% Confidence Intervals

		No. of Deaths Among Exposed		No. of Person-Years			
Exposure[a]	Excluded Area[b]	SG	CG	SG	CG	RR	95% CI
Ages 40-49 y							
Crude estimate (unadjusted)	—	803	1238	7,261,415	8,843,852	0.79	0.72-0.86
Adjusted for							
Invitation	—	619	1205	6,994,421	8,843,852	0.74	0.66-0.83
Attendance	—	523	1205	6,994,421	8,843,852	0.71	0.62-0.80
Invitation	Stockholm	619	752	6,994,421	5,459,745	0.71	0.63-0.81
Attendance	Stockholm	523	752	6,994,421	5,459,745	0.67	0.58-0.78
Ages 40-44 y							
Invitation	—	247	485	5,041,040	6,567,101	0.83	0.70-1.00
Attendance	—	217	485	5,041,040	6,567,101	0.82	0.67-1.00
Ages 45-49 y							
Invitation	—	372	720	5,071,256	6,211,523	0.68	0.59-0.78
Attendance	—	306	720	5,071,256	6,211,523	0.63	0.54-0.75

SG indicates study group; CG, control group; RR, relative risks; 95% CI, 95% confidence interval.
[a] Contamination was adjusted for in all RR estimates except the crude estimate.
[b] The Jonkoping Hoglandet area was excluded from the study group in the calculation of all estimates except for the crude estimate.

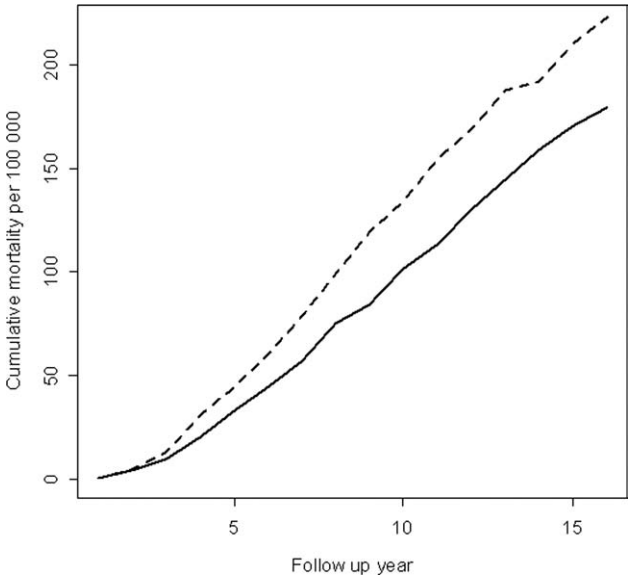

Figure 2. This chart illustrates the crude cumulative breast cancer mortality per 100,000 person-years. Solid line indicates the study group; dashed line, control group.

(95% CI, 0.54-0.75), respectively (Table 4). When these age group-specific RR estimates were weighted together to calculate the estimates for women ages 40 to 49 years, they did not differ from the unweighted RR estimates.

Adjustment for lead time for women who died from breast cancer decreased the RR estimates. With lead time at 1 month, the adjustment resulted in RR estimates <1 percentage point below those presented, whereas adjustment for a 1-year lead time resulted in estimates 5 percentage points below those presented.

The estimated NNS during a 10-year period (corresponding to about 6 mammography episodes) to save 1 life was 1252 women (95% CI, 958-1915 women). RR estimates based on excess mortality were close to the estimates based on individual cause of death. The RR estimate of the exposure invitation was 0.73 (95% CI, 0.66-0.80), and the RR estimate of the exposure attendance was 0.70 (95% CI, 0.63-0.78).

DISCUSSION

Because of the nature of the mammography screening programs in Sweden's counties, some of which invited women ages ≥40 years and some of which invited women ages ≥50 years, we were able to gather unique, comprehensive material to study the effectiveness of screening of women aged <50 years. That material included all of Sweden and an average of 16 years of screening in the study group. All estimates indicated statistically significant, lower breast cancer mortality in the counties with service screening. For the group ages 40 to 44 years, the estimated reduction in breast cancer mortality was smaller than that for the group ages 45 to 49 years. The estimated effectiveness was somewhat higher when Stockholm County was excluded from the control group.

A similar design was used for the same target group in an earlier study by Jonsson et al[11] Those authors demonstrated a statistically nonsignificant 14% reduction in mortality among women who were invited to service screening and were followed for 10 years. A study in northern Sweden revealed a statistically significant 36% to 38% reduction in mortality for women who were invited to service screening at ages 40 to 49 years.[12] In the Age trial, the estimated RR of breast cancer mortality for women who were invited to screening starting at age 40 years versus age 50 years was 0.83 (95% CI, 0.66-1.04) after 10 years of follow-up.[10] In an overview of 4 Swedish trials, the estimated RR for women who were randomized at ages 40 to 49 was 0.77 (95% CI, 0.59-1.01).[5] In the current study, the results indicated a significant reduction in breast cancer mortality that seemed to contradict the results from other studies. However, the current study had greater power, and our estimates were well within the 95% CIs from most other studies, which means that those results were in accordance with ours. Furthermore, the time with screening (trial time) for the group ages 40 to 49 years was shorter in most randomized trials. In the Age trial, women were invited to screening between ages 40 years and 49 years; however, in the current study, the follow-up was 6 years longer.

National mortality trends may not have influenced our results, because the study design was based on a geographic comparison of 34 areas. However, because the current study was not an RCT, a possible bias may exist caused by differences between the study group and the control group other than screening. Excluding Stockholm from the control group resulted in somewhat higher estimates of effectiveness, possibly because of its big-city characteristics and greater frequency of private screening. The estimated RR for the reference period, previous to the start of service screening, was 0.94 and, despite the size of the study, was not statistically significant. If this estimate had been the true difference without screening in the study period, then an adjustment would reduce the estimated mortality reduction by 5 or 6 percentage points. It is reasonable to expect that possible differences in breast cancer mortality caused by geographic differences in

breast cancer care have diminished over last 2 decades. One reason for this is the development of both national guidelines and regional care programs, which started in the early 1980s, with the purpose of ensuring similar care in the whole country. Therefore, the estimated difference in baseline mortality during the reference period probably is an overestimate of a possibly unobservable difference during the study period. The control group and the study group during the reference period differed slightly from the groups that were used during the study period, because the areas where screening activities (eg, RCTs) took place before service screening began were excluded. We chose not to adjust the results for the reference period.

The results based on individual underlying causes of death were validated by excess mortality estimates, which produced similar results. The effectiveness of the service-screening program was estimated for 2 different types of exposures: invitation to screening and attendance to screening. The former exposure holds the most interest for health planners, whereas the second exposure holds the most interest for the women themselves. The estimated effectiveness was higher when we adjusted for nonattendance. These estimates also were adjusted for contamination in the control group. No adjustment was made for contamination from opportunistic screening, because no such data were available.

In conclusion, the current large study of the Swedish service-screening program with mammography for women ages 40 to 49 revealed a reduction in breast cancer mortality. The reduction was estimated at 26% to 29%, depending on the studied exposure. The reduction was greater only when those women who actually attended screening were considered, and it also was greater among women ages 45 to 49 years than among women ages 40 to 44 years.

CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

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