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Article

The impacts of public mammography screening on the relationship between socioeconomic status and cancer stage

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A R T I C L E I N F O

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A B S T R A C T

This study aimed to investigate the relationship between socioeconomic inequality and mortality following the introduction of a public mammography screening program in Norway by exploring the role of change in stage distribution as the mechanism for differences before and after the introduction of the screening program. Attained education level was used as a measure of socioeconomic status in this population-based study. All women aged 50–69 years diagnosed with breast cancer from 1999–2008 and with follow-up data until the end of 2009 were included. The primary endpoint was all-cause mortality. The results of a mediation analysis indicated that the introduction of screening led to stage distribution related reductions of −5.6 (95% confidence interval = −6.7 to −4.5), −2.5 (−3.0 to −2.1), and −1.4 (−1.9 to −0.9) fewer deaths per 1000 women for with a primary school education, secondary school education, and university education, respectively. The study showed that stage distribution explained −5 (−5.9 to −4.1) fewer deaths among women with a university education and −2.4 (−2.9 to −2.0) fewer deaths among women with a secondary school education before program implementation when compared to the group with a primary school education. There were significant reductions in mortality due to stage distribution after program implementation with differences relative to women with primary school of −1.8 (−2.2 to −1.4) and −0.7 (−0.9 to −0.5) fewer deaths in favor of women with university education and secondary school, respectively. The results indicate reduced importance of cancer stage as a reason for differences in mortality by socioeconomic status after the introduction of a public mammography program.

1. Introduction

Despite the interest and controversy regarding the effects of breast cancer screening programs, little is known about subsequent changes related to socioeconomic inequality in mortality. Different research groups (Kalager et al., 2009; Kalager, Zelen, Langmark, & Adami, 2010; Olsen et al., 2012) have investigated the introduction of public screening in Norway; however, their principal aims were to examine the overall impacts of the program on mortality and not to describe change according to interactions with sociodemographic characteristics. Previously published studies on breast cancer and socioeconomic status (SES) have emphasized the relationship between the incidence of cancer, patient mortality, and breast cancer mortality in the general population. However, while the incidence of breast cancer and breast cancer mortality among the general population has been shown to concentrate among women with a higher SES (Braaten, Weiderpass, Kumle, & Lund, 2005; Menvielle et al., 2011; Pudrovska, Carr, McFarland, & Collins, 2013; Robsahm & Tretli, 2005; Strand et al., 2007; Strand, Tverdal, Claussen, & Zahl, 2005), this is not so for breast cancer mortality among patients.

Among patients diagnosed with breast cancer, a poor prognosis is more frequent among women with a lower SES (Byers et al., 2008; Halmin et al., 2008; Kravdal, 2000; Louwman, van de Poll-Franse, Fracheboud, Roukema, & Coebergh, 2007), and this relationship has been shown to relate to differences in cancer stage at diagnosis. Indeed, this is a finding common among a wide array of cancer types (Lyratzopoulos et al., 2012; Woods, Rachet, & Coleman, 2006). In Norway, Kravdal (2000) used pre-screening program data from 1960 to 1991 to document the importance of SES (focusing on attained education) for mortality among cancer patients in general. Furthermore, for breast cancer, Kravdal found that differences in stage distribution had a mediating role, explaining a quarter of differences between education levels. Link, Northridge, Phelan, and Ganz (1998) discussed education as an important marker of SES in the context of breast cancer since a given education leads to particular working careers and associated incomes as well as knowledge and interpersonal power.

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In the setting of screening, Yabroff and Gordis (2003) investigated the relationship between breast cancer incidence, survival, and mortality. Yabroff and Gordis stressed that the relative importance of these aspects on the overall association between SES and breast cancer mortality depends on the stage distribution of new cases and the relation of stage distribution with SES as well as the strength of the relationship between SES and survival, all aspects that are susceptible to change under new cancer control programs. These authors further mentioned that other factors, such as adjuvant therapy, may also differ by SES.

In Norwegian counties, organized mammography screening for breast cancer was introduced in phases starting in 1995/1996 and again in 2004. Following the objectives of the Norwegian Breast Cancer Screening Program (NBCSP), screening was introduced to reduce breast cancer mortality through earlier detection (Cancer Registry of Norway, 2000). It should be noted that, in Norway, higher education in public institutions is tuition-free, and universal access to health care is provided within a single-payer public system.

Any mammography screening conducted prior to the introduction of the public program in Norway has been referred to as a setting of opportunistic screening. This describes a situation where the general practitioner or social network promoted, or the women themselves pursued, unsystematic mammography screening at some, often irregular, interval (Hofvind, Vacek, Skelly, Weaver, & Geller, 2008; Lynge et al., 2011). Lynge et al. estimated that some 40% of Norwegian women had a mammography examination prior to introduction of the program. However, with the introduction of organized screening in Norway, every female aged 50–69 was invited to be screened every 2 years resulting in an overall participation rate of 77% (Giordano et al., 2012).

In addition, Link et al. (1998) point to the dynamics of changing inequalities, whereby higher SES groups are more adept to make use of technologies when introduced. Link et al. also discussed the diverging inequalities concerning mammography screening in an opportunistic screening setting. From a technology diffusion point of view, these authors did not comment on whether population-based screening programs could contribute to narrowing the gap in inequalities.

Against this background, the aims of this article are twofold. The first aim is to explore changes in patient mortality rates associated with changes in cancer stage at the introduction of the screening program for each level of education (the within-education group changes). The second aim is to describe changes to the marginal importance of cancer stage for differences by education level before and after the introduction of the screening program (the between-education group differences). Motivated by the discussion of Yabroff and Gordis (2003), a small sensitivity analysis was conducted to determine the plausibility of the results. Thus, education-specific changes in the incidence of breast cancer at the introduction of the program were investigated and the results on mortality were compared after adjusting for the association between education and the risk of dying from causes other than breast cancer.

2. Methods and setting

The data from all Norwegian women aged 50–69 who were diagnosed with breast cancer between 1999 and 2008 were collected for this study. Patients were followed until death (from any cause) or latest date of follow-up as of December 31, 2009 (maximum follow-up of 11 years). The death from any cause approach may be regarded as conservative, since this includes deaths that are possibly unrelated to breast cancer (Cuzick, 2008). During the sample period, 15 out of 19 counties in Norway implemented the program; 4 counties had already implemented the program in 1995/1996. The county specific implementation sequence and the period of data collection can be seen in Table 1. The introduction was not randomized and took place according to administrative considerations. The patients were analyzed according to the county in which they lived in the year when diagnosed with breast cancer. Information from the cancer registry, which is 99.95% complete for female breast cancer patients in Norway (Larsen et al., 2009), was linked with information on SES as well as time and cause of death from Statistics Norway.

Attained education level was used as a proxy for SES and was grouped according to primary school (6–9 years of schooling), secondary school (10–12 years of schooling), and university education. Out of a total of 15,862 women, 149 had missing data concerning education level and 92 had missing data concerning cancer stage and were excluded from the analysis leaving data for 15,622 women for analysis. Cancer stage was categorized according to tumor, node, and metastasis (TNM) staging as follows: ductal carcinoma in situ (DCIS), TNM I, TNM II, TNM III/IV.

The applied regression models sought to separate the differences in mortality due to stage distribution from the differences in mortality due to screening introduction and education. A mediation analysis was appropriate for this setting because it captures the net and gross differences in mortality as a function of exposure variables—screening introduction (via time period) and education—and a mediator (cancer stage). The part of the analysis with time period as the exposure analyzes the within-education group changes, while the part of the analysis with education as the exposure analyzes the between-education group differences (elaborated below). Thus, the analysis considered the joint exposure of screening introduction and education, of which the screening program is the exposure that was intervened upon. Primary interest lies with the indirect effects (those through cancer stage), whereas the direct effects of the exposures then consider differences other than through this mediator.

All analyses were adjusted for age at diagnosis, year of diagnosis, civil status, and parity. Civil status and parity were included because both variables reflect additional resources within the household, and parity has been found to be related to breast cancer incidence, survival, and SES (Lappegård et al., 2005; Menvielle et al., 2011). Year of diagnosis was included to capture

Table 1
Date of the NBCSP[a] introduction in Norwegian counties.

County	Date of introduction	Data collection period relative to introduction
Rogaland	November 20, 1995	3.1–13.1 years after
Oslo	January 8, 1996	3.0–12.9 years after
Hordaland	January 15, 1996	3.0–12.9 years after
Akershus	February 12, 1996	2.9–12.9 years after
Telemark	September 13, 1999	−0.8 to 9.3 years after
(1) Aust-Agder and (2) Vest-Agder	November 1, 1999	−0.8 to 9.1 years after
(1) Troms and (2) Finnmark	May 22, 2000	−1.3 to 8.5 years after
Østfold	April 17, 2001	−2.3 to 7.7 years after
Nordland	May 17, 2001	−2.4 to 7.6 years after
Buskerud	September 10, 2001	−2.7 to 7.3 years after
(1) North and (2) South Trøndelag	September 17, 2001	−2.7 to 7.3 years after
Oppland	January 15, 2002	−3.0 to 6.9 years after
Møre og Romsdal	April 14, 2002	−3.3 to 7.6 years after
Sogn og Fjordane	February 13, 2003	−4.1 to 5.9 years after
Hedmark	August 25, 2003	−4.6 to 5.3 years after
Vestfold	February 2, 2004	−5.1 to 4.9 years after

[a] NBCSP: Norwegian Breast Cancer Screening Program.

secular trends in the mortality rates over the data collection period. The continuous variables age at diagnosis and year of diagnosis were entered linearly. Nulliparity was entered as a binary variable. Civil status was entered as a categorical variable (unmarried, married, widowed, separated/divorced). The introduction of the NBCSP (time period) was entered as a binary variable to measure any immediate change as well as a continuous variable (counting the time since county-specific introduction) to capture linear trends in time after introduction reflecting the structure of an interrupted time series analysis (Penfold & Zhang, 2013).

Results are presented according to the two aims of the study, which separately considers either time period or education level as the exposure variable. For the analysis of the within-education group change, estimates of education level specific changes in mortality rates mediated by cancer stage were adjusted across periods. This analysis separated the change in mortality at the introduction of the screening program for a specific education level into (1) a change in general mortality (direct effects) and (2) a change in mortality due to cancer stage (indirect effects). Thus, for this part of the analysis time period was analyzed as the exposure variable and cancer stage as a mediator, separately for each education level. While this analysis captures any change to mortality at screening introduction as direct and indirect effects, it does not establish the extent of any pre-existing differences between education groups due to cancer stage. For the analysis of these between-education group differences, estimates of mediation by cancer stage were analyzed with education level as the exposure variable, introducing an interaction with time period. This then separated the importance of cancer stage by education level from general mortality differences between these groups in either time period, before and after screening introduction.

In the current study mediation was estimated by turning to natural effect models for direct and indirect effects using a counterfactual framework and marginal structural models, as implemented by Lange, Vansteelandt, and Bekaert (2012). As defined by Nordahl et al. (2014), and taking education as an example of the exposure variable, the natural direct effect considers the difference in mortality between the levels of an exposure (level of education, say) where the mediator (cancer stage) is that of the reference education level (primary school). The natural indirect effect of education on mortality is then represented by the mortality rate had education been fixed at a given level and had cancer stage been changed to whatever value cancer stage would take at that level of education. To implement this definition of direct and indirect effects in the same analysis, a multinomial logit model for cancer stage was estimated conditioning on all variables to preserve the model structure in a given final analysis (Lange et al., 2012). Subsequently, a new dataset was constructed that included an auxiliary variable for the indirect effect of education on cancer stage, replicating the data one time for each of the three levels of education. Based on the multinomial logit model, predicted probabilities for each cancer stage level were obtained, first using the original education variable to represent the direct effect and thereafter using the new auxiliary education variable to represent the indirect effect. These sets of predicted probabilities gave the denominator and numerator, respectively, for the weights of the marginal structural model. While the above text exemplified the implementation of the analysis with education as the exposure (i.e. the between-education group analysis), a similar interpretation can be given to the analysis that considers time period as the exposure. However, for this within-education group analysis the auxiliary variable for the indirect effects were the replications for each level of time period, i.e. before and after screening introduction. Across all the multinomial logit models no weight for any single observation was exceedingly large, and none of the estimated weights were beyond 2.5 times larger or smaller than 1. The details of these estimated models are given in the Appendix separately for the two main aims of the study (Appendices A and B).

A marginal structural model by means of additive hazard regression was thereafter applied to mortality. Additive hazard regression is a flexible model for survival analyses with the linear dependence of the model facilitating decomposition into direct, indirect, and total effects (Lange & Hansen, 2011). The Aalen additive hazard regression is, in itself, entirely non-parametric with covariate effects varying with time (Aalen, 1989). However, a reduction of the model is feasible using the Mckeague and Sasieni (1994), whereby some coefficients are time-invariant, and the Lin and Ying (1994), whereby all coefficients except the baseline are kept time-invariant. This latter model is by analogy an additive version of the Cox regression model. These methods are implemented in the timereg package in R (Scheike & Martinussen, 2006). Standard tests (Scheike & Martinussen, 2006) for the time dependence of coefficients showed that they could be kept time-invariant, thus, the coefficients were presented as the additional number of deaths per year per 1000 breast cancer patients. Similarly, the cumulative baseline mortality could be seen to increase linearly over time, and is therefore presented as the expected number of deaths per year per 1000 patients for the reference group. Direct and indirect effect estimates as well as effect estimates for the total effects were obtained by conducting a parametric bootstrap resampling with 10,000 replications as described by Nordahl et al. (2014).

To determine the plausibility of the results, a sensitivity analysis was conducted investigating education-specific changes in incidence and by adjusting for the association between education and the risk of dying from causes other than breast cancer. For the analysis of incidence, Poisson regression modeling was used. The population size data contained no information on civil status and parity, as the population at risk was defined as the aggregate population stratified by education, year of diagnosis, age at diagnosis, and year relative to the start of screening in each county. To analyze the association between education and the risk of dying from causes other than breast cancer, all-cause mortality was compared to cancer-related mortality (WHO ICDv10 C00-C97), breast-cancer specific mortality (ICDv10 C50), and excess mortality by subtracting the expected mortality by education level in the general population. The data for the sensitivity analyses are discussed in Appendix C.

3. Results

3.1. Descriptive analyses

Descriptive statistics for the breast cancer patients included in the study are presented in Table 2. Before the introduction of the program, the group with a university level education had a higher proportion of DCIS cancers and a lower proportion of late stage cancers than did the groups with a secondary and primary school education (data not shown). In the first 2 years of the program, there were relatively small differences between educational levels. Thereafter, the distribution of cases in each stage across education levels remained similar to that observed in the first 2 years, but with larger differences in the proportion of patients with DCIS and advanced stage cancers between those with a primary school education and those with a university education. In terms of age, women with a primary school education were older (mean 61.1 years) than women with a secondary school education (mean 58.5 years) and women with a university education (57.2 years). Age of

Table 2
Descriptive statistics for breast cancer patients by level of education.

Variable	Total Sample	Primary school	Secondary school	University education
Before introduction	1862 (12%)	568 (14%)	939 (12%)	355 (10%)
Mean time before introduction (years)	−1.6 (1.2)	−1.6 (1.1)	−1.6 (1.2)	−1.7 (1.2)
After introduction	13,760 (88%)	3534 (86%)	6911 (88%)	3315 (90%)
0–2 years after	2352 (15%)	745 (18%)	1169 (15%)	438 (12%)
2-4 years after	2481 (16%)	679 (17%)	1281 (16%)	521 (14%)
4-6 years after	2962 (19%)	755 (18%)	1489 (19%)	718 (20%)
6-8 years after	2410 (15%)	592 (14%)	1231 (16%)	587 (16%)
8-12 years after	3555 (23%)	763 (19%)	1741 (22%)	1051 (29%)
Mean time after introduction (years)	5.0 (3.7)	4.5 (3.6)	5.0 (3.7)	5.6 (3.8)
Mean age at diagnosis	58.9 (5.6)	60.3 (5.6)	58.8 (5.5)	57.6 (5.4)
Mean year of diagnosis	2003.7 (2.8)	2003.4 (2.8)	2003.7 (2.8)	2004 (2.8)
Stage: DCIS	1955 (13%)	449 (11%)	996 (13%)	510 (14%)
Stage: TNM I	7683 (49%)	2051 (50%)	3872 (49%)	1760 (48%)
Stage: TNM II	5240 (34%)	1355 (33%)	2610 (33%)	1275 (35%)
Stage: TNM III/IV	744 (5%)	247 (6%)	372 (5%)	125 (3%)
Widow	1032 (7%)	378 (9%)	515 (7%)	139 (4%)
Married	10,052 (64%)	2579 (63%)	5204 (66%)	2269 (62%)
Divorced	2320 (15%)	629 (15%)	1132 (14%)	559 (15%)
Unmarried	2218 (14%)	516 (13%)	999 (13%)	703 (19%)
Parous	14,001 (90%)	3733 (91%)	7086 (90%)	3182 (87%)
Nulliparous	1621 (10%)	369 (9%)	764 (10%)	488 (13%)
Mortality rate per 1000 person-years[a]	23.2 (0.5)	29.5 (1.1)	22.0 (0.7)	17.0 (1.0)
Person-years during follow-up	83,318	22,226	41,905	19,187

Data are presented as a mean and standard deviation for continuous variables and the number and percentage of persons for categorical variables.

[a] Mortality rates are age standardized according to uniform weighting of age by age group: 50–54, 55–59, 60–64 and 65–69, where each age group contributes with weight 0.25.

diagnosis was relatively similar across education levels over time. Year of diagnosis differed less over time between education levels and more according to time of program introduction (mean before implementation: 2000; mean in the first 2 years: 2002; mean after 2 years: 2004). Mortality rates decreased over time and by level of attained education.

3.2. *Within-education group changes in mortality at the introduction of screening*

Table 3 shows the change in mortality at the introduction of the NBCSP by education level. The total change in all-cause mortality across periods was −12.5 deaths per 1000 person-years for those with a primary school education [95% confidence interval (CI): −20.6, −4.3], −2.3 deaths for those with a secondary school education [CI: −6.8, 2.2, non-significant (ns.)], and −4.5 deaths for those with a university education [CI: −10.4, 1.4, ns.]. Deaths from less severe cancer stages (the indirect effects) were reduced by −5.6 for those with a primary school education [CI: −6.7, −4.5], −2.5 deaths [CI: −3.0, 2.1] for those with a secondary school education, and −1.4 deaths [CI: −0.9, −1.9] for those with a university education. The overall reduction in mortality was −5.6 deaths [CI: −9.2, −2.1], and −3.1 [CI: −3.5, −2.7] due to less severe cancers at diagnosis. None of the direct effects of program

Table 3
Within-education group comparison of mortality rate differences per 1000 person-years at the introduction of the NBCSP.[a]

Variable	Primary school Mortality rate	Secondary school Mortality rate	University education Mortality rate	Total Sample Mortality rate
Primary school				[Ref.]
Secondary school				−7.1 (−10.0, −4.3)
University education				−11.4 (−14.5, −8.3)
Before	[Ref.]	[Ref.]	[Ref.]	[Ref.]
After (direct)	−6.9 (−15.0, 1.3)	0.2 (−4.3, 4.7)	−3.1 (−9.1, 2.8)	−2.5 (−6.0, 1.0)
After (indirect)	−5.6 (−6.7, −4.5)	−2.5 (−3.0, −2.1)	−1.4 (−1.9, −0.9)	−3.1 (−3.5, −2.8)
After (total)	−12.5 (−20.6, −4.3)	−2.3 (−6.8, 2.2)	−4.5 (−10.4, 1.4)	−5.6 (−9.2, −2.1)
Time after introduction (direct)	−0.3 (−1.3, 0.8)	−0.2 (−0.9, 0.4)	−0.0 (−0.8, 0.7)	−0.2 (−0.6, 0.2)
Time after introduction (indirect)	0.2 (−0.0, 0.4)	0.1 (−0.0, 0.1)	0.0 (−0.0, 0.1)	0.1 (0.0, 0.2)
Time after introduction (total)	−0.1 (−1.0, 0.8)	−0.2 (−0.8, 0.4)	0.0 (−0.7, 0.7)	−0.1 (−0.5, 0.3)
Age (difference from 58.9)	0.9 (0.5, 1.3)	0.6 (0.4, 0.9)	0.5 (0.1, 0.8)	0.7 (0.5, 0.9)
Year (difference from July 2003)	−1.3 (−2.6, 0.1)	−0.9 (−1.7, −0.2)	−1.2 (−2.2, −0.3)	−1.1 (−1.7, −0.6)
Widow	[Ref.]	[Ref.]	[Ref.]	[Ref.]
Married	−2.8 (−12.1, 6.4)	−5.7 (−12.4, 1.1)	−1.8 (−12.5, 9.0)	−4.3 (−9.1, 0.6)
Divorced/separated	−0.3 (−11.1, 10.6)	−4.6 (−12.4, 3.2)	2.8 (−9.4, 15.0)	−2.0 (−7.6, 3.6)
Unmarried	−10.5 (−21.1, 0.1)	−9.6 (−17.4, −1.7)	−5.4 (−16.6, 5.9)	−9.0 (−14.4, −3.6)
Parous	[Ref.]	[Ref.]	[Ref.]	[Ref.]
Nulliparous	13.4 (4.3, 22.5)	11.7 (6.0, 17.5)	9.5 (3.4, 15.6)	11.6 (7.7, 15.5)
Baseline mortality rate[b]	35.7 (27.2, 44.2)	27.1 (21.1, 33.1)	19.5 (10.6, 28.3)	34.0 (29.5, 38.5)

Numbers in parentheses are 95% confidence intervals.
Separate regression models for each level of education.

[a] NBCSP: Norwegian Breast Cancer Screening Program.
[b] Cumulative baseline at 10.7 years follow-up converted into yearly rate.

introduction (those not through cancer stage) were significant nor were the linear time trends after introduction.

3.3. Between-education group differences in mortality before and after screening introduction

Table 4 shows the results of the analysis regarding the importance of stage distribution before and after introduction of the program. In the period before screening introduction, the total difference in mortality was −13.8 deaths per 1000 person-years [CI: −21.3, −6.3] for those with a secondary school education and −16 deaths [CI: −24.7, −7.3] for those with a university education relative to the group with a primary school education. Before the program, cancer stage at diagnosis mediated a difference in mortality of −2.4 deaths [CI: −2.9, −2] for the group with a secondary school education relative to the group with a primary school education. This difference was reduced at the introduction of the program by 1.8 [CI: 1.3, 2.2], leading to a marginal rate difference in the period of −0.7 [CI: −0.9, −0.5] in favor of the group with a secondary school education. The mediated difference between those with a primary school education and a university education was −5 deaths [CI: −5.9, −4]. This difference was reduced by 3.2 deaths [CI; 2.2, 4.2] at introduction of the program. The marginal rate difference due to stage of cancer was −1.8 deaths [CI: −2.2, −1.4] among the group with a university education after program introduction. Variables describing the development of direct and indirect effects over time were negative (indicative of increasing differences over time). The direct effects over time were not significant, however the interaction between time after introduction and education level was significant for the indirect effects, p-value = 0.002. The total differences in mortality after screening introduction were smaller than before, and the group with a secondary education level had −4.4 deaths [CI: −9.4, 0.6, ns] while the group with a university education had −9.1 deaths [CI: −14.9, −3.4].

The main drivers of education-specific reductions and between education differences were associated with levels of DCIS and advanced stage cancers, which upon removal reduced the indirect effects but remained significant. No substantive differences were noted in the analyses restricted to counties implementing the program in the years 1999–2004 or in analyses that included county as a covariate. Subdividing the time periods both before [< 1.5 and > 1.5 years] and after [2 year periods: 0–2, 2–4, 4–6, 6–8, 8–12] gave essentially the same results. Introducing a common model for within-group differences led to the same conclusion.

The sensitivity analysis given in Table 5 in shows that the breast cancer incidence increased more in both relative and absolute terms for the group with a primary school education compared to the group with a secondary school education or a university education. The group with a secondary school education had a

Table 4
Between-education group comparison of mortality rate differences per 1000 person-years before and after introduction of the NBCSP.[a]

	Variable	Mortality rate per 1000	Marginal rate difference in period
Before	Primary school	[Ref.]	
	Secondary school (direct)	−11.4 (−18.9, −4.0) $^{a}_{1}$	≡
	Secondary school (indirect)	−2.4 (−2.9, −2.0) $^{b}_{1}$	≡
	Secondary school (total)	−13.8 (−21.3, −6.3) $^{a}_{1}+{}^{b}_{1}$	≡
	University education (direct)	−11.1 (−19.7, −2.4) $^{a}_{2}$	≡
	University education (indirect)	−5.0 (−5.9, −4.1) $^{b}_{2}$	≡
	University education (total)	−16.0 (−24.8, −7.3) $^{a}_{2}+{}^{b}_{2}$	≡
	Before	[Ref.]	
After	After	−11.8 (−19.9, −3.9)	
	After X Secondary school (direct)	7.6 (−1.3, 16.6) $^{c}_{1}$	−3.7 (−8.9, 1.4) $^{a}_{1}+{}^{c}_{1}$
	After X Secondary school (indirect)	1.8 (1.3, 2.2) $^{d}_{1}$	−0.7 (−0.9, −0.5) $^{b}_{1}+{}^{d}_{1}$
	After X Secondary school (total)	9.4 (0.2, 18.5) $^{c}_{1}+{}^{d}_{1}$	−4.4 (−9.4, 0.6) $^{a}_{1}+{}^{c}_{1}+{}^{b}_{1}+{}^{d}_{1}$
	After X University education (direct)	3.7 (−6.6, 13.7) $^{c}_{2}$	−7.3 (−13.0, −1.7) $^{a}_{2}+{}^{c}_{2}$
	After X University education (indirect)	3.2 (2.2, 4.2) $^{d}_{2}$	−1.8 (−2.2, −1.4) $^{b}_{2}+{}^{d}_{2}$
	After X University education (total)	6.9 (−3.5, 17.3) $^{c}_{2}+{}^{d}_{2}$	−9.1 (−14.9, −3.4) $^{a}_{2}+{}^{c}_{2}+{}^{b}_{2}+{}^{d}_{2}$
Time after introduction (in years)	Time after introduction (difference from 0)	−0.0 (−0.8, 0.8)	
	Time after X Secondary school (direct)	−0.2 (−0.7, 0.3)	
	Time after X Secondary school (indirect)	−0.1 (−0.1, −0.0)	
	Time after X Secondary school (total)	−0.2 (−0.7, 0.3)	
	Time after X University education (direct)	−0.1 (−0.8, 0.5)	
	Time after X University education (indirect)	−0.0 (−0.1, 0.1)	
	Time after X University education (total)	−0.2 (−0.8, 0.5)	
	Age (difference from 58.9)	0.7 (0.5, 0.8)	
	Year (difference from July 2003)	−1.1 (−1.6, −0.6)	
	Widow	[Ref.]	
	Married	−3.5 (−7.9, 1.2)	
	Divorced/separated	−1.3 (−6.6, 3.9)	
	Unmarried	−8.5 (−13.7, −3.4)	
	Parous	[Ref.]	
	Nulliparous	11.3 (7.4, 15.0)	
	Baseline mortality rate[b]	37.8 (32.9, 42.7)	

Numbers in parentheses are 95% confidence intervals. Letters in superscript [(a,b,c,d)] outline the calculations for total effects and the marginal rate differences after NBCSP introduction.

Tests for interaction terms: X Education level (direct effects), p-value = 0.16. After X Education level (indirect effects), p-value < 0.001. Time after introduction X Education level (direct effects), p-value = 0.92. Time after introduction X Education level (indirect effects), p-value = 0.002.

[a] Norwegian Breast Cancer Screening Program.

[b] Cumulative baseline at 10.7 years follow-up converted into yearly rate.

Table 5
Poisson regression model estimates for the incidence of breast cancer.

Variable	Incidence rate ratios
Primary school	[Ref.]
Secondary school	1.231 (1.106–1.370)
University education	1.446 (1.262–1.657)
Before	[Ref.]
After	1.681 (1.513–1.867)
After X Secondary school [a]	0.862 (0.756–0.983)
After X University education [a]	0.779 (0.661–0.918)
Time after introduction (difference from 0)	0.997 (0.986–1.008)
Time after X Secondary school [b]	1.005 (0.992–1.018)
Time after X University education [b]	1.002 (0.987–1.018)
Age (difference from 58.9)	1.018 (1.015–1.021)
Year (difference from July 2003)	0.977 (0.970–0.985)
Baseline incidence per 100,000 PY	192 (175–210)

PY: person-years.
Numbers in parentheses are 95% confidence intervals.

[a] Test for interaction: after X Education level, *p*-value 0.008.

[b] Test for interaction: time after introduction X Education level, *p*-value 0.767.

23.1% higher incidence of breast cancer [CI: 10.6%, 37.0%] and the group with university education had a 44.6% higher incidence [CI: 26.2%, 65.7%] relative to the group with a primary school education, who had an incidence per 100,000 of 192 [CI: 175, 210] cases at baseline before the introduction of the program. The incidence surged in all three groups of education; however, the increase was 68.1% for the group with a primary school education, 58.7% for the group with a secondary school education, and 53% for the group with a university education. This corresponded to an absolute increase of 131, 106, and 86 more cases per 100,000 person-years, respectively.

The adjustment for the association between education and the risk of dying from causes other than breast cancer is given in Table 6. While increasing the specificity of mortality with regards to cancer stage (as would be the case when considering deaths that were either cancer-related or breast-cancer related or to the excess mortality rate compared with the general population) had little influence on the indirect effects of cancer stage it did influence the direct effects across all education levels. For cancer-related and breast-cancer specific mortality, this means that the mortality reduction associated with the introduction of the program became more uniform across levels of education.

4. Discussion

The scope of this article was to study the role of cancer stage and socioeconomic inequality in mortality. This study is inherently limited in its focus given the complex relationship between SES and breast cancer incidence and mortality in the general population (Yabroff & Gordis, 2003). Indeed, the results are in line with a central tenet of Yabroff and Gordis which stated that the relationship between SES and mortality is dependent on the relation of stage distribution with SES, which changes upon the introduction of a cancer control program.

The introduction of a public screening program was associated with an increase in the incidence of breast cancer that, to some degree, also had a leveling effect of incidence across education levels. In my view, this is supportive of the main findings in this study, since this suggests, but does not confirm, that groups with lower levels of attained education did indeed benefit more from the technology diffused by the introduction of the NBCSP. The estimates of incidence increase are comparable to those of a recent study investigating changes by cancer stage (Lousdal, Kristiansen, Moller, & Stovring, 2016).

Since the cancer registry has almost complete coverage of breast cancer incidence (Larsen et al., 2009), it follows that one can also use the data source to evaluate cancer and breast-cancer specific mortality as opposed to total mortality. When assessing mortality among breast cancer patients, the results suggested that direct differences (not through cancer stage) in mortality after the introduction of the program were more uniform across education levels, whereas the indirect effects (those through cancer stage) remained similar to results observed in the all-cause analysis. One interpretation of this finding, although not a definitive conclusion, suggests that any previous differences in breast cancer mortality (beyond what can be observed from the relationship between SES and cancer stage) would remain in future investigations, but would be more equal than differences found in analyses examining in all-cause mortality.

Cancer stage contributed to differences between socioeconomic groups before screening began by an order of magnitude similar to that found by Kravdal (2000). However, the figures are not directly comparable owing to differences in time period, design, and focus of the analysis. Nonetheless, previous studies have established a link between cancer stage at diagnosis and SES (Lyratzopoulos et al., 2012; Woods et al., 2006), and organized mammography

Table 6
Between-education group comparison of all-cause, cancer-related, breast cancer, and excess mortality rate differences per 1000 person-years.

Variable	All-cause	Cancer-related	Breast cancer	Excess mortality
Primary school	[Ref.]	[Ref.]	[Ref.]	[Ref.]
Secondary school (direct)	−11.4 (−18.8, −3.9)	−8.2 (−15.3, −1.0)	−4.1 (−10.2, 2.0)	−6.1 (−14.0, 1.9)
Secondary school (indirect)	−2.4 (−2.9, −2.0)	−2.3 (−2.7, −1.8)	−2.3 (−2.7, −1.8)	−2.5 (−2.9, −2.0)
University education (direct)	−11.1 (−19.7, −2.4)	−8.5 (−17.2, 0.2)	−4.1 (−11.8, 3.7)	−2.8 (−11.9, 6.5)
University education (indirect)	−5.0 (−5.9, −4.0)	−4.6 (−5.5, −3.7)	−4.4 (−5.3, −3.6)	−5.0 (−6.0, −4.1)
Before	[Ref.]	[Ref.]	[Ref.]	[Ref.]
After	−11.8 (−19.8, −3.8)	−10.6 (−18.2, −2.9)	−8.3 (−14.7, −1.8)	−11.4 (−20.0, −3.0)
After X Secondary school (direct)	7.6 (−1.4, 16.6)	5.4 (−3.2, 14.0)	1.9 (−5.7, 9.4)	7.4 (−2.2, 17.0)
After X Secondary school (indirect)	1.8 (1.3, 2.2)	1.6 (1.2, 2.1)	1.6 (1.2, 2.1)	1.8 (1.3, 2.3)
After X University education (direct)	3.7 (−6.6, 14.1)	3.3 (−6.8, 13.5)	0.6 (−8.5, 9.7)	3.1 (−7.9, 14.0)
After X University education (indirect)	3.2 (2.2, 4.2)	2.9 (1.9, 3.8)	2.8 (1.8, 3.7)	3.2 (2.2, 4.3)
Baseline mortality rate[a]	37.8 (32.9, 42.7)	32.5 (27.9, 37.0)	25.4 (21.4, 29.5)	29.5 (24.6, 34.4)

Numbers in parentheses are 95% confidence intervals.
All-cause analysis is provided for easy reference, and is the same model as in Table 4. The table has been abbreviated, and shows the coefficients of education and time period.

[a] Cumulative baseline at 10.7 years follow-up converted into yearly rate.

screening aims to diagnose the cancer at an earlier stage. For the relationship between cancer stage and SES, the argument from the current analysis is that the mammography screening had a leveling effect. In other words, the difference in mortality between socioeconomic groups by cancer stage decreased after program introduction.

The current study contrasts a previous study by Louwman et al. (2007) investigating the impact of screening introduction on socioeconomic variation in survival for a region in the Netherlands. Comparing periods before (< 1991), during, and after screening introduction (> 1996) these authors found that while stage distribution improved for all socioeconomic groups, this improvement favored the high status group in particular. Although noting a SES–cancer stage relationship, these authors ultimately conditioned on cancer stage in their multivariate analysis (cf. estimates of direct effects as conceptualized in the current study). While there are other important differences to Louwman et al. (2007), this complicates an at least proximal comparison. However, their results underscore the need for further studies on the impact of screening on differences by SES. Indeed participation in the Dutch screening program was higher among higher SES. While contrary to the current results, the results by Louwman et al. need therefore not be contrary to a technology diffusion process whereby the higher SES are the first to benefit from new technology (Link et al., 1998). For the Norwegian experience it seems that the current study results fit well with those of the pre-screening era, cf. Kravdal (2000). However, it is a limitation of the current study sample that the introduction for the Norwegian counties implementing screening in 1995/1996 is not included to shed further light on the historical development of the SES–cancer stage relationship.

The current analysis showed that only a part of the reduction in mortality that occurred after the introduction of screening can reasonably be ascribed to changes occurring in stage distribution. This indicates that many changes that influenced survival at the introduction of screening were unrelated to changes in cancer stage and may indeed be unrelated to screening. Furthermore, in Norway, this difference in survival may also relate to reorganization of treatment into multidisciplinary teams (Kalager et al., 2009). As emphasized by Link et al. (1998), health differences by SES might be influenced by the introduction and diffusion of new technologies. However, the current analysis was unable to link concurrent treatment changes in greater detail.

Furthermore, it is possible that unmeasured confounders account for the observed results. Although screening was introduced at separate time points in Norwegian counties and that the analysis controlled for secular trends to mortality via calendar time, the analysis lacks the existence of separate control group of counties that did not introduce screening over the same time period. This puts a limit on the ability to interpret the period effect as the effect of screening introduction. Nevertheless, it should be noted that any concurrent change should interfere primarily with the indirect effects through cancer stage to affect the main conclusions of the current study.

The estimates of direct and indirect effects are themselves subject to causal assumptions about the nature of the relationship and the absence of confounding in a tripartite relationship, namely that of screening introduction and cancer stage, screening introduction and mortality, and cancer stage and mortality (Lange et al., 2012). These relationships are all extended to also cover education. This is, in all likelihood, a strong assumption, which in addition to the assumption of absent causal factors between education and cancer stage, and between screening introduction and cancer stage, may contribute to overestimation due to residual confounding. The estimation of mortality differences was aided by comparing across different periods before and after screening introduction. Screening introduction is therefore the exposure that was intervened upon to change the effects of the mediator. It was investigated whether screening introduction affected different education groups differentially, and whether it reduced any pre-existing difference between these groups. Screening introduction was however not a randomized intervention in Norwegian counties, and so there may be confounding with both screening introduction and education. At the outset, such confounding seems likely since the counties implementing screening early were more populous, more urban, and with higher levels of education. Comparing within each level of education therefore becomes important, since this arguably considers more homogenous groups over time. The results from the analyses of within-education group change and between-education group differences can thus be seen as supportive of each other to the extent that they point towards the same conclusion, even though the analyses themselves need not be mutually exclusive. However, future studies should consider other potential mediators of the effects of screening on cancer stage.

The analysis also considered the introduction of the screening program at the aggregate level and not whether the individual woman actually underwent screening either before or after program introduction. This repeated before-after design, with each county introducing the program at different time-points, entails an ecological intention-to-screen approach to the study of individual level data. An assumption of the analysis is, therefore, that the difference in the proportion of women undergoing screening and the associated increase in breast cancer incidence is mainly driven by the onset of high participation rates.

Although the findings showed that the introduction of public mammography screening diminished the contribution of stage distribution on mortality differences related to SES, these findings should be used carefully when advocating screening as a method for cancer control in the population or as a method for reducing socioeconomic inequalities in general. The present analysis is limited and does not extend easily to other aspects of mammography screening such as overdiagnosis. However, the analysis raises important questions about the pursuit of equity and a public screening program as a means to this end. Future studies on this issue are needed to assess the generalizability of the current findings.

In conclusion, the introduction of mammography screening had implications for socioeconomic inequalities in mortality following a breast cancer diagnosis. Although inequalities remained, the introduction of public mammography screening reduced the importance of cancer stage for differences in the mortality rate by SES.

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Appendix A. Within-education group comparison. Multinomial logit for stage of cancer and resulting weights

Variable:Outcome	Primary school Log-odds (95% CI)	Secondary school Log-odds (95% CI)	University education Log-odds (95% CI)	Overall Log-odds (95% CI)
Intercept:DCIS	−0.73 (−1.46, −0.01)	−0.42 (−0.98, 0.14)	1.19 (0.04, 2.34)	−0.50 (−0.92, −0.08)
Intercept:TNM I	1.54 (0.98, 2.09)	1.51 (1.05, 1.97)	2.29 (1.22, 3.36)	1.46 (1.11, 1.80)
Intercept:TNM II	1.34 (0.77, 1.91)	1.56 (1.09, 2.03)	2.25 (1.16, 3.34)	1.40 (1.05, 1.76)
After:DCIS	1.05 (0.47, 1.62)	0.72 (0.28, 1.17)	0.12 (−0.62, 0.86)	0.68 (0.37, 0.99)
After:TNM I	0.38 (−0.04, 0.80)	0.17 (−0.18, 0.53)	0.13 (−0.54, 0.79)	0.24 (−0.01, 0.49)
After:TNM II	−0.07 (−0.50, 0.36)	−0.12 (−0.48, 0.24)	−0.19 (−0.86, 0.48)	−0.11 (−0.36, 0.15)
Time after:DCIS	0.07 (0.01, 0.13)	0.09 (0.04, 0.13)	0.08 (0.01, 0.15)	0.08 (0.05, 0.11)
Time after:TNM I	0.06 (0.01, 0.12)	0.06 (0.02, 0.10)	0.05 (−0.02, 0.12)	0.06 (0.03, 0.09)
Time after:TNM II	0.07 (0.01, 0.12)	0.03 (−0.01, 0.08)	0.03 (−0.03, 0.10)	0.04 (0.01, 0.07)
Secondary school:DCIS				0.31 (0.11, 0.51)
Secondary school:TNM I				0.20 (0.02, 0.37)
Secondary school:TNM II				0.20 (0.02, 0.37)
University education:DCIS				0.66 (0.41, 0.92)
University education:TNM I				0.47 (0.24, 0.70)
University education:TNM II				0.53 (0.30, 0.77)
Age at diagnosis:DCIS	−0.01 (−0.04, 0.01)	−0.03 (−0.05, −0.01)	−0.01 (−0.04, 0.03)	−0.02 (−0.04, 0.00)
Age at diagnosis:TNM I	0.01 (−0.02, 0.03)	−0.01 (−0.03, 0.01)	0.01 (−0.02, 0.04)	0.00 (−0.01, 0.01)
Age at diagnosis:TNM II	−0.01 (−0.03, 0.02)	−0.03 (−0.05, −0.01)	−0.01 (−0.04, 0.03)	−0.02 (−0.03, 0.00)
Year of diagnosis:DCIS	−0.03 (−0.10, 0.05)	−0.03 (−0.09, 0.03)	−0.02 (−0.11, 0.08)	−0.03 (−0.07, 0.01)
Year of diagnosis:TNM I	−0.05 (−0.11, 0.02)	−0.01 (−0.07, 0.04)	−0.02 (−0.10, 0.07)	−0.03 (−0.06, 0.01)
Year of diagnosis:TNM II	−0.04 (−0.11, 0.03)	0.02 (−0.03, 0.07)	0.00 (−0.08, 0.09)	0.00 (−0.04, 0.04)
Nulliparous:DCIS	−0.36 (−0.89, 0.18)	−0.38 (−0.77, 0.01)	−0.56 (−1.13, 0.01)	−0.40 (−0.67, −0.13)
Nulliparous:TNM I	−0.42 (−0.86, 0.02)	−0.51 (−0.85, −0.17)	−0.60 (−1.13, −0.08)	−0.50 (−0.73, −0.26)
Nulliparous:TNM II	−0.45 (−0.90, 0.00)	−0.51 (−0.86, −0.16)	−0.75 (−1.28, −0.21)	−0.54 (−0.79, −0.30)
Married:DCIS	0.21 (−0.35, 0.76)	0.43 (0.00, 0.86)	−0.35 (−1.36, 0.65)	0.23 (−0.09, 0.55)
Married:TNM I	0.03 (−0.43, 0.48)	0.55 (0.18, 0.92)	0.05 (−0.90, 1.00)	0.30 (0.03, 0.58)
Married:TNM II	0.21 (−0.27, 0.68)	0.46 (0.08, 0.84)	0.06 (−0.91, 1.03)	0.32 (0.04, 0.60)
Divorced/Separated:DCIS	0.25 (−0.41, 0.92)	0.28 (−0.23, 0.79)	−0.35 (−1.45, 0.76)	0.16 (−0.21, 0.53)
Divorced/Separated:TNM I	0.06 (−0.49, 0.62)	0.34 (−0.10, 0.78)	0.06 (−0.98, 1.10)	0.21 (−0.12, 0.53)
Divorced/Separated:TNM II	0.19 (−0.38, 0.77)	0.20 (−0.25, 0.66)	0.24 (−0.81, 1.30)	0.23 (−0.10, 0.57)
Unmarried:DCIS	−0.05 (−0.75, 0.65)	0.37 (−0.19, 0.92)	0.13 (−0.97, 1.23)	0.25 (−0.14, 0.64)
Unmarried:TNM I	−0.15 (−0.72, 0.42)	0.64 (0.16, 1.12)	0.26 (−0.77, 1.30)	0.32 (−0.02, 0.66)
Unmarried:TNM II	0.21 (−0.37, 0.80)	0.59 (0.10, 1.08)	0.49 (−0.57, 1.54)	0.46 (0.11, 0.81)
Weights				
Range (min, max)	0.43, 2.31	0.52, 1.90	0.81, 1.25	0.57, 1.76
1st, 3rd quartile	0.88, 1.0	0.95, 1.0	0.89, 1.0	0.92, 1.0
2.5%, 97.5%	0.45, 1.38	0.54, 1.28	0.86, 1.22	0.58, 1.30
Mean (standard deviation)	1 (0.22)	1 (0.17)	1 (0.11)	1 (0.17)

Reference outcome is TNM stage III/IV.

Appendix B. Between-education group comparison. Multinomial logit for stage of cancer and resulting weights

Variable:Outcome	Log-odds (95% CI)	Weights	
Intercept:DCIS	−0.76 (−1.32, −0.20)	Range (min,max)	0.45, 2.20
Intercept:TNM I	1.38 (0.97, 1.79)	1st, 3rd quartile	0.99, 1.01
Intercept:TNM II	1.39 (0.98, 1.81)	2.5%, 97.5%	0.83, 1.11
Secondary school:DCIS	0.51 (−0.08, 1.10)	Mean (standard deviation)	1 (0.08)
Secondary school:TNM I	0.30 (−0.11, 0.71)		
Secondary school:TNM II	0.20 (−0.21, 0.61)		
University education:DCIS	1.41 (0.65, 2.17)		
University education:TNM I	0.65 (0.04, 1.27)		
University education:TNM II	0.64 (0.02, 1.25)		
After:DCIS	1.05 (0.49, 1.61)		

After:TNM I	0.34 (−0.07, 0.75)
After:TNM II	−0.13 (−0.54, 0.29)
Time after:DCIS	0.07 (0.01, 0.12)
Time after:TNM I	0.05 (0.01, 0.10)
Time after:TNM II	0.05 (0.00, 0.10)
Age at diagnosis:DCIS	−0.02 (−0.04, 0.00)
Age at diagnosis:TNM I	0.00 (−0.01, 0.01)
Age at diagnosis:TNM II	−0.02 (−0.03, 0.00)
Year of diagnosis:DCIS	−0.03 (−0.07, 0.01)
Year of diagnosis:TNM I	−0.03 (−0.06, 0.01)
Year of diagnosis:TNM II	0.00 (−0.04, 0.04)
Nulliparous:DCIS	−0.40 (−0.67, −0.12)
Nulliparous:TNM I	−0.50 (−0.73, −0.26)
Nulliparous:TNM II	−0.54 (−0.79, −0.30)
Married:DCIS	0.23 (−0.09, 0.55)
Married:TNM I	0.30 (0.03, 0.58)
Married:TNM II	0.32 (0.04, 0.60)
Divorced/Separated:DCIS	0.16 (−0.21, 0.54)
Divorced/Separated:TNM I	0.21 (−0.12, 0.53)
Divorced/Separated:TNM II	0.23 (−0.10, 0.57)
Unmarried:DCIS	0.25 (−0.14, 0.64)
Unmarried:TNM I	0.32 (−0.02, 0.66)
Unmarried:TNM II	0.46 (0.11, 0.81)
Secondary school X After:DCIS	−0.32 (−1.03, 0.38)
Secondary school X After:TNM I	−0.15 (−0.68, 0.38)
Secondary school X After:TNM II	0.04 (−0.50, 0.58)
University education X After:DCIS	−0.92 (−1.84, 0.00)
University education X After:TNM I	−0.21 (−0.97, 0.56)
University education X After:TNM II	−0.06 (−0.84, 0.71)
Secondary school X Time after:DCIS	0.02 (−0.05, 0.08)
Secondary school X Time after:TNM I	0.01 (−0.05, 0.06)
Secondary school X Time after:TNM II	−0.01 (−0.07, 0.05)
University education X Time after:DCIS	0.02 (−0.06, 0.10)
University education X Time after:TNM I	0.00 (−0.07, 0.07)
University education X Time after:TNM II	−0.01 (−0.08, 0.06)

Reference outcome is TNM stage III/IV.

Appendix C

Description 1. Aggregate statistical information on Norwegian women at the national and county level.

1. Total person years on the national level by year, age, sex, and education.
   This data was input for analyses regarding the incidence of breast cancer and excess mortality. Incidence is the number of cases in a category divided by person-years (total person-years minus the contribution of breast cancer person-years at follow-up).
2. Number of deaths and person-years on the national level by year, age, sex, and education.
   This data was input for excess mortality. Excess mortality is the observed mortality rate in the patient population after subtracting the expected mortality rate in the general population, where the general population is defined in terms of year, age, sex, and level of education.
3. County population size by year and education in the 50–59 and 60–66 year old age-groups (Statistics Norway, 2014b).
   This data was input for the incidence of breast cancer by adjusting the person-year contribution by county specific education level.
4. County specific population size by year, age, and sex (Statistics Norway, 2014a).

This data was input for the incidence of breast cancer by disaggregating total person-years by county population size.

Description 2. Combining aggregate statistical information.

Enumerations of population size stratified by the county specific screening rounds.

The starting point for the current analysis was a dataset comprising the total Norwegian female population in person-time (years) and number of deaths by age, year, sex, and education level.

It was not possible to distinguish between person-time before and after screening introduction, or subsequent screening rounds at the national level, as this program was introduced at the county level. This is further complicated by counties introducing screening in different years and having a different age- and year-specific population size as well as different levels of education.

To supplement and extend the table on national person-time to reflect the introduction of screening at the county level, two aggregate tables were extracted from Statistics Norway. One table contains the proportion of women with either a primary, secondary, or university level education (Statistics Norway, 2014b) (i.e., the same classification as applied in this study). This information was available by county and stratified by year and age (50–59, 60–66, and more than 67 years old). The screening program targeted women aged 50–69. County-specific proportions regarding the education level for women aged 67–69 were assigned the values of women aged 60–66, on the assumption that this would be more reasonable than to assign flat values for all women older than 67 years.

Another table from Statistics Norway contains population size by county, age, and year (Statistics Norway, 2014a).

The start of screening in each county was used as the official date of introduction in each county (Cancer Registry of Norway, 2014). The date of screening introduction was combined with that dates for one round of screening (screening being performed biennially in Norway) to construct the year-relative-to-screening introduction-specific person-time contribution. From the information on the date of screening introduction the within-year contribution of person-time to the before–after design was calculated.

For the calculation of person-time to be distributed at the county level, the proportion of each year for each county belonging to each period relative to screening start was computed. To classify person-time during the pre-program period, the date that screening started (dd.mm.yyyy) minus date the year started (01.01.yyyy) divided by the total number of days in a year was calculated, on the assumption that the proportion of person-time is constant within years. This equation equals the proportion of time within each year at the county level before screening introduction, with the remainder belonging to the post-program period. This was, thereafter, repeated for any subsequent screening round.

The final table considered the year relative-to-screening introduction before and after screening as well as for subsequent screening rounds. It also varied by the year- and age-specific proportion of patients with either a primary, secondary, or university level education in each county.

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