Socioeconomic inequalities in stage-specific breast cancer incidence: a nationwide registry study of 1.1 million young women in Norway, 2000–2015

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Socioeconomic inequalities in stage-specific breast cancer incidence: a nationwide registry study of 1.1 million young women in Norway, 2000–2015

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ABSTRACT

Background: Women with high socioeconomic status (SES) have the highest incidence rates of breast cancer. We wanted to determine if high SES women only have higher rates of localized disease, or whether they also have higher rates of non-localized disease. To study this, we used data on a young population with universal health care, but not offered screening.

Material and methods: Using individually linked registry data, we compared stage-specific breast cancer incidence, by education level and income quintile, in a Norwegian cohort of 1,106,863 women aged 30–48 years during 2000–2015 ($N = 7531$ breast cancer cases). We calculated stage-specific age-standardized rates and incidence rate ratios and rate differences using Poisson models adjusted for age, period and immigration history.

Results: Incidence of localized and regional disease increased significantly with increasing education and income level. Incidence of distant stage disease did not vary significantly by education level but was significantly reduced in the four highest compared to the lowest income quintile. The age-standardized rates for tertiary versus compulsory educated women were: localized 28.2 vs 19.8, regional 50.8 vs 40.4 and distant 2.3 vs 2.6 per 100,000 person-years. The adjusted incidence rate ratios (tertiary versus compulsory) were: localized 1.40 (95% CI 1.25–1.56), regional 1.25 (1.15–1.35), distant 0.90 (0.64–1.26). The age-standardized rates for women in the highest versus lowest income quintile were: localized 28.9 vs 17.7, regional 52.8 vs 41.5 and distant 2.3 vs 3.2 per 100,000 person-years. The adjusted incidence rate ratios (highest versus lowest quintile) were: localized 1.63 (1.42–1.87), regional 1.27 (1.09–1.32), distant 0.64 (0.43–0.94).

Conclusion: Increased breast cancer rates among young high SES women is not just increased detection of small localized tumors, but also increased incidence of tumors with regional spread. The higher incidence of young high SES women is therefore real and not only because of excessive screening.

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Introduction

Breast cancer is the most commonly diagnosed female cancer worldwide [1,2]. Survival is better than for most other cancer types [3], but disease burden is high [4] because survivors may develop reduced health due to late effects of treatment [5]. It is not clear how the burden of breast cancer varies by socioeconomic status (SES). High SES women are more often diagnosed with breast cancer [6–8], but their breast cancer is usually detected at an earlier stage [9–17] than low SES women. It is not clear whether high SES women only have increased incidence of localized disease, or whether they also have increased incidence of non-localized disease, compared to low SES women. Previous studies have only compared the stage distribution of patients [9–17] and have not compared absolute stage-specific incidence rates. To better understand how the burden of breast cancer varies by SES, comparisons of stage-specific incidence rates are necessary.

In young women, breast cancer is less common but the disease tends to be detected later and is more often an aggressive subtype [18]. Thus, disease burden is particularly high for women diagnosed at a young age, due to the potential number of years lived in poor health or potential number of life-years lost. There is little information on how SES influences breast cancer rates in young women below screening age. Specifically, it is unknown whether absolute rates of localized, regional and distant stage disease are all higher for high SES women.

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Supplemental data for this article can be accessed here.

We took advantage of individually-linked nationwide registry data, to compare stage-specific incidence rates of first invasive breast cancer, by education and income level in 1.1 million young women in Norway during 2000–2015. We wanted to find out if high SES women only have higher incidence rates of localized disease, or whether they also have higher rates of non-localized disease in a young population covered by universal health care but not invited to organized screening.

Material and methods

Study design and population

We performed a population-wide cohort study using individually linked data from the Cancer Registry of Norway, Central Population Registry, National Education Database and Register for Personal Tax Payers. We had virtually complete follow-up of all women in Norway through updates of residential status per 1 January each year from 2000 to 2016. If women migrated or died during the previous year, we had exact date of status change.

We identified 1,223,780 potentially eligible women who resided in Norway at some time while aged between 30 and 48 years during 2000 to 2015. Of 1,223,780 potentially eligible women, 7350 (0.6%) were ineligible due to an invasive cancer diagnosis before age 30 or year 2000, and 109,569 (9.0%) were excluded from the analysis due to missing information on education or income for the entire study period. After these exclusions, there were 1,106,863 women included in the analysis.

Follow-up started at 1 January 2000, age 30 years, or after education and income were both known, whichever came last. We started follow-up from age 30 years to ensure most women had completed their education and started earning income before entry to the study. Follow-up ended on date of first invasive cancer diagnosis, date of permanent emigration, date of death, age 49 years, or 31 December 2015, whichever came first. Follow-up was restricted to age 48 years because we were interested in women diagnosed before entry to the mammography screening program, which starts at age 49 years in some counties in Norway.

Socioeconomic status

Education level was categorized as compulsory (lower secondary school or less, ≤10 years), secondary (completed upper secondary school or vocational education, 11–13 years) or tertiary (university or college education, ≥14 years). If study participants attained a higher education level during follow-up, they contributed person-years to more than one level (7.6% of women). All Norwegian educational institutions have mandatory reporting to the National Education Database, and education level was 99.7% complete for Norwegian-born women. Educational level was primarily unknown for immigrants who had not completed any education after arriving in Norway, and had not responded to surveys of education level among immigrants [19]. Education level was therefore missing for 25% of eligible immigrants, but this was only 5.3% of all eligible women.

Income quintiles were age- and period-specific for women aged 30–34, 35–39, 40–44 and 45–48 years during 2000–2004, 2005–2009 and 2010–2015. Quintiles were based on average personal income during the previous five-year period. For example, average income during 1995–1999 was used to create quintiles for follow-up in 2000–2004. Median income for each quintile is shown in Supplemental Table S1. We used past income to ensure income was earned before any cancer diagnosis, since income is known to fall after a diagnosis [20]. The Personal Tax Payers Register included all taxable persons in Norway and was 99.8% complete for Norwegian-born women. By definition, past income was missing for immigrants who did not reside in Norway during the previous five-year period. Income was therefore missing for 34% of eligible immigrants, but this was only 7.0% of all eligible women.

Breast cancer incidence and stage

Incidence rates included the first diagnosis of primary malignant breast cancer (International Classification of Diseases-10 code C50) with an epithelial morphology. We identified 7691 women with a first primary malignant breast cancer during follow-up. However, 160 of these women had a non-epithelial or unknown morphology, so were censored at diagnosis, in line with censoring of women diagnosed with other invasive cancers. This left a total of 7531 breast cancer cases included in our incidence rates. The Cancer Registry of Norway has had mandatory reporting of all new cancer cases since 1953, with 98.8% completeness and 99.3% histologically verified breast cancers [21].

Stage at diagnosis was determined by a summary stage variable created by the Cancer Registry of Norway, using pathological tumor size, nodal status and metastasis (TNM), or clinical notifications of SEER summary stage if pathological TNM was missing. In these notifications, tumors localized to the breast were classified as TNM stage I; tumors with metastasis to regional lymph nodes as TNM stage II; tumors with metastasis to skin and/or chest wall as TNM stage III; and tumors with metastasis to distant lymph nodes or other organs as TNM stage IV. If pathological TNM and clinical notifications were both missing or incomplete, stage was classified as unknown.

In our analyses, we categorized stage as localized (TNM I), regional (TNM II–III), distant (TNM IV) or unknown. It should be noted that the regional group also includes node negative tumors that are large in size or have grown into the skin and/or chest wall (pT2-4pN0). We combined TNM stages II and III because the Cancer Registry changed their coding practice for lymph node spread in 2008, resulting in a substantial migration from stages II to III. Details of the Cancer Registrýs staging and coding practices over time are reported elsewhere [22].

Statistical analysis

In descriptive analyses of education and income groups, we compared distribution of person-years at risk by age (30–34, 35–39, 40–44 and 45–48 years), calendar period (2000–2004, 2005–2009, and 2010–2015) and immigration history (Norwegian or immigrant), and calculated overall and stage-specific age-standardized rates using the world standard population as the reference population [23,24].

To conduct a Poisson regression analysis, individual data was collapsed to an aggregate data file containing the sum of person-years observation and number of breast cancer cases by stage in each covariate pattern. In Poisson analyses, we estimated with 95% confidence intervals (CI) the stage-specific incidence rate ratios and incidence rate differences per 100,000 person-years, by education level and income quintile. The incidence rate differences were post-estimated using pairwise comparisons of predicted incidence rates.

We estimated three models: (1) an education model; (2) an income model; and (3) an interaction model that compared women by their combined education and income status. In the interaction model, we were specifically interested in differentiating the most vulnerable women in the population – those with the lowest education level and lowest income, from the rest. We therefore defined secondary or tertiary education as 'high education' and the four highest income quintiles as 'high income.'

All models contained *a priori* interactions between stage and socioeconomic variables, since our main interest was stage-specific socioeconomic inequalities. We otherwise used likelihood ratio tests to test for interactions between remaining covariates when determining final models. Age, calendar period and immigration history all had significant interactions with stage, but none had interactions with socioeconomic variables. Final models were therefore adjusted for interactions between stage and age, stage and calendar period, and stage and immigration history. During the model building, age and period were tested as linear or categorical variables. The categories described above were found adequate for controlling for confounding.

We analyzed the data using STATA 15.1 [25]. A two-sided p-value less than .05 was considered statistically significant. We obtained ethical approval from the Regional Committee for Medical and Health Research Ethics in Norway (reference 2013/2376).

Results

Study cohort

Our cohort included 1,106,863 women with 9,569,368 person-years observation time. There were 7531 cases of first invasive breast cancer diagnosed; 2322 localized, 4481 regional, 233 distant and 495 with unknown stage. Compulsory educated women accounted for 21% of person-years observation, secondary for 38% and tertiary for 41% of person-years observation (Supplemental Table S2). Tertiary educated women accounted for a greater proportion of observation time in younger age groups and more recent periods compared to secondary and compulsory educated women. In other words, an increasing proportion of younger birth cohorts completed a tertiary education. Income groups were equally distributed by age group and calendar period, because income quintiles were age and period-specific. The median income in each quintile increased with older age and over time (Supplemental Table S1). Immigrant women, who comprised 10% of the study cohort, had a higher proportion of observation time in the lowest education and income groups compared to Norwegian-born women.

Overall and stage-specific incidence rates

The overall age-standardized breast cancer rate for the study cohort was 78.3 cases per 100,000 person-years (Table 1). Overall incidence rates increased with increasing education and income level, increasing age, over time, and were higher for Norwegian compared to immigrant women.

In the study cohort, the age-standardized rate for localized stage (24.2 per 100,000) was around half the rate for regional stage (46.6 per 100,000) and ten times the rate for distant stage (2.4 per 100,000) (Table 2). Localized and regional stage rates increased with increasing education and income level, whereas distant stage rates were lowest in the highest education and income groups. Figure 1 shows localized, regional and distant stage rates by combined education and income level.

Table 1. Person-years, breast cancer cases and overall age-standardized incidence rates (World standard population) [23,24].

	Person-years observation	Breast cancer cases	Age-Standardized Rate per 100,000 person-years
Total	9,569,368	7531	78.3
Education Level			
Compulsory	2,039,147	1480	67.1
Secondary	3,650,558	2894	76.5
Tertiary	3,879,663	3157	87.1
Income Quintile[a]			
Q1 (low)	1,825,452	1275	68.0
Q2	1,891,849	1356	71.0
Q3	1,939,196	1500	77.8
Q4	1,976,632	1666	85.5
Q5 (high)	1,936,239	1734	88.9
Education-Income[b]			
Low-Low	655,083	446	59.8
Low-High	1,170,369	829	73.4
High-Low	1,384,064	1034	70.8
High-High	6,359,851	5222	83.2
Age group[c]			
30–34 years	2,423,369	472	19.5
35–39 years	2,569,504	1272	49.5
40–44 years	2,586,876	2579	99.7
45–48 years	1,989,618	3208	161.2
Calendar period			
2000–2004	2,984,783	2179	75.1
2005–2009	2,991,691	2281	76.6
2010–2015	3,592,893	3071	82.6
Immigration history			
Norwegian-born	8,610,134	6871	79.0
Immigrant	959,234	660	72.1

Women 30–48 years in 2000–2015 ($N = 1{,}106{,}863$).
[a]Age and period-specific quintiles of average personal income during the previous five-year period.
[b]Education: low = compulsory; high = secondary-tertiary. Income: low = Q1, high = Q2–Q5.
[c]Incidence rates by age group are crude, not age-standardized.

Table 2. Stage-specific age-standardized incidence rates of breast cancer (World standard population) [23,24].

	Age-Standardized Rate (per 100,000 person-years)			
	Localized ($n = 2322$)	Regional ($n = 4481$)	Distant ($n = 233$)	Unknown ($n = 495$)
Total	24.2	46.6	2.4	5.2
Education level				
Compulsory	19.8	40.4	2.6	4.3
Secondary	23.1	45.9	2.4	5.1
Tertiary	28.2	50.8	2.3	5.7
Income quintile[a]				
Q1 (low)	17.7	41.5	3.2	5.5
Q2	22.1	42.1	2.3	4.5
Q3	24.5	46.3	2.1	4.9
Q4	27.3	49.8	2.2	6.0
Q5 (high)	28.9	52.8	2.3	4.8
Education-Income[b]				
Low-Low	13.4	38.1	3.4	4.9
Low-High	20.8	43.6	3.0	5.9
High-Low	23.2	41.6	2.1	3.9
High-High	26.4	49.2	2.2	5.3
Age group[c]				
30–34 years	5.1	12.2	0.8	1.4
35–39 years	13.3	31.3	1.6	3.3
40–44 years	28.8	61.3	3.3	6.2
45–48 years	55.8	90.2	4.5	10.8
Calendar period				
2000–2004	21.2	45.4	3.1	5.4
2005–2009	24.1	46.2	2.0	4.3
2010–2015	26.7	48.0	2.2	5.7
Immigration history				
Norwegian-born	24.4	46.8	2.5	5.2
Immigrant	22.0	43.8	1.4	4.9

Women 30–48 years in 2000–2015 ($N = 1,106,863$ women, $n = 7531$ breast cancer cases).
[a]Age and period-specific quintiles of average personal income during the previous five-year period.
[b]Education: low = compulsory; high = secondary-tertiary. Income: low = Q1, high = Q2–Q5.
[c]Incidence rates by age group are crude, not age-standardized.

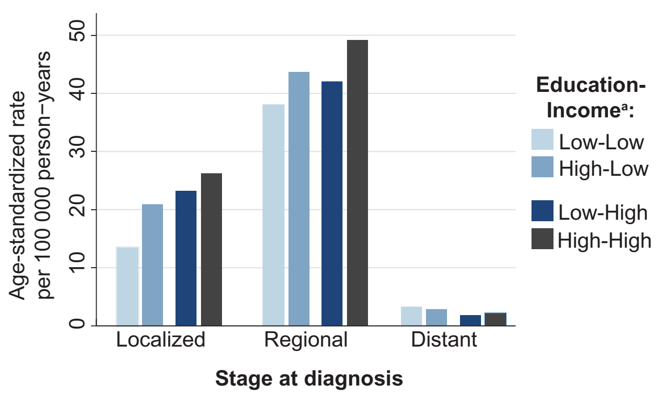

Figure 1. Age-standardized localized, regional and distant stage breast cancer rates, by combined education and income status (World standard population) [23,24]. Women 30–48 years in 2000–2015 ($N = 1,106,863$ women, 7036 breast cancer cases). [a]Education: low = compulsory; high = secondary-tertiary. Income: low = Q1, high = Q2–Q5.

Socioeconomic inequalities in stage-specific incidence

Education

After adjustment for age, period and immigration history, rates of localized and regional stage were significantly higher for secondary and tertiary compared to compulsory educated women, while rates of distant stage did not vary significantly by education level (Figure 2). Adjusted rates of unknown stage were significantly higher for tertiary versus compulsory educated women (rate ratio: 1.32, 95% CI: 1.03–1.69; rate difference: 1.4, 95% CI: 0.2–2.6 per 100,000).

Income

Income patterns for localized and regional stage were similar to patterns by education level (Figure 2). In contrast to educational inequalities for distant stage, which were not significant, the income inequalities for distant stage were significant, and the four highest income quintiles all had significantly reduced adjusted rates of distant stage compared to the lowest income quintile. Adjusted rates of unknown stage did not vary significantly by income quintile.

Combined education and income status

In the model comparing women by their combined education and income status, the adjusted relative rate of localized stage was significantly increased in all groups compared to the low education-low income group (Figure 3). The adjusted relative rate of regional stage was only significantly increased in the high education-high income group compared to the low education-low income group. For distant stage, however, the socioeconomic pattern was reversed; relative rate of distant stage was significantly decreased with high income, regardless of education level. Adjusted rates of unknown stage did not vary significantly by combined education and income status.

Discussion

In this registry-based study of 1.1 million young women in Norway, covered by universal health care but not invited to screening, women with high education or high income level had increased incidence of both localized and regional stage breast cancer, but decreased incidence of distant stage breast cancer, compared to women with low education or income. Differences in distant stage breast cancer were modest in absolute terms and only significant by income, not education.

Localized stage

Increased incidence of localized breast cancer for high compared to low SES young women was consistent with studies that have compared the stage distribution [9–11,26] or odds of early versus late stage diagnosis [12–15,17,27] of patients. In our young population that was not invited to organized screening, some of the increased rates of localized breast cancer for high SES women could be due to private opportunistic screening, which seems to be more frequent among high compared to low SES women in populations without organized screening [28,29] and also among young women below screening age [30]. Awareness of early symptoms of breast cancer may have also been greater for high compared to low SES women [31].

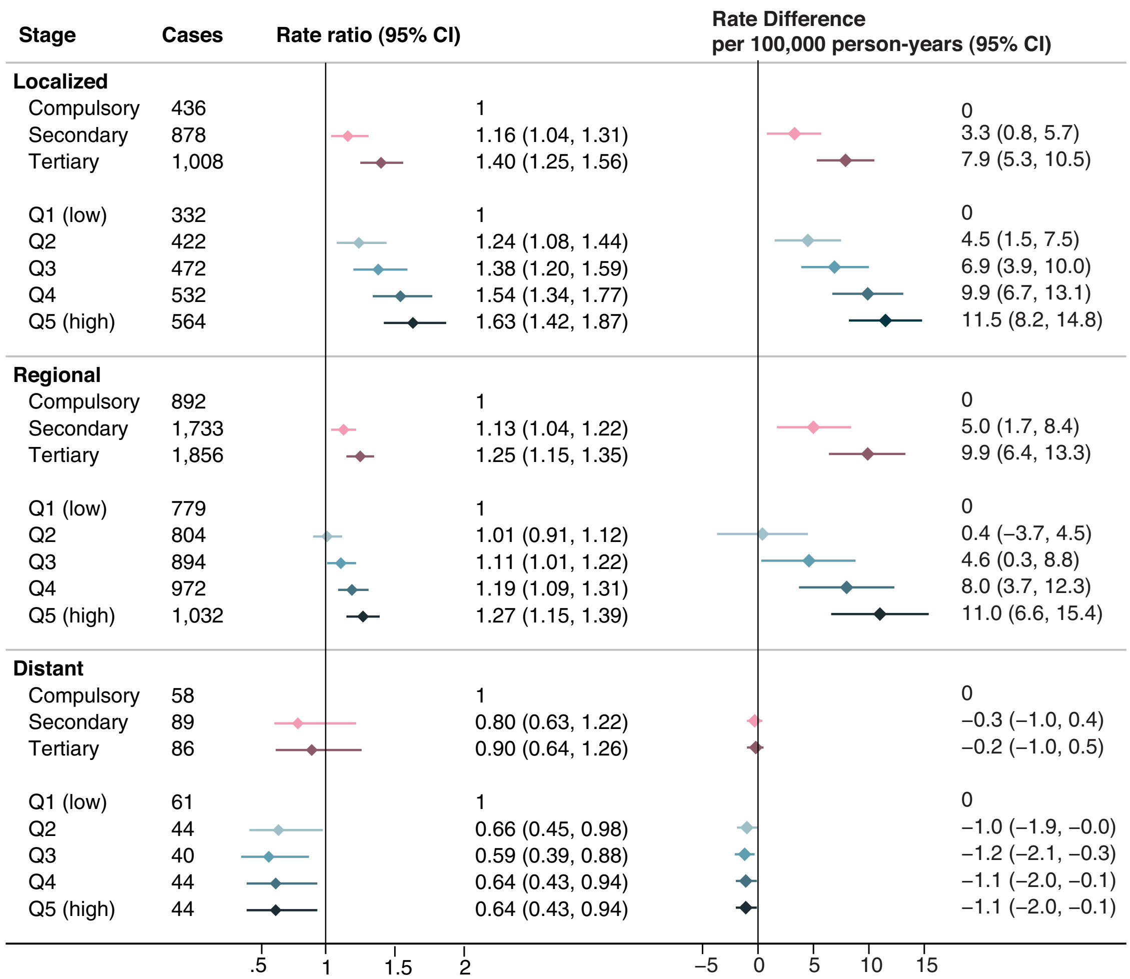

Figure 2. Adjusted stage-specific rate ratios and rate differences with 95% Confidence Intervals (CI), by education and income. Women 30–48 years, Norway, 2000–2015 ($N = 1{,}106{,}863$ women, 7036 breast cancer cases). [a]Rate differences and rate ratios are adjusted for age, period and immigration history (all as interactions with stage). [b]Income is in age- and period-specific quintiles of average personal income during the previous five-year period.

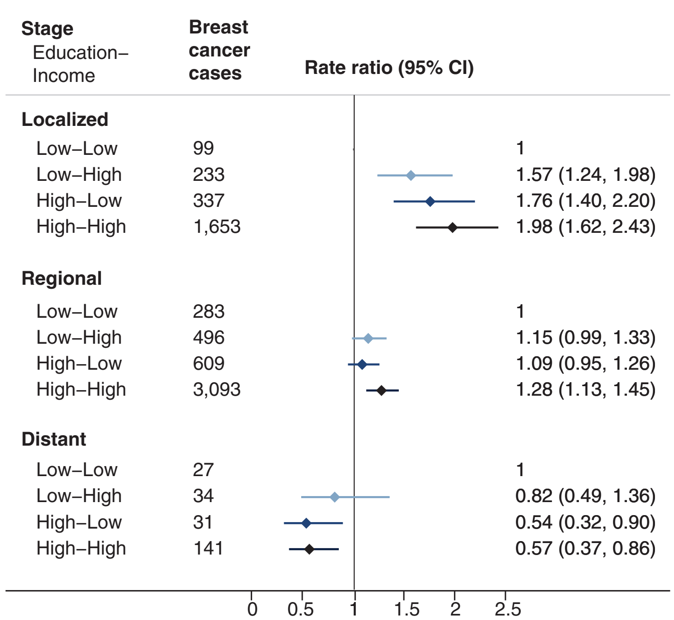

Figure 3. Adjusted stage-specific rate ratios with 95% Confidence Intervals (CI), by combined education and income status. Women 30–48 years, Norway, 2000–2015 ($N = 1{,}106{,}863$ women, 7036 breast cancer cases). [a]Rate ratios are adjusted for age, period and immigration history (all as interactions with stage). [b]Education: low = compulsory; high = secondary-tertiary. Income: low = Q1, high = Q2–Q5.

Regional stage

High SES women had significantly increased incidence of regional stage breast cancer compared to low SES women. Survival from regional stage breast cancer is reasonably high but still lower than for localized tumors [22]. Regional stage tumors may also require more aggressive treatment that can negatively influence the patient's quality of life [5]. Having the highest incidence of regional stage breast cancer was therefore a disadvantage for high SES women. In contrast to our findings, a United States study from 1991–1992 [32] of women aged 55 years or older reported no difference in regional stage breast cancer incidence for women living in affluent versus deprived counties. However, these findings may not be comparable to ours due to the different time period and age group studied, and the use of an area-based SES measure.

To our knowledge, there are no recent studies of SES and stage-specific incidence of breast cancer. Among studies that have compared the stage distribution of breast cancer patients of all ages, a recent study from Norway [11] reported a higher proportion of regional stage tumors for high versus low SES women, supporting our findings of higher regional stage incidence rates for high SES young women. However, studies in the United Kingdom [10,27], Sweden [26], United States [9], Canada [13] and New Zealand [17] have all reported decreasing proportions of regional tumors with increasing SES for women of all ages. Even with a lower proportion of regional tumors, high SES women in these countries may still have the higher absolute rates of regional stage disease, if their overall breast cancer rates are highest.

Distant stage

Reduced rates of distant stage breast cancer for high compared to low SES women was consistent with studies that have compared the stage distribution of patients by SES [9–15,17,26,27]. Some of the SES gradient for distant stage could be due to differential delay in seeking help after becoming aware of symptoms, although a British survey has found that factors relating to patient delay work both for and against high SES women [31].

Our SES gradient for distant stage was significant only for income. High-income earners and highly educated women had similar distant stage rates, whereas the low-income earners had increased distant stage rates compared to lower educated women. In Norway, poor finance rather than lack of knowledge may therefore be a somewhat greater barrier to preventing late detection of breast cancer, even with universal health care. However, absolute rates of distant stage were low, even for low-income earners. The absolute rate increase was only one case per 100,000 person-years for the lowest compared to highest income group. Good breast awareness or equitable health care may have reduced late detection rates and minimized the SES differences in late detection for this young Norwegian cohort.

Study strengths and weaknesses

A key strength of our study was the calculation of stage-specific incidence rates, enabling us to determine how the absolute burden of localized and non-localized disease varied by socioeconomic status in the population. Previous studies comparing the stage distribution of patients have not been able to shed light on whether high SES women only have increased rates of localized disease, or whether they also have higher rates of non-localized disease than low SES women. If we had also compared the stage distribution of patients, we may have overseen the increased rate of regional stage for high versus low SES women, and overemphasized the importance of SES differences in distant stage disease, which were significant for income but small in absolute terms.

Our study used high-quality registry data, with individual SES and virtually complete follow-up of all young women in Norway. Any information or selection bias was likely minimal. Almost no breast cancer tumors were not morphologically verified or based on death certificate only, considered important indicators of validity [33]. Rates of breast cancer with unknown stage were low, so SES inequalities in unknown stage were unlikely to have influenced our overall findings. Registry-based information on income and education was virtually complete for Norwegian women. We excluded nine percent of eligible women who were missing income or education, most of whom were recent immigrants to Norway. However, some of these women do not register their emigration back out of Norway, which leads to immortality bias from overestimation of person-years at risk. We therefore believe that our estimates were more accurate after we excluded women with unknown education or income.

One potential limitation of our registry-based data was that income was only available as five-year averages. Income may have fluctuated over five years due to young women recently entering the workforce or on the other hand reducing employment after childbirth. Five-year average income may have therefore differed from actual income at diagnosis. However, the five-year average should have still reflected financial resources during the years preceding diagnosis.

Conclusion

In this young population covered by universal health care but not invited to organized screening, the higher overall breast cancer incidence among women with high socioeconomic status is not just due to increased detection of localized tumors. Women with high socioeconomic status also had the highest rates of tumors with regional spread, which require more aggressive treatment and have higher mortality than localized tumors. Our results therefore indicate that the higher breast cancer incidence rates in young women with high socioeconomic status is real, and not simply an artifact caused by greater opportunistic screening use compared to women with low socioeconomic status.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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