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Social class is an important and independent prognostic factor of breast cancer mortality

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Reasons of the important impact of socioeconomic status on breast cancer prognosis are far from established. This study aims to evaluate and explain the social disparities in breast cancer survival in the Swiss canton of Geneva, where healthcare costs and life expectancy are among the highest in the world. This population-based study included all 3,920 female residents of Geneva, who were diagnosed with invasive breast cancer before the age of 70 years between 1980 and 2000. Patients were divided into 4 socioeconomic groups, according to the woman's last occupation. We used Cox multivariate regression analysis to identify reasons for the socioeconomic inequalities in breast cancer survival. Compared to patients of high social class, those of low social class had an increased risk (unadjusted hazard ratio [HR] 2.4, 95% CI: 1.6–3.5) of dying as a result of breast cancer. These women were more often foreigners, less frequently had screen-detected cancer and were at more advanced stage at diagnosis. They less frequently underwent breast-conserving surgery, hormonal therapy, and chemotherapy, in particular, in case of axillary lymph node involvement. When adjusting for all these factors, patients of low social class still had a significantly increased risk of dying of breast cancer (HR 1.8, 95% CI: 1.2–2.6). Overmortality linked to low SES is only partly explained by delayed diagnosis, unfavorable tumor characteristics and suboptimal treatments. Other factors, not measured in this study, also could play a role. While waiting for the outcome of other researches, we should consider socioeconomic status as an independent prognostic factor and provide intensified support and surveillance to women of low social class.

Key words: breast carcinoma; socioeconomic status; incidence; mortality; survival

In North America and Western Europe, breast cancer accounts for more than 30% of new cancer cases and for 25% of cancer deaths among women. Breast cancer mortality rates are now decreasing because of the widely generalized use of mammography screening and the improvement in treatment.[1] Besides stage, tumor characteristics and treatment, only few factors are recognized as independent prognostic factors. Socioeconomic status (SES) could be one of them.

Breast cancer occurs more frequently in wealthy countries[2] and among women with high SES.[3] This is partly due to a higher prevalence of breast cancer risk factors, such as older age at first pregnancy, low parity, high-calorie intake, sedentary occupation and use of hormonal replacement therapy in women with high SES.[3–5] On the other hand, breast cancer survival is in general lower in less affluent countries[6] and in women with low income or educational level.[3]

To date, the reasons for social disparities in breast cancer prognosis are far from being established. Possible explanations include differences in sector of care,[7,8] access to early diagnosis, stage at diagnosis,[9] tumor biology[10,11] such as estrogen receptor status,[10–13] grade[9,13,14] or histologic type[13] and access to optimal treatment.[10,13,15] However, despite the numerous publications on social or ethnical disparities in breast cancer outcome, we still do not know to which extent these factors explain social inequalities in breast cancer prognosis.[3,16–21]

In Switzerland, average income and life expectancy are among the highest in the world, and the healthcare system is one of the most expensive worldwide.[22,23] Particularly, in the Swiss canton of Geneva, medical facilities are easily accessible. There are 6 physicians per 1,000 inhabitants. Technical equipment is optimal with at least 3 magnetic resonance imaging facilities per 100,000 inhabitants. Every inhabitant lives in the vicinity of a medical centre or hospital (public or private). Because the access to and the quality of care are particularly high, one could expect minimal social disparities in breast cancer prognosis. However, there is no comprehensive public health strategy except for a breast cancer screening program initiated in 1999, many years after most European countries. Medical insurance is compulsory and costly (~350 € monthly per person). The Swiss government covers all medical insurance fees for 10% of the population considered as indigent and between 5 and 25% of the insurance fees for 17% of the population with low income.

In this study, we investigate the importance of social inequalities in breast cancer survival in Geneva and to which extent differences in patient, tumor and treatment characteristics explain these social disparities.

Material and methods

We used information from the population-based Geneva cancer registry to identify all female residents diagnosed with invasive breast cancer before the age of 70 years between 1980 and 2000. The registration is based on various sources of information. Completeness is considered as very high, as attested by its very low percentage (<2%) of cases recorded only from death certificates.[2] Every hospital, pathology laboratory and practitioner is requested to report all cancer cases. Trained registrars systematically abstract data from medical and laboratory reports. Physicians regularly receive questionnaires to secure missing clinical and therapeutic data. Death certificates are consulted systematically.

For every cancer patient, the Geneva cancer registry records information on sociodemographic characteristics, method of tumor detection, tumor characteristics (coded according to the International Classification of Diseases for Oncology (ICD-O)),[24] hormone receptor status, stage of disease at diagnosis (according to the tumor, lymph node and metastasis TNM classification system),[25] treatment during the first 6 months after diagnosis, type of surgery, number of removed and number of positive lymph nodes, sector of care, date and cause of death (coded according to the World Health Organization's classification).[26]

For this study, variables of interest included age (variable in continuous), country of birth (Switzerland, France, Italy, Spain and Portugal, Western and Northern Europe, Eastern Europe, other), civil status (single, married, widowed, divorced/other), method of detection (screening, symptoms and fortuitous detection during hospitalization/work-up for an unrelated medical condition) and sector of care in charge of the main breast cancer treatment, in particular, surgery (private and public). Histologic type was categorized as ductal (ICD-O codes: 8211, 8500-4, 8521), lobular (ICD-O codes: 8520, 8522), mucinous (ICD-O codes: 8480, 8481) and other. Dif-

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TABLE I – PATIENT CHARACTERISTICS, METHOD OF DETECTION AND SECTOR OF CARE ACCORDING TO SOCIOECONOMIC STATUS AMONG WOMEN AGED <70 YEARS WITH BREAST CANCER (GENEVA CANCER REGISTRY, 1980–2000)

	Socioeconomic status				p-value for χ^2 of heterogeneity[1]
	High	Middle	Low	Other	
Mean age (standard error)	52.0 (0.4)	53.3 (0.2)	54.7 (0.4)	55.6 (0.3)	$p < 0.0001$
Country of birth					$p < 0.0001$
Switzerland	266 (56.2)	1,106 (56.7)	251 (37.9)	428 (51.2)	
France	62 (13.1)	297 (15.2)	60 (9.1)	88 (10.5)	
Italy	15 (3.2)	111 (5.7)	153 (23.1)	54 (6.5)	
Spain and Portugal	7 (1.5)	68 (3.5)	132 (19.9)	26 (3.1)	
Western and Northern Europe	46 (9.7)	176 (9.0)	17 (2.6)	86 (10.3)	
Eastern Europe	27 (5.7)	38 (1.9)	10 (1.5)	20 (2.4)	
Other	50 (10.6)	153 (7.9)	39 (5.9)	134 (16.0)	
Period of diagnosis					$p < 0.0001$
1980–1984	66 (14.0)	295 (15.1)	168 (25.4)	185 (22.1)	
1985–1989	79 (16.7)	357 (18.3)	126 (19.0)	203 (24.3)	
1990–1994	106 (22.4)	463 (23.8)	162 (24.5)	234 (28.0)	
1995–2000	222 (46.9)	834 (42.8)	206 (31.1)	214 (25.6)	
Method of detection					$p = 0.0011$
Screening	136 (28.8)	523 (26.8)	129 (19.5)	228 (27.3)	
Symptoms	294 (62.2)	1,261 (64.7)	462 (69.8)	536 (64.1)	
Other	43 (9.1)	165 (8.5)	71 (10.7)	72 (8.6)	
Sector of care					$p < 0.0001$
Private	343 (72.5)	1,195 (61.3)	196 (29.6)	496 (59.3)	
Public	130 (27.5)	754 (38.7)	466 (70.4)	340 (40.7)	
Total	473 (100.0)	1,949 (100.0)	662 (100.0)	836 (100.0)	

Values indicate the number of people belonging to a particular status; values in parentheses indicate percentages.
[1]After exclusion of patients with "other" socioeconomic status.

ferentiation was considered as well differentiated, moderately differentiated, poorly differentiated and unknown. Estrogen receptor status was considered as positive (>10% of the cells expressed estrogen), negative and unknown. Pathologists assessed differentiation only from 1985 and hormone receptor status since 1995. Tumor size, in millimeter, was based on pathology reports and regrouped as ≤10, 11–20, 21–40 and ≥41. The number of removed and the number of positive axillary lymph nodes were based on pathology reports and considered as a mean number.

For staging, we used the pathological pTNM or, when absent, the clinical cTNM classification. Tumors were classified as T0 (no evidence of primary tumor), T1 (≤2 cm), T2 (2–5 cm), T3 (>5 cm), T4 (extension to chest wall/skin and inflammatory carcinoma) and TX (unknown). Lymph node invasion was classified as N0 (no invasion), N1 (metastasis to movable ipsilateral axillary node), N2 (metastasis to fixed ipsilateral axillary node) and NX (unknown) and distant metastasis as M0 (absent), M1 (present) or MX (unknown). Stage was classified in 5 groups: stage I (T1 and N0), stage II (T0 or T1 and N1, T2 and N0 or N1, T3 and N0), stage III (T0 or T1 or T2 and N2, T3 and N1 or N2, T4 and any N), stage-IV (M1) and unknown.[25]

Treatments of interest were type of surgery (breast-conserving surgery, mastectomy, unknown), radiotherapy (yes, no), hormonal therapy (essentially tamoxifen during the study period) (yes, no) and chemotherapy (yes, no).

The Geneva cancer registry systematically retrieves the patient's last occupation from the files of the Cantonal Population Office, which is in charge of the registration of the resident population. We used the classification of vital statistics which includes 12 major groups subdivided into 40 sub-major groups and 130 minor groups.[27] Occupational subgroups were classified into SES indicators in 7 levels based on the Social Classes of the British Registrar General.[28] For the purpose of this study, we regrouped SES in 4 levels only: low (manual employees, skilled and unskilled workers, including farmers), middle (nonmanual employees and administrative staff), high (professionals, executives, administrators, entrepreneurs) and other (housewives and unemployed).[29] Unfortunately, we could not distinguish between housewives and unemployed who represented less than 3% of Geneva's working population during the study period. We limited our study to women younger than 70 years, because former occupation was not systematically reported for retired women.

In addition to passive follow-up (routine examination of death certificates and hospital reports), the Cancer registry assesses survival annually through an active follow-up by linkage of the files of the Cantonal Population Office with the Geneva Cancer Registry database, using personal Id numbers. Cause of death is systematically recorded and validated by consulting medical files or by sending a questionnaire to the practitioner.

Statistical analysis

Patient and tumor characteristics, sector of care and treatment were compared between socioeconomic groups by chi-square test for heterogeneity. To examine the differences in the distribution of differentiation and estrogen receptor status by SES, we limited the study to the years with available corresponding data.

We used the actuarial method (intervals in months and standard error according to Greenwood) to calculate five-year disease specific (deaths from breast cancer) and overall (all deaths) survival and log-rank test to compare survival curves.[30]

We evaluated the effect of SES on five-year and ten-year disease specific mortality by Cox's proportional hazards analysis. *T*o evaluate if mortality risks increased when SES levels decreased, we performed trend test considering SES as a continuous variable after having excluded the category "other." To evaluate to what extent patient and tumor characteristics and treatment explained the socioeconomic differences in breast cancer survival, we gradually entered these factors in the Cox model. The multiadjusted hazard ratios of breast cancer mortality therefore reflect the remaining effect of SES on breast cancer mortality, *i.e.*, the part of overmortality not explained by patient, tumor and treatment characteristics. To evaluate if the effect of SES was similar over time, in women before and after the age of 50 years, in early and advanced disease, in Swiss born and migrants, in private and public sectors and across different treatment categories, we performed interaction tests between

TABLE II – BREAST CANCER CHARACTERISTICS ACCORDING TO SOCIOECONOMIC STATUS AMONG PATIENTS AGED <70 YEARS (GENEVA CANCER REGISTRY, 1980–2000)

	Socioeconomic status				p-value for χ^2 of heterogeneity[1]
	High	Middle	Low	Other	
Histologic subtype					$p = 0.0071$
Ductal	388 (82.0)	1,548 (79.4)	553 (83.5)	674 (80.6)	
Lobular	53 (11.2)	192 (9.9)	40 (6.0)	64 (7.7)	
Mucinous	6 (1.3)	40 (2.1)	11 (1.7)	6 (0.7)	
Other	26 (5.5)	169 (8.7)	58 (8.8)	92 (11.0)	
Differentiation[2]					$p = 0.2481$
Well	92 (22.6)	399 (24.1)	106 (21.5)	150 (23.0)	
Moderately	174 (42.8)	608 (36.8)	188 (38.1)	254 (39.0)	
Poorly	80 (19.7)	401 (24.2)	124 (25.1)	132 (20.3)	
Unknown	61 (15.0)	246 (14.9)	76 (15.4)	115 (17.7)	
Estrogen receptors status[3]					$p = 0.9170$
Positive	173 (77.9)	626 (75.1)	155 (75.2)	155 (72.4)	
Negative	37 (16.7)	156 (18.7)	37 (18.0)	38 (17.8)	
Unknown	12 (5.4)	52 (6.2)	14 (6.8)	21 (9.8)	
Tumor size (mm)					$p = 0.2035$
≤10	84 (17.8)	346 (17.8)	96 (14.5)	150 (17.9)	
11–20	187 (39.5)	718 (36.8)	233 (35.2)	304 (36.4)	
21–40	125 (26.4)	507 (26.0)	202 (30.5)	212 (25.4)	
>40	24 (5.1)	114 (5.8)	43 (6.5)	47 (5.6)	
Unknown	53 (11.2)	264 (13.5)	88 (13.3)	123 (14.7)	
Stage[4]					$p = 0.0005$
I	190 (40.2)	751 (38.5)	222 (33.5)	320 (38.3)	
II	218 (46.1)	870 (44.6)	302 (45.6)	354 (42.3)	
III	24 (5.1)	156 (8.0)	79 (11.9)	78 (9.3)	
IV	23 (4.9)	105 (5.4)	46 (6.9)	51 (6.1)	
Unknown	18 (3.8)	67 (3.4)	13 (2.0)	33 (3.9)	

Values indicate the number of people belonging to a particular status; values in parentheses indicate percentages.

[1]After exclusion of patient with "other" socioeconomic status.–[2]Information on differentiation is available only since 1985; the description in the table is limited to the period 1985–2000.–[3]Information on estrogen receptor status is available only since 1995; the description in the table is limited to the period 1995–2000.–[4]Stage is coded according to the International TNM classification.

SES and these variables.[31] We also performed subgroup analyses, in particular, among young (<50 years) and older (50–69 years) women.

All analyses were done with SPSS software (version 10 SPSS Inc. Chicago, IL). Differences were considered statistically significant at $p < 0.05$.

Results

At 5 years of follow-up, among the 3,920 patients of the cohort, 483 patients had died of breast carcinoma, 144 had died of other causes and 215 patients were lost to follow-up because they had moved from the canton. Patients of low SES were older than those of high SES (mean age 55 *vs.* 52 years), more often married (64 *vs.* 54%), more often born abroad (62 *vs.* 44%), and more often diagnosed before 1989 (46 *vs.* 31%) (Table I). They had less frequently screen-detected cancers (20 *vs.* 30%) and were mainly treated in the public sector (70 *vs.* 28%) (Table I). These patients also had less frequent lobular histology (6 *vs.* 11%) and stage I disease (34 *vs.* 40%) (Table II). Nearly all women in the other SES category were married, reflecting their housewife status. Patients belonging to other SES were comparable to women of middle SES in terms of country of birth, method of detection, sector of care and tumor stage. They were slightly older and had slightly less often information on histologic type, differentiation and estrogen receptor status.

Cancer treatment differed between the SES groups (Table III). Women of low SES less frequently underwent breast-conserving surgery than those of high SES (39 *vs.* 51%) and had less frequent lymph node dissection (84 *vs.* 89%). They had less often adjuvant radiotherapy (63 *vs.* 69%) and less frequently hormonal therapy (36 *vs.* 40%). However, among postmenopausal patients (<50 years) with estrogen receptor positive tumors, use of hormonal therapy was evenly distributed between SES groups (Table III). Chemotherapy was evenly used among women with high and low SES. Nevertheless, when considering women with axillary lymph node involvement, women of low SES less often received adjuvant chemotherapy (63 *vs.* 70%). Patients belonging to other SES less frequently had breast conserving surgery, hormonal therapy and chemotherapy for lymph node positive disease compared to that of patients of middle SES.

In addition to tumor size, lymph node status, tumor histology, differentiation and type of treatment, SES was a strong prognostic factor for breast cancer mortality. The five-year breast cancer specific survival was 91% (95% CI: 88–94%) for women of high SES, 85% (95% CI: 83–87%) for women of middle SES, and 81% (95% CI: 78–84%) for women of low SES ($p < 0.0001$) (Fig. 1). The survival of women with other SES was 86% (95% CI: 83–89%), similar to that of women of middle SES.

Table IV presents the unadjusted effect of SES on breast cancer mortality and the modification of risk when gradually accounting for other prognostic factors. Compared with that of women of high SES, the nonadjusted risk of dying of breast cancer (hazard ratio) was 1.7 (95% CI: 1.2–2.5) for women of middle SES and 2.4 (95% CI: 1.6–3.5) for women of low SES ($p_{\text{Wald test}} < 0.0001$, $p_{\text{trend test}} < 0.0001$). The relative differences between SES groups diminished but remained statistically significant after adjustment for age, period of diagnosis, civil status, country of birth, tumor characteristics, method of detection, stage, sector of care and treatment. Compared with that of women of high SES, the multiadjusted hazard ratio was 1.6 (95% CI: 1.1–2.3) for women of middle SES and 1.8 (95% CI: 1.2–2.6) for women of low SES ($p_{\text{Wald test}} = 0.0330$, $p_{\text{trend test}} = 0.0271$). The risk of dying of breast cancer for women with other SES was 1.3 (95% CI: 0.9–2.0).

We also examined the effect of each factor separately. The 2.4-fold increased breast cancer mortality risk linked to low SES compared to that of high SES decreased to 2.0 when we adjusted for

TABLE III – TREATMENT OF BREAST CANCER ACCORDING TO SOCIOECONOMIC STATUS AMONG WOMEN AGED <70 YEARS (GENEVA CANCER REGISTRY, 1980–2000)

	Socioeconomic status				p-value for χ^2 of heterogeneity[1]
	High	Middle	Low	Other	
Type of surgery					
Breast-conserving	243 (51.4)	981 (50.3)	256 (38.7)	348 (41.6)	$p < 0.0001$
Mastectomy	210 (44.4)	876 (44.9)	370 (55.9)	450 (53.8)	
Unknown[2]	20 (4.2)	92 (4.7)	36 (5.4)	38 (4.5)	
Lymph node dissection					
Yes	421 (89.0)	1,655 (84.9)	557 (84.1)	705 (84.3)	$p = 0.0465$
No	52 (11.0)	294 (15.1)	105 (15.9)	131 (15.7)	
Radiotherapy					
Yes	325 (68.7)	1,315 (67.5)	414 (62.5)	504 (60.3)	$p = 0.0383$
No	148 (31.3)	634 (32.5)	248 (37.5)	332 (39.7)	
Radiotherapy after breast conserving surgery					
Yes	226 (93.0)	910 (92.8)	238 (93.0)	316 (90.8)	$p = 0.9875$
No	17 (7.0)	71 (7.2)	18 (7.0)	32 (9.2)	
Hormonal therapy					$p = 0.2712$
Yes	191 (40.4)	749 (38.4)	237 (35.8)	245 (29.3)	
No	282 (59.6)	1,200 (61.6)	425 (64.2)	591 (70.7)	
Hormonal therapy among women > 50 years with positive estrogen receptors[3]					
Yes	105 (85.4)	391 (82.7)	95 (85.6)	111 (84.7)	$p = 0.6373$
No	18 (14.6)	82 (17.3)	16 (14.4)	20 (15.3)	
Chemotherapy					
Yes	210 (44.4)	873 (44.8)	294 (44.4)	326 (39.0)	$p = 0.9785$
No	263 (55.6)	1076 (55.2)	368 (55.6)	510 (61.0)	
Chemotherapy among women with positive lymph nodes					
Yes	115 (69.7)	511 (74.4)	163 (62.7)	198 (66.4)	$p = 0.0017$
No	50 (30.3)	176 (25.6)	97 (37.3)	100 (33.6)	

Values indicate the number of people belonging to a particular status; values in parentheses indicate percentages.

[1]After exclusion of patients with "other" socioeconomic status.–[2]Including nonoperated patients.–[3]Information on estrogen receptor status is available only since 1995; the description in the table is limited to the period 1985–2000.

stage at diagnosis. The same decrease was observed for adjustment for treatment or tumour characteristics. The risk decreased to only 2.2 when adjusting for method of detection and to only 2.3 when adjusting for country of birth.

None of the interaction tests were significant. The effect of SES did not significantly change according to patient characteristics, period, sector of care, tumor stage and treatment. Analyses by subgroups showed that the adjusted risk of breast cancer mortality in low *vs*. high SES women (HR: 1.7, in the whole study cohort) was slightly more pronounced in women born in Switzerland (HR: 2.2, 95% CI: 1.3–3.9), treated in the private sector (HR: 1.9, 95% CI: 1.0–3.6) and less pronounced among patients diagnosed during the first study period (HR: 1.3, 95% CI: 0.7–2.8).

Results by age groups were interesting. The difference in stage distribution by SES was more marked in young (<50 years) than in old women (50–69 years), while the treatment disparities were more important in old than in young women. Among young women, the proportion of stage I, II, III and IV disease was 39, 47, 2 and 5% among high SES patients *vs*. 27, 52, 14 and 7% among low SES patients (p value for X^2 of heterogeneity $p < 0.001$). Among old women (50–69 years), the proportion of mastectomy was 44% in high *vs*. 55% in low SES patients ($p < 0.001$), the use of adjuvant hormonal therapy was 54 *vs*. 41% ($p = 0.001$) and of adjuvant chemotherapy in case of positive lymph nodes was 60 *vs*. 54% ($p = 0.003$). The higher proportion of screen-detected cancers and the higher prevalence of lobular histologic type among high SES patients were present only in old women. In young women, unadjusted and multiadjusted risk linked to low SES was 3.1 (95% CI: 1.6–6.2) and 2.4 (95% CI: 1.2–4.9), respectively. After the age of 50 years, the corresponding HRs were 1.9 (95% CI: 1.2–3.1) and 1.5 (95% CI: 0.9–2.4), respectively.

We performed additional analyses to rule out putative bias linked to lack of information on receptor status and differentiation in the early period or to putative disparities between pathology laboratories. In the 1995–2000 period, the percentages of tumors with unknown estrogen receptor status and differentiation were low (7 and 9%, respectively) and the adjusted risk of breast cancer mortality linked to low SES patients remained important (HR: 3.1, 95% CI: 1.1–8.9). The effect of SES was similar between laboratories. Also, to rule out residual effect of period and nationality, which differed between SES, we adjusted for year of diagnosis (instead of period) and detailed country of birth (instead of region), but this did not modify the results.

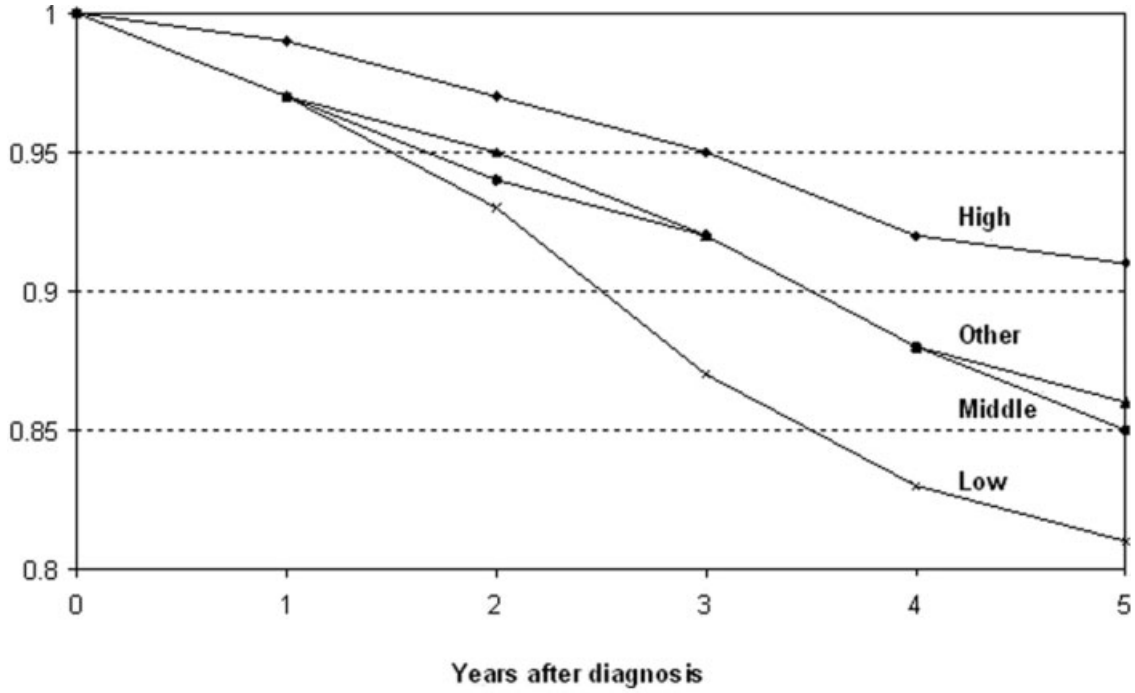
After 10 years of follow-up, the overmortality from breast cancer among low *vs*. high SES patients was slightly lowered (adjusted HR: 1.5, 95% CI: 1.1–2.1).

Overall mortality was also significantly linked to SES. Compared with that of women of high SES, the unadjusted hazard ratio of 5-year overall mortality was 1.8 (95% CI: 1.3–2.6) for women of middle SES and 2.6 (95% CI: 1.8–3.6) for women of low SES. These relative differences remained significant when adjusting for factors significantly linked to general mortality in univariate analyses (*i.e*., age, civil status, and period) with adjusted HR of 1.8 and 2.2 for middle and low SES, respectively.

Discussion

In this study, we clearly demonstrate that breast cancer patients of low SES have a significantly increased risk of dying as a result of breast cancer compared to the risk in patients of high SES. Low SES patients were diagnosed at a later stage, had different tumor characteristics and more often received suboptimal treatment. However, these important prognostic factors explained less than 50% of the overmortality linked to low SES. Even after adjusting for all these factors, the risk of dying of breast cancer remained 70% higher among patients of low SES than that among patients of high SES.

Other differences between SES groups could explain the poorer prognosis of low SES patients. Low SES patients were more often migrants treated in the public sector. They were underrepresented in the most recent period, because the increase in breast cancer



NUMBER OF WOMEN AT RISK AT THE BEGINNING OF THE PERIOD

	0 year	1st year	2nd year	3rd year	4th year	5th year
High	473	461	402	349	294	256
Middle	1,949	1,868	1,614	1,396	1,197	1,021
Low	662	623	545	472	407	364
Other	836	792	718	651	562	512

FIGURE 1 – Observed breast cancer specific survival according to socioeconomic status among women aged <70 years. (Only deaths from breast cancer are considered. Survival curves are derived from actuarial method and are not adjusted. *p* value of log-rank test <0.0001.)

TABLE IV – EVOLUTION OF THE RISK[1] (HAZARD RATIO, HR) OF DYING AS A RESULT OF BREAST CANCER ACCORDING TO SOCIOECONOMIC STATUS AMONG PATIENTS AGED <70 YEARS AFTER ADJUSTMENT STEP BY STEP ON OTHER PUTATIVE EXPLANATORY FACTORS (GENEVA CANCER REGISTRY, 1980–2000)

	Unadjusted HR (95%CI)	HR adjusted for age and period[2]	HR additionally adjusted for civil status and country of birth[3]	HR additionally adjusted for tumor characteristics[4]	HR additionally adjusted for method of detection and stage[5]	HR additionally adjusted for sector of care and treatment[6]
High	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Middle	1.7 (1.2–2.5)	1.6 (1.1–2.4)	1.7 (1.1–2.4)	1.6 (1.1–2.1)	1.6 (1.1–2.3)	1.6 (1.1–2.2)
Low	2.4 (1.6–3.5)	2.1 (1.4–3.0)	2.1 (1.4–3.1)	1.9 (1.3–2.3)	1.8 (1.2–2.6)	1.7 (1.1–2.5)
Other	1.7 (1.1–2.5)	1.4 (1.0–2.1)	1.5 (1.0–2.3)	1.4 (0.9–2.1)	1.3 (0.9–2.0)	1.3 (0.9–1.9)
p-Value for Wald test[7]	0.0001	0.0021	0.0043	0.0086	0.0169	0.0330
p-Value for trend test[7]	0.0001	0.0008	0.0007	0.0012	0.0117	0.0271

[1]Hazard ratios derived from Cox model, considering only death from breast cancer.–[2]Hazard ratios are adjusted for age at diagnosis (in continuous) and period (1980–1984, 1985–1989, 1990–1994, 1995–2000).–[3]Hazard ratios are adjusted for age, period, civil status (single, married, widowed, divorced/other) and country of birth (Switzerland, France, Italy, Spain and Portugal, West and North Europe, East Europe, other).–[4]Hazard ratios are adjusted for age, period, marital status, country of birth, histology (ductal, lobular, mucinous carcinoma, other), differentiation (well, moderately, poorly, unknown), and estrogen receptor status (positive, negative, unknown).–[5]Hazard ratios are adjusted for age, period, marital status, country of birth, histology, differentiation, estrogen receptor status, method of detection (screening, symptom, other) and stage (I, II, III, IV, unknown).–[6]Hazard ratios are adjusted for age, period, marital status, country of birth, histology, differentiation, estrogen receptor status, method of detection, stage, sector of care (private, public), type of surgery (no surgery, breast-conserving surgery, mastectomy), lymph node dissection (yes, no), radiotherapy (yes, no), hormonal therapy (yes, no), and chemotherapy (yes, no).–[7]After exclusion of patients with "other" socioeconomic status.

incidence in Geneva mainly concerned women of high SES. However, these differences explained only a small part of the overmortality associated with low SES, and the SES effect on breast cancer mortality remains present whatever the period, sector of care and place of birth.

This study has several shortcomings. The definition of SES was based on the woman's occupation and not on the husband's, which would probably better describe the family's socioeconomic situation. No information on SES was available for housewives, representing a substantial percentage of women living in Geneva. We evaluated the breast cancer mortality in this group and found a comparable risk as for patients of middle SES. We have no information on estrogen receptor status and differentiation for the beginning of the study period as these prognostic factors were not identified in routine histologic examination. However, the SES disparities remain present in the last study period, when there was adequate information on these tumor characteristics. We realize that, despite detailed information on patient and tumor characteristics and treatment, there is still room for residual confounding associated with unrecorded prognostic factors such as type and dose of adjuvant chemotherapy and the patient's compliance. Also, we have no information on comorbidity which could influence not only general mortality but also mortality linked to breast cancer itself, as comorbidity may influence the attribution of optimal treatment, compliance or host response to tumor aggression.

Health inequalities between social classes were already recognized several centuries ago. One would expect that the improvement of working and living conditions would have reduced social health inequalities but, while life expectancy has increased considerably, health inequalities have neither disappeared nor diminished.[3,32–34]

Other studies in European countries reported a cancer overmortality of 25 to 50% among breast cancer patients of low SES.[3,10,35–37] The number of cancer deaths in Europe that could potentially be avoided by eliminating social variation in cancer survival appeared particularly important for breast cancer.[38]

Even though Switzerland has one of the best equipped healthcare systems in Europe, this study shows that breast cancer patients of low SES have a 2.4-fold increased risk of dying of breast cancer compared with the risk for breast cancer patients of high SES. This difference is in fact as great as that between black and white populations in North America.[39,40] In addition, we observed that the SES differences remained and even increased during the 20-year period, despite cancer screening becoming more widely used and the irrefutable progress in medical care.

The effect of SES was particularly important among young women of low SES with at least a 3-fold increased risk of dying of breast cancer among patients of low *vs.* high SES. The public health impact of SES inequalities in breast cancer mortality is therefore even higher in terms of years of life lost due to premature death. Comparison between breast cancer and other causes of death could explain the lower impact of SES on breast cancer mortality among the elderly.

Nearly all previous studies on social disparities in breast cancer survival or mortality have reported that low SES impairs prognosis.[3,16–21] However, only few studies evaluated the reasons of such social disparities.[12,34,35,41–47] All these studies have demonstrated that differences in stage at diagnosis or in tumor characteristics only partly explain the SES differences in breast cancer mortality. To our knowledge, the present study is the first to consider, in addition to stage and tumor characteristics, other well established prognostic factors linked to patient characteristics, screening and treatment and their interaction on SES impact on breast cancer mortality. We found that all these prognostic factors only partly explained SES differences in breast cancer survival. Other reasons linked to the patient's health, like lifestyle, attitude, knowledge and convictions also could play a role. Low SES might prevent the patient to cope with the medical system, to overcome psychosocial difficulties, to endure the adverse effects of treatments and consequently to receive optimal cancer care.[18] We can also learn from the causes evoked in studies on Black and White disparities.[48] Black individuals are more likely than white individuals to have a defeatist attitude toward medical illness, to experience stigma, fear and denial related to a cancer diagnosis, to mistrust the healthcare system, to have misperceptions about cancer and treatment benefits, to miss their medical visits and to be less participatory. Medical professionals may also have more difficulty to communicate, to present treatment enthusiastically, to provide care of high quality to black or low SES patients.

We urgently need additional studies on the aetiology of social disparities in cancer outcome. Until more information on the reasons for SES disparities are available, we should consider SES as an important and independent prognostic factor. A systematic social evaluation should be part of the standard work-up of all breast cancer patients and social support should be part of the standard breast cancer treatment among low SES patients.

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