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Socioeconomic Status and Breast Cancer Survival in the Southeastern Netherlands, 1980–1989

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Socioeconomic differences in breast cancer survival in the southeastern Netherlands between 1980 and 1989 were studied (n = 3928), as was the impact of prognostic factors (stage at diagnosis, morphology, and treatment) on such differences. An area-based measure of socioeconomic status (SES) in five groups, based on the postcode of residence at the time of diagnosis, was used. In univariate analyses the relative survival rate was used to correct for causes of death other than breast cancer. The measure of outcome in multivariate analyses was the hazard ratio. The results of both univariate and multivariate analyses suggested a small survival advantage for the higher SES groups. In a model with follow-up period, SES and age, the hazard ratios with 95% confidence intervals (CI) for SES groups from high to low were: 1.00, 1.06 (0.84–1.33), 1.04 (0.86–1.26), 1.15 (0.96–1.38), 1.18 (0.99–1.42). After a correction for stage at diagnosis, differences in survival were reduced substantially. Morphology and treatment were not important explanatory factors of the SES survival association. We conclude that small socioeconomic differences in breast cancer survival exist in The Netherlands and that stage at diagnosis is the most important determinant of such differences.

Key words: survival, breast cancer, socioeconomic status, prognostic factors, The Netherlands
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INTRODUCTION

BREAST CANCER is the most common cancer among females in The Netherlands [1] as in many developed countries. Dutch women experience one of the highest incidence rates in the world [2]. The 5 year relative survival rate of breast cancer patients in the period 1975–1985 in the southeastern Netherlands was 69% [3].

Socioeconomic differences in breast cancer survival have been reported in studies from the United States [4], Finland [5], Sweden [6], Australia [7], Scotland [8] and England and Wales [9]. Except for one [9], these studies on patients diagnosed in the 1960s or later, showed that breast cancer patients of low socioeconomic status (SES) have a higher chance of dying from their disease than breast cancer patients of high SES.

This paper is the first report on the impact of SES on breast cancer survival in The Netherlands, a country that is characterised by a relative lack of geographical and financial barriers to primary and specialised care. A description of the association between an area-based measure of SES and breast cancer survival in the 1980s is given and possible explanations of this association were studied. With respect to the latter, it was tested whether the difference in survival from breast cancer in different SES groups can be explained by the distribution of a number of prognostic factors: stage at diagnosis, morphology and treatment.

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PATIENTS AND METHODS

Patients

Data for this study were derived from the population-based Eindhoven Cancer Registry, The Netherlands, which serves an area of about one million inhabitants (about 7% of the Dutch population) in the southeastern part of The Netherlands [2]. The registry identifies newly diagnosed cases of cancer through routine reports from departments of pathology and radiotherapy, through in-patient records from all eight community hospitals in the region, as well as through data from specialised departments and hospitals outside of the region [2, 10]. In this region, the distance to a hospital is always less than 30 km and that to a radiotherapy department is always less than 50 km. All hospitals use the same criteria for the clinical assessment and

treatment of breast cancer patients as they adhere to the guidelines developed by the regional Breast Cancer Study Group [11].

The records of all women diagnosed with an invasive tumour of the breast between 1980 and 1989 (n = 3959) were checked. Patients with an unknown basis of diagnosis (n = 3), diagnosis based on autopsy (n = 2), or unknown address at diagnosis (n = 21) were excluded from the basic material. The remaining 3933 patients were followed up until 1 July 1991, through the virtually complete municipal registries in the area, to determine their vital status. This was unknown for 5 patients, thus finally 3928 patients were included in the study.

Both patients with (96%) and those without (4%) a histologically confirmed breast tumour were included in the study, as there was no systematic difference in the proportion of patients with a histologically confirmed breast tumour according to SES group.

SES

Because no data on the SES of individual patients were directly available from the cancer registry, a proxy measure of SES was used, based on the place of residence at time of diagnosis of each patient. Data to develop the proxy measure were obtained from a commercial marketing agency, which had assigned each postcode (average of 16 households) in our study area to one of 45 socioeconomic categories, using a wide range of socioeconomic and sociodemographic survey data at the postcode level. The central variable in our analysis was education; the agency provided us with information on the percentage of main breadwinners in three educational groups (low, medium, high) for each of the 45 socioeconomic categories. These three educational groups encompassed several types of schooling, and we assigned an average number of years of education to each of them: 7.5 years to the lowest educational category (range of education between 6 and 9 years), 10 years to the medium educational category (years of education either 10 or 11) and 15 years to the highest educational category (range of years of education between 12 and 18).

The information on the percentage of main breadwinners in each of these three educational groups was then used to calculate a summary measure of the average number of years of education for each of the 45 socioeconomic categories. The 45 socioeconomic categories were then ranked from low (7.8 years) to high (13.8 years) according to their summary score on education, and five socioeconomic categories were constructed, based on quintiles of the underlying population. So the lowest SES category [1] contained approximately 20% of the population living in areas with the lowest educational level and the highest SES category [5] contained approximately 20% of the population living in areas with the highest education level. Finally, each woman was assigned to one of the five categories of SES through her postcode of residence at the time of diagnosis.

We validated the proxy measure of SES in a subsample of respondents to a postal survey, which had been carried out in a part of the registration area of the Eindhoven cancer registry [12]. The subsample consisted of respondents living in postcode areas for which at least six respondents were found in the survey, as the postcode area was the unit of measurement in this analysis. Each postcode could be assigned to one of the five socioeconomic categories of the proxy measure. For respondents to the survey, data on educational level were known and for each of the 381 postcodes, we calculated the average number of years of education with the survey data and then assigned each postcode to one of the five socioeconomic groups of the proxy measure (using the same procedure as with the marketing agency data).

For each postcode we thus had two scores: (1) a score from 1 to 5 based on data from the original classification of the marketing agency; and (2) a score from 1 to 5 based on data from respondents to the survey. The Pearson correlation coefficient between the two variables was 0.51, which is rather high for this type of comparison. We concluded from this exercise that validity at the postcode level was satisfactory, given that the assignment of postcodes to one of 45 categories by the marketing agency was based on a large number of socioeconomic and sociodemographic variables, of which education was only one.

Prognostic factors

We studied the impact of a number of potential confounders and intermediary variables, which were treated as categorical in the analysis. As potential confounders of the SES survival association we studied: *age at diagnosis* (three categories: younger than 50, 50 to 64, and 65 years or older), *period of diagnosis* (two categories: 1980–1984 and 1985–1989) and *degree of urbanisation* of the place of residence at diagnosis (three categories: (1) smallest municipalities; (2) intermediate; (3) largest municipalities). The following potential intermediary variables in the association between SES and survival were studied: *stage at diagnosis* (four categories: localised (only local involvement of a tumour), regional (tumour growth confined to the breast and regional lymph nodes), distant (presence of metastases to other organs), and unknown), *morphology* (three categories: ductal carcinoma, lobular carcinoma or other [13]) and *treatment* (five categories: (1) surgery only; (2) surgery and radiotherapy; (3) surgery and endocrine therapy; (4) surgery and chemotherapy; and (5) no surgery).

Univariate analysis

The survival time of patients was calculated as the number of days between the date of diagnosis and either the date of death or the end of follow-up (1 July 1991), whichever occurred first. As no information on the exact cause of death was available, the Relative Survival Rate (RSR) was used to correct for deaths due to causes other than breast cancer. The RSR [14] is the ratio of the observed survival rate for a group of cancer patients to the expected survival rate in a group similar to the patient group with respect to age, sex, and calendar period of observation. In this study, the expected survival rate was based on life tables of the population of the registration area of the Eindhoven Cancer Registry, which were obtained from The Netherlands Central Bureau of Statistics. These life tables each applied to a 2 year calendar period and were age- and sex-specific. RSRs and 95% confidence intervals (CI) were calculated with the computer programme package for cancer survival studies from the Finnish Cancer Registry [15].

Multivariate analysis

The multivariate analyses were conducted with a proportional hazards regression model which was adapted to the RSR [16] using GLIM (generalised linear interactive modelling) [17]. The measure of effect in the multivariate analyses was the hazard ratio, which expresses the probability of death from breast cancer for a specific category of patients relative to a reference category (with a hazard ratio of unity).

The entire period of follow-up was divided into two periods of 6 years: 1–6 and 7–12. Because the probability of death from breast cancer was not equal for these two periods, it was

necessary to correct for this difference in hazards by including this variable in the model. At every step in the multivariate analysis an extra variable was added to a model which contained follow-up period and SES. First, possible confounders were added to the model and then possible intermediary variables. For a variable to be included in the final model, it had to cause a change in hazard ratios of the SES variable after addition to the model. Furthermore, the reduction in deviance due to a variable, with a corresponding difference in degrees of freedom, using the chi-square distribution, had to be statistically significant ($P < 0.05$).

At each step in the analysis, a test for trend with the SES variable was also conducted by including SES as a continuous variable in the model. The reduction in deviance due to the continuous SES variable was then evaluated, using the chi-square distribution with one degree of freedom.

RESULTS

Table 1 contains the 5 and 10 year RSR for the five SES categories, uncorrected for other factors. Both the 5 and 10 year RSR appeared to be higher for the higher SES categories, although a clear gradient was not apparent and 95% CIs overlapped.

The distribution of age ($P < 0.001$) and degree of urbanisation ($P < 0.001$) differed statistically significantly per SES category (Table 2), while for the other variables this was not the case: period of diagnosis ($P = 0.61$), stage ($P = 0.08$), morphology ($P = 0.11$) and treatment ($P = 0.93$). For stage however, we saw that the percentage of patients diagnosed at a distant stage was higher in the lower SES categories.

Table 3 contains the results of the multivariate analyses, showing the hazard ratios for the five SES categories for the different models, with the highest SES category as a reference category. Period of diagnosis and degree of urbanisation were added to a model with follow-up period and SES, but appeared not to confound the SES survival association. These are, therefore, not presented in Table 3. In model 1 which included follow-up period and SES, the gradient in hazard ratios was clear and the lower SES categories showed higher hazard ratios. The P-value for the test for trend was 0.037. When age was included in the model (model 2) the hazard ratios for SES were reduced substantially, while the reduction in deviance was also statistically significant. CIs around hazard ratios for the five SES categories overlapped, but a gradient was apparent with higher hazard ratios for the lower SES categories (test for trend, $P = 0.073$). After a correction for stage (model 3), differences in hazard ratios became much smaller and the gradient disappeared ($P = 0.841$). The reduction in deviance due to stage was also statistically significant. Morphology (model 4) and treatment (model 5) changed hazard ratios only moderately but because the reduction in deviance due to these variables was statistically significant, they were retained in the final model.

Table 1. Five and 10 year relative survival rate (%) according to socioeconomic status in breast cancer patients 1980–1989, in southeastern Netherlands

SES	n (%)	5 year RSR	10 year RSR
1 (low)	902 (23.0)	73 (70–76)*	57 (50–64)*
2	987 (25.1)	72 (68–76)	61 (55–67)
3	814 (20.7)	75 (71–79)	65 (58–72)
4	430 (10.9)	74 (69–79)	64 (55–73)
5 (high)	795 (20.2)	77 (73–81)	64 (58–70)
Total	3928 (100)	74 (72–76)	62 (59–65)

*95% confidence interval in parentheses.

DISCUSSION

Our results suggest that socioeconomic differences in breast cancer survival exist in The Netherlands: after a correction for age, mortality due to breast cancer was 18% higher in the lowest SES category than in the highest SES category. Although CIs for the different SES categories overlapped, a gradient in hazard ratios for different SES categories was apparent ($P = 0.073$). Socioeconomic differences in breast cancer survival could mainly be ascribed to differences in the stage-distribution between the SES categories, particularly to differences in the percentage of patients diagnosed with a metastasis, which was 8.6 for the lowest and 5.4 for the highest SES category.

Before we continue with the interpretation of our findings, some methodological issues concerning the proxy measure of SES have to be considered. The measure of SES is ecological and based on the average number of years of education per postcode of residence, and, therefore, misclassification, resulting in an underestimation of the SES survival gradient, cannot be ruled out. The results from our validation study showed, however, that our measure of SES is a very reasonable indicator at the postcode level, which is the basic unit of measurement in our analyses. The postcode of residence at the time of diagnosis was used to assign each patient to a socioeconomic category. The area of residence of a patient and, therefore, her SES score could have changed during the follow-up period. It seems very unlikely, however, that migration after the diagnosis of cancer was differential according to SES.

Due to the use of one single life table to correct for causes of death other than breast cancer, we may have overestimated the gradient in survival by SES. Expected survival is overestimated for lower SES groups and, therefore, relative survival is underestimated and the hazard ratio is overestimated. For higher SES groups, expected survival might be underestimated, and, therefore, the relative survival is overestimated and the hazard ratio might be underestimated for these groups. In a Finnish study [5], it was shown that this overestimation of the SES survival gradient is probably not very large. In this study, the socioeconomic gradient in both corrected survival (censoring of cases dying from causes other than breast cancer) and relative survival were calculated. The ratio of survival rates of the highest and lowest social class was somewhat higher when the RSR was used (1.12) as compared to the corrected survival rate (CSR) (1.10). This overestimation of the SES survival gradient is probably smaller in The Netherlands than in Finland, as socioeconomic variation in general mortality is smaller in The Netherlands than in Finland [18].

A direct comparison of our findings with those from other studies [4–9] is rather difficult, as studies differ in design and data analysis. In most studies a better survival for higher SES groups was found. However, in a study on English breast cancer patients diagnosed between 1971 and 1981, a non-significant better survival was found for council tenants (low SES) than for owner-occupiers (high SES) [9]. In a study on Swedish breast cancer patients (period of diagnosis 1961–1979) the RSR of white collar workers was approximately 7% higher than that of blue collar workers, without a correction for other prognostic factors [6]. The relative risk of case fatality in low SES women from South Australia (1977–1982), was 1.35 (95% CI

Table 2. Distribution of possible confounders and intermediary factors according to socioeconomic status in breast cancer patients 1980–1989, in southeastern Netherlands

	SES = 1 low* 100%	SES = 2 100%	SES = 3 100%	SES = 4 100%	SES = 5 high* 100%	Total 100%	χ^2 test
Age							
≤49	24.7	30.2	25.1	29.8	34.1	28.6	$P < 0.001$
50–64	38.5	33.8	34.6	33.0	34.2	35.1	
≥65	36.8	36.0	40.3	37.2	31.7	36.3	
Period of diagnosis							
80–84	46.2	43.0	43.2	42.8	44.2	44.0	$P = 0.61$
85–89	53.8	57.0	56.8	57.2	55.8	56.0	
Degree of urbanisation							
1	8.3	15.9	10.3	3.5	2.9	9.0	$P < 0.001$
2	38.5	57.3	40.4	33.7	52.6	46.0	
3	53.2	26.8	49.3	62.8	44.5	45.0	
Stage							
Local	48.4	46.9	46.7	49.3	49.6	48.0	$P = 0.08$
Regional	31.8	33.6	33.2	31.9	35.8	33.4	
Distant	8.6	6.8	6.3	6.5	5.4	6.8	
Unknown	11.2	12.7	13.8	12.3	9.2	11.8	
Morphology							
Ductal	79.0	78.1	82.2	77.4	82.4	80.0	$P = 0.11$
Lobular	12.6	13.5	9.3	13.1	10.7	11.8	
Other	8.4	8.4	8.5	9.5	6.9	8.2	
Treatment							
Su	22.3	22.0	19.9	22.1	20.1	21.3	$P = 0.93$
Su + Ra	56.4	55.1	55.4	52.1	56.2	55.4	
Su + En	6.5	7.9	8.6	8.4	7.4	7.7	
Su + Ch	6.8	7.1	7.9	7.9	7.9	7.4	
No Su	8.0	7.9	8.2	9.5	8.4	8.3	

SES, socioeconomic status; Su, surgery; Ra, radiotherapy; En, endocrine therapy; Ch, chemotherapy.

Table 3. Hazard ratios according to socioeconomic status in breast cancer patients 1980–1989 in southeastern Netherlands: result of fitting models with several confounders and intermediary factors

Model	SES = 1 low*	SES = 2	SES = 3	SES = 4	SES = 5 high*	Test for trend
1. FU + SES	1.24 (1.03–1.49)†	1.17 (0.97–1.41)	1.09 (0.90–1.33)	1.09 (0.86–1.38)	1.00	$P = 0.037$
2. + Age	1.18 (0.99–1.42)	1.15 (0.96–1.38)	1.04 (0.86–1.26)	1.06 (0.84–1.33)	1.00	$P = 0.073$
3. + Stage	1.03 (0.87–1.22)	1.06 (0.90–1.26)	1.04 (0.87–1.25)	1.09 (0.88–1.34)	1.00	$P = 0.841$
4. + MO	1.03 (0.87–1.22)	1.06 (0.90–1.26)	1.04 (0.87–1.24)	1.07 (0.87–1.33)	1.00	$P = 0.802$
5. + TR	1.03 (0.87–1.22)	1.04 (0.88–1.23)	1.03 (0.87–1.23)	1.04 (0.84–1.29)	1.00	$P = 0.792$

*Reference category; †95% confidence intervals in parentheses; FU, follow-up period, SES, socioeconomic status; MO, morphology, TR, treatment [28].

(1.04–1.74)) after correction for age and histology [7]. 5 year survival was 66% in the highest SES group compared with 55% in the lowest SES group in patients diagnosed in the west of Scotland in the period 1980–1987, using an area-based measure of SES [8]. Even in studies which adjusted for differences in stage distribution across SES groups, a statistically significant higher risk of dying for the lowest SES group was found [4, 5], which is not the case in our study. For Finnish breast cancer patients (1971–1980) from the highest social class the relative risk of dying after correction for age, period of diagnosis, and stage was reduced to 0.78 (95% CI (0.68–0.90)) [5]. Women from the United States (1979–1983) living in areas with at least

35% working class, experienced a relative risk of mortality of 1.52 (95% CI (1.28–1.88)), compared with women living in areas with less than 35% working class, adjusted for race, age, stage and histology [4]. Our results are thus in the same direction as those from most studies conducted in other countries. The strength of the association seems to be relatively weak, however, in The Netherlands, the age-corrected hazard ratio for the lowest SES category being 1.18.

The most important explanatory factor of socioeconomic differences in breast cancer survival in our study appeared to be stage of disease at diagnosis. In several studies, it was found that women from lower SES groups are diagnosed at more advanced stages of breast cancer than women from higher SES groups [5, 19–22]. Such differences in stage distribution may be related to the length of delay between the occurrence of the first symptoms and the time of diagnosis, which might be shorter in more educated and better informed women. In some studies, delay was found to be longer for women of lower SES [22–24], and a longer delay was found to be related to more advanced stages of breast cancer [24–26], which is related to lower survival [26].

In our study, stage was only moderately associated with SES: only a distant stage was more common among lower SES women. Credit to this moderate association may be good access to primary and specialised care in the southeastern Netherlands as a result of relatively short distances to a hospital, good supply of health services and a health insurance system without major financial obstacles: in the study period only 0.4% of the Dutch population was not covered by health insurance [27].

Less attention has been given to socioeconomic differences in treatment as an explanation for survival differences. It could be argued that the choice of treatment, given the extent of disease at diagnosis, might be related to the SES of breast cancer patients. Although we found no differences in treatment according to SES adjusted for stage (results not shown), differences in the quality of treatment of breast cancer patients according to SES may exist. Such differences cannot be evaluated, however, through the rather rough indicator of treatment used in this study. In any case, such differences cannot be responsible for large differences in survival in The Netherlands.

Our findings on the influence of stage on socioeconomic differences in breast cancer survival indicate that, with regard to secondary prevention of breast cancer, special attention should be given to women of lower SES. During the study period, a breast cancer screening programme at the population level was absent, and is now being implemented in The Netherlands. Through health education programmes, women from lower SES groups should be especially encouraged to participate in such a screening programme as well as to practise breast self examination. Such programmes, together with keeping up good general access to health care facilities for the entire population, may lead to a further reduction of socioeconomic differences in breast cancer survival in The Netherlands.

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