Small but significant socioeconomic inequalities in axillary staging and treatment of breast cancer in the Netherlands

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BACKGROUND: The use of sentinel node biopsy (SNB), lymph node dissection, breast-conserving surgery, radiotherapy, chemotherapy and hormonal treatment for breast cancer was evaluated in relation to socioeconomic status (SES) in the Netherlands, where access to care was assumed to be equal.

METHODS: Female breast cancer patients diagnosed between 1994 and 2008 were selected from the nationwide population-based Netherlands Cancer Registry (N = 176,505). Socioeconomic status was assessed based on income, employment and education at postal code level. Multivariable models included age, year of diagnosis and stage.

RESULTS: Sentinel node biopsy was less often applied in high-SES patients (multivariable analyses, ≤49 years: odds ratio (OR) 0.70 (95% CI: 0.56–0.89); 50–75 years: 0.85 (0.73–0.99)). Additionally, lymph node dissection was less common in low-SES patients aged ≥76 years (OR 1.34 (0.95–1.89)). Socioeconomic status-related differences in treatment were only significant in the age group 50–75 years. High-SES women with stage T1–2 were more likely to undergo breast-conserving surgery (+ radiotherapy) (OR 1.15 (1.09–1.22) and OR 1.16 (1.09–1.22), respectively). Chemotherapy use among node-positive patients was higher in the high-SES group, but was not significant in multivariable analysis. Hormonal therapy was not related to SES.

CONCLUSION: Small but significant differences were observed in the use of SNB, lymph node dissection and breast-conserving surgery according to SES in Dutch breast cancer patients despite assumed equal access to health care.

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Breast cancer is the most common cancer in females from Western countries, particularly in Western Europe (Ferlay et al, 2010). Incidence rates are generally highest among women with high socioeconomic status (SES) (Faggiano et al, 1997; Carlsten et al, 2008; National Cancer Intelligence Network, 2009; Spadae et al, 2009). However, at least for the Netherlands, we observed age-specific differences in this association. In women aged 25–44 years, the highest incidence rates were reported for those with high SES, whereas in those aged ≥65 years rates were the lowest for those with a high SES. No socioeconomic inequalities were observed in those aged 45–64 years (Aarts et al, 2010).

Survival from breast cancer has been reported to be generally worse in those with low SES (Schrijvers et al, 1995; Bastiaannet et al, 2011), although better survival rates have been observed by others (Faggiano et al, 1997). In the Netherlands, an equal health-care system is provided and a health insurance is compulsory for all inhabitants. However, survival disparities from breast cancer have been reported. These were partly explained by tumour size (Bastiaannet et al, 2011) and by stage differences resulting from differences in attendance to the free population screening programme (Aarts et al, 2011).

Treatment disparities were present in studies from Denmark and the UK, which have shown that deprived women had higher mastectomy rates, although the odds of receiving radiotherapy after breast-conserving surgery was not associated with SES as well as chemotherapy and endocrine treatment (Norredam et al, 1998; Taylor and Cheng, 2003; Henley et al, 2005; Downing et al, 2007; Raine et al, 2010). Furthermore, the use of sentinel node biopsy (SNB) was higher in regions with a high educational level in the US (Halpern et al, 2009), but to our knowledge this has not been studied in other countries.

Although Dutch health care is supposedly equally accessible, socioeconomic treatment disparities were reported for colon, pancreas, prostate and oesophageal cancer (Aarts et al, submitted; Lemmens et al, 2005; van Oost et al, 2006; Bus et al, 2012). However, for breast cancer care it is not known whether there are differences in axillary staging and treatment. Therefore, we investigated the association between SES and the use of SNB, lymph node dissection, breast-conserving surgery, radiotherapy, chemotherapy and hormonal treatment for breast cancer in the Netherlands.

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PATIENTS AND METHODS

Patient selection

Female patients with their first primary breast cancer (invasive and in situ) diagnosed between 1994 and 2008 were selected from the Netherlands Cancer Registry. Patients with other tumours before their breast cancer were excluded. The nationwide Dutch network and registry of histopathology and cytopathology regularly submits reports of all diagnosed malignancies to the regional cancer registries. The national hospital discharge databank, which receives discharge diagnoses of admitted patients from all Dutch hospitals, completes case ascertainment. After notification, trained registry personnel collect data on diagnosis, staging and treatment from the medical records, including pathology and surgery reports, about 9 months after diagnosis, using the registration and coding manual of the Dutch Association of Comprehensive Cancer Centres.

Stage was divided according to TNM classification at the year of diagnosis. Pathological T, N and M stage was used; clinical stage was used if pathological was missing.

In the Netherlands, the SNB was gradually implemented from 1998 to 2003; we therefore studied the SNB from 2003 onwards. It is registered in six of nine regional registries; analyses on SNB were limited to these registries and to stage cT1,2N0M0,X.

National guidelines for treatment of breast cancer were introduced in the Netherlands in 2002 (Working Group Treatment Breast Cancer, 2002). Before that time, treatment was based on regional guidelines. Treatment was categorised as breast-conserving surgery, external beam radiotherapy after breast-conserving surgery, chemotherapy and hormonal therapy. The use of breast-conserving surgery and breast-conserving surgery plus external beam radiotherapy was studied among patients with stage T1,2N0M0,X breast cancer and chemotherapy and hormonal therapy in TanyN+M0,X breast cancer. The use of chemotherapy was studied from 2002 onwards, as treatment guidelines were rapidly changing before that time. The use strongly increased from 1994 to 2002 and gradually further increased afterwards. We were not able to classify chemotherapy as adjuvant or neoadjuvant.

The population-based screening programme for breast cancer in the Netherlands started around 1990 and covered in 1997 all women aged 50–69 years; in 1998 the upper age limit was extended to 75.

Socioeconomic status

Socioeconomic status was assigned to each patient using an area-based measure according to place of residence at the time of diagnosis. The area-based SES was provided by the Netherlands Institute for Social Research and consists of numbers from income, employment and education, which are provided to the institute by a private organisation that collects information by telephone calls with one person per 6-digit postal code area; this person is seen as representative for his or her area. Next, numbers are aggregated to 4-digit postal code areas. Validation studies indicate that these numbers at aggregated level approach the true situation (Tesser et al, 1995). A higher score represents a high social deprivation (low SES) and a low score represents little social deprivation and consequently a high SES. Scores were divided into quintiles.

Statistical analysis

All statistical tests were two-sided and were considered significant if P<0.05. The distribution of sociodemographic and clinical characteristics was studied across the SES strata. Significance was tested with non-parametric tests (continuous variables) and χ²-tests (categorical variables).

Analyses were stratified according to the age groups ≤49, 50–75, ≥76. The odds ratios (OR) were stratified by these age categories and adjusted for age (continuously), year of diagnosis, SES and T-stage. After excluding patients with unknown SES (N=445) and non-carcinomas (N=1548), data on 176505 patients were analysed.

RESULTS

Patients with highest SES were on average 3 years younger (P<0.0001) and had a lower stage of disease than patients with the lowest SES (P<0.0001; Table 1).

The use of the SNB procedure for stage cT1,2N0M0,X breast cancer increased from 74% in 2003 to 88% in 2008. In general, the use of SNB was higher in patients with highest SES (Table 1).

Table 1. Patient characteristics of breast cancer patients in the Netherlands, diagnosed during 1994–2008

| Socioeconomic status | 5. lowest | 4. | 3. intermediate | 2. | 1. highest |
|----------------------|-----------|----|----------------|----|-----------|
|                      | N         | %  | N             | %  | N         | %  | N         | %  | N         | %  |
| Period of diagnosis  |           |    |               |    |           |    |           |    |           |    |
| 1994–1998            | 10234     | 23 | 10296         | 18 | 10413     | 20 | 9372      | 20 | 11689     | 20 |
| 1999–2003            | 11990     | 20 | 11616         | 21 | 11580     | 19 | 12695     | 19 | 11845     | 20 |
| 2004–2008            | 13077     | 18 | 13389         | 20 | 13308     | 21 | 13234     | 21 | 11767     | 20 |
| Age at diagnosis*#   |           |    |               |    |           |    |           |    |           |    |
| Mean                 | 62.2      |    | 61.4          |    | 60.7      |    | 59.9      |    | 59.3      |    |
| 0–49                 | 7673      | 22 | 8003          | 23 | 8477      | 24 | 9128      | 26 | 10101     | 29 |
| 50–75                | 20823     | 59 | 21314         | 60 | 21339     | 60 | 21104     | 60 | 20058     | 57 |
| 76+                  | 6805      | 19 | 5984          | 17 | 5485      | 16 | 5069      | 14 | 5142      | 15 |
| TNM stage*           |           |    |               |    |           |    |           |    |           |    |
| 0 (in situ)          | 2755      | 8  | 2934          | 8  | 3100      | 9  | 3081      | 9  | 3150      | 9  |
| 1                    | 11964     | 34 | 12203         | 35 | 12384     | 35 | 12636     | 36 | 12561     | 36 |
| 2                    | 14686     | 42 | 14682         | 42 | 14402     | 41 | 14357     | 41 | 14566     | 41 |
| 3                    | 3601      | 10 | 3450          | 10 | 3434      | 10 | 3271      | 9  | 3144      | 9  |
| 4                    | 1899      | 5  | 1644          | 5  | 1601      | 5  | 1541      | 4  | 1425      | 4  |
| Unknown              | 396       | 1  | 388           | 1  | 380       | 1  | 335       | 1  | 455       | 1  |

Abbreviation: TNM = tumour–node–metastasis. *P<0.0001 (χ²-test). #P<0.0001 (t-test).
Clinical Studies

analyses (age (Table 2). These differences were significant in multivariable

Abbreviations: 95% CI = 95% confidence interval; LND = lymph node dissection; OR = odds ratio, adjusted for age, year of diagnosis, T-stage and histology; SNB = sentinel node biopsy. P-values are from $\chi^2$ test. Trend refers to P-value from trend test.

Table 3
Use of therapies for breast cancer in the Netherlands according to socioeconomic status, diagnosed during 1994–2008

Abbreviations: 95% CI = 95% confidence interval; OR = odds ratio; SES = socioeconomic status. P-value refers to $\chi^2$-test. Trend refers to P-value for trend. *OR adjusted for age (continuously), year of diagnosis, T-stage (T2N0 vs T1N0). †OR adjusted for age (continuously), year of diagnosis, T-stage (T2N0+, T3N0+, T4N0+ vs T1N0+). ‡From 2002 onwards. OR adjusted for age (continuously), year of diagnosis, T-stage (T1N0+, T3N0+, T4N0+ vs T1N0+).

high-SES patients less often received SNB, with 1–3% lower rates in high- vs low-SES patients aged <75, but not statistically significant (Table 2). These differences were significant in multivariable analyses (age <49: OR 0.70 (95% CI: 0.56–0.89); 50–75 years: 0.85 (0.73–0.99)). In the oldest age group no consistent pattern on the use of SNB appeared. Compared with high SES, rates of lymph node dissection in addition to SNB were slightly higher in low-SES patients in the youngest age group (36% vs 39%, not statistically significant), and lower in low-SES patients in the oldest group (27% in high SES vs 22% in low SES, $P = 0.01$). In multivariable
analyses, among the patients aged \( \geq 76 \) receiving SNB, those with high SES more often received lymph node dissection compared with those with low SES, although not statistically significant for the highest SES group (OR 1.34 (95% CI: 0.95–1.89)).

Small, statistically significant socioeconomic differences were present in treatment selection in those aged 50–75 years. The use of breast-conserving surgery was slightly higher in high-SES patients (stage T1,2N0M0,X), i.e. 64% of patients with high SES compared with 60% of those with low SES (\( \chi^2 \text{-test } P < 0.0001 \); Table 3). Nearly all of these patients received additional radiotherapy (97%), which was not significantly different between the SES groups. In multivariable analyses, the odds of breast-conserving surgery remained significantly increased (OR 1.15 (95% CI: 1.09–1.22) vs OR high SES), although the effect was no longer significant in multivariable analyses (Table 3). In this early stage, an inverse association was observed for mastectomy, with lower rates in high-SES women aged 50–75 years (data not shown).

In those aged 50–75 years, the use of endocrine treatment was not related to SES, neither in univariable nor in multivariable analyses (Table 3). Rates of chemotherapy for node-positive breast cancer were highest in high-SES patients (62% vs 55% in low SES, \( \chi^2 \text{-test } P < 0.0001 \)), but were no longer significant in multivariable analyses (Table 3).

Of all therapies mentioned above, none was significantly related to SES in women aged <50 years. In women of age \( \geq 76 \) years, the only significant associations were observed for breast-conserving surgery, with higher rates in the high-SES group (\( \chi^2 \text{-test } P = 0.02, \) OR high vs low SES 1.21 (95% CI: 1.06–1.38)), and for chemotherapy, in which rates were reduced in the second highest SES group (OR 0.45 (95% CI: 0.22–0.91). The use of breast-conserving surgery and radiotherapy combined, however, was not significantly related to SES (OR 1.10 (95% CI: 0.95–1.28)).

**DISCUSSION**

This study shows that in the Netherlands, a country with assumed equal access to care, breast cancer patients with high SES were less likely to undergo SNB and, in the oldest group, more likely to receive additionally lymph node dissection. Furthermore, in patients aged 50–75 years the use of high-SES group (\( \chi^2 \text{-test } P = 0.02, \) OR high vs low SES 1.21 (95% CI: 1.06–1.38)), and for chemotherapy, in which rates were reduced in the second highest SES group (OR 0.45 (95% CI: 0.22–0.91). The use of breast-conserving surgery and radiotherapy combined, however, was not significantly related to SES (OR 1.10 (95% CI: 0.95–1.28)).

A prior US study showed higher rates of lymph node biopsy/sampling, that is, either axillary lymph node dissection or SNB, in areas where the education level was higher, although the absolute difference was quite small (Halpern et al., 2009). Our data suggest a poorer staging of the axillary lymph nodes and abandoning surgery in the armpit in patients with high SES. We cannot explain this observation as we expected the rates to increase with higher SES owing to — among others — better understanding of the importance of axillary staging. Possibly, patients with high SES are more conscious of the side effects of lymph node dissection, such as lymph oedema, and therefore are more inclined not to undergo this therapy. Previously, older age was associated with reduced likelihood of receiving lymph node biopsy (Halpern et al., 2009), but the mean age differed by only 3 years in our study, suggesting that age only little affected the staging procedure. Another study stated that among women undergoing breast-conserving surgery, those with comorbid conditions were less likely to receive axillary dissection (Louwman et al., 2005). As cancer patients with high SES have fewer comorbidities (Louwman et al., 2010), higher rates of axillary dissection would be expected among high-SES patients. We had no information on comorbidities in this study, but it probably has not contributed to the lower rates of SNB in high-SES patients in our study population. Besides, in the US, patients treated in hospitals with higher patient volumes were more likely to receive lymph node biopsy (Halpern et al., 2009). Possibly this has affected our results as well. Also, in the Netherlands, staging procedures and type of surgery depended on hospital characteristics, such as volume, with reducing differences over time (van Steenbergen et al., 2010). It should be noted, however, that absolute differences in our study were small and that statistical significance may have resulted from the large number of patients.

Our results on treatment selection are in line with and the order of magnitude is fairly similar to studies from Denmark and the UK. These studies have shown that women with a lower SES had higher mastectomy rates (Norredam et al., 1998; Taylor and Cheng, 2003; Henley et al., 2005) and lower breast-conserving surgery rates (Taylor and Cheng, 2003; Downing et al., 2007; Raine et al., 2010), although an age-dependent association has been observed as well (Thomson et al., 2001). Adjustment for stage explained the higher mastectomy rates observed in low SES (Henley et al., 2005), whereas the association remained significant after stratification by tumour size (Taylor and Cheng, 2003) and stage (our study, early stage (data not shown)). This implies that type of surgery chosen for the SES groups is not fully explained by stage and age in early-stage disease. Because of higher prevalence of coexisting diseases in patients with low SES (Louwman et al., 2010), type of surgery is expected to be less invasive owing to the poor general condition in low SES patients. In fact, we observed higher invasive surgery (mastectomy) rates in low SES. Presence of comorbidities might also be indicative of mastectomy to avoid the effects of radiotherapy, but this has not been studied before. A Northern Italian study found that presence of comorbidities reduced the odds of receiving radiotherapy after breast-conserving surgery (Rosato et al., 2009). Besides, that study also reported no educational differences in treatment of early-stage breast cancer after adjustment for comorbidities and hospital characteristics (Rosato et al., 2009). As discussed previously, hospital characteristics were affecting treatment selection, including type of adjuvant therapy and use of radiotherapy, in the Netherlands as well (Vulto et al., 2005; Siesling et al., 2007; van Steenbergen et al., 2010), but we could not take these into account in our analyses. Nor were we able to investigate the contributions of ER status or grade, but previously these factors were reported to be not associated to SES (Henley et al., 2005). More active involvement of the patient in decision making led to higher mastectomy rates (Katz et al., 2005), but the effects in the Netherlands remain to be studied.

In our study, in accordance with the Dutch treatment guidelines (Oncoline. www.oncoline.nl), nearly all patients undergoing breast-conserving surgery received additional radiotherapy (97%) and no differences were observed between the SES groups. Our results differ in line with studies from the UK and US, where receiving adjuvant radiotherapy was not associated with deprivation (Downing et al., 2007). Compared with the US, our rates of adjuvant radiotherapy are high (97% vs 73%) (Smith et al., 2010). Furthermore, in the US, large SES differences were observed, with adjuvant radiotherapy rates of 67% in patients with low SES vs 78% in those with high SES in the period 1991–2002, which were not explained by stage, hormone receptor status, grade, chemotherapy, comorbidity and surgery characteristics (Hershman et al., 2008). Similar differences were observed in another US study investigating adjuvant radiotherapy rates according to race, which reported 74% in whites vs 65% in blacks (Smith et al., 2010), which remained also significant after adjustment for demographic, clinical (including comorbidities) and socioeconomic covariates.
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Previous studies have reported inconsistent results with respect to the associations between SES and adjuvant radiotherapy, chemotherapy and endocrine treatment (Macleod et al., 2000; Taylor and Cheng, 2003; Downing et al., 2007), with higher rates in high SES in some studies but no association in others (Macleod et al., 2000; Downing et al., 2007; Bhargava and Du, 2009). Low educational level was associated with reduced doses of chemotherapy, whereas presence of comorbidities was not associated (Griggs et al., 2007). No data were available on chemotherapy doses from the Netherlands Cancer Registry. Besides, we have used the pathological staging supplemented with clinical TNM in case postoperative data were missing. As we were not able to classify chemotherapy as adjuvant or neoadjuvant, the staging may not be completely correct for the patients who received neoadjuvant chemotherapy.

Higher education predicted hormonal therapy use in older US breast cancer survivors (Yen et al., 2011). For those on hormonal therapy, wealthier women and women with insurance coverage for some or all medication costs were more likely to receive an aromatase inhibitor, which is prescribed by the American Society for Clinical Oncology (ASCO) (Yen et al., 2011). Owing to the Dutch obligatory health insurance for every inhabitant, insurance status is unlikely to affect treatment selection. This is in line with our finding that hormonal therapy was not related to SES in our study.

Unfortunately, patient preferences in itself could not be taken into account in this study. For example, the choice of mastectomy depends on the interplay between the surgeon’s recommendations and patients’ preferences for treatment (Hawley, 2010). The role of patient decision making (Smith et al., 2009) is likely to be influenced by health literacy, that is, ‘The degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions’ (National Network of Libraries of Medicine, 2010). Low health literacy may lead to treatment options that are not fully understood, and therefore some patients may not receive the most appropriate treatment for their medical condition (Merriman et al., 2002). As SES can be linked with education, those with low SES are expected to be more vulnerable to low health literacy. A solution towards solving this might be to focus more on clear and adapted communication by health-care providers. In contrast, some patients do not want to be very involved in decision making (Lantz et al., 2005; Levinson et al., 2005).

Our study findings might be influenced by several limitations. First, we had no information on the presence of comorbidities, which may have affected therapy selection. Second, data on grade, ER status and PR status were not available, which might have affected our results. Third, we had no information on hospital characteristics, which affected therapy selection in Italy and the Netherlands; however, in the latter study, regional and hospital variation reduced over time (Rosato et al., 2009; van Steenbergen et al., 2010). Fourth, in this study we have used a measure of SES based on 6-digit postal code of the residential area. Our results may therefore be subject to ecological fallacy. Furthermore, our findings may be explained by some residual confounding. Although this measure of SES is not based on individual data on income, education or occupation, it covers a relatively small geographical area and thus is likely to represent a reliable approximation of individual SES. Previous studies in the Netherlands have proven that socioeconomic differences based on neighbourhood data tend to reflect socioeconomic differences accurately at the individual level (Bos et al., 2000, 2001; Smits et al., 2001). Furthermore, as the measure of SES used in this study is based on several outcomes, it also applies to older women (born before 1955), although their occupation or education does not always properly reflect their social class (Berkman and Macintyre, 1997).

Nevertheless, we have used population-based nationwide data, including all breast cancer patients from the Netherlands. We have thus provided a complete overview of the association between SES and the staging and treatment selection of breast cancer, which has not been done before.

CONCLUSION

Small but significant differences were observed in the use of SNB, lymph node dissection and breast-conserving surgery according to SES in Dutch breast cancer patients despite the assumed equal access to health care.

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Conflict of interest

The authors declare no conflict of interest.

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