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Predictors of early death in female patients with breast cancer in the UK: a cohort study

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ABSTRACT

Objective: To identify factors predicting early death in women with breast cancer.

Design: Cohort study.

Setting: 29 trusts across seven cancer networks in the North Thames area.

Participants: 15 037 women with primary breast cancer diagnosed between January 1996 and December 2005.

Methods: Logistic regression analyses to determine predictors of early death and factors associated with lack of surgical treatment.

Main exposures: Age at diagnosis, mode of presentation, ethnicity, disease severity, comorbidities, treatment and period of diagnosis in relation to the Cancer Plan (the NHS's strategy in 2000 for investment in and reform of cancer services).

Main outcome measures: Death from any cause within 1 year of diagnosis, and receipt of surgical treatment.

Results: By 31 December 2006, 4765 women had died, 980 in the year after diagnosis. Older age and disease severity independently predicted early death. Women over 80 were more likely to die early than women under 50 (OR 8.05, 95% CI 5.96 to 10.88). Presence of distant metastases on diagnosis increased the odds of early death more than eightfold (OR 8.41, 95% CI 6.49 to 10.89). Two or more recorded comorbidities were associated with a nearly fourfold increase. There was a significant decrease in odds associated with surgery (OR 0.29, 95% CI 0.24 to 0.35). Independently of disease severity and comorbidities, women over 70 were less likely than those under 50 to be treated surgically and this was even more pronounced in those aged over 80 (OR 0.09, 95% CI 0.07 to 0.10). Other factors independently associated with a reduced likelihood of surgery included a non-screening presentation, non-white ethnicity and additional comorbidities.

Conclusions: These findings may partially explain the survival discrepancies between the UK and other European countries in female patients with breast cancer. The study identifies a group of women with a particularly poor prognosis for whom interventions aiming at early detection may be targeted.

ARTICLE SUMMARY

Article focus

- Several studies have shown that the UK has lower survival for breast cancer than some other European countries with a similar expenditure on healthcare.
- Differences have been shown to occur mainly in older patients and in the first year after diagnosis.
- Several reasons/explanations have been proposed.

Key messages

- This study shows that patients with breast cancer dying in the first year after diagnosis are more likely to be older and have more advanced disease and existing comorbidities.
- Surgical treatment and (to a lesser extent) radiotherapy and tamoxifen usage were associated with a reduced risk of early death.
- The likelihood of receiving surgery was inversely related to age, independently of comorbidity and disease severity.
- These findings suggest that early detection, management of comorbidities and optimisation of treatment of older patients are important target areas to improve outcomes.

Strengths and limitations of this study

- This is a large cohort of women with a diagnosis of breast cancer, and the results may be generalisable to women treated for breast cancer in the UK during the same time period.
- Many variables that may be related to both risk factors and outcomes have not been assessed in this study. However, their correlation with death within a year would have to be very strong to explain the strong associations seen in our data.

INTRODUCTION

Despite the decline in breast cancer mortality seen in the UK since the late 1980s, survival rates are still substantially lower than in many other European countries.[1 2] It has been difficult to pinpoint the reasons for these differences. One important observation in some studies remains unexplained, namely

that of poorer survival in UK patients soon after their diagnosis. Sant *et al*[3] demonstrated a higher risk of death in women with breast cancer in the UK in the first 6 months after diagnosis than in other European countries. This was particularly pronounced for the youngest (under 29 years) and oldest (over 80 years) age groups. Six months from diagnosis, survival patterns in the UK became more similar to those in the other European countries. Further analysis of the survival differential has revealed that disparities between the UK and northern European countries (Sweden and Norway) occur mainly for older women in the first year after diagnosis.[4] Eighty-one per cent of the excess UK deaths occur within 2 years of diagnosis.

Beral and Peto[5] have suggested that observed differences in survival may be due to bias relating to artefacts in cancer registration rather than to genuine differences in diagnosis and management of breast cancer. However, a recent study by Møller *et al*[6] has shown that such effects are unlikely to make a significant contribution to observed differences in survival. The effects of incomplete ascertainment and registration from death certificates only on survival comparisons based on cancer registry data have been investigated in detail by Robinson *et al*.[7]

The aim of this study was to investigate factors associated with early mortality (within 1 year after diagnosis) in a sample of UK women given a diagnosis of breast cancer during 1996–2005. Since surgical intervention with a curative intent is strongly related to reduced mortality, a secondary aim of the study was to identify the patient characteristics most often associated with the failure to use this treatment option.

SUBJECTS AND METHODS

We conducted a cohort study using data from the North Thames Prospective Audit of Breast Cancer, set up in 1996 by Health Authorities in the North Thames area to monitor the implementation of the Calman–Hine recommendations in 29 trusts in seven participating cancer networks: North London, North East London, West London, South West London (Royal Marsden Hospital, Brompton Road), Mount Vernon, Mid-Anglia and South Essex. The audit used a common dataset and a standard proforma across the providers to collect detailed demographic, diagnostic and treatment data for all new primary cases of malignant female breast cancer diagnosed between January 1996 and December 2005. Trained data collectors used either Thames Cancer Registry (TCR) Access-based software or the British Association of Surgical Oncology software for breast audit to record information. The number of participating trusts varied from year to year, with a maximum of 26 trusts submitting partial or complete datasets in 2000 and a minimum of seven trusts submitting data in 2005.

Women were followed from their date of entry into the audit to death or censoring at 31 December 2006, an average of 5.6 years. Date of death was confirmed through linking patients to the NHS Central Register using the NHS Strategic Tracing Service or matching with records in the TCR. For those who were neither traced nor matched, date of death was taken from the breast audit database, if it was recorded. Women who were either traced or matched but who had no date of death in any of the three databases were assumed to be alive at 31 December 2006. Women who could not be traced in the NHS Central Register or matched to the TCR database and who had no date of death recorded in the audit database were excluded from analyses, as we could not be sure of their vital status. The study also excluded women with in situ breast cancer without any invasive component at diagnosis. After these exclusions, a total of 15 037 women were available for analysis.

Data on different treatment modes (surgery, radiotherapy, chemotherapy and tamoxifen) were taken from the audit database, augmented by information from the TCR database where possible. Cases were matched to Hospital Episode Statistics (HES) data using name, NHS number, date of birth and date of diagnosis within 90 days of that recorded in the audit database in order to obtain further information on receipt of surgery. Women with a C50 diagnosis (breast cancer) and a B or T8 code in the HES surgery field were regarded as having had surgery. Only 98 cases were recoded on this basis, illustrating the completeness of the audit database in this respect.

Cause of death was available from the TCR database for 85% of the women who died during the study period. A categorical variable accounting for the calendar period of diagnosis was included to adjust for diagnosis and treatment in relation to the implementation of the Cancer Plan (the NHS's strategy in 2000 for investment in and reform of cancer services). As per the methodology of Rachet *et al*,[8] the following periods were considered: before 27 September 2000 (when the plan was published); 28 September 2000 to 31 December 2003 (initialisation period); after 01 January 2004 (implementation). Patient age was categorised as: <50 years, 50–59 years, 60–69 years, 70–79 years and 80 years and over. Pathological tumour size was assigned to one of five groups: <10 mm, 10–19 mm, 20–39 mm, 40–49 mm and 50 mm and over. Information on additional diagnoses was obtained from the matched HES dataset and was used to determine the Charlson Comorbidity Index for matched patients. This is a weighted index based on the number and severity of 17 potential serious comorbid conditions that affect mortality.[9] The index was categorised into the groups 0, 1 and 2+.

Clinical, demographic, pathological and treatment-related factors were compared between women who died from any cause within 1 year of their diagnosis and those who survived beyond this year. All-cause mortality, rather than death from breast cancer, was used partly because

specific cause of death was not known in 15% of the women, but also because the international study[4] that highlighted the adverse survival in English women in the first year after diagnosis was also based on all-cause mortality. An analysis restricted to breast cancer-specific mortality produced broadly similar results.

Univariate analyses were performed using χ^2 tests and unadjusted (bivariate) logistic regression models. A multivariate logistic regression model investigated the independent contribution of all covariates. This model included surgery but not collinear covariates—that is, variables that were only known for patients who had surgery, namely tumour size and node status.

The regression models assessed the effects of age, ethnicity, mode of presentation (screening, symptoms or incidental), distant metastases at diagnosis, comorbidities, period of diagnosis and treatments (surgery, radiotherapy, tamoxifen and chemotherapy) on early death from any cause. The results are presented as ORs, both unadjusted (univariate) and fully adjusted (multivariate), with 95% CIs.

Additional logistic regression models were used to determine which factors were associated with use of surgery. All analyses were conducted using Stata V.10.

RESULTS

The study population consisted of 15 037 women, of whom 4456 (30%) were over 70 years old at the time of their diagnosis. The majority of women (78%) presented symptomatically, and 82% of those with known ethnicity were recorded as white. Over a mean follow-up of 5.6 years, there were 4765 deaths. Table 1 shows the underlying cause of death in these women. A total of 980 women (6.5% of the total cohort and 20.6% of all deaths) died within a year of their diagnosis, and, of these, 464 women were known to have died from breast cancer. Among those for whom the cause of death was known, there was no significant difference in the proportions dying from different causes between those who died within or after the first year since diagnosis (χ^2=10.6; 9 df; p=0.30). However, significantly more of the women who died early had an unrecorded cause of death (26% vs 12%).

Table 2 describes the characteristics of women who survived 1 year beyond diagnosis and those who did not, and table 3 shows the results of the logistic regression analyses. In univariate analyses (χ^2 values in table 2 and unadjusted ORs in table 3), older age (>60 years), white ethnicity, distant metastases at diagnosis, positive nodes and larger tumours (>20 mm) were all significantly linked with death within 1 year of diagnosis (p<0.001 for all χ^2 tests). Comorbidities on diagnosis were also associated with an increased likelihood of early death (Charlson Index ≥2: OR 5.55, 95% CI 4.56 to 6.76). Women presenting because of symptoms (OR 7.91, 95% CI 5.21 to 12.01) or whose cancer was discovered incidentally (OR 11.98, 95% CI 7.37 to 19.48) were significantly more likely to die early, compared with those whose cancer was identified through screening. 'Incidental' cancers comprised non-symptomatic referrals from any source other than routine screening or the patient's general practitioner.

Surgical treatment was associated with highly significantly reduced odds of early death from any cause (OR 0.12, 95% CI 0.11 to 0.14), as was treatment with chemotherapy (OR 0.60, 95% CI 0.51 to 0.71) and radiotherapy (OR 0.27, 95% CI 0.23 to 0.32). There was no significant association between tamoxifen usage and early death (OR 0.94, 95% CI 0.79 to 1.12). The time period in which women were diagnosed (before, during or after implementation of the Cancer Plan) was not significantly associated with death within a year of diagnosis in univariate models (χ^2=3.54; p=0.17).

The results of the multivariate logistic regression analysis to assess the factors independently associated with early death are shown as the adjusted ORs in table 3. This model excluded tumour size and nodal status, which are only known in women who received

Table 1 Cause of death in women with breast cancer by length of survival

Cause of death	Survival		Total
	<1 year from diagnosis Number (%)	>1 year from diagnosis Number (%)	Number (%)
Breast cancer	464 (63.9)	2015 (60.5)	2479 (61.1)
Lung cancer	4 (0.6)	38 (1.1)	42 (1.0)
Colorectal cancer	3 (0.4)	32 (1.0)	35 (0.9)
Other/unspecified cancer	39 (5.4)	232 (7.0)	271 (6.7)
Ischaemic heart disease	34 (4.7)	137 (4.1)	171 (4.2)
Stroke	14 (1.9)	79 (2.4)	93 (2.3)
Other cardiovascular disease	43 (5.9)	204 (6.1)	247 (6.1)
Senility	16 (2.2)	92 (2.8)	108 (2.7)
Pneumonia	38 (5.2)	205 (6.2)	243 (6.0)
All other causes	71 (9.8)	294 (8.8)	365 (9.0)
Total with known cause of death	726 (100.0)	3328 (100.0)	4054 (100.0)
Cause of death not known	254 (25.9)	457 (12.1)	711 (14.9)
Total cases	980	3785	4765

Table 2 Characteristics of participants who did or did not survive the first year after diagnosis

Patient characteristic	Survival <1 year from diagnosis Number (%)	Survival >1 year from diagnosis Number (%)	p Value*
Age at diagnosis (years)			
<50	88 (9.0)	3712 (26.4)	<0.001
50–59	91 (9.3)	3648 (26.0)	
60–69	148 (15.1)	2894 (20.6)	
70–79	270 (27.6)	2373 (16.9)	
≥80	383 (39.1)	1430 (10.2)	
Ethnicity			
Non-white	75 (7.7)	1983 (14.1)	<0.001
White	488 (49.8)	8610 (61.3)	
Not known	417 (42.6)	3464 (24.6)	
Distant metastases at diagnosis			
No	312 (31.8)	7977 (56.7)	<0.001
Yes	156 (15.9)	271 (1.9)	
Not known	512 (52.2)	5809 (41.3)	
Tumour size (mm)			
<10	12 (1.2)	1220 (8.7)	<0.001
10–19	73 (7.4)	4016 (28.6)	
20–39	83 (8.5)	3103 (22.1)	
40–49	86 (8.8)	1953 (13.9)	
≥50	99 (10.1)	799 (5.7)	
Not known	627 (64.0)	2966 (21.1)	
Node status			
Negative	95 (9.7)	5492 (39.1)	<0.001
Positive	167 (17.0)	4213 (30.0)	
Not known	718 (73.3)	4352 (31.0)	
Charlson Index (comorbidities)			
0 (minor)	203 (20.7)	6755 (48.1)	<0.001
1 (moderate)	48 (4.9)	359 (2.6)	
≥2 (severe)	231 (23.6)	1384 (9.8)	
Not known	498 (50.8)	5559 (39.5)	
Diagnosis date (in relation to Cancer Plan)			
Pre 2000	624 (63.7)	9057 (64.4)	0.79
2000–2003	292 (29.8)	3897 (27.7)	
Post 2003	64 (6.5)	1103 (7.8)	
Presentation			
Screening	23 (2.3)	2274 (16.2)	<0.001
Symptoms	763 (77.9)	9531 (67.8)	
Incidental	64 (6.5)	528 (3.8)	
Not known	130 (13.3)	1724 (12.3)	
Surgery			
No	489 (49.9)	1513 (10.8)	<0.001
Yes	491 (50.1)	12 544 (89.2)	
Radiotherapy			
No	454 (46.3)	3395 (24.2)	<0.001
Yes	256 (26.1)	7079 (50.4)	
Not known	270 (27.6)	3583 (25.5)	
Chemotherapy			
No	520 (53.1)	6482 (46.1)	<0.001
Yes	203 (20.7)	4200 (29.9)	
Not known	257 (26.2)	3375 (24.0)	
Tamoxifen			
No	172 (17.6)	2321 (16.5)	0.49
Yes	601 (61.3)	8630 (61.4)	
Not known	207 (21.1)	3106 (22.1)	
Total cases	980	14 057	

*p Value for comparison of proportions, excluding 'not known' category where present. For age, tumour size, Charlson Index and Cancer Plan, test is for trend; for all other factors, test is for heterogeneity.

Table 3 Crude and adjusted ORs and 95% CIs for early death from any cause

Factor	Number of cases	Early deaths, number (%)	OR (95% CI) Unadjusted	OR (95% CI) Adjusted*
Age at diagnosis (years)				
<50	3800	88 (2.3)	1.00 (–)	1.00 (–)
50–59	3739	91 (2.4)	1.05 (0.78 to 1.42)	1.41 (1.03 to 1.93)
60–69	3042	148 (4.9)	2.16 (1.65 to 2.82)	2.61 (1.94 to 3.50)
70–79	2643	270 (10.2)	4.80 (3.75 to 6.14)	4.62 (3.45 to 6.18)
≥80	1813	383 (21.1)	11.30 (8.89 to 14.36)	8.05 (5.96 to 10.88)
Ethnicity				
Non-white	2058	75 (3.6)	1.00 (–)	1.00 (–)
White	9098	488 (5.4)	1.50 (1.17 to 1.92)	1.25 (0.96 to 1.63)
Not known	3881	417 (10.7)	3.18 (2.47 to 4.09)	2.24 1.70 to 2.94)
Distant metastases at diagnosis				
No	8289	312 (3.8)	1.00 (–)	1.00 (–)
Yes	427	156 (36.5)	14.72 (11.73 to 18.47)	8.41 (6.49 to 10.89)
Not known	6321	512 (8.1)	2.25 (1.95 to 2.60)	1.35 (1.13 to 1.60)
Tumour size (mm)				
<10	1232	12 (1.0)	1.00 (–)	–
10–19	4089	73 (1.8)	1.85 (1.00 to 3.41)	–
20–39	3186	83 (2.6)	2.72 (1.48 to 5.00)	–
40–49	2039	86 (4.2)	4.48 (2.44 to 8.22)	–
≥50	898	99 (11.0)	12.60 (6.87 to 23.08)	–
Not known	3593	627 (17.4)	21.49 12.09 to 38.20)	–
Node status				
Negative	5587	95 (1.7)	1.00 (–)	–
Positive	4380	167 (3.8)	2.29 (1.78 to 2.96)	–
Not known	5070	718 (14.2)	9.54 (7.67 to 11.86)	–
Charlson Index (comorbidities)				
0 (minor)	6958	203 (2.9)	1.00 (–)	1.00 (–)
1 (moderate)	407	48 (11.8)	4.45 (3.19 to 6.20)	2.54 (1.77 to 3.65)
2+ (severe)	1615	231 (14.3)	5.55 (4.56 to 6.76)	3.55 (2.85 to 4.42)
Not known	6057	498 (8.2)	2.98 (2.52 to 3.52)	1.10 (0.90 to 1.34)
Diagnosis date (in relation to Cancer Plan)				
Pre 2000	9681	624 (6.4)	1.00 (–)	1.00 (–)
2000–2003	4189	292 (7.0)	1.09 (0.94 to 1.26)	0.90 (0.75 to 1.07
Post 2003	1167	64 (5.5)	0.84 (0.65 to 1.10)	0.71 (0.52 to 0.98)
Presentation				
Screening	2297	23 (1.0)	1.00 (–)	1.00 (–)
Symptoms	10 294	763 (7.4)	7.91 (5.21 to 12.01)	3.31 (2.13 to 5.14)
Incidental	592	64 (10.8)	11.98 (7.37 to 19.48)	3.92 (2.30 to 6.66)
Not known	1854	130 (7.0)	7.46 (4.76 to 11.67)	2.77 (1.72 to 4.48)
Surgery				
No	2002	489 (24.4)	1.00 (–)	1.00 (–)
Yes	13 035	491 (3.8)	0.12 (0.11 to 0.14)	0.29 (0.24 to 0.35)
Radiotherapy				
No	3849	454 (11.8)	1.00 (–)	1.00 (–)
Yes	7335	256 (3.5)	0.27 (0.23 to 0.32)	0.61 (0.51 to 0.74)
Not known	3853	270 (7.0)	0.56 (0.48 to 0.66)	0.65 (0.48 to 0.87)
Chemotherapy				
No	7002	520 (7.4)	1.00 (–)	1.00 (–)
Yes	4403	203 (4.6)	0.60 (0.51 to 0.71)	1.49 (1.19 to 1.86)
Not known	3632	257 (7.1)	0.95 (0.81 to 1.11)	1.20 (0.89 to 1.62)
Tamoxifen				
No	2493	172 (6.9)	1.00 (–)	1.00 (–)
Yes	9231	601 (6.5)	0.94 (0.79 to 1.12)	0.64 (0.51 to 0.80)
Not known	3313	207 (6.2)	0.90 (0.73 to 1.11)	0.93 (0.70 to 1.24)

*Adjusted for all other factors—that is, based on model that includes all factors.

surgical treatment. There was a clear and independent association between increasing age and the risk of early death, with an eightfold increase in the odds of early death in women aged 80 or more compared with those aged <50 at diagnosis (OR: 8.05, 95% CI 5.96 to 10.88). In this adjusted analysis, white ethnicity was not independently associated with early death. The significant associations noted in the univariate analyses were upheld (although generally attenuated) in the multivariate model, except for chemotherapy. Women receiving chemotherapy were more likely than those not treated with chemotherapy to die within a year of their diagnosis (OR 1.49, 95% CI 1.19 to 1.86). Surgery was associated with a reduced risk of early death (OR 0.29, 95% CI 0.24 to 0.35), as was radiotherapy (OR 0.61, 95% CI 0.51 to 0.74) and also tamoxifen (OR 0.64, 95% CI 0.51 to 0.80). Women who were most recently diagnosed with breast cancer (post-2003) were less likely to die early (OR 0.71, 95% CI 0.52 to 0.98). Women with missing data for ethnicity, presentation or metastases were at increased risk of early death compared with the reference categories.

Overall, 13.3% of women did not have surgery as part of their treatment (table 2), and this proportion was significantly greater in women who died within a year of diagnosis (50% vs 11%). The characteristics of women who did or did not receive surgical treatment are shown in table 4. Those receiving surgery were significantly younger, and were more likely to present via screening, to be free of metastases at diagnosis, and to have fewer comorbidities. For those of known ethnicity, there was no difference in the proportions receiving surgery between white and non-white women. However, the proportion of cases with unknown ethnicity was significantly greater in those not receiving surgery (38.7% vs 23.8%).

In multivariate analysis (table 5), mode of presentation, older age (particularly ≥80 years), distant metastases on presentation and comorbidities were independent predictors of no surgical treatment (70–79 years old vs <50 years old: OR 0.27, 95% CI 0.23 to 0.33; ≥80 years old versus <50 years old: OR 0.09, 95% CI 0.07 to 0.10; symptomatic presentation versus screening: OR 0.34, 95% CI 0.26 to 0.45; incidental presentation versus screening: OR 0.28, 95% CI 0.20 to 0.40; distant metastases on diagnosis: OR 0.16, 95% CI 0.12 to 0.20; severe comorbidities: OR 0.50, 95% CI 0.41 to 0.62). White ethnicity was independently linked with an increased likelihood of surgical treatment compared with non-white ethnicity (OR 1.39, 95% CI 1.16 to 1.65).

Table 4 Characteristics of women who did or did not have surgery

Patient characteristic	Surgery, number (%)		p Value*
	No	Yes	
Age at diagnosis (years)			
<50	213 (10.6)	3587 (27.5)	<0.001
50–59	182 (9.1)	3557 (27.3)	
60–69	219 (10.9)	2823 (21.7)	
70–79	526 (26.3)	2117 (16.2)	
≥80	862 (43.1)	951 (7.3)	
Ethnicity			
Non-white	238 (11.9)	1820 (14.0)	0.36†
White	989 (49.4)	8109 (62.2)	
Not known	775 (38.7)	3106 (23.8)	
Distant metastases at diagnosis			
No	680 (34.0)	7609 (58.4)	<0.001
Yes	151 (7.5)	276 (2.1)	
Not known	1171 (58.5)	5150 (39.5)	
Charlson Index (comorbidities)			
0	309 (15.4)	6649 (51.0)	<0.001
1	47 (2.3)	360 (2.8)	
≥2	81 (9.0)	1434 (11.0)	
Not known	1465 (73.2)	4592 (35.2)	
Diagnosis date (in relation to Cancer Plan)			
Pre 2000	1336 (66.7)	8345 (64.0)	0.025
2000–2003	522 (26.1)	3667 (28.1)	
Post 2003	144 (7.2)	1023 (7.8)	
Presentation			
Screening	61 (3.0)	2236 (17.2)	<0.001
Symptoms	1527 (76.3)	8767 (67.3)	
Incidental	117 (5.8)	475 (3.6)	
Not known	297 (14.8)	1557 (11.9)	
Radiotherapy			
No	1014 (50.6)	2835 (21.7)	<0.001
Yes	339 (16.9)	6996 (53.7)	
Not known	649 (32.4)	3204 (24.6)	
Chemotherapy			
No	1107 (55.3)	5895 (45.2)	<0.001
Yes	311 (15.5)	4092 (31.3)	
Not known	584 (29.2)	3048 (23.4)	
Tamoxifen			
No	260 (13.0)	2233 (17.1)	<0.001
Yes	1315 (65.7)	7916 (60.7)	
Not known	427 (21.3)	2886 (22.1)	
Total cases	2002	13 035	

*p Value for comparison of proportions, excluding 'not known' category where present. For age, Charlson Index and Cancer Plan, test is for trend; for all other factors, test is for heterogeneity.
†p Value when 'not known' category is included: <0.001.

DISCUSSION

Poorer prognosis of older women with breast cancer has been attributed variously to treatment received,[10–17] more severe disease on presentation,[13 18–21] and the presence of comorbidities.[10] Stage was identified as the most important factor explaining breast cancer survival discrepancies between European countries for women given a diagnosis between 1990 and 1992,[19] particularly in older age groups.

This study in more than 15 000 women diagnosed as having breast cancer in the North Thames area found that age and disease severity at diagnosis were independent predictors of early death from any cause. In the women analysed here, distant metastases on diagnosis were a strong predictor of early death, increasing the odds of dying within a year of diagnosis more than eightfold (OR 8.41, 95% CI 6.49 to 10.89). This effect

Table 5 Crude and adjusted ORs and 95% CIs for surgical treatment

Factor	Number of cases	Surgical cases, number (%)	OR (95% CI) Unadjusted	OR (95% CI) Adjusted*
Age at diagnosis (years)				
<50	3800	3587 (94.4)	1.00 (–)	1.00 (–)
50–59	3739	3557 (95.1)	1.16 (0.95 to 1.42)	0.99 (0.80 to 1.22)
60–69	3042	2823 (92.8)	0.77 (0.63 to 0.93)	0.73 (0.59 to 0.89)
70–79	2643	2117 (80.1)	0.24 (0.20 to 0.28)	0.27 (0.23 to 0.33)
≥80	1813	951 (52.5)	0.07 (0.06 to 0.08)	0.09 (0.07 to 0.10)
Ethnicity				
Non-white	2058	1820 (88.4)	1.00 (–)	1.00 (–)
White	9098	8109 (89.1)	1.07 (0.92 to 1.25)	1.39 (1.16 to 1.65)
Not known	3881	3106 (80.0)	0.52 (0.45 to 0.61)	0.93 (0.77 to 1.11)
Distant metastases at diagnosis				
No	8289	7609 (91.8)	1.00 (–)	1.00 (–)
Yes	427	276 (64.6)	0.16 (0.13 to 0.20)	0.16 (0.12 to 0.20)
Not known	6321	5150 (81.5)	0.39 (0.36 to 0.43)	0.36 (0.31 to 0.40)
Charlson Index (comorbidities)				
0 (minor)	6958	6649 (95.6)	1.00 (–)	1.00 (–)
1 (moderate)	407	360 (88.5)	0.36 (0.26 to 0.49)	0.70 (0.49 to 0.99)
2+ (severe)	1615	1434 (88.8)	0.37 (0.30 to 0.45)	0.50 (0.41 to 0.62)
Not known	6057	4592 (75.8)	0.15 (0.13 to 0.17)	0.20 (0.17 to 0.23)
Diagnosis date (in relation to Cancer Plan)				
Pre 2000	9681	8345 (86.2)	1.00 (–)	1.00 (–)
2000–2003	4189	3667 (87.5)	1.12 (1.01 to 1.25)	1.11 (0.97 to 1.27)
Post 2003	1167	1023 (87.7)	1.14 (0.95 to 1.37)	0.75 (0.60 to 0.94)
Presentation				
Screening	2297	2236 (97.3)	1.00 (–)	1.00 (–)
Symptoms	10294	8767 (85.2)	0.16 (0.12 to 0.20)	0.34 (0.26 to 0.45)
Incidental	592	475 (80.2)	0.11 (0.08 to 0.15)	0.28 (0.20 to 0.40)
Not known	1854	1557 (84.0)	0.14 (0.11 to 0.19)	0.39 (0.29 to 0.53)

*Adjusted for all other factors—that is, based on model that includes all factors.

was independent of age and treatment. It was also independent of patient comorbidities, although this should be interpreted with some caution, as comorbidity data were available only for the 60% of participants who could be successfully linked to the HES dataset. Surgery was strongly associated with a reduced risk of early death, and older patients were less likely to receive surgery.

Great improvements in cancer services have been made during the past decade. To investigate whether the implementation of the Cancer Plan has had any observable effect on survival, this research included a categorical variable controlling for calendar period of diagnosis in the multivariate analyses. This method was similar to that used by Rachet *et al*[8] in their assessment of the NHS Cancer Plan for England. In our study, women given a diagnosis after 2003 had reduced odds of early death compared with women given a diagnosis before the Cancer Plan was published (OR 0.71, 95% CI 0.52 to 0.98). This suggests a survival benefit resulting from changes to cancer services after 2000.

While women of white ethnicity were at greater odds of early death in univariate analyses, this association was no longer significant when the model was adjusted for the other covariates. The white women were in general older than the non-white women, and this may explain these findings. However, in the adjusted analysis, white women were more likely to be treated surgically than those belonging to non-white ethnic groups. These results should perhaps be treated with caution, given the large proportion (26%) of cases for which ethnicity was not known.

Radiotherapy and tamoxifen treatments were independently associated with reduced likelihood of early death, while chemotherapy was associated with increased odds of dying within a year of diagnosis (OR 1.49, 95% 1.19 to 1.86). This relationship with chemotherapy is likely to be a reflection of selection bias, whereby only the most severe cases are given this form of treatment. A similar bias, but in the opposite direction, may apply to surgery—that is, with very ill patients selectively not being operated upon. However, the association between surgery and death within 1 year remained apparent in a model correcting for age and comorbidity. These findings are consistent with those in a recent study by Brewster *et al*[22] that found age, deprivation, emergency admission, tumour stage, and grade and absence of treatment were independent factors associated with death within 30 days of diagnosis.

A recent report from the National Cancer Intelligence Network based on data from 2007 confirms that a high proportion of older women in the UK do not receive surgical treatment: 61% of women aged over 80 did not

have surgery.[23] This group is likely to have a particularly poor prognosis. Nearly 40% of women who died early in our study were aged 80 years or over, and 66% (252/383) of them had not had surgery.

In our study, age was strongly inversely associated with the likelihood of receiving surgery. This reflects the well-described pattern in other studies of older women being less likely to receive treatment than younger women.[10 24] Women over 80 years old attending breast units in Manchester in 2002, for example, were less likely to have surgery than women aged 65–79 years even after adjustment for poorer general health, including comorbidities.[11]

Patient comorbidity has been shown to be a potentially important confounder in studies of treatment received,[15 25] but our analyses suggest that older women are less likely to receive surgery even after adjustment for comorbidities. Comorbidity data were missing for approximately 40% of participants. Patients with missing comorbidity data were less likely to receive surgery, although there was no association between these missing data and early death after adjustment for other factors.

One potential limitation of this study is missing information. Women with missing data on ethnicity, presentation and distant metastases were more likely to die within a year of their diagnosis and were less likely to receive surgical treatment. They may represent women who were seriously ill at diagnosis and who were not scheduled for surgery. An analysis of the characteristics of patients with several missing data elements suggests that these women tend to be older, have more severe disease (as determined by a proxy of tumour size), and are more likely to die early. In addition, a failure to record important details relating to their diagnosis and treatment may be an indication that such patients are receiving worse care. With respect to this study, if women with missing information have worse disease and are generally older, then the estimates of association between these variables and early death will be biased towards underestimates of the true effects.

Retrospective analyses rely on records in which some information may be inaccurate. In this study a particular effort was made to ensure that the surgical status of women was recorded correctly, as this was considered an important marker of the quality of treatment and was expected to be strongly associated with outcome. Time and resource constraints precluded this additional effort being extended to other variables to verify database entries. However, an earlier study looking at trends in the treatment of breast cancer[26] concluded that the audit database was a reasonably reliable source of such data.

The effects of deprivation on disease severity and ultimately on mortality were not explored in this study. Such analyses rely on potential patient identifiers, such as postcode data, that were not available to us. Deprivation has been linked to poorer patient outcomes for UK patients with breast cancer in several studies,[22 27–29] and stated aims of the Cancer Plan and the Cancer Reform

Table 6 Comparison of audit cohort and registered North Thames cases

Year of diagnosis	Cancer registry database				Breast audit database				
	No of registered North Thames cases	Mean (SD) age at diagnosis	Total deaths	Deaths within 1 year*	No of cases submitted†	Mean (SD) age at diagnosis	Total deaths	Deaths within 1 year*	No of trusts submitting
1996	4068	61.5 (14.9)	1829	283 (7.0%)	1380 (33.9%)	61.6 (14.8)	577	68 (4.9%)	21
1997	4254	61.4 (14.6)	1734	312 (7.3%)	2611 (61.4%)	60.8 (14.3)	1022	161 (6.2%)	23
1998	4121	62.0 (15.2)	1581	325 (7.9%)	2133 (51.8%)	61.8 (15.3)	859	144 (6.8%)	24
1999	4269	61.7 (14.7)	1513	332 (7.8%)	2004 (46.9%)	61.4 (14.9)	680	130 (6.5%)	24
2000	4100	61.7 (14.9)	1309	372 (9.1%)	2065 (50.4%)	61.2 (14.9)	630	159 (7.7%)	26
2001	4086	61.8 (15.2)	1160	328 (8.0%)	1600 (39.2%)	61.3 (15.4)	448	120 (7.5%)	20
2002	4006	61.6 (14.5)	922	312 (7.8%)	1280 (32.0%)	60.1 (14.9)	280	83 (6.5%)	16
2003	4359	61.6 (14.8)	832	331 (7.6%)	797 (18.3%)	58.7 (15.1)	149	51 (6.4%)	13
2004	4238	61.9 (14.6)	591	316 (7.5%)	563 (13.3%)	58.4 (14.8)	81	36 (6.4%)	8
2005	3400	61.4 (14.6)	282	220 (6.5%)	604 (17.8%)	59.0 (14.5)	39	28 (4.6%)	7
Total	40 901	61.7 (14.8)	11 753	3131 (7.7%)	15 037 (36.8%)	60.9 (14.9)	4765	980 (6.5%)	29

*Figures in parentheses are deaths within 1 year as a percentage of total cases.
†Figures in parentheses are audit cases as a percentage of total registered cases.

Strategy[30–32] are to tackle the inequalities in cancer survival between different socioeconomic groups in England.

We suspect a complex relationship between the exposures studied here, some of which may be on the same causal pathway for early death. For example, high age and comorbidity may be rational and adequate reasons for not offering surgery. While a number of patient and treatment characteristics were strongly and independently linked with early death, these associations must be interpreted with caution and with a consideration for unmeasured confounding factors. For instance, the selection of a patient's treatment will depend on a number of factors, including some not measured here, such as their own preferences or established practices within the organisation in which they are treated.[33] Furthermore, their presentation to health services depends, among other factors, on access to those services and knowledge of cancer symptoms. Many of these variables may be linked to both risk factors and outcomes and they have not been assessed in this study. However, for any underlying confounder to explain the strong statistical associations seen in our data, they would need to have a very strong correlation with death within a year of diagnosis.

Five-year relative survival in our sample (based on life tables for London during the period 1996–2001) was 84.1%. This is similar to recent estimates from the Office for National Statistics,[34] which reports a value of 82% for women given a diagnosis between 2000 and 2006. Thus our cohort sample is likely to be reasonably representative of the UK population of women diagnosed as having breast cancer during this period. Table 6 compares the audit data with the total registrations for female breast cancer in the North Thames region at TCR. Mean age at diagnosis was similar throughout the study period. Likewise, the proportion of patients dying within 1 year of diagnosis was broadly similar, although slightly lower in the audit database (6.5% vs 7.7% overall.) The proportion of total cases represented in the audit varied between 61% in 1997 and 13% in 2004, with an overall figure of 37%. (The decrease in the number of registered cases in 2005 is an artefact due to changes in the TCR catchment area.) In general, there was a higher representation in the earlier years, which may have implications for the applicability of the results to more recent times.

CONCLUSIONS

Our findings offer detailed insights into the determinants of death in the first year after a diagnosis of breast cancer, a period shown to be important in international comparisons. As expected, early death is linked to older age and to the presence of comorbidities. Comorbidities can be addressed in the long run through general health policy, but two other determinants of early death identified by this study are potential avenues for intervention.

First, the findings relating to disease severity lend empirical support to the notion that late diagnosis is a major determinant of early death. This supports the rationale for projects that focus on increasing awareness of breast symptoms and the importance of screening. Second, surgery is independently associated with a large reduction in the risk of early death, and older women were—independently of disease severity and comorbidity—much less likely to receive surgery. Assuming surgery is an indicator of attempts at curative treatment, there may be benefits of increased treatment activity for older women.

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