Prognostic factors in women with breast cancer: distribution by socioeconomic status and effect on differences in survival

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Abstract

***Study objective*—To quantify and investigate differences in survival from breast cancer between women resident in affluent and deprived areas and define the contribution of underlying factors to this variation.**

***Design*—Analysis of two datasets relating to breast cancer patients in Scotland: (1) population-based cancer registry data; (2) a subset of cancer registration records supplemented by abstraction of prognostic variables (stage, node status, tumour size, oestrogen receptor (ER) status, type of surgery, use of radiotherapy and use of adjuvant systemic therapy) from medical records.**

***Setting*—Scotland.**

***Patients*—(1) Cancer registration data on 21 751 women aged under 85 years diagnosed with primary breast cancer between 1978 and 1987; (2) national clinical audit data on 2035 women aged under 85 years diagnosed with primary breast cancer during 1987 for whom adequate medical records were available.**

***Main results*—Survival differences of 10% between affluent and deprived women were observed in both datasets, across all age groups. In the audit dataset, the distribution of ER status varied by deprivation group (65% ER positive in affluent group *v* 48% ER positive in deprived group; under 65 age group). Women aged under 65 with non-metastatic disease were more likely to have breast conservation than a mastectomy if they were affluent (45%) than deprived (32%); the affluent were more likely to receive endocrine therapy (65%) than the deprived (50%). However, these factors accounted for about 20% of the observed difference in survival between women resident in affluent and deprived areas.**

***Conclusions*—Deprived women with breast cancer have poorer outcomes than affluent women. This can only partly be explained by deprived women having more ER negative tumours than affluent women. Further research is required to identify other reasons for poorer outcomes in deprived women, with a view to reducing these survival differences.**

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Women with breast cancer from lower socioeconomic groups have relatively lower survival than affluent women and this difference in outcomes seems independent of the measure of socioeconomic status used.[1] The clinical importance of this observation depends on the magnitude of the difference in survival. A recent review of cancer registration data from England and Wales indicated a difference of 5%–10% both for absolute and relative survival between the affluent and deprived groups depending on the period of diagnosis[2]; similar figures were reported in the US,[3] Finland,[4] the Netherlands[5] and by other British cancer registry studies.[6–10] These differences equate to hazard ratios for the deprived women of between 1.16[8] to 1.49.[11] Considering that five year observed survival for women with breast cancer in Scotland improved by just six percentage points (from 50% to 56%) in the 16 years from 1970 to 1985,[10] the potential benefit of understanding and remedying the difference between socioeconomic groups is substantial. So far, attempts to explain socioeconomic differences on the basis of stage and treatment have produced conflicting findings,[3–5 7 8 11] which may well reflect the differing health service provisions and socioeconomic structures in the countries in which the studies have been carried out.

In Scotland, it is possible to bring together high quality cancer registry data covering the whole country over a prolonged period with nationally conducted clinical audit data for a single year. The Scottish Cancer Therapy Network (SCTN) breast cancer audit[12] of women diagnosed in 1987 collected a wide range of demographic and biological variables at presentation and details of treatment and outcome. This study builds on this earlier analysis of these data that examined survival among the surgically treated breast cancer patients only. That analysis confirmed the lower survival of women with breast cancer living in deprived areas and showed a difference in oestrogen receptor (ER) status between affluent and deprived patients[12]; the potential contribution to differences in outcome from variation in ER status was unclear.

The first aim of this study was to establish that the effect of deprivation on survival observed in the registry data could be confirmed in the corresponding group of women in the audit, and not just in the subgroup of women treated surgically. Secondly, we wanted to assess the impact of differences in ER status and other prognostic factors on the effect of deprivation on survival in the well characterised group of patients in the audit. Finally, we sought to quantify the extent to which variations in ER status may account for the observed differences in survival in the same group of women. The importance of the difference in the proportion of ER status by deprivation group needs to be investigated as women with ER negative tumours usually have poorer prognoses than women with ER positive tumours. Additionally, ER status should affect which form of adjuvant systemic therapy is given.

Methods

STUDY POPULATIONS

Cancer registration data

Data from the Scottish Cancer Registry were used to enable a precise estimate of the difference in the survival rates of women with breast cancer between socioeconomic groups to be obtained. Eligibility criteria for inclusion in survival analyses based on these data are detailed in a recent publication from the Scottish Cancer Intelligence Unit.[13] Women were included if they had no previous history of malignancy, were resident in Scotland, aged under 85 years, registered as having invasive breast cancer (ICD-9 174) and diagnosed between 1978 and 1987 (before the introduction of the national breast screening programme in 1988); cases where the only record supporting a diagnosis of cancer was the death certificate were excluded. The DCO (death certificate only) rate covering the time period studied was 3% in Scotland. Deprivation groups were defined using the Carstairs Index,[14] an area based score derived from 1981 census data, based on the postcode of residence at diagnosis. These scores were split into quintiles of the Scottish population and then combined into three groups (1) affluent, the least deprived quintile; (2) intermediate, quintiles 2, 3 and 4; and (3) deprived, the most deprived quintile. In Scotland, patients with cancer are not actively followed up to death by the cancer registry. Therefore, death information from the General Register Office (Scotland) was linked by probability matching[15] until the end of 1996 and supplemented by deaths recorded on the cancer file for 1997 and 1998.

National Audit data

A national population-based study of all women with invasive breast cancer recorded by the Scottish Cancer Registry in 1987[16] was undertaken by the SCTN, with the aim of documenting patterns of care of patients resident in Scotland. The Medical Director of each Trust Hospital, the Chief Administrative Medical Officer of each Health Board and individual consultants were contacted to obtain permission to examine the case notes; all cooperated in the study. Specially trained SCTN data managers examined the case notes for all women eligible for inclusion in the audit.

The clinical factors examined in the audit were (1) "clinical stage", adapted from that defined by TNM criteria[17] in five categories (TNM stages I-III in patients undergoing surgery; an extra category for all TNM stage I-III non-surgical patients; TNM stage IV (metastatic) patients), (2) pathological tumour size (analysed in 1 cm bands), (3) pathological node status (positive; inadequate negative sample (INS-1, 2, 3 or unknown number sampled, all negative); negative (4 or more nodes sampled, all negative)) and (4) ER status (positive > 20 fmol/mg cytosolic protein or ⩾ 10% staining). Histological grade was collected but not included in the analysis because 61% of women of all ages (and 56% of those under 65) did not have this information recorded.

The treatment factors available for analysis included type of surgery (mastectomy; breast conservation; none), use of radiotherapy to the breast, chest wall or axilla, and prescription of adjuvant systemic treatment, comprising endocrine therapy (tamoxifen; ovarian ablation) or chemotherapy, or both. A variable giving the possible combinations of any surgery, use of radiotherapy and any adjuvant systemic therapy was also investigated. Survival data for deaths up until 31 December 1998 (provisional for 1998) were obtained by probabilistic linkage[15] with the death records from the General Register Office (Scotland).

DATA ANALYSIS

All of the clinical and treatment factors were examined to investigate whether any of them were associated with deprivation category, both in the overall group and stratified by age. Results are presented for age groups under and over 65 years, mainly to abrogate the influence of "missing data" that tended to be concentrated in the older age groups, and partly to allow comparison with the analysis of data from south east England.[7] The significance of these relations was assessed by performing χ^2 tests of association. These comparisons were made both with and without the inclusion of the missing values to determine whether any apparently significant differences may have been attributable to variation in the proportion of missing values between deprivation categories. The treatment factors were examined only for women with no evidence of metastatic disease at presentation because it is in this group that any differences in the management of the disease are most likely to influence their longer term survival.

Kaplan-Meier estimates of survival at 5 and 10 years using both all cause mortality and breast cancer specific mortality were obtained for both the registry and the audit data. The breast cancer specific mortality was derived using the main underlying cause of death recorded by the Registrar General, Scotland and a breast cancer specific death was assumed when any of the following ICD-9 codes were recorded as the underlying cause on the death certificate: 174; 195.1; 196–198; 199; 217; 238.3; 238.9; 239.3; 239.9.(Scottish Cancer Intelligence Unit[13]; appendix 7). Cox's proportional hazards modelling was applied to the audit data to examine the effect of introducing other variables into the model on the relative hazard ratios for the intermediate and most deprived groups relative to the affluent group.

Results

All of the 21 751 eligible women aged under 85 years recorded on the Scottish Cancer Registry (SCR) as having invasive breast cancer diagnosed during the years 1978 to 1987 were included in the analysis of registry data. The numbers of women in the three deprivation groups were 5080, 12 895 and 3719 for the affluent, intermediate and deprived groups, respectively. For 57 women, a deprivation score could not be assigned. For the audit, 2581 women were registered with the SCR at the start of data collection in 1994, of whom 2115 were eligible for the analysis. The remaining 466 women were excluded for the following reasons: death certificate only registrations (n=79); patients diagnosed and treated outside Scotland (n=16) or outwith the audit window (three months outside of 1987, n=35); those with non-invasive disease (n=36); not primary breast cancer (n=48); their records could not be traced (n=163) or their case notes had been destroyed (n=89). To be comparable with the registry data, a further 80 women aged 85 and over at diagnosis were also excluded from the study population. Therefore, the audit data analyses are based on 2035 women. There were 496 women in the affluent group, 1234 women in the intermediate group and 303 women in the deprived group for this dataset. Only two women could not be assigned a deprivation score.

SURVIVAL

Table 1 shows the Kaplan-Meier estimates of survival at 5 and 10 years for women with breast cancer diagnosed between 1978 and 1987 for the registry data and the 1987 audit data, based on breast cancer specific mortality for both datasets. Highly significant trends for better survival among the affluent are seen in each age group and across all ages in the registry data. The difference in breast cancer specific survival between the affluent and deprived groups was 8.7% (SE = 1.1%) at five years and 10.2% (SE = 1.1%) at 10 years. There was no evidence that the effect of deprivation category on survival varied significantly by age group (test for interaction p= 0.98) or that it decreased over the period 1978 to 1987 (test for interaction p= 0.06 for deprivation with year of diagnosis fitted as a continuous variable). Similar results were seen for the audit data, with differences in five year survival of 9.2% (SE = 3.5%) and 10 year survival of 13.0% (SE = 3.8%).

Similar differences in survival between the affluent and deprived groups were evident when any cause of death was used as the end point. The differences for the registry data were 8.7% (SE = 1.1%) and 10.1% (SE = 1.0%) at 5 and 10 years, respectively; for the corresponding audit data, the differences were 7.1% (SE = 3.6%) and 9.4% (SE = 3.6%), respectively. From the registry data, the hazard ratios relative to the affluent groups, after adjustment for age group, for the intermediate and deprived groups were 1.20 (95% CI 1.15, 1.26) and 1.37 (95% CI 1.29, 1.45), respectively. These were strikingly similar to those from the audit data, although the standard errors differed because of the far greater number of women in the registry data set compared with the audit. The corresponding age adjusted hazard ratios from the audit dataset were 1.19 (95% CI 1.01, 1.41) and 1.42 (95% CI 1.15, 1.76), respectively.

PROGNOSTIC FACTORS

The distribution of the clinical factors by deprivation category derived from the audit is shown in table 2. The percentages are presented as totals of the known values only. Tests of association were performed with and without the inclusion of the unknown categories; in general the results were very similar with and without the unknowns. When the unknowns were excluded, no differences were seen for women under 65 years of age, over 65 years or for all ages combined, in the distribution of "clinical stage" (p = 0.07, 0.23 and 0.45 for <65 years, 65–84 and 0–84, respectively), pathological node status (p = 0.41, 0.35 and 0.20, respectively) or pathological tumour size (p = 0.17, 0.12 and 0.17, respectively). However, differences by deprivation group were apparent for ER status that were significant for the under 65 age group and all ages

Table 1 Kaplan-Meier survival at 5 and 10 years for Registry data for 1978–1987 for breast cancer and for the Audit data (1987). Breast cancer specific deaths as endpoint

	5 years			*% Diff (Aff–Dep)*	*p for trend*	*10 years*			*% Diff (Aff–Dep)*	*p for trend*
	Aff	*Interm*	*Dep*			*Aff*	*Interm*	*Dep*		
Registry data										
Total number*	5080	12 895	3719	n/a	n/a	5080	12 895	3719	n/a	n/a
Age group										
25–44 (n=3012)	71.9%	69.2%	63.0%	8.9%	0.0009	61.5%	56.9%	52.2%	9.3%	0.0004
45–54 (n=4513)	71.7%	65.7%	60.8%	10.9%	<0.0001	61.2%	53.3%	49.4%	11.8%	<0.0001
55–64 (n=5265)	69.6%	63.3%	60.0%	9.6%	<0.0001	57.1%	50.3%	45.5%	11.6%	<0.0001
65–74 (n=5258)	67.3%	63.5%	59.3%	8.0%	0.0004	54.0%	49.4%	44.2%	9.8%	0.0001
75–84 (n=3683)	61.1%	56.9%	56.3%	4.8%	0.0189	46.1%	41.4%	36.7%	9.4%	0.0024
All (0–84)† (n=21 751)	68.6%	63.6%	59.9%	8.7%	<0.0001	56.5%	50.5%	46.3%	10.2%	<0.0001
Audit data										
Total number‡	496	1234	303	n/a	n/a	496	1234	303	n/a	n/a
Age group										
25–44 (n=295)	71.3%	72.6%	55.5%	15.8%	0.18	61.3%	60.8%	50.2%	11.1%	0.29
45–54 (n=409)	72.3%	67.9%	62.8%	9.5%	0.18	66.1%	56.1%	43.6%	22.5%	0.009
55–64 (n=486)	78.5%	67.4%	72.6%	5.9%	0.21	61.3%	56.0%	58.3%	3.0%	0.49
65–74 (n=479)	73.7%	69.1%	62.1%	11.6%	0.21	64.4%	54.1%	43.6%	20.8%	0.023
75–84 (n=363)	62.0%	60.8%	59.2%	2.8%	0.58	45.3%	49.5%	42.3%	3.0%	0.67
All (0–84)§ (n=2035)	72.2%	67.7%	63.0%	9.2%	0.009	60.7%	55.5%	47.7%	13.0%	0.001

*A deprivation category could not be assigned to 57 cases. †There were 20 cases aged under 25 years included in the 0–84 group. ‡A deprivation category could not be assigned to two cases. §There were three cases aged under 25 years included in the 0–84 group.

Table 2 Distribution of cases (%) for the clinical factors in the deprivation groups by age group. Note that the percentages for the known values are based on the total of known cases (that is, excluding the unknowns)

	<65							65–84*							0–84*						
	Aff		Interm		Dep			Aff		Interm		Dep			Aff		Interm		Dep		
	No	%	No	%	No	%	p value§	No	%	No	%	No	%	p value§	No	%	No	%	No	%	p value§
Total	293	n/a	728	n/a	172	n/a		203	n/a	506	n/a	131	n/a		496	n/a	1234	n/a	303	n/a	
Clinical factors																					
"Clinical stage"†							0.07							0.23							0.45
Stage I (surgical)	63	25.8	139	22.6	32	22.9		18	10.1	42	9.6	11	9.6		81	19.2	181	17.2	43	16.9	
Stage II (surgical)	145	59.4	322	52.4	76	54.3		55	30.9	173	39.7	40	34.8		200	47.4	495	47.1	116	45.5	
Stage III (surgical)	14	5.7	69	11.2	14	10.0		20	11.2	52	11.9	11	9.6		34	8.1	121	11.5	25	9.8	
Non-metastatic, non-surgical	4	1.6	36	5.9	7	5.0		67	37.6	113	25.9	39	33.9		71	16.8	149	14.2	46	18.0	
Metastatic	18	7.4	49	8.0	11	7.9		18	10.1	56	12.8	14	12.2		36	8.5	105	10.0	25	9.8	
Unknown	49	n/a	113	n/a	32	n/a		25	n/a	70	n/a	16	n/a		74	n/a	183	n/a	48	n/a	
ER status							0.01							0.71							0.02
Positive	133	64.6	252	58.1	61	48.0		49	70.0	134	66.3	36	63.2		182	65.9	386	60.7	97	52.7	
Negative	73	35.4	182	41.9	66	52.0		21	30.0	68	33.7	21	36.8		94	34.1	250	39.3	87	47.3	
Unknown	87	n/a	294	n/a	45	n/a		133	n/a	304	n/a	74	n/a		220	n/a	598	n/a	119	n/a	
Node status							0.41							0.35							0.20
Positive	118	49.2	250	49.2	66	54.1		44	57.1	111	53.4	28	50.0		162	51.1	361	50.4	94	52.8	
INS‡	51	21.3	132	26.0	27	22.1		12	15.6	52	25.0	11	19.6		63	19.9	184	25.7	38	21.3	
Negative	71	29.6	126	24.8	29	23.8		21	27.3	45	21.6	17	30.4		92	29.0	171	23.9	46	25.8	
Unknown	53	n/a	220	n/a	50	n/a		126	n/a	298	n/a	75	n/a		179	n/a	518	n/a	125	n/a	
Tumour size							0.17							0.12							0.17
≤1 cm	24	10.6	82	16.0	12	9.2		7	6.8	23	7.8	3	4.8		31	9.4	105	13.0	15	7.8	
>1≤2 cm	99	43.8	178	34.8	49	37.7		34	33.0	120	41.0	19	30.2		133	40.4	298	37.0	68	35.2	
>2≤3 cm	58	25.7	139	27.1	34	26.2		35	34.0	75	25.6	16	25.4		93	28.3	214	26.6	50	25.9	
>3≤4 cm	21	9.3	57	11.1	13	10.0		15	14.6	31	10.6	10	15.9		36	10.9	88	10.9	23	11.9	
>4≤5 cm	14	6.2	30	5.9	10	7.7		4	3.9	25	8.5	11	17.5		18	5.5	55	6.8	21	10.9	
>5 cm	10	4.4	26	5.1	12	9.2		8	7.8	19	6.5	4	6.3		18	5.5	45	5.6	16	8.3	
Unknown	67	n/a	216	n/a	42	n/a		100	n/a	213	n/a	68	n/a		167	n/a	429	n/a	110	n/a	

*A deprivation category could not be assigned to two cases. †TNM clinical stage for non-metastatic, surgical cases (I, II or III) with extra categories for non-metastatic, non-surgical and metastatic cases. ‡Inadequate negative sample = 1, 2, 3, or unknown number of nodes sampled, all negative. §χ^2 test of association excluding the unknown category.

(both p ≤ 0.02) but not for the subgroup of women aged over 65 (p = 0.71). For women with known ER status, 65% of affluent women, 58% of the intermediate group and 48% of the deprived cases were ER positive in the under 65 age group. When the tests of association were performed with unknowns included in the analysis, the association between ER status and deprivation for both the under 65 age group and all ages remained significant (both p < 0.001) and a significant difference was apparent for node status among women under 65 years of age (p = 0.003) but not for all ages (p=0.08) or those over 65 (p = 0.50). The discrepant result for node status reflects a difference in the distribution of the unknown node status by deprivation group for women aged under 65 years. None of the other tests of association were significant when the unknowns were included.

TREATMENT

The pattern of treatment factors across deprivation categories in women with no evidence of metastatic spread at diagnosis are shown in table 3. Although the numbers of women aged over 65 treated by surgery alone were small, there seemed to be a significant difference in the proportion treated in this manner according to deprivation category (7.0%, 8.0% and 17.1% of women, respectively from affluent, intermediate and deprived groups having surgery alone, p < 0.001). Overall, in women of all ages there appeared to be no significant difference in the type of surgery by deprivation group (p = 0.19). Among women aged over 65 there was, however, slightly more breast conservation in the deprived group (p = 0.04). The reverse was true in the under 65 age group with 54% of affluent women having a mastectomy compared with 64% of the deprived women (p = 0.008). Affluent women of all ages were more likely to receive endocrine therapy than their deprived counterparts (74% and 60%, respectively; p = 0.001); this difference was significant both in those under 65 years of age (65% and 50%, respectively; p = 0.008), and those aged over 65 (87% and 75%, respectively; p = 0.03). However, limiting this analysis to women whose ER status was known, deprivation did not affect whether or not women received adjuvant endocrine therapy for any of the age groups (p values all greater than 0.25).

EFFECT OF ADJUSTING FOR PROGNOSTIC FACTORS

Table 4 shows the effect on the relative hazard ratio (RHR) for deprivation by adjusting for age, ER status, node status, tumour size and "clinical stage". For women under 65, the addition of ER status to a model containing age and deprivation reduced the RHR from 1.41 to 1.33 for the deprived group and from 1.23 to 1.18 for the intermediate group.

Discussion

We have shown in 21 751 women diagnosed with breast cancer between 1978 and 1987 that there is a strong gradient between socioeconomic status and survival for women in

Table 3 Distribution of cases (%) for the treatment combinations and type of surgery in the deprivation groups by age group for women with non-metastatic disease only

	<65							65–84*							0–84*						
	Aff		Interm		Dep			Aff		Interm		Dep			Aff		Interm		Dep		
	No	%	No	%	No	%	p value†	No	%	No	%	No	%	p value†	No	%	No	%	No	%	p value†
Total	275	n/a	679	n/a	161	n/a		185	n/a	450	n/a	117	n/a		460	n/a	1129	n/a	278	n/a	
Treatment combinations							0.07							<0.001							0.003
No treatment	0	0	3	0.4	1	0.6		7	3.8	6	1.3	4	3.4		7	1.5	9	0.8	5	1.8	
Surgery only	33	12.0	107	15.8	36	22.4		13	7.0	36	8.0	20	17.1		46	10.0	143	12.7	56	20.1	
RT only	1	0.4	3	0.4	1	0.6		0	0	0	0	1	0.9		1	0.2	3	0.3	2	0.7	
CT/hormone only	0	0	10	1.5	3	1.9		54	29.2	99	22.0	33	28.2		54	11.7	109	9.7	36	12.9	
Surgery + RT	40	14.5	119	17.5	26	16.1		4	2.2	33	7.3	1	0.9		44	9.6	152	13.5	27	9.7	
Surgery + CT/hormone	101	36.7	205	30.2	47	29.2		81	43.8	200	44.4	42	35.9		182	39.6	405	35.9	89	32.0	
RT + CT/hormone only	3	1.1	20	2.9	2	1.2		6	3.2	8	1.8	1	0.9		9	2.0	28	2.5	3	1.1	
Surgery + RT + CT/hormone	97	35.3	212	31.2	45	28.0		20	10.8	68	15.1	15	12.8		117	25.4	280	24.8	60	21.6	
Type of surgery							0.008							0.04							0.19
Mastectomy	147	53.5	382	56.3	103	64.0		74	40.0	191	42.4	46	39.3		221	48.0	573	50.8	149	53.6	
Conservation	124	45.1	261	38.4	51	31.7		44	23.8	146	32.4	32	27.4		168	36.5	407	36.0	83	29.9	
None	4	1.5	36	5.3	7	4.3		67	36.2	113	25.1	39	33.3		71	15.4	149	13.2	46	16.5	
Any hormone therapy							0.008							0.03							0.001
Given	178	64.7	395	58.2	80	49.7		161	87.0	372	82.7	88	75.2		339	73.7	767	67.9	168	60.4	
None	97	35.3	284	41.8	81	50.3		24	13.0	78	17.3	29	24.8		121	26.3	362	32.1	110	39.6	
Any hormone therapy by ER status																					
ER positive							0.76							0.29							0.62
Hormone given	91	72.2	168	68.9	41	71.9		43	91.5	107	82.3	25	80.6		134	77.5	275	73.5	66	75.0	
No hormone	35	27.8	76	31.1	16	28.1		4	8.5	23	17.7	6	19.4		39	22.5	99	26.5	22	25.0	
ER negative							0.53							0.45							0.31
Hormone given	29	40.8	66	38.4	20	31.7		14	70.0	46	71.9	12	57.1		43	47.3	112	47.5	32	38.1	
No hormone	42	59.2	106	61.6	43	68.3		6	30.0	18	28.1	9	42.9		48	52.7	124	52.5	52	61.9	
ER unknown							0.009							0.21							0.003
Hormone given	58	74.4	161	61.2	19	46.3		104	88.1	219	85.5	51	78.5		162	82.7	380	73.2	70	66.0	
No hormone	20	25.6	102	38.8	22	53.7		14	11.9	37	14.5	14	21.5		34	17.3	139	26.8	36	34.0	

*A deprivation category could not be assigned to two cases. †χ^2 test of association.

Scotland. The size of this difference (8.7% at 5 years and 10.2% at 10 years) seems to be consistent across the age groups and over time. We confirmed this effect in women diagnosed over a single year in whom a detailed analysis of prognostic and treatment factors identified differences in ER status between deprivation categories. We were able to show, however, that the higher incidence of ER negative tumours in deprived women accounted only in part for the poorer outcome in these women.

The data supporting an effect of deprivation on survival in women with breast cancer are robust. Several other British studies, one national[2] and the others from different cancer registries in England[6–9] reported differences in survival between deprived and affluent women of a similar magnitude to that we describe. The differences in survival by deprivation group remain in the latest registry data available for Scotland.[13] The suggestion that the effect of deprivation on survival varied by age and was larger for women aged over 65[7] is not supported by our results.

Questions have been raised regarding the reliability of cause of death information from death certificates.[18] However, they seem not to constitute a bias here as differences between the affluent and deprived groups are of a similar order of magnitude whether all cause or breast cancer specific mortality is used as the end point. In this analysis we chose to look at breast cancer specific deaths.

Cancer registry data in Scotland are known to be of high quality both in terms of accuracy[19] and completeness.[20] The registry and audit data complement each other and have different strengths. The registry data benefit from large numbers and accuracy; the audit studied fewer women but the additional data on demography, pathology and treatment provided more detailed information. Our audit data are based on the single year 1987. By contrast, the cancer registry data cover the period 1978 to 1987, accumulating a large number of cases to give a more precise estimate of differences in survival. This period was chosen as being prior to the introduction of the national breast screening programme, avoiding problems of lead and length time bias artefactually extending survival times.

Looking at the two datasets, an important issue is whether the difference between survival rates for affluent and deprived women obtained from the single year is representative of the precise estimate derived from the 10 year period. We confirmed this first by showing there was no evidence of an interaction between year of diagnosis and survival difference between the affluent and the deprived groups in the registry data. Secondly, the difference in survival derived from the audit data was extremely close to that from the registry data (9.2% and 8.7% at five years, respectively). We believe, therefore, that the audit is representative and an appropriate dataset in which to examine prognostic and treatment factors in detail.

Having confirmed the effect of deprivation on survival in the audit dataset, one concern is

Table 4 Relative hazard ratios (RHR) with 95% confidence intervals for the groups of deprivation when different factors are entered into separate Cox models, with the affluent group as the baseline for all relative hazard ratios. Breast cancer specific deaths as endpoint

Factors forced into model	*Group*	*RHR for deprivation groups (95% CI) <65*	*p value* for <65 analysis*	*RHR for deprivation groups (95% CI) 65–84†*	*p value* for 65–84 analysis*	*RHR for deprivation groups (95% CI) 0–84†*	*p value* for 0–84 analysis*
Deprivation (Dep) alone			0.0367		0.1117		0.0042
	Intermediate	1.23 (0.99, 1.53)		1.14 (0.88, 1.48)		1.20 (1.01, 1.42)	
	Most Deprived	1.43 (1.08, 1.89)		1.42 (1.02, 1.98)		1.43 (1.16, 1.78)	
Dep + Age group			0.0467		0.0972		0.0058
	Intermediate	1.23 (0.99, 1.52)		1.14 (0.88, 1.49)		1.19 (1.01, 1.41)	
	Most Deprived	1.41 (1.06, 1.87)		1.44 (1.03, 2.01)		1.42 (1.15, 1.76)	
Dep + Age + ER status			0.1272		0.0826		0.0153
	Intermediate	1.18 (0.95, 1.47)		1.16 (0.89, 1.52)		1.17 (0.99, 1.38)	
	Most Deprived	1.33 (1.00, 1.76)		1.46 (1.05, 2.04)		1.37 (1.11, 1.70)	
Dep + Age + ER status + node status			0.3839		0.0401		0.0399
	Intermediate	1.13 (0.91, 1.41)		1.16 (0.89, 1.51)		1.14 (0.96, 1.34)	
	Most Deprived	1.20 (0.91, 1.60)		1.53 (1.10, 2.14)		1.32 (1.07, 1.64)	
Dep + Age + ER status + node status + tumour size			0.4753		0.1315		0.0780
	Intermediate	1.11 (0.90, 1.38)		1.22 (0.94, 1.59)		1.15 (0.98, 1.36)	
	Most Deprived	1.18 (0.89, 1.57)		1.40 (1.00, 1.97)		1.27 (1.03, 1.58)	
Dep + Age + ER status + node status + tumour size + "clinical stage"			0.2213		0.4416		0.0926
	Intermediate	1.21 (0.97, 1.51)		1.10 (0.84, 1.44)		1.18 (1.00, 1.40)	
	Most Deprived	1.18 (0.89, 1.57)		1.25 (0.89, 1.75)		1.23 (0.99, 1.53)	
Dep + Age + ER status + node status + tumour size + "clinical stage" + interaction of node status by tumour size			0.2603		0.4163		0.0977
	Intermediate	1.20 (0.96, 1.50)		1.08 (0.83, 1.42)		1.18 (1.00, 1.40)	
	Most Deprived	1.16 (0.87, 1.54)		1.26 (0.89, 1.77)		1.23 (0.99, 1.53)	

*p values are the Wald statistics for the deprivation factor in the model, conditional on the other factors being present. †A deprivation category could not be assigned to two cases.

KEY POINTS

- There was a 10% survival difference at 10 years between women from affluent and deprived areas.
- No differences were observed in tumour size or nodal status at presentation between the deprivation groups.
- Deprived women were more likely to have oestrogen receptor negative tumours.
- This difference in distribution of oestrogen receptor status by deprivation group explains about a third of the difference in survival between affluent and deprived women.

whether there are biases in evaluating prognostic factors. By their nature, many prognostic factors are available only for surgical cases. A large proportion of the "missing data" in the audit comprises non-surgical/non-metastatic patients and those with metastatic disease at presentation. For the under 65 years age group, these two groups represent about 10% of all cases, whereas in the older age group, this rises to approximately 37%. This is a potentially serious source of bias but our decision to examine results in women under 65 years of age (as well as for all ages), where the effect of deprivation on survival is equally strong, reduces our dependence on these missing data.

In the audit dataset, "clinical stage", tumour size and nodal status were not related to deprivation. Other studies[3–5 7 8] defined extent of disease as localised, regional or distant metastases, while two separate Scottish studies looked at early, locally advanced or metastatic disease[21] and pathological factors.[21 22] Where the distributions of stage with deprivation were examined, three studies showed a slight excess of more advanced disease in the lower socioeconomic groups.[4 7 21] Others, however, found no associations between stage[3] or for pathological factors[22] and deprivation. The inclusion of stage into survival models affected the size of the deprivation effect on survival in some,[4 5 7] but not all studies.[3] In our audit dataset, the only prognostic factor that seemed to be correlated with deprivation was ER status. This varied from 35% of the affluent women under 65 being ER negative to 52% of those who were deprived. These data need to be interpreted with caution; ER data were missing for approximately one third of women, although this did not vary systematically by deprivation category. A previous study from the USA reported a relation between ER negative tumours and low economic or educational levels[23] while a study from the west of Scotland showed no such relation.[22] The latest available data from the Scottish Cancer Registry (1997), which now includes some basic staging and treatment details, support our findings and show that more women with ER negative tumours are observed in the deprived group than expected by chance (unpublished data). The cause of this variation in ER status by deprivation is unclear. It may, however, have important implications as women with ER negative tumours generally have a worse prognosis and should receive different adjuvant treatment compared with those with ER positive tumours.

Two treatment factors also emerged that differed between the affluent and deprived women with non-metastatic disease, although neither of these factors seemed to be important in relation to older women. Firstly, affluent women under 65 years of age were more likely to receive conservation surgery compared with mastectomy. This may reflect in part the higher proportion of deprived women with large (> 4 cm) tumours, although this association was not statistically significant (p = 0.17). However, in terms of survival, breast conservation is no more effective than mastectomy so the differential application of these two types of surgery to affluent and deprived women should have no effect on outcome.[24] The second treatment difference observed in the audit dataset was that affluent women were more likely to receive endocrine therapy. This probably reflects the higher incidence of ER positive tumours in these women. Neither type of surgery nor use of endocrine therapy differed between affluent and deprived women in the separate West of Scotland study of women with early breast cancer aged under 75 years.[25]

As differences in treatment between affluent and deprived women do not seem to account for their differing survival, can it be explained by the differences in ER status we observed? Survival for patients with ER negative tumours is poorer than for those with ER positive disease, differences of around 10% being reported.[26–29] For women under 65 years, our own audit dataset indicates a larger difference in five year survival of 22% (81% and 59% for ER positive and negative patients, respectively). If we assume that ER status specific survival rates are the same for affluent and deprived women, it is possible to calculate the difference in survival between affluent and deprived women that would be expected solely because of the higher proportion of ER positive patients in the affluent group. The higher proportion of ER positive tumours in affluent women (0.65) would equate to a five year survival of 73.3% ($0.65 \times 81 + 0.35 \times 59$). For the deprived women, with a lower incidence of ER positive tumours (0.48), this equates to a five year survival of 69.6% ($0.48 \times 81 + 0.52 \times 59$). This calculation estimates that the difference in survival rates attributable to the differing proportions of ER status would be just 3.7%; if the same calculation is repeated with a "not known" category included, the difference in survival is 2.2% (the five year survival for women with ER status unknown is 65%). These differences are substantially less than the differences in breast cancer specific survival seen in either the audit or registry datasets, suggesting that other factors also account for the poorer survival of deprived women with breast cancer.

This study has confirmed the adverse effect of deprivation on breast cancer specific survival in Scotland, which is equally large in women aged under and over 65 years of age. Deprived women under 65 are more likely than affluent women to have ER negative tumours but the difference in breast cancer specific survival we observed was much greater than could be explained by differences in ER status alone (9.2% and 3.7%, respectively). Likewise, in the audit dataset the age adjusted excess risk of death of 41% in women from deprived areas falls only to 33% with the inclusion of ER status in the multivariate model of survival. It is unlikely, therefore, that variations in the incidence of ER positive tumours are the major reason for survival differences between socioeconomic groups in Scotland. These differences in outcome between the affluent and deprived groups are substantially larger than the known benefit of adjuvant systemic therapy on survival,[30] suggesting factors such as comorbidity, immunological competence and nutrition may be involved. Although Macleod *et al*[25] suggested comorbidity may indeed be important, these areas have received relatively little attention and warrant further investigation.

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1 Kogevinas M, Porta M. *Socioeconomic differences in cancer survival: a review of the evidence*. IARC Scientific Publications. Vol 138. IARC: Lyon, 1997:177–206.
2 Coleman MP, Babb P, Damiecki P, *et al*. *Cancer survival trends in England and Wales 1971–1995: deprivation and NHS region. Series SMPS no 61.* London: The Stationery Office, 1999.
3 Berg JW, Ross R, Latourette HB. Economic status and survival of cancer patients. *Cancer* 1977;**39**:467–77.
4 Karjalainen S, Pukkala E. Social class as a prognostic factor in breast cancer survival. *Cancer* 1990;**66**:819–26.
5 Schrijvers CTM, Coebergh JWW, van der Heijden LH, *et al*. Socioeconomic variation in Cancer survival in the Southeastern Netherlands, 1980–1989. *Cancer* 1995;**75**:2946–53.
6 Yorkshire Cancer Organisation. *Cancer in Yorkshire. Cancer registry report series, 3: breast cancer.* Leeds: YCO, 1995.
7 Schrijvers CTM, Mackenbach JP, Lutz JM, *et al*. Deprivation and survival from breast cancer. *Br J Cancer* 1995;**72**:738–43.
8 Sainsbury R, Haward B, Rider L, *et al*. Influence of clinician workload and patterns of treatment on survival from breast cancer. *Lancet* 1995;**345**:1265–70.
9 Pollock AM, Vickers N. Breast, lung and colorectal cancer incidence and survival in South Thames Region, 1987–1992: the effect of social deprivation. *J Public Health Med* 1997;**19**:288–94.
10 Black RJ, Sharp L, Kendrick SW. *Trends in cancer survival in Scotland 1968–1990* . Edinburgh: ISD, 1993:138.
11 Gordon NH, Crowe JP, Brumberg DJ, *et al*. Socioeconomic factors and race in breast cancer recurrence and survival. *Am J Epidemiol* 1992;**135**:609–18.
12 Twelves CJ, Thomson CS, Gould A, *et al*. Variation in the survival of women with breast cancer in Scotland. *Br J Cancer* 1998;**78**:566–71.
13 Scottish Cancer Intelligence Unit. *Trends in cancer survival in Scotland 1971–1995.* Edinburgh: Information and Statistics Division, 2000.
14 Carstairs V, Morris R. *Deprivation and health in Scotland*. Aberdeen: Aberdeen University Press, 1991.
15 Kendrick S, Clarke J. The Scottish Record Linkage System. *Health Bull (Edinb)* 1993; **51**:72–9
16 Scottish Breast Cancer Focus Group, Scottish Cancer Trials Breast Group, Scottish Cancer Therapy Network. *Scottish Breast Cancer Audit 1987 and 1993*. Edinburgh: Scottish Cancer Therapy Network, 1996.
17 UICC (International Union Against Cancer). *TNM classification of malignant Tumours*. 4th ed. Berlin: Springer-Verlag, 1987.
18 Maudsley G, Williams EMI. Death certification by House Officers and General Practitioners—practice and performance. *J Public Health Med* 1993;**15**:192–201.

19 Brewster D, Crichton J, Muir C. How accurate are Scottish cancer registration data? *Br J Cancer* 1994;**70**:954–9.
20 Brewster D, Crichton J, Harvey JC, *et al*. Completeness of case ascertainment in a Scottish regional cancer registry for the year 1992. *Public Health* 1997;**111**:339–43.
21 Macleod U, Ross S, Gillis C, *et al*. Socio-economic deprivation and stage of disease at presentation in women with breast cancer. *Ann Oncol* 2000;**11**:105–7.
22 Carnon AG, Ssemwogerere A, Lamont DW, *et al*. Relation between socioeconomic deprivation and pathological prognostic factors in women with breast cancer. *BMJ* 1994;**309**:1054–7.
23 Gordon NH. Association of education and income with estrogen receptor status in primary breast cancer. *Am J Epidemiol* 1995;**142**:796–803.
24 Early Breast Cancer Trialists' Collaborative Group. Effects of radiotherapy and surgery in early breast cancer: an overview of the randomised trials. *N Engl J Med* 1995;**333**:1444–55.
25 Macleod U, Ross S, Twelves C, *et al*. Primary and secondary care management of women with early breast cancer from affluent and deprived areas: retrospective review of hospital and general practice records. *BMJ* 2000;**320**:1442–5.
26 Chevallier B, Heintzmann F, Mosseri V, *et al*. Prognostic value of estrogen and progesterone receptors in operable breast cancer. Results of a univariate and multivariate analysis. *Cancer* 1988;**62**:2517–24.
27 Shek LLM, Godolphin W. Model for breast cancer survival: relative prognostic roles of axillary nodal status, TNM stage, estrogen receptor concentration, and tumor necrosis. *Cancer Res* 1988;**48**:5565–9.
28 Crowe JP, Gordon NH, Hubay CA, *et al*. Estrogen receptor determination and long term survival of patients with carcinoma of the breast. *Surg Gynaecol Obstetr* 1991;**173**:273–8.
29 Newman SC, Lees AW, Jenkins HJ. The effect of body mass index and oestrogen receptor level on survival of breast cancer patients. *Int J Epidemiol* 1997;**26**:484–90.
30 Early Breast Cancer Trialists' Collaborative Group. Systemic treatment of early breast cancer by hormonal, cytotoxic or immune therapy. *Lancet* 1992;**339**:1–15, 71–85.