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Socio-economic status and survival from breast cancer for young, Australian, urban women

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Abstract

Objective—To estimate the association between measures of socio-economic status (SES) and breast cancer (BC) survival for young, urban Australian women.

Methods—We used a population-based sample of 1,029 women followed prospectively for a median of 7.9 years. SES was defined by education and area of residence. Hazard ratios (HRs) associated with SES measures were estimated for (i) distant recurrence (DR) and (ii) all-cause mortality as end-points.

Results—HRs for area of residence were not significantly different from unity, with or without adjustment for age at diagnosis and education level. The univariable HR estimate of DR for women with university education compared with women with incomplete high school education was 1.51 (95% CI = 1.08 – 2.13, p = 0.02), which reduced to 1.20 (95% CI = 0.85 – 1.72, p = 0.3) after adjusting for age at diagnosis and area of residence. Adjusting for prognostic factors

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differentially distributed across SES groups did not substantially alter the association between survival and SES.

Conclusions—Among young, urban Australian women there is no association between SES and BC survival.

Implications—This lack of estimates of association may be partly attributed to universal access to adequate breast cancer care in urban areas.

Keywords

Breast cancer; socioeconomic status; Australia; survival

In Australia between 1968 and 2001, breast cancer (BC) mortality declined from 22.5 to 19 per 100,000 women.[1] Korda and Butler[1] suggest that this decline is at least partly attributable to improvements in healthcare, but over the last two decades Australians of higher socio-economic status (SES) have experienced a greater decline in avoidable mortality than those of lower SES, consistent with a disproportionate distribution of the benefits of improved healthcare.[2] This differential decline might have maintained existing SES-related differences in prognosis for many diseases and medical conditions, such as BC. In other Western countries, which have also experienced healthcare related mortality reductions, there is some evidence that lower SES is associated with reduced survival following a BC diagnosis.[3-5]

The reasons for SES-related differences in BC survival might include differences in: tumour characteristics at diagnosis;[6-8] adequacy and type of treatment;[9,10] existence of co-morbid conditions;[11] and lifestyle factors, such as timing of pregnancy.[12] Research conducted in other Western countries has shown that at least some of these factors might partly account for SES differences in BC survival.[3,5]

In Australia, BC incidence has been higher for women with high SES,[13] but BC survival has been lower for women with low SES. During 2000 to 2002, BC incidence for women living in the highest SES areas was 134 per 100,000 women while for those in the lowest SES areas it was 110 per 100,000.[14] Survival following BC diagnosis might also be related to area-based SES. Studies of women living in New South Wales and Western Australia have reported that women residing in lower SES areas had a worse prognosis following BC diagnosis compared with women living in the highest SES areas, with hazard ratio (HR) estimates ranging from 1.26 to 1.45.[15,16] No Australian information is currently available on the relationship between BC survival and individual level SES, the latter measured by, for example, occupation or education. Additionally, only limited research has been conducted on whether established prognostic factors account for any disparity in survival between SES groups in Australia, as has been found in other Western countries.

Our aims were two-fold. First, to determine whether survival of young, urban, Australian women diagnosed with BC between 1991 and 1998 is associated with area-level and individual-level SES. Second, to examine whether any association of BC survival with SES could be attributed to differences related to known prognostic factors such as tumour characteristics, obesity, or timing of pregnancy.

Subjects and methods

Subjects

The Australian Breast Cancer Family Study (ABCFS) is a population-based case-control family study of genetic, environmental and lifestyle factors associated with BC and is the

Australian component of the Breast Cancer Family Registry.[17] It commenced in 1992 and recruited incident cases (women with primary BC) residing in Sydney or Melbourne, Australia via the respective state cancer registries. Reporting to cancer registries is a legislative requirement in Australia. A major focus of the ABCFS was genetic factors, so younger women were over-sampled. Study approval was obtained from the ethics committees of The University of Melbourne and The Cancer Councils of Victoria and New South Wales. All subjects provided written informed consent for participation. Overall participation of cases was 69%. Non-participation was due to attrition by death (2%), refusal by the attending doctor (8%), refusal by the case patient (16%), non-response by the attending doctor (1%), non-response by the case (1%), or inability to locate the case (2%). The recruitment strategy, participation and baseline data collection methods for the study have previously been described.[18]

To be eligible for the current study, women had to be diagnosed with non-metastatic breast cancer before age 60 years, have no history of other invasive cancer (apart from non-melanocytic skin cancer), and data on individual and area-level SES had to be available.

Data collection

Questionnaires

At study entry, participants were administered a questionnaire via face-to-face interview, which addressed education, physical characteristics and history of pregnancy, as previously described.[18] The median time between diagnosis and interview was 10.4 months (inter-quartile range 5.1 to 14 months).

Medical history

Tumour characteristics including size, grade, and number of involved axillary nodes were abstracted from pathology reports by trained research assistants. Five per cent of pathology data record abstractions by each research assistant were checked for accuracy by author KAP who is a Consultant Medical Oncologist. For 30 subjects data was abstracted independently by both research assistants and inter-rater reliability for the data relevant to this validation study was 100%.[19] Information on first distant recurrence and death was also abstracted from medical records. Record of distant recurrence, metastases, or other evidence of cancer recurrence by the treating doctor in the patient medical record was accepted as evidence for distant recurrence. In the vast majority of cases there was confirmatory evidence from diagnostic imaging reports. If date of death was not available from the medical record, information was obtained from cancer registries and death certificates. Variables describing tumour characteristics were converted to ordinal variables representing clinically important categories.

Socio-economic status

Both individual and area-level measures of SES were obtained as these measures may index different factors related to healthcare utilisation.[20] Education, the individual measure of SES, was defined in categories corresponding to the highest level achieved: incomplete high school, complete high school, and university level (Bachelor's degree or higher). Information on occupation was not available. The area-based measure was the Index of Relative Socioeconomic Disadvantage (IRSD), a composite measure developed by the Australian Bureau of Statistics, and based upon 20 variables related to a specific census collection district (CCD) including average family income, education, occupation, and employment.[21] The index has a mean of 1,000, with lower values indicating greater socio-economic disadvantage. The IRSD was assigned to participants using their residential

address at the first contact after their diagnosis, and the IRSD for that area at the closest census date. This index was categorised as quintiles for analysis.

Statistical methods

Associations between SES measures and demographic and prognostic measures were evaluated using Pearson's chi-squared test. Demographic and prognostic factors considered were age at diagnosis in years (<35, 35-39, 40-49, 50-59), number of involved axillary nodes (0, 1-3, ≥4, unknown), tumour size (≤20 mm, >20 mm, unknown), tumour grade (1, 2, 3, unknown), obesity based on body mass index (≤30 kg/m^2, >30, unknown)[22] and time in years to diagnosis from last full-term pregnancy (nulliparous, <2, 2-4.99, ≥5).[23] For age at diagnosis and tumour grade the smallest group was used as the reference category, which could result in an under-estimate of the confidence intervals for associations with these variables. However, given that these categories are still relatively large in the context of the overall sample size this is unlikely to substantially affect results.

Due to the anticipated association between SES and age at diagnosis, associations with demographic and prognostic factors were adjusted for age at diagnosis. This was undertaken for each variable by fitting ordinal logistic regression models in which the SES measure was the dependent variable and the demographic or prognostic factor was the independent variable, with age at diagnosis included as a covariate. The significance of the association between each demographic and prognostic variable and the SES measures was evaluated using the likelihood ratio test.

Cox proportional hazard models were fitted for two endpoints: (i) distant recurrence (DR); (ii) death from any cause. For both endpoints, time was measured from date of diagnosis, with subjects' data left-truncated at date of interview for all-cause mortality. For the analysis of DR, date of DR was used as time of the event of interest. In the DR analysis, for women who died without a known DR the event was assumed to have occurred on the date they died (a plausible assumption given the young age of the cohort). Those alive at the last follow-up date (date of last contact with ABCFS staff or date of last medical follow-up) were censored at date of last contact. For all-cause mortality, date of death was used as the date of event for women who died. Women not known to have died were censored at date of last contact.

Hazard ratios (HR) associated with SES were estimated separately for each SES measure for DR and for death, without correction for other factors. Models adjusting for demographic and prognostic factors were then fitted, and the impact of these factors on the HRs associated with SES measures evaluated. For all models, Schoenfeld residuals and log-minus-log plots were used to assess the proportional hazards assumption. Complete case analyses were conducted, but as women who died during follow-up were more likely to have data missing, models were re-fitted to the total eligible sample with dummy categories specified for missing values to determine whether the pattern of missing data altered results. Our study had approximately 60% power to detect a 1.3-fold gradient in association across extreme quintiles, similar to that observed in previous studies. All statistical analyses were conducted using Stata version 10.1.[24] All tests and p values were two-tailed, with nominal significance identified at $\alpha = 0.05$, as per convention.

Results

A total of 1,132 cases were recruited to the original study. We excluded eight who were diagnosed at age 60 years, 11 with metastatic disease, 17 who had previously had cancer, and 67 without complete SES data, leaving a sample of 1,029 women. For the eligible sample, median age at interview was 41 years (ranging from 23 to 59 years). Median follow-up time was 7.9 years, (range three months to 14.4 years). There were 235 (23%) deaths and

267 diagnosed incidents of distant recurrence (26%); cause of death information was unavailable for only 26 women.

Index of relative socio-economic disadvantage

There was a strong positive association between IRSD and education ($p<0.001$; see Table 1). Adjustmenting for age at diagnosis, there was evidence for a negative association between IRSD and obesity ($p=0.002$), a negative association with tumour size ($p=0.02$), and a positive association with recency of pregnancy ($p=0.03$).

Education level

Education was associated with age at BC diagnosis ($p<0.001$, see Table 2). The majority of women with at least complete high school education were diagnosed before age 40 years, whereas the majority of women with incomplete high school education were diagnosed after age 40 years. There was a negative association between obesity and education ($p=0.01$), which persisted after adjustment for age at diagnosis ($p=0.03$). Education was negatively associated with time from last full-term pregnancy to BC diagnosis ($p<0.001$), even after adjustment for age at diagnosis ($p=0.005$).

Survival

As shown in Table 3, four Cox Proportional Hazards models were fitted to the data for DR. IRSD and education were first modelled individually, without inclusion of other variables (models 1 and 2, respectively). Next, both SES measures, and age at diagnosis, were included (model 3). Finally, tumour characteristics and other prognostic factors were included (model 4). No evidence of departure from the proportional hazards assumption was observed for any variable in any model.

The results from model 1 indicate that IRSD was not a predictor of distant disease-free survival (DDFS) ($p=0.8$), and there were no differences in DDFS by quintile of IRSD. Model 2 results suggest that education level was a predictor of DDFS ($p=0.04$). Women with a university education had a greater risk of DR than those with an incomplete high school education (HR = 1.51, 95% CI = 1.08-2.13, $p=0.02$), while the risk for women with complete high school education was intermediate between the two (HR = 1.38, 95% CI = 1.03-1.85, $p=0.03$).

The results from model 3 demonstrate that adjusting for age at diagnosis attenuates the association between education and DDFS to the extent that there is little difference in prognosis between education levels (results were the same regardless of IRSD inclusion). When known prognostic factors were included in the model the HR estimates did not alter substantially for either IRSD or education (see model 4, Table 3). Results did not differ substantially when cases with missing data were included in analyses, or when all-cause mortality was used as the endpoint (results not shown).

Discussion

This study of women living in Australia's two largest capital cities, Sydney and Melbourne, found no evidence that survival over an average of eight years following diagnosis of BC in the mid-to-late 1990s differed according to SES, as measured by education or area of residence. The HRs for quintiles of IRSD were all close to unity, even after adjustment for age at diagnosis and education. For education level, the crude HR estimates suggested that women with university education faced a greater risk of DR following BC diagnosis (H.R. compared with women with incomplete high school education = 1.51, 95% CI = 1.08 – 2.13). However, after adjusting for age at diagnosis and IRSD the association with education

level was substantially reduced and no longer statistically significant (H.R. = 1.2, 95% CI = 0.85 – 1.72). Adjusting for prognostic factors differentially distributed across SES groups, such as obesity and recency of pregnancy, did not substantially alter the association between survival and either measure of SES.

These results are not fully consistent with previous reports of SES and BC survival in Australia. Yu et al.[16] found that women living in the most disadvantaged areas (lower 20% of IRSD) of New South Wales had 30% greater risk of mortality following BC diagnosis than those living in the highest SES areas (upper 20% of IRSD), even after adjustment for age at diagnosis, year of follow-up, and stage of cancer. Hall et al.[15] also found an association between area of residence in Western Australia and BC survival, after adjusting for age, co-morbidity, marital status, indigenous status, surgical treatment, location and status of hospital, insurance, and urbanicity. These studies had larger sample sizes than ours, being based upon data from entire Australian states drawn from record linkage or a state-wide registries, and followed cases diagnosed in a similar time period for five years. Neither of these studies adjusted for tumour characteristics (beyond stage) or known risk factors such as obesity or pregnancy, which others have found to be associated with survival.[6-8,12,22] On the other hand, a recent report of period survival from Victoria for prevalent cases of breast cancer (unadjusted for prognostic or SES factors) found no statistically significant differences between Melbourne and the rest of the state, nor between the Integrated Cancer Services regions.[25]

ABCFS participants were − by the inclusion criteria − living in the metropolitan areas of Sydney and Melbourne at diagnosis, therefore our study considers the associations across the SES gradient within these cities, not across the state. Previous research has shown no difference in risk of death due to BC across NSW by the Accessibility/Remoteness Index of Australia (ARIA).[26] Jong et al. compared the 83% who live in highly accessible areas with three other much smaller categories of lower accessibility and remoteness, so they had little power to detect urban/rural differences. The distribution of the IRSD in our study was slightly negatively skewed and the participation rate was only 69%, indicating the ABCFS may have under-sampled women from lower SES areas. This is an inherent limitation of studies of this kind as persons with high SES are more likely to participate in voluntary research,[27] especially when risk of disease is associated with SES.

The results presented here suggest that, at least across the metropolitan areas of Sydney and Melbourne in the 1990s, there were no significant differences in survival following BC diagnosis that were related to SES. A plausible explanation is that, in these urban areas, ease of access to healthcare facilities facilitated by both geography and government funding, eradicated the SES differences in BC survival seen in other studies. This issue should be investigated further in studies that recruit participants from both urban and rural areas, collect detailed information on utilisation of healthcare resources, and focus on obtaining equivalent participation across SES.

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Table 1

Associations between demographic/prognostic factors and Index of Relative Socio-economic Disadvantage quintiles.

Characteristic	Quintiles of Index of Relative Socio-economic Disadvantage												χ^2(df) *p*	*p* [a]
	Lowest		Quintile 2		Quintile 3		Quintile 4		Highest		Total			
%	No.	%	No.	%	No.	%	No.	%	No.	%	No.			
Highest level of education														
Incomplete high school	43.2	89	31.1	64	25.7	53	22.3	46	12.2	25	26.9	277		
High school	42.2	87	51.5	106	56.3	116	56.8	117	55.1	113	52.4	539		
University	14.6	30	17.5	36	18.0	37	20.9	43	32.7	67	20.7	213	65.35(8), <0.001	<0.001
Age at diagnosis														
<35 years	21.4	44	22.3	46	17.0	35	14.1	29	12.2	25	17.4	179		
35-39 years	27.7	57	29.6	61	32.5	67	31.1	64	27.3	56	29.6	305		
40-49 years	25.2	52	22.8	47	25.7	53	27.7	57	34.1	70	27.1	279		
50-59 years	25.7	53	25.2	52	24.8	51	27.2	56	26.3	54	25.9	266	16.57(12), 0.17	N/A
Tumour size														
<20 mm	64.6	133	65.0	134	67.5	139	70.4	145	75.1	154	68.5	705		
>20 mm	34.5	71	34.5	71	32.0	66	29.6	61	24.9	51	31.1	320	6.51(4), 0.26	0.02
Unknown	1.0	2	0.5	1	0.5	1	0	0	0	0	0.4	4		
Tumour grade score														
1	14.6	30	11.7	24	14.6	30	13.6	28	16.6	34	14.2	146		
2	32.0	66	33.5	69	32.5	67	42.7	88	39.0	80	36.0	370		
3	46.6	96	51.0	105	47.1	97	40.8	84	40.5	83	45.2	465	10.29(8), 0.24	0.12
Unknown	6.8	14	3.9	8	5.8	12	2.9	6	3.9	8	4.7	48		
Number of involved nodes														
0	54.9	113	55.3	114	54.9	113	48.5	100	60.0	123	54.7	563		
1 to 3	29.1	60	27.7	57	27.2	56	30.6	63	23.9	49	27.7	285		
>4	14.6	30	13.6	28	13.6	28	17.5	36	11.7	24	14.2	146	6.84(8), 0.55	0.84
Unknown	1.5	3	3.4	7	4.4	9	3.4	7	4.4	9	3.4	35		
Obese in year prior to diagnosis														
No	83.5	172	84.5	174	87.4	180	88.3	182	92.7	190	87.3	898		
Yes	14.6	30	15.5	32	12.1	25	10.2	21	6.8	14	11.9	122	9.65(4), 0.05	0.002
Unknown	1.9	4	0	0	0.5	1	1.5	3	0.5	1	0.9	9		

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Characteristic	Quintiles of Index of Relative Socio-economic Disadvantage												χ^2(df) *p*	*p* [a]
	Lowest		Quintile 2		Quintile 3		Quintile 4		Highest		Total			
%	No.	%	No.	%	No.	%	No.	%	No.	%	No.			
Years since last full-term pregnancy														
Nulliparous	28.2	58	23.3	48	25.7	53	14.1	29	25.4	52	23.3	240		
<2 years	6.3	13	6.3	13	5.3	11	8.3	17	5.4	11	6.3	65		
2-4 years	9.2	19	12.6	26	14.6	30	17.5	36	12.7	26	13.3	137	18.62(12), 0.1	0.03
>5 years	56.3	116	57.8	119	54.4	112	60.2	124	56.6	116	57.0	587		

N/A indicates the test was not applicable. The χ^2 test statistic, associated degrees of freedom (df), and p-value (P) are shown for the unadjusted tests. *p*-values for the age-adjusted test as also presented.

Notes:

[a]Adjusted for age at diagnosis. Individuals with missing data were excluded from all tests of association.

Table 2

Associations between demographic/prognostic factors and highest level of education.

Characteristic	Highest level of education achieved								χ^2(df), *p*	*p*
	Incomplete high school		High school		University		Total			
	%	No.	%	No.	%	No.	%	No.		
Age at diagnosis										
<35 years	9.7	27	21.2	114	17.8	38	17.4	179		
35-39 years	20.9	58	31.0	167	37.6	80	29.6	305		
40-49 years	28.5	79	24.7	133	31.5	67	27.1	279		
50-59 years	40.8	113	23.2	125	13.1	28	25.9	266	67.19(6), <0.001	N/A
Tumour size										
<20 mm	70.8	196	66.8	360	70.0	149	68.5	705		
>20 mm	28.9	80	32.7	176	30.0	64	31.1	320	1.43(2), 0.49	0.89
Unknown	0.4	1	0.6	3	0	0	0.4	4		
Tumour grade score										
1	14.4	40	14.1	76	14.1	30	14.2	146		
2	37.5	104	35.4	191	35.2	75	36.0	370		
3	43.0	119	44.9	242	48.8	104	45.2	465	0.99(4), 0.91	0.45
Unknown	5.1	14	5.6	30	1.9	4	4.7	48		
Number of involved nodes										
0	58.1	161	51.6	278	58.2	124	54.7	563		
1 to 3	25.6	71	28.4	153	28.6	61	27.7	285		
>4	13.7	38	15.8	85	10.8	23	14.2	146	5.24(4), 0.26	0.67
Unknown	2.5	7	4.3	23	2.3	5	3.4	35		
Obese in year prior to diagnosis										
No	82.3	228	87.6	472	93.0	198	87.3	898		
Yes	15.5	43	11.9	64	7.0	15	11.9	122	8.82(2), 0.01	0.03
Unknown	2.2	6	0.6	3	0	0	0.9	9		
Years since last pregnancy										
Nulliparous	18.4	51	23.4	126	29.6	63	23.3	240		
<2 years	4.3	12	7.6	41	5.6	12	6.3	65		
2-4 years	6.9	19	13.9	75	20.2	43	13.3	137		

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Characteristic	Highest level of education achieved								χ^2(df), *p*	*p*
	Incomplete high school		High school		University		Total			
	%	No.	%	No.	%	No.	%	No.		
>5 years	70.4	195	55.1	297	44.6	95	57	587	40.91(6), <0.001	0.004

N/A indicates the test was not applicable. The χ^2 test statistic, associated degrees of freedom (df), and *p*-value are shown for the unadjusted tests. *p*-values for the age-adjusted test as also presented.

Note: a) Adjusted for age at diagnosis Individuals with missing data were excluded from all tests of association.

Table 3

Hazard ratio estimates for distal recurrence and death for sequential models.

Characteristics	Model 1			Model 2			Model 3			Model 4		
	HR	**95% CI**	***p***	**HR**	**95% CI**	***p***	**HR**	**95% CI**	***p***	**HR**	**95% CI**	***p***
Index of Relative Socio-economic Disadvantage												
Lowest IRSD	Ref.		0.83§				Ref.		0.81§	Ref.		0.96§
Quintile 2	1.07	0.75, 1.53	0.7				1.03	0.72, 1.48	0.85	1.09	0.75, 1.61	0.6
Quintile 3	1.00	0.70, 1.43	1.0				0.97	0.67, 1.39	0.85	1.00	0.68, 1.48	1.0
Quintile 4	1.08	0.76, 1.54	0.7				1.13	0.79, 1.61	0.52	1.12	0.76, 1.64	0.6
Highest IRSD	0.88	0.60, 1.28	0.5				0.90	0.61, 1.32	0.59	1.00	0.67, 1.49	1.0
Education												
Incomplete High school				Ref.		0.04§	Ref.		0.55§	Ref.		0.3§
High school				1.38	1.03, 1.85	0.03	1.15	0.85, 1.55	0.36	1.19	0.86, 1.65	0.3
University				1.51	1.08, 2.13	0.02	1.20	0.85, 1.72	0.3	1.34	0.92, 1.96	0.1
Age at diagnosis												
<35 years							Ref.		<0.001§	Ref.		<0.01§
35-39 years							1.03	0.77, 1.38	0.9	1.05	0.76, 1.45	0.8
40-49 years							0.56	0.39, 0.79	<0.001	0.71	0.47, 1.08	0.1
50-59 years							0.34	0.23, 0.51	<0.001	0.47	0.28, 0.77	
<0.001												
Tumour size												
<20 mm										Ref.		
>20 mm										1.43	1.10, 1.85	0.01
Tumour grade score												
1										Ref.		<0.01§
2										2.36	1.34, 4.16	
<0.001												
3										2.56	1.46, 4.48	
<0.001												
Number of involved nodes												
0										Ref.		<0.001§

Characteristics	Model 1			Model 2			Model 3			Model 4		
	HR	95% CI	*p*	HR	95% CI	*p*	HR	95% CI	*p*	HR	95% CI	*p*
1 to 3										1.78	1.33, 2.37	
<0.001												
>4										3.18	2.31, 4.38	
<0.001												
Obese in year prior to diagnosis												
No										Ref.		
Yes										1.12	0.78, 1.63	0.5
Years since last pregnancy												
Nulliparous										Ref.		0.09[§]
<2 years										1.56	0.98, 2.48	0.06
2-4 years										1.47	1.01, 2.15	0.05
>5 years										1.07	0.75, 1.51	0.7
Number of cases included in the model			1,029			1,029			1,029		940	

Model 1 includes the Index of Relative Socio-economic Disadvantage (IRSD) as the explanatory variable, without adjustment for any other factors. Model 2 includes highest level of education achieved as the sole explanatory variables. In Model 3, both measures of SES (IRSD and education level) are included as explanatory variables, as well as age at diagnosis. Model 4 includes both SES measures, age at diagnosis, and all other prognostic factors. H.R. denotes the hazard ratio and 95% C.I. indicates the 95% confidence interval for the hazard ratio point estimate.

[§]**indicates the overall significance of ordinal variables.**