Original Article

Socioeconomic Status and Survival After an Invasive Breast Cancer Diagnosis

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BACKGROUND: Women who live in geographic areas with high poverty rates and low levels of education experience poorer survival after a breast cancer diagnosis than women who live in communities with indicators of high socioeconomic status (SES). However, very few studies have examined individual-level SES in relation to breast cancer survival or have assessed the contextual role of community-level SES independent of individual-level SES. **METHODS:** The authors of this report examined both individual-level and community-level SES in relation to breast cancer survival in a population-based cohort of women ages 20 to 69 years who were diagnosed with breast cancer in Wisconsin between 1995 and 2003 (N = 5820). **RESULTS:** Compared with college graduates, women who had no education beyond high school were 1.39 times more likely (95% confidence interval [CI], 1.10-1.76) to die from breast cancer. Women who had household incomes <2.5 times the poverty level were 1.46 times more likely (95% CI, 1.10-1.92) to die from breast cancer than women who had household incomes ≥5 times the poverty level. Adjusting the analysis for use of screening mammography, disease stage at diagnosis, and lifestyle factors eliminated the disparity by income, but the disparity by education persisted (hazard ratio [HR], 1.27; 95% CI, 0.99-1.61). In multilevel analyses, low community-level education was associated with increased breast cancer mortality even after adjusting for individual-level SES (HR, 1.57; 95% CI, 1.09-2.27 for ≥20% vs <10% of adults without a high school degree). **CONCLUSIONS:** The current results indicated that screening and early detection explain some of the disparity according to SES, but further research will be needed to understand the additional ways in which individual-level and community-level education are associated with survival. ***Cancer* 2011;117:1542–51.** © *2010 American Cancer Society.*

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Significant progress has been achieved over the past 30 years in improving survival rates after an invasive breast cancer diagnosis in the United States. Nationally, the 5-year relative survival rate among women who were diagnosed between 1999 and 2005 exceeds 90% compared with a rate of 75% among women who were diagnosed between 1975 and 1977.[1] This improvement probably is the result of advances in the efficacy of breast cancer treatments and the widespread use of screening mammography to detect cancers at an early stage.[2] Early screening both improves treatment effectiveness and makes survival rates appear longer because of lead-time bias and overdiagnosis.[3,4]

Unfortunately, not all women have benefited equally from these advances in breast cancer detection and treatment. Women who live in communities with high poverty rates and low levels of education experience poorer survival rates after a breast cancer diagnosis.[5-11] These disparities according to community-level socioeconomic status (SES) may be caused by several factors, including differences in the use of screening, tumor aggressiveness, lifestyle behaviors and environmental exposures, and access to treatment.[6,12,13] Elucidation of the relative roles of these factors could guide interventions to reduce disparities in survival.

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One primary limitation in the evaluation of the role of socioeconomic factors in breast cancer survival has been a dependence on community-level markers of SES.[14,15] Nearly all studies to date have relied on geography-based (eg, United States Census) measures of SES as a proxy for individual-level SES.[12,13,16] Although both individual-level and community-level SES can influence health,[14,17] very few studies have been able to evaluate both in relation to breast cancer survival.

We examined individual-level and community-level SES in relation to breast cancer survival in a population-based cohort of women who had incident invasive breast cancer diagnosed in Wisconsin during the period from 1995 to 2003. We also examined variation in individual-level screening use, disease stage at diagnosis, and lifestyle factors as potential mediators of a relation between SES and survival.

MATERIALS AND METHODS

We used data on Wisconsin women with breast cancer from 2 population-based, case-control studies of breast cancer, both of which have been described previously.[18,19] The studies were conducted according to protocols approved by the University of Wisconsin Institutional Review Board. All women provided verbal informed consent.

Study Population

Women ages 20 years to 69 years who were residents of Wisconsin and had a first diagnosis of invasive breast cancer during 1995 to 2003 were identified from the mandatory statewide cancer registry. Eligibility was limited to women with listed telephone numbers, driver's licenses verified by self-report (if aged <65 years of age for comparability with controls in the case-control studies), and known dates of diagnosis (from the cancer registry). Of 7471 eligible women, 79% (N = 5865) were interviewed.

Data Collection

On average, telephone interviews were conducted 16.4 months (standard deviation, 6.0 months) after diagnosis. The interview elicited information on SES, reproductive and menstrual history, height and weight, use of hormones, personal and family medical history, mammography screening use, and demographic factors. Socioeconomic data collected included the highest degree or year of school completed, annual household income 1 year before diagnosis, and household size 1 year before diagnosis. The women reported which of the following categories matched their household income: <$15,000, from $15,000 to $29,999, from $30,000 to $49,999, from $50,000 to $99,999, and ≥$100,000. Mammography screening was assessed by asking women to report the number of mammograms they had in the 5 years before their diagnosis.

Community-level socioeconomic data were collected for census tracts from the Year 2000 United States Census.[20] The residential locations of all women were geocoded to census tracts based on home address and zip code using previously described methods.[21,22] Then, each woman was assigned census-tract level data from the 2000 US Census for the percentage of families in poverty and the percentage of the population aged >25 years without a high school diploma.

Information regarding each woman's tumor characteristics was obtained from the Wisconsin Cancer Registry and included date of diagnosis, stage at diagnosis, and tumor histology. Tumor histology was defined using the International Classification of Diseases for Oncology[23] codes as either lobular (code 8520) or nonlobular (all other codes).

Vital status was determined through December 31, 2006, using automated searches of the National Death Index.[24] The underlying cause of death on the death certificate was assigned according to the International Classification of Diseases, Ninth Revision (ICD-9) (through 1998) and the 10th Revision (ICD-10) (from 1999 to 2006).[25,26] Deaths from breast cancer (ICD-9 code 174 and ICD-10 code C50) and from all causes were evaluated.

Statistical Analyses

The residential location of 45 women (0.8%) was unknown; thus, census-level SES information could not be ascertained for those women, and they were excluded from all analyses, leaving a total of 5820 women available for analysis. Household income and household size were used to determine an income-to-poverty ratio based on federal poverty guidelines. The midpoint of each income category was taken as the household income value. For the lowest and highest categories, $15,000 and $100,000 were used as the household income values, respectively. The income-to-poverty ratio was calculated by dividing the household income value by the appropriate poverty-level income based on household size according to the Year 2000 United States poverty guidelines.[27]

The inclusion of questions on household income and household size varied during the course of the studies, and some women refused to answer these questions when

they were included. Consequently, 2596 women were missing data on income-to-poverty ratio. Of these, 1642 women were not asked about their income, and 954 women chose not to answer. Education information was missing for 68 women. Many covariates were missing data for a small fraction of women (see Table 1). Multiple imputation was used to impute missing data for individual-level income, education, and all covariates listed in Table 1. Ten imputations were conducted using the Markov Chain Monte Carlo method,[28] which was implemented in SAS statistical software (version 9; SAS Institute, Inc., Cary, NC). The imputation model contained all variables listed in Tables 1 and 2. For subsequent analyses, each model was fit separately to the 10 imputed datasets, and their results were combined for statistical inferences using the methods of Rubin.[29]

Multivariate logistic regression models were fit to estimate the odds ratios (OR) and 95% confidence intervals (CIs) describing the association between SES factors and both mammography screening use and stage at diagnosis. Each model was adjusted for patient age and calendar year at diagnosis. Cox proportional-hazards models were used to estimate the hazard ratios (HR) and 95% CIs associated with SES factors for breast cancer and all-cause mortality. To examine potential mediators of the association between SES and mortality, variables that represented screening use, tumor characteristics, and lifestyle factors were added sequentially to the models (according to the parameters listed in Table 1). In addition, a model that contained both individual-level and community-level SES variables was constructed to examine the independent effects of these factors. To account for the clustering of individuals within communities, a robust sandwich estimate for the covariance matrix was used in the Cox regression model with the census tract clustering variable specified.[30] For all analyses, survival was calculated as the number of days from diagnosis to either death or the date of last follow-up, December 31, 2006, when all remaining women were censored. In analyses of breast cancer mortality, deaths from other causes were censored at the time of death. Women who were diagnosed with breast cancer and died before they could be interviewed could not be included in the study; therefore, all models were adjusted for this left truncation of survival times.[31]

RESULTS

On average, the 5820 study participants were followed for 7.2 years (standard deviation, 2.1 years) from the date of their diagnosis. There were 690 total deaths, including 469 deaths (68%) from breast cancer. Characteristics of the study cohort are listed in Table 1. Approximately 67% of the cancers were diagnosed at a local stage. Women with less education were more likely to be older, postmenopausal, obese, and current smokers at the time of diagnosis and were less likely to report annual screening mammograms before their diagnosis or to have used postmenopausal hormones.

There was a high degree of association between each of the SES variables. Table 2 displays the distribution of each SES variable stratified by individual-level education. Women with a college degree were much more likely than those without a degree to have a high income-to-poverty ratio and to live in an area in which there was low percentage of adults without a high school degree and a low percentage of families in poverty.

After adjusting for age and year of diagnosis, low levels of each SES indicator were associated with a reduced likelihood of having had annual screening mammograms before diagnosis (Table 3). For instance, women with an income-to-poverty ratio <2.5 were less than half as likely to have had annual mammograms as women with an income-to-poverty ratio ≥ 5 (OR, 0.49; 95% CI, 0.39-0.61). There was no association between individual-level education and disease stage at diagnosis. The likelihood of having distant-stage cancer at diagnosis was elevated among women who had a low income-to-poverty ratio and low levels of both community-level SES indicators (Table 3).

In the models that were adjusted for patient age and year of diagnosis, breast cancer-specific mortality was elevated at low levels of each SES indicator (Table 4, Model 1). Community-level education had the strongest association: Women who lived areas in which $\geq 20\%$ of adults did not have a high school education were 1.61 times more likely (95% CI, 1.21-2.15) to die from their breast cancer than women who lived in areas in which $<10\%$ of adults did not have a high school education. After adjusting for disease stage at diagnosis, tumor histology, and mammography use, only individual-level and community-level education retained an association with breast cancer mortality (Table 4, Model 2). Further adjustment for variation in lifestyle factors had a minor attenuating effect on these associations (Table 4, Model 3). In the full model that contained both individual-level and community-level SES factors (Table 4, Model 4), community-level education was associated with breast cancer mortality (HR, 1.57; 95% CI, 1.09-2.27).

Table 1. Characteristics of Women With Breast Cancer: Wisconsin, 1995-2003

Characteristic	No. of Women (%)		
	All Women, N=5820[a]	No College, N=2728	Some College/College Degree, N=3024
Age at diagnosis, y			
20-34	147 (2.5)	49 (1.8)	96 (3.2)
35-44	889 (15.3)	336 (12.3)	547 (18.1)
45-54	1897 (32.6)	737 (27)	1145 (37.9)
55-64	2037 (35)	1057 (38.7)	951 (31.4)
≥65	850 (14.6)	549 (20.1)	285 (9.4)
Menopausal status[b]			
Premenopausal	2134 (36.7)	810 (29.7)	1322 (43.7)
Postmenopausal	3252 (55.9)	1775 (65.1)	1444 (47.8)
Unknown	434 (7.5)	143 (5.2)	258 (8.5)
Family history of breast cancer[c]			
No	4419 (75.9)	2062 (75.6)	2354 (77.8)
Yes	1217 (20.9)	611 (22.4)	606 (20)
Unknown	184 (3.2)	55 (2)	64 (2.1)
Recent mammography use[d]			
None	388 (10)	243 (12.1)	145 (8)
<1/y	742 (19.1)	402 (20)	340 (18.7)
Annual	2685 (68.9)	1358 (67.4)	1327 (72.8)
Unknown	80 (2.1)	11 (0.6)	11 (0.6)
History of postmenopausal hormone use[b,e]			
Never	1292 (39.7)	848 (47.8)	442 (30.6)
Ever	1925 (59.2)	925 (52.1)	999 (69.2)
Unknown	35 (1.1)	2 (0.1)	3 (0.2)
Body mass index, kg/m^2[b]			
<18.5	77 (1.3)	33 (1.2)	44 (1.5)
18.5-24.9	2537 (43.6)	1055 (38.7)	1471 (48.6)
25.0-29.9	1838 (31.6)	912 (33.4)	915 (30.3)
≥30.0	1282 (22)	695 (25.5)	579 (19.1)
Unknown	86 (1.5)	33 (1.2)	15 (0.5)
Smoking history[b]			
Never	2956 (50.8)	1295 (47.5)	1651 (54.6)
Former	1714 (29.5)	809 (29.7)	901 (29.8)
Current	1083 (18.6)	614 (22.5)	466 (15.4)
Unknown	67 (1.2)	10 (0.4)	6 (0.2)
Disease stage at diagnosis			
Localized	3911 (67.2)	1825 (66.9)	2041 (67.5)
Regional	1678 (28.8)	780 (28.6)	881 (29.1)
Distant	107 (1.8)	50 (1.8)	54 (1.8)
Unknown	124 (2.1)	73 (2.7)	48 (1.6)
Histologic type			
Lobular	554 (9.5)	270 (9.9)	278 (9.2)
Nonlobular	5266 (90.5)	2458 (90.1)	2746 (90.8)

[a] This group included 68 women who were missing information on education.
[b] Menopausal status, recent mammography use, history of postmenopausal hormone use, body mass index, and smoking history refer to characteristics at 1 year prior to diagnosis.
[c] Women reported their current knowledge of a family history of breast cancer at the time of the interview.
[d] Mammography use during the 5 years before the date of diagnosis was recorded; the analysis was limited to women aged ≥50 years.
[e] This analysis was limited to postmenopausal women.

Table 2. Socioeconomic Status Among Women With Breast Cancer: Wisconsin, 1995-2003

Characteristic	No. of Women (%)				
	All Women, N=5820[a]	No High School Degree, N=277	High School Degree, N=2451	Some College, N=1497	College Degree, N=1527
Individual-level variables					
Income-to-poverty ratio					
≥5.0	1079 (18.5)	13 (4.7)	292 (11.9)	299 (20)	475 (31.1)
2.5-4.9	1312 (22.5)	41 (14.8)	566 (23.1)	368 (24.6)	337 (22.1)
<2.5	833 (14.3)	71 (25.6)	458 (18.7)	206 (13.8)	98 (6.4)
Unknown	2596 (44.6)	152 (54.9)	1135 (46.3)	624 (41.7)	617 (40.4)
Community-level variables					
Percentage without a high-school diploma					
0-9.9	1820 (31.3)	33 (11.9)	580 (23.7)	483 (32.3)	710 (46.5)
10.0-19.9	3224 (55.4)	166 (59.9)	1512 (61.7)	827 (55.2)	681 (44.6)
≥20	776 (13.3)	78 (28.2)	359 (14.7)	187 (12.5)	136 (8.9)
Percentage in poverty					
0-4.9	2862 (49.2)	99 (35.7)	1116 (45.5)	782 (52.2)	833 (54.6)
5-9.9	2096 (36)	99 (35.7)	983 (40.1)	503 (33.6)	490 (32.1)
≥10	862 (14.8)	79 (28.5)	352 (14.4)	212 (14.2)	204 (13.4)

[a] This group included 68 women who were missing information on education.

Table 3. The Association Between Socioeconomic Status and Mammographic Screening Before Diagnosis and Disease Stage at Diagnosis Among 5820 Women With Breast Cancer: Wisconsin, 1995-2003

Characteristic	OR (95% CI)			
	Annual Screening Mammogram[a,b]	Local Stage at Diagnosis[b]	Regional Stage at Diagnosis[b]	Distant Stage at Diagnosis[b]
Individual-level variables				
Education				
College degree	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Some college	0.79 (0.64-0.98)[c]	1.05 (0.90-1.23)	0.95 (0.81-1.11)	0.99 (0.58-1.68)
No college[d]	0.66 (0.55-0.79)[c]	0.97 (0.84-1.12)	1.03 (0.89-1.19)	1.03 (0.64-1.66)
Income-to-poverty ratio				
≥5.0	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
2.5-5.0	0.72 (0.59-0.88)[c]	0.86 (0.74-1.01)	1.12 (0.95-1.31)	1.73 (0.86-3.48)
<2.5	0.49 (0.39-0.61)[c]	0.85 (0.70-1.03)	1.11 (0.92-1.35)	2.06 (1.03-4.11)[c]
Community-level variables				
Percentage without a high school diploma				
0-9.9	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
10.0-19.9	0.80 (0.68-0.93)[c]	0.97 (0.86-1.11)	1.00 (0.88-1.14)	1.41 (0.88-2.25)
≥20	0.77 (0.61-0.97)[c]	0.95 (0.79-1.14)	0.99 (0.82-1.20)	2.00 (1.11-3.60)[c]
Percentage in poverty				
0-4.9	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
5-9.9	0.85 (0.73-0.99)[c]	0.99 (0.87-1.12)	1.02 (0.90-1.15)	0.94 (0.61-1.46)
≥10	0.75 (0.61-0.92)[c]	0.89 (0.76-1.05)	1.08 (0.91-1.27)	1.53 (0.93-2.53)

OR indicates odds ratio; CI, confidence interval.
[a] This analysis was limited to women aged ≥50 years.
[b] This analysis was adjusted for age and year of diagnosis.
[c] Estimates are statistically significant ($P < .05$).
[d] This analysis included 277 women without a high school diploma and 2451 women with a high school diploma.

Table 4. The Association Between Socioeconomic Status and Breast Cancer Mortality After a Breast Cancer Diagnosis Among 5820 Women With Breast Cancer: Wisconsin, 1995-2003

	HR (95% CI)			
Characteristic	Model 1[a]	Model 2[b]	Model 3[c]	Model 4[d]
Individual-level variables				
Education				
College degree	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Some college	1.28 (0.99-1.67)	1.24 (0.95-1.63)	1.20 (0.91-1.57)	1.15 (0.88-1.51)
No college	1.39 (1.10-1.76)[e]	1.35 (1.06-1.71)[e]	1.27 (0.99-1.61)	1.20 (0.94-1.55)
Income-to-poverty ratio				
≥5.0	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
2.5-5.0	1.14 (0.83-1.55)	0.97 (0.70-1.34)	0.95 (0.68-1.32)	0.90 (0.64-1.25)
<2.5	1.46 (1.10-1.92)[e]	1.14 (0.84-1.55)	1.09 (0.79-1.49)	0.99 (0.71-1.38)
Community-level variables				
Percentage without a high school diploma				
0-9.9	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
10-19.9	1.37 (1.10-1.70)[e]	1.32 (1.06-1.64)[e]	1.29 (1.04-1.87)[e]	1.40 (1.09-1.78)[e]
≥20	1.61 (1.21-2.15)[e]	1.45 (1.09-1.93)[e]	1.40 (1.04-1.87)[e]	1.57 (1.09-2.27)[e]
Percentage in poverty				
0-4.9	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
5-9.9	0.97 (0.79-1.19)	0.94 (0.76-1.15)	0.91 (0.74-1.12)	0.78 (0.62-0.98)[e]
≥10	1.25 (0.98-1.61)	1.09 (0.85-1.41)	1.06 (0.83-1.37)	0.86 (0.63-1.19)

HR indicates hazard ratio; CI, confidence interval; Ref, reference category.
[a] This model was adjusted for age and year of diagnosis.
[b] This model was adjusted for age, year of diagnosis, histologic type, stage at diagnosis, and mammography use.
[c] This model was adjusted for age, year of diagnosis, histologic type, stage at diagnosis, mammography use, smoking history, family history of breast cancer, body mass index, and postmenopausal hormone use.
[d] This model was adjusted for age, year of diagnosis, histologic type, stage at diagnosis, mammography use, smoking history, family history of breast cancer, body mass index, postmenopausal hormone use, and all socioeconomic variables.
[e] Estimates are statistically significant ($P < .05$).

The association between SES and all-cause mortality largely mirrored that observed for breast cancer mortality (data not shown). In the models that were adjusted only for age and year of diagnosis, all-cause mortality was elevated at low levels of each SES indicator. In the final model that included all SES variables, only community-level education was associated with all-cause mortality (HR, 1.42; 95% CI, 1.05-1.92) for ≥20% vs <10% of adults without a high school degree.

DISCUSSION

Few studies have been able to examine both individual-level and community-level SES in relation to breast cancer survival. We observed that survival rates among women who were diagnosed with breast cancer were lower for those who had less education, reported less income, or lived in areas with low community-level education or income. These lower survival rates were explained in part by lower use of screening mammography and a higher likelihood of being diagnosed with distant-stage breast cancer. Adjustment for these factors substantially attenuated, but did not eliminate, the association between SES and breast cancer survival. These results suggest that socioeconomic disparities in breast cancer survival could be reduced substantially by improving early detection among women of low SES. However, independent of screening and early detection, survival rates were lower among women who had less education and among those who lived in communities with lower education.

Previous studies of breast cancer survival in relation to SES in the United States have focused almost exclusively on community-level factors because of their ready availability in many datasets.[5-11] A recent study examined disparities in breast cancer survival among >100,000 women with breast cancer in the National Cancer Institute's Surveillance, Epidemiology, and End Results Program.[7] A composite community-level SES variable was created from the percentage of adults with <12 years of education and the percentages of families that were living below the federal poverty line in the county. Women in

the lowest SES quartile were 1.19 times more likely (95% CI, 1.13-1.26 times more likely) to die from breast cancer than women in the highest SES group. Women living in low SES counties also were more likely to have advanced-stage disease and were less likely to have received radiation or surgery during their first course treatment. After adjusting for these differences, the association between SES and breast cancer survival was greatly attenuated (HR, 1.08; 95% CI, 1.03-1.14). Similar results were observed in the Patterns of Care Study by the National Program of Cancer Registries.[6] Again, the lower survival rate among women who lived in low SES areas (mortality HR, 1.59) was attenuated substantially after adjustment for disease stage and treatment (HR, 1.16).

Women in our study who had college degrees were more likely to live in highly educated communities compared with women who never attended college. However, there is substantial evidence that community-level SES variables do not serve as simple proxies for individual-level SES.[14,32] Rather, community-level socioeconomic context can affect health through independent pathways related to the physical, social, and service environments of the community.[14,17] The few studies that have examined individual-level SES in relation to breast cancer survival have focused on economic indicators of access to health care.[33-36] In a clinic-based study, Franzini et al[36] used an "ability-to-pay" scale (reflecting income, the number of dependents, and insurance coverage) as an SES indicator and observed that all-cause mortality among women with breast cancer was 1.69 times greater (95% CI, 1.15-2.48 times greater) in women who ranked lowest in SES compared with those ranked highest, even after adjusting for disease stage at diagnosis, treatment, and tumor histology. In a population-based study of women who were diagnosed with breast cancer in New Jersey, Ayanian et al[33] observed that uninsured women and those who were covered by Medicare were more likely to be diagnosed with distant-stage disease than women who had private insurance. Analyses adjusted for stage indicated that the uninsured and Medicaid women with breast cancer experienced a 40% to 50% increased rate of death compared with privately insured women. Similar results have been reported in studies of women who were diagnosed with breast cancer in Michigan.[34,35]

SES can influence breast cancer survival through several mechanisms, as indicated in the review by Cross et al.[13] Women with low SES may develop more aggressive breast cancers, may be screened less intensively for early detection, may be exposed to lifestyle or environmental factors that accelerate tumor progression, or may receive inadequate treatment. Elucidation of the primary mechanisms by which SES influences breast cancer survival may provide targets for interventions to reduce these disparities. We used a model-building technique in which groups of variables were added sequentially in an attempt to distinguish which of these mechanisms may be most relevant to the socioeconomic disparities in breast cancer survival observed in our cohort.

In the basic model, which was adjusted only for patient age and year of diagnosis, there were marked differences in breast cancer survival according to each indicator of SES. Numerous studies have demonstrated that women with low income or education levels are less likely to receive regular screening mammography.[37-40] In large part because of this deficit in screening, women with low education and income levels also are more likely to be diagnosed with late-stage disease.[41-43] These patterns also were observed in our study sample. Adjustment for mammography use and disease stage at diagnosis dramatically attenuated the disparities associated with individual-level and community-level income. These results are consistent with the hypothesis that women with lower household income are experiencing lower breast cancer survival because they do not receive regular screening mammograms and, thus, are diagnosed with later stage disease. Similarly, women who live in high poverty areas may have less access to mammography facilities. Adjustment for screening also may capture variation in other unknown factors that are associated with participation in screening. Women who participate in mammography or other cancer screening programs generally may be healthier or may differ in other important ways from women who do not participate. For instance, women who volunteered for participation in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial had all-cause and breast cancer-specific mortality rates that were 62% and 72% lower, respectively, than the general population.[44] Thus, some of the improved survival associated with screening in an observational study may be attributable not to screening but to other factors.[45] In contrast to the results regarding income, the relation between individual-level and community-level education largely remained elevated even after adjusting for screening use and disease stage at diagnosis.

Health-related behaviors, including smoking and obesity, vary according to SES[37,46] and may influence breast cancer survival.[47] We observed that women who had less education were more likely to be obese and to be

current smokers, and they also were less likely to have used postmenopausal hormones. At least 2 studies have reported that a history of postmenopausal hormone use is associated with better prognosis after a breast cancer diagnosis.[48,49] However, further adjustment in our models for such lifestyle factors had only a modest effect on the HRs, and a statistically significant association between education and breast cancer survival persisted.

The differences we observed in education and income reinforce the idea that education and income, although both are measures of SES, are separate constructs and cannot be used interchangeably.[14] Although individual-level education and income were correlated in our study, education levels varied substantially across all income groups. In addition, whereas both education and income may be associated with economic resources, education also can reflect noneconomic social characteristics that influence health, such as health-related knowledge, problem-solving skills, and influence over one's life.[14] It is noteworthy that, in the current study, community-level education was associated strongly with breast cancer survival even after adjusting for individual-level education in the multilevel model.

A substantial portion of the decline in breast cancer mortality has been attributed to the increased use of adjuvant systemic therapy.[2,50] Education may play a pivotal role in access and adherence to adjuvant treatment regimens.[6,12,13] Unfortunately, we had limited data on treatment within this cohort and, thus, could not examine the role of treatment in mediating the observed socioeconomic disparities in breast cancer survival. Our study has other limitations that also should be considered. The study sample was 95% non-Hispanic white; thus, we had no ability to examine the potential interactions between SES and race. Women with low SES may be more likely to have tumors that are more aggressive and less responsive to treatment.[16] Breast cancers that do not express the estrogen receptor (ER), progesterone receptor (PR), or human epidermal growth factor receptor 2 (HER2) are not amenable to endocrine therapy; and women who have these "triple-negative" breast cancers experience poorer survival than women who have cancers that express either ER, PR, or HER2.[51] Even after adjusting for disease stage and tumor grade, Bauer et al[51] observed that women who lived in low SES areas were 12% more likely (95% CI, 1%-24%) to have triple-negative breast cancer than women who lived in high SES areas. Although we observed little difference in tumor histology (lobular vs nonlobular) according to education, data on the expression of these tumor biomarkers were not available for our study participants and could not be addressed in this analysis.

Data on household income were missing for a large portion of our sample (45%). Many women simply were not asked about household income, whereas a substantial number who were asked refused to answer. Those who refused to answer were more likely to be less educated and varied according to other observed variables. In analyses that were limited to women who reported household income ($N = 3224$), we also observed elevated breast cancer mortality (HR, 1.52; 95% CI, 1.07-2.17 for an income-to-poverty ratio <2.5 vs ≥ 5.0). The exclusion of women with missing data not only can reduce precision but also can lead to bias because of the association between missing data and other covariates.[52] Thus, we used multiple imputation to impute missing data, such that all the data could be used while accounting for the uncertainty in the missing data.

Finally, we acknowledge the challenges in measuring SES at either the individual or community level.[14] Education and income are crude measures of SES that fail to capture variation in prestige and quality of education and accumulated wealth. With assessment at only 1 point in time, we also failed to capture variation in SES at earlier life stages. This study also had several important strengths, including a large population-based sample, a high participation rate, substantial duration of follow-up, and detailed screening history and lifestyle information.

In summary, Wisconsin women with low SES and those living in low SES communities experienced an elevated mortality rate after a breast cancer diagnosis. Lower use of screening mammography and late stage at diagnosis accounted for a substantial fraction of these disparities. Although improving access to screening and early detection should reduce socioeconomic disparities in breast cancer survival, further research will be necessary to understand the additional mechanisms through which education affects this important health outcome. The current results also suggest that community-level education is associated with breast cancer survival independent of individual-level SES. Intervention strategies that target communities with low education levels should be evaluated for their potential to improve outcomes for women who are diagnosed with breast cancer.

CONFLICT OF INTEREST DISCLOSURES

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REFERENCES

1. Horner MJ, Ries LAG, Krapcho M, et al. SEER Cancer Statistics Review, 1975-2006. Bethesda, MD: National Cancer Institute; 2008. http://seer.cancer.gov/csr/1975_2006/ based on November 2008 SEER data submission, posted to the SEER website, 2009. Accessed on October 13, 2010.
2. Berry DA, Cronin KA, Plevritis SK, et al. Effect of screening and adjuvant therapy on mortality from breast cancer. *N Engl J Med.* 2005;353:1784-1792.
3. Shwartz M. Estimates of lead time and length bias in a breast cancer screening program. *Cancer.* 1980;46:844-851.
4. Jemal A, Clegg LX, Ward E, et al. Annual report to the nation on the status of cancer, 1975-2001, with a special feature regarding survival. *Cancer*. 2004;101:3-27.
5. Harper S, Lynch J, Meersman SC, Breen N, Davis WW, Reichman MC. Trends in area-socioeconomic and race-ethnic disparities in breast cancer incidence, stage at diagnosis, screening, mortality, and survival among women ages 50 years and over (1987-2005). *Cancer Epidemiol Biomarkers Prev.* 2009;18:121-131.
6. Byers TE, Wolf HJ, Bauer KR, et al. The impact of socioeconomic status on survival after cancer in the United States: findings from the National Program of Cancer Registries Patterns of Care Study. *Cancer.* 2008;113:582-591.
7. Yu XQ. Socioeconomic disparities in breast cancer survival: relation to stage at diagnosis, treatment and race [serial online]. *BMC Cancer*. 2009;9:364.
8. Gordon NH, Crowe JP, Brumberg DJ, Berger NA. Socioeconomic factors and race in breast cancer recurrence and survival. *Am J Epidemiol.* 1992;135:609-618.
9. Bassett MT, Krieger N. Social class and black-white differences in breast cancer survival. *Am J Public Health.* 1986;76:1400-1403.
10. Gorey KM, Luginaah IN, Holowaty EJ, Fung KY, Hamm C. Breast cancer survival in Ontario and California, 1998-2006: socioeconomic inequity remains much greater in the United States. *Ann Epidemiol.* 2009;19:121-124.
11. Greenwald HP, Polissar NL, Dayal HH. Race, socioeconomic status and survival in 3 female cancers. *Ethn Health.* 1996;1:65-75.
12. Bigby J, Holmes MD. Disparities across the breast cancer continuum. *Cancer Causes Control.* 2005;16:35-44.
13. Cross CK, Harris J, Recht A. Race, socioeconomic status, and breast carcinoma in the US: what have we learned from clinical studies. *Cancer.* 2002;95:1988-1999.
14. Braveman PA, Cubbin C, Egerter S, et al. Socioeconomic status in health research: 1 size does not fit all. *JAMA.* 2005;294:2879-2888.
15. Baquet CR, Commiskey P. Socioeconomic factors and breast carcinoma in multicultural women. *Cancer.* 2000; 88(5 suppl):1256-1264.
16. Vona-Davis L, Rose DP. The influence of socioeconomic disparities on breast cancer tumor biology and prognosis: a review. *J Womens Health (Larchmt).* 2009;18:883-893.
17. Robert SA. Socioeconomic position and health: the independent contribution of community socioeconomic context. *Annu Rev Sociol.* 1999;25:489-516.
18. Sprague BL, Trentham-Dietz A, Newcomb PA, Titus-Ernstoff L, Hampton JM, Egan KM. Lifetime recreational and occupational physical activity and risk of in situ and invasive breast cancer. *Cancer Epidemiol Biomarkers Prev.* 2007;16: 236-243.
19. Nelson SE, Gould MN, Hampton JM, Trentham-Dietz A. A case-control study of the HER2 Ile655Val polymorphism in relation to risk of invasive breast cancer. *Breast Cancer Res.* 2005;7:R357-R364.
20. US Census Bureau. 2000 Census of Population and Housing, Summary File 3: Washington, DC: US Census Bureau; 2002. http://www.census.gov/census2000/sumfile3.html. Accessed on October 13, 2010.
21. McElroy JA, Remington PL, Trentham-Dietz A, Robert SA, Newcomb PA. Geocoding addresses from a large population-based study: lessons learned. *Epidemiology.* 2003;14:399-407.
22. Robert SA, Strombom I, Trentham-Dietz A, et al. Socioeconomic risk factors for breast cancer: distinguishing individual- and community-level effects. *Epidemiology.* 2004;15:442-450.
23. Fritz A, Percy C, Jack A, et al. International Classification of Diseases for Oncology, 3rd Edition., Geneva, Switzerland: World Health Organization; 2000.
24. Calle EE, Terrell DD. Utility of the National Death Index for ascertainment of mortality among cancer prevention study II participants. *Am J Epidemiol.* 1993;137:235-241.
25. World Health Organization. International Classification of Diseases, 9th Revision (ICD-9). Geneva, Switzerland: World Health Organization; 1977.
26. World Health Organization. International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10). Geneva, Switzerland: World Health Organization; 1994.
27. United States Department of Health and Human Services, Office of the Secretary. Annual update of the HHS Poverty Guidelines. *Fed Reg*. 2000;65:7555-7557.
28. Schafer JL. Analysis of incomplete multivariate data. New York: Chapman and Hall; 1997.
29. Rubin DB. Multiple Imputation for Nonresponse in Surveys. New York: John Wiley & Sons; 1987.
30. Lin DY, Wei LJ. The robust inference for the proportional hazards model. *J Am Stat Assoc.* 1989;84:1074-1078.
31. Klein JP, Moeschberger ML. Survival Analysis: Techniques for Censored and Truncated Data. New York: Springer; 1997.
32. Geronimus AT, Bound J. Use of census-based aggregate variables to proxy for socioeconomic group: evidence from national samples. *Am J Epidemiol.* 1998;148:475-486.
33. Ayanian JZ, Kohler BA, Abe T, Epstein AM. The relation between health insurance coverage and clinical outcomes among women with breast cancer. *N Engl J Med.* 1993;329: 326-331.
34. Bradley CJ, Given CW, Roberts C. Disparities in cancer diagnosis and survival. *Cancer.* 2001;91:178-188.
35. Bradley CJ, Given CW, Roberts C. Race, socioeconomic status, and breast cancer treatment and survival. *J Natl Cancer Inst.* 2002;94:490-496.
36. Franzini L, Williams AF, Franklin J, Singletary SE, Theriault RL. Effects of race and socioeconomic status on survival of 1332 black, Hispanic, and white women with breast cancer. *Ann Surg Oncol.* 1997;4:111-118.

37. National Center for Health Statistics. Health, United States, 2008 with Chartbook, 2008. Hyattsville, Md: National Center for Health Statistics; 2008.
38. Katz SJ, Zemencuk JK, Hofer TP. Breast cancer screening in the United States and Canada, 1994: socioeconomic gradients persist. *Am J Public Health.* 2000;90:799-803.
39. Swan J, Breen N, Coates RJ, Rimer BK, Lee NC. Progress in cancer screening practices in the United States: results from the 2000 National Health Interview Survey. *Cancer.* 2003;97:1528-1540.
40. Dailey AB, Kasl SV, Holford TR, Calvocoressi L, Jones BA. Neighborhood-level socioeconomic predictors of nonadherence to mammography screening guidelines. *Cancer Epidemiol Biomarkers Prev.* 2007;16:2293-2303.
41. Clegg LX, Reichman ME, Miller BA, et al. Impact of socioeconomic status on cancer incidence and stage at diagnosis: selected findings from the Surveillance, Epidemiology, and End Results National Longitudinal Mortality Study. *Cancer Causes Control.* 2009;20:417-435.
42. Hahn KM, Bondy ML, Selvan M, et al. Factors associated with advanced disease stage at diagnosis in a population-based study of patients with newly diagnosed breast cancer. *Am J Epidemiol.* 2007;166:1035-1044.
43. Lannin DR, Mathews HF, Mitchell J, Swanson MS, Swanson FH, Edwards MS. Influence of socioeconomic and cultural factors on racial differences in late-stage presentation of breast cancer. *JAMA.* 1998;279:1801-1807.
44. Pinsky PF, Miller A, Kramer BS, et al. Evidence of a healthy volunteer effect in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial. *Am J Epidemiol.* 2007;165:874-881.
45. Moss SM, Summerley ME, Thomas BT, Ellman R, Chamberlain JO. A case-control evaluation of the effect of breast cancer screening in the United Kingdom trial of early detection of breast cancer. *J Epidemiol Commun Health.* 1992;46:362-364.
46. Mokdad AH, Ford ES, Bowman BA, et al. Prevalence of obesity, diabetes, and obesity-related health risk factors, 2001. *JAMA.* 2003;289:76-79.
47. Soerjomataram I, Louwman MW, Ribot JG, Roukema JA, Coebergh JW. An overview of prognostic factors for long-term survivors of breast cancer. *Breast Cancer Res Treat.* 2008;107:309-330.
48. Newcomb PA, Egan KM, Trentham-Dietz A, et al. Prediagnostic use of hormone therapy and mortality after breast cancer. *Cancer Epidemiol Biomarkers Prev.* 2008;17:864-871.
49. Schairer C, Gail M, Byrne C, et al. Estrogen replacement therapy and breast cancer survival in a large screening study. *J Natl Cancer Inst.* 1999;91:264-270.
50. Early Breast Cancer Trialists' Collaborative Group. Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. *Lancet*. 2005;365:1687-1717.
51. Bauer KR, Brown M, Cress RD, Parise CA, Caggiano V. Descriptive analysis of estrogen receptor (ER)-negative, progesterone receptor (PR)-negative, and HER2-negative invasive breast cancer, the so-called triple-negative phenotype: a population-based study from the California Cancer Registry. *Cancer.* 2007;109:1721-1728.
52. Greenland S, Finkle WD. A critical look at methods for handling missing covariates in epidemiologic regression analyses. *Am J Epidemiol.* 1995;142:1255-1264.