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Post-diagnosis social networks and breast cancer mortality in the After Breast Cancer Pooling Project (ABCPP)

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Abstract

Background—Large social networks have been associated with better overall survival though not consistently with breast cancer (BC)-specific outcomes. We evaluated associations of post-diagnosis social networks and BC outcomes in a large cohort.

Methods—9,267 women from the After Breast Cancer Pooling Project provided data on social networks within approximately two years following diagnosis. A social network index was derived from information about the presence of a spouse/partner, religious ties, community ties, friendship ties, and numbers of first-degree, living relatives. We used Cox models to evaluate associations, and meta-analysis to determine whether effect estimates differed by cohort. We stratified by demographic, social, tumor, and treatment factors.

Results—There were 1,448 recurrences and 1,521 deaths, 990 from BC. Associations were similar in three of four cohorts. After covariate adjustment, socially isolated women (small

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networks) had higher risks of recurrence (HR=1.43, 95% CI:1.15–1.77), BC-specific mortality (HR=1.64, 95% CI:1.33–2.03), and total mortality (HR=1.69, 95% CI:1.43–1.99), compared to socially integrated women; associations were stronger in those with stage I/II cancer. In the fourth cohort, there were no significant associations with BC-specific outcomes. A lack of a spouse/partner (p=0.02) and community ties (p=0.04) predicted higher BC-specific mortality in older, White, but not other, women. However, a lack of relatives (p=0.02) and friendship ties (p=0.01) predicted higher BC-specific mortality in non-White women only.

Conclusions—In a large pooled cohort, larger social networks were associated with better BC-specific and overall survival. Clinicians should assess social networks information as a marker of prognosis considering that critical supports may differ by sociodemographic factors.

Condensed abstract

In this large, prospective, pooled cohort study of 9,267 women with breast cancer, women who were socially isolated had higher risks of recurrence, breast cancer-specific mortality, and overall mortality. In analyses of specific ties and outcomes, specific associations differed by age, race/ethnicity, and country of origin suggesting that critical supports differ by sociodemographic factors.

Keywords

Social networks; social support; breast cancer; survival; mortality

Introduction

Social networks are defined as the web of social relationships surrounding an individual[1]. It is well established that larger social networks predict lower overall mortality in healthy populations[2] and in breast cancer (BC) patients[3–8]. However, associations with BC-specific outcomes have been mixed. In 2,835 postmenopausal BC survivors in the Nurses' Health Study (NHS), Kroenke et al., found that socially isolated women, i.e., women with small networks, assessed prior to diagnosis were twice as likely to die of BC than were socially integrated women[3]. Reynolds et al. found suggestive but nonsignificant associations of social network size assessed at diagnosis with BC-specific survival in 1,011 women with both DCIS and invasive BC from the Black and White Study[7]. Two larger studies in women with invasive BC found significant associations with overall, but not BC-specific mortality. However, each of these studies included BC survivors years after initial diagnosis, two years on average post-diagnosis in one cohort (N=2,264) and six years post-diagnosis in a second cohort of 4,589 BC survivors[4, 6]. It is unclear whether discrepancies in associations are due to differences in study size, population characteristics, methodologic differences, or other factors.

Determining whether social networks influence BC-specific outcomes and in whom, is necessary to developing effective social and clinical interventions. Therefore, we examined associations between post-diagnosis social networks and prognosis in a pooled cohort of four cohorts of 9,267 women with invasive BC from the After Breast Cancer Pooling Project

(ABCPP), stratifying additionally by age, race, time since diagnosis, tumor characteristics, and levels of social support or social strain.

METHODS

The After Breast Cancer Pooling Project

The ABCPP is an international collaboration of four prospective cohorts including 18,333 women[9] from multiple U.S. sites and Shanghai, China who were diagnosed with stages I–IV invasive BC. The goal of the collaboration was to examine the roles of physical activity, adiposity, dietary factors, supplement use, and quality of life in BC prognosis. Three of the cohorts, the Shanghai Breast Cancer Survival Study (SBCSS)[10], the LACE Study[11], and the Women's Healthy Eating and Living (WHEL) Study[12], specifically recruited BC patients. The fourth cohort included BC patients diagnosed in the NHS, a prospective study of female nurses[13]. Each study collected data on clinical, social, reproductive, and lifestyle factors. Data were harmonized into a common dataset. Individual study investigators received Institutional Review Board (IRB) approval from their respective institution(s) to participate in this collaboration.

Study sample—We described derivation of the cohort (including LACE, NHS, SBCSS, and WHEL cohorts) previously[14]. Briefly, data on social factors were collected approximately six months post-diagnosis in SBCSS and on average 1.8 years post-diagnosis in WHEL and LACE. In the NHS, we used data collected within two years (mean, median=0.9 year) post-diagnosis. Women were excluded if they were missing data on >2 social ties (N=485 or 5%). Otherwise we assumed that missing data signified a lack of a social tie. We included 1,947 women from the LACE cohort, 2,221 from the NHS cohort, 2,127 from the SBCSS cohort, and 2,972 from the WHEL cohort (N=9,267).

Data Collection

Social networks—The ABCPP Social Network Index (ABCPP-SNI)[14] used in this analysis was adapted from the Berkman-Syme Social Networks Index[15] (B-SNI), which is frequently used in epidemiological research and includes five components: a spouse/intimate partner, number of relatives, friendship ties, religious/social ties, and community ties. Women were assigned 1 or 0 points depending on whether or not they were married/in an intimate relationship, engaged in volunteer work, or engaged in religious participation, and 1, 2, or 3 points for cohort-specific (approximate) tertiles of the sum of relatives or friends. A higher score signifies greater social integration. We calculated the ABCPP-SNI separately in each cohort and divided the index into cohort-specific tertiles of women who were socially isolated, moderately integrated, and socially integrated. We also standardized the continuous social network score and created a Z-score (mean=0, standard deviation=1) for analyses of trend. The ABCPP-SNI was developed and validated previously against the B-SNI and showed good agreement ($r=0.72$, $p<0.001$, $\kappa=0.60$)[14].

Sociodemographic and reproductive characteristics—Available sociodemographic and reproductive data included race/ethnicity (Non-Hispanic White, Non-Hispanic Black, Asian, Hispanic, Other), education (<high school, high school, some college, college

graduate), menopausal status at diagnosis (premenopausal, postmenopausal, unknown), parity, and age at first birth.

Lifestyle factors and body mass index—Lifestyle factors were measured at the time as the social variable assessments. Smoking history was self-reported (never, past, current). Recreational physical activity in metabolic equivalents (MET-hours/week) was determined from validated semi-quantitative questionnaires[16]. Height and weight were self-reported in LACE and NHS; in the SBCSS and WHEL, height and weight were measured during study visits. Body mass index (BMI) in kg/m^2 was derived from weight and height. Information on alcohol intake (g/d) was derived from validated food frequency questionnaires[17].

Clinical characteristics and breast cancer treatment—Available clinical and treatment data included age at diagnosis (years), American Joint Committee on Cancer (AJCC) stage (I, II, III, IV), estrogen receptor (ER)/progesterone receptor (PR) status, nodal status, HER2 status, and comorbidity (defined as diabetes, hypertension, myocardial infarction, or stroke). Treatment information included data on surgery, chemotherapy, radiation therapy, and hormonal therapy.

Ascertainment of BC outcomes—Main outcomes were BC recurrence, BC-specific mortality, and total mortality. Recurrence was defined as recurrence/metastasis or development of new primary BC. Each study followed participants to ascertain BC outcomes. Detailed methods were previously published for each study[9]; in brief, outcomes were ascertained through a combination of self-report, medical record review and linkage to vital statistics registries.

Statistical analyses

Using analysis of covariance and Mantel-Haenszel chi-square tests, we examined age-adjusted associations between social network categories and potential confounding variables.

Analyses of social networks and outcomes—We examined associations between social networks assessed within approximately two years following diagnosis and outcomes. Each analysis involved three steps. First, Cox proportional hazard regression models were used to estimate study-specific adjusted hazard ratios (HRs) and 95% confidence intervals (CI) for associations of social networks with each outcome (i.e., recurrence, BC-specific mortality, total mortality, non-BC mortality). Second, a meta-analysis was conducted, combining study-specific HRs using inverse-variance weights in random-effects models[18]. The Q statistic was used to assess heterogeneity in relative risk estimates across cohorts[19]. When there was no evidence for heterogeneity (P>0.10), cohorts were pooled and associations between social networks and outcomes were evaluated using proportional hazards regression, adjusted for cohort in addition to covariates listed below. When associations differed across cohorts, we reported the Q statistic and separately reported associations for differing groups. Tests for linear trend of social network size were conducted using the standardized, continuous measure.

We conducted initial models adjusted for age and time between diagnosis and the social assessment (lag time). A second set of models adjusted additionally for cohort, AJCC stage, race/ethnicity, education, parity, menopausal status at diagnosis, hormone receptor status, Her2 neu status, and comorbidity. Covariates were chosen based on *a priori* determination from literature review. We allowed missing categories for covariates. However, we compared results using this approach against complete case ascertainment.

In a recent paper in the ABCPP, we reported that socially isolated women had more adverse lifestyle characteristics and a lower likelihood of receiving chemotherapy[14]. Therefore, we also considered a final set of models adjusted additionally for treatment, smoking, physical activity, alcohol, and post-diagnosis BMI to determine whether treatment and lifestyle factors explained associations between social networks and survival. We determined the degree to which adjustment for these variables attenuated associations by evaluating percent change in effect estimates. We also conducted sensitivity analyses with complete case ascertainment and excluding data provided ≤6 months since diagnosis, since associations may differ in women undergoing initial treatment (N=8,001). We conducted tests of proportionality with variable by time interactions.

We evaluated analyses stratified by demographic, social, BC tumor and treatment variables including social support levels, as well as caregiving obligations and social strain levels since these can have negative effects on health[20–22]. We computed interaction terms based on the cross product of the continuous social networks variable and each of the dichotomous stratification variables and evaluated interactions with Wald χ^2 tests when analyses suggested differences in associations across strata. We also evaluated associations between each type of social tie and outcomes, stratified by age (≤ vs.> median=56.1y), White vs. non-White race, and country (US vs. Shanghai, China). Associations with reported $p<0.05$ were statistically significant. All statistical tests were two-sided.

RESULTS

Among 9,267 women, there were 1,448 recurrences and 1,521 deaths, with 990 from breast cancer. Follow-up from diagnosis ranged from 0.2 to 20.9 years (median=10.6 years). Socially isolated women were more likely to be Caucasian, college educated, and nulliparous. Socially isolated women were also more likely to have lower levels of physical activity, be current smokers, drink more than recommended, and be obese. Finally, social isolation was associated with a lower likelihood of receiving chemotherapy or hormonal therapy and a higher likelihood of lumpectomy (Table 1). Age, menopausal status at diagnosis, cancer stage, and treatment with radiation were not related to social network size.

Social networks and outcomes

In meta-analysis, associations for non-BC mortality did not differ by cohort, so we pooled all four cohorts. Women with smaller social networks had a higher risk of non-BC mortality (HR=1.82, 95% CI:1.44–2.30, p-trend<0.001). By contrast, associations between social isolation (vs. social integration) and recurrence (Q=6.31, p=0.10), BC-specific mortality (Q=7.69, p=0.05), and total mortality (Q=6.17, p=0.10) differed statistically and/or

qualitatively by cohort so data were not pooled; associations were highly similar in the LACE, NHS, and SBCSS cohorts and differed in WHEL.

After adjustment for potential confounding variables in LACE/NHS/SBCSS, socially isolated women had higher risks of recurrence (OR=1.43, 95% CI:1.18–1.74, p-trend<0.001), BC-specific mortality (OR=1.64, 95% CI:1.33–2.03, p-trend=<0.001), and total mortality (OR=1.69, 95% CI:1.43–1.99, p-trend<0.001), compared to socially integrated women (Table 2). Adjusting for lifestyle and treatment factors attenuated results for the linear social network variable by 13% for recurrence, 18% for BC mortality, and 26% for total mortality, but associations remained significant after adjustment for these potential mediating factors. In WHEL, those in the middle tertile of social networks had nonsignificant lower risks of outcomes in fully adjusted models (Table 2). Results were similar in analyses with complete case ascertainment or when we restricted analyses to women with data provided ≥6 months post-diagnosis. In proportional hazards tests, treatment effects varied by time. However, modeling these effects did not materially influence associations of interest so we retained original variables which represent time-averaged treatment effects.

In stratified analyses, in the LACE/NHS/SBCSS cohort, associations with recurrence and BC mortality were stronger for those with stage I/II vs. stage III (recurrence) or stage III/IV (BC-specific mortality) cancer though only the interaction term for BC mortality was statistically significant (p=0.02) (Table 3). Associations did not differ by age, time since diagnosis, ER/PR status, Her2neu status, or treatment (data not shown). Qualitatively, associations appeared stronger for non-White vs. White women, although differences were not statistically significant (data not shown).

Types of social ties and outcomes

Being unmarried/unpartnered was associated with worse BC-specific (HR=1.37, 95% CI: 1.06–1.77) and total (HR=1.45, 95% CI:1.21–1.74) mortality in older White women but it was not associated with outcomes in non-White or younger White, women. Small friendship and relative networks predicted significantly worse recurrence, BC-specific mortality, and total mortality in non-White, but not White, women. Religious participation was not associated with outcomes. Community ties predicted lower risks of BC-specific (HR=0.80, 95% CI:0.65–0.99) and total mortality (HR=0.79, 95% CI:0.68–0.92) in older White and Asian, but not other, women (Table 4).

DISCUSSION

In the LACE, NHS, and SBCSS cohorts, socially isolated BC survivors had higher risks of recurrence, BC-specific mortality, and total mortality; associations were stronger in those with earlier stage disease. Controlling for treatment and lifestyle factors attenuated effect estimates but did not fully account for the observed associations. By contrast, in the WHEL cohort, associations between social networks and BC-specific outcomes were generally nonsignificant. Smaller social networks predicted higher non-BC mortality in all cohorts. Ties to family and relatives predicted lower mortality in non-White women whereas a spouse predicted lower mortality in older White women. Community ties predicted better outcomes

in older Whites and Asians. To our knowledge, this is the largest study examining associations between social networks and BC survival in a diverse population of BC survivors with extensive data on potential confounding and mediating variables.

Consistent with previous studies[4, 6, 23, 24], smaller social networks were strongly related to non-BC outcomes in all four cohorts. Associations with BC-specific outcomes were more complex. Our main effects associations were strikingly similar in LACE, NHS, and SBCSS, consistent with the previous NHS study[3], suggesting that most BC survivors do benefit from larger networks. Findings differed in WHEL which were similar to those reported in Beasley et al., who also showed a U-shaped association between social connectedness and BC-specific mortality. The authors did not discuss this association but two other studies may provide insights. In the Black and White Study[7], Reynolds et al. found stronger evidence of an association of social network size and BC mortality in Whites than Blacks. Though neither association was significant, the effect size of the association reported in Whites was similar to that in our findings (HR~1.4). In the NHS data, though numbers of close friends and relatives predicted lower BC-specific mortality, neither community ties, religious ties, nor a spouse were related to this outcome[3]. Religious ties[4], marital ties[25], ties to relatives[3], and community ties[4] have each been related to better cancer prognosis. However, taken together, these findings suggest that not all ties are equally helpful to all women.

In fact, there were substantial differences in associations between specific social ties and outcomes in subgroups by age, race/ethnicity and country of origin. Similar to results reported in Table 4 which include the WHEL participants, we noted that associations with BC-specific outcomes within WHEL also differed by sociodemographic factors such as race and age (data not shown). Differences in associations may be due to population differences in social networks as well as differences in characteristics of informal caregivers. In the National Survey of Families and Households, Blacks, Asians, and Hispanics were shown to rely more on relatives compared with Whites[26]; Asians and Whites were more likely than others to participate in recreational groups[26]. The marital benefit seen in the older White women in this study may be due in part to the higher likelihood of spouses assuming caregiving roles in Whites[27] whereas non-White informal caregivers are more likely to be friends and family[27–29]. It is unclear why there were no significant associations between any social tie and outcomes in younger White women though possible reasons include sufficient levels of support from proximal ties when networks are small[30]; inadequate support from important ties, e.g., if a spouse cannot take off time from work to provide care; or possibly to diminished strength of ties in White women who are more likely to move away from extended families than women of other racial/ethnic groups[31, 32]. Future research in diverse cancer populations should clarify these findings. Nonetheless, similar main effects associations in three cohorts, with subgroup differences as to which ties were most predictive provided evidence that women, depending on demographic, cultural, and tumor characteristics, depend differently on their social networks[33, 34]. This suggests that a social network index may not be the optimal summary measure of the influence of social relationships on outcomes in certain sociodemographic groups. These novel findings were facilitated by the large pooled cohort.

Given that patient needs differ by stage, needs for and the influence of social support may also differ by stage. Weaker associations in late stage cancer patients suggest that resources provided within naturally-occurring networks may not be well-matched to the needs of those with late stage cancer[35]. Managing relationships with family and friends providing caregiving may be difficult when both patients and caregivers are coping with feelings of high distress[36] and expectations regarding needs differ[37]. In the Pathways Study, Kroenke et al. found that tangible support was most important to quality of life (QoL) in women with late-stage cancer but that affectionate support, while related to higher QoL in earlier stage patients, predicted lower QoL in later stage patients[38]. Specific training could be needed to help assist late-stage cancer patients. However, since previous randomized studies show little effect of social support interventions in metastatic patients[39, 40], the impact of social relationships on survival in women with late-stage disease may be limited, and social interventions might best target women with earlier stage cancer.

A major strength of the current analysis was the ability to examine associations in a large cohort of ethnically and geographically diverse BC survivors. Another strength was the ability to harmonize the studies to develop a consistent post-diagnosis social networks measure. In addition, we minimized confounding by adjusting for variables related to BC severity, including stage, hormone receptor status, and HER2 status, and reproductive history, lifestyle, demographic, and socioeconomic variables.

One limitation was the lack of complete social network information across cohorts though study-specific social network categories helped address this. Women of lower socioeconomic status (SES) were not well-represented in this population, which may lead to an underestimate of the association since women of low SES tend to have smaller social networks[41] and poorer survival. Furthermore, African-American and Hispanic women were also not well-represented in the cohort. Future studies should include larger numbers of, and should validate social networks measures in, these women, important given that most previous studies have been conducted in primarily White populations. However, this study supports the use of a social networks measure in a Chinese population.

We considered that disease severity could influence social network size. However, older women's social networks have been shown to be relatively stable across diagnosis[3, 42] though the fact that younger women's networks are less stable[42] could help explain the lack of association in younger White women in the current study. Studies should examine changes in social networks over time and outcomes. Other limitations include the somewhat different timing of social networks measures in the cohorts and missing covariate data. However, complete case ascertainment and sensitivity analyses by time of the social networks measures relative to diagnosis resulted in similar associations (data not shown).

To summarize, smaller social networks were related to higher risks of recurrence and mortality in BC survivors, particularly in women with earlier stage cancer. Health care providers need to assess information on social networks at the time of diagnosis and during follow-up since this may be a potential marker of prognosis.

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Table 1

Selected baseline characteristics* by category of social network size, in the After Breast Cancer Pooling Project (N=9,267)

	Size of social networks			
	Socially integrated	**Moderately integrated**	**Socially isolated**	**p-value****
N	3,153	4,161	1,953	
Mean time from diagnosis to post-diagnosis assessment (days)	494	499	508	0.38
Comorbidity (%)	8.1	8.2	8.7	0.33
Study (%)				
LACE	24.3	20.8	16.1	<0.001
NHS	24.1	23.9	23.9	
SBCSS	25.2	23.3	18.6	
WHEL	26.5	31.9	41.4	
Demographic variables				
Age at diagnosis (mean years)	57	57	56	<0.001
Ethnicity (%)				
Caucasian	64.9	66.6	71.6	<0.001
African-American	2.6	2.3	2.1	
Asian	27.2	26.0	21.0	
Hispanic/Latino	3.0	3.3	3.3	
Other	2.3	1.9	2.1	
Education				
Less than HS	13.6	12.6	10.8	<0.001
HS	18.6	17.5	15.9	
Some college	18.9	20.0	19.3	
College degree or greater	48.9	49.9	54.1	
Severity of disease				
Stage (%)				
I	45.9	44.9	43.8	0.50
II	40.7	42.0	42.1	
III	12.9	12.7	14.0	
IV	0.4	0.4	0.1	
ER positive tumor (%)	75.5	76.2	76.5	0.34
HER-2-neu positive (%) (N=5930)	19.2	18.2	15.9	0.05
Treatment factors				
Chemotherapy (%)	66.3	64.0	63.3	<0.001
Radiation (%)	53.5	54.4	54.9	0.57
Lumpectomy (%)	36.8	38.6	41.0	0.001
No hormonal therapy (%)	28.7	30.1	30.9	0.03
Reproductive factors				
Postmenopausal at diagnosis (%)	64.7	62.7	59.8	0.15

	Size of social networks			
	Socially integrated	**Moderately integrated**	**Socially isolated**	**p-value****
Nulliparous (%)	16.4	25.4	37.8	<0.001
Lifestyle and related factors				
Body mass index (kg/m^2)				
<25	46.1	48.5	47.3	<0.001
25–<30	35.0	31.6	29.5	
30–<35	12.8	12.5	14.3	
35+	6.2	7.4	8.9	
Physical activity (MET-hr/wk)				
<3	22.6	24.1	29.3	<0.001
3–<10	24.0	25.1	24.0	
10–<21	26.3	26.4	22.4	
21+	27.1	24.5	24.3	
Smoking status (%)				
Never	65.8	60.2	54.8	<0.001
Past	31.1	34.6	37.3	
Current	3.0	5.1	7.8	
Alcohol intake (g/d)				
0	57.5	54.6	52.9	<0.001
>0–<1.7	8.2	9.4	8.8	
1.7–<15	12.0	10.3	10.4	
15+	22.3	25.7	27.8	

*Except for age, all variables age-adjusted

**p-value, continuous variable, or p-value, Mantel-Haenszel $\chi 2$ test for categorical variables

Table 2

Relative hazard of breast cancer outcomes by level of social integration in the ABCPP (N=9,267[*]).

	Socially integrated	Moderately integrated	Socially isolated	p-value[**]
N, LACE, NHS, SBCSS	2,319	2,832	1,144	
Recurrence	286	419	187	
Age, lag time-adjusted HR[†]	1.00	**1.25**	**1.39**	**0.002**
95% CI		**(1.07, 1.46)**	**(1.15, 1.68)**	
Model II HR[‡]	1.00	**1.25**	**1.43**	**<0.001**
95% CI		**(1.07, 1.46)**	**(1.18, 1.73)**	
Model III HR[§]	1.00	**1.23**	**1.35**	**0.005**
95% CI		**(1.06, 1.44)**	**(1.11, 1.64)**	
Breast cancer-specific mortality	204	295	151	
Age, lag time-adjusted HR	1.00	**1.20**	**1.52**	**<0.001**
95% CI		**(1.01, 1.44)**	**(1.24, 1.88)**	
Model II HR	1.00	**1.21**	**1.64**	**<0.001**
95% CI		**(1.01, 1.45)**	**(1.33, 2.03)**	
Model III HR[§]	1.00	1.16	**1.43**	**0.002**
95% CI		(0.97, 1.39)	**(1.15, 1.77)**	
All-cause mortality	332	496	259	
Age, lag time-adjusted HR	1.00	**1.26**	**1.61**	**<0.001**
95% CI		**(1.10, 1.45)**	**(1.37, 1.90)**	
Model II HR	1.00	**1.25**	**1.69**	**<0.001**
95% CI		**(1.08, 1.43)**	**(1.43, 1.99)**	
Model III HR[§]	1.00	**1.17**	**1.42**	**<0.001**
95% CI		**(1.02, 1.35)**	**(1.16, 1.52)**	
N, WHEL[¶]	834	1,329	809	
Recurrence	158	234	164	
Age, lag time-adjusted HR	1.00	0.92	1.07	0.40
95% CI		(0.75, 1.12)	(0.86, 1.34)	
Model II HR	1.00	0.92	0.99	0.92
95% CI		(0.75, 1.13)	(0.79, 1.25)	
Model III HR	1.00	0.86	0.91	0.43
95% CI		(0.70, 1.05)	(0.72, 1.14)	
Breast cancer-specific mortality	102	136	102	
Age, lag time-adjusted HR	1.00	0.82	1.07	0.58
95% CI		(0.64, 1.06)	(0.81, 1.41)	
Model II HR	1.00	0.83	1.00	0.91
95% CI		(0.64, 1.08)	(0.75, 1.34)	
Model III HR	1.00	0.78	0.90	0.42
95% CI		(0.60, 1.01)	(0.67, 1.20)	

	Socially integrated	Moderately integrated	Socially isolated	p-value**
All-cause mortality	120	180	134	
Age, lag time-adjusted HR	1.00	0.94	**1.28**	**0.04**
95% CI		(0.75, 1.19)	**(1.00, 1.63)**	
Model II HR	1.00	0.93	1.16	0.23
95% CI		(0.73, 1.17)	(0.90, 1.51)	
Model III HR	1.00	0.86	1.04	0.93
95% CI		(0.68, 1.09)	(0.80, 1.35)	
Non-breast cancer mortality, All	146	245	140	
Age, lag time-adjusted HR	1.00	**1.36**	**1.85**	**<0.001**
95% CI		**(1.11, 1.67)**	**(1.46, 2.33)**	
Model II HR	1.00	**1.34**	**1.82**	**<0.001**
95% CI		**(1.09, 1.65)**	**(1.44, 2.30)**	
Model III HR	1.00	**1.25**	**1.52**	**<0.001**
95% CI		**(1.01, 1.54)**	**(1.20, 1.93)**	

*Analyses of recurrence include 9,237 women and do not include the 30 women with stage IV cancer.

**p-value, standardized, continuous measure of social network size

†Age- and lag time-adjusted model adjusted for age (continuous) and time between diagnosis and social network assessment (continuous).

‡Model II adjusted additionally for covariates including cohort (LACE, NHS (ref), WHEL, SBCSS), education (<HS, HS, some college, college degree or greater (ref)), race (White (ref), Black, Asian, Hispanic, other), stage (I (ref), II, III, IV), estrogen receptor status (no (ref), yes), Her2 neu status (no (ref), yes), parity (nulliparous, 1 pregnancy>20 weeks and age at first birth<20, 1 pregnancy>20 weeks and age at first birth≥20, 2+ and age at first birth<20, 2+ and age at first birth≥20), menopausal status (premenopausal, postmenopausal (ref)), comorbidity (no (ref), yes).

§Model III adjusted additionally for possible mediating (lifestyle and treatment) variables including chemotherapy (no (ref), yes), radiation (no (ref), yes), surgery (no, lumpectomy, mastectomy (ref), other), hormonal therapy (none (ref), tamoxifen, aromatase inhibitors, or both), alcohol intake (none (ref), >0–<1.7, 1.7–<15, 15+ g/d), smoking (never (ref), past, current), physical activity (0–<10 (ref), 10–<20, 20+ METS/wk), and body mass index (<18.5, 18.5–25 (ref), 25–<30, 30+ kg/m2).

¶The association between social isolation and outcomes differed in WHEL for recurrence (Q=6.31, p=0.10), breast cancer-specific mortality (Q=7.69, p=0.05), and total mortality, (Q=6.17, p=0.10).

Table 3

Relative hazards of social networks and outcomes, stratified by stage and subcohort (N=9,267*)

	Level of social integration			
	Socially integrated	**Moderately integrated**	**Socially isolated**	**p****
LACE/NHS/SBCSS				
Stage I/II	1,983	2,420	968	
Recurrence†	186	305	125	0.36
HR	1.00	**1.36**	**1.42**	
95% CI		**(1.13, 1.65)**	**(1.12, 1.80)**	
Breast cancer mortality	111	175	95	**0.02**
HR	1.00	1.26	**1.72**	
95% CI		(0.99, 1.60)	**(1.30, 2.28)**	
Total mortality	227	348	186	**0.01**
HR	1.00	**1.19**	**1.52**	
95% CI		**(1.01, 1.41)**	**(1.25, 1.86)**	
Stage III/IV	274	337	136	
Recurrence†	103	106	54	
HR	1.00	0.81	1.18	
95% CI		(0.60, 1.10)	(0.81, 1.71)	
Breast cancer mortality	91	102	51	
HR	1.00	0.88	0.92	
95% CI		(0.56, 1.37)	(0.56, 1.53)	
Total mortality	102	127	65	
HR	1.00	0.93	1.28	
95% CI		(0.70, 1.23)	(0.91, 1.81)	
WHEL				
Stage I/II	696	1,130	676	
Recurrence	113	156	116	0.39
HR	1.00	**0.77**	0.92	
95% CI		**(0.60, 0.99)**	(0.70, 1.21)	
Breast cancer mortality	64	81	63	0.30
HR	1.00	0.72	0.93	
95% CI		(0.52, 1.02)	(0.63, 1.35)	
Total mortality	80	119	92	0.12
HR	1.00	0.85	1.11	
95% CI		(0.64, 1.14)	(0.81, 1.54)	
Stage III/IV	138	199	133	
Recurrence†	45	78	48	
HR	1.00	0.91	1.13	
95% CI		(0.58, 1.43)	(0.77, 1.67)	
Breast cancer mortality	38	55	39	

	Level of social integration			
	Socially integrated	**Moderately integrated**	**Socially isolated**	**p****
HR	1.00	0.88	0.92	
95% CI		(0.56, 1.37)	(0.56, 1.53)	
Total mortality	40	61	42	
HR	1.00	0.91	0.95	
95% CI		(0.60, 1.40)	(0.58, 1.55)	

* Analyses of recurrence include 9,237 women and do not include the 30 women with stage IV cancer

** p-value, test for interaction

† Models adjusted for covariates in Table 2, Model III. Analyses adjusted for variables other than those specifically analyzed or restricted.

Table 4

Relative hazards* of breast cancer outcomes by type of social tie in women in the ABCPP

	N	Recur	HR	95% CI	Breast cancer-specific mortality	HR	95% CI	Total mortality	HR	95% CI
Older White**										
Married/partner	2,810	432	1.00		284	1.00		540	1.00	
No partner	688	109	0.97	(0.77, 1.23)	99	**1.37**	**(1.06, 1.77)**	201	**1.45**	**(1.21, 1.74)**
p-value†			0.81			**0.02**			**<0.001**	
Non-White and Younger White**										
Married/partner	4,479	697	1.00		474	1.00		595	1.00	
No partner	1,260	210	0.90	(0.77, 1.06)	133	0.92	(0.75, 1.13)	185	0.93	(0.78, 1.11)
p-value			0.22			0.42			0.42	
p-interaction			0.66			**0.02**			**0.001**	
White										
Large friend network	3,248	529	1.00		333	1.00		545	1.00	
Moderate friend network	1,773	292	1.01	(0.87, 1.17)	193	1.02	(0.85, 1.22)	303	0.96	(0.83, 1.11)
Small friend network	1,171	203	1.06	(0.89, 1.24)	139	1.04	(0.85, 1.28)	237	1.04	(0.89, 1.22)
p-value			0.56			0.66			0.64	
Non-White										
Large friend network	1,865	222	1.00		174	1.00		217	1.00	
Moderate friend network	620	97	1.15	(0.89, 1.47)	72	1.09	(0.81, 1.45)	111	**1.35**	**(1.06, 1.71)**
Small friend network	560	105	**1.43**	**(1.12, 1.84)**	79	**1.40**	**(1.05, 1.86)**	108	**1.43**	**(1.12, 1.83)**
p-value			**0.002**			**0.01**			**<0.001**	
p-interaction			**0.02**			0.08			**0.01**	
Older White and Asian										
No community ties	3,816	546	1.00		447	1.00		735	1.00	
Community ties	2,020	284	0.93	(0.77, 1.11)	179	**0.80**	**(0.65, 0.99)**	321	**0.79**	**(0.68, 0.92)**
p-value			0.39			**0.04**			**0.003**	
Younger White, Black, Hispanic										
No community ties	2,010	345	1.00		193	1.00		263	1.00	

	N	Recur	HR	95% CI	Breast cancer-specific mortality	HR	95% CI	Total mortality	HR	95% CI
Community ties	1,391	273	1.13	(0.95, 1.34)	171	1.18	(0.94, 1.48)	202	1.12	(0.91, 1.37)
p-value			0.17			0.16			0.28	
p-interaction			0.15			**0.003**			**<0.001**	
All groups‡										
Religious participation	4,669	763	1.00		473	1.00		775	1.00	
No religious participation	2,452	423	1.03	(0.91, 1.18)	269	1.07	(0.91, 1.26)	436	1.06	(0.94, 1.21)
p-value			0.62			0.39			0.35	
White										
Large relative network	3,016	497	1.00		322	1.00		501	1.00	
Moderate relative network	1,509	237	1.00	(0.84, 1.18)	161	1.00	(0.82, 1.22)	274	1.02	(0.87, 1.20)
Small relative network	1,667	290	0.99	(0.85, 1.15)	182	0.86	(0.71, 1.04)	310	0.97	(0.83, 1.12)
p-value			0.86			0.14			0.77	
Non-White										
Large relative network	1,713	224	1.00		170	1.00		230	1.00	
Moderate relative network	514	86	**1.33**	**(1.02, 1.73)**	68	**1.42**	**(1.05, 1.92)**	91	**1.38**	**(1.06, 1.78)**
Small relative network	818	114	1.21	(0.95, 1.54)	87	**1.33**	**(1.01, 1.76)**	115	**1.35**	**(1.06, 1.72)**
p-value			0.07			**0.02**			**0.003**	
p-interaction			0.21			**0.03**			**0.05**	

Analyses of recurrence do not include 30 women with stage IV cancer.

*Models adjusted for covariates in Table 2, Model III and simultaneously adjusted for the different social ties. Analyses adjusted for variables other than those specifically analyzed or restricted.

**Older whites included white women older than the median age=56.1. Younger whites included white women younger than the median age.

†p-value=p-value, dichotomous or ordinal variable; p-interaction=p-value, test for interaction

‡This value does not include data from the SBCSS study which did not include data on religious participation.