

# **HHS Public Access**

Breast Cancer Res Treat. Author manuscript; available in PMC 2016 May 04.

### Published in final edited form as:

Author manuscript

Breast Cancer Res Treat. 2012 May; 133(1): 375-385. doi:10.1007/s10549-012-1962-3.

# Social networks, social support and burden in relationships, and mortality after breast cancer diagnosis

# Candyce H. Kroenke,

Kaiser Permanente, Division of Research, 2101 Webster, 20th Floor, Oakland, CA 94612, USA

# Yvonne Michael,

Department of Epidemiology and Biostatistics, Drexel University School of Public Health, 1505 Race Street, 6th Floor, MS 1033, Philadelphia, PA 19102, USA

# Hilary Tindle,

Division of General Internal Medicine, University of Pittsburgh, Pittsburgh, PA, USA

# Elizabeth Gage,

School of Public Health, University at Buffalo, State University of New York, Buffalo, NY, USA

# Rowan Chlebowski,

David Geffen School of Medicine, University of California, Los Angeles, CA, USA

# Lorena Garcia,

School of Medicine, University of California, Davis, CA, USA

# Catherine Messina,

Department of Preventive Medicine, Stony Brook University, Stony Brook, NY, USA

# JoAnn E. Manson, and

Division of Preventive Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

# Bette J. Caan

Kaiser Permanente, Division of Research, 2000 Broadway, Oakland, CA 94612, USA

Candyce H. Kroenke: Candyce.h.kroenke@kp.org

# Abstract

Though larger social networks are associated with reduced breast cancer mortality, there is a need to clarify how both social support and social burden influence this association. We included 4,530 women from the Women's Health Initiative who were diagnosed with breast cancer between 1993 and 2009, and provided data on social networks (spouse or intimate partner, religious ties, club ties, and number of first-degree relatives) before diagnosis. Of those, 354 died during follow-up, with 190 from breast cancer. We used Cox proportional hazards regression to evaluate associations of social network members with risk of post-diagnosis mortality, further evaluating associations by social support and social burden (caregiving, social strain). In multivariate-adjusted analyses,

Correspondence to: Candyce H. Kroenke, Candyce.h.kroenke@kp.org.

Conflict of interest The authors declare that they have no financial conflicts of interest.

among women with high but not low social support, being married was related to lower all-cause mortality. By contrast, among women with high but not low social burden, those with a higher number of first-degree relatives, including siblings, parents, and children, had higher all-cause and breast cancer mortality (among caregivers: 0-3 relatives (ref), 4-5 relatives, HR = 1.47 (95% CI: 0.62-3.52), 6-9 relatives, HR = 2.08 (95% CI: 0.89-4.86), 10+ relatives, HR = 3.55 (95% CI: 1.35-9.33), *P*-continuous = 0.02, *P*-interaction = 0.008). The association by social strain was similar though it was not modified by level of social support. Other social network members were unrelated to mortality. Social relationships may have both adverse and beneficial influences on breast cancer survival. Clarifying these depends on understanding the context of women's relationships.

#### Keywords

Social networks; Social support; Social burden; Social relationships; Caregiving; Stress; Breast cancer; Mortality; Women

# Introduction

Social networks are defined as the web of social relationships that surround an individual [1]. The most commonly examined aspect of social networks with regard to breast cancer survival has been social network size (i.e., the number of network members); previous studies have found that larger networks (i.e., greater social integration) are associated with better survival after breast cancer diagnosis [2–7]. In a Nurses' Health Study (NHS) of 2,835 women with any stage breast cancer, Kroenke and colleagues found that socially isolated women were twice as likely to die of their breast cancer than socially integrated women [4]. In particular, greater numbers of living children, friends, and close relatives were each related to lower mortality.

Previous studies of social networks and breast cancer survival have often used the Berkman– Syme social network index (B–SNI) which assesses numbers of friends and "close" relatives in addition to marital status, community participation, and religious participation and heavily weights friends and close relatives in the computation of the index [8]. However, this research has omitted study of the benefits that accrue to women who describe relationships as "close", as well as the costs of social relationships on breast cancer prognosis.

Though large social networks may increase the odds that women will have friends and family to rely on for instrumental (e.g., rides to the hospital, trips to the pharmacy, assistance with exercise, or provision of healthy meals [9, 10]) and social-emotional support, they can also increase the likelihood of caregiving obligations to network members since women comprise up to three-quarters of informal caregivers [11, 12]. While potentially rewarding or beneficial [13], caregiving can be physically and emotionally demanding, and has been linked to lowered immune function [14], poorer mental health [15], lower cognitive function [16], higher coronary heart disease risk [17, 18], and higher mortality [19]. Caregiving responsibilities can lead to strained relationships between network members; large family networks may produce substantial demands. Although larger social networks can increase levels of social-emotional support, the emotionally sustaining quality of a relationship,

outcomes.

social networks can also produce relational strain or conflicts between members, increasing stress and causing biological effects [20] that jeopardize survival [21–23]. No one has examined whether social burden modifies the influence of social networks on breast cancer

Therefore, we evaluated associations between social network members, i.e., the presence of a spouse or intimate partner, number of first degree relatives, club participation, and religious participation, with mortality outcomes, considering the modifying influence of both social support and social burden. We examined several social network members with outcomes, consistent with previous analyses though the Women's Health Initiative (WHI) cohort lacked specific information on numbers of friends. We focused particularly on relative networks based on the strength of previous findings of relatives with breast cancer mortality [4], because people often turn to family in need [24, 25], and because people rely more on relatives than friends for instrumental types of support [26]. We hypothesized that larger social networks, particularly relative networks, would be related to lower mortality in women with breast cancer in those with higher perceived social support, and that women with high levels of social burden would experience less benefit from network members. We considered associations in 4,530 postmenopausal women from the WHI with invasive breast cancer.

#### **Methods**

#### Study population

The design of the WHI has been previously described [27, 28]. In brief, the WHI observational study (OS) is a multiethnic cohort of 93,676 post-menopausal women, ages 50–79, enrolled 1993–1998 at 40 geographically diverse clinical centers throughout the United States. Eligibility criteria included (1) ages 50–79, (2) postmenopausal status, (3) willingness to provide informed consent, and (4) at least a three-year life expectancy. The WHI clinical trials (CT) study includes 68,132 women with the same basic eligibility who agreed to participate in controlled clinical trials of diet or hormone therapy. Recruitment methods are detailed elsewhere [29].

At baseline, participants provided detailed information about demographics, psychosocial factors, medical history, and known or suspected risk factors for cancer through a self-administered questionnaire. Medical history was updated annually in the OS and every six months in the CT, by mail and/or telephone questionnaires. Human Subjects Review Committees at each participating institution approved the protocol.

We included participants with data at baseline on social networks, social support, and social burden from both the OS and CT (<5% missing data for each social variable), without a history of breast cancer (3.6%) at baseline (N= 136,886). Those missing social data had less education (34 vs. 40% college graduates), lower social support (35.6 vs. 36.0 points), higher social strain (6.7 vs. 6.5 points), lower physical activity (11.9 vs. 12.5 METS), and higher BMI (28.4 vs. 27.9 kg/m<sup>2</sup>), and were less likely to have had a mammogram in the prior two years (80 vs. 84%) (all comparisons, P< 0.001). Prior to study end in 2009, 4,530 were diagnosed with invasive breast cancer. Study participants contributed 31,184 person-years

follow-up. Follow-up ranged from 0 to 14.4 years with a median follow-up of 6.9 years. Of these women, 354 died during follow-up, with 190 from breast cancer.

#### **Data collection**

**Breast cancer ascertainment**—Breast cancer cases were initially identified from annual self-report of medical history and then confirmed by medical record and pathology report review (available in 98.2% of participants) by physician adjudicators at local clinics. All cases were centrally adjudicated and characteristics coded (histology, extent of disease, receptor status) using the Surveillance, Epidemiology, and End Results (SEER) coding system [30]. Invasive breast cancers confirmed by central review were included as cases. Final adjudication and coding of histology, hormone receptor status (positive or negative), and HER2 status was based on pathology report review and performed at the WHI Clinical Coordinating Center using the SEER coding system [31].

**Mortality**—Attribution of cause of death was based on medical record review by physician adjudicators at the local clinical centers who were blinded to information about social networks, with central final adjudication [30]. The National Death Index was crosschecked with participants at 2–3-year intervals.

**Social networks**—Social network members included: a spouse/intimate partner, club ties, religious ties, and first-degree relatives. Women were asked, "Are you currently married or in an intimate relationship with at least one person?" Women were also asked, "How often have you gone to meetings of clubs, lodges, or parent groups in the last month?" and, "How often have you gone to a religious service or to church during the past month?" For these questions, response options included: (1) not at all in the past month, (2) once in the past month, (3) 2–3 times in the past month, (4) once a week, (5) 2–6 times a week, and (6) every day.

In addition, women were asked whether or not they had sons, daughters, sisters, and brothers and if yes, how many. Women were asked further whether their mother and father were still alive. Women reported 0–23 first-degree relatives with an average of 3 male (SD = 2) and 3 (SD = 2) female relatives. We categorized this variable to enable comparison to previous analyses of relatives as part of the B–SNI [8] (see Table 1). Though social network members were similar to those included in the B–SNI, questions about relative networks did not ask about degree of closeness and information on friends was not collected. Therefore, we analyzed each network member separately and did not evaluate a composite measure.

**Social support**—Social support was assessed using nine items chosen from the Medical Outcomes Study (MOS) questionnaire [32]. Participants ranked on a 5-point scale how often specific types of support, including emotional support, affection, tangible support, and positive interaction, were available. The summary score ranged from 9 to 45 (mean = 36.1, SD = 7.6), with a higher score indicating more social support. Internal consistency for the score was high (standardized Cronbach's alpha = 0.93). No clinically meaningful categories exist for the MOS social support scale [33], so we categorized social support into quartiles based on the distribution of women in this study.

**Social burden**—Social burden included both caregiving responsibilities and social strain, as in previous WHI analysis [34]. Caregiving responsibilities were assessed by: "Are you now helping at least one sick, limited, or frail family member or friend on a regular basis?" (yes/no) Social strain was evaluated with four items derived from a measure of the negative aspects of social relationships [35]. Women were asked, "Of the people who are important to you, how many,": (1) "get on your nerves", 2) "ask too much of you," (3) "do not include you," (4) "try to get you to do things you do not want to do". Responses ranged from "none" (1) to "all" (5). Items were summed to yield a social strain score that ranged from 4 to 20, with higher scores indicating greater social strain. Internal consistency for the score was high (standardized Cronbach's alpha = 0.72). Social strain was also categorized into quartiles.

**Covariates**—Collection of data for breast cancer-related variables was previously described. Information on other covariates was self-reported at the time of the social assessment.

Initial analyses were adjusted for age, study arm (CT vs. OS), and time between social assessment and breast cancer diagnosis. Aside from age, we included in minimally-adjusted models those factors inherent to the study that may influence associations but were not population characteristics. Analyses were adjusted additionally for family history of breast cancer, mammogram within the past two years, disease severity (stage, tumor size, HER-2 neu status, nodal status, estrogen receptor status), sociodemographic characteristics (race, income, education), reproductive variables (age at first birth), behavioral and related factors [body mass index (BMI), smoking, physical activity], and comorbidity (see Tables 1, 2, 3, 4). We considered other covariates as presented in Table 1 but only included those in analysis that were significantly associated with the outcome (P < 0.10) in minimally-adjusted analyses, or that influenced the magnitude of the association of interest by at least 10%. Covariates included those considered a priori to be important potential confounders of the association between social networks and breast cancer mortality.

#### Statistical analyses

Using analysis of covariance, we regressed potential confounding variables against categories of relative network size, adjusted for continuous age (Table 1).

**Analyses of social network members and mortality outcomes**—We employed Cox proportional hazards models (SAS PROC PHREG; SAS Institute, Cary, NC, USA) for failure-time data to assess associations of categories of social network members, assessed at study onset, with time to event. Our primary aim was to evaluate associations stratified by levels of social support and burden. However, we analyzed and reported main effects in the text to facilitate comparison to previous papers. Therefore, we evaluated associations of social network members with time to breast cancer-specific mortality and all-cause mortality [36, 37]. Person-years of follow-up were counted from the date of diagnosis until the date of death or end of follow-up, whichever came first. We conducted tests for linear trend, computing Wald statistics. For all analyses, minimally-adjusted results were compared with

**Stratified analyses**—We evaluated effect modification by social support and strain, stratifying women by high and low levels of social support or strain using both a median split, to maximize power, and a split between the third and fourth quartiles, to capture associations among those with very high levels of support or strain, compared to those with lower levels. To assess the potential influence of social networks on mortality in the context of caregiving, we stratified by caregiving status (yes/no). When associations differed across strata, we used Wald tests to evaluate interaction terms of dichotomous stratification variables and either continuous or dichotomous variables, as indicated. Results for minimally-adjusted models were similar to those adjusted for multiple covariates as presented in Tables 2, 3, 4. Therefore, because of the complexity of the data, we have presented multivariate-adjusted associations only.

All statistical tests were two-sided; the criterion for statistical significance was P < 0.05.

# Results

Women with larger relative networks had a greater likelihood of a live birth, an earlier age at first birth, and a larger number of children. They were more likely to be married, provide caregiving, and indicate religious participation, but less likely to participate in clubs. Those with larger relative networks were less likely to have a college education and had lower income. Whites were less likely than nonwhites to have large relative networks. Relative network size was related to behaviors consistent with a pattern of responsible caregiving, including lower alcohol intake and a greater likelihood of never smoking, but was otherwise related to a lower level of daily self-care exhibited by lower levels of physical activity and higher BMI. However, larger relative network size was related to a higher likelihood of having a mammogram within the past two years. Disease characteristics were largely unrelated to relative networks though women with fewer relatives had more hormone receptor positive tumors (Table 1).

#### Main effects analyses

**Social support, social burden, and all-cause mortality**—In analyses adjusted for age, study arm, and time between psychosocial assessment and diagnosis, social support (continuous variable, HR = 0.98, 95% CI: 0.97–1.00, P= 0.01), social strain (continuous variable, HR = 1.05, 95% CI: 1.01–1.10, P= 0.03), and caregiving (dichotomous variable, HR = 0.82, 95% CI: 0.65–1.02, P= 0.07) were each marginally associated with all-cause mortality. Results were qualitatively similar in multivariate-adjusted analyses (social support, HR = 0.99, 95% CI: 0.98–1.00, P= 0.09; social strain, HR = 1.04, 95% CI: 1.00–1.09, P= 0.07, caregiving, HR = 0.84, 95% CI: 0.55–1.04, P= 0.10) though associations were nonsignificant. These variables were not associated with breast cancer-specific mortality (data not shown).

**Social networks and mortality**—In main effects analyses of social network members, being married was weakly related to lower all-cause mortality in minimally-adjusted models,

(HR = 0.82, 95% CI: 0.66–1.01, P= 0.06), but adjustment for income attenuated the association (data not shown). Neither religious nor club participation was related to outcomes in minimally- or in multivariate-adjusted analyses (data not shown). In minimally-adjusted analyses, relative network size was inversely related to all-cause (P= 0.002) and breast cancer-specific mortality (P= 0.01) though adjustment for covariates, particularly sociodemographic factors, attenuated associations (data not shown). In sensitivity analysis, results were qualitatively similar (data not shown).

#### Stratified analyses

**Social networks and mortality stratified by levels of social support**—Social support did not modify associations between relative, club, and religious network members and mortality but it did modify the association between having a spouse/partner and mortality (Table 2). Specifically, split along median levels of support, being married was related to lower all-cause mortality among women reporting higher but not lower than median levels of social support. In contrast, being married was related to higher breast cancer mortality among women reporting lower but not higher than median levels of social support (Table 2). There were no apparent differences by levels of social support split at the third and fourth quartiles (data not shown).

**Social networks and mortality stratified by levels of social burden**—Caregiving responsibilities strongly modified the relationship between relative network size, though not other network members, and risk of mortality; the positive relationship between number of relatives and mortality appeared exclusively among caregivers (Table 3). The pattern of association, particularly for breast cancer-specific mortality, was positive and monotonic with higher categories of relatives.

Positive relationships between relative network size (but not other network members) and all-cause and breast cancer mortality outcomes were somewhat stronger among those with higher levels of social strain, when analyzed by median levels of social strain (data not shown), but this pattern was more evident in the highest quartile of social strain (Table 4). There were no other significant differences by social strain for mortality outcomes, regardless of approach to stratification. In sensitivity analyses, omitting those who died in the first year after baseline, results in stratified analyses were qualitatively similar (data not shown).

# Discussion

Consistent with expectation, associations of social network members and mortality depended on levels of social support and burden. Being married predicted lower all-cause mortality among women reporting high, not low, social support. By contrast, greater relative network size was related to higher all-cause and breast cancer-specific mortality among those with high levels of social burden—those providing care to friends or relatives, or those experiencing high levels of social strain. Adjustment for sociodemographic and other covariates did not attenuate these findings. These findings suggest the need to assess the context of support and burden in women's social relationships to understand their influence on breast cancer survival.

In general, researchers have found that larger network size predicts lower post-diagnosis mortality [2–6]. Kroenke reported striking findings showing that larger numbers of living children, close relatives, and friends were each related to lower breast cancer-specific mortality [4]. These findings described associations between "close" relatives and outcomes, although the WHI and NHS did ask similar questions about numbers of children.

Findings suggest that results depend on how social networks are measured and that feelings of "closeness" capture benefits inherent in relationships but that alternate approaches are needed to explore costs. No previous work addresses this specifically though previous findings point to the possibility that network members can create burdens for women post-diagnosis [5]. Although a larger number of friends and relatives was related to earlier diagnosis and better survival in white women in the Black/White Cancer Survival study [5], women reporting less frequent contact with friends and relatives were conversely more likely to present with early stage disease (*P*-trend = 0.05) and had a commensurate lower risk of mortality, OR = 0.5 (0.2-1.2).

Supportive social network members can confer benefit, consistent with our findings regarding a supportive spouse. However, women with larger relative networks may also have greater obligations and stresses that impinge directly on health or preclude prioritizing daily self-care. In the WHI, a larger number of relatives was related, for example, to lower physical activity and higher BMI, two risk factors for poor breast cancer prognosis [38, 39]. Frequent contact with friends and relatives, in the context of strained relationships or caregiving, may have adverse consequences for health with important implications for longevity. Strained relationships may lead to earlier mortality [22, 23]. That a larger number of relatives was associated with higher mortality among those providing caregiving suggests that negative relationship dynamics within families may have adverse consequences for health. Further research is needed to understand the mechanisms of social networks on breast cancer survival.

Thus, the nature and quality of women's relationships matter to health. No one has previously examined this within the context of breast cancer; these findings are novel. These findings suggest a great need for understanding how social burden influences the impact of social relationships on women's health. Future research should consider this question in larger groups of women of different ethnicities and socioeconomic status.

A study strength was the ability to adjust for variables related to breast cancer mortality including stage, tumor size, nodal status, grade, hormone receptor status, and HER2 status. A second strength was its size, with over 4,500 women. Another strength was the ability to adjust carefully for lifestyle, demographic, and socioeconomic variables.

One important limitation was the lack of data on friendship networks; we were unable to draw conclusions regarding their influence. These findings likely underestimate the benefits of social networks on breast cancer survival though missing data may also lead to an underestimate of the costs since women missing any social data reported higher social strain and lower social support. Despite a large sample size, we had limited power to assess associations of modest size. Related to this was the inability to fully examine associations

for each type of relative. Nevertheless, a post hoc analysis revealed that the positive association of relative network size and mortality was driven primarily by a positive association between numbers of siblings and mortality, particularly among women with high social burden (data not shown). Future research should consider the impact of specific types of relationships.

Another limitation was the inability to adjust for breast cancer treatment. However, disease severity influences treatment course and adjustment for treatment has not substantially influenced associations over and above careful adjustment for disease severity in other studies [4, 40]. We cannot rule out that this may affect findings; women with few relatives were more likely to have ER-positive cancer, which has better prognosis than ER-negative cancer. However, adjustment for breast cancer treatment as a confounding variable may be inappropriate since treatment is unlikely to influence social network size. It may be more useful to determine how network members influence treatment decisions.

A final limitation was that social measures were not updated in these analyses nor was there assessment of social history before study enrollment. Numbers of relatives were assessed at baseline only and follow-up measures of social support and burden were inconsistent across the OS and CT cohorts. Though social network size appears consistent over time [4], levels of support and strain may change over time. The assessment of social networks at one time may capture the cumulative, biological impact of social relationships over time inaccurately. However, the evaluation of the impact of social networks on mortality after breast cancer reflecting potential costs, not just benefits, is unique in the breast cancer literature.

To summarize, the presence of a supportive spouse predicted lower mortality but larger relative networks predicted adverse outcomes among those with high levels of social burden. Given the rising costs of health care and the aging of the population, there is a growing need to understand how social relationships influence disease progression.

# References

- Berkman, L.; Glass, TA. Social integration, social networks, social support, and health. In: Berkman, L.; Kawachi, I., editors. Social epidemiology. Oxford University Press; New York: 2000.
- Beasley JM, Newcomb PA, Trentham-Dietz A, Hampton JM, Ceballos RM, Titus-Ernstoff L, Egan KM, Holmes MD. Social networks and survival after breast cancer diagnosis. J Cancer Surviv. 2010; 4(4):372–380. [PubMed: 20652435]
- Chou AF, Stewart SL, Wild RC, Bloom JR. Social support and survival in young women with breast carcinoma. Psychooncology. 2012; 21(2):125–133. [PubMed: 20967848]
- Kroenke CH, Kubzansky LD, Schernhammer ES, Holmes MD, Kawachi I. Social networks, social support, and survival after breast cancer diagnosis. J Clin Oncol. 2006; 24(7):1105–1111. [PubMed: 16505430]
- Reynolds P, Boyd PT, Blacklow RS, Jackson JS, Greenberg RS, Austin DF, Chen VW, Edwards BK. The relationship between social ties and survival among black and white breast cancer patients. National Cancer Institute Black/White Cancer Survival Study Group. Cancer Epidemiol Biomark Prev. 1994; 3(3):253–259.
- Waxler-Morrison N, Hislop TG, Mears B, Kan L. Effects of social relationships on survival for women with breast cancer: a prospective study. Soc Sci Med. 1991; 33(2):177–183. [PubMed: 1887281]

- 7. Pinquart M, Duberstein PR. Associations of social networks with cancer mortality: a meta-analysis. Crit Rev Oncol Hematol. 2011; 75(2):122–137. [PubMed: 19604706]
- Berkman LF, Syme SL. Social networks, host resistance, and mortality: a nine-year follow-up study of Alameda County residents. Am J Epidemiol. 1979; 109(2):186–204. [PubMed: 425958]
- 9. Hirschman KB, Bourjolly JN. How do tangible supports impact the breast cancer experience? Soc Work Health Care. 2005; 41(1):17–32. [PubMed: 16048854]
- Woloshin S, Schwartz LM, Tosteson AN, Chang CH, Wright B, Plohman J, Fisher ES. Perceived adequacy of tangible social support and health outcomes in patients with coronary artery disease. J Gen Intern Med. 1997; 12(10):613–618. [PubMed: 9346457]
- 11. Arno, PS. The economic value of informal caregiving, U.S., 2000. Paper presented at the annual meeting of the American Association for Geriatric Psychiatry; Orlando, Florida. 2002.
- Arno PS, Levine C, Memmott MM. The economic value of informal caregiving. Health Aff (Millwood). 1999; 18(2):182–188. [PubMed: 10091447]
- Brown SL, Smith DM, Schulz R, Kabeto MU, Ubel PA, Poulin M, Yi J, Kim C, Langa KM. Caregiving behavior is associated with decreased mortality risk. Psychol Sci. 2009; 20(4):488– 494. [PubMed: 19320860]
- Kiecolt-Glaser JK, Glaser R, Shuttleworth EC, Dyer CS, Ogrocki P, Speicher CE. Chronic stress and immunity in family caregivers of Alzheimer's disease victims. Psychosom Med. 1987; 49(5): 523–535. [PubMed: 3671639]
- Cannuscio CC, Jones C, Kawachi I, Colditz GA, Berkman L, Rimm E. Reverberations of family illness: a longitudinal assessment of informal caregiving and mental health status in the nurses' health study. Am J Public Health. 2002; 92(8):1305–1311. [PubMed: 12144989]
- Lee S, Kawachi I, Grodstein F. Does caregiving stress affect cognitive function in older women? J Nerv Ment Dis. 2004; 192(1):51–57. [PubMed: 14718776]
- Lee S, Colditz G, Berkman L, Kawachi I. Caregiving to children and grandchildren and risk of coronary heart disease in women. Am J Public Health. 2003; 93(11):1939–1944. [PubMed: 14600070]
- Lee S, Colditz GA, Berkman LF, Kawachi I. Caregiving and risk of coronary heart disease in U.S. women: a prospective study. Am J Prev Med. 2003; 24(2):113–119. [PubMed: 12568816]
- 19. Schulz R, Beach SR. Caregiving as a risk factor for mortality: the caregiver health effects study. JAMA. 1999; 282(23):2215–2219. [PubMed: 10605972]
- Adam EK, Gunnar MR. Relationship functioning and home and work demands predict individual differences in diurnal cortisol patterns in women. Psychoneuroendocrinology. 2001; 26(2):189– 208. [PubMed: 11087964]
- Sephton SE, Sapolsky RM, Kraemer HC, Spiegel D. Diurnal cortisol rhythm as a predictor of breast cancer survival. J Natl Cancer Inst. 2000; 92(12):994–1000. [PubMed: 10861311]
- Antonucci TC, Birditt KS, Webster NJ. Social relations and mortality: a more nuanced approach. J Health Psychol. 2010; 15(5):649–659. [PubMed: 20603288]
- 23. Birditt K, Antonucci TC. Life sustaining irritations? Relationship quality and mortality in the context of chronic illness. Soc Sci Med. 2008; 67(8):1291–1299. [PubMed: 18662845]
- 24. White LK, Riedmann A. Ties among adult siblings. Soc Forces. 1992; 71(1):85–102.
- Wellman B, Wortley S. Different strokes from different folks: community ties and social support. Am J Sociol. 1990; 96(3):558–588.
- 26. Adams RG, Blieszner R. Aging well with friends and family. Am Behav Sci. 1995; 39:209-224.
- 27. Matthews KA, Shumaker SA, Bowen DJ, Langer RD, Hunt JR, Kaplan RM, Klesges RC, Ritenbaugh C. Women's health initiative. Why now? What is it? What's new? Am Psychol. 1997; 52(2):101–116. [PubMed: 9104085]
- Women's Health Initiative Study Group. Design of the women's health initiative clinical trial and observational study. The Women's Health Initiative Study Group. Control Clin Trials. 1998; 19(1): 61–109. [PubMed: 9492970]
- Hays J, Hunt JR, Hubbell FA, Anderson GL, Limacher M, Allen C, Rossouw JE. The women's health initiative recruitment methods and results. Ann Epidemiol. 2003; 13(9 Suppl):S18–S77. [PubMed: 14575939]

- Curb JD, McTiernan A, Heckbert SR, Kooperberg C, Stanford J, Nevitt M, Johnson KC, Proulx-Burns L, Pastore L, Criqui M, et al. Outcomes ascertainment and adjudication methods in the Women's Health Initiative. Ann Epidemiol. 2003; 13(9 Suppl):S122–S128. [PubMed: 14575944]
- Cunningham, J.; Hankey, B.; Lyles, B.; Percy, C.; Ries, L.; Seiffert, J., et al. The SEER Program Code Manual. Revised. Cancer Statistics Branch, Surveillance Program, Division of Cancer Prevention and Control, National Cancer Institute; 1992.
- Sherbourne CD, Stewart AL. The MOS social support survey. Soc Sci Med. 1991; 32(6):705–714. [PubMed: 2035047]
- Hardy SE, Concato J, Gill TM. Resilience of community-dwelling older persons. J Am Geriatr Soc. 2004; 52(2):257–262. [PubMed: 14728637]
- Messina CR, Lane DS, Glanz K, West DS, Taylor V, Frishman W, Powell L. Relationship of social support and social burden to repeated breast cancer screening in the women's health initiative. Health Psychol. 2004; 23(6):582–594. [PubMed: 15546226]
- Antonucci, TC.; Kahn, RL.; Akiyama, H. Psychosocial factors and the response to cancer symptoms. In: Yancik, R.; Yates, JW., editors. Cancer in the elderly: Approaches to early detection and treatment. Springer Publishing Co.; New York: 1989. p. 40-52.
- 36. Cox D. Regression models and life-tables. J R Stat Soc (B). 1972; 34:187-220.
- Cupples LA, D'Agostino RB, Anderson K, Kannel WB. Comparison of baseline and repeated measure covariate techniques in the Framingham heart study. Stat Med. 1988; 7(1–2):205–222. [PubMed: 3353604]
- Kroenke CH, Chen WY, Rosner B, Holmes MD. Weight, weight gain, and survival after breast cancer diagnosis. J Clin Oncol. 2005; 23(7):1370–1378. [PubMed: 15684320]
- Holmes MD, Chen WY, Feskanich D, Kroenke CH, Colditz GA. Physical activity and survival after breast cancer diagnosis. JAMA. 2005; 293(20):2479–2486. [PubMed: 15914748]
- 40. Irwin ML, McTiernan A, Manson JE, Thomson CA, Sternfeld B, Stefanick ML, Wactawski-Wende J, Craft L, Lane D, Martin LW, et al. Physical activity and survival in postmenopausal women with breast cancer: results from the women's health initiative. Cancer Prev Res (Phila). 2011; 4(4):522–529. [PubMed: 21464032]

Kroenke et al.

_
0
Ň
4
" >
5
VHI (
M
6
th
ii.
e,
siz
¥
0
ţ
ne
ě
ti
ela
Ĩ
ee
50
ġ
ŝ
fir
off
~ >>
5
- Ee
cal
Å
9
ic.
ist
fer
act
ar
Сĥ
ē
lii
S
base
ed base
cted base
elected base
Selected base

	0-3	4-5	6-9	10 or more	P-trend
Z	1,218	1,513	1,412	387	
Person-years	8,519	10,450	9,632	2,583	
Family history of breast cancer (%)	16.1	17.2	21.8	24.5	<0.001
Medical visit within last year (%)	83.2	82.4	82.7	81.6	0.54
Mammogram within last 2 years (%)	11.6	12.5	14.1	16.6	0.005
Demographic variables					
Age (mean years)	63.8	63.7	63.7	63.9	0.85
Ethnicity (%)					
Caucasian	90.5	91.9	85.9	70.2	<0.001 **
African–American	6.3	6.1	4.3	16.6	
Asian	1.1	1.3	3.8	4.4	
Hispanic/Latino	1.2	1.7	2.8	6.5	
Other	0.7	0.8	1.1	1.0	
Education college (%)	81.1	73.7	66.5	51.3	<0.001
Income (\$, mean)	55,983	56,051	50,806	41,629	<0.001
Severity of disease					
Stage					
Localized (%)	73.3	72.5	73.8	69.4	$0.41^{**}$
Regional (%)	22.8	24.9	22.9	27.0	
Distant (%)	1.1	0.9	1.1	1.5	
No nodal involvement (%)	72.8	72.5	74.0	69.4	0.35
Tumor $>3 \text{ mm}(\%)$	94.6	92.2	93.8	92.5	0.45
ER positive tumor (%)	<i>9.17</i>	76.7	74.7	71.5	0.004
HER-2-neu receptor + (%)	19.5	18.7	19.1	24.0	0.24
Behavioral factors					
Body mass index (kg/m <sup>2</sup> )	27.6	28.0	28.5	29.9	<0.001
Physical activity (METS/wk)	17 3	12.2	11.9	111	000

Author Manuscript

Kroenke	et	al	
KIUCHKU	υı	aı.	

	Size of	Size of relative networks	letworks		
	0–3	4-5	6-9	10 or more	P-trend
Never smokers (%)	86.1	89.1	88.1	88.6	0.37
Fat intake >30% (%)	61.4	62.8	64.8	72.9	<0.001
Alcohol intake (servings/wk)	3.4	2.8	2.3	1.4	<0.001
Reproductive factors					
Age at menopause (mean years)	48.9	48.9	48.6	48.6	0.12
Ever live birth (%)	65.0	92.0	95.8	97.2	<0.001
Age at menarche <12 years (%)	25.6	24.6	21.5	23.0	0.02
Age at first birth >30 years (%)	21.0	11.4	7.2	8.2	<0.001
Ever breast feeding (%)	34.6	52.1	58.5	61.3	<0.001
Social variables					
Social support score (mean)	35.4	36.5	36.5	35.4	0.23
Social strain score (mean)	1.6	1.6	1.6	1.8	< 0.001
Provide caregiving (%)	37.0	37.9	42.3	39.3	0.03
Number of children (mean)	1.1	2.4	3.3	4.3	< 0.001
First-degree relatives (mean)	2.2	4.5	7.0	11.7	< 0.001
Married (%)	53.8	66.6	66.4	66.3	< 0.001
Religious participation (%)	35.0	40.5	47.8	57.8	< 0.001
Club participation (%)	59.4	58.7	55.8	52.0	< 0.001

Except for age, all variables age-adjusted

\*\* P value, Mantel–Haenszel  $\chi^2$  test, not for trend, age-adjusted

Page 13

2	
e	
Tab	
-	

Relative risk of mortality by presence of social network member and level of social-emotional support, among 4,530 participants diagnosed with breast cancer from the WHI, 1993–2009

	Total person- time	High support	ort		Low support	1100		1 Inddne ugur					
		All-cause death	$\mathrm{HR}^{*}$	95% CI	All-cause death	, HR*	95% CI	Breast cancer death	$\mathrm{HR}^{*}$	95% CI	Breast cancer death	$\mathrm{HR}^{*}$	95% CI
Married													
No	11,082	52	1.00		66	1.00		26	1.00		42	1.00	
Yes	20,101	109	0.67	(0.47 - 0.97)	94	1.31	(0.95 - 1.81)	62	0.79	(0.47 - 1.33)	60	1.82	(1.15–2.88)
Pvalue			0.03			0.10			0.38			0.01	
P-interaction				0.02						0.005			
Relatives													
0–3	8,519	36	1.00		57	1.00		20	1.00		23	1.00	
4-5	10,450	47	0.93	(0.58 - 1.49)	50	0.84	(0.57 - 1.27)	30	1.12	(0.59 - 2.15)	30	1.13	(0.63–2.02)
6-9	9,632	57	1.07	(0.67 - 1.70)	61	1.04	(0.70 - 1.56)	26	0.93	(0.48 - 1.81)	36	1.36	(0.76–2.44)
10 or more	2,583	21	1.52	(0.84–2.72)	25	1.20	(0.71 - 2.05)	12	2.02	(0.90 - 4.52)	13	1.14	(0.53 - 2.43)
<i>P</i> -continuous			0.47			0.28			0.34			0.51	
<b>P-interaction</b>				0.91						0.79			
Club participation													
No	13,033	63	1.00		87	1.00		40	1.00		49	1.00	
Yes	18,150	98	1.00	(0.72 - 1.40)	106	1.07	(0.79 - 1.44)	48	0.75	(0.48 - 1.19)	53	1.01	(0.67 - 1.53)
Pvalue			0.99			0.68			0.46			0.97	
<b>P</b> -interaction				0.89						0.34			
Religious participation	on												
No	11,452	43	1.00		71	1.00		36	1.00		34	1.00	
Yes	19,731	108	1.18	(0.83 - 1.68)	122	0.96	(0.71 - 1.31)	52	0.94	(0.59 - 1.53)	68	1.08	(0.69 - 1.67)
Pvalue			0.36			0.80			0.82			0.74	
<i>P</i> -interaction				0.47						0.36			

Breast Cancer Res Treat. Author manuscript; available in PMC 2016 May 04.

any involvement), estrogen-receptor status (positive, negative [ref]), age at first birth (never pregnant, never had term pregnancy, <20, 20-29, 30 years [ref]), smoking status (never [ref], past, current), BMI (<25 [ref] 25-29, 30+ kg/m<sup>2</sup>), physical activity (<3 [ref], 3-17, 18+

mets/week), comorbidity (yes, no [ref]), mammography within the last two years (yes, no [ref])

Results in bold were statistically significant (P<0.05)

Author Manuscript

Auth
Nor N
Mani
anuscr
þ

Kroenke et al.

Table 3

Relative risk of mortality by the presence of social network member and level of caregiving among 4,530 participants diagnosed with breast cancer from the WHI, 1993–2009

	Total person- time	Provide caregiving	aregiving		0	ŀ		D			5		
		All-cause death	HR*	95% CI	All-cause death	$\mathrm{HR}^{*}$	95% CI	Breast cancer death	$\mathrm{HR}^{*}$	95% CI	Breast cancer death	HR*	95% CI
Married													
No	11,082	50	1.00		101	1.00		26	1.00		42	1.00	
Yes	20,101	70	0.91	(0.60 - 1.39)	133	1.04	(0.77 - 1.39)	44	0.93	(0.53 - 1.65)	78	1.60	(1.03-2.48)
Pvalue			0.67			0.80			0.80			0.04	
P-interaction				0.61						0.19			
Relatives													
0–3	8,519	25	1.00		68	1.00		10	1.00		33	1.00	
4–5	10,450	23	0.75	(0.41 - 1.37)	74	0.88	(0.62 - 1.26)	17	1.47	(0.62–3.52)	43	1.03	(0.62 - 1.69)
69	9,632	51	1.50	(0.88–2.57)	67	0.86	(0.60 - 1.24)	29	2.08	(0.89 - 4.86)	33	0.85	(0.50 - 1.44)
10 or more	2,583	21	2.06	(1.06-4.01)	25	0.92	(0.56 - 1.52)	14	3.55	(1.35-9.33)	11	0.79	(0.37 - 1.67)
<i>P</i> -continuous	*		0.01			0.38			0.02			0.44	
P-interaction				0.008						0.008			
Club participation	-												
No	13,033	49	1.00		101	1.00		32	1.00		57	1.00	
Yes	18,150	71	0.86	(0.58 - 1.26)	133	1.13	(0.87 - 1.49)	38	0.68	(0.40 - 1.16)	63	1.00	(0.69 - 1.47)
Pvalue			0.44			0.36			0.16			0.98	
P-interaction				0.34						0.26			
Religious participation	ation												
No	11,452	35	1.00		89	1.00		20	1.00		50	1.00	
Yes	19,731	85	1.32	(0.87 - 2.02)	145	0.95	(0.72 - 1.25)	50	1.56	(0.87–2.79)	70	0.79	(0.54 - 1.16)
Pvalue			0.20			0.72			0.14			0.23	
P-interaction				0.23						0.08			

Breast Cancer Res Treat. Author manuscript; available in PMC 2016 May 04.

any involvement), estrogen-receptor status (positive, negative [ref]), age at first birth (never pregnant, never had term pregnancy, <20, 20–29, 30 years [ref]), smoking status (never [ref]), past, current), BMI (<25 [reference] 25–29, 30+ kg/m<sup>2</sup>), physical activity (<3 [ref], 3–17,

18+ mets/week), comorbidity (yes, no[ref]), mammography within the last two years (yes, no [ref])

Results in bold were statistically significant (P<0.05)

Author Manuscript

Author
Manuscript

Author Manuscript

Kroenke et al.

Relative risk of mortality by the presence of social network member and level of social strain, among 4,530 participants diagnosed with breast cancer from the WHI, 1993–2009

	Iotal person- time	High social strain	u strain		LUW SUCIAI 341 AILI								
		All-cause death	$\mathrm{HR}^{*}$	95% CI	All-cause death	$\mathrm{HR}^{*}$	95% CI	Breast cancer death	$\mathrm{HR}^{*}$	95% CI	Breast cancer death	$HR^*$	95% CI
Married													
No	11,082	47	1.00		104	1.00		19	1.00		49	1.00	
Yes	20,101	99	1.12	(0.73–1.72)	137	0.98	(0.74 - 1.31)	40	1.83	(0.96 - 3.48)	82	1.26	(0.84 - 1.91)
P value			0.59			06.0			0.07			0.27	
P-interaction				0.54						0.23			
Relatives													
0–3	8,519	22	1.00		71	1.00		10	1.00		33	1.00	
4-5	10,450	27	1.21		70	0.77	(0.54 - 1.09)	16	2.57	(1.02-6.47)	44	1.01	(0.62 - 1.64)
69	9,632	48	2.06	(1.16–3.65)	70	0.76	(0.53 - 1.09)	25	3.39	(1.40 - 8.17)	37	0.83	(0.50 - 1.40)
10 or more	2,583	16	1.53		30	1.22	(0.76 - 1.94)	8	2.53	(0.84–7.59)	17	1.40	(0.74-2.68)
<i>P</i> -continuous	*		0.10			0.98			0.07			0.56	
P-interaction				0.06						0.20			
Club participation													
No	13,033	50	1.00		100	1.00		33	1.00		56	1.00	
Yes	18,150	63	0.98	(0.66 - 1.45)	141	1.05	(0.80 - 1.37)1	26	0.59	(0.33 - 1.05)	75	1.07	(0.74 - 1.55)
Pvalue			06.0			0.72			0.07			0.71	
P-interaction				0.78						0.08			
Religious participation	ation												
No	11,452	37	1.00		87	1.00		17	1.00		53	1.00	
Yes	19,731	76	1.05	(0.69 - 1.58)	154	1.00	(0.76 - 1.31)	42	1.21	(0.65–2.27)	78	0.82	(0.57 - 1.20)
Pvalue			0.83			0.70			0.55			0.31	
P-interaction				0.73						0.17			

Breast Cancer Res Treat. Author manuscript; available in PMC 2016 May 04.

any involvement), estrogen-receptor status (positive, negative [ref]), age at first birth (never pregnant, never had term pregnancy, <20, 20–29, 30 years [ref]), smoking status (never [ref], past, current), BMI (<25 [reference] 25–29, 30+ kg/m<sup>2</sup>), physical activity (<3 [ref], 3–17,

18+ mets/week), comorbidity (yes, no[ref]), mammography within the last two years (yes, no [ref])

Results in bold were statistically significant (P<0.05)

Author Manuscript