HHS Public Access

Author manuscript

Cancer. Author manuscript; available in PMC 2022 April 01.

Published in final edited form as:

Cancer. 2021 April 01; 127(7): 1114–1125. doi:10.1002/cncr.33348.

Health-Related Quality of Life Outcomes Among Breast Cancer Survivors

Jihye Park, MSPH[1], **Juan L. Rodriguez, MPH, MS, PhD**[2], **Katie M. O'Brien, PhD**[3], **Hazel B. Nichols, PhD**[1], **M. Elizabeth Hodgson, PhD**[4], **Clarice R. Weinberg, PhD**[5], **Dale P. Sandler, PhD**[3]

[1]Department of Epidemiology, University of North Carolina Gillings School of Global Public Health, Chapel Hill, North Carolina

[2]Division of Cancer Prevention and Control, Centers for Disease Control and Prevention, Atlanta, Georgia

[3]Epidemiology Branch, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, North Carolina

[4]Social and Scientific Systems, Inc, Durham, North Carolina

[5]Biostatistics and Computational Biology Branch, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, North Carolina

Abstract

BACKGROUND: Data from a nationwide sample of US breast cancer survivors were used to examine associations between patient characteristics (breast cancer clinical features, prognostic factors, and treatments) and health-related quality of life (HRQOL). Associations between postdiagnosis HRQOL and mortality were then evaluated.

METHODS: The authors identified female breast cancer survivors (n = 2453) from the Sister Study or Two Sister Study who were at least 1 year from breast cancer diagnosis and who had responded to a survivorship survey in 2012. HRQOL was assessed with the Patient-Reported Outcomes Measurement Information System (PROMIS) Global 10 measures. Multivariable linear regression was used to assess predictors associated with HRQOL. Cox regression was used to

Corresponding Author: Dale P. Sandler, PhD, Epidemiology Branch, National Institute of Environmental Health Sciences, National Institutes of Health, 111 TW Alexander Dr, MD A3-05, Research Triangle Park, NC 27709 (sandler@niehs.nih.gov).

AUTHOR CONTRIBUTIONS

Jihye Park: Conceptualization, formal analysis, methodology, visualization, and writing–original draft. **Juan L. Rodriguez:** Conceptualization, methodology, resources, and writing–review and editing. **Katie M. O'Brien:** Data curation, validation, and writing–review and editing. **Hazel B. Nichols:** Methodology and writing–review and editing. **M. Elizabeth Hodgson:** Data curation and writing–review and editing. **Clarice R. Weinberg:** Investigation and writing–review and editing. **Dale P. Sandler:** Conceptualization, funding acquisition, investigation, supervision, and writing–review and editing.

Some of these results were presented as a poster at the 44th Annual Virtual Conference of the American Society of Preventive Oncology on March 28, 2020.

We appreciate the helpful comments of Dr. Alexandra (Lexie) White and Dr. Jennifer Woo.

Additional supporting information may be found in the online version of this article.

CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

calculate hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between HRQOL and all-cause mortality.

RESULTS: HRQOL, assessed an average of 4.9 years after the cancer diagnosis (standard deviation of 1.9 years), was negatively associated with a higher cancer stage at diagnosis; a higher comorbidity score at the survey; experience of surgical complications; dissatisfaction with breast surgery; and experience of any recent recurrence, metastasis, or secondary malignancy. Since the completion of the survey, there were 85 deaths (3.5%) during a mean follow-up of 4 years (standard deviation of 0.5 years). In multivariate models, decreases in PROMIS physical T scores and mental T scores were associated with increased mortality (HR for physical T scores, 1.08; 95% CI, 1.05–1.11; HR for mental T scores, 1.03; 95% CI, 1.01–1.06).

CONCLUSIONS: Prognostic and cancer treatment–related factors affect HRQOL in breast cancer survivors and may inform targeted survivorship care. PROMIS global health measures may offer additional insights into patients' well-being and mortality risk.

LAY SUMMARY:

• Findings from a study suggest that prognostic and cancer treatment–related factors affect health-related quality of life (HRQOL) in breast cancer survivors and that poor HRQOL may increase the mortality risk.

• The evaluation of HRQOL is important because it may hold potential as a tool for optimizing survivorship care.

Keywords

breast neoplasms; cancer survivors; comorbidity; mastectomy; mental health; prognosis; quality of life; survival rate; survivorship

INTRODUCTION

Breast cancer is the most commonly diagnosed cancer among women in the United States, with more than 250,000 new cases diagnosed each year.[1] Advances in early detection methods and treatment options over past decades have resulted in a steady increase in 5-year survival for breast cancer.[2] With increasing survival after breast cancer, it is important to quantify the impact of a cancer diagnosis and its treatment on long-term health outcomes.[3,4]

Beyond cancer-related outcomes such as recurrence, mortality, and clinician-assessed toxicity, there is increasing interest in understanding the survivorship experience through patient-reported outcomes.[5] Health-related quality of life (HRQOL), a key patient-reported outcome measure, is consistently associated with mortality risk[6–9] and is increasingly considered an important endpoint in cancer clinical trials, where it is used to inform patient-centered care, clinical decision making, and health policy or reimbursement decisions.[10,11]

Previous work has shown that women with breast cancer may experience impaired physical and emotional functioning after cancer treatment.[12–24] Several demographic and clinical determinants may negatively influence survivors' HRQOL.[12–18] For instance, breast cancer survivors with comorbid conditions, such as heart failure,[19] arthritis,[13,20] diabetes,[13] and

lymphedema,[20,21] have poorer physical and mental health outcomes than those without these conditions.[20,22–24] Women who have had reconstruction after breast cancer are more likely to report better mental HRQOL, reduced stress, and lower anxiety levels in comparison with women without breast reconstruction, although women who have had reconstruction are more likely to experience physical discomfort.[25]

A deeper understanding of underlying factors associated with poor HRQOL is needed to identify women at highest risk of mortality, and this may inform the development of targeted supportive interventions.[4] In this analysis, we assessed physical and mental HRQOL according to cancer prognostic factors, initial treatment, and clinical predictors within a large sample of US women with a breast cancer diagnosis. Furthermore, we evaluated whether postdiagnosis HRQOL was associated with mortality.

MATERIALS AND METHODS

This project was nested within the Sister Study and the Two Sister Study. The Sister Study is a prospective cohort study of women residing in the United States (including Puerto Rico). From 2003 to 2009, approximately 50,884 eligible women were enrolled in the study if they were between the ages of 35 and 74 years and had a sister who had breast cancer.[26] The Two Sister Study (2008–2010) is a retrospective study of 1422 women with young-onset breast cancer (<50 years old at diagnosis) who had a sister in the Sister Study cohort.[27] The detailed design and inclusion criteria of the parent studies have been described elsewhere.[26,27] The project analysis used cross-sectional data from a Sister Study survivorship survey supported by the Centers for Disease Control and Prevention and carried out by the National Institute of Environmental Health Sciences in 2012. Sister Study participants were eligible to receive the survivorship survey if they had an incident breast cancer diagnosis (including invasive breast cancer, ductal carcinoma in situ [DCIS], and lobular carcinoma in situ) before sample identification on October 9, 2012.[28] Two Sister Study participants were enrolled in the parent study after diagnosis, and thus all were eligible for the survivorship survey. The survey queried about medical history, health behaviors, depressive symptoms, HRQOL, and other aspects of the survivor experience.[28] All participants provided informed consent, and study protocols were approved by the institutional review boards of the National Institute of Environmental Health Sciences/National Institutes of Health and the Copernicus Group. This project was also approved by the University of North Carolina institutional review board (#19–2659).

Population for Analysis

A total of 2537 English-speaking women completed the survey via a mailed paper questionnaire or a computer-assisted telephone interview with a response rate of 90.3%.[28] For this project analysis, we first restricted our sample to participants who had been diagnosed with invasive breast cancer or DCIS (2003–2011), who were at least 1 year from breast cancer diagnosis, and who had completed the survivorship survey (n = 2482). Women with an unknown cancer stage (n = 7), unstageable breast cancer (n = 7), or missing HRQOL information (n = 15) were excluded. In total, 2453 women were included in the final analytical sample.

Measures

Demographic and clinical characteristics—Demographic characteristics were ascertained from questionnaires completed at Sister Study and Two Sister Study enrollment. Medical records were used to ascertain clinical characteristics (age at breast cancer diagnosis, cancer type, cancer stage, and hormone receptor status) for 95.5% of the participants and cancer treatment data (including breast surgery, radiation, chemotherapy, and endocrine therapy) for 80.2% of the participants. If this information was missing from the medical records or records were not retrieved, it was taken from self-reported measures. Mortality information was obtained from death certificates and/or linkages to the National Death Index (with a mortality cutoff date of December 31, 2016) for 96% of the participants.[26]

HRQOL measures—The 10-item Patient-Reported Outcomes Measurement Information System (PROMIS) global health scale (PROMIS Global 10)[29] was used to assess HRQOL domains, including general health, physical health, mental health, social health, pain, and fatigue. Prior research on PROMIS Global 10 has identified 2 HRQOL factors with 4 domains each: physical HRQOL (overall physical health, physical functioning, pain, and fatigue) and mental HRQOL (quality of life, mental health, satisfaction with social activities, and emotional problems).[29]

Because 1 item was not included in the survivorship survey (global04: “In general, how would you rate your mental health, including your mood and your ability to think?”), we conducted multiple imputation to estimate the missing item for our participants. We did so by using data from an external sample of 382 breast cancer survivors who had completed the 2010 National Health Interview Survey.[30] The imputation model included the following covariates: 3 PROMIS items (global02, global05, and global10, which were used to create the mental HRQOL summed score), age at diagnosis, time since diagnosis, race/ethnicity, and education. We ran the imputation model 100 times and present the combined results.

The physical and mental HRQOL summary scores were calculated as instructed in the scoring manual[31] and were transformed to T-score distributions with a mean of 50 and a standard deviation (SD) of 10. The PROMIS T-score distribution and population norms were developed on the basis of a sample that is representative of the US adult general population.[32]

Other measures—Many breast cancer survivors have coexistent chronic diseases or comorbidities at the time of their cancer diagnosis that have been negatively associated with patients’ quality of life.[13] To summarize the overall influence of comorbidities on quality-of-life scores, we created a comorbidity score using data from the survivorship survey. The comorbidity score was defined as the sum of the number of chronic conditions reported in the survey. The survey asked participants if they were receiving treatment or taking medications for any of the following comorbid conditions: hypertension or high blood pressure, diabetes, stomach or intestinal problems, high cholesterol, arthritis, pulmonary diseases, depression, anxiety, kidney problems, and chronic liver conditions. If participants were receiving treatment for other conditions that were not listed in the survey, they were

asked to specify the names of the conditions. They were also asked about specific cardiovascular diseases, including congestive heart failure, myocardial infarction, and coronary heart disease, since their breast cancer diagnosis. Among the specified conditions, we captured 15 comorbidities that were identified as markers of poor function in the Charlson index.[33] Our survey captured a mix of prevalent conditions and conditions for which women were being treated. Although we were not able to calculate the Charlson index per se, we calculated a comorbidity score by summing the number of relevant conditions reported without applying any weights. Specifically for our assessment of breast cancer survivors, we also evaluated other comorbidities as potential predictors for poor HRQOL, including experience of lymphedema, neuropathy, heart disease, and osteoporosis since the breast cancer diagnosis, as well as coexisting psychiatric conditions such as anxiety and depression.

Given that a history of cancer other than breast cancer was not considered a basis for exclusion in the parent studies,[26] we evaluated participants' personal history of cancer other than breast cancer or nonmelanoma skin cancer as a predictor for poor HRQOL and mortality outcomes. Self-reporting on recent recurrence, secondary malignancy, or metastasis from the survey was also evaluated as we hypothesized that this could strongly influence current quality of life. We considered only the recent cases occurring before survey completion because the questionnaire queried women's experience of any recurrence, secondary malignancy, or metastasis during the last 12 months. However, we did not expect this to produce any bias because the overall rate of all potential cases approximated from all available data sources was very close to the rate of self-reported recent cases (5.0% vs 4.9%).

For women who underwent a mastectomy with or without breast reconstruction, the survey queried about satisfaction with their decision. The items were each rated on a 5-point ordinal scale ranging from "very satisfied" to "very dissatisfied." Women who had a mastectomy were also asked to report any complications that occurred during or after surgery.

Statistical Analysis

Descriptive statistics were used to summarize demographics, breast cancer–related characteristics, and HRQOL measures among all participants. To evaluate how clinical characteristics, treatment history, comorbidities present at the survey, and breast cancer–related survivorship experience were associated with HRQOL measures, ordinary least squares regression models were fitted to estimate marginal means and 95% confidence intervals (CIs) of the physical and mental HRQOL T scores. We calculated unadjusted means and differences between adjusted means of groups within a category and corresponding 95% CIs. We identified minimally sufficient sets of confounders by using directed acyclic graphs,[34] and we considered covariates that were potentially associated with both breast cancer–related characteristics and quality-of-life scores. Multivariate models were fitted after adjustments for different covariate subsets tailored to yield total effect estimates for covariates.[35]

To evaluate associations between HRQOL scores after diagnosis and all-cause mortality, we used Cox proportional hazards regression and calculated hazard ratios (HRs) and 95% CIs.

When estimating the effects of HRQOL scores on mortality risk, we evaluated the effects of both continuous linear changes in scores and dichotomized categories (poor vs good) based on existing literature.[4,36] For the categorization, HRQOL T scores < 1 SD below the US population mean (T scores < 40) were considered to indicate poor functioning. The time to event was defined as the time from the survey to the date of death or mortality cutoff date (December 31, 2016). Individuals without the event were censored as of the same date. To avoid a selection bias due to immortal person-time, we considered breast cancer survivors to be at risk starting at the time of HRQOL assessment (not at cancer diagnosis) because women had to survive to be surveyed.[37]

All Cox models were adjusted for the following: survivor's age at diagnosis (years, continuously); time from diagnosis to survey (years, continuously); menopausal status at diagnosis (premenopausal vs postmenopausal); American Joint Committee on Cancer (AJCC) stage (stage 0, I, II, III, or IV); hormone receptor status (estrogen receptor [ER]– or progesterone receptor [PR]–positive vs ER- and PR-negative); cancer treatment (lumpectomy alone, mastectomy with or without lumpectomy, any radiation therapy, or any chemotherapy); comorbidity score (0, 1, or ≥2); and experience of any recent recurrence, metastasis, or secondary malignancy (yes vs no). Proportional hazards assumptions were tested via the plotting of the negative log of the cumulative hazard as well as testing of the likelihood ratio of HRQOL-by-time product terms.

In a sensitivity analysis, we limited our analysis to 1968 participants who had a diagnosis of invasive breast cancer (AJCC stages I-IV). SAS software (version 9.4; SAS Institute, Inc, Cary, North Carolina) was used for all statistical analyses. R software (version 3.6.3) was used for generating figures.

RESULTS

A total of 2453 women aged 28 to 80 years at diagnosis with a diagnosis of DCIS or invasive breast cancer were included. At the time of the survey, the time from diagnosis to survey ranged from 1 to 8.6 years and averaged 4.9 years (SD, 1.9 years). Table 1 presents characteristics of participants included in the analysis. The majority were non-Hispanic White and highly educated. At the time of diagnosis, most were married or in a significant relationship, had been employed for wages, and had health insurance. In our sample, 13% had any history of cancer other than breast cancer or nonmelanoma skin cancer before their first breast cancer diagnosis. Unadjusted mean scores for the physical HRQOL and mental HRQOL of the survivors were 51.50 (95% CI, 51.18–51.83) and 51.56 (95% CI, 51.20–51.92), respectively, which indicated higher HRQOL than that of the US general population (mean T score, 50). The characteristics of participants with an invasive cancer stage are shown in Supporting Table 1.

Participants' clinical characteristics, treatment history, comorbidities present at the survey, and breast cancer–related survivorship experience are shown in Table 2. Adjusted mean PROMIS T scores according to characteristics are shown as well. Overall, 20% of the women were classified with AJCC stage 0 disease, 46% were classified with stage I disease, 25% were classified with stage II disease, 8% were classified with stage III disease, and 1%

were classified with stage IV disease at diagnosis. Nearly 85% were diagnosed with ER- or PR-positive breast cancer. A minority of survivors (5%) reported any recurrence, metastasis, or secondary malignancy during the 12 months before the survey. For the initial treatment of breast cancer, 2% had undergone lumpectomy or breast-conserving surgery (BCS) alone, 17% had undergone mastectomy with no adjuvant therapy, 31% had received radiation with or without breast surgery, and 51% had received any chemotherapy (with or without breast surgery). Among survivors who were diagnosed with ER- or PR-positive cancer, 88% had received endocrine therapy. Survivors generally reported being in good health (67% had a comorbidity score of 0 at the survey). Among survivors who had breast surgery, approximately 15% reported that they had experienced surgical complications. Most reported that they were satisfied with their mastectomy and/or reconstruction surgery. When the analysis was limited to participants with invasive cancer, a majority of the survivors (87%) had received adjuvant radiation therapy and/or chemotherapy (Supporting Table 2). Among those who had ER- or PR-positive invasive breast cancer, 84% of the survivors had received endocrine therapy for their initial treatment.

Survivors diagnosed with a higher cancer stage had lower mean T scores for physical and mental health than those with a lower stage (Table 2). Survivors who received adjuvant therapy had lower mean T scores for physical function than those who underwent lumpectomy or BCS alone; the adjusted mean physical T score for survivors who received any chemotherapy was 3.69 points lower than the mean for those who underwent lumpectomy or BCS alone (95% CI, −6.29 to −1.10). No substantial differences in adjusted mean T scores by initial treatment type were observed for mental health. Among survivors who underwent mastectomy, receipt of breast reconstruction surgery was associated with higher T scores for physical health alone (mean difference, −1.44; 95% CI, −2.54 to −0.34). Survivors with a higher comorbidity score had substantially lower mean physical and mental T scores in comparison with those with zero comorbidity even after adjustments for age, race/ethnicity, socioeconomic status, any history of other cancer, cancer stage, and cancer treatment. Survivors who experienced any cancer recurrence, metastasis, or secondary malignancy within the 12 months before the survey had lower mean T scores than those who did not for both physical health (mean difference, −4.84; 95% CI, −6.38 to −3.30) and mental health (mean difference, −3.45; 95% CI, −5.18 to −1.72). Among survivors who underwent breast surgery, experience of surgical complications during or after a surgery was inversely associated with mean T scores. Moreover, dissatisfaction with mastectomy or reconstruction surgery was associated with lower mean T scores. When the analysis was restricted to participants with invasive cancer (Supporting Table 2), survivors with ER- and PR-negative invasive breast cancer had lower mean T scores for mental health alone in comparison with those with ER- or PR-positive cancer (mean difference, −1.19; 95% CI, −2.31 to −0.08). No statistically significant associations between receipt of adjuvant chemotherapy or radiation therapy and lower mean T scores were observed among survivors with invasive breast cancer. Aside from that, we generally observed similar patterns for the associations.

Differences between adjusted mean PROMIS T scores (95% CIs) for physical and mental HRQOL associated with comorbidities present at the survey are shown in Figure 1. Among survivors who underwent any breast surgery, the diagnosis of lymphedema after the

completion of surgery was associated with lower mean T scores. In addition, among survivors who underwent any chemotherapy, the diagnosis of neuropathy after the completion of chemotherapy was associated with lower mean T scores. The diagnosis of heart disease and osteoporosis subsequent to breast cancer and the receipt of treatment for anxiety and depression were negatively associated with estimated mean T scores. Similar patterns of the associations were observed when the analysis was restricted to survivors of invasive breast cancer (Supporting Fig. 1).

Multivariable analyses of associations between PROMIS T scores and all-cause mortality are shown in Table 3. Since the survey, there were 85 deaths (3.5%) with an average of 4 years of follow-up (SD, 0.5). Survivors who died had reported lower mean T scores than those who did not (physical mean T score, 42.6 vs 51.8; mental mean T score, 46.4 vs 51.7). Decreases in PROMIS physical T scores and mental T scores were associated with increased mortality (HR for physical T scores, 1.08; 95% CI, 1.05–1.11; HR for mental T scores, 1.03; 95% CI, 1.01–1.06) after adjustments for age at diagnosis; time from diagnosis to survey; menopausal status at diagnosis; cancer stage; hormone receptor status; cancer treatment; comorbidity score; and any experience of recent recurrence, metastasis, or secondary malignancy. Survivors with poor physical HRQOL (T score < 1 SD below the US population mean) had increased mortality in comparison with those with good physical HRQOL (HR, 3.14; 95% CI, 1.92–5.14). Likewise, poor mental HRQOL was associated with increased mortality (HR, 2.24; 95% CI, 1.31–3.84). When the analysis was restricted to participants with invasive cancer, again, both poor physical T scores and poor mental T scores were associated with increased mortality (Supporting Table 3).

DISCUSSION

In one of the largest studies evaluating HRQOL among US breast cancer survivors, we found that HRQOL surveyed at an average of 5 years after the cancer diagnosis was associated with a higher cancer stage at diagnosis; a higher comorbidity score at the survey; experience of surgical complications; dissatisfaction with breast surgery; and experience of any recent recurrence, metastasis, or secondary malignancy. Survivors' physical HRQOL was also associated with receipt of breast reconstruction surgery and adjuvant treatment. Our findings also suggest that HRQOL measured after breast cancer is associated with survivors' mortality even after adjustments for prognostic factors and cancer treatment.

The increased HRQOL among women who underwent breast reconstruction in the current study was consistent with findings from prior work.[24,25] However, few studies have assessed whether HRQOL outcomes differ by women's satisfaction with reconstruction surgery or their experience of surgery complications. In our sample, women who underwent breast reconstruction after mastectomy had a higher physical HRQOL score than women who did not, but their physical and mental HRQOL scores decreased when they were dissatisfied with mastectomy and reconstruction surgery. We also found that the experience of surgical complications during or after a breast surgery (eg, infection, implant rupture, or hematoma) was a predictor associated with lower HRQOL. Although identifying whether the decision-making process of mastectomy and reconstruction met patient expectations was beyond the scope of our investigation, we were able to determine that dissatisfaction with surgery and

experience of postsurgery complications could negatively affect the quality of life of breast cancer survivors. Therefore, when treatment options are being discussed, it is important that patients be informed of possible long-term impairments.

Comorbidities were assessed in this study through patient self-report, and 33% of the women had a comorbidity score of 1 or higher. Although agreement between patient-reported breast cancer and medical records has been extremely high, the same may not be true for other medical conditions.[38] Although agreement is likely to vary with the health condition of interest, it is reassuring that in this population, agreement between medical records and self-report of breast cancer was better than 99%.[38] Comorbidities assessed in our study also included the following conditions (some of which are associated with breast cancer treatments) that were not incorporated into the calculation of the comorbidity score: lymphedema, neuropathy, osteoporosis, anxiety, and depression. We found that lower HRQOL scores were associated with a higher comorbidity score and the presence of specific comorbidities in agreement with other studies.[13,20,39] A prevalent diagnosis of anxiety and depression had the strongest association with lower physical and mental HRQOL. Although we did not have care-related information (eg, access to survivorship care, quality of comorbidity management, and pharmacotherapy), our findings reinforce the importance of supportive physical and psychological care for breast cancer survivors.

Many, but not all, studies have reported that HRQOL is a prognostic indicator for survival in patients with breast cancer.[6–8,40,41] Two studies have reported that a quality-of-life assessment at the time of diagnosis can help to predict overall survival in advanced breast cancer but not in early stages of the disease.[7,42] Studies differ in the timing and tools used to assess quality of life. We are unaware of any studies using the PROMIS global health scale to examine the association between HRQOL and overall survival in breast cancer survivors. In our study, we found that poor physical and mental HRQOL, as measured by the PROMIS global health scale an average of 5 years after diagnosis, was predictive of breast cancer mortality, even after adjustments for important prognostic factors. PROMIS global health measures may hold potential as a tool for oncology providers to optimize survivorship care.

Besides the known clinical measures that were controlled in the multivariate model, quality of life itself might be a significant independent predictor of breast cancer survival, although a causal association should be evaluated with caution. One explanation for the statistically significant association between decreased T scores and increased mortality is that the patient-reported quality-of-life data might be a sensitive surrogate marker for an unrecognized biological prognostic factor because the quality-of-life data can pick up patients' well-being and symptoms that are separate from a physician's observed indicators.[7] Moreover, quality-of-life scores might be markers of patients' behavior and perceived social support, which have been hypothesized to affect disease progression and subsequent responses to treatment in patients with cancer.[43–46] However, we cannot rule out that these associations are due to reverse causation; participants who are sicker may report worse quality of life. Although we adjusted for all known clinical predictors, including cancer stage, hormone receptor status, cancer treatment, comorbidity score, and any experience of recent recurrence, metastasis or secondary malignancy, it is possible that survivors who

reported a decreased quality-of-life score were more likely than those who reported an increased score to suffer from undiagnosed or more severe disease.

The Sister Study and the Two Sister Study provided a unique opportunity for examining HRQOL in a nationwide sample of US female breast cancer survivors treated at multiple institutions. We had detailed and validated cancer characteristics and treatment information as well as survivors' vital status. This allowed us to identify predictors of poor quality of life and mortality. We had detailed information on cancer diagnosis, treatment, HRQOL measures, and mortality with a clearly established timeline, and this was harmonized across the parent studies, survivorship survey, medical records, and National Death Index database. However, self-reported data on comorbid conditions relied on participants' recall, which may have been subject to misclassification. Additionally, we had relatively small numbers for some racial/ethnic categories, which limited subgroup analyses. Future studies could investigate these relationships among more diverse samples of breast cancer survivors. We studied women who had a family history of breast cancer (the Sister Study participants) or were diagnosed at younger ages (Two Sister participants), and this may limit the generalizability of the study results.

In conclusion, prognostic and cancer treatment–related factors are important predictors of HRQOL, which, together with comorbidity, is associated with mortality risk in breast cancer survivors. PROMIS global health measures may offer additional insights into patients' well-being and mortality risk. If our results are replicated, future investigations could seek ways to improve HRQOL in breast cancer survivors, potentially through targeted survivorship care.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

FUNDING SUPPORT

This research was supported in part by the Intramural Research Program of the National Institutes of Health (National Institute of Environmental Health Sciences grant Z01 ES-044005 to Dale P. Sandler) and by the Division of Cancer Prevention and Control of the Centers for Disease Control and Prevention (survivorship survey). The findings and conclusions in the report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

REFERENCES

1. U.S. Cancer Statistics Working Group. U.S. Cancer Statistics Data Visualizations Tool, Based on 2019 Submission Data (1999–2017). US Department of Health and Human Services; 2020.
2. National Cancer Institute. Cancer Stat Facts: Female Breast Cancer. Accessed July 7, 2020. https://seer.cancer.gov/statfacts/html/breast.html
3. Javid SH, Lawrence SO, Lavallee DC. Prioritizing patient-reported outcomes in breast cancer surgery quality improvement. Breast J. 2017;23:127–137. [PubMed: 27779352]
4. Weaver KE, Forsythe LP, Reeve BB, et al. Mental and physical health–related quality of life among U.S. cancer survivors: population estimates from the 2010 National Health Interview Survey. Cancer Epidemiol Biomarkers Prev. 2012;21:2108–2117. [PubMed: 23112268]

5. Shisler R, Sinnott JA, Wang V, Hebert C, Salani R, Felix AS. Life after endometrial cancer: a systematic review of patient-reported outcomes. Gynecol Oncol. 2018;148:403–413. [PubMed: 29150143]
6. Efficace F, Therasse P, Piccart MJ, et al. Health-related quality of life parameters as prognostic factors in a nonmetastatic breast cancer population: an international multicenter study. J Clin Oncol. 2004;22:3381–3388. [PubMed: 15310784]
7. Montazeri A Quality of life data as prognostic indicators of survival in cancer patients: an overview of the literature from 1982 to 2008. Health Qual Life Outcomes. 2009;7:102. [PubMed: 20030832]
8. Quinten C, Coens C, Mauer M, et al. Baseline quality of life as a prognostic indicator of survival: a meta-analysis of individual patient data from EORTC clinical trials. Lancet Oncol. 2009;10:865–871. [PubMed: 19695956]
9. Epplein M, Zheng Y, Zheng W, et al. Quality of life after breast cancer diagnosis and survival. J Clin Oncol. 2011;29:406–412. [PubMed: 21172892]
10. Lipscomb J, Reeve BB, Clauser SB, et al. Patient-reported outcomes assessment in cancer trials: taking stock, moving forward. J Clin Oncol. 2007;25:5133–5140. [PubMed: 17991933]
11. Calvert M, Blazeby J, Altman DG, et al. Reporting of patient-reported outcomes in randomized trials: the CONSORT PRO extension. JAMA. 2013;309:814–822. [PubMed: 23443445]
12. Teo I, Reece GP, Christie IC, et al. Body image and quality of life of breast cancer patients: influence of timing and stage of breast reconstruction. Psychooncology. 2016;25:1106–1112. [PubMed: 26360810]
13. Fu MR, Axelrod D, Guth AA, et al. Comorbidities and quality of life among breast cancer survivors: a prospective study. J Pers Med. 2015;5:229–242. [PubMed: 26132751]
14. Jones SM, LaCroix AZ, Li W, et al. Depression and quality of life before and after breast cancer diagnosis in older women from the Women's Health Initiative. J Cancer Surviv. 2015;9:620–629. [PubMed: 25708515]
15. Dialla PO, Chu WO, Roignot P, et al. Impact of age-related socioeconomic and clinical determinants of quality of life among long-term breast cancer survivors. Maturitas. 2015;81:362–370. [PubMed: 25911244]
16. Cho J, Jung SY, Lee JE, et al. A review of breast cancer survivorship issues from survivors' perspectives. J Breast Cancer. 2014;17:189–199. [PubMed: 25320616]
17. Smith AW, Alfano CM, Reeve BB, et al. Race/ethnicity, physical activity, and quality of life in breast cancer survivors. Cancer Epidemiol Biomarkers Prev. 2009;18:656–663. [PubMed: 19190157]
18. Pinheiro LC, Tan X, Olshan AF, et al. Examining health-related quality of life patterns in women with breast cancer. Qual Life Res. 2017;26:1733–1743. [PubMed: 28247314]
19. Harrison JM, Davis MA, Barton DL, Janz NK, Pressler SJ, Friese CR. Functional status and quality of life among breast cancer survivors with heart failure: results of the Medicare Health Outcomes Survey. Support Care Cancer. 2017;25:2463–2473. [PubMed: 28275898]
20. Lim JW. The impact of comorbidity on the relationship between life stress and health-related quality of life for Chinese- and Korean-American breast cancer survivors. Ethn Health. 2018;23:16–32. [PubMed: 27764966]
21. Pusic AL, Cemal Y, Albornoz C, et al. Quality of life among breast cancer patients with lymphedema: a systematic review of patient-reported outcome instruments and outcomes. J Cancer Surviv. 2013;7: 83–92. [PubMed: 23212603]
22. Bellury L, Pett MA, Ellington L, Beck SL, Clark JC, Stein KD. The effect of aging and cancer on the symptom experience and physical function of elderly breast cancer survivors. Cancer. 2012;118:6171–6178. [PubMed: 22674036]
23. Ashing K, Rosales M, Lai L, Hurria A. Occurrence of comorbidities among African-American and Latina breast cancer survivors. J Cancer Surviv. 2014;8:312–318. [PubMed: 24473830]
24. Fanakidou I, Zyga S, Alikari V, Tsironi M, Stathoulis J, Theofilou P. Mental health, loneliness, and illness perception outcomes in quality of life among young breast cancer patients after mastectomy: the role of breast reconstruction. Qual Life Res. 2018;27:539–543. [PubMed: 29119452]

25. Platt J, Zhong T. Patient-centered breast reconstruction based on health-related quality-of-life evidence. Clin Plast Surg. 2018;45: 137–143. [PubMed: 29080656]
26. Sandler DP, Hodgson ME, Deming-Halverson SL, et al. The Sister Study cohort: baseline methods and participant characteristics. Environ Health Perspect. 2017;125:127003. [PubMed: 29373861]
27. Fei C, Deroo LA, Sandler DP, Weinberg CR. Fertility drugs and young-onset breast cancer: results from the Two Sister Study. J Natl Cancer Inst. 2012;104:1021–1027. [PubMed: 22773825]
28. Buchanan ND, Dasari S, Rodriguez JL, et al. Post-treatment neurocognition and psychosocial care among breast cancer survivors. Am J Prev Med. 2015;49(6 suppl 5):S498–S508. [PubMed: 26590645]
29. Hays RD, Bjorner JB, Revicki DA, Spritzer KL, Cella D. Development of physical and mental health summary scores from the Patient-Reported Outcomes Measurement Information System (PROMIS) global items. Qual Life Res. 2009;18:873–880. [PubMed: 19543809]
30. National Center for Health Statistics. Data File Documentation, National Health Interview Survey, 2010 (Machine Readable Data File and Documentation). Centers for Disease Control and Prevention; 2011.
31. PROMIS Network. Scoring PROMIS Global Short Form. Accessed October 10, 2019. http://www.healthmeasures.net/images/PROMIS/manuals/PROMIS_Global_Scoring_Manual.pdf
32. Liu H, Cella D, Gershon R, et al. Representativeness of the Patient-Reported Outcomes Measurement Information System internet panel. J Clin Epidemiol. 2010;63:1169–1178. [PubMed: 20688473]
33. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40:373–383. [PubMed: 3558716]
34. Greenland S, Pearl J, Robins JM. Causal diagrams for epidemiologic research. Epidemiology. 1999;10:37–48. [PubMed: 9888278]
35. Westreich D, Greenland S. The table 2 fallacy: presenting and interpreting confounder and modifier coefficients. Am J Epidemiol. 2013;177:292–298. [PubMed: 23371353]
36. Rodriguez JL, Hawkins NA, Berkowitz Z, Li C. Factors associated with health-related quality of life among colorectal cancer survivors. Am J Prev Med. 2015;49(6 suppl 5):S518–S527. [PubMed: 26590647]
37. Lash TL, Cole SR. Immortal person-time in studies of cancer outcomes. J Clin Oncol. 2009;27:e55–e56. [PubMed: 19597013]
38. D'Aloisio AA, Nichols HB, Hodgson ME, Deming-Halverson SL, Sandler DP. Validity of self-reported breast cancer characteristics in a nationwide cohort of women with a family history of breast cancer. BMC Cancer. 2017;17:692. [PubMed: 29058598]
39. Harrison SE, Watson EK, Ward AM, et al. Primary health and supportive care needs of long-term cancer survivors: a questionnaire survey. J Clin Oncol. 2011;29:2091–2098. [PubMed: 21519023]
40. Kenne Sarenmalm E, Odén A, Ohlén J, Gaston-Johansson F, Holmberg SB. Changes in health-related quality of life may predict recurrent breast cancer. Eur J Oncol Nurs. 2009;13:323–329. [PubMed: 19596212]
41. Coates AS, Hürny C, Peterson HF, et al. Quality-of-life scores predict outcome in metastatic but not early breast cancer. International Breast Cancer Study Group. J Clin Oncol. 2000;18:3768–3774. [PubMed: 11078489]
42. Groenvold M, Petersen MA, Idler E, Bjorner JB, Fayers PM, Mouridsen HT. Psychological distress and fatigue predicted recurrence and survival in primary breast cancer patients. Breast Cancer Res Treat. 2007;105:209–219. [PubMed: 17203386]
43. Gotay CC, Kawamoto CT, Bottomley A, Efficace F. The prognostic significance of patient-reported outcomes in cancer clinical trials. J Clin Oncol. 2008;26:1355–1363. [PubMed: 18227528]
44. Kroenke CH, Kubzansky LD, Schernhammer ES, Holmes MD, Kawachi I. Social networks, social support, and survival after breast cancer diagnosis. J Clin Oncol. 2006;24:1105–1111. [PubMed: 16505430]
45. Pinquart M, Duberstein PR. Associations of social networks with cancer mortality: a meta-analysis. Crit Rev Oncol Hematol. 2010;75: 122–137. [PubMed: 19604706]

46. Nausheen B, Gidron Y, Peveler R, Moss-Morris R. Social support and cancer progression: a systematic review. J Psychosom Res. 2009;67:403–415. [PubMed: 19837203]

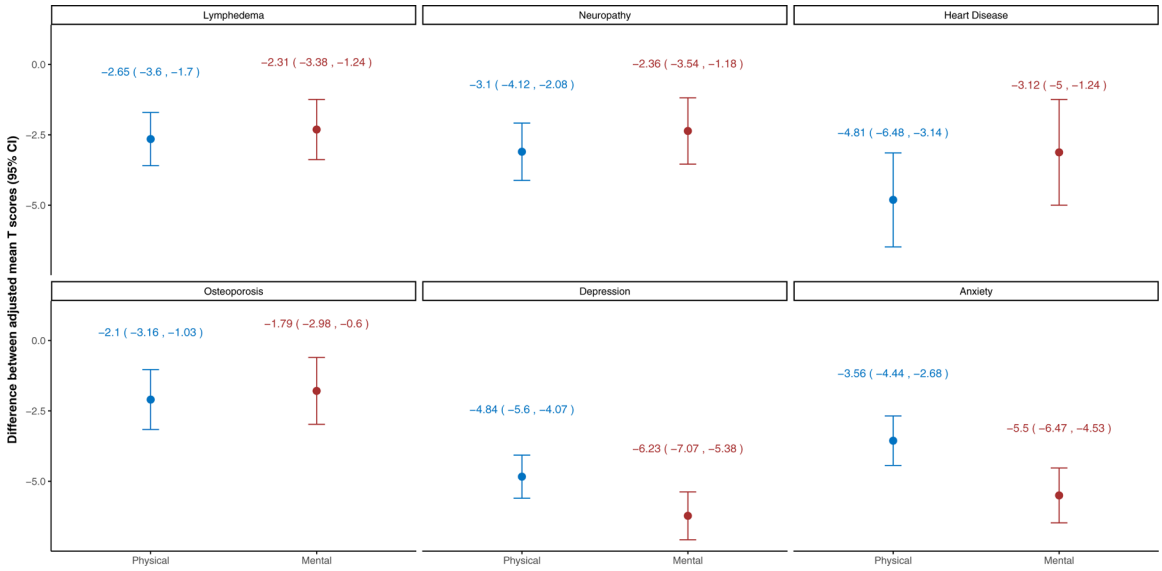

Figure 1.

Differences between adjusted mean PROMIS T scores (95% CIs) for physical and mental HRQOL associated with comorbidities present in the survivorship survey. Marginal means and 95% CIs for physical and mental HRQOL T scores associated with the presence of each comorbidity were estimated first; then, differences between the means of groups within a category and corresponding 95% CIs were calculated (eg, difference between adjusted mean T scores = adjusted mean T score$_{(\text{yes comorbidity})}$ − adjusted mean T score$_{(\text{no comorbidity})}$). Ordinary least squares regression models that were used to estimate marginal means were adjusted for age at diagnosis, race/ethnicity, socioeconomic status (education, income, employment status, and insurance coverage), any history of other cancer (excluding nonmelanoma skin cancer), cancer stage, and cancer treatment. Analyses for lymphedema and neuropathy were limited to those who underwent any breast surgery (n = 2425) and those who underwent any chemotherapy (n = 1239), respectively. Prevalence counts and proportions for each condition were as follows: lymphedema after the completion of surgery, 366 of 2410 (15%); neuropathy after the completion of chemotherapy, 356 of 1217 (29%); heart disease after breast cancer, 91 of 2423 (4%); osteoporosis after breast cancer, 256 of 2417 (11%); currently receiving treatment or taking medications for depression, 529 of 2441 (22%); and currently receiving treatment or taking medications for anxiety or nervousness, 393 of 2445 (16%). CI indicates confidence interval; HRQOL, health-related quality of life; PROMIS, Patient-Reported Outcomes Measurement Information System.

TABLE 1.

Study Participant Characteristics (n = 2453)

Characteristic	Value	
Study, No. (%)		
Sister Study	1337	(55)
Two Sister Study	1116	(45)
Age at diagnosis, mean (SD), range, y	53.2 (10.5), 28–80	
Age at diagnosis, No. (%)		
<45 y	527	(22)
45–54 y	983	(40)
55–64 y	491	(20)
≥65 y	452	(18)
Time since diagnosis at survey, mean (SD), range, y	4.9 (1.9), 1–8.6	
Time since diagnosis at survey		
1≤5 y	1109	(45)
≥5 y	1344	(55)
Race/ethnicity, No. (%)		
Non-Hispanic White	2201	(90)
Non-Hispanic Black	113	(5)
Hispanic	75	(3)
Other[a]	62	(2)
Missing	2	
Education, No. (%)		
High school/GED or lower	319	(13)
Associate’s degree/some college	695	(28)
Bachelor’s degree	773	(32)
Graduate or professional degree	664	(27)
Missing	2	
Annual household income per person		
<$25,000	561	(24)
$25,000–$37,499	419	(18)

Characteristic	Value	
$37,500–$74,999	883	(37)
≥$75,000	509	(21)
Missing	81	
Married, living with someone as married, or in significant relationship at diagnosis, No. (%)		
No	425	(17)
Yes	2023	(83)
Missing	5	
Menopausal status at diagnosis, No. (%)		
Premenopausal	1248	(51)
Postmenopausal	1205	(49)
Employment status at diagnosis, No. (%)		
Employed for wages	1630	(67)
Out of work/unable to work	317	(13)
Retiree	461	(19)
Other	36	(1)
Missing	9	
Health insurance coverage during breast cancer treatment, No. (%)		
Fully covered	2361	(97)
Partially covered	44	(2)
Not covered	26	(1)
Missing	22	
Any history of other cancer excluding NMSC, No. (%)		
No	2132	(87)
Yes	321	(13)

Abbreviations: GED, generalized education development; NMSC, nonmelanoma skin cancer; SD, standard deviation.

[a] *Other* includes those who identified as Asian/Pacific Islander, American Indian/Alaskan Native, or multiracial.

Cancer. Author manuscript; available in PMC 2022 April 01.

TABLE 2.

Unadjusted Means With 95% CIs and Differences Between Adjusted Means With 95% CIs for PROMIS T Scores for Physical and Mental HRQOL Associated With Clinical Characteristics, Treatment History, Comorbidities Present at the Survey, and Breast Cancer–Related Survivorship Experience

			PROMIS T Score for Physical HRQOL				PROMIS T Score for Mental HRQOL			
	No. (%)		Unadjusted Mean (95% CI)		Difference Between Adjusted Means (95% CI)		Unadjusted Mean (95% CI)		Difference Between Adjusted Means (95% CI)	
Breast cancer characteristics										
AJCC stage at diagnosis[a]										
0	485	(20)	52.76	(52.03 to 53.49)		Reference	52.31	(51.51 to 53.12)		Reference
I	1131	(46)	51.97	(51.49 to 52.44)	−0.77	(−1.64 to 0.09)	52.08	(51.55 to 52.61)	−0.32	(−1.29 to 0.65)
II	610	(25)	50.48	(49.83 to 51.13)	−2.36	(−3.34 to −1.37)	50.88	(50.16 to 51.59)	−1.07	(−2.17 to 0.03)
III	206	(8)	49.70	(48.59 to 50.81)	−3.08	(−4.42 to −1.74)	49.04	(47.81 to 50.27)	−2.55	(−4.05 to −1.05)
IV	21	(1)	45.21	(41.72 to 48.70)	−7.15	(−10.64 to −3.66)	50.92	(47.06 to 54.78)	−0.45	(−4.35 to 3.46)
Hormone receptor status[b,c]										
Any ER(+) or PR(+)	2039	(85)	51.53	(51.17 to 51.89)		Reference	51.70	(51.31 to 52.10)		Reference
ER(−) and PR(−)	374	(15)	51.28	(50.45 to 52.12)	−0.23	(−1.14 to 0.68)	50.72	(49.80 to 51.64)	−0.81	(−1.82 to 0.20)
Missing	40									
Breast cancer treatment history										
Initial treatment[d]										
No treatment	5	(0.2)	45.18	(38.00 to 52.36)	−6.44	(−13.89 to 1.01)	46.04	(38.11 to 53.97)	−3.46	(−11.82 to 4.90)
Lumpectomy or breast-conserving surgery alone	44	(2)	54.28	(51.86 to 56.70)		Reference	51.93	(49.23 to 54.63)		Reference
Mastectomy with no adjuvant therapy	411	(17)	52.33	(51.54 to 53.13)	−2.42	(−4.97 to 0.13)	52.59	(51.72 to 53.47)	0.73	(−2.13 to 3.59)
Radiation therapy with or without breast surgery	754	(31)	52.12	(51.53 to 52.71)	−2.75	(−5.24 to −0.25)	52.12	(51.47 to 52.76)	−0.08	(−2.88 to 2.72)
Any chemotherapy	1239	(51)	50.78	(50.32 to 51.24)	−3.69	(−6.29 to −1.10)	50.89	(50.39 to 51.39)	−0.05	(−2.96 to 2.86)
Breast reconstruction surgery[d,e]										
Yes	785	(32)	52.19	(51.61 to 52.76)		Reference	51.56	(50.90 to 52.21)		Reference
No	371	(68)	49.69	(48.85 to 50.53)	−1.44	(−2.54 to −0.34)	50.83	(49.87 to 51.78)	−0.71	(−1.99 to 0.58)
Missing	7									
Endocrine therapy for initial treatment[d,f]										

	No. (%)		PROMIS T Score for Physical HRQOL				PROMIS T Score for Mental HRQOL			
			Unadjusted Mean (95% CI)		Difference Between Adjusted Means (95% CI)		Unadjusted Mean (95% CI)		Difference Between Adjusted Means (95% CI)	
Endocrine therapy	1796	(88)	51.40	(51.02 to 51.78)		Reference	51.65	(51.23 to 52.07)		Reference
No endocrine therapy	242	(12)	52.56	(51.53 to 53.59)	0.74	(−0.45 to 1.93)	52.07	(50.92 to 53.22)	0.23	(−1.11 to 1.56)
Missing	41									
Comorbidities present at survey										
Comorbidity score[g]										
0	1636	(67)	50.03	(52.65 to 53.41)		Reference	52.29	(51.85 to 52.72)		Reference
1	599	(24)	49.91	(49.29 to 50.54)	−3.96	(−4.79 to −3.14)	50.99	(50.27 to 51.71)	−2.27	(−3.24 to −1.31)
≥2	218	(9)	44.43	(43.39 to 45.47)	−9.76	(−11.03 to −8.49)	47.66	(46.47 to 48.85)	−5.92	(−7.39 to −4.45)
Breast cancer–related survivorship experience										
Any recent recurrence, metastasis, or secondary malignancy (past 12 mo)[h]										
No	2306	(95)	51.81	(51.48 to 52.14)		Reference	51.75	(51.38 to 52.11)		Reference
Yes	120	(5)	45.86	(44.42 to 47.31)	−4.84	(−6.38 to −3.30)	48.14	(46.53 to 49.75)	−3.45	(−5.18 to −1.72)
Missing	27									
Any complications during or after a breast surgery[i,j]										
Did not experience surgical complications	2054	(85)	51.86	(51.50 to 52.21)		Reference	51.93	(51.54 to 52.32)		Reference
Experienced surgical complications	371	(15)	49.62	(48.79 to 50.46)	−2.21	(−3.11 to −1.31)	49.55	(48.63 to 50.47)	−2.10	(−3.11 to −1.09)
Missing	1									
Satisfaction with mastectomy[k,l]										
Satisfied	1053	(92)	51.62	(51.13 to 52.12)		Reference	51.77	(51.22 to 52.33)		Reference
Neither satisfied nor dissatisfied	59	(5)	50.19	(48.09 to 52.28)	−1.60	(−3.75 to 0.54)	47.54	(45.20 to 49.89)	−4.21	(−6.63 to −1.80)
Dissatisfied	28	(3)	43.89	(40.85 to 46.93)	−7.41	(−10.48 to −4.34)	41.33	(37.93 to 44.74)	−10.44	(−13.89 to −6.98)
Missing	23									
Satisfaction with reconstruction surgery[k,m]										
Satisfied	589	(77)	53.13	(52.51 to 53.75)		Reference	52.60	(51.87 to 53.34)		Reference
Neither satisfied nor dissatisfied	43	(6)	50.88	(48.57 to 53.20)	−2.20	(−4.60 to 0.21)	50.86	(48.14 to 53.57)	−1.68	(−4.51 to 1.14)
Dissatisfied	135	(18)	48.46	(47.17 to 49.75)	−4.69	(−6.13 to −3.26)	46.38	(45.29 to 48.36)	−5.91	(−7.61 to −4.20)

		PROMIS T Score for Physical HRQOL		PROMIS T Score for Mental HRQOL	
	No. (%)	Unadjusted Mean (95% CI)	Difference Between Adjusted Means (95% CI)	Unadjusted Mean (95% CI)	Difference Between Adjusted Means (95% CI)
Missing	25				

Abbreviations: AJCC, American Joint Committee on Cancer; CI, confidence interval; ER, estrogen receptor; HRQOL, health-related quality of life; PR, progesterone receptor; PROMIS, Patient-Reported Outcomes Measurement Information System.

Higher PROMIS T scores represent better HRQOL. Higher comorbidity scores represent a greater number of conditions. The comorbidity score is defined as the sum of the number of chronic conditions reported in the survivorship survey.

[a] Adjusted for age at diagnosis, race/ethnicity, socioeconomic status (education, income, employment status, and insurance coverage), and any history of other cancer excluding NMSC.

[b] Adjusted for age at diagnosis, race/ethnicity, and menopausal status.

[c] Borderline results for both ER and PR were combined with the any ER(+) or PR(+) category.

[d] Adjusted for age at diagnosis, race/ethnicity, socioeconomic status (education, income, employment status, and insurance coverage), any history of other cancer excluding NMSC, and cancer stage.

[e] Analysis was limited to women who underwent mastectomy (n = 1162).

[f] Analysis was limited to women with ER(+) or PR(+) breast cancer (n = 2039).

[g] Adjusted for age at diagnosis, race/ethnicity, socioeconomic status (education, income, employment status, and insurance coverage), any history of other cancer excluding NMSC, cancer stage, and cancer treatment.

[h] Adjusted for age at diagnosis, race/ethnicity, any history of other cancer excluding NMSC, cancer stage, hormone receptor status, and cancer treatment.

[j] Adjusted for age at diagnosis, cancer stage, and race/ethnicity.

[j] Analysis was limited to women who underwent any breast surgery (n = 2425).

[k] Adjusted for age at diagnosis, race/ethnicity, and time from diagnosis to survey.

[l] Analysis was limited to women who underwent mastectomy (n = 1162).

[m] Analysis was limited to women who underwent breast reconstruction surgery (n = 785).

TABLE 3.

Multivariable Analyses of Associations Between PROMIS T Scores and All-Cause Mortality

	Alive (n = 2368)	All-Cause Deaths (n = 85)	Adjusted HR (95% CI)[a]
Physical health[b]			
Decrease in PROMIS T score (continuous), mean (SD)	51.8 (8.1)	42.6 (8.0)	1.08 (1.05–1.11)
Good (T score ≥ 1 SD below US population mean), No. of participants	2120	49	Reference
Poor (T score < 1 SD below US population mean), No. of participants	241	36	3.14 (1.92–5.14)
Mental health[c]			
Decrease in PROMIS T score (continuous), mean (SD)	51.7 (9.0)	46.4 (9.7)	1.03 (1.01–1.06)
Good (T score ≥ 1 SD below US population mean), No. of participants	2119	60	Reference
Poor (T score < 1 SD below US population mean), No. of participants	245	25	2.24 (1.31–3.83)

Abbreviations: CI, confidence interval; HR, hazard ratio; HRQOL, health-related quality of life; PROMIS, Patient-Reported Outcomes Measurement Information System; SD, standard deviation.

Higher PROMIS T scores represent better HRQOL.

[a]HRs were adjusted for age at diagnosis; time from diagnosis to survey; menopausal status at diagnosis; cancer stage; hormone receptor status; cancer treatment; comorbidity score; and any experience of recent recurrence, metastasis, or secondary malignancy.

[b]Seven women with missing physical HRQOL scores were excluded.

[c]Four women with missing mental HRQOL scores were excluded.