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Differential impact of symptom prevalence and chronic conditions on quality of life in cancer survivors and non-cancer individuals: a population study

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Abstract

Background—To compare associations of symptom prevalence, chronic conditions, and health-related quality of life (HRQOL) between cancer survivors and non-cancer individuals using the U.S. National Health Interview Survey.

Methods—Study samples comprised 604 survivors and 6,166 non-cancer individuals. Symptoms included sensation abnormality, pain, fatigue, cognitive disturbance, depression, and anxiety. Physical and mental HRQOL was measured by the Patient-Reported Outcomes Measurement Information System.

Results—Compared to non-cancer individuals, survivors had higher prevalence in sensation abnormality (OR=2.4; 95% CI=1.9 to 3.0), pain (OR=2.1; 95% CI=1.7 to 2.6), and fatigue (OR=1.4; 95% CI=1.1 to 1.8), and decremented physical HRQOL (difference=−3.7; 95% CI=−4.7 to −2.6). Prevalence of individual symptoms was significantly associated with decremented physical HRQOL (range=−5.9 [anxiety] to −8.9 [pain]) and mental HRQOL (range=−4.7 [sensation] to −8.4 [depression]). Association between cancer experience and physical and mental HRQOL was chiefly explained by the prevalence of six symptoms and presence of chronic conditions. Pain (beta=−4.0; 95% CI=−4.5 to −3.6) and ≥2 chronic conditions (beta=−9.2; 95% CI=−10.2 to −8.2) significantly decremented physical HRQOL. Depression (beta=−5.2; 95% CI=−5.8 to −4.6) and ≥2 chronic conditions (beta=−3.3; 95% CI=−4.4 to −2.3) significantly decremented mental HRQOL.

Conclusions—Cancer survivors experience more symptom burden than non-cancer individuals, which is associated with more chronic conditions and impaired HRQOL.

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AVAILABILITY OF DATA AND MATERIAL

The dataset generated for statistical analyses during the current study is available through the U.S. CDC's website (http://www.cdc.gov/nchs/nhis/nhis_2010_data_release.htm). The dataset is also available from the corresponding author on reasonable request.

Impacts—Interventions to manage symptom prevalence especially for older cancer survivors and survivors with more chronic conditions may improve their HRQOL outcomes.

Keywords

Cancer survivors; chronic conditions; National Health Interview Survey; non-cancer individuals; quality of life; symptoms

INTRODUCTION

In 2014, approximately 15 million Americans were cancer survivors, and this number will reach 19 million by 2024 (1). Following anticancer therapy, survivors may develop late effects inclusive of second malignancy, various chronic conditions, and physical and psychological symptoms. Maintaining normal daily activity and quality of life is the primary goal of cancer survivorship.

A recent study based on the National Health Interview Survey (NHIS) found that 25% and 10% of cancer survivors in the U.S. had suboptimal physical and mental health-related quality of (HRQOL), respectively (2). Although vulnerable demographic and treatment factors have been associated with impaired HRQOL (2), these factors are antecedent to survivors' HRQOL. In contrast, symptom prevalence and chronic conditions are deemed to be the proximal factors on the impact of daily functioning or quality of life (3).

Previous research suggests that cancer survivors without chronic conditions had equivalent or better HRQOL than general population with chronic conditions (4, 5); yet survivors had decremented HRQOL if they developed chronic conditions. Compared to the general population, cancer survivors with more chronic conditions are more likely to co-occur different symptoms (6). Indeed, the mechanisms between the prevalence of multiple symptoms and chronic conditions are complicated, and the relative impact of symptom prevalence and chronic conditions on HRQOL in cancer survivors are understudied. In an era of patient-centered oncological care, specific attention has been paid to address the issues related to symptom burden that represent one's perceived abnormal physical, emotional, cognitive, or psychosomatic state (7, 8).

Symptom burden has been commonly investigated in cancer patients during and shortly after completion of therapy but not in long-term survivors (5 years post-diagnosis). Symptoms resulting from anticancer therapy can persist over time, and new symptoms may emerge decades after therapy completion. A rehabilitation study found that survivors 10 years post-diagnosis had symptom prevalence above the severe threshold, including fatigue (65%), sleep disturbance (46%), lack of concentration (45%), and joint/muscle pain (44%) (9). Symptom prevalence in cancer populations, especially fatigue, has a strong predictive validity for survival (10). Our previous study demonstrated that prevalence of 12 symptoms (e.g., pain, perceived cognitive problems, distress, and sensation abnormalities) in adult survivors of childhood cancer was independently associated with decreased HRQOL (11). Prevalence of these symptoms explained 60% and 56% of the variance in the SF-36's physical and mental summary scores (PCS/MCS), respectively, whereas demographic and clinical variables explained up to 15% and 10% of the variance in PCS and MCS,

respectively. However, how socio-demographic factors, cancer experience (i.e., survivors vs. non-cancer individuals) and chronic conditions are related to symptom prevalence, as well as the extent to which these factors collectively impact HRQOL were not evaluated in the previous study.

It is our hope to treat symptoms as an avenue toward improving daily activity and HRQOL of cancer survivors. Clinical implications for this initiative can be intensified if the prevalence of symptom phenotypes is high in cancer survivors vs. non-cancer individuals and if the association of decreased HRQOL with cancer experience is significantly explained by symptom prevalence. Previous HRQOL studies in cancer survivorship often used convenience or matched samples as comparison groups (12); however, most studies have not taken symptom prevalence into consideration. It is therefore not surprising that mixed evidence has emerged (13), including worse (12, 14) and equivalent (15, 16) HRQOL between survivors and comparison groups.

This study addressed two specific aims: Aim 1 was to compare the prevalence of six symptom phenotypes (sensation abnormality, pain, fatigue, cognitive disturbance, depressive symptom, and anxiety) between survivors of adult cancers and non-cancer individuals, and identify the determinants for the prevalence of individual symptoms. Aim 2 was to examine the association between cancer experience and HRQOL by accounting for the influence of the six selected symptom prevalence, chronic conditions, and socio-demographic factors. We hypothesize that the prevalence of individual symptom phenotypes is higher and HRQOL is worse in cancer survivors than non-cancer individuals. Additionally, we hypothesize that both symptom prevalence and co-occurring chronic conditions will significantly impact HRQOL regardless of the status of survivorship, and the effect of multiple symptoms on HRQOL will be larger than that of chronic conditions. This study used 2010 NHIS data comprised of representative cancer survivors and non-cancer non-institutionalized individuals in the U.S; therefore, our findings can be generalized to the non-institutionalized U.S. population.

MATERIALS AND METHODS

Study participants

NHIS is an annual survey conducted by the U.S. Center for Disease Control and Prevention through computer-assisted personal interviews to investigate health status and utilization issues (17). A national representative sample using households was selected by means of a complex sampling framework.

The survey is comprised of three core components (family, sample adult, and sample child) and different supplements focusing on specific public health issues. In this study, family and sample adult components as well as cancer control and quality of life supplements were used. The cancer control supplement is completed every five years and the quality of life supplement was completed in 2010. All members of the household 18 years of age and above who were at home at the time of the survey were invited to complete the family component. One adult per household was randomly selected to complete the sample adult

component and cancer control supplement; one quarter of the sample adults were randomly selected to complete the quality of life supplement.

Given the use of secondary, de-identified data from the U.S. federal government which is also publicly available, a waiver was granted by Institutional Review Board of University of Florida where the study was conducted.

Measures

Symptom phenotypes—Because items capturing the concept of symptom prevalence are scattered throughout the NHIS and standard symptom tools are not used by the NHIS, we developed a three-step strategy to identify appropriate symptom items. The first step was to create a list of symptom phenotypes based on the framework of our previous study (11). The second step was to search for the items measuring symptoms listed in the sample adult component and quality of life supplement of the questionnaire. Individual items were independently documented using an extraction form by the first author and a research coordinator. Each item was assigned to one of the symptom phenotypes based on the previous study's framework (11), and then classified by the following attributes: symptom presence, symptom intensity, and symptom behavior. Only items measuring the attribute of symptom presence were included in this study. The third step was for the two co-authors (ICH and KRK) to evaluate the quality of individual items and select appropriate items. Discrepancies were adjudicated by consensus in a group meeting.

The research team established *a priori* criteria to set aside items containing a vague concept of symptoms or having no clear time frame. In total, 18 out of 65 items were retained to capture the prevalence of the six symptom phenotypes: sensation abnormality (6 items), pain (6 items), fatigue (1 item), cognitive disturbance (3 items), depression (1 item), and anxiety (1 item) (Table 1). Symptom presence was denoted if individuals endorsed "yes," "some days/most days/every day," or "some difficulty/a lot of difficulty" for items measuring a specific phonotype.

HRQOL—HRQOL was self-reported using the Global Health Scale of the Patient-Reported Outcomes Measurement Information System (PROMIS®). PROMIS applies modern test theory to develop reliable, valid, flexible, and precise tools for assessing HRQOL (18). The Global Health Scale is a 10-item scale measuring physical and mental HRQOL (19). The scores of individuals' physical and mental HRQOL were calculated and normalized to T-scores (mean=50, SD=10). Higher scores indicate better HRQOL.

Socio-demographics, clinical, and cancer-related variables—Several important socio-demographic characteristics collected from the NHIS were used in analyses. Race/ethnicity was grouped as Hispanic, non-Hispanic White, non-Hispanic Black, Non-Hispanic Asian, and non-Hispanic other. Marital status was classified as separated, divorced, married, single/never married, and widowed. Education was classified as below high school, high school/GED, some college, bachelor degree, and graduate degree. For clinical variables, chronic conditions were self-reported by cancer survivors and non-cancer individuals; type of cancer and anticancer therapy were self-reported by cancer survivors. Years since cancer diagnosis was calculated based on the difference between year at diagnosis and year at

interview. Survivors with <5 vs. ≥ 5 years since diagnosis were defined as recent and long-term survivors, respectively. Chronic conditions were selected based on known primary conditions (20) and classified by the absolute number (none, 1, and 2 and above).

Statistical analyses

Standard psychometric analyses were performed to test measurement properties of the symptom phenotypes used in this study; these methods include the Kuder-Richardson Formula-20 for estimating scale reliability and confirmatory factory analysis for testing construct validity. To test Aim 1, raw differences in the prevalence of individual symptom phenotypes between cancer survivors and non-cancer individuals were compared using odds ratios (ORs) by conducting logistic regression. The independent effect of cancer experience (survivors vs. non-cancer individuals) on the prevalence of each symptom was compared using ORs by conducting logistic regression adjusted for chronic conditions, age, sex, race/ethnicity, marital status, and education. To test Aim 2, raw differences in physical/mental HRQOL associated with the prevalence of each symptom phenotype were tested using t-tests. The independent effect of all symptoms and cancer experience (survivors vs. those without cancer) on physical/mental HRQOL was tested using linear regression adjusted for the aforementioned covariates. We performed a two-step approach (i.e., two models) to test the impact of cancer experience on HRQOL. Model 1 included individual symptom phenotypes plus socio-demographic variables as predictors of HRQOL, and Model 2 included number of chronic health conditions in addition to the predictors described in Model 1. Since some individuals who experience symptoms also have co-occurring chronic health conditions that further impact HRQOL (6, 21), this two-step approach helps elucidate whether the inclusion of chronic health conditions influences the estimated association of cancer experience with HRQOL when prevalence of individual symptoms is included in the model. All analyses were performed by STATA 13.1 through the weighted procedures to address unequal probability of selection due to a complex sampling design of the NHIS.

RESULTS

Participant characteristics (Table 2)

Of the 6,770 participants, 604 were cancer survivors and 6,166 did not have a cancer history. The sample is representative of the approximately 230 million U.S. non-institutionalized adults (cancer survivors: 8.9%; non-cancer individuals: 91.1%). Half of the cancer survivors (49.9%) were ≥65 years of age which was higher than non-cancer individuals (13.7%; $p<0.001$). More survivors were female (56.6%) and non-Hispanic White (85.6%) compared to non-cancer individuals (51.2% female, 66.8% non-Hispanic White; p's<0.001). More survivors reported having at least one chronic condition (45.3%) than non-cancer individuals (22.0%; $p<0.001$). Approximately 66% of the survivors were long-term survivors.

Prevalence of symptom phenotypes and HRQOL between survivors and non-cancer individuals: bivariate analyses (Table 3)

Psychometric analysis reveals acceptable scale reliability and construct validity (Table 1). Cancer survivors overall reported a higher prevalence of individual symptom phenotypes than non-cancer individuals in sensation abnormality (61.0% vs. 39.3%; $p<0.001$), pain

(73.5% vs. 56.6%; p<0.001), fatigue (68.6% vs. 61.0%; p<0.01), cognitive disturbance (32.2% vs. 21.1%; p<0.001), depression (43.4% vs. 41.2%; p>0.05), and anxiety (62.9% vs. 59.4%; p>0.05). Long-term survivors had a slightly higher prevalence in individual symptom phenotypes (except fatigue) than did recent survivors. Without adjusting for covariates, ORs of symptom prevalence were significantly higher for survivors in sensation (OR=2.4; 95% CI=1.9 to 3.0), pain (OR=2.1; 95% CI=1.7 to 2.6), fatigue (OR=1.4; 95% CI=1.1 to 1.8), and cognitive disturbance (OR=1.8; 95% CI=1.4 to 2.3). Compared to non-cancer individuals, survivors reported significantly lower raw physical HRQOL scores (−3.7; 95% CI=−4.7 to −2.6), but equivalent raw mental HRQOL scores.

Association of symptom prevalence with HRQOL: bivariate analyses (Table 4)

Among the six symptoms, individuals experiencing pain had the largest decrease in physical HRQOL scores when compared to those without pain (−8.9), followed by cognitive disturbance vs. no (−8.4), fatigue vs. no (−7.8), depressive symptom vs. no (−7.1), sensation abnormality vs. no (−6.1), and anxiety vs. no (−5.9) (p's<0.001). In contrast, individuals experiencing depressive symptom had the largest decrease in mental HRQOL scores when compared to those without depressive symptom (−8.4), followed by cognitive disturbance vs. no (−7.9), anxiety vs. no (−6.6), fatigue and pain vs. no (both −5.5), and sensation abnormality vs. no (−4.7) (p's<0.001).

Effects of socio-demographic, clinical, and cancer experience factors on the prevalence of individual symptoms: multivariable analyses (Table 5)

Compared to non-cancer individuals, survivors had significantly higher odds of experiencing sensation abnormality (OR=1.3; 95% CI=1.0 to 1.7), pain (OR=1.5; 95% CI=1.1 to 1.9), and fatigue (OR=1.4; 95% CI=1.1 to 1.8) after adjusting for various covariates. Individuals having more chronic conditions had significantly higher odds of experiencing all six symptoms than those having fewer chronic conditions (p's<0.001). Specifically, having ≥2 and 1 chronic conditions increased the odds of pain by approximately 27-fold (95% CI=16.8 to 44.3) and 7-fold (95% CI=5.3 to 8.2), respectively, when compared to having no chronic conditions. Additionally, having an older age at the time of the survey was associated with higher odds of sensation abnormality and cognitive disturbance but lower odds of fatigue and anxiety. Females were more likely to report pain (OR=1.4; 95% CI=1.2 to 1.6), fatigue (OR=1.7; 95% CI=1.5 to 1.9), depressive symptom (OR=1.6; 95% CI=1.4 to 1.8), and anxiety (OR=1.6; 95% CI=1.4 to 1.8) than males.

Effects of symptom prevalence and cancer experience on HRQOL: multivariable analyses (Table 6)

Multivariable analyses revealed that prevalence of six symptoms and chronic conditions independently impacted physical HRQOL (Model 1b). Cancer experience impacted physical HROQL only when chronic conditions were excluded from the analysis (Model 1a). Pain had the strongest impact on physical HRQOL (beta=−4.0; 95% CI=−4.5 to −3.6), followed by fatigue (beta=−3.3; 95% CI=−3.8 to −2.9), depressive symptom (beta=−2.5; 95% CI=−3.1 to −2.0), cognitive disturbance (beta=−2.3; 95% CI=−2.9 to −1.8), sensation abnormality (beta=−1.1; 95% CI=−1.5 to −0.7), and anxiety (beta=−0.9; 95% CI=−1.4 to −0.4). Individuals having 1 and ≥2 chronic conditions reported decremented physical

HRQOL by 4.8 points (95% CI=−5.5 to −4.1) and 9.2 points (95% CI=−10.2 to −8.2) compared to those without chronic conditions, respectively. Across the two models, decremented physical HRQOL was significantly associated with older age, non-Hispanic Black (vs. non-Hispanic White), and lower education (below high school, high school/GED, and some college vs. graduate degree).

Symptom prevalence alone rather than cancer experience significantly impacted mental HRQOL regardless of the inclusion of chronic conditions (Models 2a and 2b). After adjusting for chronic conditions, prevalence of depressive symptom had the strongest effect on mental HRQOL (beta=−5.2; 95% CI=−5.8 to −4.6), followed by cognitive disturbance (beta=−3.3; 95% CI=−4.0 to −2.7), anxiety (beta=−1.9; 95% CI=−2.4 to −1.3), pain (beta=−1.8; 95% CI=−2.2 to −1.3), fatigue (beta=−1.2; 95% CI=−1.7 to −0.7), and sensation abnormality (beta=−0.9; 95% CI=−1.4 to −0.4). Individuals occurring with 1 and ≥2 chronic conditions had decremented mental HRQOL by 1.8 points (95% CI=−2.5 to −1.1) and 3.3 points (95% CI=−4.4 to −2.3) compared to those without chronic conditions, respectively. Across the two models, decremented mental HRQOL was significantly related to being currently unmarried (separated, divorced, single/never married, and widowed status vs. married), and having a lower education (below high school, high school/GED, some college, and bachelor degree vs. graduate degree).

DISCUSSION

This study demonstrates that cancer survivors experienced a significantly higher symptom prevalence, especially in sensation abnormality, pain, and fatigue, than non-cancer individuals. Chronic conditions were significantly related to the prevalence of all six symptoms. Survivors reported significantly worse physical HRQOL than non-cancer individuals, yet survivorship status did not significantly affect mental HRQOL. Instead of cancer experience, both prevalence of symptom phenotypes and chronic conditions independently impacted physical and mental HRQOL. Older age, non-Hispanic Black, currently being unmarried, and lower education were related to decremented physical and/or mental HRQOL.

Because survivors of adult cancers tend to be older in age, a higher prevalence of symptom phenotypes may be due to issues related to aging (e.g., more chronic conditions) (22). Indeed, we found that the presence of individual symptoms was linked to a greater number of chronic conditions. We further discovered that the inclusion of chronic conditions alongside socio-demographic factors in the multivariable models indicated a higher prevalence of individual symptom phenotypes (e.g., sensation abnormality, pain, and fatigue) among cancer survivors compared to that reported by non-cancer individuals (Table 5). This finding implies that chronic conditions and socio-demographics alone may not fully explain the variation of symptom burden, and the residual symptom burden in cancer survivors may be caused by symptom-specific mechanisms, particularly in relation to treatment exposures, such as autonomic nervous system activation, systemic inflammation, alteration of hypothalamic-pituitary-adrenal axis, and endothelial dysfunction (23). Longitudinal studies evaluating the onset of individual symptoms beginning with therapy completion and continuing throughout different survivorship stages are required to guide the

development of a heuristic model for elucidating the complex nature of symptoms related to toxic therapy, aging, and chronic conditions.

Most impressively, we observed that cancer survivors and non-cancer individuals reported comparable physical and mental HRQOL given the same magnitude of symptom burden (insignificant coefficients −0.65 and −0.23 on cancer experience; Table 6). However, physical and mental HRQOL is substantially decreased (approximately 14 points or 1.4 SD on both domains; Table 6) among cancer and non-cancer individuals who experienced all six symptoms compared to that of asymptomatic individuals. Our study also suggests that the effect of multiple symptoms on HRQOL seems larger than that of chronic conditions, which is consistent with the previous cancer survivorship studies (24, 25). Interestingly, the magnitude of all six symptoms (Table 6) was smaller than the summated effects of individual symptoms on physical and mental HRQOL (approximately 30 and 32 points or 3.0 and 3.2SD, respectively; results upon request), suggesting the effects of individual symptoms on HRQOL are antagonistic rather than additive. Although our study highlights the influence of symptom prevalence on impaired HRQOL after controlling for chronic conditions and socio-demographics, other factors related to survivorship (e.g., poor coping skill and social support) (26, 27) that are not being measured by the NHIS may explain the residual variance.

We have argued that the mixed results (12–14, 16) of HRQOL between survivors and non-cancer individuals may mislead clinical relevance if symptom burden and chronic conditions are not taken into consideration. Although symptomatology plays a key role in patient-centered oncological research, how symptom manifestation influences our interpretation of health outcomes remains to be determined (28). Cancer survivors often experience two or more concurrent symptoms, known as symptom clusters (29), and multiple symptoms may influence each other and act as mediators to explain the association between cancer experience and HRQOL (3). Cancer patients/survivors with symptom clusters (30) have shown a higher risk of premature death than those without symptom clusters. Although this study focused on the impact of individual symptom prevalence on HRQOL, future studies are warranted to elucidate possible clusters of symptom prevalence and test the association between cluster prevalence and HRQOL. This alternate approach will help identify symptom clusters that may share common etiology for clinical interventions.

Our results have implications for designing prospective research of delayed occurrences of morbidity, mortality, and impaired HRQOL for cancer survivors. If the causal links between symptom burden and future health outcomes are established, symptoms can be used as sentinel indictors of an early diagnosis for adverse events (e.g., unexplained cardiac arrest) (31) and functional status decline. Although survivorship guidelines have noted the importance of screening for symptoms (e.g., fatigue, depression, and anxiety) as an avenue for ascertaining chronic problems (32, 33), cancer survivors have received infrequent screening and inadequate care for symptoms.

This study contains several limitations. First, NHIS collects data from the civilian of non-institutionalized population. Excluding institutionalized individuals who are likely older and severely ill will limit the generalizability of our findings to the entire U.S. population.

Second, cancer information (e.g., diagnosis and treatment) was self-reported by participants. Although experiencing cancer is a significant event, self-reporting may cause information recall bias, especially in elderly participants. Third, symptom phenotypes were generated using the items in NHIS, and measurement properties were determined by content and construct validity. Using standard symptom measures with sophisticated measurement properties is warranted to replicate our findings. Fourth, only six symptom phenotypes were investigated. Excluding other important symptoms (e.g., respiratory, sexual, and sleep disturbance) that were not contained in NHIS may underestimate the impact of symptom burden on HRQOL.

CONCLUSIONS

Compared to non-cancer individuals, cancer survivors suffer significantly from various symptoms, typically sensation abnormality, pain, and fatigue. However, asymptomatic cancer survivors appear to experience physical and mental HRQOL comparable to individuals who have not had cancer. When survivors develop symptoms and chronic conditions, their HRQOL substantially decreases. Interventions to control symptoms especially for older survivors and survivors with more chronic conditions may improve their HRQOL outcomes.

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References

1. DeSantis CE, Lin CC, Mariotto AB, Siegel RL, Stein KD, Kramer JL, et al. Cancer treatment and survivorship statistics, 2014. CA Cancer J Clin. 2014; 64(4):252–71. [PubMed: 24890451]
2. Weaver KE, Forsythe LP, Reeve BB, Alfano CM, Rodriguez JL, Sabatino SA, 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(11):2108–17. [PubMed: 23112268]
3. Wilson IB, Cleary PD. Linking clinical variables with health-related quality of life. A conceptual model of patient outcomes. JAMA. 1995; 273(1):59–65. [PubMed: 7996652]
4. Dowling EC, Chawla N, Forsythe LP, de Moor J, McNeel T, Rozjabek HM, et al. Lost productivity and burden of illness in cancer survivors with and without other chronic conditions. Cancer. 2013; 119(18):3393–401. [PubMed: 23794146]
5. Heins MJ, Korevaar JC, Hopman PE, Donker GA, Schellevis FG, Rijken MP. Health-related quality of life and health care use in cancer survivors compared with patients with chronic diseases. Cancer. 2016; 122(6):962–70. [PubMed: 26748907]
6. Mao JJ, Armstrong K, Bowman MA, Xie SX, Kadakia R, Farrar JT. Symptom burden among cancer survivors: Impact of age and comorbidity. J Am Board Fam Med. 2007; 20(5):434–43. [PubMed: 17823460]
7. Basch E. Missing patients' symptoms in cancer care delivery-the importance of patient-reported outcomes. JAMA Oncol. 2016; 34(6):557–65.

8. Basch E, Deal AM, Kris MG, Scher HI, Hudis CA, Sabbatini P, et al. Symptom monitoring with patient-reported outcomes during routine cancer treatment: A randomized controlled trial. J Clin Oncol. 2016; 34(6):557–65. [PubMed: 26644527]
9. Kjaer TK, Johansen C, Ibfelt E, Christensen J, Rottmann N, Hoybye MT, et al. Impact of symptom burden on health related quality of life of cancer survivors in a Danish cancer rehabilitation program: A longitudinal study. Acta Oncol. 2011; 50(2):223–32. [PubMed: 21091085]
10. Quinten C, Maringwa J, Gotay CC, Martinelli F, Coens C, Reeve BB, et al. Patient self-reports of symptoms and clinician ratings as predictors of overall cancer survival. J Natl Cancer Inst. 2011; 103(24):1851–8. [PubMed: 22157640]
11. Huang IC, Brinkman TM, Kenzik K, Gurney JG, Ness KK, Lanctot J, et al. Association between the prevalence of symptoms and health-related quality of life in adult survivors of childhood cancer: A report from the St. Jude Lifetime Cohort study. J Clin Oncol. 2013; 31(33):4242–51. [PubMed: 24127449]
12. Fossa SD, Hess SL, Dahl AA, Hjermstad MJ, Veenstra M. Stability of health-related quality of life in the Norwegian general population and impact of chronic morbidity in individuals with and without a cancer diagnosis. Acta Oncol. 2007; 46(4):452–61. [PubMed: 17497312]
13. Wu HS, Harden JK. Symptom burden and quality of life in survivorship: A review of the literature. Cancer Nurs. 2015; 38(1):E29–54. [PubMed: 24831042]
14. Mykletun A, Dahl AA, Haaland CF, Bremnes R, Dahl O, Klepp O, et al. Side effects and cancer-related stress determine quality of life in long-term survivors of testicular cancer. J Clin Oncol. 2005; 23(13):3061–8. [PubMed: 15860864]
15. Klein D, Mercier M, Abeilard E, Puyraveau M, Danzon A, Dalstein V, et al. Long-term quality of life after breast cancer: A French registry-based controlled study. Breast Cancer Res Treat. 2011; 129(1):125–34. [PubMed: 21340477]
16. Wikman A, Djarv T, Johar A, Lagergren P. Health-related quality of life does not differ between short-term, long-term and very long-term cancer survivors in the Swedish general population. Psychooncology. 2013; 22(6):1369–74. [PubMed: 22888065]
17. Schiller JS, Lucas JW, Ward BW, Peregoy JA. Summary health statistics for U.S. adults: National Health Interview Survey, 2010. Vital Health Stat. 2012; 10(252):1–207.
18. Cella D, Riley W, Stone A, Rothrock N, Reeve B, Yount S, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005–2008. J Clin Epidemiol. 2010; 63(11):1179–94. [PubMed: 20685078]
19. 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(7):873–80. [PubMed: 19543809]
20. Yabroff KR, Lawrence WF, Clauser S, Davis WW, Brown ML. Burden of illness in cancer survivors: Findings from a population-based national sample. J Natl Cancer Inst. 2004; 96(17): 1322–30. [PubMed: 15339970]
21. Klassen AF, Anthony SJ, Khan A, Sung L, Klaassen R. Identifying determinants of quality of life of children with cancer and childhood cancer survivors: A systematic review. Support Care Cancer. 2011; 19(9):1275–87. [PubMed: 21611865]
22. Keating NL, Norredam M, Landrum MB, Huskamp HA, Meara E. Physical and mental health status of older long-term cancer survivors. J Am Geriatr Soc. 2005; 53(12):2145–52. [PubMed: 16398900]
23. Whooley MA, Wong JM. Depression and cardiovascular disorders. Annu Rev Clin Psychol. 2013; 9:327–54. [PubMed: 23537487]
24. Cohen HJ, Lan L, Archer L, Kornblith AB. Impact of age, comorbidity and symptoms on physical function in long-term breast cancer survivors (CALGB 70803). J Geriatr Oncol. 2012; 3(2):82–9. [PubMed: 22707996]
25. Deimling GT, Arendt JA, Kypriotakis G, Bowman KF. Functioning of older, long-term cancer survivors: The role of cancer and comorbidities. J Am Geriatr Soc. 2009; 57(Suppl 2):S289–92. [PubMed: 20122020]

26. Kenzik K, Huang IC, Rizzo JD, Shenkman E, Wingard J. Relationships among symptoms, psychosocial factors, and health-related quality of life in hematopoietic stem cell transplant survivors. Support Care Cancer. 2015; 23(3):797–807. [PubMed: 25193598]
27. Kroenke CH, Kwan ML, Neugut AI, Ergas IJ, Wright JD, Caan BJ, et al. Social networks, social support mechanisms, and quality of life after breast cancer diagnosis. Breast Cancer Res Treat. 2013; 139(2):515–27. [PubMed: 23657404]
28. Trotti A, Colevas AD, Setser A, Basch E. Patient-reported outcomes and the evolution of adverse event reporting in oncology. J Clin Oncol. 2007; 25(32):5121–7. [PubMed: 17991931]
29. Dodd MJ, Miaskowski C, Paul SM. Symptom clusters and their effect on the functional status of patients with cancer. Oncol Nurs Forum. 2001; 28(3):465–70. [PubMed: 11338755]
30. Cheville AL, Novotny PJ, Sloan JA, Basford JR, Wampfler JA, Garces YI, et al. The value of a symptom cluster of fatigue, dyspnea, and cough in predicting clinical outcomes in lung cancer survivors. J Pain Symptom Manage. 2011; 42(2):213–21. [PubMed: 21398089]
31. Krahn AD, Healey JS, Simpson CS, Chauhan VS, Birnie DH, Champagne J, et al. Sentinel symptoms in patients with unexplained cardiac arrest: From the cardiac arrest survivors with preserved ejection fraction registry (CASPER). J Cardiovasc Electrophysiol. 2012; 23(1):60–6. [PubMed: 21955300]
32. Andersen BL, DeRubeis RJ, Berman BS, Gruman J, Champion VL, Massie MJ, et al. Screening, assessment, and care of anxiety and depressive symptoms in adults with cancer: An American Society of Clinical Oncology guideline adaptation. J Clin Oncol. 2014; 32(15):1605–19. [PubMed: 24733793]
33. Bower JE, Bak K, Berger A, Breitbart W, Escalante CP, Ganz PA, et al. Screening, assessment, and management of fatigue in adult survivors of cancer: An American Society of Clinical Oncology Clinical Practice Guideline Adaptation. J Clin Oncol. 2014; 32(17):1840–50. [PubMed: 24733803]

Table 1

Items selected from the 2010 NHIS for measuring the concept of six symptom phenotypes

Symptom	Item
Sensation abnormality	Item content: • Do you have difficulty seeing, even when wearing glasses? … Would you say no difficulty, some difficulty, a lot of difficulty, or are you unable to do this? • Do you have difficulty clearly seeing someone's face across a room? … Would you say no difficulty, some difficulty, a lot of difficulty, or are you unable to do this? • Do you have difficulty clearly seeing the picture on a coin? … Would you say no difficulty, some difficulty, a lot of difficulty, or are you unable to do this? • Do you have difficulty hearing, even when using a hearing aid? … Would you say no difficulty, some difficulty, a lot of difficulty, or are you unable to do this? • Do you have difficulty hearing what is said in a conversation with one other person in a quiet room? … Would you say no difficulty, some difficulty, a lot of difficulty, or are you unable to do this? • Do you have difficulty hearing what is said in a conversation with one other person in a noisier room? … Would you say no difficulty, some difficulty, a lot of difficulty, or are you unable to do this? Measurement properties: • Scale reliability: Kuder–Richardson Formula-20 (KR-20)=0.70 • Construct validity: RMSEA=0.03; CFI=0.96
Pain	Item content: • Did you have severe headache or migraine? • Did you have neck pain? • Did you have low back pain? • Have you had any symptoms of pain, aching, or stiffness in or around a joint? • Did you have facial ache or pain in the jaw muscles or the joint in front of the ear? • Do you have frequent pain? Measurement properties: • Scale reliability: Kuder–Richardson Formula-20 (KR-20)=0.71 • Construct validity: RMSEA=0.04; CFI=0.98
Fatigue	Item content: • How often did you feel very tired or exhausted? … Would you say never, some days, most days, or every day?
Cognitive disturbance	• Do you have difficulty remembering or concentrating? … Would you say no difficulty, some difficulty, a lot of difficulty, or are you unable to do this? • Do you have difficulty learning the rules for a new game? … Would you say no difficulty, some difficulty, a lot of difficulty, or are you unable to do this? • Do you have difficulty understanding and following instructions for example, to use a cell phone or to get to a new place? … Would you say no difficulty, some difficulty, a lot of difficulty, or are you unable to do this? Measurement properties: • Scale reliability: Kuder–Richardson Formula-20 (KR-20)=0.72 • Construct validity: RMSEA=0.01; CFI=0.99
Depression	Item content: • How often do you feel depressed? … Would you say daily, weekly, monthly, a few times a year, or never?

Symptom	Item
	Measurement properties: • N/A: based on a single item
Anxiety	Item content: • How often do you feel worried, nervous or anxious? … Would you say daily, weekly, monthly, a few times a year, or never? Measurement properties: • N/A: based on a single item

RMSEA: root mean square error of approximation; CFI: confirmatory fit index

Cut-points for acceptable models include KR-20≥0.7; RMSEA<0.06; CFI>0.95.

Table 2

Characteristics of cancer survivors and non-cancer individuals from the 2010 NHIS (N=6,770)

	Cancer survivors (N=604)	Non-cancer individuals (N=6,166)	
	Raw N (%) #	Raw N (%) #	Statistical difference
Age at survey (years)			
18–44.9	53 (9.85)	3,082 (51.83)	X^2=276.10 (p<0.001)
45–64.9	229 (40.27)	2,028 (34.51)	
≥65	322 (49.86)	1,056 (13.65)	
Gender			
Male	234 (43.44)	2,782 (48.83)	X^2=4.81 (p<0.05)
Female	370 (56.56)	3,384 (51.17)	
Race/ethnicity			
Hispanic	49 (5.87)	1,219 (14.78)	X^2=106.29 (p<0.001)
Non-Hispanic White	475 (85.63)	3,458 (66.80)	
Non-Hispanic Black	66 (6.52)	1,048 (12.48)	
Non-Hispanic Asian	10 (1.39)	402 (5.02)	
Non-Hispanic other races	4 (0.58)	39 (0.93)	
Marital status			
Separated	23 (3.17)	239 (2.62)	X^2=166.67 (p<0.001)
Divorced	112 (14.43)	856 (10.57)	
Married	271 (57.26)	2,719 (53.87)	
Single/never married	59 (8.31)	1,804 (27.53)	
Widowed	137 (16.84)	523 (5.41)	
Education			
Below high school	87 (12.84)	1,053 (14.16)	X^2=7.49 (p=0.119)
High school/GED	151 (25.45)	1,641 (27.15)	
Some college	199 (32.75)	1,833 (30.87)	
Bachelor degree	92 (15.80)	1,071 (18.83)	
Graduate degree	73 (13.16)	540 (8.99)	
Number of non-cancer chronic conditions			
None	321 (54.70)	4,722 (78.05)	X^2=75.59 (p<0.001)
1	208 (32.92)	1,065 (16.60)	
2	47 (8.73)	221 (3.06)	
3	17 (2.20)	83 (1.20)	
≥4	11 (1.44)	75 (1.09)	
Cancer sites by human body systems			
Blood/circulation	27 (4.16)	–	
Bone	7 (0.95)	–	
Brain	2 (0.42)	–	

	Cancer survivors (N=604)	Non-cancer individuals (N=6,166)	
	Raw N (%) #	Raw N (%) #	Statistical difference
Breast (female only)	127 (32.56)	–	
Digestive system	60 (8.85)	–	
Endocrine system	13 (2.08)	–	
Genitourinary system	20 (3.41)	–	
Reproductive system	165 (28.72)	–	
Head and neck	5 (1.11)	–	
Respiratory	19 (3.12)	–	
Skin	189 (34.32)	–	
Soft tissue	1 (0.27)	–	
Cancer-related therapy			
Surgery	391 (72.38)	–	
Chemotherapy	120 (21.01)	–	
Radiotherapy	105 (19.23)	–	
Hormonal therapy	37 (5.90)	–	
Bone marrow/steam cell transplant	2 (0.25)	–	
Years since cancer diagnosis			
<5	200 (34.40)	–	
5–14.9	233 (37.97)	–	
15–24.9	89 (14.06)	–	
≥25	82 (13.57)	–	

% was weighted to reflect the entire U.S. non-institutionalized adults (N=229,377,665; ≥18 years of age) including cancer survivors (8.9%) and non-cancer individuals (91.1%).

Table 3

Bivariate analysis for the difference in symptom prevalence and HRQOL between cancer survivors and non-cancer individuals[#]

	All cancer survivors[†] (Recent and long-term)	Recent survivors[†]	Long-term survivors[†]	Non-cancer individuals (Reference)[†]
Sensation abnormality				
Prevalence, %	60.99	59.16	62.22	39.28
OR (95% CI)[‡]	2.42*** (1.92, 3.04)	2.24*** (1.59, 3.16)	2.55*** (1.91, 3.39)	1.00
Pain				
Prevalence, %	73.47	71.87	74.56	56.63
OR (95% CI)[‡]	2.12*** (1.71, 2.64)	1.95*** (1.38, 2.77)	2.24*** (1.72, 2.93)	1.00
Fatigue				
Prevalence, %	68.58	69.70	67.84	60.99
OR (95% CI)[‡]	1.40** (1.11, 1.76)	1.47* (1.03, 2.10)	1.35 (0.99, 1.83)	1.00
Cognitive disturbance				
Prevalence, %	32.22	30.24	33.55	21.07
OR (95% CI)[‡]	1.78*** (1.40, 2.26)	1.62** (1.15, 2.28)	1.89*** (1.41, 2.54)	1.00
Depression				
Prevalence, %	43.43	43.09	43.65	41.23
OR (95% CI)[‡]	1.09 (0.87, 1.37)	1.08 (0.08, 1.50)	1.10 (0.83, 1.46)	1.00
Anxiety				
Prevalence, %	62.86	58.82	65.55	59.35
OR (95% CI)[‡]	1.16 (0.94, 1.44)	0.98 (0.69, 1.39)	1.30* (1.01, 1.69)	1.00
Physical HRQOL				
Raw score	49.60	49.31	49.79	53.24
Difference (95% CI)[‡]	−3.65*** (−4.71, −2.58)	−3.46*** (−4.73, −2.18)	−3.93*** (−5.68, −2.18)	1.00
Mental HRQOL				
Raw score	52.76	52.77	52.76	53.85
Difference (95% CI)[‡]	−1.09 (−2.19, 0.02)	−1.09 (−2.49, 0.31)	−1.09 (−2.57, 0.40)	0

[#]Numbers in the Table were weighted to represent the entire U.S. non-institutionalized adults.

[†]Two models were implemented: Model 1 compared the difference between all cancer survivors and non-cancer individuals (two groups), and Model 2 compared difference between recent survivors, long-term survivors, and non-cancer individuals (three groups).

[‡]Raw ORs and differences without covariate adjustment.

*p<0.05;

**p<0.01,

*** p<0.001.

Table 4

Bivariate analysis for HRQOL differences by the prevalence of individual symptoms[#]

	Physical HRQOL			Mental HRQOL		
	Symptom presence	**No symptom presence**	**Difference (95% CI)[†]**	**Symptom presence**	**No symptom presence**	**Difference (95% CI)[†]**
Sensation abnormality	49.37	55.43	−6.06*** (−6.58, −5.53)	50.99	55.69	−4.70*** (−5.26, −4.15)
Pain	49.04	57.90	−8.86*** (−9.35, −8.36)	51.37	56.85	−5.48*** (−5.97, −5.00)
Fatigue	50.00	57.76	−7.76*** (−8.28, −7.25)	51.68	57.17	−5.49*** (−6.03, −4.95)
Cognition disturbance	46.40	54.82	−8.42*** (−9.12, −7.71)	47.64	55.50	−7.86*** (−8.55, −7.18)
Depression	48.86	55.94	−7.08*** (−7.61, −6.55)	48.88	57.32	−8.44*** (−8.97, −7.89)
Anxiety	50.59	56.52	−5.93*** (−6.44, −5.43)	51.15	57.71	−6.56*** (−7.06, −6.06)

[#]Numbers in the Table were weighted to represent the entire U.S. non-institutionalized adults.

[†]Raw difference without covariate adjustment.

***p<0.001.

Table 5

Multivariable analysis for the factors contributing to the prevalence of individual symptoms[#]

	Sensation abnormality[†]	Pain[†]	Fatigue[†]	Cognitive disturbance[†]	Depression[†]	Anxiety[†]
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Cancer experience (Ref: Non-cancer individuals)						
Cancer survivors	1.31* (1.01, 1.70)	1.47** (1.14, 1.89)	1.36* (1.05, 1.75)	1.05 (0.80, 1.39)	1.05 (0.81, 1.35)	1.18 (0.94, 1.48)
Number of chronic conditions (Ref: none)						
1	2.27*** (1.92, 2.69)	6.58*** (5.30, 8.16)	3.40*** (2.76, 4.17)	3.01*** (2.46, 3.69)	2.38*** (2.00, 2.85)	2.37*** (2.00, 2.80)
2 and above	4.49*** (3.35, 6.03)	27.02*** (16.8, 44.3)	6.48*** (4.58, 9.16)	3.66*** (4.98, 8.88)	3.68*** (2.82, 4.81)	3.65*** (2.67, 5.00)
Age at survey (Ref: 18–44.9 years old)						
45–64.9 years old	1.73*** (1.47, 2.03)	1.02 (0.86, 1.20)	0.68*** (0.58, 0.80)	1.43*** (1.17, 1.74)	0.81* (0.67, 0.95)	0.82* (0.69, 0.98)
≥65 years old	2.39*** (1.89, 3.01)	0.78* (0.62, 0.98)	0.40*** (0.32, 0.49)	1.67*** (1.29, 2.16)	0.46 (0.36, 0.58)	0.45*** (0.36, 0.56)
Gender (Ref: Male)						
Female	0.88 (0.77, 1.01)	1.37*** (1.20, 1.56)	1.66*** (1.45, 1.90)	0.98 (0.83, 1.15)	1.59*** (1.39, 1.82)	1.55*** (1.36, 1.78)
Race/ethnicity (Ref: White)						
Hispanic	0.65*** (0.54, 0.79)	0.70*** (0.59, 0.84)	0.59*** (0.49, 0.71)	0.89 (0.71, 1.12)	0.62*** (0.51, 0.75)	0.67*** (0.55, 0.82)
Non-Hispanic Black	0.73** (0.60, 0.88)	0.83 (0.69, 1.01)	0.60** (0.56, 0.85)	0.89 (0.70, 1.14)	0.72** (0.59, 0.87)	0.57*** (0.47, 0.69)
Non-Hispanic Asian	0.79 (0.60, 1.04)	0.54*** (0.41, 0.71)	0.71* (0.53, 0.94)	0.96 (0.68, 1.35)	0.61** (0.45, 0.82)	0.78 (0.60, 1.02)
Non-Hispanic other races	2.05* (1.00, 4.19)	1.01 (0.52, 1.97)	0.68 (0.31, 1.50)	0.55 (0.17, 1.75)	0.81 (0.37, 1.78)	0.48 (0.20, 1.17)
Marital status (Ref: Married)						
Separated	1.26 (0.87, 1.82)	1.48* (1.03, 2.14)	1.15 (0.77, 1.72)	1.54* (1.03, 2.30)	1.67** (1.18, 2.38)	1.80** (1.25, 2.60)

	Sensation abnormality†	Pain†	Fatigue†	Cognitive disturbance†	Depression†	Anxiety†
	OR (95% CI)	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Divorced	1.10 (0.92, 1.34)	1.29* (1.06, 1.56)	1.23 (0.99, 1.53)	1.10 (0.87, 1.39)	1.34** (1.11, 1.62)	1.15 (0.95, 1.39)
Single/never married	0.90 (0.75, 1.07)	0.91 (0.77, 1.07)	0.90 (0.76, 1.08)	1.04 (0.82, 1.32)	1.17 (0.98, 1.39)	1.14 (0.97, 1.34)
Widowed	1.27 (0.97, 1.66)	0.94 (0.71, 1.25)	0.82 (0.63, 1.05)	1.25 (0.88, 1.61)	1.22 (0.96, 1.55)	0.97 (0.76, 1.24)
Education (Ref: Graduate degree)						
Below high school	1.26 (0.98, 1.64)	1.09 (0.83, 1.44)	0.90 (0.68, 1.19)	2.18*** (1.56, 3.04)	1.16 (0.87, 1.55)	0.83 (0.64, 1.09)
High school/GED	1.04 (0.84, 1.29)	1.12 (0.87, 1.43)	0.91 (0.72, 1.15)	1.61** (1.19, 2.18)	1.00 (0.79, 1.28)	0.86 (0.69, 1.08)
Some college	0.99 (0.79, 1.25)	1.20 (0.95, 1.53)	0.92 (0.73, 1.15)	1.35 (0.89, 1.87)	0.98 (0.77, 1.25)	0.96 (0.77, 1.21)
Bachelor degree	0.91 (0.72, 1.14)	0.90 (0.69, 1.18)	0.82 (0.63, 1.05)	1.06 (0.74, 1.51)	0.94 (0.72, 1.23)	1.12 (0.87, 1.45)

#Numbers were weighted to represent the entire U.S. non-institutionalized adults.

†Six multivariable models were performed to identify the determinants for the prevalence of individual symptom phenotypes.

*p<0.05;

**p<0.01,

***p<0.001.

Table 6

Multivariable analysis for the factors contributing to decremented HRQOL[†,#]

Independent variables	Physical HRQOL		Mental HRQOL	
	Model 1a	Model 1b	Model 2a	Model 2b
	Beta (95% CI)	Beta (95% CI)	Beta (95% CI)	Beta (95% CI)
Sensation abnormality	−1.44*** (−1.87, −1.01)	−1.09*** (−1.48, −0.69)	−1.04*** (−1.54, −0.54)	−0.91*** (−1.41, −0.41)
Pain	−5.24*** (−5.72, −4.76)	−4.01*** (−4.46, −3.55)	−2.21*** (−2.68, −1.74)	−1.76*** (−2.23, −1.28)
Fatigue	−3.74*** (−4.24, −3.25)	−3.31*** (−3.78, −2.85)	−1.33*** (−1.83, −0.83)	−1.17*** (−1.66, −0.67)
Cognition disturbance	−3.38*** (−4.01, −2.75)	−2.32*** (−2.90, −1.75)	−3.70*** (−4.35, −3.06)	−3.31*** (−3.95, −2.66)
Depression	−2.72*** (−3.29, −2.16)	−2.54*** (−3.07, −2.00)	−5.27*** (−5.88, −4.65)	−5.20*** (−5.81, −4.59)
Anxiety	−0.94** (−1.48, −0.41)	−0.91*** (−1.42, −0.41)	−1.87*** (−2.42, −1.33)	−1.86*** (−2.40, −1.32)
Cancer experience (Ref: Non-cancer individuals)				
Cancer survivors	−0.59* (−1.81, −0.09)	−0.65 (−1.43, 0.13)	−0.35 (−1.29, 0.59)	−0.23 (−1.18, 0.72)
Number of chronic conditions (Ref: None)				
1	N/A	−4.81*** (−5.47, −4.14)	N/A	−1.79*** (−2.46, −1.11)
2 and above	N/A	−9.16*** (−10.17, −8.16)	N/A	−3.34*** (−4.36, −2.32)
Age at survey (Ref: 18–44.9 years old)				
45–64.9 years old	−1.55*** (−2.04, −1.06)	−0.87*** (−1.34, −0.41)	−0.84** (−1.37, −0.31)	−0.59* (−1.13, −0.06)
≥65 years old	−2.60*** (−3.34, −1.87)	−1.01** (−1.74, −0.28)	−0.24 (−0.94, 0.47)	0.34 (−0.40, 1.08)
Gender (Ref: Male)				
Female	−0.46* (−0.89, −0.03)	−0.37 (−0.77, 0.03)	0.43* (0.02, 0.85)	0.46* (0.05, 0.88)
Race/ethnicity (Ref: White)				
Hispanic	−0.59 (−1.24, 0.06)	−0.73* (−1.35, −0.10)	−1.02** (−1.66, −0.37)	−1.07** (−1.71, −0.43)
Non-Hispanic Black	−1.12** (−1.81, −0.43)	−0.95** (−1.60, −0.29)	−1.44*** (−2.08, −0.79)	−1.37*** (−2.02, −0.73)
Non-Hispanic Asian	0.06 (−0.80, 0.92)	−0.03 (−0.85, 0.79)	−1.56** (−2.46, −0.67)	−1.60** (−2.50, −0.70)
Non-Hispanic other races	−2.45* (−4.52, −0.38)	−1.44 (−3.67, 0.80)	−3.00* (−5.55, −0.45)	−2.64* (−5.03, −0.24)
Marital status (Ref: Married)				
Separated	−0.91 (−2.30, 0.49)	−1.10 (−2.40, 0.20)	−3.66*** (−4.79, −2.52)	−3.73*** (−4.85, −2.61)
Divorced	−0.63 (−1.36, 0.11)	−0.40 (−1.12, 0.33)	−2.19*** (−2.87, −1.51)	−2.11*** (−2.79, −1.42)
Single/never married	−0.07 (−0.60, 0.45)	−0.04 (−0.54, 0.45)	−1.53*** (−2.09, −0.98)	−1.52*** (−2.07, −0.97)
Widowed	−1.34** (−2.20, −0.49)	−0.61 (−1.42, 0.21)	−1.39** (−2.24, −0.54)	−1.12** (−1.96, −0.28)
Education (Ref: Graduate degree)				
Below high school	−4.58*** (−5.56, −3.60)	−3.91*** (−4.86, −2.96)	−6.00*** (−6.97, −5.03)	−5.76*** (−6.73, −4.79)
High school/GED	−2.76*** (−3.52, −2.00)	−2.32*** (−3.04, −1.59)	−4.16*** (−5.03, −3.28)	−3.99*** (−4.97, −3.12)

Independent variables	Physical HRQOL		Mental HRQOL	
	Model 1a	Model 1b	Model 2a	Model 2b
	Beta (95% CI)	Beta (95% CI)	Beta (95% CI)	Beta (95% CI)
Some college	−2.35*** (−3.09, −1.61)	−1.91*** (−2.60, −1.22)	−2.80*** (−3.63, −1.98)	−2.64*** (−3.46, −1.83)
Bachelor degree	−0.35 (−1.13, 0.42)	−0.16 (−0.89, 0.57)	−1.08* (−1.93, −0.24)	−1.01* (−1.85, −0.17)
Variance explained, %	43.3%	49.3%	37.0%	37.8%

[#]Numbers in the Table were weighted to represent the entire U.S. non-institutionalized adults.

[†]Based on multivariable analyses adjusting for independent variables: Models 1a and 2a included the following independent variables: 6 symptom phenotypes, cancer experience, and age, sex, race/ethnicity, marital status, and education; Models 1b and 2b included the independent variables listed in Models 1a and 2a plus chronic conditions.

*p<0.05

**p<0.01,

***p<0.001.