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The prevalence and risk of symptom and function clusters in colorectal cancer survivors

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Abstract

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Code availability Not applicable.

Ethics approval An exemption from IRB review was granted by the Georgetown-Medstar Oncology IRB because the project was deemed “not human subjects research” (secondary analysis of de-identified, secondary data).

Consent to participate Not applicable.

Consent for publication Not applicable.

Conflict of interest The authors declare no competing interests.

Purpose—Our purpose was to describe the prevalence and predictors of symptom and function clusters in a diverse cohort of colorectal cancer survivors.

Methods—We used data from a cohort of 909 adult colorectal cancer survivors. Participants were surveyed at a median of 9 months after diagnosis to ascertain the co-occurrence of eight distinct symptom and functional domains. We used factor analysis to identify co-occurring domains and latent profile analysis (LPA) to identify subgroups of survivors with different symptom and function clusters. Multinomial logistic regression models were used to identify risk/protective factors.

Results—Factor analysis demonstrated a single underlying factor structure that included all eight health domains with depression and anxiety highly correlated ($r = 0.87$). The LPA identified three symptom and function clusters, with 30% of survivors in the low health-related quality of life (HRQOL) profile having the highest symptom burden and lowest functioning. In multivariable models, survivors *more* likely to be in the low HRQOL profile included being non-White, female, those with a history of cardiac or mental health conditions, and chemotherapy recipients. Survivors *less* likely to be in the low HRQOL profile included those with older age, greater financial well-being, and more spirituality.

Conclusion—Nearly one-third of colorectal cancer survivors experienced a cluster of physical and psychosocial symptoms that co-occur with clinically relevant deficits in function.

Implications for Cancer Survivors—Improving the identification of risk factors for having the highest symptom and lowest function profile can inform the development of clinical interventions to mitigate their adverse impact on cancer survivors' HRQOL.

Keywords

Colorectal neoplasms; Quality of life; Cancer survivors; Symptom assessment; Population health

Introduction

Patient-reported outcomes (PROs) are widely accepted by the healthcare practice, research, and policy communities as valid descriptions of an individual's symptoms and functional status that determine their health-related quality of life (HRQOL). Multiple co-occurring symptoms (or "symptom clusters") are highly prevalent in persons with chronic diseases and, specifically, in persons with cancer [1]. Symptom clusters involve 2 or more concurrent symptoms that are distinct from other symptom clusters; they may share underlying causal mechanisms and outcomes and usually have a temporal dimension [2]. Symptom clusters are particularly relevant to oncology care providers, who often report patients experiencing multiple symptoms that are often associated with deficits in function [3]. For example, the cluster of pain, fatigue, and sleep disturbance negatively affects patients' functional status and HRQOL [4]. Treatment for one symptom is often associated with reductions in severity of other symptoms in the cluster and improvements in functional status [5].

Strong evidence indicates cancer and its treatment can result in long-term or late-occurring symptoms and *functional deficits* [6–10]. Cancer survivors often have multiple comorbid conditions that are associated with chronic symptoms and functional impairments [11].

Most prior symptom cluster research with cancer survivors has assessed only symptoms such as pain, fatigue, depression, and sleep disturbance that are common in oncology, but not co-occurring deficits in physical, cognitive, and social function. Therefore, we focus on investigating the phenomenon of symptom and function clusters (hereafter, "clusters"). This approach accounts for the impact of cancer on the HRQOL of survivors that is more comprehensively measured by the concurrent evaluation of co-occurring symptoms and deficits in functioning that is a priority for the FDA [12]. We also used state-of-the-art psychometrically validated continuous scales from the Patient-Reported Outcomes Measurement Information System® (PROMIS®) to more accurately assess the severity of each symptom and functional domain than by using simple binary indicators of the presence of symptoms.

We analyzed a previously surveyed cohort of 909 adult colorectal cancer (CRC) survivors using various psychometric and statistical methods to identify subgroups with differing symptom and functional status *profiles* indicative of low, moderate, and high HRQOL. We next identified survivors' demographic and clinical characteristics associated with HRQOL profile membership and predicted which survivors were likely to be in the low HRQOL profile. The identification of risk factors for being in the low HRQOL profile is an important first step in the development of assessment tools to more accurately identify at-risk cancer survivors and in the design of interventions to provide evidence-based supportive care for cancer survivors to mitigate the impact of clusters and associated impairments in HRQOL.

Methods

Participants and data collection procedures

We recruited patients with cancer as part of the Measuring Your Health (MY-Health) study [13]. Four population-based cancer registries, which are part of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program in 3 states (California, Louisiana, and New Jersey), enrolled 5506 participants within 6 to 13 months (median 9 months) after they were diagnosed with one of seven different cancer types, including 909 participants with primary invasive CRC. We oversampled younger age groups and racial-ethnic minority groups to ensure a heterogeneous sample, addressing limitations of prior research with predominately non-Hispanic White samples. Enrolled participants completed a self-administered mailed baseline survey. The study was approved by all participating sites' IRBs.

Patient characteristics

We obtained clinical data on the date of cancer diagnosis, cancer type, cancer stage, and initial surgery and radiation therapy from the cancer registry databases. The participant baseline survey included items on sociodemographics, financial variables (e.g., healthcare coverage, financial well-being) [14], health behaviors (e.g., smoking status, physical activity, BMI), social support (marital status, ability to find companionship when needed), spirituality [15], history of selected comorbid conditions, and receipt of ambulatory systemic cancer therapy as this data is incomplete in most cancer registries.

Outcomes: symptoms and functioning

The PROMIS® domains used in the MY-Health study included short form measures of five symptoms (fatigue, pain interference, anxiety, depression, and sleep disturbance) and three functional domains (physical function, ability to participate in social roles (social function), and cognitive function) [13]. These domains were selected because of their prevalence and impact in cancer survivors and their relevance for most other chronic conditions that frequently co-occur in cancer survivors. All PROMIS® scores are reported as T-scores and calibrated based on a US sample with a mean of 50 and a standard deviation (SD) of 10 points. Higher PROMIS® scores for symptoms reflect worse symptom burden and for functioning reflect better functioning.

Analysis

We first used Pearson correlations to evaluate the relationships among the eight PROMIS® HRQOL domain indicators. Factor analysis was then used to determine the lower dimensional factor structure that guided us to reduce the number of indicators if needed.

Following the identification of clusters, we used latent profile analysis (LPA) to identify distinct groups of CRC patients with different levels of symptoms or functional deficits simultaneously across the eight PROMIS® indicators and then groups cancer survivors based on their similarity of symptom/function scores to identify HRQOL profiles. We generated a series of hierarchically nested profiles that varied in the number of survivor subgroup profiles (starting with two profiles). To determine a final LPA model, we used multiple goodness-of-fit statistics and clinical interpretability. We used a multinomial logistic regression model to determine the demographic and clinical factors associated with HRQOL profile membership determined by the final LPA model and reported adjusted odds ratios (ORs) and their 95% Wald confidence intervals. To evaluate the overall classification accuracy of the regression model, we provided hit rate and hit rate by chance, which is the recommended effect size for determining whether the classification model performs better than chance [16]. We also estimated Huberty's I index; a value above 0.35 supports "good" prediction of the model [17]. We used M-Plus (V 8) to implement the factor analyses and the LPA, and SAS (V 9.4) for the data summary and regression analysis.

Results

Table 1 provides the demographic and clinical characteristics of the 909 CRC patients included in the study. The sample was diverse with respect to race/ethnicity (40% non-Hispanic White, 23% Black, 18% Asian, and 19% Hispanic), age, gender, education, and smoking status.

Association among symptom and function domains

A majority of the correlations among the eight PROMIS® symptom and function domains ranged in absolute value between 0.42 and 0.69, thus supporting the grouping of symptom and function domains in clusters. The strongest correlation ($r = 0.87$) was between depression and anxiety. Given our objective of conducting the most parsimonious analysis possible, we opted to exclude depression in subsequent analyses because anxiety is more

frequent, related to HRQOL, and associated with fear of recurrence later in the cancer trajectory [18–21].

Identifying colorectal cancer survivor subgroup profiles

Table 2 provides fit statistics for 2-, 3-, 4-, and 5-profile solutions of the LPA model. Although the 4-profile model was empirically the best statistical fit, the 3-profile solution was the more clinically interpretable solution with sufficient sample size in each profile. The 3-profiles consisted of low, moderate, and high HRQOL groups. As shown in Fig. 1, the low HRQOL profile, representing approximately 30% of the CRC patient sample, reported impaired functional status with mean PROMIS® scores ranging between 35 and 41 and high symptom burden scores ranging from 59 to 65. The high HRQOL profile, representing approximately 26% of the sample, reported high functioning with PROMIS scores ranging from 54 to 62 and low symptom burden ranging from 40 to 43, nearly an entire standard deviation below the US norms for the PROMIS® measures (e.g., better functioning and fewer symptoms). The moderate HRQOL profile subgroup fell between the low and high HRQOL profiles and represented 44% of the sample, with mean PROMIS functioning scores ranging from 44 to 52 and symptom burden ranging from 48 to 53.

Patient characteristics associated with profile membership

Table 3 shows the frequency distributions (unadjusted) of CRC survivors with membership in each of the three HRQOL profiles (low, moderate, high). Table 4 presents the adjusted ORs and 95% CIs from the multinomial logistic regression model for each characteristic having a statistically significant association with profile membership in the model. After adjusting for all other variables, characteristics of survivors *more* likely to be in the low HRQOL profile than in the high HRQOL profile included being female (OR = 2.30, 95% CI 1.29–4.10) compared to male; Asian (OR = 2.81, 1.11–7.09) or Black (OR = 3.41, 1.54–7.56) compared to non-Hispanic White; not working (OR = 4.04, 2.07–7.89) compared to working status; having a cardiac-related condition (OR = 4.17, 1.90–9.13), mental health–related condition (OR = 8.24, 3.38–20.13), or sleep disturbance (OR = 9.88, 3.50–27.92) compared with not having the condition; and reporting the receipt of chemotherapy (OR = 8.12, 3.47–18.98) compared with reporting no chemotherapy. Factors *less* likely to be in the low HRQOL vs high HRQOL profile group included older age at diagnosis (OR = 0.83, 0.72–0.95, for 5-year increase in age), greater financial well-being (OR = 0.83, 0.71–0.96 for a half SD [13.3] increase in financial well-being score), and more spirituality (OR = 0.51, 0.43–0.61 for a half SD [4.8] increase in spirituality score).

Among CRC patients, the regression model accurately predicted 55% were in the high HRQOL group, 68% in the moderate HRQOL profile, and 60% in the low HRQOL profile (Fig. 2). The classification hit rate was 64.44%, the hit rate by chance was 35.31%, and Huberty's I index was 0.45. As a sensitivity analysis, we excluded all non-significant factors from the multinomial model and found similar classification performance (e.g., Huberty's I index = 0.40), suggesting an improvement-over-chance classification [17].

Discussion

Examining symptom and function clusters in adult cancer survivors is important because in oncology clinical practice, most survivors present with more than one symptom or functional deficit, and these deficits are likely associated with each other [3]. We initiated this work using CRC survivors' data because it is one of the most prevalent cancers, affects both sexes, and is associated with numerous persistent and late-occurring adverse effects of local and systemic therapies. We identified three profile groups among adult CRC survivors with respect to these clusters, with 30% in the low HRQOL profile. We found several risk factors for being in the low HRQOL profile, including younger age, belonging to a racial-ethnic minority group, being female, a history of cardiac or mental health conditions, lower financial well-being, and less spirituality.

A recent NIH panel of experts on symptom science noted that "research on symptom clusters is extremely limited" [1]. Although most of the research on symptom clusters has been conducted in oncology vs other chronic diseases and conditions, the majority of prior cancer-related research has been done in patients with advanced cancer or was focused on acute, transient symptoms during active cancer treatment [23–28]. Our focus on cancer survivors is somewhat different but extends recent work in this population [29–31]. Our use of LPA detected a 4-group profile, consistent with a prior investigation of breast cancer symptom clusters using the MY-Health cohort [30]. Despite these differences, our findings for adult CRC survivors are consistent with prior studies of patients in different phases of their cancer trajectory showing that symptoms are highly correlated with deficits in function that reflect poorer HRQOL [3, 24]. This finding supports a common clinical perception that symptoms are inter-related, often exacerbate each other, and co-occur with clinically meaningful declines in physical, cognitive, and social functioning.

We found that 30% of adult CRC survivors were in the low HRQOL profile group, with PROMIS domain scores at least 10 points below the general US population PROMIS norm values for most of the seven HRQOL domains within the group. Clinically meaningful differences on most PROMIS® domain scores for cancer patients are in the 3–6 point range [32];thus, the 10-point differences we observed for the low HRQOL group represent significant decrements in HRQOL in comparison to US norms and to the other profile groups in this study. The moderate HRQOL profile group, the largest at 44% of the cohort, was characterized by PROMIS® scores close to US norms of 50, except for physical function that had a mean of 44. The scores for the low HRQOL group reflect a moderate to severe level of symptoms and functional deficits relative to the other groups based on clinically meaningful thresholds established for cancer survivors for some domains [33]. Thus, this group will be the one likely to benefit from targeted interventions to enhance HRQOL.

We examined the sociodemographic and clinical variables that were most closely associated with being in this low HRQOL profile in the multinomial regression model. In the model, we observed that younger age was associated with belonging to the low HRQOL group compared to the high HRQOL group, consistent with prior studies of survivors of breast cancer [30, 34, 35]. This may be due in part to the multiple challenges faced by

younger survivors, including managing multiple responsibilities (e.g., child care and work), experiencing cancer at an unexpectedly early age, and greater negative effects of a diagnosis and treatment on psychological, sexual, and social functioning in this group compared to older survivors [36]. However, our findings diverge from other studies. One study of colorectal cancer survivors found that older age was associated with poorer overall HRQOL [37], while another study in the Netherlands found that an emotional and a pain symptom cluster were each independent of age [10].

Consistent with studies involving patients with mixed cancer types [6, 38, 39] and studies of colorectal cancer survivors [40, 41], we found that women were more likely to have worse symptom burden than men. Our work extends the literature because we are unaware of prior research of symptom and function clusters that report these findings in CRC survivors, as the majority of prior studies of symptom clusters in oncology have focused on breast cancer. The findings that Asians and non-Hispanic Blacks were at greater risk for low HRQOL compared to non-Hispanic Whites is a fairly novel finding, which may be due in part to inadequate access to high-quality oncology and overall supportive care for post-acute adverse effects and other systemic inequities distinct from measures we controlled for in our model (such as education, income, and financial well-being). These findings suggest that additional efforts to develop culturally sensitive tailored interventions, which both accurately identify cancer survivors at risk for impaired HRQOL and promote HRQOL in these groups of survivors, may be warranted.

We did find a significantly higher risk of being in the low HRQOL group among those with worse financial well-being adjusting for all other factors, which may be related to the financial hardship of cancer and/or fewer resources for accessing high-quality symptom-related care, and with lower spirituality. The findings for financial well-being are consistent with several prior studies showing that higher symptom burden is associated with lower education level, lower income, and with unemployment among cancer survivors [30, 31, 34, 41, 42]. Our findings for spirituality are novel and may be associated with the use of more effective coping mechanisms for dealing with symptoms, particularly mental health, having a greater sense of meaning and purpose, or being part of a faith community [43].

We also observed a strong association of comorbidities with being in the low HRQOL profile group, consistent with prior studies of colorectal cancer survivors [39, 41]. As expected, we observed an association of receipt of chemotherapy with the low HRQOL profile group, but found no association of late-stage diagnosis with poorer HRQOL, as previously reported [41].

We examined how well our multinomial regression model was able to identify the HRQOL profile subgroup to which each survivor belonged. Our ability to successfully identify 60% of the participants into the low HRQOL profile group using multinomial regression models that included numerous sociodemographic, behavioral, and clinical characteristics, including stage and some treatment information, represents an advance in symptom cluster research; however, uncertainty remains whether this is sufficiently accurate to guide clinical decision-making. There is clearly a need to develop more comprehensive prediction models that include additional details to enable more precise identification of risk for, and more

effective management of, symptom clusters. Identifying individuals who may have higher rates of clinically significant, long-term side effects would help clinicians create more precise, patient-specific survivorship care plans and to promote using the most appropriate supportive care management strategies.

One of the key limitations of prior research is the poor understanding of how symptom and function clusters vary across different subgroups defined by race-ethnicity, socio-economic status, age, and sex. We assessed clusters in a uniquely large and diverse group of long-term CRC survivors treated in diverse community settings. Our cohort was comprised of 60% racial-ethnic minorities and 22% with less than a high school education. Our approach enhances the impact of our findings by also including the most vulnerable groups with major chronic diseases: older adults; persons with fewer economic resources; and those with multimorbidity. We used state-of-the-art PROMIS® measures that provide a continuous metric of symptom severity or functional limitation, which have an important advantage over many prior symptom cluster studies that used only a binary indicator of presence or absence of a symptom. The continuous PROMIS® score range provides a more precise estimate of the severity of symptoms and extent of impairment on functioning that each HRQOL profile is experiencing. PROMIS® measures have also been extensively cross-culturally validated, thus enhancing their applicability and validity across different populations [44–46]. Some studies on symptom clusters have treated cancer survivors as one homogeneous population using methods based on a common mean and standard deviation [27, 39]. This one group approach does not capture the heterogeneity of cancer survivors who experience persistent, co-occurring symptoms and related functional limitations. In contrast, our use of LPA of multiple symptom and function domains simultaneously, coupled with clinical insight, enabled us to identify and describe subgroups of CRC survivors who may be at higher risk and require earlier identification and management for optimal outcomes.

Despite these strengths, our study was limited to eight symptoms and function domains, although these domains are among the most common and impactful for most cancer survivors. For example, the inclusion of gastrointestinal symptoms for CRC survivors (e.g., nausea, diarrhea, cramping) would be important, but were not collected in MY-Health. In addition, we had limited treatment data and missing information on dose, type, and duration of therapy that can only be collected from medical records. Although we presented results for a single time point, we will conduct longitudinal analyses of symptom clusters and functional status to evaluate predictors of longitudinal transitions in these clusters. Finally, the MY-Health survey cohort did not include a pre-treatment assessment of HRQOL that would have allowed us to measure changes in symptoms and functional deficits related to the diagnosis and initial treatment of CRC.

In summary, we found that among adult survivors of CRC, there was a large group (30%) belonging to a low HRQOL profile defined as experiencing co-occurring functional deficits and significant symptom burden. We identified numerous fixed and mutable risk factors for being in this low HRQOL profile that may be useful in the development of interventions to mitigate their clinical impact. Our creation of a prediction model is an early first step towards developing more precise clinical tools to promote earlier identification and

management of CRC survivors at risk for clusters of symptoms and functional deficits that result in impaired HRQOL.

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Data availability

Data underlying this article are available with permission from the following data repository: Potosky, Arnold L.; Moinpour, Carol, 2016, “PROMIS 2 MY Health”, https://doi.org/10.7910/DVN/XD1A6B, Harvard Dataverse, V1, UNF:6:No/Ha2bxUBEO7nsiGeazsg = = [fileUNF].

References

1. Miaskowski C, Barsevick A, Berger A, Casagrande R, Grady PA, Jacobsen P, et al. Advancing symptom science through symptom cluster research: expert panel proceedings and recommendations. J Natl Cancer Inst. 2017;109:djw253. 10.1093/jnci/djw253.
2. Miaskowski C, Aouizerat BE, Dodd M, Cooper B. Conceptual issues in symptom clusters research and their implications for quality-of-life assessment in patients with cancer. J Natl Ca Inst Monographs. Oxford University Press; 2007;2007:39–46. 10.1093/jncimonographs/lgm003.
3. Buckner TW, Wang J, DeWalt DA, Jacobs S, Reeve BB, Hinds PS. Patterns of symptoms and functional impairments in children with cancer. Pediatric blood & cancer. Wiley Online Library; 2014;61:1282–8. 10.1002/pbc.25029. [PubMed: 24634396]
4. Illi J, Miaskowski C, Cooper B, Levine JD, Dunn L, West C, et al. Association between pro- and anti-inflammatory cytokine genes and a symptom cluster of pain, fatigue, sleep disturbance, and depression. Cytokine. 2012;58:437–47. 10.1016/j.cyto.2012.02.015. [PubMed: 22450224]
5. Kwekkeboom KL, Abbott-Anderson K, Cherwin C, Roiland R, Serlin RC, Ward SE. Pilot randomized controlled trial of a patientcontrolled cognitive-behavioral intervention for the pain, fatigue, and sleep disturbance symptom cluster in cancer. J Pain Symptom Manage. 2012;44:810–22. 10.1016/j.jpainsymman.2011.12.281. [PubMed: 22771125]
6. Jefford M, Ward AC, Lisy K, Lacey K, Emery JD, Glaser AW, et al. Patient-reported outcomes in cancer survivors: a population-wide cross-sectional study. Support Care Cancer. 2017;25:3171–9. 10.1007/s00520-017-3725-5. [PubMed: 28434095]
7. Faury S, Rullier E, Denost Q, Quintard B. Quality of life and fatigue among colorectal cancer survivors according to stoma status – the national VICAN survey. J Psychosoc Oncol. 2020;38:89–102. 10.1080/07347332.2019.1638481. [PubMed: 31304892]
8. Matias M, Baciarello G, Neji M, Di Meglio A, Michiels S, Partridge AH, et al. Fatigue and physical activity in cancer survivors: a cross-sectional population-based study. Cancer Med. 2019;8:2535–44. 10.1002/cam4.2060. [PubMed: 30864301]
9. Mazor M, Cataldo JK, Lee K, Dhruva A, Cooper B, Paul SM, et al. Differences in symptom clusters before and twelve months after breast cancer surgery. Eur J Oncol Nurs. 2018;32:63–72. 10.1016/j.ejon.2017.12.003. [PubMed: 29353634]

10. Agasi-Idenburg SC, Thong MSY, Punt CJA, Stuiver MM, Aaronson NK. Comparison of symptom clusters associated with fatigue in older and younger survivors of colorectal cancer. Support Care Cancer. 2017;25:625–32. 10.1007/s00520-016-3451-4. [PubMed: 27770205]
11. Smith AW, Reeve BB, Bellizzi KM, Harlan LC, Klabunde CN, Amsellem M, et al. Cancer, comorbidities, and health-related quality of life of older adults. Health Care Financ Rev. 2008;29:41–56. [PubMed: 18773613]
12. Kluetz PG, Slagle A, Papadopoulos EJ, Johnson LL, Donoghue M, Kwitkowski VE, et al. Focusing on core patient-reported outcomes in cancer clinical trials: symptomatic adverse events, physical function, and disease-related symptoms. Clinical Cancer Research AACR. 2016;22:1553–8.
13. Jensen RE, Moinpour CM, Keegan THM, Cress RD, Wu X-C, Paddock LE, et al. The Measuring Your Health Study: leveraging community-based cancer registry recruitment to establish a large, diverse cohort of cancer survivors for analyses of measurement equivalence and validity of the Patient Reported Outcomes Measurement Information System® (PROMIS®) short form items. Psychological Test and Assessment Modeling [Internet]. 2016 [cited 2020 Oct 19];58. Available from: https://www.ptam.klaus-kubinger.com/index.php/ptam/article/view/58
14. Patient Satisfaction Questionnaires (PSQ-III and PSQ-18) [Internet]. Patient Satisfaction Questionnaire from RAND Health Care | RAND. [cited 2021 Mar 26]. Available from: https://www.rand.org/health-care/surveys_tools/psq.html
15. Peterman AH, Fitchett G, Brady MJ, Hernandez L, Cella D. Measuring spiritual well-being in people with cancer: The functional assessment of chronic illness therapy—spiritual well-being scale (FACIT-Sp). Ann Behav Med. 2002;24:49–58. [PubMed: 12008794]
16. Boedeker P, Kearns NT. Linear discriminant analysis for prediction of group membership: a user-friendly primer. Adv Methods Pract Psychol Sci. 2019;2:250–63. 10.1177/2515245919849378.
17. Huberty CJ, Lowman LL. Group overlap as a basis for effect size. Educ Psychol Measur. 2000;60:543–63. 10.1177/0013164400604004.
18. Aminisani N, Nikbakht H, Jafarabadi MA, Shamshirgaran SM. Depression, anxiety, and health related quality of life among colorectal cancer survivors. Journal of Gastrointestinal Oncology. AME Publications; 2017;8:81. 10.21037/jgo.25l7.01.12. [PubMed: 28280612]
19. Qaderi SM, Ezendam NP, Verhoeven RH, Custers JA, de Wilt JH, Mols F. Follow-up practice and healthcare utilisation of colorectal cancer survivors. European Journal of Cancer Care. Wiley Online Library; 2021;e13472. 10.1111/ecc.13472. [PubMed: 34081367]
20. Koch L, Bertram H, Eberle A, Holleczek B, Schmid-Höpfner S, Waldmann A, et al. Fear of recurrence in long-term breast cancer survivors-still an issue. Results on prevalence, determinants, and the association with quality of life and depression from the cancer survivorship--a multi-regional population-based study. Psychooncology. England; 2014;23:547–54. 10.1002/pon.34526
21. Götze H, Taubenheim S, Dietz A, Lordick F, Mehnert-Theuerkauf A. Fear of cancer recurrence across the survivorship trajectory: results from a survey of adult long-term cancer survivors. Psychooncology. England; 2019;28:2033–41. 10.1002/pon.5188.
22. Bredle JM, Salsman JM, Debb SM, Arnold BJ, Cella D. Spiritual well-being as a component of health-related quality of life: the functional assessment of chronic illness therapy—spiritual wellbeing scale (FACIT-Sp). Religions Molecular Diversity Preservation International. 2011;2:77–94. 10.3390/rel2010077.
23. Thavarajah N, Chen E, Zeng L, Bedard G, Di Giovanni J, Lemke M, et al. Symptom clusters in patients with metastatic cancer: a literature review. Expert Rev Pharmacoecon Outcomes Res. 2012;12:597–604. 10.1586/erp.12.41. [PubMed: 23186400]
24. Lin Y, Bailey DE, Docherty SL, Porter LS, Cooper BA, Paul SM, et al. Distinct profiles of multiple co-occurring symptoms in patients with gastrointestinal cancers receiving chemotherapy. Support Care Cancer [Internet]. 2021 [cited 2021 Mar 23]; Available from: http://link.springer.com/10.1007/s00520-020-05946-410.1007/s00520-020-05946-4
25. Papachristou N, Barnaghi P, Cooper BA, Hu X, Maguire R, Apostolidis K, et al. Congruence between latent class and K-modes analyses in the identification of oncology patients with distinct symptom experiences. Journal of pain and symptom management. Elsevier; 2018;55:318–333.e4. [PubMed: 28859882]

26. Miaskowski C, Cooper BA, Aouizerat B, Melisko M, Chen L-M, Dunn L, et al. The symptom phenotype of oncology outpatients remains relatively stable from prior to through 1 week following chemotherapy. European journal of cancer care. Wiley Online Library; 2017;26:e12437.
27. Miaskowski C, Dunn L, Ritchie C, Paul SM, Cooper B, Aouizerat BE, et al. Latent class analysis reveals distinct subgroups of patients based on symptom occurrence and demographic and clinical characteristics. Journal of pain and symptom management. Elsevier; 2015;50:28–37. [PubMed: 25647419]
28. Miaskowski C, Cooper BA, Melisko M, Chen L-M, Mastick J, West C, et al. Disease and treatment characteristics do not predict symptom occurrence profiles in oncology outpatients receiving chemotherapy. Cancer. Wiley Online Library; 2014;120:2371–8. [PubMed: 24797450]
29. Berger A, Kumar G, LeVan T, Meza J. Symptom clusters and quality of life over 1 year in breast cancer patients receiving adjuvant chemotherapy. Asia Pac J Oncol Nurs. 2020;7:134. 10.4103/apjon.apjon_57_19. [PubMed: 32478130]
30. Lee L, Ross A, Griffith K, Jensen R, Wallen G. Symptom clusters in breast cancer survivors: a latent class profile analysis. Onc Nurs Forum. 2020;47:89–100. 10.1188/20.ONF.89-100.
31. Roiland RA, Heidrich SM. Symptom clusters and quality of life in older adult breast cancer survivors. Oncol Nurs Forum. 2011;38:672–80. 10.1188/11.ONF.672-680. [PubMed: 22037330]
32. Yost KJ, Eton DT, Garcia SF, Cella D. Minimally important differences were estimated for six Patient-Reported Outcomes Measurement Information System-Cancer scales in advanced-stage cancer patients. J Clin Epidemiol. 2011;64:507–16. 10.1016/j.jclinepi.2010.11.018. [PubMed: 21447427]
33. Cella D, Choi S, Garcia S, Cook KF, Rosenbloom S, Lai J-S, et al. Setting standards for severity of common symptoms in oncology using the PROMIS item banks and expert judgment. Qual Life Res. 2014;23:2651–61. 10.1007/s11136-014-0732-6. [PubMed: 24938431]
34. Shi Q, Smith TG, Michonski JD, Stein KD, Kaw C, Cleeland CS. Symptom burden in cancer survivors 1 year after diagnosis: a report from the American Cancer Society's Studies of Cancer Survivors. Cancer. 2011;117:2779–90. 10.1002/cncr.26146. [PubMed: 21495026]
35. Avis NE, Levine B, Marshall SA, Ip EH. Longitudinal examination of symptom profiles among breast cancer survivors. Journal of Pain and Symptom Management. Elsevier; 2017;53:703–10. [PubMed: 28042076]
36. Colorectal Cancer Alliance. Never Too Young Survey Report [Internet]. Never Too Young Survey and Report | Colorectal Cancer Alliance. [cited 2021 Mar 23]. Available from: https://www.ccalliance.org/about/never-too-young/survey
37. Rodriguez JL, Hawkins NA, Berkowitz Z, Li C. Factors associated with health-related quality of life among colorectal cancer survivors. American Journal of Preventive Medicine. Elsevier; 2015;49:S518–27. 10.1016/j.amepre.2015.08.007. [PubMed: 26590647]
38. Batra A, Yang L, Boyne DJ, Harper A, Cuthbert CA, Cheung WY. Symptom burden in patients with common cancers near end-of-life and its associations with clinical characteristics: a real-world study. Supportive Care in Cancer. Springer; 2021;29:3299–309. 10.1007/s00520-020-05827-w. [PubMed: 33104922]
39. Thomas BC, Waller A, Malhi RL, Fung T, Carlson LE, Groff SL, et al. A longitudinal analysis of symptom clusters in cancer patients and their sociodemographic predictors. J Pain Symptom Manage. 2014;47:566–78. 10.1016/j.jpainsymman.2013.04.007. [PubMed: 24035068]
40. Laghousi D, Jafari E, Nikbakht H, Nasiri B, Shamshirgaran M, Aminisani N. Gender differences in health-related quality of life among patients with colorectal cancer. Journal of Gastrointestinal Oncology. AME Publications; 2019;10:453. 10.21037/jgo.2019.02.04. [PubMed: 31183195]
41. Adams SV, Ceballos R, Newcomb PA. Quality of life and mortality of long-term colorectal cancer survivors in the Seattle Colorectal Cancer Family Registry. Montazeri A, editor. PLoS ONE. 2016;11:e0156534. 10.1371/journal.pone.0156534. [PubMed: 27253385]
42. McDougall JA, Blair CK, Wiggins CL, Goodwin MB, Chiu VK, Rajput A, et al. Socioeconomic disparities in health-related quality of life among colorectal cancer survivors. J Cancer Surviv. 2019;13:459–67. 10.1007/s11764-019-00767-9. [PubMed: 31111302]

43. Salsman JM, Yost KJ, West DW, Cella D. Spiritual well-being and health-related quality of life in colorectal cancer: a multi-site examination of the role of personal meaning. Support Care Cancer. 2011;19:757–64. 10.1007/s00520-010-0871-4. [PubMed: 20405147]

44. Reeve BB, Pinheiro LC, Jensen RE, Teresi JA, Potosky AL, McFatrich MK, et al. Psychometric evaluation of the PROMIS® fatigue measure in an ethnically and racially diverse population-based sample of cancer patients. Psychological Test and Assessment Modeling. PABST Science Publishers; 2016;58:119.

45. Jensen RE, Potosky AL, Reeve BB, Hahn E, Cella D, Fries J, et al. Validation of the PROMIS physical function measures in a diverse US population-based cohort of cancer patients. Qual Life Res. 2015;24:2333–44. 10.1007/s11136-015-0992-9. [PubMed: 25935353]

46. Teresi JA, Ocepek-Welikson K, Cook KF, Kleinman M, Ramirez M, Reid MC, et al. Measurement equivalence of the Patient Reported Outcomes Measurement Information System® (PROMIS®) pain interference short form items: application to ethnically diverse cancer and palliative care populations. Psychol Test Assess Model. 2016;58:309–52. [PubMed: 28983449]

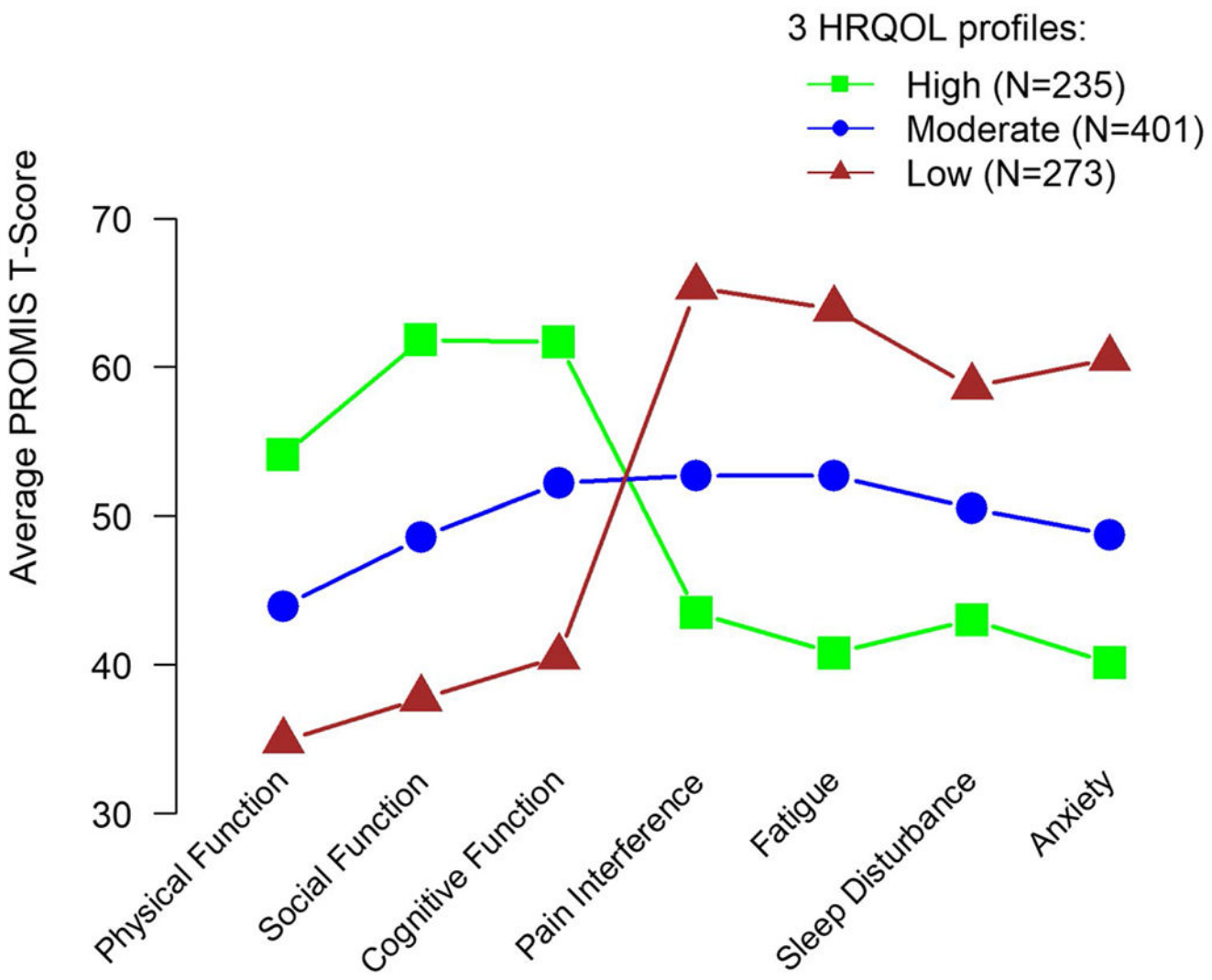

Fig. 1.

Latent profile analysis 3 profile subgroup result (*N* = 909 colorectal cancer survivors). X-axis: health-related quality of life (HRQOL) domains. Y-axis: average PROMIS T-score. PROMIS®, Patient-Reported Outcomes Measurement Information System. PROMIS® measures use a T-score metric in which 50 is the mean of a relevant reference population and 10 is the standard deviation (SD) of that population

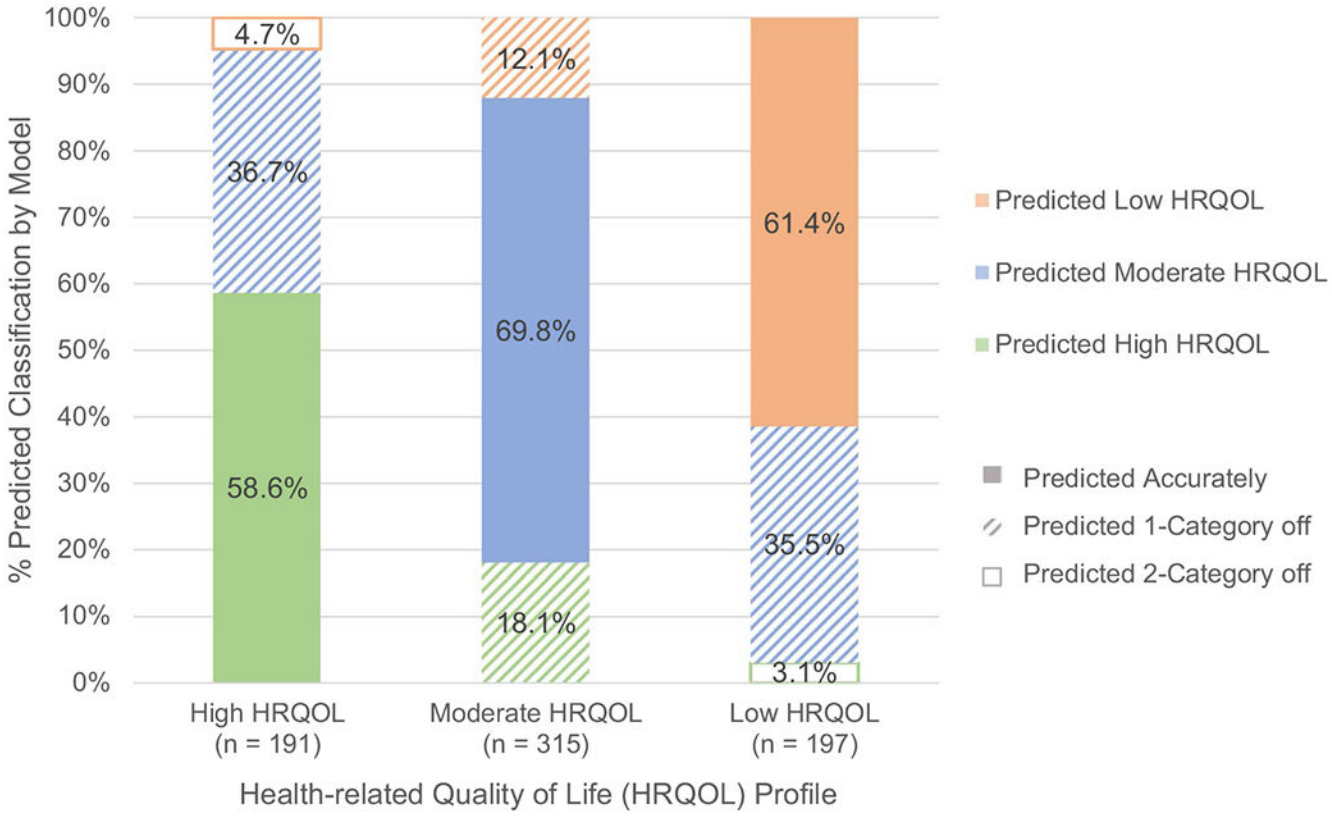

Fig. 2.

Prediction accuracy of profile membership by the multinomial logistic regression model. X-axis: health-related quality of life (HRQOL) profile. Y-axis: % predicted classification by model. Colored bars show the percent predicted by the multinomial model as being members in either the low (red), moderate (blue), or high (green) HRQOL profile groups. Shaded bars indicate the accuracy of the model's prediction classification as either accurate (fully shaded), 1-category off (hatched fill), or 2-categories off (no fill)

Table 1

Characteristics of colorectal cancer survivors in study cohort ($N = 909$)

Variable	Level	Overall ($N = 909$)*
Race/ethnicity	Non-Hispanic White	351 (39.9%)
	Non-Hispanic Black	202 (23.0%)
	Hispanic	170 (19.3%)
	Non-Hispanic Asian	156 (17.7%)
Age at diagnosis	21–39	33 (3.6%)
	40–49	129 (14.2%)
	50–59	216 (23.8%)
	60–69	243 (26.7%)
	70–79	233 (25.6%)
	80+	55 (6.1%)
Sex	Male	441 (48.5%)
	Female	468 (51.5%)
Body mass index	Underweight/normal	334 (37.7%)
	Overweight	315 (35.6%)
	Obese	236 (26.7%)
Marital status	Married (living with partner)	526 (58.7%)
	Single (includes never married, divorced, widowed)	370 (41.3%)
Educational attainment	College or graduate degree	221 (24.7%)
	High school (HS) grad or some college	480 (53.6%)
	Did not graduate HS	195 (21.8%)
Survey language	English	820 (90.2%)
	Spanish or Chinese	89 (9.8%)
Cancer type	Colon cancer	660 (72.6%)
	Rectal cancer	249 (27.4%)
Stage at diagnosis	Stage I	226 (25.6%)
	Stage II	225 (25.5%)
	Stage III	286 (32.4%)
	Stage IV	147 (16.6%)

Variable	Level	Overall (*N* = 909)*
Smoker status	Current smoker	94 (10.6%)
	Former smoker	298 (33.6%)
	Never smoker	494 (55.8%)
Comorbidity**		
Heart-related conditions		146 (16.1%)
Chronic obstructive pulmonary disease (COPD) or asthma		147 (16.2%)
Depression or anxiety		230 (25.3%)

*Not all columns add to 100% due to between 0 and 3% missing, unknown, refused to answer, or “other” values

**Participants were asked if they had ever been told by a healthcare professional that they had any of 15 different chronic conditions including heart-related conditions (heart attack, heart failure, stroke), asthma, chronic obstructive pulmonary disease (COPD), depression, and anxiety

Table 2

Latent profile analysis fit statistics for different number of profiles

Profile #	AIC	BIC	Adj. BIC	VLMR LRT	LMR LRT	Entropy
2	45,309.40	45,415.27	45,345.40	2632.34, $p < .01$	2584.90, $p < .01$	0.883
3	44,488.01	44,632.38	44,537.11	837.39, $p < .01$	822.299, $p < .01$	0.874
4	44,184.76	44,367.63	44,246.95	319.25, $p = .01$	313.499, $p = .01$	0.855
5	44,100.41	44,321.78	44,175.69	100.35, $p = .14$	98.544, $p = .14$	0.867

Note: *AIC* Akaike information criterion, *BIC* Bayesian information criterion, *Adj. BIC* adjusted BIC, *VLMR LRT* Vuong-Lo-Mendell-Rubin likelihood ratio test, *LMR LRT* Lo-Mendell-Rubin adjusted likelihood ratio test

Goodness-of-fit statistics included Akaike information criterion (AIC), Bayesian information criterion (BIC), adjusted BIC, Vuong-Lo-Mendell-Rubin likelihood ratio (VLMR-LR) test, Lo-Mendell-Rubin adjusted likelihood ratio (LMR-LR) test, and entropy. Lower AIC, BIC, and adjusted BIC reflect better model fit. Both the VLMR-LR and the LMR-LR tests compare one nested LPA model to another model with one additional profile, with statistically significant improvement ($p < .05$) suggesting the model with more profiles reflects better fit. Entropy is a measure of uncertainty in the posterior classifications of the model with higher entropy values reflecting less uncertainty

Table 3

Characteristics of colorectal cancer survivors by membership in health-related quality of life subgroup profiles (*N* = 909)

Characteristics		High HRQOL (N = 235)	Moderate HRQOL (N = 401)	Low HRQOL (N = 273)	*P*-value*
Race/ethnicity	Non-Hispanic White	112 (48.7%)	159 (41.1%)	80 (30.5%)	< 0.01
	Non-Hispanic Black	40 (17.4%)	86 (22.2%)	76 (29.0%)	
	Hispanic	39 (17.0%)	66 (17.1%)	65 (24.8%)	
	Non-Hispanic Asian	39 (17.0%)	76 (19.6%)	41 (15.6%)	
Age at diagnosis	21–39	9 (3.8%)	13 (3.2%)	11 (4.0%)	< 0.01
	40–49	19 (8.1%)	59 (14.7%)	51 (18.7%)	
	50–59	55 (23.4%)	80 (20.0%)	81 (29.7%)	
	60–69	67 (28.5%)	108 (26.9%)	68 (24.9%)	
	70–79	72 (30.6%)	117 (29.2%)	44 (16.1%)	
	80+	13 (5.5%)	24 (6.0%)	18 (6.6%)	
Sex	Male	127 (54.0%)	193 (48.1%)	121 (44.3%)	0.09
	Female	108 (46.0%)	208 (51.9%)	152 (55.7%)	
Body mass index	Underweight/normal	89 (38.5%)	150 (37.9%)	95 (36.8%)	0.95
	Overweight	85 (36.8%)	138 (34.8%)	92 (35.7%)	
	Obese	57 (24.7%)	108 (27.3%)	71 (27.5%)	
Marital status	Married (living with partner)	138 (59.7%)	244 (61.3%)	144 (53.9%)	0.16
	Single (includes never married, divorced, widowed)	93 (40.3%)	154 (38.7%)	123 (46.1%)	
Educational attainment	College/grad degree	72 (31.0%)	103 (25.9%)	46 (17.2%)	< .01
	High school (HS) grad/some college	123 (53.0%)	225 (56.7%)	132 (49.4%)	
	Did not complete HS	37 (15.9%)	69 (17.4%)	89 (33.3%)	
Survey language	English	216 (91.9%)	361 (90.0%)	243 (89.0%)	0.54
	Spanish/Chinese	19 (8.1%)	40 (10.0%)	30 (11.0%)	
Health coverage	Private or private + public	166 (71.6%)	246 (63.6%)	137 (53.1%)	< 0.01
	Public only	66 (28.4%)	141 (36.4%)	121 (46.9%)	
Current employment	Working	113 (49.1%)	148 (37.4%)	69 (26.5%)	< 0.01
	Not working	117 (50.9%)	248 (62.6%)	191 (73.5%)	
Cancer type	Colon cancer	178 (75.7%)	300 (74.8%)	182 (66.7%)	0.03
	Rectal cancer	57 (24.3%)	101 (25.2%)	91 (33.3%)	

Characteristics		High HRQOL (N = 235)	Moderate HRQOL (N = 401)	Low HRQOL (N = 273)	*P*-value*
Stage at diagnosis	Stage I	76 (33.3%)	94 (24.0%)	56 (21.1%)	< 0.01
	Stage II	69 (30.3%)	107 (27.4%)	49 (18.5%)	
	Stage III	59 (25.9%)	128 (32.7%)	99 (37.4%)	
	Stage IV	24 (10.5%)	62 (15.9%)	61 (23%)	
Smoker status	Current smoker	18 (7.9%)	37 (9.4%)	39 (14.8%)	0.12
	Former smoker	78 (34.1%)	134 (34.1%)	86 (32.6%)	
	Never smoker	133 (58.1%)	222 (56.5%)	139 (52.7%)	
Chemotherapy (self-report)	Yes	97 (41.6%)	245 (62.2%)	197 (73.8%)	< 0.01
	No	136 (58.4%)	149 (37.8%)	70 (26.2%)	
Frequency of moderate physical activity per week[d]	2 or more times	128 (54.9%)	142 (35.6%)	47 (17.5%)	< 0.01
	None/once	105 (45.1%)	257 (64.4%)	221 (82.5%)	
Able to find companionship when needed	Never/rarely	15 (6.5%)	44 (11.2%)	53 (20.4%)	< 0.01
	Sometimes	15 (6.5%)	71 (18.0%)	70 (26.9%)	
	Often/always	201 (87.0%)	279 (70.8%)	137 (52.7%)	
Financial well-being [14]	Mean	66.0	56.0	49.4	< 0.01
	SD	25.4	25.9	26.5	
Spirituality (FACIT-Sp) [15]	Mean	40.9	37.5	31.9	< 0.01
	STD	7.4	8.7	10.2	
Comorbid conditions					
Heart-related	Yes	25 (10.6%)	60 (15.0%)	61 (22.3%)	< 0.01
	No	210 (89.4%)	341 (85.0%)	212 (77.7%)	
Asthma or COPD	Yes	29 (12.3%)	62 (15.5%)	56 (20.5%)	0.04
	No	206 (87.7%)	339 (84.5%)	217 (79.5%)	
Depression or anxiety	Yes	13 (5.5%)	90 (22.4%)	127 (46.5%)	< 0.01
	No	222 (94.5%)	311 (77.6%)	146 (53.5%)	
Sleep disturbance	Yes	10 (4.3%)	50 (12.5%)	71 (26.0%)	< 0.01
	No	225 (95.7%)	351 (87.5%)	202 (74.0%)	

*Note: *P*-values were calculated by comparing non-missing row values only; these percentages sum to 100%. The percent of missing values for row variables is not shown and ranged from 0 to 5%

P-values are based on Pearson chi-square tests for all categorical row variables and chi-square rank based group means score statistics for all continuous/ordinal row variables

[a]The survey item used was: "Now think about activities that take moderate physical effort that you did in your free time during the last 7 days. Moderate physical activities make you breathe somewhat harder than normal, such as bicycling, dancing, swimming, and gardening. Do not include walking. In the past 7 days, how many times did you do such activities?"

Table 4

Factors associated with membership in low and moderate health-related quality of life profiles using multinomial logistic regression (n = 703) (The full regression model adjusted for age, race/ethnicity, sex, body mass index, marital status, educational attainment, survey language, geographic region, employment status, health coverage, smoking status, cancer type, geographic region, stage at diagnosis, reported ever receiving chemotherapy, ability to find companionship, financial well-being, spirituality and comorbidities including a history of heart-related conditions, asthma or COPD, depression or anxiety, or sleep disturbance condition. Only variables statistically associated (p < .05) with the outcome (HRQOL profile) are presented in this table.)

Variable (*denotes reference category)	Comparator vs reference HRQOL profile	Adjusted odds ratio (95% Wald CI)
Age at diagnosis (per 5-year increase)	Moderate vs high	0.97 (0.87, 1.08)
	Low vs high	0.83 (0.72, 0.95)
	Low vs moderate	0.86 (0.77, 0.96)
Race/ethnicity		
Hispanic vs non-Hispanic White*	Moderate vs high	0.95 (0.48, 1.87)
	Low vs high	2.36 (1.00, 5.54)
	Low vs moderate	2.50 (1.24, 5.04)
Asian vs non-Hispanic White*	Moderate vs high	1.55 (0.78, 3.06)
	Low vs high	2.81 (1.11, 7.09)
	Low vs moderate	1.82 (0.85, 3.88)
Black vs non-Hispanic White*	Moderate vs high	1.77 (0.94, 3.33)
	Low vs high	3.41 (1.54, 7.56)
	Low vs moderate	1.93 (1.04, 3.57)
Sex		
Female vs male	Moderate vs high	1.57 (1.01, 2.43)
	Low vs high	2.30 (1.29, 4.10)
	Low vs moderate	1.46 (0.91, 2.35)
Educational attainment		
Less than high school vs college or graduate degree*	Moderate vs high	0.59 (0.28, 1.23)
	Low vs high	1.76 (0.70, 4.41)
	Low vs moderate	2.98 (1.44, 6.16)
High school or some college vs college or graduate degree*	Moderate vs high	0.79 (0.47, 1.31)
	Low vs high	1.03 (0.51, 2.07)
	Low vs moderate	1.31 (0.74, 2.31)

Variable (*denotes reference category)	Comparator vs reference HRQOL profile	Adjusted odds ratio (95% Wald CI)
Current employment status		
Not working vs working*	Moderate vs high	1.97 (1.20, 3.25)
	Low vs high	4.04 (2.07, 7.89)
	Low vs moderate	2.05 (1.18, 3.55)
Insurance		
Government/no insurance vs private or private + government)*	Moderate vs high	1.85 (1.12, 3.08)
	Low vs high	1.09 (0.57, 2.09)
	Low vs moderate	0.59 (0.35, 0.97)
Cancer type		
Rectal cancer vs colon cancer*	Moderate vs high	0.79 (0.49, 1.30)
	Low vs high	1.74 (0.95, 3.21)
	Low vs moderate	2.20 (1.34, 3.61)
History of heart-related conditions		
Yes vs no*	Moderate vs high	1.52 (0.79, 2.93)
	Low vs high	4.17 (1.90, 9.13)
	Low vs moderate	2.74 (1.52, 4.95)
History of anxiety or depression		
Yes vs no*	Moderate vs high	5.04 (2.21, 11.51)
	Low vs high	8.24 (3.38, 20.13)
	Low vs moderate	1.63 (1.00, 2.68)
History of sleep disturbance condition		
Yes vs no*	Moderate vs high	3.35 (1.32, 8.50)
	Low vs high	9.88 (3.50, 27.92)
	Low vs moderate	2.95 (1.58, 5.53)
Received chemotherapy (self-reported)		
Yes vs no*	Moderate vs high	2.29 (1.24, 4.24)
	Low vs high	8.12 (3.47, 18.98)
	Low vs moderate	3.55 (1.75, 7.18)
Financial well-being [14] (per ½ SD increase)		
	Moderate vs high	0.84 (0.74, 0.94)
	Low vs high	0.83 (0.71, 0.96)

Variable (*denotes reference category)	Comparator vs reference HRQOL profile	Adjusted odds ratio (95% Wald CI)
Spirituality (FACIT-SP) [22] (per ½ SD increase)	Low vs moderate	0.99 (0.88, 1.11)
	Moderate vs high	0.76 (0.66, 0.88)
	Low vs high	0.51 (0.43, 0.61)
	Low vs moderate	0.67 (0.59, 0.77)

The sample size was 703 (out of 909) due to missing values for some covariates. In a separate model including only the statistically significant variables that are shown in this table, the sample size was 795. In this model, there were no changes in the variables that were significantly associated with HRQOL profile membership