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Examination of individual and multiple comorbid conditions and health-related quality of life in older cancer survivors

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Abstract

Purpose Older cancer survivors (≥ 65 years at diagnosis) are at high-risk for multimorbidity (2 + comorbid conditions). However, few studies have utilized a generalizable sample of older cancer survivors to understand how individual comorbid conditions, as opposed to total comorbidity burden, are associated with health-related quality of life (HRQOL). We examined associations between HRQOL outcomes (pain, fatigue, physical function), individual comorbidities (cardiovascular disease [CVD], lung disease, diabetes, arthritis) and total comorbidity (cancer-only, cancer + 1 condition, cancer + 2 or more conditions).

Methods Utilizing a population-based sample of 2019 older cancer survivors, we tested associations between comorbid conditions and the HRQOL outcomes using generalized linear models. HRQOL domains were assessed using Patient-Reported Outcome Measurement Information System® (PROMIS®) measures. Comorbidity was assessed via self-report.

Results Cancer survivors with lung disease reported significantly worse physical functioning ($\beta = -4.96$, $p < 0.001$), survivors with arthritis reported significantly higher pain ($\beta = 4.37$, $p < 0.001$), and survivors with CVD reported significantly higher fatigue ($\beta = 3.45$, $p < 0.001$) compared to survivors without each condition. Having cancer + 1 condition was not as strongly associated with all outcomes as when individual conditions were tested (e.g. pain: $\beta = 3.09$, $p < 0.001$). Having 2+ comorbidities had a stronger association with all outcomes (e.g. physical function: $\beta = -7.51$, $p < 0.001$) than examining conditions individually.

Conclusions Knowing the specific comorbid condition profile of an older cancer survivor provides insight into specific HRQOL outcomes that may be impaired in cancer survivorship, but understanding total comorbidity burden, regardless of the specific conditions, sheds light on survivors at-risk for multiple impairments in HRQOL. This information, taken together, can inform risk-stratified survivorship care.

Keywords Symptoms · Cancer · Comorbidity · Older adults · Health-related quality of life

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Plain English summary

Older cancer survivors (≥ 65 years at diagnosis) are often managing multiple chronic health conditions (e.g. heart disease, diabetes) while undergoing and after cancer treatment. Previous research has most often examined how the total number of chronic conditions influences health-related quality of life (HRQOL), but few studies have explored whether specific chronic conditions influence specific areas of HRQOL, like pain. We tested the association between HRQOL domains (pain, fatigue, physical function) and individual comorbid conditions (heart disease, lung disease, diabetes, arthritis) in a sample of older cancer survivors. We also tested the association between the same three HRQOL domains and the total number of comorbid

conditions. Our results found that when examining only one additional chronic condition, knowing the specific condition (e.g. heart disease) has a larger influence on HRQOL than when examining the total count of conditions. However, if a survivor has two or more chronic health conditions, they are at increased risk for poor HRQOL in all the domains we examined, regardless of the specific chronic condition. The results of this study provide useful information for risk-stratified survivorship care and identifying older cancer survivors who will require tailored and timely symptom management.

Introduction

Approximately 67% of older adults (age ≥ 65) in the USA have multimorbidity (2+ co-occurring comorbid conditions) [1], and the risk for multimorbidity is higher among older cancer survivors [2, 3]. Both cancer treatment and common comorbid conditions (e.g. cardiovascular disease [CVD]) can impact an older survivor's symptom burden and overall health-related quality of life (HRQOL) [4–6]. Pain, fatigue, and physical function limitations are some of the most commonly impaired domains of HRQOL reported by older cancer survivors [7–11]. Understanding how multimorbidity may influence older cancer survivors' outcomes following diagnosis is an important step in identifying and tailoring symptom management for survivors.

Multimorbidity is commonly captured as a numerical count or as a comorbidity index (e.g. Charlson Comorbidity Index, NCI Comorbid Index). These indices were developed and weighted to assess the role of comorbidity on overall survival [12–15], not HRQOL, and therefore may not appropriately weight conditions likely to impact HRQOL. Identification of the specific relationships between types of comorbidities and HRQOL provide a window into the survivors most at-risk for problematic outcomes after cancer treatment, and can assist with providing more specific recommendations to heath care providers who care for older cancer survivors.

Research involving cancer survivors with multimorbidity has shown variable relationships between multimorbidity and cancer outcomes including overall survival [16–22], treatment complications [23, 24], and lower likelihood of guideline-concordant care [25–27]. Some studies also suggest significantly lower HRQOL among multimorbid survivors [28–30], but few studies have explored individual comorbidities and their associations with specific HRQOL outcomes.

In this study we aimed to tease out the differences in HRQOL when examining comorbid conditions both separately and as a count variable. We examined associations between CVD, lung disease, diabetes, arthritis and three common HRQOL outcomes (pain, fatigue, physical function) in a population-based sample of older cancer survivors 6–12 months postdiagnosis. We also tested the association between a comorbid count variable (cancer-only, cancer + 1 condition, cancer + 2 or more conditions) and pain, fatigue, and physical function to determine if the conclusions differ when looking at the independent association of each comorbid condition compared to a categorical count of the total number of conditions.

Methods

Data collection and study population

The current study used data from the population-based Measuring Your Health (MY-Health) study. The MY-Health study design and methods have been described in detail elsewhere [31]. Briefly, 15,300 individuals diagnosed with cancer between 2010 and 2012 were contacted by four Surveillance, Epidemiology, and End Results (SEER) cancer registries (California [2], Louisiana, and New Jersey). A total of 5506 individuals completed a self-report, mail-based survey for a response rate of 36%. We used the following inclusion criteria: (1) completed the baseline MY-Health survey between 6 and 12 months from diagnosis ($N = 162$ excluded), (2) were diagnosed with their first cancer (prostate, colorectal, non-small cell lung, Non-Hodgkin lymphoma, female breast, uterine, or cervical) at the age of 65 years or older ($N = 3240$ excluded), and (3) had Stage I–IV cancer based on the derived AJCC 7th edition staging criteria ($N = 85$ excluded). The final sample was $N = 2019$. The research design and study methods for the MY-Health study were approved by the Institutional Review Board at Georgetown University.

Measures

Health-related quality of life

In this study, we examined three HRQOL domains (pain, fatigue, and physical function) using Patient Reported Outcomes Measurement Information System® (PROMIS®) tailored short forms [31]. Pain interference was measured using 11 items selected from the Pain Interference PROMIS item bank v1.0 (Cronbach's alpha [α] = 0.91), fatigue with 14 items selected from the Fatigue PROMIS item bank v1.0 ($\alpha = 0.89$), and physical function with 16 items selected from the Physical Function PROMIS item bank v1.0 ($\alpha = 0.92$). All PROMIS short forms were scored using a T-score metric with a mean of 50 and standard deviation (SD) of 10 and were normalized to the general US population, meaning that

a score of 50 represents the average US adult's experience of the HRQOL domain of interest [32]. For pain and fatigue, higher scores represent greater symptom burden. For physical functioning, higher scores represent better functioning.

Multimorbidity

Patients self-reported their history of ten comorbid conditions: (1) heart attack; (2) heart failure or congestive heart failure; (3) stroke; (4) asthma; (5) lung disease; (6) diabetes; (7) arthritis; (8) depression; (9) anxiety; and (10) a sleep disorder. For each condition, survivors were categorized as having the condition (responding 'Yes' to survey item) or not having the condition (responding 'No,' 'Unsure,' or missing survey item). We focused on four of these comorbidities (CVD, lung disease, diabetes, arthritis) common among older adults (hereafter 'selected conditions') [1]. Survivors were coded as having a history of CVD if they answered 'yes' to either heart attack and/or heart failure.

To control for the presence of other comorbid conditions in our analyses and examine the independent effect of the selected conditions, we created an additional comorbid conditions indicator using the 10 comorbidities identified in the survey (excluding the condition being independently examined in the model). Other conditions were coded as either 0 = no additional condition or 1 = one or more additional comorbid conditions. Finally, we created a comorbid count variable (cancer-only, cancer + 1 condition, cancer + 2 or more conditions) using all 10 self-reported comorbid conditions.

Sociodemographic variables

Sociodemographic characteristics were obtained from self-report data and through SEER. Self-report variables included: education attainment (< high school graduate, high school graduate or GED/some college, ≥ college degree), race/ethnicity (Non-Hispanic White, Non-Hispanic Black, Hispanic, Non-Hispanic Asian, Other race/ethnicity/multiracial), and marital status (married/living with a partner, never married/separated/divorced/widowed). We obtained data on survivors' sex (male/female) from SEER.

Cancer clinical variables

Survivors' clinical characteristics were obtained through self-report and SEER. SEER data included: cancer site (lung cancer, breast cancer, gynecologic cancer [uterine, cervical], colorectal cancer, non-Hodgkin lymphoma, prostate cancer), stage (as measured by American Joint Committee on Cancer, 7th edition: early stage [I/II], advanced stage [III/IV]), and

age at diagnosis. We combined uterine and cervical cancer into one 'gynecologic cancer' category due to small sample size. Cancer treatment information was collected via self-report. Older cancer survivors were asked, separately, if they ever received chemotherapy [yes/no], radiation [yes/no], and/or surgery [yes/no] as part of their cancer treatment.

Statistical analysis

We computed descriptive statistics for sociodemographic, clinical, and outcome variables. We created generalized linear models for each selected condition and each outcome measure (pain, fatigue, physical function). Each generalized linear model included self-reported history of the selected condition as the primary independent variable, and was adjusted for sociodemographic characteristics, clinical characteristics, and presence of other comorbid conditions. We also tested a generalized linear model for each outcome (pain, fatigue, physical function) using the comorbid count variable as the primary independent variable. The fully adjusted models controlled for sociodemographic and clinical characteristics. To identify possible differences in the associations between comorbid count and each outcome across cancer type, we also conducted a sensitivity analysis that stratified the comorbid count models by the four most common cancer types in our sample (lung cancer, colorectal cancer, breast cancer, and prostate cancer). We were unable to conduct these sensitivity analyses for the selected conditions models because of small sample sizes.

Previous research in cancer survivors has identified ranges of PROMIS T-scores that indicate minimally important differences between groups for fatigue (2.5–5.0 points), pain interference (4.0–6.0 points), and physical function (4.0–6.0 points) [33]. Minimally important differences have been used in previous work with PROMIS data to suggest clinically meaningful results, and we examine differences between survivors with and without the four selected conditions using the lower bound of these ranges as the threshold for clinically meaningful results. All tests were two-sided, the significance level was set at 0.001 to account for the multiple comparisons, and analyses were completed using SAS 9.4 (Cary, NC).

Results

We found that 74% (N = 1494) of cancer survivors were multimorbid (at least 1 additional comorbidity), and just under half had 2 or more comorbid conditions (45.7%; Table 1). Overall, cancer survivors reported physical function limitations notably below the US population average of 50 (Mean [M] = 43.7, Standard Deviation [SD] = 9.8) [32]. In contrast, the overall sample reported pain (M = 51.8, SD = 10.4) and

Table 1 Sociodemographic and clinical characteristics of older cancer survivors (N = 2019)

	N (%)
Age at diagnosis (mean, standard deviation)	71.8 (4.97)
Sex	
Male	1029 (51.0)
Female	990 (49.0)
Marital status	
Married/living with a partner	1246 (62.3)
Never married/separated/divorced/widowed	755 (37.7)
Education	
Less than high school grad	436 (21.9)
High school grad or completed some college	1028 (51.6)
Completed a college degree or higher	527 (26.5)
Race/ethnicity	
Non-Hispanic White	985 (48.8)
Non-Hispanic Black	358 (17.7)
Hispanic	333 (16.5)
Non-Hispanic Asian	288 (14.3)
Other race/multiple races	55 (2.7)
Cancer site	
Lung cancer	372 (18.4)
Breast cancer	414 (20.5)
Gynecologic cancer	115 (5.7)
Colorectal cancer	380 (18.8)
Non-Hodgkin lymphoma	178 (8.8)
Prostate cancer	560 (27.7)
Stage of disease	
Stage I/II	1441 (71.4)
Stage III/IV	578 (28.6)
History of chemotherapy	
Received chemotherapy	782 (39.8)
Did not receive chemotherapy	1183 (60.2)
History of radiation	
Received radiation	830 (41.9)
Did not receive radiation	1151 (58.1)
Comorbid conditions	
Cardiovascular disease	264 (13.1)
Arthritis	852 (42.2)
Diabetes	577 (28.6)
Lung disease	312 (15.5)
Total number of comorbid conditions	
Cancer only	525 (26.0)
1	571 (28.3)
2	431 (21.4)
3	246 (12.2)
4 or more	246 (12.3)

fatigue levels (M = 51.0, SD = 10.5) similar to the general population. When examining the characteristics of survivors with each of the four selected conditions, we saw differences

Table 2 Adjusted mean scores for pain, fatigue, and physical function PROMIS measures by comorbidity

Outcome	Cardiovascular disease[a]		Lung disease[a]		Diabetes[a]		Arthritis[a]		Comorbid count[b]		
	Yes N=264	No N=1755	Yes N=312	No N=1442	Yes N=577	No N=1707	Yes N=852	No N=1167	Cancer only N=525	Cancer+1 N=571	Cancer+2 or more N=923
Physical function	40.2 (38.9–41.4)	43.8 (43.1–44.5)	38.8 (37.6–40.0)	43.5 (42.8–44.2)	41.4 (40.5–42.3)	43.9 (43.2–44.6)	40.8 (40.0–41.6)	44.0 (43.2–44.7)	46.3 (45.4–47.2)	43.2 (42.4–44.1)	38.8 (38.0–39.6)
Pain	55.0 (53.6–56.4)	52.1 (51.3–52.9)	54.7 (53.3–56.0)	52.4 (51.6–53.3)	54.4 (53.4–55.5)	52.3 (51.5–53.1)	55.9 (54.9–56.8)	51.5 (50.7–52.4)	49.7 (48.6–50.7)	52.9 (51.9–53.9)	56.8 (55.9–57.8)
Fatigue	54.6 (53.3–56.0)	51.2 (50.4–52.0)	55.8 (54.5–57.2)	51.6 (50.7–52.4)	53.5 (52.4–54.5)	51.6 (50.7–52.4)	53.7 (52.8–54.6)	51.2 (50.4–52.0)	49.0 (48.0–50.0)	51.5 (50.6–52.5)	56.0 (55.1–56.9)

[a]Models adjusted for: age at diagnosis, race/ethnicity, education, sex, marital status, other comorbid conditions, cancer site, chemotherapy, radiation, surgery, cancer stage

[b]Model adjusted for: age at diagnosis, race/ethnicity, education, sex, marital status, cancer site, chemotherapy, radiation, surgery, cancer stage

in sociodemographic and clinical characteristics (Supplemental Table 1) and in physical function, fatigue, and pain (Table 2). Survivors diagnosed with cardiovascular disease or lung disease were more likely to have been diagnosed with lung cancer. Survivors with arthritis were significantly more likely to be women (57.3%) and have early stage cancer (76.5%) compared to survivors without arthritis. Survivors diagnosed with diabetes were more likely to have less than a high school education (28.4%) compared to survivors without diabetes (19.3%).

After controlling for sociodemographic characteristics, clinical characteristics, and history of other comorbid conditions, cancer survivors with CVD reported lower physical functioning ($\beta = -3.85$, $p < 0.001$; Table 3), higher pain ($\beta = 2.74$, $p < 0.001$; Table 3), and higher fatigue ($\beta = 3.45$, $p < 0.001$; Table 3) compared to survivors without CVD. The adjusted means for fatigue reached the threshold for a minimally important difference between survivors with CVD and those without CVD (Table 2).

After controlling for all other characteristics, cancer survivors with lung disease had significantly lower physical functioning ($\beta = -4.96$, $p < 0.001$; Table 3) and higher levels of pain ($\beta = 2.45$, $p < 0.001$; Table 3) and fatigue ($\beta = 4.49$, $p < 0.001$; Table 3) compared to survivors without lung disease. The adjusted means for both physical function and fatigue reached the threshold for a minimally important difference between survivors with lung disease and those without lung disease (Table 2).

After controlling for all other characteristics, cancer survivors with diabetes had significantly worse physical functioning ($\beta = -2.05$, $p < 0.001$; Table 3) and higher levels of pain ($\beta = 1.93$, $p < 0.001$; Table 3) and fatigue ($\beta = 1.87$ $p < 0.001$; Table 3) compared to survivors without diabetes. None of the adjusted means reached the threshold for minimally important differences between survivors with and without diabetes (Table 2).

After controlling for sociodemographic characteristics, clinical characteristics, and history of other comorbid conditions, cancer survivors with arthritis had significantly worse physical function ($\beta = -3.32$, $p < 0.001$; Table 3) and higher levels of pain ($\beta = 4.34$, $p < 0.001$; Table 3) and fatigue ($\beta = 2.57$, $p < 0.001$; Table 3) compared to survivors without arthritis. The adjusted means for pain and fatigue reached the threshold for a minimally important difference between survivors with arthritis and those without arthritis (Table 2).

Cancer survivors with 1 comorbid condition reported significantly worse physical functioning ($\beta = -3.24$, $p < 0.001$), higher pain ($\beta = 3.11$, $p < 0.001$), and higher fatigue ($\beta = 2.72$, $p < 0.001$) compared to survivors with only a cancer history (Table 4). Cancer survivors with a history of 2 or more comorbid conditions reported even worse physical functioning ($\beta = -7.63$, $p < 0.001$), higher pain ($\beta = 7.27$, $p < 0.001$), and higher fatigue ($\beta = 7.25$, $p < 0.001$) compared

to survivors with only a cancer history. For both physical function and pain, the adjusted means reached the threshold for a minimally important difference between cancer only and cancer + 2 or more and between cancer + 1 and cancer + 2 or more. The fatigue adjusted means reached the threshold for a minimally important difference between all groups. The results of our sensitivity analysis are reported in Supplemental Table 1. Overall, these findings found that the direction of the associations (worse physical functioning and higher symptoms among survivors with more comorbidities) was consistent across cancer types and with the non-stratified models.

Discussion

Our study found that three-quarters of older cancer survivors were multimorbid, which is similar to findings in the broader Medicare population. Specifically, 63% of Medicare beneficiaries 65–74 years report multimorbidity, and 78% of Medicare beneficiaries 75–84 years report multimorbidity [1]. Older survivors with arthritis reported clinically relevant pain and fatigue, survivors with lung disease reported clinically relevant physical function limitations and fatigue, survivors with CVD reported clinically relevant fatigue, and survivors with diabetes did not report any clinically relevant symptoms or functioning concerns, consistent with prior literature [1]. Lung disease has previously been found to be associated with impaired physical function and increased total symptom burden [34, 35]. Similarly, prior work has found that diabetes is not as strongly associated with HRQOL compared to other comorbid conditions [36, 37]. A strength of our study is the utilization of population-based cancer registries (SEER) to identify and recruit the sample, providing a more generalizable estimate of the multimorbidity burden and HRQOL of older cancer survivors. Overall, our study results suggest that understanding older cancer survivor's multimorbidity profile may be clinically important to mitigate potentially adverse outcomes following a cancer diagnosis.

We also compared associations between specific comorbid conditions and the total burden of multimorbidity on HRQOL. We found that the presence of any single comorbid condition (cancer + 1 condition) had a lower symptom burden than a comorbid condition with an identified HRQOL deficit. For example, pain reported by older cancer survivors with arthritis was higher than for cancer survivors reporting any comorbid condition. These findings are consistent with existing evidence that identified stronger associations between certain comorbid conditions and specific outcomes [28].

Previous research has also indicated that having multiple comorbid conditions is associated with lower HRQOL

Table 3 Generalized linear models examining each selected comorbidity and the PROMIS domains

	Cardiovascular disease		Arthritis		Diabetes		Lung disease	
	B (SE)	p value	B (SE)	p value	B (SE)	p value	B (SE)	p value
Physical function								
History of selected condition (ref = no)								
Yes	− 3.68 (0.58)	< 0.001	− 3.16 (0.40)	< 0.001	− 2.08 (0.43)	< 0.001	− 5.10 (0.57)	< 0.001
Other comorbid conditions (ref = no)								
Yes	− 5.33 (0.43)	< 0.001	− 4.62 (0.40)	< 0.001	− 5.34 (0.41)	< 0.001	− 4.78 (0.42)	< 0.001
Age at diagnosis	− 0.23 (0.58)	< 0.001	− 0.24 (0.04)	< 0.001	− 0.24 (0.04)	< 0.001	− 0.24 (0.04)	< 0.001
Sex (ref = male)								
Female	− 1.68 (0.58)	0.004	− 1.38 (0.58)	0.016	− 1.20 (0.58)	0.039	− 1.58 (0.57)	0.006
Race/ethnicity (ref = non-Hispanic White)								
Non-Hispanic Black	− 0.95 (0.56)	0.091	− 0.93 (0.56)	0.098	− 0.95 (0.57)	0.094	− 1.08 (0.56)	0.054
Hispanic	− 1.59 (0.59)	0.007	− 1.42 (0.59)	0.016	− 1.58 (0.60)	0.008	− 1.86 (0.59)	0.002
Non-Hispanic Asian	− 1.24 (0.59)	0.037	− 1.35 (0.59)	0.022	− 1.37 (0.60)	0.022	− 1.55 (0.59)	0.009
Other race/multiple races	− 0.88 (1.21)	0.465	− 0.96 (1.20)	0.422	− 1.04 (1.21)	0.386	− 0.98 (1.20)	0.413
Education (ref = completed college degree or higher)								
< High school (HS) grad	− 3.57 (0.60)	< 0.001	− 3.57 (0.60)	< 0.001	− 3.82 (0.60)	< 0.001	− 3.59 (0.60)	< 0.001
HS grad or some college	− 1.66 (0.47)	< 0.001	− 1.73 (0.47)	< 0.001	− 1.93 (0.47)	< 0.001	− 1.77 (0.47)	< 0.001
Marital status (ref = married/partnered)								
Not partnered*	− 0.87 (0.42)	.042	− 0.73 (0.42)	0.083	− 0.85 (0.42)	0.045	− 0.79 (0.42)	0.061
Cancer site (ref = prostate)								
Breast	− 2.42 (0.86)	0.005	− 2.40 (0.85)	0.005	− 2.62 (0.86)	0.002	− 2.37 (0.85)	0.006
Lung	− 5.06 (0.70)	< 0.001	− 5.24 (0.69)	< 0.001	− 5.32 (0.69)	< 0.001	− 4.11 (0.72)	< 0.001
Colorectal	− 2.59 (0.73)	< 0.001	− 2.85 (0.73)	< 0.001	− 2.81 (0.73)	< 0.001	− 2.44 (0.73)	< 0.001
Non-Hodgkin lymphoma	− 1.59 (0.85)	0.062	− 1.77 (0.84)	0.036	− 1.95 (0.85)	0.022	− 1.46 (0.84)	0.083
Gynecologic	− 3.22 (1.08)	0.003	− 3.20 (1.08)	0.003	− 3.35 (1.08)	0.002		
Chemotherapy (ref = no)								
Yes	− 2.83 (0.48)	< 0.001	− 2.93 (0.48)	< 0.001	− 2.90 (0.48)	< 0.001	− 2.85 (0.48)	< 0.001
Radiation (ref = no)								
Yes	− 0.72 (0.42)	0.090	− 0.73 (0.42)	0.082	− 0.70 (0.42)	0.098	− 0.57 (0.42)	0.177
Surgery (ref = no)								
Yes	0.68 (0.49)	0.164	0.68 (0.48)	0.159	0.70 (0.49)	0.149	0.70 (0.48)	0.145
Stage (ref = early stage)								
Late stage	− 1.57 (0.51)	0.002	− 1.58 (0.51)	0.002	− 1.57 (0.51)	0.002	− 1.58 (0.51)	0.002
Pain								
History of selected condition (ref = no)								
Yes	2.83 (0.67)	< 0.001	4.32 (0.46)	< 0.001	1.97 (0.50)	< 0.001	2.39 (0.66)	< 0.001
Other comorbid conditions (ref = no)								
Yes	5.29 (0.50)	< 0.001	3.77 (0.46)	< 0.001	5.05 (0.47)	< 0.001	5.34 (0.49)	< 0.001
Age at diagnosis	− 0.08 (0.05)	0.091	− 0.07 (0.05)	0.098	− 0.06 (0.05)	0.172	− 0.07 (0.05)	0.108
Sex (ref = male)								
Female	0.32 (0.67)	0.635	− 0.06 (0.66)	0.927	− 0.07 (0.67)	0.913	0.16 (0.67)	0.807
Race/ethnicity (ref = non-Hispanic White)								
Non-Hispanic Black	1.56 (0.65)	0.016	1.50 (0.64)	0.019	1.55 (0.65)	0.018	1.58 (0.65)	0.015
Hispanic	2.58 (0.69)	< 0.001	2.47 (0.68)	< 0.001	2.57 (0.69)	< 0.001	2.65 (0.69)	< 0.001
Non-Hispanic Asian	3.01 (0.68)	< 0.001	3.15 (0.67)	< 0.001	3.14 (0.69)	< 0.001	3.09 (0.68)	< 0.001
Other race/multiple races	4.68 (1.38)	.001	4.86 (1.36)	< 0.001	4.90 (1.38)	< 0.001	4.72 (1.38)	0.001
Education (ref = completed college degree or higher)								
< High School (HS) grad	4.01 (0.69)	< 0.001	3.95 (0.68)	< 0.001	4.23 (0.69)	< 0.001	4.12 (0.69)	< 0.001

Table 3 (continued)

	Cardiovascular disease		Arthritis		Diabetes		Lung disease	
	B (SE)	p value	B (SE)	p value	B (SE)	p value	B (SE)	p value
HS grad or some college	2.10 (0.54)	<0.001	2.14 (0.53)	<0.001	2.32 (0.54)	<0.001	2.25 (0.54)	<0.001
Marital status (ref=married/partnered)								
Not partnered*	0.82 (0.49)	0.093	0.73 (0.48)	0.131	0.81 (0.49)	0.098	0.78 (0.49)	0.112
Cancer site (ref=prostate)								
Breast	1.18 (0.99)	0.235	1.09 (0.98)	0.264	1.35 (0.99)	0.175	1.22 (0.99)	0.218
Lung	2.08 (0.80)	0.010	2.34 (0.79)	0.003	2.29 (0.80)	0.004	1.97 (0.83)	0.018
Colorectal	0.92 (0.84)	0.274	1.34 (0.83)	0.108	1.09 (0.84)	0.195	0.98 (0.84)	0.244
Non-Hodgkin lymphoma	0.41 (0.98)	0.674	0.60 (0.96)	0.535	0.73 (0.98)	0.457	0.40 (0.98)	0.681
Gynecologic	1.32 (1.25)	0.290	1.33 (1.23)	0.279	1.43 (1.25)	0.252	1.41 (1.25)	0.258
Chemotherapy (ref=no)								
Yes	2.33 (0.55)	<0.001	2.40 (0.55)	<0.001	2.39 (0.55)	<0.001	2.35 (0.55)	<0.001
Radiation (ref=no)								
Yes	1.00 (0.49)	0.040	1.11 (0.48)	0.021	1.00 (0.49)	0.040	0.97 (0.49)	0.048
Surgery (ref=no)								
Yes	0.34 (0.56)	0.540	0.34 (0.55)	0.535	0.33 (0.56)	0.557	0.31 (0.56)	0.577
Stage (ref=early stage)								
Late stage	1.28 (0.59)	0.030	1.43 (0.58)	0.014	1.29 (0.59)	0.028	1.27 (0.59)	0.031
*Fatigue**								
History of selected condition (ref=no)								
Yes	3.42 (0.66)	<0.001	2.51 (0.45)	<0.001	1.91 (0.49)	<0.001	4.56 (0.65)	<0.001
Other comorbid conditions (ref=no)								
Yes	4.85 (0.49)	<0.001	4.74 (0.45)	<0.001	4.81 (0.47)	<0.001	4.24 (0.48)	<0.001
Age at diagnosis	0.03 (0.04)	0.471	0.05 (0.04)	0.282	0.05 (0.04)	0.278	0.04 (0.04)	0.314
Sex (ref=male)								
Female	1.31 (0.66)	0.046	1.10 (0.65)	0.912	0.87 (0.66)	0.187	1.21 (0.65)	0.064
Race/ethnicity (ref=non-Hispanic White)								
Non-Hispanic Black	− 0.96 (0.64)	0.134	− 0.98 (0.63)	0.122	− 0.97 (0.64)	0.133	− 0.84 (0.64)	0.186
Hispanic	− 0.14 (0.68)	0.839	− 0.34 (0.67)	0.615	− 0.15 (0.68)	0.824	0.10 (0.67)	0.882
Non-Hispanic Asian	0.11 (0.67)	0.865	0.23 (0.67)	0.727	0.24 (0.68)	0.720	0.39 (0.67)	0.566
Other race/multiple races	2.51 (1.35)	0.064	2.56 (1.34)	0.057	2.72 (1.36)	0.045	2.68 (1.35)	0.048
Education (ref=completed college degree or higher)								
<High school (HS) grad	3.11 (0.68)	<0.001			2.25 (0.68)	<0.001	3.14 (0.68)	<0.001
HS grad or some college	1.81 (0.53)	0.001	1.85 (0.53)	0.001	2.07 (0.53)	<0.001	1.92 (0.53)	<0.001
Marital status (ref=married/partnered)								
Not partnered*	0.90 (0.48)	0.062	0.74 (0.48)	0.121	0.89 (0.48)	0.065	0.84 (0.48)	0.079
Cancer site (ref=prostate)								
Breast	0.71 (0.97)	0.465	0.66 (0.97)	0.494	0.92 (0.98)	0.345	0.70 (0.97)	0.469
Lung	3.65 (0.79)	<0.001	3.70 (0.78)	<0.001	3.92 (0.79)	<0.001	2.83 (0.82)	0.001
Colorectal	1.78 (0.83)	0.032	1.94 (0.82)	0.019	2.00 (0.83)	0.016	1.66 (0.83)	0.045
Non-Hodgkin lymphoma	1.43 (0.96)	0.137	1.57 (0.96)	0.100	1.78 (0.96)	0.064	1.34 (0.96)	0.163
Gynecologic	1.66 (1.23)	0.175	1.60 (1.22)	0.189			1.75 (1.22)	0.153
Chemotherapy (ref=no)								
Yes	3.34 (0.55)	<0.001	3.43 (0.54)	<0.001	3.40 (0.55)	<0.001	3.35 (0.54)	<0.001
Radiation (ref=no)								
Yes	1.79 (0.48)	<0.001	1.77 (0.48)	<0.001	1.77 (0.48)	<0.001	1.65 (0.48)	0.001
Surgery (ref=no)								
Yes	− 0.58 (0.55)	0.290	− 0.59 (0.54)	0.283	− 0.61 (0.55)	0.265	− 0.62 (0.55)	0.260

Table 3 (continued)

	Cardiovascular disease		Arthritis		Diabetes		Lung disease	
	B (SE)	p value	B (SE)	p value	B (SE)	p value	B (SE)	p value
Stage (ref = early stage)								
Late stage	2.13 (0.58)	< 0.001	2.10 (0.57)	< 0.001	2.12 (0.58)	< 0.001	2.13 (0.58)	< 0.001

*Not partnered marital status includes: never married, divorced, widowed, or separated

Table 4 Generalized linear models examining total number of comorbid conditions and PROMIS domains

	Physical function		Pain		Fatigue	
	B (SE)	p value	B (SE)	p value	B (SE)	p value
Comorbid conditions (ref = 0)						
1 condition	− 3.08 (0.50)	< 0.001	3.24 (0.58)	< 0.001	2.55 (0.57)	< 0.001
2+ condition	− 7.52 (0.47)	< 0.001	7.20 (0.54)	< 0.001	7.03 (0.53)	< 0.001
Age at diagnosis	− 0.25 (0.04)	< 0.001	− 0.06 (0.05)	0.177	0.05 (0.04)	0.242
Sex (ref = male)						
Female	− 1.44 (0.57)	0.011	0.15 (0.66)	0.821	1.10 (0.65)	0.090
Race/ethnicity (ref = non-Hispanic White)						
Non-Hispanic Black	− 1.01 (0.56)	0.070	1.60 (0.64)	0.013	− 0.91 (0.63)	0.149
Hispanic	− 1.54 (0.59)	0.009	2.52 (0.68)	< 0.001	− 0.21 (0.67)	0.754
Non-Hispanic Asian	− 1.47 (0.59)	0.012	3.22 (0.68)	< 0.001	0.35 (0.66)	0.593
Other race/multiple races	− 1.07 (1.19)	0.368	4.87 (1.36)	< 0.001	2.75 (1.34)	0.042
Education (ref = completed college degree or higher)						
< High school (HS) grad	− 3.68 (0.59)	< 0.001	4.09 (0.69)	< 0.001	3.21 (0.67)	< 0.001
HS grad or some college	− 1.85 (0.46)	< 0.001	2.24 (0.53)	< 0.001	1.98 (0.52)	< 0.001
Marital status (ref = married/partnered)						
Not partnered[a]	-0.64 (0.42)	0.130	0.62 (0.49)	0.205	0.66 (0.48)	0.164
Cancer site (ref = prostate)						
Breast	− 2.27 (0.85)	0.008	1.01 (0.98)	0.304	0.54 (0.96)	0.577
Lung	− 4.93 (0.69)	< 0.001	1.92 (0.79)	0.016	3.49 (0.78)	< 0.001
Colorectal	− 2.60 (0.72)	< 0.001	0.91 (0.83)	0.274	1.78 (0.82)	0.030
Non-Hodgkin lymphoma	− 1.65 (0.84)	0.049	0.45 (0.97)	0.645	1.48 (0.95)	0.119
Gynecologic	− 3.03 (1.07)	0.005	1.13 (1.24)	0.359	1.46 (1.21)	0.227
Chemotherapy (ref = no)						
Yes	− 3.01 (0.48)	< 0.001	2.48 (0.55)	< 0.001	3.52 (0.54)	< 0.001
Radiation (ref = no)						
Yes	− 0.66 (0.42)	0.115	0.96 (0.48)	0.047	1.74 (0.47)	< 0.001
Surgery (ref = no)						
Yes	0.68 (0.48)	0.154	0.34 (0.55)	0.533	− 0.59 (0.54)	0.279
Stage (ref = early stage)						
Late stage	− 1.56 (0.50)	0.002	1.29 (0.58)	0.027	2.13 (0.57)	< 0.001

[a]Not partnered marital status includes: never married, divorced, widowed, or separated

among older cancer survivors and may be associated with lower overall survival [34–39]. Our results support previous research, indicating that cumulative multimorbidity burden may be associated with lower HRQOL, regardless of the specific chronic conditions. Older cancer survivors with two or more additional comorbid conditions reported worse pain, fatigue, and greater physical function limitations compared to survivors reporting only one comorbidity and survivors without any additional comorbidities. The current COVID-19 pandemic has highlighted both risks associated with having underlying health conditions [40], and challenges with getting needed care, given stay-at-home orders and social distancing guidelines. For cancer patients with multimorbidity, such challenges are even greater. The healthcare

workforce, primarily within primary care and oncology, is already experiencing problems in providing timely, high-quality care to all cancer survivors [41]. As a result, it is critical to find ways to identify those patients who may have greater symptom burden and functional decline, to both support ways to help patients manage at home and make referrals to appropriate care when needed. Consideration of various potential risk factors for poor outcomes, including the presence of other chronic conditions, is a necessary step to identify older survivors who may need more regular monitoring and assistance in symptom management as they transition to survivorship.

Our findings should be interpreted considering the study limitations. First, the survey was a cross-sectional assessment of health outcomes 6 to 12 months after a cancer diagnosis. This precludes our ability to examine the predictive nature of multimorbidity on health outcomes after cancer, and the patterns of associations between multimorbidity and HRQOL may look different in survivors further away from diagnosis. Additionally, we do not know when each of these conditions was diagnosed in relation to survivors' cancer diagnoses and treatment; this timing may be important [42]. We also do not have information on the severity or longevity of each of these conditions and thus are unable to indicate the true level of multimorbidity burden [43]. Beyond the timing of diagnosis and severity of the comorbidities, there may also be additional missing variables (e.g. geographic region, annual income) that could affect the associations presented in this study. Finally, although the sample used in the current study was recruited through the population-based SEER cancer registries, we only utilized four of the SEER registries. This may limit the generalizability of our study findings to the broader population of older cancer survivors in the US.

The transition from active treatment to post-treatment survivorship is a critical point in the care of cancer survivors and includes the management of the physical and psychosocial effects of cancer and its treatment [44, 45]. Our results complement and extend a growing interest in survivorship research—risk stratification of survivorship care [41]. Risk-stratified care involves identifying those patients who have the greatest needs and then 'triaging' patients to different care pathways based on their level of risk. Patients with the highest risk (for example, determined by the type and count of comorbidity, prognosis/risk of recurrence, late effects and/or ability to self-manage) could continue their follow-up with oncology providers, while individuals at moderate or low risk could be seen by advanced practice providers, primary care or both [41]. Examining select comorbid conditions may identify survivors at risk for specific poor outcomes (e.g. arthritis and pain), but examining the total number of conditions may identify survivors at risk for multiple poor outcomes. Recognizing the key role of multimorbidity

in the health of older cancer survivors will aid in the timely identification of problematic symptoms and the introduction of personalized and appropriate strategies for prevention or management.

Compliance with ethical standards

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