Relationship between sleep and exercise as colorectal cancer survivors transition off treatment

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Abstract

Purpose The primary objective of this study was to evaluate the relationship between exercise and sleep disturbance in a sample of individuals diagnosed with stage I, II, and III colorectal cancer (CRC) as patients transitioned off first-line treatment. We also sought to identify heterogeneity in the relationship between sleep disturbance and exercise.

Methods Data were obtained from the MY-Health study, a community-based observational study of adults diagnosed with cancer. Patient-Reported Outcomes Measurement Information System® (PROMIS) measures (e.g., PROMIS Sleep) were administered, and participants self-reported demographics, comorbidities, cancer treatment, and exercise. Regression mixture and multiple regression models were used to evaluate the relationship between sleep disturbance and exercise cross-sectionally at an average of 10 months after diagnosis, and the change in sleep disturbance over a 7-month period, from approximately 10 to 17 months post-diagnosis.

Results Patients whose exercise was categorized as likely at or above American College of Sports Medicine's guidelines did not report statistically better sleep quality compared to patients who were classified as not active. However, retirement (B = −2.4), anxiety (B = 0.21), and fatigue (B = 0.24) had statistically significant relationships with sleep disturbance ($p < 0.05$). Increase in exercise was not significantly associated with a decrease in sleep disturbance. No statistical heterogeneity was revealed in the relationship between sleep and exercise.

Conclusions Further prospective research using an objective measure of exercise is warranted to confirm or refute the nature of the relationship between exercise and sleep disturbance in individuals diagnosed with CRC transitioning off first-line treatment.

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Background

Between 30 and 87% of individuals diagnosed with cancer experience sleep disturbance [1], yet few studies examine sleep quality in the colorectal cancer (CRC) population. Individuals diagnosed with CRC manage unique consequences of CRC treatment such as bowel control and stomas, and common cancer-related symptoms such as fatigue, anxiety, pain, nausea, all of which have implications for sleep quality. Consequences of sleep disturbance include decreased cognitive functioning [2], fatigue [3], loss in work productivity and quality, and increased visits to health professionals [4].

Few treatment options are available for sleep disturbance. The two most widely used treatment options include cognitive behavioral therapy (CBT) and pharmacotherapies. CBT includes relaxation therapy, sleep hygiene, and cognitive therapy. Unfortunately, there are an inadequate number of providers trained in CBT for sleep disturbance, and patient adherence issues pose considerable barriers to the adequacy of sleep treatment [2]. Pharmacologic treatments are associated with adverse daytime side effects such as sedation or dizziness. Individuals diagnosed with cancer may experience disturbed sleep for a substantially longer duration than the 4 to 6 weeks, the maximum period of time for which pharmacologic sleep aids are recommended [5]. There is growing evidence that a third option, exercise, improves sleep quality in healthy individuals [6] and in specific cancer populations [7].

Exercise, unlike CBT and pharmacologic treatments, is not associated with side effects such as sedation. Exercise is linked to additional benefits such as improved aerobic fitness in individuals diagnosed with various cancers [8]. Exercise is also associated with a reduction in anxiety, pain, and fatigue in cancer populations, all of which are associated with sleep disturbance [7]. Exercise is potentially more accessible (and less expensive than CBT and pharmacologic treatments) because patients can exercise at home [9, 10].

Two observational studies assessed the relationship between sleep disturbance and exercise including individuals diagnosed with CRC: one in individuals diagnosed with stage II or III CRC undergoing chemotherapy in Taiwan [11] and another in women diagnosed with CRC and ovarian or breast cancer starting chemotherapy [12]. These studies did not find a statistically significant relationship between sleep and exercise, but sample sizes were small and sleep was not the primary outcome; studies were not powered to detect differences in sleep outcomes [11, 12]. Quality of life outcomes differ by cancer site [13]; therefore, the study including patients from mixed sites does not address sleep specifically in CRC. There are currently no published studies assessing the relationship between sleep and exercise specifically in CRC survivors who are transitioning off treatment. Chemotherapy is associated with disturbed sleep [1]; patients not on chemotherapy may experience different sleep outcomes. Exercise may be more effective in ameliorating sleep disturbance for some individuals and not for others, which could attenuate sleep outcomes between exercise treatment groups and usual care groups. The literature currently does not include a study exploring characteristics of possible subgroups of CRC survivors with similar sleep outcomes.

This observational study builds on the published literature by examining the relationship between sleep and exercise specifically in a large sample of individuals diagnosed with stage I, II, or III CRC in the USA. Exercise activity was self-reported at two time points after CRC diagnosis: 10 months after CRC diagnosis on average and approximately 17 months after CRC diagnosis, as patients transition off treatment and may be more physically active [14]. The first objective was to evaluate the relationship between sleep and exercise cross-sectionally (approximately 10 months after diagnosis) and over time from approximately 10 to 17 months after CRC diagnosis on average. It was hypothesized that patients whose exercise was categorized as moderately or highly active would self-report less sleep disturbance than patients who did not exercise. We also test the hypothesis that patients who increase exercise activity between study assessments would experience a decline in sleep disturbance. The second objective of this study was to uncover possible variability among patients and reveal relationships between sleep disturbance and exercise that may differ depending on severity of sleep disturbance using regression mixture models (RMMs).

Methods

MY-Health study design

This secondary data analysis was conducted using data from Georgetown University's Measuring Your Health (MY-Health) study [15, 16]. Potential study participants were identified from four Surveillance, Epidemiology, and End Results Program (SEER) cancer registries located in California (2), Louisiana, and New Jersey. Individuals aged 21–84 years diagnosed with cancer were invited to participate in the MY-Health study via mail. Participants included in this secondary analysis had been diagnosed with stage I, II, or III CRC and were able to perform physical activity, defined as patients who were able to get out of bed (self-reported). Questionnaires were administered to patients at two time points: 10 months on average after diagnosis (SD = 1.6, range for CRC patients 5.5 to 21.3, $n = 734$, referred to as month 10 data collection) and a 6-month follow-up approximately 17 months after diagnosis on average (SD = 2.0, range 12.8 to 26.4, $n = 400$, referred to as the month 17 data collection). The MY-Health study oversampled black, Hispanic, and Asian individuals and patients under 65. Additional details on the study design and procedures have been published [15]. This secondary data analysis was deemed non-human subjects research by the University of North Carolina IRB.

Measures

Dependent variable

Patient-Reported Outcomes Measurement Information System (PROMIS) Sleep Disturbance items were administered to patients at both study time points. PROMIS Sleep Disturbance includes a 7-day recall. Sleep disturbance is defined as "perceptions of sleep quality, sleep depth, and restoration associated with sleep" including perceived difficulties and concerns with getting to sleep or staying asleep, as well as perceptions of the adequacy of and satisfaction with sleep and does not include symptoms of specific sleep disorders or subjective estimates of sleep quantities [17]. A custom six-item short form was scored; the psychometric properties of the six-item form were evaluated in individuals enrolled in the MY-Health study (Cronbach's $\alpha = 0.88$–0.95) [18]. PROMIS Sleep Disturbance is a continuous variable scored on a T-score metric with a mean of 50 and standard deviation (SD) of 10 based on the referent population (mixture of clinical and the general US population [19]), and higher scores indicate worse sleep disturbance. Positive change over time is indicative of worsening sleep. Retrospective anchor-based mean change thresholds were estimated between 3 and 5 points for worsening sleep and between − 0.6 and − 2 points for improvement on PROMIS Sleep Disturbance [20].

Independent variables

Exercise Based on patients' responses to three exercise items, patients' exercise was categorized into one of four activity levels reflecting the American College of Sports Medicine's (ACSM) recommendation that individuals diagnosed with cancer achieve 150 min of moderate-intensity exercise per week or 75 min of vigorous exercise per week [21]: (1) not active, (2) slightly active, (3) moderately active, (4) highly active. Patients classified in the "not active" or "slightly active" groups likely did not meet the minimum ACSM guideline [21]. See supplemental materials for additional details on exercise level derivation.

Patient-level factors associated with sleep disturbance Cancer treatment type (e.g., surgery [22], chemotherapy [23]) and most recent date of treatment were self-reported. Comorbid conditions [24] were self-reported and categorized as no comorbid diseases, 1 comorbid disease, 2 or more comorbid diseases. Three PROMIS domains were included in the models as independent variables to assess aspects of health-related quality of life known to be associated with sleep disturbance: anxiety (11 items), fatigue [25] (14 items), and pain interference (11 items) [26]. PROMIS measures are normed to the general US population [19], and higher scores indicate worse anxiety, fatigue, and pain, respectively. Nausea severity was measured using a five-point nausea [27] item from the FACT-G physical well-being (PWB) subscale [28] with a recall period of the "past 7 days" and response choices ranging from 0 = "not at all" to 4 = "very much." Other characteristics known to be associated with different levels of sleep disturbance were included in the models such as age at diagnosis [27], sex [29], time since diagnosis [30], employment status [31], and an indicator for living with children under 18 [31]. Age and race were also included in the model to account for the over-sampling of younger and minority persons.

Factors associated with exercise Exercise participation is partially determined by patients' ability to perform activities [32]; thus patients' PROMIS physical function scores were included in the models (higher scores indicate better physical function). Social support is associated with participation in exercise and was measured using PROMIS ability to participate in social roles and activities (higher scores represent fewer social limitations). Higher weight is associated with less exercise; therefore, body mass index (BMI) was derived from patient-reported weight and height [29]. Other factors already included in the model that are associated with participation in exercise and affect sleep include increased age, parenthood, sex, and race [32–34].

Analyses

Analyses were conducted twice: cross-sectionally at approximately 10 months after diagnosis (month 10 analyses) and longitudinally from approximately 10 to 17 months after diagnosis (change analyses). Complete case analyses were conducted for all models. Due to missing data, 587 out of the 734 participants were included in the month 10 analyses. For the change analyses, 348 participants were included in the analyses.

Relationships between candidate independent variables were evaluated for collinearity by calculating bivariate correlations and variance inflation factor (VIF) within multiple regression models ($VIF \geq 10$). All categorical variables were entered into the model as indicator variables (except for the FACT-G PWB item which was entered as a continuous variable) because categorical response choices/levels were not necessarily evenly spaced.

RMMs [35] are special cases of finite mixture models, which model weighted combinations of different distributions. With RMMs, the component membership to each distribution is unobservable. In this study, we employed RMMs to test if heterogeneity was present in the associations between sleep disturbance and exercise. RMMs were estimated using Dual Quasi-Newton optimization [36], and models ranging from 1 to 4 classes were evaluated. The final models (e.g., choice of number of classes) were chosen based on fit (e.g., smallest Bayesian information criterion index (BIC), Akaike information criterion (AIC)) and interpretability. If the single class model was identified, then multiple regression (which assumes one common class of sleep disturbance) was used to model factors associated with sleep disturbance.

Supporting analyses

Sensitivity analysis on persistent exercise levels Patients classified as having no change in exercise may have had exercise levels above ACSM guidelines. Therefore, a sensitivity analysis was conducted to split the no change category into two persistent exercise categories: (1) no change in exercise activity—persistently not active or slightly active [reference category] and (2) no change in exercise activity—persistently moderately or highly active.

Loss to follow-up There was substantial patient attrition from the month 10 survey data collection to month 17 survey data collection. Patients who participated in month 10 and month 17 survey administrations (outcome = 1) were compared with patients who participated in month 10 but not month 17 (outcome = 0). The logistic model included patient characteristics at month 10 that were related to sleep disturbance and potentially associated with patient attrition.

Power Power to detect multiple classes using RMMs was evaluated and confirmed using simulations based on MY-Health study data, which provided information about the covariance structure among the independent variables. Subsamples were randomly drawn from the study dataset to simulate 1000 datasets for each of the parameter modifications in the simulation: overall sample size, numeric differences between coefficients in each latent class, variance of the error term used to simulate sleep disturbance scores, and proportion of sample within each class. For the month 10 analyses, power to detect multiple classes was above 95% for all circumstances when the mean difference between simulated sleep disturbance between classes differed by approximately 9 and 17 points, and the variance of the error term used to simulate sleep disturbance scores was less than 8. The proportion of the sample designated to each class was modified in the simulations, but the effect on power was negligible.

Power to detect an exercise effect was calculated for a sample size of 350. When the sample size was 350 and the partial correlation was set at 0.20 or higher, power was 0.85 at the lowest.

Analysis conventions An alpha of 0.05 or less was chosen as the criterion for statistical significance. All analyses were performed using SAS version 9.3 (SAS Institute Inc., Cary, NC, USA). SAS PROC FMM was used for RMMs [37].

Results

Patient, disease, and treatment characteristics were similar for the month 10 and change analysis samples (Table 1). Almost two thirds of the sample was moderately or highly active at the first data collection (month 10 analysis sample: 60.3%, change analysis sample: 60.9%). Mean PROMIS Sleep Disturbance scores hovered around the average scores observed in the referent population (i.e., patients who went to sleep clinics and healthy sleepers) (month 10 analysis sample: mean = 50.4; change analysis sample at month 10: mean = 49.5).

Bivariate relationships between sleep disturbance and exercise levels and change in sleep disturbance and change in exercise levels are presented in Tables 2 and 3, respectively. More severe sleep disturbance was observed in individuals reporting lower levels of exercise (Table 2). The mean change in PROMIS Sleep Disturbance scores for patients who increased activity from months 10 to 17 were negative, indicating improvement.

Regression mixture models

Model fit

For the month 10 model, the smallest BIC (1-class 4188.6, 2-class 4367.1, 3-class 4545.6, 4-class 4724.1) and AIC (1-class 4070.4, 2-class 4126.4, 3-class 4182.4, 4-class 4238.4) were associated with the one-class model. Therefore, a multivariable regression was chosen for the month 10 model.

Regarding the change model, the smallest BIC and AIC were associated with the two-class model (1-class: AIC = 2308.8, BIC = 2424.2; 2-class: AIC = 2069.8, BIC = 2304.8; 3-class: AIC = 2156.5, BIC = 2510.9; 4-class: AIC = 2432.6, BIC = 2906.5,). The two-class model chosen using SAS starting values [Supplemental Table 1] included one large class (mixing probability = 0.90) and a small class (mixing probability = 0.10). The regression coefficients for the smallest class were all statistically significant, and the variance for smallest class was less than 0.001, suggesting that

Table 1 Patient characteristics at month 10

Patient characteristics	Month 10 analysis sample ($n = 587$)	Change analysis sample ($n = 348$)
Age at diagnosis		
Mean (SD), median, min-max	62.1 (12.4), 64.0, 22–84	63.4 (11.3), 65.0, 30–84
Sex		
Female	308 (52.5%)	169 (48.6%)
BMI		
Mean (SD), median, min-max	28.8 (7.1), 27.4, 14–71	29.2 (7.4), 27.9, 17–71
Race		
White	325 (55.4%)	177 (50.9%)
Black	108 (18.4%)	63 (18.1%)
Other or multiple[a]	154 (26.2%)	108 (31.0%)
Employment status		
Working full time, part time or a student	233 (39.7%)	131 (37.6%)
Retired	250 (42.6%)	169 (48.6%)
Unemployed or disabled	104 (17.7%)	48 (13.8%)
Living status		
Live with child(ren) under 18 years old	97 (16.5%)	50 (14.4%)
Relevant comorbidities[b]		
No comorbid conditions	232 (39.5%)	140 (40.2%)
1 comorbid condition	155 (26.4%)	92 (26.4%)
2 or more comorbid conditions	200 (34.1%)	116 (33.3%)
Colorectal cancer stage		
Stage I	169 (28.8%)	99 (28.4%)
Stage II	183 (31.2%)	113 (32.5%)
Stage III	235 (40.0%)	136 (39.1%)
Level of exercise activity		
Not active	132 (22.5%)	75 (21.6%)
Slightly active	101 (17.2%)	61 (17.5%)
Moderately active	271 (46.2%)	160 (46.0%)
Highly active	83 (14.1%)	52 (14.9%)
Months since chemotherapy		
0 = never	263 (44.8%)	154 (45.8%)
1 = current	123 (21.0%)	72 (21.4%)
2 = 1–2 months	103 (17.5%)	65 (19.3%)
3 = > 2 months	98 (16.7%)	45 (13.4%)
Months since surgery		
0 = never	47 (8.0%)	21 (6.5%)
1 = 0–4 months	54 (9.2%)	28 (8.7%)
2 = more than 4 months	486 (82.8%)	272 (84.7%)
Months since diagnosis at data collection		
Mean (SD), median, min-max	9.7 (1.6), 9.5, 6–21	9.5 (1.3), 9.4, 6–15
PROMIS Sleep Disturbance T-score		
Mean (SD), median, min-max	50.4 (9.7), 51.2, 30–75	49.5 (9.7), 50.2, 30–75
PROMIS anxiety T-score		
Mean (SD), median, min-max	49.3 (10.7), 49.4, 36–84	47.6 (10.2), 47.4, 36–84
PROMIS depression T-Score		
Mean (SD), median, min-max	48.2 (10.3), 48.0, 36–81	46.6 (9.7), 45.2, 36–72
PROMIS fatigue T-score		
Mean (SD), median, min-max	51.9 (10.3), 51.7, 29–78	51.2 (10.2), 51.4, 29–78
PROMIS pain interference T-score		

Table 1 (continued)

Patient characteristics	Month 10 analysis sample ($n = 587$)	Change analysis sample ($n = 348$)
Mean (SD), median, min-max	52.9 (10.8), 54.6, 40–79	51.9 (10.8), 52.5, 40–79
PROMIS physical functioning T-score		
Mean (SD), median, min-max	44.8 (9.1), 43.8, 15–62	45.1 (8.8), 44.7, 21–62
PROMIS ability to participate in social roles and activities T-score		
Mean (SD), median, min-max	49.9 (10.0), 49.4, 25–66	50.6 (9.8), 50.1, 25–66
FACT-G physical well-being nausea item		
Mean (SD), median, min-max	0.6 (1.0), 0.0, 0–4	0.5 (0.9), 0.0, 0–4

Note: Percent calculated out of non-missing responses

BMI body mass index, *FACT-G* Functional Assessment of Cancer Therapy-General, *max* maximum, *min* minimum, *PROMIS* Patient-Reported Outcomes Measurement Information System, *SD* standard deviation

[a] Includes patients who categorized themselves as Asian, American Indian or Alaska Native, Asian Hawaiian or Pacific Islander, other, or a combination of races

[b] Includes heart failure, asthma, lung disease (e.g., emphysema, chronic bronchitis, chronic obstructive pulmonary disease), joint diseases (e.g., arthritis, rheumatism), anxiety, depression, stroke, mini-stroke, blood clot or bleeding in the brain, diabetes, sleep disorder, and HIV or AIDS

Table 2 Mean PROMIS Sleep Disturbance by exercise categories ($n = 587$)

Exercise category	PROMIS sleep disturbance scores at month 10					
	N	Mean	SD	Median	Min	Max
Not active	132	53.0	10.3	53.9	29.7	75.2
Slightly active	101	52.4	9.8	53.1	29.7	75.2
Moderately active	271	48.9	9.3	50.1	29.7	75.2
Highly active	83	48.5	8.8	48.8	29.7	71.6

PROMIS Patient-Reported Outcomes Measurement Information System, *SD* standard deviation, *Min* minimum, *Max* maximum

class was modeling outliers. Therefore, a multiple regression (1-class model) was chosen for the analysis.

Month 10 model

Table 4 presents the results of the month 10 model. Patients achieving moderate or highly active exercise levels did not have significantly better sleep than patients who were classified as not active. Being retired (compared to working), worse anxiety, and worse fatigue had statistically significant relationships with sleep disturbance. Although the coefficients on anxiety and fatigue were statistically significant, they were small (less than 1); a 25-point improvement in PROMIS fatigue would be associated with a 6-point improvement in PROMIS Sleep Disturbance.

Change model

Multiple regression results for the change analyses are presented in Table 5. Change in exercise level was not statistically significantly associated with change in sleep disturbance from months 10 to 17. Change in fatigue and sleep disturbance at month 10 had statistically significant relationships with change in sleep disturbance from month 10 to month 17, but coefficients were small: a 35-point improvement in

Table 3 Mean change in PROMIS sleep disturbance by change in exercise categories from month 10 to month 17 ($n = 348$)

	Change in PROMIS Sleep Disturbance					
Change in exercise categories	*N*	Mean	SD	Median	Minimum	Maximum
Less active by 2 or 3 exercise categories	18	2.61	8.09	2.0	− 14.8	19.2
Less active by 1 exercise category	44	0.04	7.97	1.4	− 20.0	12.6
No change	182	0.15	7.18	0.0	− 25.0	19.0
Persistently not active or slightly active[a]	49	− 0.7	6.9	0.0	− 21.7	15.8
Persistently moderately or highly active[a]	133	0.5	7.3	0.0	− 25.0	19.0
More active by 1 exercise category	68	− 0.57	6.77	0.0	− 22.3	14.2
More active by 2 or 3 exercise categories	36	− 0.96	5.49	0.0	− 10.8	9.8

PROMIS Patient-Reported Outcomes Measurement Information System, *SD* standard deviation

[a] Subset of the "no change" category

Table 4 Multiple regression results: relationship between PROMIS Sleep Disturbance and exercise from approximately 10 months after CRC diagnosis (*n* = 587)

Effect	Categories	Estimate	Standard error	Z	*P* value
Intercept		35.799	7.48	4.78	< 0.0001
Exercise group at month 10	Highly active	1.564	1.15	1.36	0.1738
	Moderately active	0.451	0.86	0.53	0.5989
	Slightly active	− 0.200	1.01	− 0.20	0.8428
	Not active	ref	–	–	–
Months between chemotherapy and month 10 data collection	1 = current	− 0.286	0.96	− 0.30	0.7650
	2 = 1–2 months	− 1.540	0.92	− 1.67	0.0956
	3 = > 2 months	− 0.294	0.93	− 0.31	0.7529
	0 = never	ref	–	–	–
Months between surgery and month 10 data collection	1 = 0–4 months	− 0.560	1.56	− 0.36	0.7200
	2 = more than 4 months	− 0.108	1.17	− 0.09	0.9260
	0 = never	ref	–	–	–
Race (collected at month 10)	Black	1.362	0.86	1.59	0.1113
	Other or multiple[a]	0.090	0.76	0.12	0.9059
	White	ref	–	–	–
Number of relevant comorbidities at month 10[b]	1 comorbid condition	1.517	0.80	1.91	0.0567
	2 or more comorbid conditions	0.826	0.81	1.03	0.3054
	No comorbid conditions	Ref	–	–	–
Sex (collected via SEER)	Female	0.363	0.64	0.56	0.5722
	Male	ref	–	–	–
Live with child under 18 years old at month 10	Checked	1.070	0.93	1.15	0.2490
	Unchecked	ref	–	–	–
Employment at month 10	Retired	− 2.426	0.89	− 2.72	0.0066
	Unemployed or disabled	− 0.686	0.96	− 0.72	0.4732
	Working full time, part time or student	ref	–	–	–
Months between diagnosis and month 10 data collection		0.024	0.20	0.12	0.9034
Age at diagnosis (years) (collected via SEER)		− 0.059	0.04	− 1.53	0.1266
BMI (collected at Month 10)		0.046	0.05	1.00	0.3169
PROMIS anxiety at month 10		0.207	0.04	4.90	< 0.0001
PROMIS fatigue at month 10		0.243	0.06	4.38	< 0.0001
PROMIS pain interference at month 10		0.044	0.04	1.04	0.2963
PROMIS physical functioning at month 10		−0.099	0.06	− 1.62	0.1063
PROMIS social functioning at month 10		−0.081	0.06	− 1.37	0.1706
FACT-G physical well-being nausea item at month 10		0.014	0.41	0.03	0.9734
Variance		54.840	3.20	_	_

BMI body mass index, *FACT-G* Functional Assessment of Cancer Therapy-General, *PROMIS* Patient-Reported Outcomes Measurement Information System, *SD* standard deviation

[a] Includes patients who categorized themselves as Asian, American Indian or Alaska Native, Asian Hawaiian or Pacific Islander, other, or a combination of races

[b] Includes heart failure, asthma, lung disease (e.g., emphysema, chronic bronchitis, chronic obstructive pulmonary disease), joint diseases (e.g., arthritis, rheumatism), anxiety, depression, stroke, mini-stroke, blood clot or bleeding in the brain, diabetes, sleep disorder, and HIV or AIDS

PROMIS fatigue would be associated with a 5.3-point improvement in PROMIS Sleep Disturbance. Poor sleep disturbance 10 months after diagnosis was associated with improvement in sleep disturbance from 10 to 17 months after CRC diagnosis (B = − 0.23).

Supporting analyses

Sensitivity analysis on persistent exercise levels

Change in exercise was not statistically associated with change in sleep disturbance (Supplemental Table 2).

Table 5 Multiple regression results: relationship between change in PROMIS Sleep Disturbance and change in exercise from approximately 10 to 17 months after CRC diagnosis ($n = 348$)

Effect	Categories	Estimate	Standard error	Z	*P* value
Intercept		7.488	5.06	1.48	0.1390
Exercise group change (month 17–month 10)	Less active by 1 exercise category	0.365	1.08	0.34	0.7355
	Less active by 2 or 3 exercise categories	2.579	1.57	1.64	0.1006
	More active by 1 exercise category	− 0.024	0.91	− 0.03	0.9791
	More active by 2 or 3 exercise categories	0.318	1.20	0.26	0.7913
	No change	ref	–	–	–
Months between chemotherapy and month 17 data collection	1 = current	1.502	1.72	0.87	0.3823
	2 = 1–2 months	0.515	1.76	0.29	0.7694
	3 = > 2 months	0.151	0.76	0.20	0.8422
	0 = never	ref	–	–	–
Months between surgery and month 17 data collection	1 = 0–4 months	− 2.570	1.77	− 1.45	0.1458
	2 = more than 4 months	− 0.451	1.25	− 0.36	0.7185
	0 = never	ref	–	–	–
Race (collected at month 10)	Black	− 0.421	0.90	− 0.47	0.6418
	Other or multiple[a]	− 0.292	0.89	− 0.33	0.7438
	White	ref	–	–	–
Number of relevant comorbidities at month 10[b]	1 comorbid condition	0.915	0.89	1.03	0.3046
	2 or more comorbid conditions	− 0.258	0.85	− 0.30	0.7610
	No comorbid conditions	ref	–	–	–
Sex (collected via SEER)	Female	− 0.073	0.69	− 0.11	0.9147
	Male	ref	–	–	–
Live with child under 18 years old at month 10	Checked	− 0.383	1.09	− 0.35	0.7247
	Unchecked	ref	–	–	–
Employment at month 10	Retired	− 1.297	0.95	− 1.37	0.1710
	Unemployed or disabled	− 0.636	1.11	− 0.58	0.5651
	Work	Ref	–	–	–
Months between diagnosis and month 17 data collection		0.124	0.17	0.73	0.4681
Age at diagnosis (years) (collected via SEER)		0.012	0.05	0.26	0.7931
BMI (collected at month 10)		0.070	0.05	1.46	0.1451
PROMIS sleep disturbance at month 10		− 0.225	0.04	− 6.01	< 0.0-001
PROMIS anxiety change (month 17–month 10)		0.091	0.06	1.63	0.1034
PROMIS depression change (month 17–month 10)		0.055	0.06	0.98	0.3267
PROMIS fatigue change (month 17–month 10)		0.152	0.05	2.87	0.0042
PROMIS pain interference change (month 17–month 10)		− 0.007	0.04	− 0.16	0.8740
PROMIS physical functioning (month 17–month 10)		0.006	0.07	0.09	0.9287
PROMIS social roles and activities (month 17–month 10)		− 0.083	0.06	− 1.51	0.1322
FACT-G physical well-being nausea item change (month 17–-month 10)		0.065	0.39	0.17	0.8688
Variance		37.481	2.84	_	_

BMI body mass index, *FACT-G* Functional Assessment of Cancer Therapy-General, *PROMIS* Patient-Reported Outcomes Measurement Information System.

[a] Includes patients who categorized themselves as Asian, American Indian or Alaska Native, Asian Hawaiian or Pacific Islander, other, or a combination of races

[b] Includes heart failure, asthma, lung disease (e.g., emphysema, chronic bronchitis, chronic obstructive pulmonary disease), joint diseases (e.g., arthritis, rheumatism), anxiety, depression, stroke, mini-stroke, blood clot or bleeding in the brain, diabetes, sleep disorder, and HIV or AIDS

Change in fatigue and sleep disturbance at month 10 had statistically significant relationships with change in sleep disturbance from 10 to 17 months after diagnosis.

Loss to follow-up

We compared patient characteristics for patients who were included in the RMM/multiple regression models ($n = 348$), with patients who were not included in the models due to missing values or survey attrition ($n = 386$) (Supplemental Table 3). Patients who were retired were more likely to participate in the month 10 data collection and follow-up survey (OR = 1.69), and minorities (Asian, American Indian or Alaska Native, Asian Hawaiian or Pacific Islander, patients who categorized their race as other, or a combination of races) were less likely to participate in both surveys (OR = 0.53).

Discussion

This observational study examined the relationship between sleep and exercise specifically in individuals diagnosed with stage I, II, or III CRC. We did not find a statistically significant relationship between sleep disturbance and exercise (or change in sleep and change in exercise), and this relationship did not differ by *severity* of (or magnitude of change) in sleep disturbance. This study confirms findings from previous studies showing that patients who are employed [31], anxious [38], or fatigued [39] also report worse sleep quality.

Approximately 40% of individuals in this study likely did not achieve the ACSM recommendations for exercise (150 min of moderate-intensity exercise per week or 75 min of vigorous exercise per week [21]) approximately 10 months after diagnosis. Between month 10 and month 17, almost 30% of the sample increased exercise categories by at least one level, and only 18% reduced exercise activity. These results reflect a previous study on exercise habits in CRC survivors showing that after treatment, CRC patients tend to increase exercise activity on average [40].

Patients may attribute sleep disturbance to general cancer-related factors such as the anxiety of cancer diagnosis, but reasons for sleep disturbance vary by cancer site. For example, estrogen deficiency caused by treatments for breast cancer are associated with hot flashes and sweating, both known disrupters of sleep [41]. Xerostomia (mouth dryness) is often experienced by individuals diagnosed with head and neck cancer and has been shown to be detrimental to sleep in this population [42]. It is possible that exercise may be more effective in reducing particular aggravating factors of sleep disturbance in some cancer populations but not in others, thus explaining why exercise is associated with improved sleep disturbance in breast cancer or mixed cancer studies but not overwhelmingly so in individuals diagnosed with CRC.

The results of this study should be considered in light of some limitations. Exercise activity levels presented some measurement limitations that precluded us from objectively and more precisely categorizing patients as achieving or not achieving ACSM exercise recommendations (e.g., *duration* of exercise not captured, exercise items not psychometrically evaluated, social desirability bias [43]). Randomized trials using objective measures of exercise for both the treatment and control arms will provide more clarity on the relationship between sleep and exercise. Patients were not randomized to participate in exercise, introducing selection bias. There are a few omitted variables that that would be beneficial to include in the models discussed in this study, that without which, make it more difficult to control for patients' exercise participation. We did not have information on self-efficacy, one of the most important predictors of exercise. We also did not have access to an indicator for previous exercise habits prior to CRC diagnosis, which are indicative of current or future exercise habits. Another omitted variable is information on patients' physical activity, which is a much broader concept including any body movement that requires energy expenditure. Some patients may not exercise but engage in significant physical activity throughout the day. For example, some patients may walk to work or have a labor-intensive job that involves heavy lifting. By only including exercise in the model, we may limit the conclusions and recommendations on exercise; some estimates may be biased because we are not including information on more general physical activity. Finally, our study cannot address issues of causality between sleep and exercise as this is an observational study.

Although polysomnography is considered the gold standard for sleep assessment, as a lab-based measure, polysomnography is burdensome for patients over time, and it may not adequately characterize sleep disturbance during real-life situations outside of the lab [44]. PROMIS Sleep Disturbance scale addresses this weakness because it is a short (6 item) questionnaire that assessed sleep quality during real-life situations.

As a large community-based observational study, the MY-Health data provide information on experiences from a very diverse sample of patients who were evaluated during the course of usual care without controlled interventions.

Conclusion

Using self-reported measures of exercise participation and sleep disturbance, no significant relationships between exercise participation and sleep disturbance (or change in exercise and change in sleep) was observed in a cohort of individuals diagnosed with stage I, II, and III CRC transitioning off treatment. Furthermore, being retired, anxiety and fatigue, and changes in fatigue were statistically related to sleep disturbance. Further prospective research including objective measurements of physical activity is warranted to confirm or refute the nature of the relationship between exercise and sleep disturbance in individuals diagnosed with stage I, II, or III CRC who had recently completed first-line cancer treatment.

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Compliance with ethical standards

Ethical approval This secondary data analysis was deemed non-human subjects research by the University of North Carolina IRB; formal consent is not required. The MY-Health study was approved through Georgetown University's IRB (approval 2009-436).

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