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Associations between Cancer History and Sleep Related Variables in Long-term Cancer Survivors

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Abstract

Introduction. Although sleep complaints are common and distressing in cancer patients, relatively little is known about sleep related outcomes in long-term cancer survivors. The aim of this study was to determine if sleep disturbance (daytime sleepiness, sleep medication use, sleep duration) is more common among cancer survivors compared to non-cancer controls.

Methods. Cancer survivors were sent two surveys, one for themselves and a second to be completed by their spouse or a friend. Eligible survivors had a history of at least 1 cancer diagnosis in the past 2 to 10 years. Logistic regression models were used to estimate the association between sleep related variables and history of cancer. Stratified subgroup analyses were also conducted to identify subgroups of cancer survivors for whom sleep problems might be most relevant.

Results. After adjustment for demographic covariates, cancer survivors had greater daytime sleepiness (measured by the Epworth Sleepiness Scale) compared to controls (23% of cancer survivors and 16% of controls scored $\geq$ 10 which is indicative of excessive sleepiness). Overall, neither sleep medication use nor sleep duration were associated with being a cancer survivor. The association between sleep duration and cancer survivorship differed by sex. Male survivors reported longer sleep duration compared to controls (OR= 1.22, 95% CI: 1.01, 1.49), while females tended to have shorter sleep duration compared to controls (OR=0.82, 95% CI: 0.67, 1.01). Associations were similar regardless of time since diagnosis, history of multiple cancers, histology, and treatment history.

Conclusions. Differences in sleep remain prevalent in cancer survivors, even many years post-diagnosis.

Implications for Cancer Survivors. Monitoring sleep related concerns should be part of survivorship care plans. More research is needed to clearly identify which cancer survivors are at most risk for chronic sleep disturbance and mechanisms by which sleep problems are maintained.

Introduction

Problems with disturbed sleep are among the most common and distressing complaints reported by persons with cancer (1-4). However, the persistence of sleep disturbances among long term cancer survivors is less well established (1). Chronic difficulties with sleep are important because these can have profound effects on physical, cognitive, and emotional functioning (5, 6). Additionally, reports have emphasized survivorship care plans for those who have had cancer (7, 8) and research is needed to more clearly identify important areas of potential difficulty for cancer survivors.

Spielman's three factor model of insomnia (also known as the 3 P's model) is a cognitive-behavioral model of sleep disturbance that can be applied to cancer survivors to understand why cancer might be associated with sleep disturbance (9-11). The model considers three types of factors in sleep disturbance: (1) predisposing factors which increase the individual's general susceptibility to develop sleep problems; (2) precipitating (i.e., situational) factors that trigger the onset of sleep disturbance; and (3) perpetuating factors which contribute to the maintenance of sleep disturbance over time. Some important predisposing factors relevant to cancer survivors might include female sex, older age, and psychiatric comorbidities such as a mood or anxiety disorder. Sleep related problems in cancer patients can be more immediately precipitated by the cancer disease process, cancer treatments (e.g., chemotherapy, radiotherapy, hormone therapy, hospitalization, bone marrow transplantation), symptoms or problems associated with cancer or it's treatment (e.g., pain, delirium, abrupt menopause), or the cognitive and emotional sequela often associated with cancer diagnosis and treatment (e.g., ruminative thoughts, worry about health, depressed mood). Previous work indicates that cancer can influence sleep disturbance not only by initiating problems with sleep, but also by exacerbating

preexisting sleep difficulties (10). For example, occasional sleep difficulties that do not require special intervention may become severe and chronic as a result of cancer disease or cancer treatment.

Once initiated or exacerbated, sleep disturbances can become chronic for some persons. Difficulties may be perpetuated by the continued presence of precipitating factors (e.g., chronic pain, depressed mood) and maintenance of maladaptive sleep behaviors initially performed to compensate for sleep disturbances (e.g., napping, excessive time spent in bed). Sleep problems can also be perpetuated by dysfunctional thought patterns related to sleep that cause physiological arousal which ultimately interferes with sleep, such as feeling pressure to sleep and rumination about the consequences of poor sleep (9-11). Cancer may also impact daytime sleepiness and sleep medication use by way of its effect on sleep quality and quantity over time.

There is a sizeable literature including studies on sleep related outcomes in persons with relatively recent cancer diagnoses (e.g., within approximately 1 year) or undergoing treatment (5, 6, 12-26). However, there are relatively fewer papers examining sleep related outcomes in cancer survivors over longer-term follow-up (e.g., time since most recent diagnosis of greater than 1 year) and with adequate comparison groups, both of which are necessary to accurately understand the association between cancer survivorship and sleep related outcomes.

Four studies have examined sleep related variables in cancer survivors compared to a non-cancer comparison group (27-30). The average survivorship time of these study samples ranged from fewer than 5 years to greater than 10 years. Lower quality sleep compared to non-cancer controls was reported in lung cancer survivors and breast cancer survivors (29, 30) but not among testicular cancer survivors compared to non-cancer controls (28). A small study of breast cancer survivors (N=15) (27) observed similar quality of sleep between breast cancer survivors

and women with disturbed sleep due to menopausal hot flashes. Sleep efficiency (i.e., the percentage of time spent in bed during which the person is sleeping) was reportedly lower in lung cancer survivors (29) but not breast cancer survivors (27, 30) relative to controls. Three studies have found no differences in sleep medication use between survivors of testicular cancer or breast cancer compared to non-cancer controls (27, 28, 30), while one study reported that lung cancer survivors used more sleep medications than controls (29). Two studies reported lower sleep duration in breast cancer survivors than non-cancer controls (27, 30). No studies have compared daytime sleepiness in long-term cancer survivors to non-cancer controls.

There are multiple limitations in this literature on sleep related outcomes in long-term cancer survivors. The cancer subgroups based on cancer site that have been studied relative to cancer free controls are limited. Two of the 4 studies examined breast cancer survivors, while one paper studied testicular cancer survivors, and 1 study reported on lung cancer survivors. No studies have examined a large heterogeneous sample with regards to cancer site, which may limit the generalizability of previous studies to diverse cancer populations. There has been a call for more descriptive studies of sleep problems in long-term survivors incorporating more heterogeneous samples in terms of cancer site (1). Additionally, an important sleep related outcome, daytime sleepiness, has not been investigated in controlled studies of long-term survivors. Moreover, the methodological rigor of the existing controlled studies of cancer survivors varies. One study reported univariate associations only (29) without adjusting for potential confounders (e.g., sex, age). No studies adjusted for psychological distress or pain, both of which have clear associations with cancer status and sleep (31-35). Additionally, differences in the cancer subpopulations studied may explain some inconsistencies in inferences regarding sleep related outcomes across studies and more types of cancer need to be studied. Finally,

previous studies comparing cancer survivors to non-cancer controls have not addressed potential differences in effect estimates due to important characteristics such as histology (invasive versus insitu), treatment history, or history of multiple cancers. These comparisons may provide important information about which cancer survivors are at the most risk for long-term problems with sleep.

The primary aim of the current study was to test for associations between cancer history and sleep related variables (day-time sleepiness, sleep medication use, sleep duration). It was hypothesized that cancer survivors would report greater day-time sleepiness, greater sleep mediation use, and shorter sleep duration compared to a convenience sample of non-cancer controls. The second aim of this study was to test for differences in the association between cancer history and sleep related variables across subgroups such as sex, cancer site, cancer histology, time since diagnosis, history of multiple cancers, and treatment history in order to identify the subgroups for which associations between cancer history and sleep related variables are relevant.

Methods

Study Design and Subject Recruitment

This study was approved by the Institutional Review Board. The study was based on cross-sectional survey data that was collected in order to determine the main symptoms facing long term cancer survivors in order to develop institution-specific programs. Cancer survivors with a history of cancer and date of diagnosis more than 2 years but less than 10 years were identified through the Mercy Medical Cancer Registry. Questionnaires with addressed and stamped returned envelopes were mailed to 4401 individuals in the registry. The first mailing was conducted in June 2008 and a second mailing was done in November 2009. Consent was

implied with return of the questionnaire. The questionnaires required approximately 20 minutes to complete. A "control" survey was included in each packet and survivors were asked to give that survey to a spouse or friend without a history of cancer. Persons with any cancer diagnosis within the past 2 years (either their first diagnosis or a subsequent cancer) were excluded from the current study do to our focus on cancer survivorship. Survey respondents who reported either no history of cancer or a history of basal or squamous cell skin cancer only were classified as controls. It is possible that some spouses or friends completing the survey reported a history of cancer and were classified as survivors.

Measures

Participants completed multiple questionnaire items pertaining to their demographics (sex, age, race, educational attainment, marital status) and medical history. Survivors were asked to report all previous cancers, including the age at which each cancer was diagnosed. Self-report information was supplemented with data in the hospital tumor registry when necessary, such as to determine the cancer histology (invasive versus in-situ) or to fill in missing data (e.g., age at which cancer was diagnosed). Cancer survivors were asked to indicate in a yes/no format whether or not they received radiation therapy, surgical treatment, chemotherapy or hormone therapy for cancer(s). Time since diagnosis was calculated for every cancer diagnosis reported by each participant. For the purposes of this study, participants were grouped into two categories with respect to the time since their most recent cancer diagnosis (2 to 4 years, $\geq$ 5 years).

All participants were asked about the extent to which they are bothered other medical conditions and symptoms, some of which may relate to sleep outcomes (e.g., pain, leg cramps, frequent urination at night, etc.) on a scale from 1 (*not at all*) to 5 (*extremely*). Respondents

selecting a score of 3 (*moderately*) or higher were identified as being bothered by these symptoms.

Participants completed the Epworth Sleepiness Scale (ESS) as a measure of daytime sleepiness (36). The ESS is an 8-item questionnaire assessing propensity for sleep in 8 common situations (e.g., watching television, talking with someone). Subjects rate their likelihood of dozing in each situation on a scale of 0 (*would never doze*) to 3 (*high chance of dozing*). The ESS score is the sum of the 8 items. Total scores range from 0 to 24. A score of 10 of higher is used in clinical settings as an indicator of excessive sleepiness (37). The ESS has demonstrated high internal consistency (Chronbach's alpha= .88), high test-retest reliability (r=.82), and the ability to discriminate between persons with sleep disturbance of varying severity (36, 38, 39).

Frequency of sleep medication use (including melatonin or any medication taken to aid sleep) over the past year was self-reported as never, rarely (one day/month or less), sometimes (2-4 days/month), often (5-15 days/month), or almost always (16-30 days/month). A binary variable was created, with responses categorized as either "one day/month or less" or "more than once a month" in order to distinguish participants reported infrequent use of sleep medications from those using sleep medications more regularly.

Average sleep duration was self-reported separately for workday or weekday nights and non-workday or weekend nights. A weighted average score for sleep duration was created by the following procedure: [(weekday sleep duration * 5) + (weekend sleep duration *2)] / 7.

Depressive symptoms were assessed with the Center for Epidemiologic Studies Depression Scale (40) (CES-D). Respondents are asked to rate the frequency with which each item occurred over the previous 7 days on a 4-point Likert scale ranging from 0 (*Rarely, less than 1 day*) to 3 (*Most or all of the time, 5-7 days*). Total scores range from 0 to 60, with higher

scores indicating greater depressive symptoms. Radloff (40) reported that the CES-D demonstrated high reliability in a general population ($\alpha = .85$).

Statistical Procedures

All analyses were performed using STATA 11.0 (41). Prior to analysis, the data were explored using frequencies and descriptive statistics. Normality was tested using the Shapiro-Wilk test. Differences between cancer survivors and controls on demographic characteristics and symptom comorbidities were tested using one-way Analysis of Variance (ANOVA), Wilcoxon-Mann-Whitney test, or χ^2 tests.

A series of nested logistic regression models was preformed separately for each sleep related variable: 1) daytime sleepiness, 2) sleep medication use, and 3) sleep duration. First, log odds of cancer survivorship (0 = no history of cancer, 1= history of cancer(s)) was regressed on the sleep related variable. Next, demographic covariates (age, sex, race, educational attainment) were entered in the model as a group. The Likelihood Ratio Test (LRT) was used to determine whether the extended model explained significantly more variance than the simpler model ($p < .05$ for the F-test indicates significant contribution to the model). Finally, symptom covariates were added to the model as a group and the LRT was used to test the significance of the extended model. Covariate blocks were kept in the model only if the group made a significant contribution to the model based on the LRT. Symptom covariates may be on the causal pathway between cancer and long-term sleep disturbance, thus attenuation of measures of association by symptom covariates may reflect mediation rather than adjustment for confounding. Measures of association should be considered both before and after adjustment for symptom covariates.

The same series of logistic regression models described were also tested separately in 3 specific subgroups based on cancer site (breast cancer, colorectal cancer, prostate cancer) that

included at least 50 survivors. Subgroup analyses were also performed on persons with a history of more than one cancer diagnosis, regardless of the site(s) of their diagnoses. For sex-specific cancer sites, analyses were restricted by sex, (i.e. breast cancer survivors were compared to female controls only and prostate cancer survivors were compared to male controls only), while models testing associations in colorectal survivors or survivors of multiple cancers statistically adjusted for sex.

Finally, stratified analyses were used to test for differences in the association between sleep related variables and cancer history based on sex or cancer specific factors. The same series of logistic regression models was again repeated separately within strata for each of the following factors: sex (males or females), time since most recent cancer diagnosis (2 to 4 years or ≥ 5 years), history of multiple cancers (yes or no), history of chemotherapy (yes or no), history of radiation therapy (yes or no), history of surgical treatment for cancer (yes or no), history of hormone therapy for cancer (yes or no), and histology (history of at least one invasive cancer or history of insitu only). The generalized inverse variance method was used to test for heterogeneity of effects across pairs of strata with $Q > 3.84$ indicating $p < .05$ and significant heterogeneity of effects.

Sample Characteristics

A total of 1512 surveys were returned. Of these, 69 were ineligible for the current study because they had a cancer diagnosis within the last 2 years. 1189 were classified as cancer survivors eligible for the study because they reported a history of at least 1 cancer diagnosis, with a diagnosis date of at least 2 years prior to survey completion and 254 respondents were classified as controls (no cancer history other than possible basal or squamous skin cancer). Thus, the total sample size of eligible respondents was 1443 (1189 cases and 254 controls). Analyses

were limited to those who responded to all items included in the regression models, leaving 1028 cases, 209 controls. There were no differences between those with missing data and those with complete data on daytime sleepiness, sleep medication use, sleep duration or likelihood of being a case; however, those excluded due to incomplete data were older ($\chi^2(1)$= 4.38, p = .04), had lower educational attainment ($\chi^2(3)$= 20.18, p < .001), and were more likely to be male ($\chi^2(1)$= 6.80, p = .01) and African-American ($\chi^2(2)$= 26.51, p < .001) than those with complete data.

Results

See Table 1 for a description of demographic variables by cancer history. Compared to controls, cancer survivors were more likely to be female, older, and African-American less likely to have graduate level education. There are also significant differences in the distribution of marital status between cancer survivors and controls, such that cancer survivors are more likely to be single or widowed than controls. This is likely attributable to nature of the control sample recruited (spouses or friends of cases). Table 1 also contains information on other comorbid symptoms that may be associated with sleep and fatigue related variables. Cancer survivors reported higher CESD scores than controls and were also more likely to report moderate or severe problems with feeling hot, urination at night, and pain.

Characteristics of the cancer survivors are described in Table 2. Most of the participants had a history of only one cancer (85.4%), although some participants reported up to 4 cancers. The most common diagnosis for the first occurring cancer in the sample was breast (66.1%), followed by prostate (12.5%) and colorectal (6.3%). Survivorship times range from 2 to 45 years across all cancers. On average, the first diagnosis of cancer occurred approximately 8 years prior to study participation. Most survivors have a history of at least 1 invasive cancer (87.5%). The most commonly reported treatment received was surgical (90.5%), followed by chemotherapy

(52.9%), hormone therapy (43.4%), and radiation (39.8%). Twenty-two cancer survivors (2.1%) denied receipt of any of these forms of treatment, 273 (26.6%) reported receiving 1 of these forms of treatment, 282 (27.4%) reported receiving 2 of these forms of treatment, 313 (30.5%) reported receiving three of these kinds of treatment, and 138 (13.4%) indicated they received all 4 forms of treatment (chemotherapy, surgery, radiation, and hormone therapy).

Differences in the sleep variables are reported in Table 3. Univariate tests indicate that cancer survivors report higher daytime sleepiness scores and greater likelihood of using sleep medications more than once per week than controls.

Daytime Sleepiness

See Table 4 for results of models related to daytime sleepiness. Cancer survivors reported greater daytime sleepiness, even after adjusting for demographic variables. Symptom covariates did not make a significant contribution to the model ($LR\ \chi^2(4) = 7.68$, $p = .10$) and were not kept in the model.

When limited to breast cancer survivors compared to female controls, daytime sleepiness was not statistically different from controls. The association was also not statistically significant among the colorectal or prostate survivor subgroups. However, the point estimate of the association observed in the three subgroups based on site is comparable to that seen in the overall sample (ORs range from 1.04 to 1.06), but precision is lower among the subgroups. Finally, among persons with a history of more than one cancer diagnosis, cancer survivors report higher ESS scores after adjusting for demographic covariates. Symptom covariates did not make a significant contribution to the model ($LR\ \chi^2(4) = 4.28$, $p = .37$).

For daytime sleepiness, the measure of association was similar across levels of sex, time since most recent cancer diagnosis, history of multiple cancers, history of chemotherapy, history

of radiation therapy, history of surgical treatment for cancer, history of hormone therapy for cancer, and histology (all $Q < 3.84$, $p > .05$).

Sleep Medication Use

Table 5 displays models of the association between cancer history and frequency of sleep medication use. Cancer survivors reported a greater likelihood of using sleep medications more than once per month compared to controls; however both the demographic covariates and symptom covariates made significant contributions to the model which attenuated the observed association. There were no statistically significant associations (either univariate or adjusted) observed among breast cancer, colorectal or prostate cancer survivor subgroups There was an association between sleep medication use and cancer survivorship observed among survivors of multiple cancers; however, this association attenuated after adjustment for the contribution of demographic covariates.

For sleep medication use, the measure of association was similar across levels of sex, time since most recent cancer diagnosis, history of multiple cancers, history of chemotherapy, history of radiation therapy, history of surgical treatment for cancer, history of hormone therapy for cancer, and histology (all $Q < 3.84$, $p > .05$).

Sleep Duration

Models of the association between cancer history and sleep duration are reported in Table 6. There was no association observed between sleep duration and cancer survivorship, either before of after adjustment for demographic and symptom covariates when considering the entire sample. However, among breast cancer survivors, cancer survivorship was associated with shorter sleep duration. Neither the demographic covariates ($LR\ \chi^2(6) = 2.65$, $p = .62$) nor the symptom covariates ($LR\ \chi^2(4) = 2.65$, $p = .62$) accounted for significant variance in this model.

Among prostate survivors, cancer survivorship was associated with longer sleep duration after adjustment for demographic covariates but the association was attenuated after adjustment for symptom covariates. Among colorectal cancer survivors, there was no association observed between sleep duration and cancer survivorship.

Based on stratified analyses, the association between cancer history and sleep duration was different between males and females (Q = 6.58 for univariate model and Q = 8.22 for the fully adjusted model). Stratified logistic regression models are presented in Table 6. Male survivors report longer sleep duration than controls after adjustment for demographic and symptom covariates. Female survivors tended to report shorter sleep duration than controls, although this was only marginally significant. Neither the demographic covariates ($LR\ \chi^2(6)$= 1.41, p = .97) nor the symptom covariates ($LR\ \chi^2(4)$= 2.87, p = .58) were maintained in the model due to the lack of significant contributions. The association between cancer history and sleep duration was similar across levels of time since most recent cancer diagnosis, history of multiple cancers, history of chemotherapy, history of radiation therapy, history of surgical treatment for cancer, history of hormone therapy for cancer, and histology (all $Q < 3.84$, $p > .05$).

Discussion

The current results demonstrate that differences in sleep between cancer survivors and controls remain prevalent, even many years after diagnosis. Cancer survivorship is associated with greater daytime sleepiness. Approximately 23% of cancer survivors scored at or above 10 on the Epworth Sleepiness Scale (i.e., at or above the clinical cutoff for determining excessive sleepiness), while 16% of controls scored 10 or higher. This association appears to be similar regardless of sex, cancer histology, having had multiple cancers, time since most recent cancer diagnosis, and treatments received.

This study did not find an overall association between cancer survivorship and sleep medication use after adjustment for demographic variables, nor was an association observed within breast, colorectal, or prostate survivors specifically. This results is consistent with studies among breast and testicular cancer survivors that have found similar frequencies of sleep medication use between cancer survivors and controls (27, 28, 30), but one study found that lung cancer survivors (at least 5 years post-diagnosis) used more sleep medications than controls (29). One explanation for the significant finding among lung cancer survivors is that only the unadjusted association was reported in this study, while all other studies have adjusted for sex and other covariates. Alternatively, there may be factors associated with lung cancer survivors that were not measured in the current study which promote more frequent sleep medication use among certain survivors.

Although no overall association was observed between cancer survivorship and sleep duration, stratified analyses reveal that the association varied by sex. Male cancer survivors, including prostate survivors specifically, report significantly longer sleep duration than controls, while female survivors, including breast cancer survivors specifically, tended to report shorter sleep duration. No association was observed between survivorship and sleep duration in the subgroups of cancer survivors that had both men and women (colorectal survivors, survivors of multiple cancers). The association between cancer history and sleep duration was similar across levels of time since diagnosis, histology, and treatment history. Although there were differences observed in sleep duration, measures of sleep quality (e.g., number of interruptions, feeling rested in the morning) may be more relevant.

For all sleep variables, the observed associations with cancer history were independent of cancer characteristics including time since diagnosis, history of multiple cancers, treatment

history, and histology. These results are consistent with a previous study which reported that, among cancer patients treated within the last six months, sleep problems were comparable among those treated with chemotherapy, radiation treatment, and surgery (5). Overall, there is limited research available on potential modifiers of associations between cancer history and sleep outcomes.

This study has a number of strengths. The sample was larger and more diverse in terms of cancer site than previous studies. This allows for more general inferences about cancer survivors to add to the generalizability of findings. We were also able to perform subgroup analyses on groups of survivors of cancers that have not been previously studied (colorectal, prostate, multiple cancers). Further, our sample was a sample from a community hospital and may be more representative of the general survivor population than studies that recruit in tertiary care centers or from clinical trial populations that have rigid inclusion criteria. Additionally, the current analyses adjusted more fully for demographic and symptom covariates, including depressive symptoms and pain than previous studies. Finally, this study reports on daytime sleepiness among cancer survivors which has not been reported and is a clinically useful screen for propensity for daytime sleep.

There are limitations to the current study. A major limitation is the low response rate to the survey. It is unknown if non-respondents did not complete the survey as a result of either more or fewer symptom complaints. Further, a convenience sample of spouses or friends was used for the control group leading to imbalances in sample size and sex distribution between cases and control. While using friends or spouses may also lead to unintended matching on factors, the impact of this matching should be limited because there were many more cases than controls. Additionally, the current analyses were limited to those participants who answered all

questions utilized in the regression models. Those eliminated for missing data tended to be older, less well educated, male, and African-American. The observed results may be biased due to exclusions based on missing data. Moreover, although survivors were at least 2 years past their most recent cancer diagnosis at the time of study participation, it cannot be confirmed that they were disease free at the time of participation or under active treatment, which would have influenced their reporting of symptoms. Finally, the data are cross-sectional; therefore causal inferences about the effect of cancer survivorship on sleep related outcomes cannot be made.

Although there is evidence that differences in sleep persist for many years post-diagnosis, research suggests that survivors typically do not speak with their medical providers about chronic sleep complaints and that medical providers typically do not initiate conversations about this topic (29). A better understand of the lasting effects of cancer on sleep and sleep related outcomes will inform the development of clinical practice guidelines for optimal follow-up care for long-term survivors (1). Ultimately, a better understanding of chronic sleep difficulties may improve the quality of life of long-term survivors. More research is needed to clearly identify which cancer survivors are at most risk for chronic sleep disturbance and mechanisms by which sleep problems are maintained.

Table 1. Demographic and covariate variables by cancer history

	Cancer Survivors (N=1028)	**Non-cancer Controls (N=209)**	***p* value** [a]
Demographic Variables			
Sex (%)			**<.001**
Male	218 (21.2%)	139 (66.5%)	
Female	810 (78.8%)	70 (33.5%)	
Age, mean (SD)	63.56 (11.54)	60.56 (11.2)	**<.001**
Race, N (%)			**.01**
White	851 (82.8%)	189 (90.4%)	
Black	151 (14.7%)	15 (7.2%)	
Other	26 (2.5%)	5 (2.4%)	
Education, N (%)			**.002**
Less than high school	26 (2.5%)	2 (1.0%)	
High school	328 (31.9%)	43 (20.6%)	
College/technical school	432 (42.0%)	99 (43.4%)	
Graduate school	242 (23.5%)	65 (31.1%)	
Marital status, N (%)			**<.001**
Single	275 (26.8%)	15 (7.2%)	
Married/cohabitating	618 (60.1%)	189 (90.4%)	
Widowed	135 (13.1%)	5 (2.4%)	
Smoking Status, N (%)			.49
Current	75 (7.3%)	21 (10.1%)	
Former	464 (45.1%)	95 (45.5%)	
Never	479 (46.6%)	92 (44.0%)	
BMI, N (%)			.11
Between 18.5 and 25	387 (37.7%)	68 (32.6%)	
Between 25 and 30	326 (31.7%)	86 (41.2%)	
Greater than 30	282 (27.4%)	49 (23.4%)	
Symptom Covariates			
CESD, median (range)	15 (6 – 54)	12 (8 – 50)	**<.001**
Feeling hot, N (%)			**<.001**
No	870 (84.6%)	197 (94.3%)	
Yes	158 (15.4%)	12 (5.7%)	
Leg cramps at night, N (%)			.29
No	970 (94.4%)	201 (96.2%)	
Yes	58 (5.6%)	8 (3.8%)	
Urination at night, N (%)			**.02**
No	898 (87.4%)	195 (93.3%)	
Yes	130 (12.6%)	14 (6.7%)	
Pain, N (%)			**.04**
No	823 (80.1%)	180 (86.1%)	
Yes	205 (19.9%)	29 (13.9%)	

a. tests of difference between cancer survivors and non-cancer controls based on one-way ANOVAs for normally distributed continuous variables (age), Wilcoxon-Mann-Whitney tests for non-normally distributed continuous variables (CESD) and χ^2 tests for categorical variables.

Table 2. Characteristics of cancer survivors

	Cancer Survivors (N=1028)		
Total Number of cancers [a], N(%)			
1	878 (85.4%)		
2	129 (12.6%)		
3	17 (1.7%)		
4	4 (0.4%)		
Site for first cancer, N(%)			
Bladder	13(1.3%)		
Breast	678 (66.1%)		
Hematopoietic	27 (2.6%)		
Cervical	7 (0.7%)		
Colorectal	65 (6.3%)		
Endometrial	8 (0.8%)		
Head/neck	7 (0.7%)		
Kidney	15 (1.5%)		
Liver	2 (0.2%)		
Lung	13 (1.3%)		
Melanoma	13 (1.3%)		
Nerve sheath	1 (0.1%)		
Ovarian	9 (0.9%)		
Pancreas	1 (0.1%)		
Peritoneal	2 (0.2%)		
Prostate	128 (12.5%)		
Sarcoma	4 (0.4%)		
Testicular	4 (0.4%)		
Thyroid	22 (2.1%)		
Upper gastrointestinal	6 (0.6%)		
Unknown	1 (0.1%)		
Missing	2 (0.2%)		
	Mean (SD)	Median	(Range)
Years since diagnosis [b]			
First cancer *(n= 1026, 2 missing)*	8.02 (5.95)	7	(2 – 45)
Second cancer *(n= 150)*	7.06 (5.25)	6	(2 – 38)
Third cancer *(n= 21)*	7.76 (6.36)	7	(2 – 31)
Fourth cancer *(n= 4)*	4.0 (2.31)	4	(2 – 6)
Time since most recent cancer diagnosis, N(%)			
2 to 4 years	359 (35.0%)		
≥ 5 years	667 (65.0%)		
Missing	2 (0.2%)		
Histology, N(%)			
History of invasive cancer(s)	900 (87.5%)		
History of insitu cancer(s) only	128 (12.5%)		
Treatments Received for Cancer [c], N(%)			
Radiation Therapy	409 (39.8%)		
Chemotherapy	544 (52.9%)		
Surgery	930 (90.5%)		
Hormone Therapy			
Yes	445 (43.3%)		
Not sure	59 (5.7%)		

a. cancers diagnosed as basal or squamous cell skin cancer are not included as cancers for the purpose of this study.

b. Of the 1028 cancer survivors, 150 reported a second cancer, 21 reported a third cancer, and 4 reported a fourth cancer. Survivorship time is reported separately for each of these subsequent cancer diagnoses.
c. treatment categories are not mutually exclusive. Survivors may have received more than 1 treatment modality.

Table 3. Sleep related variables by cancer history

	Cancer Survivors (N=1028)	**Non-cancer Controls (N=209)**	***p* value** [a]
Epworth Sleepiness Scale			
Median (range)	6 (0 – 24)	5 (0 – 23)	**.02**
N(%) with Epworth score > 10	231 (22.5%)	33 (15.8%)	**.03**
Sleep medication use, N (%)			
1 or fewer times/month	759 (73.83%)	172 (82.3%)	**.01**
More than 1 time/month	269 (26.2%)	37 (17.7%)	
Sleep duration			.84
Median (range)	7 (2 – 12)	7 (3 – 10)	

a. tests of difference between cancer survivors and non-cancer controls based on Wilcoxon-Mann-Whitney tests for non-normally distributed continuous variables (Epworth scores and sleep duration) and χ^2 tests for categorical variables.

Table 4. Logistic Regression Models: Associations between daytime sleepiness (Epworth Sleepiness Scale) and cancer survivorship

	Bivariate Association			***Adjusted for demographic covariates*** [a]		
	OR	**(95% CI)**	***p* value**	**OR**	**(95% CI)**	***p* value**
Overall *(1028 cases, 209 controls)*	**1.04**	**(1.00, 1.08)**	**.04**	**1.05**	**(1.01, 1.10)**	**.01**
Subgroup analyses						
Breast *(642 cases, 70 female controls)*	1.06	(0.99, 1.13)	.08	1.06	(0.99, 1.13)	.08
Colorectal *(51 cases, 209 controls)*	1.04	(0.96, 1.11)	.33	1.04	(0.96, 1.13)	.26
Prostate *(112 cases, 139 male controls)*	1.04	(0.98, 1.10)	.22	1.03	(0.96, 1.11)	.46
History of multiple cancer diagnoses *(150 cases, 209 controls)*	1.03	(0.97, 1.08)	.33	**1.08**	**(1.01, 1.15)**	**.03**

a. adjusted for sex, age, race, educational attainment. However, cases and controls for the beast cancer subgroup were only female and cases and controls for the prostate group were only males so these 2 comparisons include sex as a covariate.

Note: Measures of association after adjustment for symptom variables is not reported here. Symptom variables only made a significant contribution among prostate survivors. However, even among this group, further adjustment did not change the effect estimate or inference.

Table 5. Logistic Regression Models: Association between sleep medication use frequency and cancer survivorship

	Bivariate Association			***Adjusted for demographic covariates*** [a]			***Adjusted for demographic and symptom covariates*** [b]		
	OR	**(95% CI)**	***p* value**	**OR**	**(95% CI)**	***p* value**	**OR**	**(95% CI)**	***p* value**
Overall *(1028 cases, 209 controls)*	**1.65**	**(1.12, 2.41)**	**.01**	1.24	(0.81, 1.89)	.32	1.13	(0.72, 1.74)	.60
Subgroup Analyses									
Breast *(642 cases, 70 female controls)*	1.12	(0.64, 1.95)	.69	-- [c]			--		
Colorectal *(51 cases, 209 controls)*	1.13	(0.52, .247)	.75	1.07	(0.47, 2.43)	.87	0.95	(0.40, 2.24)	.90
Prostate *(112 cases, 139 male controls)*	0.88	(0.41, 1.89)	.75	0.95	(0.36, 2.48)	.91	0.96	(0.36, 2.58)	.94
History of multiple cancer diagnoses *(150 cases, 209 controls)*	**2.12**	**(1.29, 3.48)**	**.003**	1.35	(0.76, 2.41)	.32	--		

a. adjusted for sex, age, race, educational attainment. However, cases and controls for the beast cancer subgroup were only female and cases and controls for the prostate group were only males so these 2 comparisons did not include sex as a covariate.
b. in addition to demographic variables, adjusted for depressive symptoms, feeling hot, urination at night, leg cramps at night, and pain
c. Covariate adjustment was conducted in two blocks (demographic variables, symptom variables). The blocks were retained in the model only when a significant contribution was made to the model by the covariate group according to the Likelihood Ratio Test.

Table 6. Logistic Regression Models: Association between sleep duration and cancer survivorship

	Bivariate Association			***Adjusted for demographic covariates*** [a]		
	OR	(95% CI)	*p* value	OR	(95% CI)	*p* value
Overall *(1028 cases, 209controls)*	1.01	(0.98, 1.14)	.86	1.04	(0.91, 1.19)	.56
Subgroup Analyses						
Breast *(642 cases, 70 female controls)*	**0.80**	**(0.65, 0.98)**	**.03**	-- [c]		
Colorectal *(51 cases, 209 controls)*	1.08	(0.81, 1.43)	.61	1.09	(0.81, 1.48)	.56
Prostate *(112 cases, 139 male controls)*	1.20	(0.97, 1.47)	.10	**1.33**	**(1.02, 1.73)**	**.04**
History of multiple cancer diagnoses *(150 cases, 209 controls)*	0.98	(0.82, 1.17)	.82	0.83	(0.66, 1.04)	.10
Stratified by Sex						
Males *(218 cases, 139 controls)*	1.15	(0.98, 1.36)	.08	**1.22**	**(1.01, 1.49)**	**.04**
Females *(810 cases, 70 controls)*	0.82	(0.67, 1.01)	.06	0.82	(0.67, 1.01)	.06

a. adjusted for sex, age, race, educational attainment. However, cases and controls for the beast cancer subgroup were only female and cases and controls for the prostate group were only males so these 2 comparisons did not include sex as a covariate.
b. in addition to demographic variables, adjusted for depressive symptoms, feeling hot, urination at night, leg cramps at night, and pain.
c. Covariate adjustment was conducted in two blocks (demographic variables, symptom variables). The blocks were retained in the model only when a significant contribution was made to the model by the covariate group according to the Likelihood Ratio Test.
Note: Measures of association after adjustment for symptom variables is not reported here. Symptom variables only made a significant contribution for the overall comparison. However, even among this group, further adjustment did not change the effect estimate or inference.

Goals Analysis

This Capstone project helped me to meet a number of my goals for the MPH year. The project provided my first in depth exploration of the literature on cancer survivorship. It also exposed me to the complexity involved in the measurement and quantification of the cancer experience. The project allowed me the opportunity to work collaboratively on a team with professionals from a variety of disciplines. It also gave me the opportunity to practice new analysis techniques learned throughout the MPH year. The work and iterations of this project have continued to shape my methodological and critical thinking skills and helped me to further my development towards becoming an independent researcher.

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