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# Short Sleep Duration and Physical and Psychological Health Outcomes Among Adult Survivors of Childhood Cancer

**Margaret M. Lubas, PhD, LCSW**[1], **Belinda N. Mandrell, PhD RN PNP**[2], **Kirsten K. Ness, PhD**[1], **Deo Kumar Srivastava, PhD**[3], **Matthew J. Ehrhardt, MD, MS**[1,4], **Zhaoming Wang, PhD**[1], **Melissa M. Hudson, MD**[1,4], **Leslie L. Robison, PhD**[1], **Kevin R. Krull, PhD**[1,5], **Tara M. Brinkman, PhD**[1,5]

[1]Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital

[2]Department of Pediatric Medicine, St. Jude Children's Research Hospital

[3]Department of Biostatistics, St. Jude Children's Research Hospital

[4]Department of Oncology, St. Jude Children's Research Hospital

[5]Department of Psychology, St. Jude Children's Research Hospital

## Abstract

**Background:** To examine associations between phenotypes of short sleep duration and clinically-assessed health conditions in long-term survivors of childhood cancer.

**Methods:** Survivors recruited from the St. Jude Lifetime Cohort (n=911; 52% female; mean age 34 years; 26 years post-diagnosis) completed behavioral health surveys and underwent comprehensive physical examinations. Sleep was assessed with the Pittsburgh Sleep Quality Index. Short sleep was defined as ≤ 6hours per night with phenotypes of short sleep including poor sleep efficiency (<85%), prolonged sleep onset latency (≥30 minutes), and wake after sleep onset (≥3 times per week). Covariates included childhood cancer treatment exposures, demographics, body mass index, and physical inactivity. Separate modified Poisson regression models were computed for each health category to estimate relative risks (RR) and 95% confidence intervals (CI). Multinomial logistic regression models examined associations between sleep and an aggregated burden of chronic health conditions.

**Results:** Short sleep duration was reported among 44% (95% CI 41%−47%) of survivors. In multivariable models, short sleep duration alone was associated with pulmonary (RR=1.35, 95% CI 1.08–1.69), endocrine (RR=1.22, 95% CI 1.06–1.39) and gastrointestinal/hepatic conditions (RR=1.46, 95% CI 1.18–1.79), and anxiety (RR 3.24, 95% CI 1.64–6.41) and depression (RR=2.33, 95% CI 1.27–4.27). Short sleep with prolonged SOL was associated with a high/severe burden of health conditions (OR=2.35, 95% CI 1.12–4.94).

**Corresponding author:** Tara M. Brinkman, PhD, St. Jude Children's Research Hospital, Department of Epidemiology and Cancer Control, 262 Danny Thomas Place, MS 735, Memphis, TN, 38105, tara.brinkman@stjude.org, Phone: 901-595-5891, Fax: 901-595-5845.

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**Data Availability Statement:** The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Conclusions:** Short sleep duration was associated with multiple clinically-ascertained adverse health conditions. Although the temporality of these associations cannot be determined in this cross-sectional study, sleep is modifiable, and improving sleep may improve long-term health in survivors.

### Keywords

short sleep duration; chronic health conditions; anxiety; depression

## Introduction

Despite advances in cancer therapy and survival, childhood cancer survivors experience a lifelong risk for treatment-related late effects.[1] Compared to the general population, long-term survivors have an increased risk of cardiovascular disease,[2] metabolic syndrome,[2] and obesity.[2] Compared to sibling comparisons or non-cancer controls, long-term survivors have a higher prevalence of cerebrovascular events,[3] gastrointestinal complications,[4] and pulmonary deficits.[5] Adult survivors of childhood cancer experience a high and variable burden of chronic health conditions[6] increasing their risk of early mortality.[7]

While risk of adverse health outcomes in survivors is largely driven by treatment exposures, chronic health conditions can be exacerbated by poor health behaviors. Among a large cohort of adult survivors of childhood cancer, the observed association between unhealthy lifestyle behaviors (e.g. diet, physical activity) and metabolic syndrome was stronger than the association between cranial radiation and metabolic syndrome.[8] Adherence to a Mediterranean diet has been associated with lower body mass index and lower risk of metabolic syndrome among leukemia survivors.[9] Moreover, physical activity has been associated with decreased mortality risk among childhood cancer survivors.[10] Identifying and promoting modifiable lifestyle behaviors may be essential to improving the health outcomes and quality of life of long-term survivors.

Associations between sleep and health have not been fully elucidated in survivors; however, in the general population sleep duration is widely associated with several chronic health conditions. In cross-sectional examinations of national samples, short and long sleep durations have been associated with metabolic syndrome,[11] cardiovascular disease,[12] and chronic kidney disease.[13] Moreover, prospective associations between sleep disturbances and diabetes,[14] depression,[15] gastrointestinal disease[16], and progression to end-stage renal disease[17] have also been reported. The high prevalence of self-reported sleep disturbances among survivors of childhood cancer has been well characterized;[18, 19] however, few studies have examined health status and poor sleep among childhood cancer survivors. The purpose of this study was to examine associations between short sleep duration and clinically-assessed health conditions among adult survivors of childhood cancer.

# Methods

## Study Participants

Study participants were recruited from the St. Jude Lifetime Cohort Study (SJLIFE),[20] a retrospective cohort of childhood cancer survivors who participate in prospective medical assessments. The cohort was initiated in 2007 and includes survivors of childhood cancer who are ≥5 years post-diagnosis of a pediatric cancer treated at St. Jude Children's Research Hospital. For the current study, survivors enrolled in SJLIFE who were ≥18 years of age and ≥10 years post diagnosis were recruited for a randomized controlled trial focused on sleep and cognition. We identified and screened 3,348 potentially eligible SJLIFE participants. Among these survivors, 562 refused participation in the intervention and 1,875 did not meet initial study specific inclusion/exclusion criteria (see Supplementary Table S1 intervention inclusion/exclusion criteria). This resulted in 911 participants who completed baseline evaluations to confirm eligibility for the intervention study and who form the study population for the current analysis. All participants provided written informed consent and the study was approved by the Institutional Review Board at St. Jude Children's Research Hospital.

## Measures

### Health outcomes

**Physical health outcomes.:** Clinically-assessed health conditions were evaluated during on-campus medical evaluations and defined using modified Common Terminology Criteria for Adverse Events (CTCAE) version 4.03 criteria adapted for childhood cancer survivors.[21] Comprehensive medical assessments included diagnostic procedures, an assessment of neuromuscular function, and a physical evaluation with a standardized laboratory battery. At the time of assessment, if survivors reported any chronic health conditions previously diagnosed, medical records were obtained to validate these diagnoses. The following organ systems were evaluated during the medical assessment and included as outcome variables: cardiac, pulmonary, renal, endocrine, gastrointestinal/hepatic, neurologic and musculoskeletal. CTCAE grades range from 1–4 (mild [grade 1], moderate [grade 2], severe or disabling [grade 3], life-threatening [grade 4]), and adverse health conditions were defined as grade ≥2 for each condition (i.e. moderate to life threatening). Supplemental Tables S2a–g present the frequency of grade 2–4 conditions for study participants, classified by each organ system. Chronic health conditions were included if they were diagnosed prior to and up to three months following the sleep assessment.

In addition to evaluating health conditions by each organ system, we created a composite measure assessing the burden/severity of the survivor's physical health. A method developed by Geenen et al.[22] was employed to aggregate chronic health conditions across organ systems (cardiovascular, pulmonary, endocrine, neurologic, gastrointestinal, musculoskeletal, and renal), taking into account the frequency and grade of conditions. For survivors who had multiple chronic health conditions within the same organ system, the highest grade within that organ system was utilized. This chronic health burden score was classified via the following categories: none, low (only grade 1 events), medium (having ≥1 grade 2 event and/or 1 grade 3 event), high (having ≥ 2 grade 3 events or 1 grade 4 event and

at most 1 grade 3 event), and severe (>1 grade 4 events or ≥ 2 grade 3 events and 1 grade 4 event).

**Psychological health outcomes.:** The Brief Symptom Inventory-18 (BSI-18)[23] was administered at the time of the participant's sleep evaluation to assess clinically significant anxiety and depression. Using sex-specific normative data, survivors with a T-score ≥63 ($90^{th}$ percentile) on either subscale were classified with clinically significant anxiety and/or depression. The BSI-18 has been previously validated in childhood cancer survivors.[24]

**Self-reported sleep and short sleep duration (primary predictor).—**Phenotypes of self-reported short sleep were defined a priori by utilizing questions from The Pittsburgh Sleep Quality Index (PSQI),[25] which measures sleep quality and quantity over the previous month. Individual questions were used to operationalize phenotypes of habitual short sleep duration. Sleep duration was assessed via the question, "during the past month, how many hours of actual sleep did you get a night?" Short sleep was defined as self-reported sleep duration of ≤ 6 hours per night and was determined according to the National Sleep Foundation's recommendations for adults.[26] Questions about sleep onset latency (SOL), wake after sleep onset (WASO), and sleep efficiency (SE) were also utilized to examine short sleepers with an additional sleep disturbance. Short sleepers with a prolonged SOL were defined as individuals who reported a SOL ≥ 30 minutes at least three times per week. Short sleepers with a WASO impairment were defined as individuals who reported waking up late at night or early in the morning at least three times a week. Short sleepers with poor SE were defined by a SE < 85% which was calculated from the PSQI as the ratio of total sleep time compared to total time spent in bed. These classifications were not mutually exclusive and were defined as additional sleep disturbances among short sleepers.

**Covariates—**Treatment exposures (e.g. individual chemotherapeutic agents and radiation) known to increase the risk of chronic health conditions in survivors were selected *a priori* and informed by Children's Oncology Group guidelines version 5.0.[27] Specific treatment exposures were selected for each health outcome in order to provide adequate adjustment for treatment exposures in separate models (see Table 1 for a description of treatment exposures included for each health outcome). Age at evaluation, age at cancer diagnosis, sex, race/ethnicity, body mass index (BMI) and physical inactivity were included as covariates in all models. Physical inactivity was defined as not meeting Centers for Disease Control recommendation for physical activity (75 minutes of vigorous or 150 minutes of moderate activity per week).[28] Weekly moderate and vigorous activities were converted into metabolic equivalents (METS), individuals who reported <450 METS per week were classified as inactive. Age at evaluation, BMI and physical activity were assessed at the time of the sleep survey.

## Statistical analysis

Descriptive statistics were calculated for all exposures, outcomes, and covariates. Differences between study variables by short sleep duration were reported by using Chi-square statistics for categorical variables and t-tests for continuous variables. Modified Poisson regression models with robust error variance[29] were used to examine associations

between phenotypes of short sleep duration and health outcomes. Separate models were conducted for each phenotype of short sleep and each health outcome, while adjusting for age at evaluation, sex, race/ethnicity, age at diagnosis, BMI, physical inactivity and condition-specific treatment exposures. When examining the associations between phenotypes of short sleep duration and the composite burden score of physical health outcomes, multinomial logistic regression was employed. Burden models were adjusted for age at evaluation, sex, race/ethnicity, BMI, and physical inactivity. All analyses were completed using SAS v9.4. All tests were two-sided and a p-value ≤ .05 was considered statistically significant.

## Results

### Self-Reported Sleep Characteristics

Self-reported sleep characteristics of the study participants are shown in Table 2. On average participants reported a sleep duration of 6 hours and 38 minutes. Forty-four percent of the sample were classified as short sleepers, reporting a sleep duration of ≤ 6 hours per night. Only 14 participants reported a long sleep duration, defined as ≥10 hours per night. As previous research identifies a u-shaped relationship between sleep duration and adverse health outcomes,[30, 12, 13] the fourteen participants reporting long sleep duration were removed from subsequent analyses due to the inability to examine long sleepers separately.

### Demographic, Survivorship, and Health Characteristics

Demographic, treatment exposures, and chronic health conditions among survivors with short and typical sleep duration are summarized in Table 3. Survivors were 51.8% female, predominately non-Hispanic white (84.1%), an average of 34 years of age, and 26 years from their cancer diagnosis. Leukemia (41.4%), non-central nervous system solid tumors (23.4%), and Hodgkin lymphoma (13.2%) were the most common diagnoses among participants. Grade 2 or higher cardiac (40.8%), endocrine (50.0%), neurologic (31.0%), gastrointestinal/hepatic (31.1 %), musculoskeletal (30.1%) and pulmonary (26.3%) conditions were prevalent in the sample. Grade 2 or higher renal conditions (9.9%), anxiety (6.7%) and depression (7.6%) were less common among survivors. Several health outcomes were more prevalent among short sleepers (≤ 6hours) compared to those with typical sleep duration (7 to 9 hours) such as: anxiety 10.6% vs. 3.4% ($p<0.0001$), depression 10.3% vs. 5.2% ($p=0.0100$), endocrine 55.8% vs. 45.5% ($p=0.0022$), pulmonary 30.3% vs. 23.0% ($p=0.0147$), and gastrointestinal/hepatic conditions 37.0% vs. 26.3% ($p=0.0006$) (Table 3).

### Multivariable Analyses

**Health Outcomes—**In multivariable models adjusted for condition-specific treatment exposures, demographic factors, BMI, and physical inactivity, all phenotypes of short sleep duration were associated with grade 2–4 pulmonary, endocrine, and gastrointestinal/hepatic conditions (Table 4). For example, short sleep duration alone was associated with a 22–46% increased prevalence of pulmonary, (RR 1.35, 95% CI 1.08–1.69), endocrine (RR 1.22, 95% CI 1.06–1.39), and gastrointestinal/hepatic conditions (RR 1.46, 95% CI 1.18–1.79) (Table 4). Short sleep with a prolonged SOL was associated with neurologic conditions (RR 1.32, 95% CI 1.04–1.68) and short sleep with prolonged WASO with cardiac (RR 1.21, 95% CI

1.02–1.42) and neurologic conditions (RR 1.25, 95% CI 1.01–1.57) (Table 4). All phenotypes of short sleep duration were associated with anxiety (e.g. short sleep duration RR 3.24, 95% CI 1.64–6.41) and depression (e.g. short sleep duration, RR 2.33, 95% CI 1.27–4.27) (Table 4).

**Severity/Burden—**When aggregating physical health conditions to assess the burden of conditions, 34% of participants (n=307) were classified as having a high to severe burden score, 56% were classified as having a medium burden and 10% (n=90) were classified in the none to low reference group (Supplemental Table S3). In models adjusted for age, sex, race/ethnicity, BMI, and physical inactivity, short sleep duration with a prolonged SOL was associated with a high/severe burden of chronic health conditions (OR 2.35, 95% CI 1.12–4.94) compared to those with a low to none burden. No other measures of short sleep duration were significantly associated with medium or high/severe burden of health conditions (Figure 1, Supplemental Table S4).

## Discussion

In a large heterogeneous sample of adult survivors of childhood cancer, we found associations between phenotypes of short sleep duration and clinically assessed physical and psychological health outcomes. Short sleep duration with prolonged sleep onset latency increased risk of high/serve burden of chronic health conditions greater than 2-fold. Associations between all phenotypes of short sleep duration and psychological health outcomes ranged from 2 to 3-fold in strength. While we did not observe large differences in the strength of associations between our phenotypes of short sleep duration and health outcomes, short sleep with prolonged SOL or WASO yielded consistent and strong associations to several health outcomes, including pulmonary, endocrine, gastrointestinal, neurologic, anxiety, and depression.

In our sample, 44% of survivors reported a habitual short sleep duration of six or less hours per night. Among survivors with a short sleep duration, 21–27% also reported a prolonged SOL and/or WASO, and nearly 30% of short sleepers met criteria for a poor sleep efficiency defined as <85%. Overall, 57% of the sample scored above the PSQI clinical cut-off for poor sleep quality (> 5), a composite score based on seven components of the measure with possible scores ranging from 0–21.[25] Consistent with previous literature,[19, 18] these findings underscore the severity and prevalence of sleep disturbances among survivors. Additionally, sleep disturbances[31] and fatigue are associated with reduced quality of life,[19] neurocognitive impairment,[31] and depression[19] among cross-sectional studies of childhood cancer survivors. One longitudinal study reported associations between dimensions of self-reported sleep and new onset psychological distress and new onset migraines.[18] However, this study relied on self-reported health conditions. The current study utilized clinically-ascertained health conditions and highlights the range in which sleep duration relates to many biological systems (i.e. cardiac, pulmonary, gastrointestinal, and neurologic) and dimensions of psychological health.

Strong associations were observed between phenotypes of self-reported short sleep duration and anxiety and depression, which is consistent with previous literature identifying high

comorbidity rates between sleep disturbances and psychological distress.[32, 33] Previous prospective studies have identified the presence of bidirectional relationships between sleep disturbances and depression[34, 35] and anxiety,[35] suggesting that short sleep duration can be both a causal factor and/or a consequence of psychological distress. Further, it is possible that associations between short sleep and psychological distress are amplified when relying on self-reported short sleep, of which recall of self-reported sleep can also be influenced psychological factors.

While our analyses were cross-sectional and we cannot determine directionality, there are several physiological pathways through which sleep duration could relate to adverse health conditions or overall poorer physical functioning. For example, sleep and immune functioning are bidirectionally related. Immune activation can alter sleep quality and patterns, while changes in sleep patterns can also impact the body's inflammatory response.[36] Sleep patterns and duration are associated with the release of several hormones that regulate appetite, metabolism, and glucose tolerance.[37, 38] Other physiological processes follow diurnal patterns and may be disrupted by sleep disturbances. For instance, blood pressure often decreases at night (i.e. nocturnal dipping) and lack of decrease (i.e. non-dipping), which is associated with increased risk of cardiovascular disease,[38] is more prevalent among individuals with sleep disturbances, such as obstructive sleep apnea and advanced sleep cycles.[39]

The potential causal significance of poor sleep and its associations with adverse health outcomes are reinforced by several prospective studies[17, 15, 16]/reviews.[14, 30] However, though there are several biological pathways through which sleep patterns and sleep disturbances could affect chronic health conditions, these relationships and their directions have not been fully elucidated. Conversely, it is possible that adverse health conditions and/or medications associated with the treatment of such health conditions could also contribute to sleep disturbances. Several medications used to treat chronic health conditions (such as corticosteroids,[40] SSRIs,[41] and beta-blockers [42]) could contribute to sleep disturbances, either through changes in sleep architecture (e.g. decreases in REM or slow wave sleep, changes in endogenous melatonin) or through additional side effects that may disrupt sleep. Moreover, it is possible that symptoms from some chronic conditions, such as pain, could mediate the relationship between sleep and health.[43] However, a reciprocal relationship between pain and sleep has also been supported with several longitudinal studies demonstrating sleep disturbances increase the risk of future chronic pain disorders.[44] Thus, untangling the directionality of associations between sleep and health pose several measurement challenges that are difficult to ascertain even in longitudinal studies due to complex and overlapping physiological systems.

Understanding associations between sleep duration and chronic health conditions in childhood cancer survivors is important because sleep may serve as a modifiable point of intervention to improve the health of this vulnerable population. In survivorship, excess risk of chronic conditions is driven by treatment exposures; however, intervening on lifestyle factors can improve health outcomes in this population[45]. Several behavioral sleep interventions in non-cancer samples have been successful in improving sleep quantity and quality[46, 47] and some provide preliminary support for health improvements[48–50] and

thus, merit further study among cancer survivors. While understanding the directionality between sleep and health outcomes remains an important area of future research, the treatment or even resolution of chronic health conditions do not guarantee an improvement in sleep. Pharmacologic interventions aimed to treat chronic health conditions may further disrupt sleep. In addition, even with the resolution of symptom-related factors that may have previously disrupted sleep (such as pain, physical inactivity, and/or nocturia), sleep disturbances are likely to be maintained post-resolution due to behavioral reinforcements that occurred while symptoms were active. Thus, irrespective of the directionality of associations between sleep and an array of health outcomes, if sleep is disrupted among individuals with chronic health conditions intervening on sleep may have some positive health effect.

The results of our study should be considered within the context of several limitations. Study participants involved a select group of survivors who were undergoing recruitment and screening for participation in a sleep and cognitive intervention. As these survivors expressed interest in an intervention, they may have been more likely to experience sleep or cognitive difficulties than survivors who did not express interest in participating. Because our analyses were cross-sectional and sleep was measured at only one time point, we cannot assess the temporality of associations between sleep and health outcomes. In addition, chronic health conditions were assessed from the time of cohort participation up to three months after the sleep assessment. Although we acknowledge short sleep duration may have been chronic as well, we were unable to assess this in the current study. While there are several prospective studies identifying sleep preceding chronic health conditions, there is also strong potential for bidirectional associations. Moreover, as we examined a range of health conditions that were grouped into general organ systems, it is possible that some chronic conditions could cause or contribute to sleep disturbances, while for others, sleep may be the antecedent. However, because of the small number of conditions by different sleep phenotypes we did not have sufficient power to examine chronic health conditions individually. Despite our inability to ascertain the directionality of our found associations and to further assess the contribution of several potentially mediating factors, such as pain, fatigue, or additional sleep data (e.g. napping behaviors), sleep is modifiable and may serve as an important component of lifestyle interventions that aim to improve health among survivors. Interventions targeting sleep may be necessary irrespective of whether it is an antecedent or consequent of chronic health conditions.

The present study of long-term survivors of childhood cancer identifies associations between short sleep duration and several physical and psychological health conditions. While short sleep duration alone was consistently associated with several health conditions (e.g. pulmonary, endocrine, gastrointestinal/hepatic), short sleepers with prolonged SOL and/or WASO were associated with two additional health conditions (e.g., cardiac and neurologic conditions). Examining additional sleep disturbances among short sleepers may serve as a sensitive measure between sleep and health outcomes. In addition, SOL and/or WASO may severe as additional points of interventions when targeting sleep extension.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Abbreviation Key

| | |
|---|---|
| **RR** | Relative risk |
| **CI** | Confidence interval |
| **SJLIFE** | St. Jude Lifetime Cohort Study |
| **CTCAE** | Common Terminology Criteria for Adverse Events |
| **BSI-18** | Brief Symptom Inventory-18 |
| **PSQI** | Pittsburgh Sleep Quality Index |
| **SOL** | Sleep onset latency |
| **WASO** | Wake after sleep onset |
| **SE** | Sleep efficiency |
| **BMI** | Body mass index |
| **METS** | Metabolic equivalent |

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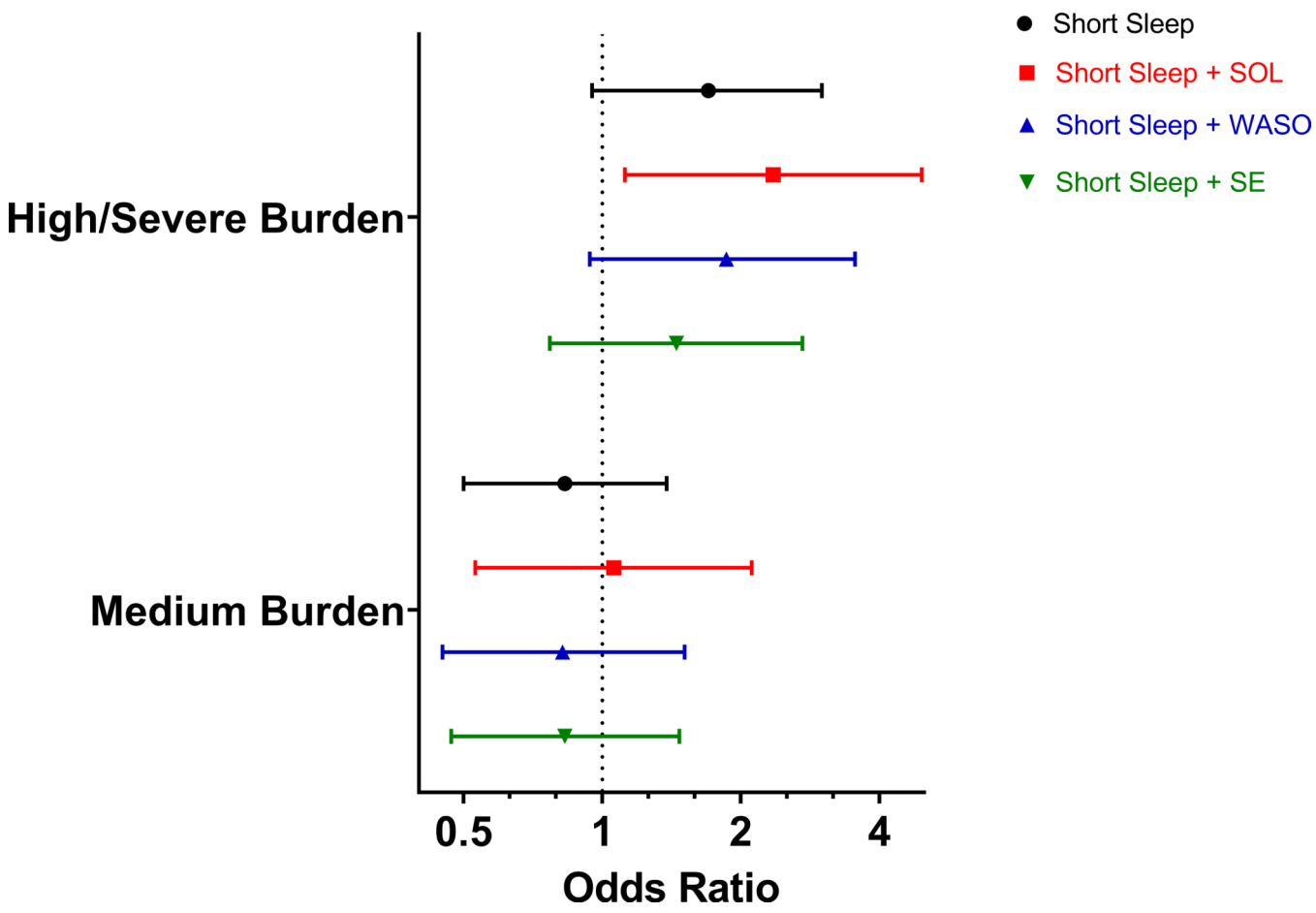


**Figure 1. Multivariable Associations between Phenotypes of Short Sleep and Severity/Burden of Physical Health Conditions**

Reference group = low burden/none; models adjusted for age, sex, race/ethnicity, body mass index, physical inactivity; long sleepers removed from analyses.

## Table 1

List of Treatment Exposures Included in Multivariable Models for Each Health Condition

| Health Condition[a] | Condition-Specific Treatment Exposures[c] |
|---|---|
| **Cardiac** | chest radiation, anthracyclines, alkylating agents (heavy metal, classic) |
| **Pulmonary** | chest radiation, bleomycin, alkylating agents (classic) |
| **Endocrine**[b] | Cranial and neck radiation, corticosteroids, methotrexate |
| **Renal** | abdominal radiation, ifosfamide, alkylating agents (heavy metal) |
| **Neurology** | cranial radiation, high dose intravenous methotrexate, intrathecal methotrexate/cytarabine |
| **Gastrointestinal/Hepatic** | neck, chest, and abdominal radiation |
| **Musculoskeletal** | cranial, chest, and abdominal radiation, methotrexate, corticosteroids, |
| **Anxiety/Depression** | cranial radiation, intrathecal methotrexate/cytarabine, high dose intravenous methotrexate, corticosteroids |

[a] in addition to treatment exposures, all models were adjusted for the following covariates: age at evaluation, age at diagnosis, sex, race/ethnicity, body mass index (BMI), and physical inactivity

[b] BMI removed as a covariate in the endocrine models because obesity is an outcome, grade 2 obesity excluded

[c] treatment exposures classified as yes/no variables

## Table 2

Self-Reported Habitual Sleep Characteristics[a] of the SJLIFE Sample (n=911)

| Sleep Characteristic | M (SD) |
|---|---|
| Sleep duration (hours) | 6.6 (1.4) |
| Sleep onset latency (minutes) | 35.0 (39.1) |
| Sleep efficiency (%) | 85.6 (19.7) |
| PSQI total score | 6.8 (2.9) |
| | **N (%)** |
| Short sleep duration (≤ 6 hours per evening) | 402 (44.1) |
| Long sleep duration (≥ 10 hours per evening) | 14 (1.5) |
| Typical sleep duration | 495 (54.3) |
| Short sleep duration + prolonged SOL | 192 (21.4) |
| Short sleep duration + WASO | 239 (26.6) |
| Short sleep duration + SE | 262 (29.2) |
| Poor sleep quality (PSQI > 5) | 503 (56.9) |

PSQI, Pittsburgh Sleep Quality Index; SOL, sleep onset latency; WASO, wake after sleep onset; SE, sleep efficiency

[a]All variables from the Pittsburgh Sleep Quality Index

## Table 3

Demographic, Treatment, and Health Characteristics of SJLIFE Sample (n=897)[a]

| Variable | Short Sleep Duration n=400 | Typical Sleep Duration n=495 | p[e] |
|---|---|---|---|
| | M (SD) | M (SD) | |
| Age at evaluation, years | 35.1 (8.5) | 33.8 (9.2) | 0.0397 |
| Age at diagnosis, years | 8.6 (5.7) | 8.8 (5.6) | 0.5239 |
| BMI, amputation adjusted (kg/m$^2$) | 29.4 (7.5) | 28.2 (6.7) | 0.0137 |
| | N (%) | N (%) | |
| Sex | | | |
| Female | 212 (53.0) | 252 (50.9) | 0.5337 |
| Male | 188 (47.0) | 243 (49.1) | |
| Race/Ethnicity | | | |
| White, non-Hispanic | 324 (81.0) | 429 (86.7) | 0.0211 |
| Other | 76 (19.0) | 66 (13.3) | |
| Diagnosis | | | |
| Leukemia | 150 (37.5) | 220 (44.4) | 0.0945 |
| CNS tumor | 24 (6.0) | 42 (8.5) | |
| Non-CNS solid tumor | 108 (27.0) | 101 (20.6) | |
| Hodgkin lymphoma | 51 (12.8) | 66 (13.4) | |
| Non-Hodgkin lymphoma | 28 (7.0) | 28 (5.7) | |
| Ewing/osteosarcoma | 32 (8.0) | 29 (5.9) | |
| Other | 7 (1.8) | 8 (1.6) | |
| Radiation | | | |
| Cranial radiation | | | |
| ≥ 20 Gy | 58 (12.3) | 80 (16.9) | 0.5078 |
| < 20 Gy | 44 (11.5) | 56 (11.9) | |
| No cranial radiation | 285 (74.2) | 335 (70.8) | |
| Chest radiation | 72 (18.7) | 111 (23.5) | 0.0865 |
| Abdominal radiation | 67 (17.4) | 95 (20.1) | 0.3095 |
| Neck radiation | 65 (16.8) | 109 (23.0) | 0.0244 |
| Chemotherapy | | | |
| High dose IV methotrexate | 118 (29.5) | 162 (32.7) | 0.3005 |
| Intrathecal methotrexate/cytarabine | 167 (41.8) | 225 (45.5) | 0.2667 |
| Corticosteroids | 202 (50.5) | 269 (54.3) | 0.2522 |
| Anthracyclines | 246 (61.5) | 320 (64.7) | 0.3317 |
| Alkylating agents (classic) | 232 (58.0) | 300 (60.6) | 0.4299 |
| Alkylating agents (heavy metal) | 37 (9.3) | 48 (9.7) | 0.8206 |
| Ifosfamide | 29 (7.3) | 37 (7.5) | 0.8982 |
| Physically inactive[b,c] | 162 (47.7) | 183 (42.2) | 0.1279 |

| Variable | Short Sleep Duration n=400 | Typical Sleep Duration n=495 | P[e] |
|---|---|---|---|
| Psychological distress[d,c] | | | |
| BSI anxiety | 35 (10.6) | 13 (3.4) | <0.0001 |
| BSI depression | 34 (10.3) | 20 (5.2) | 0.0100 |
| Chronic conditions | | | |
| Cardiac conditions (Grade ≥2) | 173 (43.3) | 192 (38.8) | 0.1768 |
| Endocrine conditions (Grade ≥2) | 223 (55.8) | 225 (45.5) | 0.0022 |
| Pulmonary conditions (Grade ≥2) | 121 (30.3) | 114 (23.0) | 0.0147 |
| Renal conditions (Grade ≥2) | 46 (11.5) | 43 (8.7) | 0.1621 |
| Neurologic conditions (Grade ≥2) | 130 (32.5) | 147 (29.7) | 0.3671 |
| Gastrointestinal conditions (Grade ≥2) | 148 (37.0) | 130 (26.3) | 0.0006 |
| Musculoskeletal conditions (Grade ≥2) | 123 (30.8) | 146 (29.5) | 0.6839 |

CNS, central nervous system; GY, gray; IV, intravenous; BSI, Brief Symptom Inventory; M, mean; SD, standard deviation

[a]Participants with long sleep duration removed (n=14)

[b]Physically inactive was defined according to CDC criteria of 450 MET-minutes per week

[c]Psychological distress defined as T-score ≥63

[d]The following variables had >10% missing: physically inactive (n=121); anxiety and depression (n=182)

[e]Chi-square test or t-test for comparison of continuous variables between short and typical sleep duration groups, all tests were two-sided

**Table 4**

Multivariable Associations[a] Between Phenotypes of Short Sleep Duration and Physical and Psychological Health Conditions (n=897)[b]

| | Cardiac | Pulmonary | Endocrine | Renal | Neurologic | GI/Hepatic | Musculoskeletal | Anxiety | Depression |
|---|---|---|---|---|---|---|---|---|---|
| **Self-Report** | ***RR (95% CI)*** | ***RR (95% CI)*** | ***RR (95% CI)*** | ***RR (95% CI)*** | ***RR (95% CI)*** | ***RR (95% CI)*** | ***RR (95% CI)*** | ***RR (95% CI)*** | ***RR (95% CI)*** |
| **Short sleep** | 1.10 (0.94–1.30) | **1.35 (1.08–1.69)** | **1.22 (1.06–1.39)** | 1.23 (0.80–1.90) | 1.18 (0.95–1.46) | **1.46 (1.18–1.79)** | 1.06 (0.85–1.31) | **3.24 (1.64–6.41)** | **2.33 (1.27–4.27)** |
| **Short sleep + SOL** | 1.18 (0.98–1.40) | **1.36 (1.05–1.75)** | **1.20 (1.04–1.39)** | 1.50 (0.94–2.41) | **1.32 (1.04–1.68)** | **1.30 (1.04–1.62)** | 1.15 (0.90–1.48) | **3.30 (1.81–6.04)** | **3.13 (1.75–5.60)** |
| **Short sleep + WASO** | **1.21 (1.02–1.42)** | **1.44 (1.14–1.81)** | **1.17 (1.02–1.35)** | 1.26 (0.80–2.00) | **1.25 (1.01–1.57)** | **1.43 (1.16–1.76)** | 1.03 (0.81–1.31) | **3.80 (2.05–7.02)** | **2.74 (1.56–4.83)** |
| **Short sleep + SE** | 1.17 (0.98–1.39) | **1.43 (1.14–1.80)** | **1.16 (1.01–1.34)** | 1.01 (0.64–1.61) | 1.20 (0.96–1.49) | **1.45 (1.19–1.78)** | 1.00 (0.79–1.27) | **1.94 (1.05–3.58)** | **1.98 (1.11–3.52)** |

GI, gastrointestinal; RR, risk ratio; CI, confidence interval; SOL, sleep onset latency; WASO, wake after sleep onset; SE, sleep efficiency

[a] models adjusted for: age at evaluation, sex, race/ethnicity, age at diagnosis, body mass index, physical inactivity and condition specific treatment exposures

[b] long sleepers removed

**Bold indicates P ≤0.05**