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REVIEW

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A call to action for expanded sleep research in pediatric oncology: A position paper on behalf of the International Psycho-Oncology Society Pediatrics Special Interest Group

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on behalf of the International Psycho-Oncology Society Pediatrics Special Interest Group

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Abstract

Sleep and circadian rhythms are closely related to physical and psychosocial well-being. However, sleep and circadian rhythm disruptions are often overlooked in children with cancer, as they are frequently considered temporary side effects of therapy that resolve when treatment ends. Yet, evidence from adult oncology suggests a bidirectional relationship wherein cancer and its treatment disrupt sleep and circadian rhythms, which are associated with negative health outcomes such as poor immune functioning and lower survival rates. A growing body of research demonstrates that sleep problems are prevalent among children with cancer and can persist into survivorship. However, medical and psychosocial outcomes of poor sleep and circadian rhythmicity have not been explored in this context. It is essential to increase our understanding because sleep and circadian rhythms are vital components of health and quality of life. In children without cancer, sleep and circadian disturbances respond well to intervention, suggesting that they may also be modifiable in children with cancer. We present this paper as a call to (a) incorporate sleep or circadian rhythm assessment into pediatric cancer clinical trials, (b) address gaps in understanding the bidirectional relationship between sleep or circadian rhythms and health throughout the cancer trajectory, and (c) integrate sleep and circadian science into oncologic treatment.

KEYWORDS

actigraphy, circadian rhythms, pediatric cancer, sleep, sleep disorders

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1 | INTRODUCTION

Sleep disruptions are frequently reported in children with cancer, both during treatment (see Supplemental File A for Reviews in Child Cancer) and well into survivorship.[1-3] Dysregulated circadian rhythms (weakening of circadian rhythmicity), indicated by irregular rest-activity rhythms, are common in adult oncology,[4] and a small but growing body of literature suggests similar disruption to the circadian system in pediatric oncology.[5,6] However, many questions on the etiology, prevalence, and impact of sleep throughout the child's cancer trajectory remain unanswered. Healthy sleep is essential for overall well-being, including mood regulation, learning and cognition, immune function, weight management, and quality of life (QoL; see Supplemental File A Health Benefits). Epidemiological and animal models suggest that disrupted sleep, sleep disorders such as obstructive sleep apnea (OSA), and circadian dysregulation are associated with increased cancer incidence, more rapid tumor growth, and decreased survival (see Supplemental File A Epidemiological/Animal). Clinical research in adult oncology connects sleep and circadian dysregulation with symptom burden, tumor progression, and cancer prognosis (see Supplemental File A Adult Oncology). Research testing these outcomes in pediatric oncology is currently limited to the association between sleep or circadian rhythms and fatigue, or their inclusion in symptom clusters in children on active treatment.[6-9] There are no longitudinal studies evaluating the effect of sleep disturbances (symptoms of inadequate or unrefreshing sleep), clinical sleep disorders (eg, insomnia, OSA, narcolepsy, excessive daytime sleepiness), or circadian dysregulation on cancer outcomes, leaving large gaps in our understanding of how sleep may affect cancer prognosis or other health-related outcomes.

Sleep problems affect up to 25% of healthy children.[10] Thus, many children with cancer have preexisting sleep problems that may be exacerbated by their illness and its treatment. Some studies have highlighted the direct effects of specific treatments (eg, corticosteroids[11]) and diagnoses (eg, brain tumors[12]) on sleep. Indirect effects of cancer treatment, such as hospitalizations,[13] are also possible risk factors for poor sleep. Accurate assessment of children's sleep patterns and habits as well as a clear understanding of risk factors (eg, gender, age, cancer diagnosis, type of cancer treatment) and when sleep problems are likely to develop are crucial to achieve the ultimate goal of improving sleep and its associated outcomes in children with cancer. However, much of the existing literature on child sleep includes cross-sectional, single-center studies with small samples, despite families and providers indicating that this is a priority area for research and clinical practice.[14,15] Adult oncology research has better integrated sleep as a meaningful outcome and correlate of medical and psychosocial outcomes. Thus, the current paper draws on the adult literature to determine a course for advancing pediatric sleep research and subsequently improving health and QoL outcomes. The following recommendations are a collaborative effort by an international group of sleep researchers, offered as a call for pediatric oncology investigators to consider including sleep assessment in their research. Expanded sleep measurement will enable us to better identify the direct and indirect effects of cancer on sleep and its associated outcomes, guiding future intervention development.

1.1 | Recommendations

1.1.1 | Recommendation 1: Incorporate sleep or circadian rhythms assessment into pediatric cancer clinical trials

We currently have limited understanding of how sleep may serve as a predictor of health, QoL, and neurocognitive outcomes, a mediator or moderator of treatment outcomes, and an outcome itself in children with cancer. Some clinical trial protocols are beginning to incorporate measures of symptom burden and QoL with a particular focus on patient-reported outcomes. The addition of sleep measures to large-scale pediatric cancer clinical trials would expand our opportunity to determine the effects of insufficient or fragmented sleep, sleep disorders, or dysregulated circadian rhythms on outcomes. To date, progress has been hampered by small sample sizes and the need to take into account differences in diagnoses, treatment types, age, and treatment phase. Possible approaches to measuring sleep in children with cancer are summarized below and in Table 1.

Subjective assessment of sleep disturbances

Patient-reported outcomes are an essential component of evaluation in clinical trials because patients understand their own experience far better than clinicians, and incorporating their symptom burden can improve clinical trial development.[31] Regular screening by self- and parent-proxy report for sleep disturbances including poor sleep quality and whether sleep duration meets recommendations for age,[32] as well as sleep disorder screening, should be incorporated into clinical trials to learn when children are most likely to develop sleep problems and to delineate the range of sleep problems that can occur. Early recognition of sleep problems is important to expedite intervention.

Patient- or proxy-reported sleep quantity is best measured in the patient's natural environment (unless the inpatient environment is the variable of interest) and can be assessed using a daily sleep diary.[33] Identifying appropriate screening instruments for sleep quality is more

TABLE 1 Selection of self- and parent-proxy report of sleep habits, behaviors, and sleep disorders

Scale Name	Items/Subscales	Forms Available	Recommended for
Selected measures: General measures			
PROMIS Sleep Health Scales[16]	4-, 8-, and 12-item scales Sleep Disturbances and Sleep-Related Interference scales	Self-report (ages 8-17) Parent proxy-report (ages 5-17) Adult self-report forms also available (ages 18+)	General assessment of sleep disturbances and daytime impairment, through online scoring can obtain t-scores with as little as 1 item, preliminary evidence of clinical validity in pediatric oncology.[17]
Sleep Disturbances Scale for Children[18]	26 items 6 subscales Disorders of: initiating/maintaining, sleep breathing, arousals, sleep-wake transition, excessive somnolence, hyperhidrosis	Parent proxy-report (ages 5-15)	Widely used measure of general child sleep habits, has been used in pediatric oncology previously
Children's Sleep Habits Questionnaire[19]	35 items Bedtime resistance, sleep onset delay, sleep duration, sleep anxiety, night wakings, parasomnias, sleep-disordered breathing, daytime sleepiness	Parent proxy-report (ages 4-10)	Widely used measure of general child sleep habits, has been used in pediatric oncology previously
Selected measures: Condition specific measures			
Pediatric Sleep Questionnaire—Sleep-Disordered Breathing Subscale[20]	15-item subscale	Parent-proxy report (ages 2-18)	Screening for sleep-disordered breathing when objective assessment (polysomnography) is not feasible.
Pediatric Insomnia Severity Index[21]	6-item scale	Parent proxy-report (ages 4-10)	Brief screening regarding insomnia symptoms in young children
Modified Epworth Sleepiness Scale[22,23]	8-item scale	Self-report (ages 12-18) Parent proxy-report (2-18 y)	Assessing daytime sleepiness, has been used previously in children with cancer.
Relevant actigraphy outcomes for sleep[24]			
Sleep efficiency	Percent of time in bed spent asleep		
Sleep onset latency	Length of time from reported bedtime, typically assessed using an event marker on the actigraph or a sleep diary, to initial onset of sleep		
Total nap time	Minutes scored as sleep during combined daytime sleep episodes (naps) per day		
Total sleep time	Number of minutes scored as nighttime sleep, from initial sleep onset to final awakening in the morning (sleep offset). For hospitalized children on an irregular sleep-wake schedule due to illness, environmental disruptors, etc, this may be calculated over 24-h periods or separately for defined periods such as 12 h daytime and 12 h nighttime periods.		
Wake after sleep onset	Minutes scored as wake between initial sleep onset and final sleep offset		
Percent sleep	Percent of minutes during a defined period (eg, 12 h or 24 h) that are scored as sleep. This can be useful for hospitalized children on an irregular sleep-wake schedule.		
Average duration of sleep episodes	Average length of sleep episodes during a defined period (eg, 12 h or 24 h). Sleep episodes are defined as lasting longer than a predefined number of minutes (eg, 5 min). Longer duration and occurring at night indicate better sleep.		
Sleep episodes	Number of sleep episodes that are longer than a predefined number of minutes (eg, 0.5 min).		
Wake episodes	Number of wake episodes that are longer than a predefined number of minutes (eg, 5 min). Lower numbers indicate more consolidate and healthier sleep.		
Longest wake episode	How long patient is awake during one wake period, noting when this occurs. Longer is better during the day than at night. Note that longest sleep episode can also be calculated.		
Relevant actigraphy outcomes for circadian analysis[6,25]			
Acrophase[26]	Clock time of peak activity		

(Continues)

TABLE 1 (Continued)

Scale Name	Items/Subscales	Forms Available	Recommended for
Amplitude	Difference between peak activity and trough activity in a 24-h period		
Midline estimating statistic of rhythm (MESOR)	Half-way between peak and trough activity in a 24-h period		
Autocorrelation Coefficient[27]	Using cosinor analysis—measures the consistency between actigraphy rhythms across days of measurement.		
I < O Dichotomy Ratio[28-30]	Computes a ratio of in-bed versus out-of-bed activity, more activity during the day indicates more robust circadian rhythm.		
Intradaily variability (IV)	An estimate of the 24-h rest-activity rhythm and reflects the fragmentation of the rhythm, a higher IV indicates a more fragmented rhythm.		
Interdaily stability (IS)	An estimate of the stability of the rhythm and describes the synchronization of the rhythm, wherein 1 signifies a perfect synchronization to the dark-light cycle.		
L5counts	Activity counts of the least active 5 h of the day.		
M10counts	Activity counts of the most active 10 h of the day.		
Relative amplitude[27]	Nonparametric method that does not rely on cosine fit. Ratio of the difference and the sum of M10 and L5. A higher RA indicates a bigger difference between the least and most active period during the day, hence a better sleep-wake rhythm.		

challenging. Instruments should ideally be applicable across the entire pediatric age range to allow uniform longitudinal assessment of sleep. This is a major challenge considering the developmental changes in normal sleep and the need for proxy-respondents in young children who cannot provide self-reports. Instruments should be methodologically robust, available in multiple languages, and provide normative values (for recent reviews of pediatric measures, see previous works[34,35]). The National Institutes of Health Patient-Reported Outcomes Measurement Information System (PROMIS) sleep item banks fulfill many of the abovementioned requirements for assessing overall sleep quality. The PROMIS Sleep Disturbance item bank assesses difficulties with sleep onset, continuity, and quality, and the Sleep-Related Impairment item bank allows additional investigation into daytime impairments associated with sleep problems, including daytime sleepiness, mood and behavior difficulties, and impact on engagement in daily activities.[16] The PROMIS scales can also be applied in more participant-friendly formats such as short forms and computerized adaptive tests. Preliminary evidence demonstrating clinical validity of these scales in pediatric oncology is promising.[17]

Objective assessment of sleep disturbances

Sleep characteristics, including sleep duration, can be objectively assessed by actigraphy. This technique measures movement by using an accelerometer to estimate sleep with algorithms validated relative to the gold standard for sleep assessment, polysomnography. The non-invasive nature of actigraphy makes it ideal for use in children. Considerations for improving the reliability and validity of actigraphy have been well described.[36,37] Where possible, a minimum of 3 days and up to 7 days of actigraphy, which would include both weekdays or school days and weekends or nonschool days, are preferable.[38] Conventional methods of measuring sleep from bedtime at night to awakening in the morning, and conventional sleep parameters such as total sleep time, sleep latency, and sleep efficiency, are useful for measuring sleep in the home environment during stable periods (defined in Table 1). However, these variables may be inadequate to accurately capture sleep patterns of hospitalized children. As such, we propose additional, innovative actigraphy variables for assessment of sleep in hospitalized children (26; Table 1).

Circadian activity rhythms (CARs), defined as the rest-activity rhythm across time, can be measured directly by actigraphy using actigraphy activity counts. Traditional cosinor analysis yielding variables, such as acrophase, amplitude, and midline estimating statistic of rhythm (MESOR), have been suggested as minimum CAR variables to report, and newer extended cosine models and nonparametric approaches that better detect rhythm fragmentation, such as the 24-hour autocorrelation and dichotomy index, can be used.[25,39] While there is no consensus regarding the analytic approach, rhythm fragmentation disrupts the sinusoidal pattern of the rest-activity pattern,[39] making nonparametric approaches attractive for analysis of CARs in ill children. Given the early stage of this research, the best CAR variables for analysis in children with cancer have yet to be determined. Several studies have measured sleep or CARs in children by using actigraphy, both during and after completing cancer treatment, with measurements taken at home during stable periods and during hospitalization.[11,40-42] Clinical-grade actigraphs are recommended over consumer sleep technologies; such as activity trackers, smart watches, or smartphone apps. Although consumer-grade technologies present an interesting opportunity to study sleep in large numbers of people, access to raw data is not always possible, and validity data suggest that these devices are not precise enough for use in research.[43]

Assessment of sleep disorders

Existing research has provided valuable information about sleep characteristics, mostly associated with insomnia, which is characterized by difficulty initiating and/or maintaining sleep, along with daytime sequelae due to poor sleep. Insomnia has been the most widely studied sleep disorder among children with cancer; however, measures specific to insomnia in pediatrics are limited.[35] The Pediatric Insomnia Severity Index[21] was recently developed for children and adolescents. Subscales of generic measures such as The Sleep Disturbances Scale for Children[18] and the Children's Sleep Habits Questionnaire[19] are also relevant for assessing insomnia, although none of these measures have been validated in pediatric oncology patients (select measures are described in Table 1). A recent review of sleep measures for oncology focused primarily on adults may also be of interest.[44]

Evidence on the prevalence of other sleep disorders in children with cancer is scarce. One study indicated a 19% risk of OSA in survivors[45] compared with 1% to 4% in healthy children.[46,47] As obesity increases the risk for OSA, children with specific cancer diagnoses or treatments that are associated with increased risk of obesity may be at greater risk. Children having prolonged exposure to corticosteroids during treatment, such as those with acute lymphoblastic leukemia (ALL) and those with central nervous system (CNS) tumors that affect the hypothalamic-pituitary-adrenal (HPA) axis, are at increased risk of obesity.[48] Therefore, it is essential to assess the development of OSA in children with cancer by including questionnaires related to the symptomology of sleep-disordered breathing. A widely used measure validated in children and adolescents 2 to 18 years of age is the Sleep-Disordered Breathing Subscale of the Pediatric Sleep Questionnaire.[20] For patients with risk factors of obesity or HPA axis tumor involvement as well as those screening above clinical cutoffs on a sleep-disordered breathing screening tool, incorporating in-laboratory nocturnal polysomnography or even home sleep testing into treatment protocols can provide invaluable diagnostic information related to their nighttime breathing, which may change as cancer-related late effects develop. In addition to promoting better understanding of the impact of cancer-directed therapy on at-risk patient populations, regular polysomnography would also likely provide clinical benefit through identification of patients in need of sleep interventions.

Excessive daytime sleepiness is also common in patients with cancer, especially in survivors of CNS tumors with tumors affecting the HPA axis and hormonal secretion.[49] Excessive daytime sleepiness can be a symptom of OSA, narcolepsy, or idiopathic hypersomnia; a stand-alone clinical diagnosis; or a cancer-related late effect. For example, survivors of CNS tumors appear to be at a heightened risk for such sleepiness in the absence of OSA.[49] For children treated for craniopharyngioma, damage to the HPA axis may manifest as narcolepsy.[50] To screen for daytime sleepiness, the modified Epworth Sleepiness Scale has been used in pediatric populations,[22] including children with cancer.[12] The differential diagnosis between OSA with excessive daytime sleepiness, excessive daytime sleepiness due to a medical condition, and narcolepsy due to a medical condition typically warrants nocturnal polysomnography followed by a multiple sleep latency test, which gives patients multiple nap opportunities to objectively determine daytime sleep propensity and sleep stages during naps.

The use of different measures to evaluate sleep should vary according to the outcomes of interest. For example, self-report measures are appropriate for assessing insomnia and general symptoms of sleep disturbances, whereas polysomnography is the gold standard for evaluating OSA, and actigraphy is necessary for evaluating circadian rhythms and sleep or wake patterns in the natural environment (Table 1).

1.1.2 | Recommendation 2: Address gaps in understanding the bidirectional relationship between sleep or circadian rhythms and health throughout the cancer trajectory

Determine mechanisms underlying the relationship between sleep and cancer outcomes

Psychoneuroendocrine and psychoneuroimmune pathways may offer insight into the mechanisms between sleep and cancer-related outcomes. These pathways may represent positive-feedback loops through which sleep and circadian rhythms, psychological factors, and tumor growth interact and destabilize the circadian, endocrine, and immune systems over the course of cancer treatment.[51] Identifying and understanding proximal biomarkers of the impact of poor sleep and dysregulated CARs on the endocrine and immune systems are essential to estimate the impact of sleep on survival and cancer outcomes. To our knowledge, endocrine (cortisol, endogenous melatonin) and immune biomarkers (eg, c-reactive protein, interleukin-6, tumor necrosis factor) have not yet been investigated in relation to sleep and circadian rhythms in pediatric oncology. As mentioned above, the use of actigraphy to measure sleep and CARs in children with cancer can be expanded to investigate the effect of individual chemotherapeutic agents on CARs, the ability of children's CARs to recover between treatments and at the end of treatment, and outcomes of dysregulated CARs based on age at diagnosis and other key sociodemographic variables.

Animal models may also offer insights into the relationship between sleep and cancer outcomes. Recent research suggests that intermittent hypoxia and sleep fragmentation, both hallmarks of sleep-disordered breathing, contribute to tumor growth (see Supplemental File A Sleep-Disordered Breathing). Further research on the connection between sleep-disordered breathing and tumor growth in children with cancer may be especially relevant to patients with CNS tumors who are at heightened risk for OSA.

Some psychosocial mechanisms may also be influenced by poor sleep, which can affect health outcomes. Neurocognitive functioning is also affected by poor sleep and OSA.[52] In brain tumor survivors, total sleep problems were moderately related to parent reports of executive functioning.[53] Adult survivors of childhood cancer with poor sleep are more vulnerable to neuropsychological consequences of poor sleep than sibling controls.[54] Studies focused on identifying and mitigating neurocognitive late effects (subjective report, actigraphy, and/or polysomnography) should also consider sleep as a correlate of neurocognitive functioning as well as an intervention target to improve functioning.

Inadequate sleep (not meeting minimum recommended duration for age) and dysregulated circadian rhythms are closely related to depression and anxiety in adult oncology[55] and children without cancer.[56] When insomnia is successfully treated, depressive symptoms improve in adolescents,[57] adults,[58] and adults with cancer.[59] Furthermore, for patients who exhibit dysregulated rhythms, which often include sleeping during the day and engagement with hospital staff and supportive care activities during the day such as child life specialists, physical therapy, occupational therapy, and psychology, are likely to be limited, which may indirectly affect adjustment and recovery. Understanding these psychosocial mechanisms may offer insights into novel sleep-related intervention targets that could impact health outcomes.

Identify risk factors for poor sleep

A child's sleep during cancer treatment can vary considerably by tumor type and the nature of cancer treatment. Hospitalization, type and intensity of treatment, age, and gender are the known risk factors for poor sleep. Demographic factors such as preexisting developmental vulnerabilities, socioeconomic status, and race or ethnicity should also be considered given their role in impacting sleep in children without cancer (see Supplemental File A Demographic Risk for Poor Sleep). Control groups are needed to disentangle the myriad of influences on sleep. For example, incorporating peer control groups without cancer or including within-subject designs where a patient can serve as their own comparison would help isolate disease and treatment-related sleep disturbances. Inpatient hospitalizations disrupt a child's sleep,[13] due in part to the frequency of nocturnal awakenings for care provision,[41] potentially resulting in delirium, which has not been studied in oncology. Even a comprehensive intervention intended to improve sleep in patients with CNS tumors receiving conditioning chemotherapy before hematopoietic stem cell transplantation could not increase total sleep time compared with controls because of the care required throughout the night.[24,60] Past studies show that sleep disturbances (including difficulty initiating and maintaining sleep, daytime napping, and variable sleep patterns) are common in ALL patients[11] and can substantially impact their QoL.[61] Adolescents, females, those receiving corticosteroid pulses (dexamethasone having a higher impact than prednisone), and high-risk patients (due to differences in dexamethasone clearance) are at increased risk (see Supplemental File A Sleep in ALL). Because much of the existing research has focused on sleep in patients with ALL, future research should attend to the different sleep experiences of children by cancer type.

Sleep also needs to be more fully described longitudinally throughout treatment and into survivorship. Longitudinal studies will improve our understanding of trajectories of sleep disturbances and differentiate patients who would most benefit from early intervention to prevent further worsening of sleep from those who have temporary sleep disturbances that resolve as each treatment is completed.

Investigate the role of sleep in health and survival posttreatment

Improvements in cancer diagnosis and treatment have led to an increase in the number of childhood cancer survivors. Minimizing the long-term effects of cancer treatment and promoting QoL, including improved sleep outcomes after treatment, have, therefore, become a priority. Studies show that 47% to 69% of adolescent and young adult cancer survivors report sleep disturbances such as prolonged sleep onset latency, poor sleep efficiency, early waking, inadequate total sleep time, and nonrefreshing sleep.[8,62] Survivors experiencing disrupted sleep report lower overall health and higher levels of anxiety and depression than do survivors without sleep disruption.[8] However, few studies describe the prevalence, predictors, and consequences of sleep disturbance among childhood cancer survivors. It is also unclear whether sleep disturbances change or resolve at different stages after treatment completion. Preliminary evidence suggests that as time from treatment increases, young adult survivors report fewer sleep concerns, whereas adolescent survivors report more sleep concerns, suggesting developmental differences in posttreatment sleep.[62] Ongoing investigation into the risk factors associated with sleep problems across the survivorship trajectory and potential interventions to meet the specific needs of this growing population is warranted.

1.1.3 | Recommendation 3: Integrate sleep and circadian science into oncologic treatment

Explore the role of circadian timing of treatments

A growing body of literature reports that circadian dysregulation in adults with cancer is prognostic of survival and related to symptom burden, suggesting that maintaining regular circadian rhythms may improve health and QoL outcomes and increase survival rates (for a review, see previous work[4]). Only two studies have investigated CARs measured by actigraphy in children or adolescents with cancer.[6] The first demonstrated that CARs were dysregulated after dexamethasone therapy was initiated in children with ALL, while the second demonstrated dysregulated CARs in hospitalized children and adolescents with CNS tumors on high dose chemotherapy compared with published values, and that fatigue was associated with greater CAR dysregulation.[63] With broader study of CARs in pediatric oncology, the field can begin to test relationships between dysregulated CARs and prognosis, as well as the impact of strengthening CARs on health and QoL outcomes.

Drug metabolism and cellular proliferation vary over the 24-hour period through the influence of the circadian timing system.[64] As a result, efficacy of cancer therapies can vary greatly depending on the phase of the circadian cycle at which they are given. Therefore, a potential mechanism for taking advantage of the relationship between the circadian system and cancer treatment is time of the administration of chemotherapeutic agents or radiation therapy to increase their effectiveness and reduce toxicity. Chronomodulated delivery of cancer therapies has shown greater effectiveness than fixed schedules in adults at equivalent doses while minimizing side effects, or potentially reducing dosages but maintaining equivalent efficacy (for a review, see previous work[65]). Given variations in effectiveness, there have been calls to personalize chronotherapy by gender and individual circadian timing and biomarkers.[4] Studies

examining the relationship between timing of chemotherapy and radiation relative to efficacy and side effect profiles are extremely limited in pediatric oncology.[66,67]

In hospitalized patients, the timing of treatment delivery is largely determined by the complexities of the hospital system rather than by an individual patient's circadian clock. Patients receive treatments based on provider availability, treatment preparation, access to rooms or beds, pretreatment needs, and staffing—all complex system issues that can result in variable treatment administration. Research evaluating the role of personalized circadian-based chemotherapy and radiation delivery in pediatric oncology has great potential to influence hospital systems to prioritize patient-based timing of treatment rather than basing treatment delivery on the hospital system's timing. Chronomodulated treatment delivery is complex and will necessitate multidisciplinary collaboration and systems level changes. This is, however, an important direction of research for the field and builds on current research efforts describing and protecting sleep and CARs in children with cancer.

Develop and evaluate interventions to improve sleep in patients and survivors

Parents express an interest in behavioral interventions that target difficulties falling asleep, and oncologists report a desire for interventions targeting their patients' irregular sleep habits.[68] However, few studies have tested or modified existing behavioral sleep interventions for pediatric oncology patients. Cognitive behavioral therapy for insomnia has been adapted for adolescent and young adult survivors, demonstrating large effects on sleep variables that were sustained across the 2-month follow-up period.[69] Yoga has also been employed as a potentially efficacious intervention for sleep in hospitalized children and adolescents.[70] Massage is another promising intervention for sleep, demonstrating feasibility and acceptability in hospitalized adolescents with cancer as well as trends towards longer overnight sleep when compared with a waitlist control.[71] A cross-sectional study of children with ALL, lymphoma, brain tumors, or solid tumors showed that improved sleep quality was associated with higher average daily activity and identified exercise as a potential intervention target for improving sleep.[42]

Hospital-based interventions that seek to provide education about sleep and fatigue management,[72] encourage physical activity,[41] and protect 90-minute windows for sleep[73] have been tested in small pilot studies in oncology. Because the hospital system is extremely disruptive to sleep and represents a potentially modifiable target, systems level interventions should be considered. Specifically, modifications that protect nighttime sleep through decreasing environmental noise and light, promoting regular developmentally appropriate bedtimes and wake times, minimizing room entries for patient care, and encouraging out-of-bed activity during the day are essential to reduce the impact of cancer treatment on sleep.

Parenting strategies and cultural practices shape childhood sleep habits, especially in young children. Previous studies in Western countries have found that parents of children with cancer are often more protective, less strict with discipline, and more likely to be permissive with their child than are parents of healthy children.[74] Changes in parenting practices may impact sleep through irregular sleep patterns, increased use of electronics around bedtime, and increased cosleeping.[68] Such behaviors, including reactive cosleeping[75] as a method to manage child behavior, offer modifiable intervention targets that could improve sleep in children with cancer. Further studies of cultural differences in parenting practices in non-Western countries are needed to tailor interventions to different patient populations and help families develop sleep habits that are consistent with their cultural beliefs.

Melatonin is widely used in pediatrics for sleep induction, despite limited evidence of its safety or effectiveness (see Supplemental File A). Recent studies in adult oncology suggest that melatonin may be helpful for sleep promotion[76,77]; however, the American Academy of Sleep Medicine does not recommend melatonin in adults with insomnia symptoms because of weak evidence.[78] Further research into the use of melatonin in pediatric cancer is warranted to guide its use.

Morning bright light therapy has been successfully used to improve dysregulated CARs, sleep, mood, fatigue, and QoL in various populations, including adult patients with cancer (see Supplemental File A Light Therapy for references). A recently completed randomized controlled trial to reduce fatigue using light therapy in newly diagnosed adolescents and young adults with solid tumors on treatment found that this intervention was feasible and acceptable.[79] Light therapy offers several advantages, including simplicity of use, low cost, portability to enable delivery to multiple settings (eg, home, temporary housing [eg, Ronald McDonald House], or inpatient unit), with little staff delivery involvement other than the initial instructions provided to the participant and parents. Its good safety profile and simplicity of use make it an attractive potential intervention for pediatric oncology patients. Although light therapy in adults with cancer and adolescents without cancer has shown no significant adverse effects (see Supplemental File A Light Therapy for references), further research is needed to definitively demonstrate its safety and effectiveness in improving outcomes such as sleep and circadian rhythmicity in children and adolescents being treated for cancer, especially in patients receiving cranial radiation or photosensitizing chemotherapy agents. In addition to light therapy, physical activity, timed meals, and increased social interaction could be incorporated into interventions aimed at improving circadian synchronization.[4]

Hydrocortisone may also provide a novel treatment for patients with dexamethasone-related sleep disturbances. For some patients on dexamethasone, cortisol depletion is a potential cause of the neuropsychological side effects exhibited, which include clinically significant sleep disturbances. For these patients, preliminary evidence supports the use of hydrocortisone to decrease sleep disruptions,[80] and a larger trial is currently underway.

2 | SUMMARY

In the last decade, our understanding of sleep and circadian rhythms in children with cancer has dramatically improved. However, many

questions remain unanswered, such as identifying demographic and treatment-related risk factors for sleep difficulties, testing the effect of sleep disturbances on outcomes, and trialing efficacious interventions to maintain or improve sleep and circadian robustness in children treated for cancer. We present this call to action to encourage broader incorporation of validated sleep measures into pediatric oncology research. This will allow pooling of data across trials, which is crucial to address gaps in studies on this group of diseases that are, thankfully, fairly rare in children. Understanding how sleep and circadian rhythms impact health during and after treatment will help us to better identify intervention targets and appropriate timing of interventions to improve sleep patterns in children with cancer. Poor sleep is more than just a side effect of treatment, and because it persists in many patients and interacts with the disease process, more research is needed to understand the role of sleep in the health and well-being of children with cancer.

AUTHORS' NOTE

We are an interdisciplinary and international group of psychologists, pediatricians, and nurse researchers devoted to advancing the understanding and treatment of sleep and circadian disturbances in pediatric oncology during treatment and into survivorship. We met monthly over the course of 6 months to determine the most relevant sleep or circadian research priorities for pediatric oncology and an outline for the current position paper. All authors drafted a portion of the paper and were involved in editing all sections.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

ETHICS APPROVAL

This manuscript was prepared in consultation with all authors. No new data was collected and no ethical board approval was needed.

DATA SHARING

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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REFERENCES

1. Daniel LC, Kazak AE, Li Y, et al. Relationship between sleep problems and psychological outcomes in adolescent and young adult cancer survivors and controls. *Support Care Cancer*. 2016;24(2):539-546.
2. Daniel LC, Wang M, Mulrooney DA, et al. Sleep, emotional distress, and physical health in survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. *Psychooncology*. 2019;28(4):903-912.
3. Zhou ES, Recklitis C. Insomnia in adult survivors of childhood cancer: a report from project REACH. *Support Care Cancer*. 2014;22(11):3061-3069.
4. Innominato PF, Roche VP, Palesh OG, Ulusakarya A, Spiegel D, Lévi FA. The circadian timing system in clinical oncology. *Ann Med*. 2014;46(4):191-207.
5. Pickering L, Jennum P, Gammeltoft S, Poulsgaard L, Feldt-Rasmussen U, Klose M. Sleep–wake and melatonin pattern in craniopharyngioma patients. *Eur J Endocrinol*. 2014;170(6):873-884.
6. Rogers VE, Zhu S, Ancoli-Israel S, Hinds PS. Impairment in circadian activity rhythms occurs during dexamethasone therapy in children with leukemia. *Pediatr Blood Cancer*. 2014;61(11):1986-1991.
7. Hockenberry MJ, Hooke MC, Gregurich M, McCarthy K, Sambuco G, Krull K. Symptom clusters in children and adolescents receiving cisplatin, doxorubicin, or ifosfamide. *Oncol Nurs Forum*. 2010;37(1):E16-E27.
8. Russo S, Fardell JE, Signorelli C, Wakefield CE, Mcloone JK, Cohn RJ. Sleep disturbances in childhood cancer survivors. *Pediatr Blood Cancer*. 2016;63(4):759-760.
9. Zupanec S, Jones H, Stremler R. Sleep habits and fatigue of children receiving maintenance chemotherapy for ALL and their parents. *J Pediatr Oncol Nurs*. 2010;27(4):217-228.
10. Owens J. Classification and epidemiology of childhood sleep disorders. *Sleep Med Clin*. 2007;2(3):353-361.
11. Hinds PS, Hockenberry MJ, Gattuso JS, et al. Dexamethasone alters sleep and fatigue in pediatric patients with acute lymphoblastic leukemia. *Cancer*. 2007;110(10):2321-2330.
12. Brimeyer C, Adams L, Zhu L, et al. Sleep complaints in survivors of pediatric brain tumors. *Support Care Cancer*. 2016;24(1):23-31.
13. Lee S, Narendran G, Tomfohr-Madsen L, Schulte F. A systematic review of sleep in hospitalized pediatric cancer patients. *Psychooncology*. 2017;26(8):1059-1069.
14. Hooke MC, Linder LA. Symptoms in children receiving treatment for cancer—part I: fatigue, sleep disturbance, and nausea/vomiting. *J Pediatr Oncol Nurs*. 2019;36(4):244-261.
15. Williams LK, McCarthy MC. Parent perceptions of managing child behavioural side-effects of cancer treatment: a qualitative study. *Child Care Health Dev*. 2014;41(4):611-619.
16. Forrest CB, Meltzer LJ, Marcus CL, et al. Development and validation of the PROMIS Pediatric Sleep Disturbance and Sleep-Related Impairment item banks. *Sleep*. 2018;41(6):zsy054.
17. Daniel LC, Gross JY, Flannery JL, Forrest CB, Barakat LP, editors. Evaluating the Validity of Patient-Reported Outcomes Measurement Information System (PROMIS) Pediatric Sleep Health Measures Among Children in Active Cancer Treatment. Society of Pediatric Psychology Annual Conference; 2019; New Orleans.
18. Bruni O, Ottaviano S, Guidetti V, et al. The sleep disturbance scale for children (SDSC). Construction and validation of an instrument to evaluate sleep disturbances in childhood and adolescence. *J Sleep Res*. 1996;5(4):251-261.
19. Owens JA, Spirito A, McGuinn M. The Children's Sleep Habits Questionnaire (CSHQ): psychometric properties of a survey instrument for school-aged children. *Sleep*. 2000;23(8):1043-1051.
20. Chervin RD, Hedger K, Dillon JE, Pituch KJ. Pediatric sleep questionnaire (PSQ): validity and reliability of scales for sleep-disordered breathing, snoring, sleepiness, and behavioral problems. *Sleep Med*. 2000;1(1):21-32.

21. Byars KC, Simon SL, Peugh J, Beebe DW. Validation of a brief insomnia severity measure in youth clinically referred for sleep evaluation. *J Pediatr Psychol*. 2017;42(4):466-475.
22. Melendres MC, Lutz JM, Rubin ED, Marcus CL. Daytime sleepiness and hyperactivity in children with suspected sleep disordered breathing. *Pediatrics*. 2004;114(3):768-775.
23. Janssen KC, Phillipson S, O'Connor J, Johns MW. Validation of the Epworth Sleepiness Scale for children and adolescents using Rasch analysis. *Sleep Med*. 2017;33:30-35.
24. Rogers VE, Zhu S, Ancoli-Israel S, Liu L, Mandrell BN, Hinds PS. A pilot randomized controlled trial to improve sleep and fatigue in children with central nervous system tumors hospitalized for high-dose chemotherapy. *Pediatr Blood Cancer*. 2019;n/a:e27814.
25. Berger AM, Wielgus KK, Young-McCaughan S, Fischer P, Farr L, Lee KA. Methodological challenges when using actigraphy in research. *J Pain Symptom Manage*. 2008;36(2):191-199.
26. Nelson W, Tong YL, Lee JK, Halberg F. Methods for cosinor-rhythmometry. *Chronobiologia*. 1979;6(4):305-323.
27. Van Someren EJ, Swaab DF, Colenda CC, Cohen W, McCall WV, Rosenquist PB. Bright light therapy: improved sensitivity to its effects on rest-activity rhythms in Alzheimer patients by application of nonparametric methods. *Chronobiol Int*. 1999;16(4):505-518.
28. Lévi F, Dugué P-A, Innominato P, et al. Wrist actimetry circadian rhythm as a robust predictor of colorectal cancer patients survival. *Chronobiol Int*. 2014;31(8):891-900.
29. Mormont M-C, Langouët AM, Claustrat B, et al. Marker rhythms of circadian system function: a study of patients with metastatic colorectal cancer and good performance status. *Chronobiol Int*. 2002;19(1):141-155.
30. Mormont M-C, Waterhouse J, Bleuzen P, et al. Marked 24-h rest/activity rhythms are associated with better quality of life, better response, and longer survival in patients with metastatic colorectal cancer and good performance status. *Clin Cancer Res*. 2000;6(8):3038-3045.
31. Basch E, Bennett AV. Patient-reported outcomes in clinical trials of rare diseases. *J Gen Intern Med*. 2014;29(3):801-803.
32. Hirshkowitz M, Whiton K, Albert SM, et al. National Sleep Foundation's sleep time duration recommendations: methodology and results summary. *Sleep Health*. 2015;1(1):40-43.
33. Acebo C, Sadeh A, Seifer R, Tzischinsky O, Hafer A, Carskadon MA. Sleep/wake patterns derived from activity monitoring and maternal report for healthy 1- to 5 year-old children. *Sleep*. 2005;28(12):1568-1577.
34. Ji X, Liu J. Subjective sleep measures for adolescents: a systematic review. *Child Care Health Dev*. 2016;42(6):825-839.
35. Lewandowski AS, Toliver-Sokol M, Palermo TM. Evidence-based review of subjective pediatric sleep measures. *J Pediatr Psychol*. 2011;36(7):780-793.
36. Ancoli-Israel S, Martin JL, Blackwell T, et al. The SBSM guide to actigraphy monitoring: clinical and research applications. *Behav Sleep Med*. 2015;13(sup1):S4-S38.
37. Meltzer LJ, Montgomery-Downs HE, Insana SP, Walsh CM. Use of actigraphy for assessment in pediatric sleep research. *Sleep Med Rev*. 2012;16(5):463-475.
38. Acebo C, Sadeh A, Seifer R, et al. Estimating sleep patterns with activity monitoring in children and adolescents: how many nights are necessary for reliable measures? *Sleep*. 1999;22(1):95-103.
39. Marler MR, Gehrman P, Martin JL, Ancoli-Israel S. The sigmoidally transformed cosine curve: a mathematical model for circadian rhythms with symmetric non-sinusoidal shapes. *Stat Med*. 2006;25(22):3893-3904.
40. Greenfeld M, Constantini S, Tauman R, Sivan Y. Sleep disturbances in children recovered from central nervous system neoplasms. *J Pediatr*. 2011;159(2):268-272. e1
41. Hinds PS, Hockenberry M, Rai SN, et al. Nocturnal awakenings, sleep environment interruptions, and fatigue in hospitalized children with cancer. *Oncol Nurs Forum*. 2007;34(2):393-402.
42. Orsey AD, Wakefield DB, Cloutier MM. Physical activity and sleep among children and adolescents with cancer. *Pediatr Blood Cancer*. 2013;60(11):1908-1913.
43. Khosla S, Deak MC, Gault D, et al. Consumer sleep technology: an American Academy of Sleep Medicine position statement. *J Clin Sleep Med*. 2018;14(05):877-880.
44. Redeker NS, Pigeon WR, Boudreau EA. Incorporating measures of sleep quality into cancer studies. *Support Care Cancer*. 2015;23(4):1145-1155.
45. Ruble K, George A, Gallicchio L, Gamaldo C. Sleep disordered breathing risk in childhood cancer survivors: an exploratory study. *Pediatr Blood Cancer*. 2015;62(4):693-697.
46. Bixler EO, Vgontzas AN, Lin H-M, et al. Sleep disordered breathing in children in a general population sample: prevalence and risk factors. *Sleep*. 2009;32(6):731-736.
47. Spilsbury JC, Storfer-Isser A, Rosen CL, Redline S. Remission and incidence of obstructive sleep apnea from middle childhood to late adolescence. *Sleep*. 2015;38(1):23-29.
48. Lustig RH, Post SR, Srivannaboon K, et al. Risk factors for the development of obesity in children surviving brain tumors. *J Clin Endocrinol Metabol*. 2003;88(2):611-616.
49. Mandrell BN, Wise M, Schoumacher RA, et al. Excessive daytime sleepiness and sleep-disordered breathing disturbances in survivors of childhood central nervous system tumors. *Pediatr Blood Cancer*. 2012;58(5):746-751.
50. Müller H, Bruhnken G, Emser A, et al. Longitudinal study on quality of life in 102 survivors of childhood craniopharyngioma. *Childs Nerv Syst*. 2005;21(11):975-980.
51. Eismann EA, Lush E, Sephton SE. Circadian effects in cancer-relevant psychoneuroendocrine and immune pathways. *Psychoneuroendocrinology*. 2010;35(7):963-976.
52. Owens JA. Neurocognitive and behavioral impact of sleep disordered breathing in children. *Pediatr Pulmonol*. 2009;44(5):417-422.
53. van Kooten JAMC, Maurice-Stam H, Schouten AYN, et al. High occurrence of sleep problems in survivors of a childhood brain tumor with neurocognitive complaints: the association with psychosocial and behavioral executive functioning. *Pediatr Blood Cancer*. 2019;n/a:e27947.
54. Clanton NR, Klosky JL, Li C, et al. Fatigue, vitality, sleep, and neurocognitive functioning in adult survivors of childhood cancer. *Cancer*. 2011;117(11):2559-2568.
55. Ancoli-Israel S, Liu L, Rissling M, et al. Sleep, fatigue, depression, and circadian activity rhythms in women with breast cancer before and after treatment: a 1-year longitudinal study. *Support Care Cancer*. 2014;22(9):2535-2545.
56. Chorney DB, Detweiler MF, Morris TL, Kuhn BR. The interplay of sleep disturbance, anxiety, and depression in children. *J Pediatr Psychol*. 2008;33(4):339-348.
57. Clarke G, McGlinchey EL, Hein K, et al. Cognitive-behavioral treatment of insomnia and depression in adolescents: a pilot randomized trial. *Behav Res Ther*. 2015;69:111-118.
58. van der Zweerde T, van Straten A, Effting M, Kyle SD, Lancee J. Does online insomnia treatment reduce depressive symptoms? A

randomized controlled trial in individuals with both insomnia and depressive symptoms. *Psychol Med*. 2019;49(3):501-509.

59. Fleming L, Randell K, Harvey CJ, Espie CA. Does cognitive behaviour therapy for insomnia reduce clinical levels of fatigue, anxiety and depression in cancer patients? *Psychooncology*. 2014;23(6):679-684.
60. Graef DM, Crabtree VM, Srivastava DK, et al. Sleep and mood during hospitalization for high-dose chemotherapy and hematopoietic rescue in pediatric medulloblastoma. *Psychooncology*. 2018;27(7):1847-1853.
61. van Litsenburg RR, Huisman J, Hoogerbrugge PM, Egeler RM, Kaspers GJ, Gemke RJ. Impaired sleep affects quality of life in children during maintenance treatment for acute lymphoblastic leukemia: an exploratory study. *Health Qual Life Outcomes*. 2011;9(1):25.
62. Daniel LC, Aggarwal R, Schwartz LA. Sleep in adolescents and young adults in the year after cancer treatment. *J Adolesc Young Adult Oncol*. 2017;6(4):560-567.
63. Rogers VE, Zhu S, Mandrell BN, Ancoli-Israel S, Liu L, Hinds PS. Relationship between circadian activity rhythms and fatigue in hospitalized children with CNS cancers receiving high-dose chemotherapy. *Support Care Cancer*. 2019;n/a:1-9.
64. Zmrzljak UP. Circadian rhythms and new options for novel anticancer therapies. *ChronoPhysiology and Therapy*. 2015;5:1.
65. Ballesta A, Innominato PF, Dallmann R, Rand DA, Levi FA. Systems chronotherapeutics. *Pharmacol Rev*. 2017;69(2):161-199.
66. Koren G, Ferrazzini G, Sohl H, Robieux I, Johnson D, Giesbrecht E. Chronopharmacology of methotrexate pharmacokinetics in childhood leukemia. *Chronobiol Int*. 1992;9(6):434-438.
67. Vassal G, Challine D, Koscielny S, et al. Chronopharmacology of high-dose busulfan in children. *Cancer Res*. 1993;53(7):1534-1537.
68. Daniel LC, Schwartz LA, Mindell JA, Tucker CA, Barakat LP. Initial validation of the sleep disturbances in pediatric cancer model. *J Pediatr Psychol*. 2016;41(6):588-599.
69. Zhou ES, Vrooman LM, Manley PE, Crabtree VM, Recklitis CJ. Adapted delivery of cognitive-behavioral treatment for iInsomnia in adolescent and young adult cancer survivors: a pilot study. *Behav Sleep Med*. 2016;15(4):288-301.
70. Diorio C, Schechter T, Lee M, et al. A pilot study to evaluate the feasibility of individualized yoga for inpatient children receiving intensive chemotherapy. *BMC Complement Altern Med*. 2015;15(1):2.
71. Jacobs S, Mowbray C, Cates LM, et al. Pilot study of massage to improve sleep and fatigue in hospitalized adolescents with cancer. *Pediatr Blood Cancer*. 2016;63(5):880-886.
72. Genc RE, Conk Z. Impact of effective nursing interventions to the fatigue syndrome in children who receive chemotherapy. *Cancer Nurs*. 2008;31(4):312-317.
73. Mandrell BN, Pritchard M, Browne E, Clifton S, Crabtree VM. *A pilot study to examine sleep in pediatric brain tumor patients hospitalized for high dose chemotherapy*. Baltimore, MD: Associated Professional Sleep Socities; 2013.
74. Vance Y, Eiser C. Caring for a child with cancer—a systematic review. *Pediatr Blood Cancer*. 2004;42(3):249-253.
75. McCarthy MC, Bastiani J, Williams LK. Are parenting behaviors associated with child sleep problems during treatment for acute lymphoblastic leukemia? *Cancer Med*. 2016;5(7):1473-1480.
76. Innominato PF, Lim AS, Palesh O, et al. The effect of melatonin on sleep and quality of life in patients with advanced breast cancer. *Support Care Cancer*. 2016;24(3):1097-1105.
77. Madsen MT, Hansen MV, Andersen LT, et al. Effect of melatonin on sleep in the perioperative period after breast cancer surgery: a randomized, double-blind, placebo-controlled trial. *J Clin Sleep Med*. 2016;12(02):225-233.
78. Sateia MJ, Buysse DJ, Krystal AD, Neubauer DN, Heald JL. Clinical practice guideline for the pharmacologic treatment of chronic insomnia in adults: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med*. 2017;13(02):307-349.
79. Crabtree VM. Feasibility and acceptability of light therapy to increase energy in adolescents and young adults newly diagnosed with solid tumors. Paper presented at Society of Pediatric Psychology Annual Conference; April 5, 2019; New Orleans, LA 2019.
80. Warris LT, Den Heuvel-Eibrink V, Marry M, et al. Hydrocortisone as an intervention for dexamethasone-induced adverse effects in pediatric patients with acute lymphoblastic leukemia: results of a double-blind, randomized controlled trial. *J Clin Oncol*. 2016;34(19):2287-2293.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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