Title: Sleep in Hematopoietic Stem Cell Transplant Patients

Short Title Sleep in HSCT

eIRB Number IRB 18-015878

Protocol Date: 1/29/2019

Amendment 1 Date: 4/2/19

Amendment 2 Date: 5/21/19

Amendment 3 Date: 9/2/19

Amendment 4 Date: 1/10/2020

Amendment 5 Date: 5/28/2020

Amendment 10 Date: 7/29/2020

Amendment 14 Date 3/12/2021

Amendment 15 Date: 8/2/21

Amendment 16 Date 3/14/22

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ABBREVIATIONS AND DEFINITIONS OF TERMS

HSCT	Hematopoietic stem cell transplant
HRQL	Health-related quality of life
AE	Adverse event
EHR	Electronic Health Record
MRN	Medical Record Number

ABSTRACT

Context: Patients undergoing treatment for cancer face disease, treatment, and environmental obstacles to sufficient, sound sleep[1]. Hospitalizations can further worsen sleep quality and quantity due to overnight vitals checks, medication administration, blood draws, and environmental noise and light[2]. For patients undergoing hematopoietic stem cell transplant (HSCT), the risk for poor sleep is especially high due to protracted hospitalization, frequent vitals checks resulting in multiple night awakenings[3], and high symptom burden peaking approximately 10 days post-transplant[4].

Objectives:

Primary: Test the acceptability and feasibility of protecting one 6-hour window for nighttime sleep (intervention) relative to regular vitals checks (observation only periods) during HSCT recovery.

Secondary: Assess the effect of one 6-hour window for nighttime sleep on subject sleep and engagement in supportive care on the HSCT unit.

Study Design:

Aggregated N=1 randomized controlled design. All participants will undergo a 5 day observation and then be randomized to receive the 5 day intervention (extended vitals checks) during either nights of days +5-+9 or days +10-+14.

Setting/Participants:

Inpatients on the HSCT Unit at CHOP

Study Interventions and Measures:

Intervention—increasing time between vitals checks from every 4 hours to one 6-hour period at night.

Subjects will wear an actigraph for the duration of the study, complete a daily sleep diary, and complete self- and parent-proxy psychosocial measures (symptom burden, health related quality of life, sleep) and acceptability. Medical record review will also be conducted to assess vitals check frequency.

TABLE 1: SCHEDULE OF STUDY PROCEDURES

Visit	Purpose	Main Procedures	Duration
Visit 1 Pre-transplant	Baseline measures	Complete Informed consent Complete CEFIS Complete self-report measures Give actigraph	35 minutes
Visit 2, Transplant Day 0	Start actigraph	Review actigraphy procedures	5 minutes
Visit 3, Transplant Day +5	Randomization	Randomize to intervention start Complete self-report measures	20 minutes
Visit 4, Transplant Day +10	Psychosocial measures	Complete self-report measures	15 minutes
Visit 5, Transplant Day +15	End of Study	Return actigraph, Complete self-report measures including acceptability measure	20 minutes

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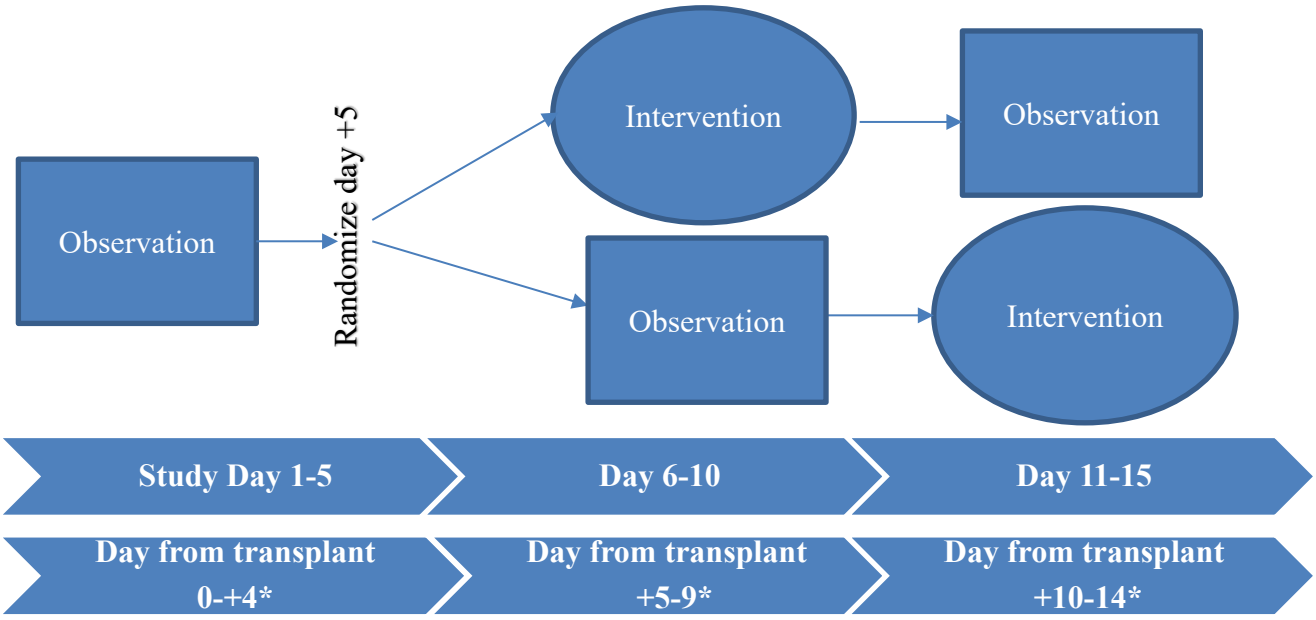
FIGURE 1: STUDY DIAGRAM



*Each study period will include nights and symptom burden and sleep will be collected the day following the end of the study period. For example, sleep from night +4 and symptom burden for the day 0-+4 period will be collected on day +5.

1 BACKGROUND INFORMATION AND RATIONALE

1.1 Introduction

Patients undergoing treatment for cancer face disease, treatment, and environmental obstacles to sufficient, sound sleep[1]. Hospitalizations can further worsen sleep quality and quantity due to overnight vitals checks, medication administration, blood draws, and environmental noise and light[2]. For patients undergoing HSCT, the risk of poor sleep is especially high due to protracted hospitalization, frequent vitals checks resulting in multiple night awakenings[3], and high symptom burden peaking approximately 10 days post-transplant[4]. Sleep quality and quantity is associated with immune functioning[5], wound healing[6], and resistance to infection[7], all critical to physical recovery from cancer and cancer treatments. Poor sleep may also have a psychosocial impact by limiting engagement in supportive care (PT/OT/School/Creative Arts Therapy/Psychology) due to compensatory daytime sleep and fatigue[8]. Together the physical impact of poor sleep and limited engagement in supportive care may hinder HSCT recovery. Frequent vitals checks are one potential intervention target when seeking to improve sleep. Vitals checks every 4 hours are necessary during conditioning and immediately post-transplant, but for many patients extending the time between vitals checks is possible. Through an aggregated N=1 randomized controlled design (each patient will serve as their own control, with the timing of the 5-day intervention period determined by randomization), the current study will test acceptability, feasibility, and impact on sleep and supportive care engagement of protecting one 6-hour window for nighttime sleep (intervention) relative to regular vitals checks (observation) during HSCT recovery.

1.2 Name and Description of Investigational Product or Intervention

The intervention tested is protecting one 6-hour window for nighttime sleep (intervention) relative to regular vitals checks (observation) during HSCT recovery.

1.3 Relevant Literature and Data

Sleep disturbances are common in pediatric oncology. Sleep disturbances frequently occur across the continuum of cancer treatment into survivorship[9]. Sleep is an understudied area of health-related quality of life[10] (HRQL) that can significantly impact cognitive functioning[11], behavior[12], mood[13], academic progress[13], and parental and family functioning[14]. Sleep quality and quantity is also associated with immune functioning[5], wound healing[6], and resistance to infection[7], all critical to physical recovery from cancer and cancer treatments. Thus, sleep is a logical and important target of assessment and intervention to improve HRQL and health outcomes for individuals—especially children receiving treatment for cancer.

Sleep is central to the experience of cancer-related symptoms. Disrupted sleep can exacerbate the physiological processes of pain[15] and fatigue[16]. Psychologically, poor sleep impacts cognitive appraisals of symptoms and symptom-related coping efforts the following day, which may amplify the patient's experience of symptoms[17]. Symptoms may then interfere with sleep the following night resulting in a vicious cycle between sleep and symptoms that can be difficult to stop. In pediatric cancer, sleep disturbances are closely related to general symptom burden. Pediatric cancer patients report between 6 (outpatient) and 12 (inpatient) symptoms that co-occur during cancer treatment, with prevalence rates of fatigue, insomnia, pain, and psychological symptoms ranging from 30-50%[18]. Studies describing the symptom

cluster of sleep disturbances, fatigue, and pain indicate that fatigue and sleep predict depression and behavior changes in adolescents but not younger patients[19], suggesting a developmental component unique to older pediatric patients in the response to cancer and its treatment. Disturbed sleep may precipitate symptoms or be the result of higher symptom burden, potentially exacerbating symptoms over time.

The hospital environment is extremely disruptive to sleep. Patients undergoing treatment for cancer face disease, treatment, and hospital environmental obstacles to sufficient, sound nighttime sleep[1]. Hospitalizations can further worsen sleep quality and quantity due to overnight vitals checks, medication administration, blood draws, and environmental noise and light[2]. For patients undergoing hematopoietic stem cell transplant (HSCT), the risk for poor sleep is especially high due to the protracted hospitalization, frequent vitals checks resulting in multiple night awakenings[3], and high symptom burden peaking approximately 10 days post-transplant[4].

Limited research has examined sleep in pediatric HSCT patients. Sleep, as measured by one global question about sleep quality, worsens from 1-week pre-transplant through 3-weeks post-transplant before improving[20]. To our knowledge only one study has focused on sleep in pediatric HSCT patients using objective measurement (actigraphy) in 8 children; results indicated patients awaken 12 times per night on average and hospital rooms were entered approximately the same number of times[3], suggesting that hospital staff play a role in sleep disruption. In adults, 77% of patients undergoing HSCT report clinically significant poor sleep, and that poor sleep is related to increased fatigue and decreased physical functioning during the hospitalization[21] while good sleep quality is related to better pre/post HSCT monocytic chemokines, biomarkers indicating immune recovery[22]. Sleep improves post-transplant; however, at day 100+ 28% of adult patients still report clinically significant sleep disturbances[21].

Interventions to promote sleep and physical activity have been piloted in pediatric oncology, but they are often not sustainable outside of research. Hospital-based interventions that seek to provide education about sleep and fatigue management[23], encourage physical activity[24], and protect 90-minute windows for sleep[25] have been tested in small pilot studies in oncology. Generally, families report interventions to be acceptable, but many interventions are not clinically feasible, requiring substantial support to continue outside of the context of research. Scalable interventions that can be integrated into clinical practice are needed to improve the psychosocial health of patients during hospitalizations.

The contribution of staff room entries to poor sleep[3] is a logical intervention target. Frequent vitals checks are necessary early in the transplant process but become less necessary post-transplant, thus extending time between vitals checks is likely feasible and has the potential to increase total sleep time. By altering hospital procedures to maximize sleep, we have the opportunity to address hospital-related sleep disruptions and improve outcomes in patients in need of sufficient sleep—patients recovering from HSCT. It is hypothesized that patients who obtain uninterupted sleep would perhaps participate more in therapies (PT/OT) to regain physical stamina, school activities, creative art therapy, and psychological services to continue cognitive recovery and bolster HRQL. Taken in sum, it is hypothesized that more sleep and increased participation in these activities would ultimately accelerate their recovery and physical functioning.

1.4 Compliance Statement

This study will be conducted in full accordance all applicable Children's Hospital of Philadelphia Research Policies and Procedures and all applicable Federal and state laws and regulations including 45 CFR 46. All episodes of noncompliance will be documented.

The investigators will perform the study in accordance with this protocol, will obtain consent and assent, and will report unanticipated problems involving risks to subjects or others in accordance with The Children's Hospital of Philadelphia IRB Policies and Procedures and all federal requirements. Collection, recording, and reporting of data will be accurate and will ensure the privacy, health, and welfare of research subjects during and after the study.

2 STUDY OBJECTIVES

The purpose of the study is to assess the acceptability and feasibility of a novel intervention to improve sleep in the hospital setting, which will provide evidence for a clinical intervention that can improve patient functioning during hospitalizations.

2.1 Primary Objective (or Aim)

The primary aim of the study is to assess the feasibility and acceptability of increasing time between vitals checks in HSCT.

2.2 Secondary Objectives (or Aim)

The secondary objectives are to:

Test the relationship between increasing time between vital checks and sleep.

Compare engagement in supportive care interventions (PT/OT/School/Creative Arts Therapy/Psychology), HRQL, and symptom burden between observation and intervention periods.

3 INVESTIGATIONAL PLAN

3.1 General Schema of Study Design

Patients undergoing HSCT face many challenges to restful sleep during the hospitalization for transplant. Frequent vitals checks, necessary during conditioning and immediately post-transplant, may be less necessary as time from transplant increases. Utilizing an aggregated N=1 randomized trial design (Figure 1. Study Flow), the current study will test protecting one 6-hour window for sleep within patients recovering from HSCT. This study will assess the acceptability and feasibility of this intervention, evaluate the impact on patient sleep, and test how sleep is related to symptom burden, engagement in supportive services, and HRQL during HSCT recovery. Participants will wear an actigraph for the duration of the study (day of the transplant [day 0] through the night of Day +14post-transplant, removing the actigraph upon awakening on Day +15) to measure sleep accompanied by a brief sleep diary sent daily by text messages delivered via REDCap and its integration with Twilio. Participants will complete self-report measures of sleep, symptom burden, and HSCT related

HRQL at baseline and at the end of each study period (Day +5, +10, +15; Table 1 Study Procedures).

3.1.1 Screening Phase

Potential subjects will be identified through the Stem Cell Transplant List using inclusion criteria for enrollment: ages 8-21, receiving HSCT at CHOP, English speaking, with no history of developmental delays. Subjects will be recruited into two strata, children ages 8-12 years and adolescents and young adults ages 13-21 years.

Parental/guardian permission (informed consent) and, if applicable, child assent, will be obtained prior to any study-related procedures being performed. Eligibility criteria will be confirmed by the subject's oncologist. Participants will be approached about study participation on transplant education day or during the conditioning admission, if interested the study team will follow up with the family 1-2 days before the transplant to complete the informed consent process and the baseline measures.

3.1.2 Study Treatment Phase (start of the study intervention)

One-two days before the transplant, a study team member will meet with the family to complete the informed consent, baseline measures, and give actigraphy instructions. All patients will wear an actigraph from the day of the transplant until day +5 from the transplant to serve as the "observation baseline" for each patient.

3.1.3 Phase 2

On Day +5, to reduce the impact of expectancies during the first observation period, patients will be randomized to ABA (observation/intervention/observation) or AAB (observation/observation/intervention), with each period lasting 5 days (Fig. 1). Block randomization stratified by age will be used to ensure similar age distribution between groups. The two group design will allow for the comparison of altering vitals checks before/after engraftment and peak symptom burden (typically on day $+10^4$). On each intervention night, the research team will verify with the child's provider that it is acceptable for the patient to have a 6-hour window between vitals checks. This confirmation will be communicated to the child's nighttime nurse. For the 5 days of the child's intervention period, the nurse will be instructed to conduct the last vitals check between 9pm-1am. After the last vitals check, the patient will be given 6 hours until the next vitals check, unless the caregiver/patient request nursing. Patients will continue to wear the actigraph until the end of the study. The patient can remove the actigraph upon awakening on Day +15.

Eligibility for extended vitals check, assessed daily: 1) No fever in the last 24 hours; 2) No concurrent chemotherapy administration; 3) No ongoing or active infection; and 4) No organ toxicity requiring labs more than every 6 hours. Even if a patient is ineligible for extended vitals checks they are asked to continue to wear the actigraph.

After each patient has completed both the intervention and a second observation (either BA or AB), they will be asked to complete final study measures and measures of acceptability of the intervention.

3.2 Allocation to Treatment Groups and Blinding

Participants will be randomized to either Observation/Intervention or Intervention/Observation on day +5 post-transplant. The research coordinator will generate a randomization sequence using a random number generator, with block randomization occurring based on participant age (8-12 or 13-21). Blinding will not be possible, but randomization will occur on day +5 to minimize the impact of the intervention on the initial observation period.

3.3 Study Duration, Enrollment and Number of Sites

3.3.1 Duration of Study Participation

The study duration per subject will be up to approximately 17 days, from the beginning of data collection (the day before the transplant), up to 5 days Phase 1 and up to 10 days Phase 2.

3.3.2 Total Number of Study Sites/Total Number of Subjects Projected

The study will only be conducted at The Children's Hospital of Philadelphia.

Recruitment will stop when approximately 55 subjects and their parent caregivers are enrolled. It is expected that approximately 55 subjects will be enrolled to produce 50 evaluable subjects. Subject nurses will also be enrolled, it is expected that each subject may have between 1 and 5 nurses involved in care during the extended vitals check period, Because some nurses will likely provide care to multiple patients, we expect to enroll 75 nurses.

3.4 Study Population

3.4.1 Inclusion Criteria

(Patient Subjects)

1) Males or females age 8 to 21 years.

2) Undergoing HSCT at The Children's Hospital of Philadelphia

3) Parent/guardian permission (informed consent) and if appropriate, child assent.

(Nurse Subjects)

4) HSCT Nurse working night shift during subject's extended vitals check.

3.4.2 Exclusion Criteria

1) History of developmental delays given the relationship to sleep/wake patterns

2) Sleep disorder diagnosis as documented in the medical record

3) Cognitive delays that impact the ability to complete study measures

4) Not proficient in English

Subjects that do not meet all of the enrollment criteria may not be enrolled. Any violations of these criteria must be reported in accordance with IRB Policies and Procedures.

4 STUDY PROCEDURES

4.1 Screening Visit

- Patients and families will be presented the study on Family Edcation Day prior to admission for HSCT

4.2 Study Treatment Phase

General overview of this phase.

4.2.1 Visit 1 Day -2 to Day -1 before transplant

- Informed Consent
- Medical Record Review
- Demographic, COVID-19 Impact measure, and Psychosocial Measures (Symptom Burden, HRQL, and Sleep)
- Introduce actigraph and electronic sleep diary.

4.2.2 Visit 2 Day 0

- Place actigraph on patient's non-dominant wrist. Patient is asked to wear the actigraph for the duration of the study (morning of Day 0- the night of Day +14). The patient can remove the actigraph upon awakening on Day +15.
- Review actigraph and electronic sleep diary procedures.

4.2.3 Visit 3 Day +5

- Randomization
- Psychosocial Measures (Symptom Burden, HRQL, and Sleep)

4.2.4 Visit 4 Day +10

- Psychosocial Measures

4.2.5 Visit 5 Day +15

- Psychosocial Measures
- Return Actigraph
- Acceptability survey
- Subject payment

4.2.6 Nurse Study Proecdure

Visit 1 Morning after patient completes extended vitals check night
Informed Consent, will take place either by phone or on the HSCT Unit with study staff
Acceptability Survey

4.3 Unscheduled Visits

Subjects will be hospitalized for the duration of the study. Should the family or the treatment team have concerns about the subject's participation or study procedures, the study team will meet with the patient to discuss whether the family would like to remain in the study.

4.4 Subject Completion/Withdrawal

Subjects may withdraw from the study at any time without prejudice to their care. They may also be discontinued from the study at the discretion of the Investigator for lack of adherence to study treatment or visit schedules, AEs, or due to a change in medical status. The Investigators may also withdraw subjects who violate the study plan, or to protect the subject for reasons of safety or for administrative reasons. It will be documented whether or not each subject completes the clinical study. If the Investigators become aware of any serious, related adverse events after the subject completes or withdraws from the study, they will be recorded in the source documents and on the CRF.

4.4.1 Early Termination Study Visit

Subjects who withdraw from the study will be asked to return the actigraph and complete the acceptability measure.

5 STUDY EVALUATIONS AND MEASUREMENTS

5.1 Screening and Monitoring Evaluations and Measurements

5.1.1 Medical Record Review

Include a listing of the variables that will be abstracted from the medical chart (paper or electronic).

- Date of birth
- Date of diagnosis and treatment history
- Medications
- Length of hospitalization prior to starting the study
- Number of visits completed or declined with supportive services (physical therapy, occupational therapy, school, creative arts therapies, and/or psychology) for each study period (Days 0-+4 including nights, Days +5-+9 including nights, Days +10-+14 including nights).
- Frequency and timing of vitals checks for each day in the study.
- Medications used for supportive care for each study period (Days 0-+4 including nights, Days +5-+9 including nights, Days +10-+14).
- Transplant parameters including: type of transplant, disease status, cell processing, GVHD prophylaxis and infectionus prophylaxis.

5.1.2 Other Evaluations, Measures

Subjects and caregivers will complete the following measures:

Table 1. Study Measures.		**Baseline**	**Day +5**	**Day +10**	**Day +15**
Construct	**Measure**				
Acceptability	Patient, caregiver, and nurse will respond to a brief questionnaire of acceptability of adjusting vitals checks.				x
Demographics	Report of sex, race/ethnicity, age of child and caregiver	x			
COVID-19 Impact	COVID-19 Exposure and Family Impact Survey (CEFIS) to assess family exposure to and experience with COVID-19 through Yes/No responses (25 items); 12 items assessing the impact of the pandemic on	x			

	self/family with 1-4 intensity scale and 1 open-ended item				
HRQL and related symptoms	Pediatric Quality of Life Inventory—Stem Cell Transplant Module. This measure assesses HRQL and syptoms relevant to patients undergoing HSCT. The measure includes questions about pain, fatigue/sleep, nausea, communication, worry, nutrition, thinking and other symptoms answered on parallel child and adolescent with parent proxy forms (41 items).[26]	x	x	x	x
Sleep	PROMIS Sleep Measures—Sleep disturbance, sleep-related impairment, and sleep hygiene over the past week-parallel parent/child forms (24 items)[27].	x	x	x	x
Supportive Care Use	EHR review to document engagement or refusal of PT/OT/School/Creative Art Therapy/ Psychology for each 5 day period.		x	x	x
Actigraphy	Worn by participant day 0-night of Day +14, removing on awakening on Day+15. To validate actigraphy: bedtime, waketime, night awakenings, naps, time actigraph was off reported daily through text messages delivered via REDCap and its integration with Twilio.				

5.2 Efficacy Evaluations

5.2.1 Diagnostic Tests, Scales, Measures, etc.

Actigraphy will be used to track the impact of extending vitals check on sleep.

5.3 Safety Evaluation

Subject safety will be monitored by adverse events, study visits, and daily checks with the subject's treatment team during the intervention (i.e., extended vitals checks) period.

6 STATISTICAL CONSIDERATIONS

6.1 Primary Endpoint

The primary endpoint is the acceptability and feasibility of the intervention. Acceptability will be measured by subjects, caregivers, and nursing ratings of the intervention. Feasibility will be measured through study staff documented medical eligibility to participate in the intervention each eligible day and by tracking compliance with extended vitals checks, through electronic health record (EHR) review.

6.2 Secondary Endpoints

Secondary endpoints will include the following:

- The change in sleep between observation and intervention period as measured by actigraphy sleep efficiency, total sleep time, and number of awakenings.
- The change in engagement in supportive services between observation and intervention period (physical therapy, occupational therapy, school and/or psychology) as measured through EHR review.

6.3 Statistical Methods

6.3.1 Baseline Data

Baseline and demographic characteristics will be summarized by standard descriptive summaries (e.g. means and standard deviations for continuous variables such as age and percentages for categorical variables such as gender).

6.3.2 Efficacy Analysis

Using descriptive statistics, feasibility will be determined by assessing medical eligibility for the intervention and the delivery of the intervention. Descriptive statistics will be used to characterize acceptability measure responses

Secondary endpoints will include the change in sleep parameters and engagement in supportive care services. We will utilize hierarchical multilevel mixed-effects models for daily diary data, which uses all available data, allows for multilevel nesting (e.g., daily data nested within participants, nested within condition), and are fairly robust to missing data (models are valid under Missing At Random assumption)[28]. Fixed and random effects models will be fit to the data[29] to estimate the impact of the intervention on nocturnal sleep (sleep efficiency, total sleep time, night awakenings); Aim 2) and engagement in supportive care, HRQL, and symptom burden (Aim 3). We will test for carryover effects of the intervention and adjust analyses as needed[29].

6.3.3 Safety Analysis

AE incidence will be summarized along with the corresponding exact binomial 95% two-sided confidence intervals.

6.4 Sample Size and Power

The current study is a pilot that is seeking to test the acceptability and feasibility of an intervention to increase sleep during HSCT. 16 subjects will yield an adequate sample size for a pilot study[30] to estimate effect sizes for a future trial.

7 STUDY INTERVENTION

7.1 Description

For the 5 day-intervention period, the study staff will work with the subject's nurse to plan on 6-hour extended period between vitals checks, occurring overnight. On each intervention night, the research team will verify with the child's oncology provider that it is acceptable for the patient to have a 6-hour window between vitals checks. This confirmation will be communicated to the child's nighttime nurse. For the 5 days of the child's intervention period, the nurse will be instructed to conduct the last vitals check between 9pm-1am. After the last vitals check, the patient will be given 6 hours until the next vitals check, unless the caregiver/patient request nursing.

8 SAFETY MANAGEMENT

8.1 Clinical Adverse Events

Clinical adverse events (AEs) will be monitored throughout the study.

8.2 Adverse Event Reporting

Since the study procedures are not greater than minimal risk, SAEs are not expected. If any unanticipated problems related to the research involving risks to subjects or others happen during the course of this study (including SAEs) they will be reported to the IRB in accordance with CHOP IRB SOP 408: Unanticipated Problems Involving Risks to Subjects. AEs that are not serious but that are notable and could involve risks to subjects will be summarized in narrative or other format and submitted to the IRB at the time of continuing review.

9 STUDY ADMINISTRATION

9.1 Treatment Assignment Methods

9.1.1 Randomization

Participants will be randomized to either Observation/Intervention or Intervention/Observation on day +5 post-transplant. The research coordinator will generate a randomization sequence using a random number generator, with block randomization occurring based on participant age (8-12 or 13-21). Blinding will not be possible, but randomization will occur on day +5 to minimize the impact of the intervention on the initial observation period.

9.2 Data Collection and Management

Electronic health record data.
Investigators will generate a list of MRNs for participants with positive parental consent who have completed the survey. A trained research assistant with limited EHR access will extract treatment related data from the EHR. To obtain a password for the EHRs, all staff must complete training on the importance of patient privacy. Training on the Health Insurance Portability and Accountability Act (HIPAA) is required for all employees. With the EHRs, patient privacy is protected by multi-step, system wide processes. Anyone

wishing to view the charts of patients for whom they do not provide care must "break the glass." This system requires a declaration of why the chart is being viewed and sends a message to both an employee's supervisor and the hospital's privacy officer. In summary, the inappropriate access to electronic health information is carefully monitored and strictly prohibited. All study files retained on CHOP's secure network or within secure REDCap database will be accessed only by study staff using a CHOP issued, password-protected computer.

Child- and parent-report data:
Participants will complete daily sleep diary questions using REDCap and the integration with Twilio (a text messaging platform that integrates with REDCap). No PHI will be transmitted over text message. Electronic demographic, psychosocial, and acceptability surveys will also be obtained using REDCap. The CHOP Research Institute Center for Biomedical Informatics (CBMi) will be used as a central location for data processing and management. These data will be stored within REDCap by participant study ID.

Nurse acceptability data:
Nurses will complete acceptability questionnaires for each night they care for the child during the extended vitals check portion of the study using REDCap and the integration with Twilio (a text messaging platform that integrates with REDCap). No PHI will be transmitted over text message. The CHOP Research Institute Center for Biomedical Informatics (CBMi) will be used as a central location for data processing and management. These data will be stored within REDCap by participant study ID.

Confidentiality of On-Line Assessment.
Participants will complete self-report questionnaires through internet access to REDCap. Daily text messages will be completed and stored within REDcap via the integration with the text messaging platform Twilio. No PHI will be transmitted over text message. Participants will complete questionnaires that are only identified with a unique Study ID, which will be assigned during recruitment. The CHOP Research Institute Center for Biomedical Informatics (CBMi) will be used as a central location for data processing and management. CBMi represents CHOP in a consortium of over three hundred academic research institutions led by Vanderbilt University. Vanderbilt, with assistance from the consortium, has developed a software toolset and workflow methodology for electronic collection and management of research and clinical trial data. REDCap (Research Electronic Data Capture) data collection projects rely on a thorough study-specific data dictionary defined in an iterative self-documenting process by all members of the research team with planning assistance from CBMi. The iterative development and testing process results in a well-planned data collection strategy for individual studies. REDCap is also a powerful tool for building and managing online surveys. The research team can create and design surveys in a web browser and engage potential respondents using a variety of notification methods. REDCap provides secure, web-based applications that are flexible enough to be used for a variety of types of research, provide an intuitive interface for users to enter data and have real time validation rules (with automated data type and range checks) at the time of entry. These systems offer easy data manipulation with audit trails for reporting, monitoring, and querying patient records, and an automated

export mechanism to common statistical packages (SPSS, SAS, Stata, R/S-Plus). Within REDCap, all data are stored by study ID number only.

9.3 Confidentiality

No identifiable data will be used for future study without first obtaining IRB approval. The investigator will obtain a data use agreement between the provider (the PI) of the data and any recipient researchers (including others at CHOP and Rutgers University) before sharing a de-identified data set (all dates and zipcodes will be removed).

9.4 Regulatory and Ethical Considerations

9.4.1 Data and Safety Monitoring Plan

An independent Data Safety and Monitoring Board will not be instituted due to the low degree of risk with this study. The PI will oversee all data collection through the implementation of standardized data collection procedures. Safety monitoring will include careful assessment and appropriate reporting of AEs as indicated below, and will also include a regular assessment of the number and type of serious AEs. Any serious AEs that might reasonably be due to the study will be reported to the CHOP IRB within 24 hours of its occurrence. Events that are not related to the study but classified as imminent risk to the subjects will be reported to the investigators and appropriate clinical referrals will be made.

9.4.2 Risk Assessment

The risks associated with this study are minimal and generally not in excess of those encountered in the hospital stay. Specifically, risks include: 1) breach of confidentiality; 2) discomfort from questions regarding cancer history and current symptoms; 3) inconvenience of study procedures. Because participants are assessed on a daily basis for whether they are medically able to participate in extended vitals checks, the medical risk for extending time between vitals checks by 2 hours is assumed minimal. If a participant develops a fever during the extended vitals checks portion of the study, there is a risk that it will not be detected for an additional 2 hours. All participants can contact their nurse at any time between vitals checks for usual care or concerns such as fever. All participants will be informed of these risks prior to participation and will be informed of the right to discontinue participation if they are uncomfortable with the study. If participants become upset, Dr. Barakat (licensed clinical psychologist, Director of Psychosocial Services in Oncology at CHOP) will assess the level of distress of the patient and determine the need for additional psychosocial support.

9.4.3 Potential Benefits of Trial Participation

The current research study seeks to improve sleep during the hospital stay for HSCT, although the short intervention period my not provide any direct benefit to the participants. The research proposed has the potential to improve clinical care of patients undergoing HSCT by reducing some overnight sleep disruptions, which may improve the patient's functioning the following day.

9.4.4 Risk-Benefit Assessment

Patients undergoing HSCT are a vulnerable and understudied group who exhibit many symptom management needs, including long-term sleep disruptions. Because poor sleep is implicated in psychosocial functioning and physical health, the results of the current study have the potential to identify a clinically relevant intervention that can improve sleep during hospital stays. Findings will inform HSCT patient care and future research on sleep in pediatric oncology. The potential benefits from the knowledge gained through this study, which has the potential to improve patient care and psychosocial outcomes, outweigh the minimal risks associated with participation.

9.5 Recruitment Strategy

After IRB approval, potential patient participants will be identified through the CHOP Stem Cell Transplant list and cleared by the patient's primary oncologist. Potential participants will be invited to participate in the study during family education day prior to the stem cell transplant admission. Families will be given the "Fast Facts" flyer about the study.

To enable the study coordinator scheduling and to allow for the extraction of EHR data, it will be necessary to maintain a "tracking" database that contains information about potentially eligible participants (e.g., parent name, child name, appointment time and location, date of birth, and MRN). Potential participant information will be added to the database from the Stem Cell Transplant List and will be updated through weekly chart review. This database will be maintained on a CHOP password-protected computer. All potential participants will be randomly assigned a participant ID number when their information is entered into the tracking database.

9.6 Informed Consent/Assent and HIPAA Authorization

Consent/assent for all participants will take place in person on the Stem Cell Transplant Unit at CHOP. Patients who are interested in participating will provide written consent (parents/legal guardians of children < 18 years old and AYA ≥ 18 years) and assent (children < 18 years of age). A study team member will review the informed consent document with prospective participants and caregivers and answer any questions about study procedures. Separate consent forms will be reviewed and signed by patients and their caregivers, as needed. HIPAA Authorization will be obtained through a combined consent-authorization document.

Nurse Consent Plan: After subjects have completed study participation, all nurses who were involved in the subject's care during the extended vitals check period (either nights of days 5-9 or 10-14) will be contacted to invite study participation. Consent will take place on the Stem Cell Transplant Unit at CHOP or by phone prior to asking the nurse to complete the study acceptability measure. Written consent will be obtained from nurse subjects enrolled in person on the Stem Cell Transplant Unit at CHOP, while verbal consent will be obtained from nurse subjects enrolled via phone.

9.7 Payment to Subjects/Families

9.7.1 Payments to subject for time, effort and inconvenience (i.e. compensation)

Subjects will receive payments in the form of giftcards for taking part in this study. Subjects will receive $1 per day for wearing the actigraph, $1 for completing the daily sleep diary text messages, and $5 for completing each of the 4 self-report measure packets. Subjects will receive a $25 bonus for completing the study. Subjects can earn up to $75 for time and effort. Caregivers will receive $5 for completing each of the 4 caregiver report measure packets for a total of $20. If subjects withdraw, they will be paid on a pro rata basis for participation until study withdrawal.

10 PUBLICATION

The data on feasibility and acceptability of this pilot study will be submitted for publication by CHOP and Rutgers Univesrity investigators to a pediatric oncology journal at the culmination of the study.

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APPENDIX

A Consent with assent

B Survey Items (Demographic form, psychosocial measures, Acceptability measure)