

ROSTERS

Randomized Order Safety Trial Evaluating Resident Schedules

*A Multi-Center Trial of Limiting PGY 2&3 Resident Work
Hours on ICU Patient Safety*

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PROTOCOL SUMMARY**Objective:**

To conduct a multi-center randomized crossover trial in six pediatric ICUs staffed by PGY2 and PGY3 residents to compare the effectiveness and safety of a sleep and circadian science-based (SCS) intervention schedule [also known as a rapidly cycling work roster (RCWR)] with a traditional schedule [also known as an extended duration work roster (EDWR)] that includes frequent shifts of 24 hours or longer.

Study Population:

Second and third year (PGY2 and PGY3) residents

Study Design:

Multi-center randomized crossover trial

Interventions:

Sleep and circadian science-based intervention schedule versus a traditional schedule

Primary outcomes:

Resident-related preventable adverse events and near misses

Secondary Outcomes:

ICU-wide preventable adverse events and near misses

Resident neurobehavioral performance and predicted driving safety

Study Duration:

12 months (4 month wash-in period followed by 8 months of data collection)

1.1 STUDY AIMS

1.1.1 Aim 1:

To test the hypothesis that PGY2&3 residents working on an *SCS intervention schedule* will make significantly fewer harmful medical errors (preventable adverse events) and other serious medical errors (near misses) while caring for ICU patients than residents working on a *traditional schedule*; (*primary endpoints: resident-related preventable adverse events and near misses*)

1.1.2 Aim 2:

To test the hypothesis that rates of harmful medical errors (preventable adverse events) and other serious medical errors (near misses) *throughout the ICU* (i.e., those involving and those not involving residents) will be lower in ICUs when PGY2&3 residents work on an *SCS intervention schedule* than when residents work on a *traditional schedule*; (*major secondary endpoints: ICU-wide preventable adverse events and near misses*)

1.1.3 Aim 3:

To test the hypothesis that resident physicians' risk of neurobehavioral performance failures and motor vehicle crashes – as assessed through drive diaries, End of Rotation Survey and simple visual reaction time tasks [Psychomotor Vigilance Task (PVT) lapses] – will be lower on the *SCS intervention schedule* than on the *traditional schedule*. (*major secondary endpoints: resident neurobehavioral performance and predicted driving safety*)

1.2 BACKGROUND AND RATIONALE

Sleep deficiency and circadian disruption degrade human alertness and performance both in laboratory and occupational settings. Over the past decade, a series of studies have found that first-year residents (interns; PGY1s) working recurrent extended duration shifts (≥ 24 hours) make more serious medical errors than do those working shifts of ≤ 16 consecutive hours; moreover, PGY1s working extended duration shifts suffer more injuries on the job, and have an increased risk of motor vehicle crashes (MVCs) on the drive home from work.(1-8) In 2009, after a year-long comprehensive study, the Institute of Medicine (IOM) concluded that while it remained unclear whether resident sleep deprivation led to patient harm, “the scientific evidence base establishes that human performance begins to deteriorate after 16 hours of wakefulness.”(9;10) They consequently called for the elimination of all resident physician shifts without sleep over 16 consecutive hours.

In response, beginning in July 2011, the Accreditation Council for Graduate Medical Education (ACGME) limited interns to no more than 16 consecutive hours of work; second year (PGY2) and higher residents, however, will continue to work for up to 28 consecutive hours.(11) In choosing not to more substantively limit the hours of PGY2 and higher residents – who represent approximately 80% of all physicians-in-training – the ACGME indicated that in its view, insufficient data existed to support policy change for more senior trainees.

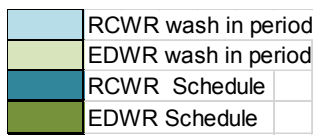
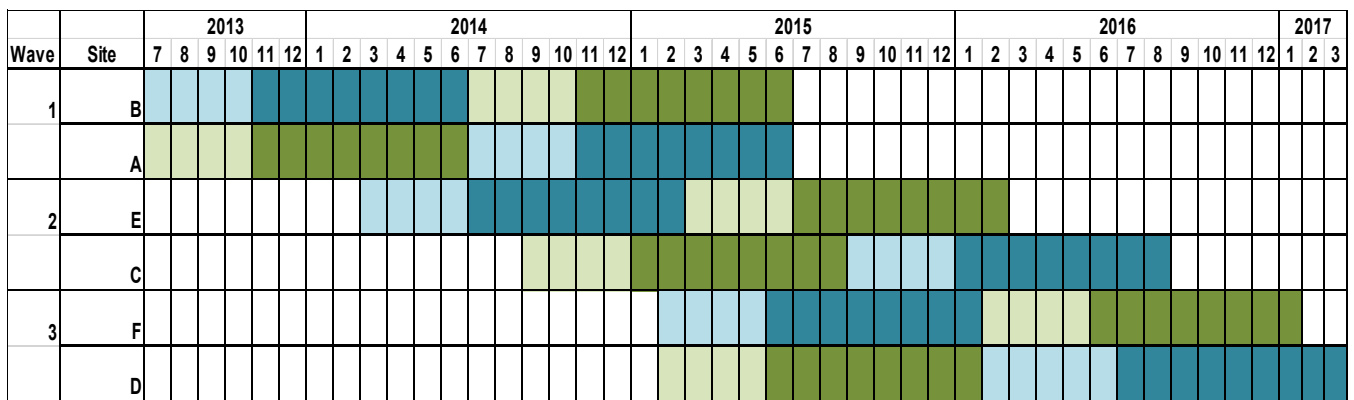
In this study, we seek to conclusively address two knowledge gaps: 1) the lack of data on the relationship between PGY2 and higher sleep deprivation and patient safety; and 2) the lack of data on the relationship between resident sleep deprivation and preventable patient injuries.

1.3 STUDY DESIGN AND INTERVENTIONS

The study is a clustered randomized controlled trial to evaluate the effectiveness of eliminating residents’ traditional 24-hour shifts in ICUs. The trial will take place in 6 academic medical centers nationwide, in three waves of two centers each.(Figure 1) One of each pair of units will initially be randomly assigned to the traditional schedule (i.e., in which overnight shifts of 24-28 hours continue to occur every 4 nights), or to the SCS intervention schedule (i.e., in which residents are limited to 16 consecutive work hours; sleep before night duty is promoted; and time off is arranged to allow recovery from sleep debt.)

Our planned timeline will be as follows: after a 2 month planning and startup period, during which staff will be recruited and hired, the intervention will be implemented in one randomly selected PICU in study wave 1; the traditional schedule will continue in the other PICU. There will be a 4-month wash-in period, after which time 8 months of data collection will take place in intervention (in black, Figure 1) and traditional (in blue) ICUs. After 8 months of data collection, the units will cross over (traditional to intervention schedule; intervention to traditional). Following another 4-month wash-in period, there will be 8 additional months of data collection. Study sites in waves two and three will follow the same pattern. Of note, each intervention period will be scheduled to occur entirely within a single academic year, and will be preceded or followed (12 months apart) by a control period that will also occur entirely within an academic year.

Figure 1. Timeline



1.4 SELECTION AND ENROLLMENT OF PARTICIPANTS

All second and third year residents at the six clinical centers will be invited to enroll in the study. The only exclusion criteria is that the resident is at least 21 years of age. Four to eight residents will be recruited per month at each clinical center for total of approximately 50 residents per site and approximately 300 subjects study-wide.

1.4.1 Recruitment

Sites will submit a waiver of informed consent for the collection of patient data, but will obtain residents' written informed consent to observe them, and collect resident-specific data. Working with program directors at each hospital, the Principal Investigators will make presentations each year to all residents to describe our study and request volunteer participants. Residents are free not to participate in the study; if they choose not to participate, they will not be followed by observers and no other data will be collected from them, but the unit schedule will proceed on the *traditional* or *SCS intervention schedule* as planned.

1.4.2 Randomization

The intervention will be implemented in one randomly assigned study site in each of the three waves and the second site will remain on the traditional schedule. After 8 months of data collection, the units will cross over (traditional to intervention schedule; intervention to traditional). The Data Coordinating Center (DCC) will be responsible for randomly assigning sites to their initial study arm.

1.4.3 Preparation of subjects

Before the start of each study, volunteers will receive a detailed explanation of the procedures involved in the study. They will also attend an educational seminar prior to the implementation of the intervention schedule designed to provide an overview of sleep and circadian science, and to convey the importance of complying with the protocol by attempting to sleep prior to night shifts. They will be asked to complete a baseline survey, which will include the Sleep Disorders and Berlin Sleep Questionnaires.

1.5 STUDY PROCEDURES

The study will take place in pediatric intensive care units (PICUs). In general, subjects will continue to carry out their normal activities and responsibilities when working either the intervention or traditional schedule. Throughout the PICU rotations, subjects will complete a daily sleep diary and wear actiwatches, described further below, to validate the results of self-reported sleep.. They will also periodically complete psychomotor vigilance tests (PVTs) to monitor their vigilance. At the completion of their rotations, all subjects will complete an End of Rotation survey. For every experimental intervention, there will be written protocols and checklists used to insure uniformity in the execution of standard procedures.

1.5.1 Detection of Errors and Adverse Events

We will use a very intensive, four-pronged data collection approach to comprehensively measure rates of all errors and adverse events.

1.5.1.1 Continuous Observation

A team of five physician research associates will conduct direct observation of resident subjects working in the units, 24 hours per day, 7 days per week. The observers will share this responsibility, working in eight-hour shifts. All suspected adverse events and errors will be documented on tablet-based data forms, and transmitted to the research nurse, who will gather follow-up data on them while conducting his or her daily chart reviews, as described below. The observer will also record and classify all medical activities in which the study subject engages, including but not limited to performance of procedures, test and medication ordering, and test interpretation. Suspected adverse events and incidents will be identified and classified. Follow-up of all suspected adverse events and errors detected by the observers will be performed by the nurse data extractors, who will collect additional information.

1.5.1.2 Voluntary and solicited reports

Forms will be made available and prominently posted in the ICUs to facilitate voluntary reporting of possible errors and events by nurses and other clinical staff. Chart reviewers will also request reports from staff of errors and adverse events 5 days per week. Any reported error or event will be pursued by the nurse data extractors, who will collect additional information.

1.5.1.3 Collection of formal incident reports

In each hospital, formal incident reports will be collected if permitted; if any institutions will not allow access to these data, we will request that duplicate study reports be filed by clinical staff on our study units when they complete formal reports. In addition, in any hospitals with computerized adverse event detection systems, the computerized AE monitors will also be interrogated for study-unit events. Nurse data extractors will collect additional information on each incident identified.

1.5.1.4 Chart surveillance

The nurse data extractors will serve as the focal point for data collection and organization, and will follow up and review all data collected by observers, reported by staff, and detected via incident reporting systems. In addition to coordinating collection from other sources, reviewers will examine all orders and charts 5 days per week; a focused version of the Institute for Healthcare Improvement (IHI) Global Trigger Tool (consisting of the intensive care module, cares module, and medication module triggers)(12) will be used to increase the sensitivity of adverse event detection. Reviews on Monday will include a review of the weekend. Data collected for each incident will include a description and classification of the event, patient information, services and personnel involved, and additional work resulting from the event. Medication incidents will further include name, dose, route and category of the drug involved.

1.5.2 Classification by severity, attribution, and preventability

Physician observers and research nurses will identify suspected errors and adverse events. Two independent physician reviewers will subsequently classify events as errors, potential adverse

events (near misses), or adverse events. All events will be rated on severity using the modified NCC-MERP scale.(12;13) Preventability will be rated using a four point Likert scale. Disagreements will be resolved by discussion. Events for which consensus cannot be reached will be re-rated by a third reviewer. Pre-discussion inter-rater reliability will be evaluated with the Kappa statistic.

1.5.3 Identification of patient risk factors

Clinical and demographic data for all patients admitted to study units will be collected by the research nurses from patient records and institutional administrative databases during lulls in unit activity. Severity of illness will be assessed using ICD-9 codes.

1.5.4 Measuring Sleep and Fatigue

In addition to data on patient safety, we will collect data on residents' sleep and work hours using the methods described below.

1.5.4.1 Sleep and work logs

A diary of sleep and wake times will be maintained by the research volunteers. A post-sleep questionnaire will be completed immediately following wake time from all sleep episodes and will provide information on subjective evaluation of sleep onset, duration, consolidation, quality, and wakefulness during sleep, as well as daily work hours. Our sleep and work logs have previously been validated; hours of sleep and work reported using this methodology have a high correlation with polysomnographically-validated total sleep time ($r=0.94$) as well as 3rd-party documented work hours ($r=0.98$).⁽²⁾

1.5.4.2 Ambulatory physiologic monitoring

To further validate reported sleep times in this study, wrist activity and ambient light levels will be monitored for the entire duration of residents' rotations with a solid-state, portable data collection device (Motionlogger BASIC; Ambulatory Monitoring, Inc., Ardsley, NY). The Motionlogger recorder is a small wrist worn device that measures activity and ambient light exposure; it is waterproof and powered by a 3V, 150 mAmp-hr Lithium Manganese battery that has a lifetime of 60 days. Data are preserved if the battery expires.

1.5.5 Measuring Resident Vigilance

1.5.5.1 PVT.

In the proposed study, we will also have resident physician subjects complete Psychomotor Vigilance Testing – an established metric of vigilance that is sensitive to sleep deprivation and circadian misalignment (14) – during one shift per week, every five hours. Completing the PVT requires 10 minutes and provides data on vigilance that will be used to derive an independent measure of neurobehavioral performance while subjects are on the job. Subjects will also be asked to complete the Karolinska Sleepiness Scale (KSS), a self-report scale that measures alertness, before and after each test.

1.5.6 Additional Measures

1.5.6.1 Self-reported attentional failures, motor vehicle crashes (MVCs), and percutaneous injuries

Through end-of-rotation surveys, we will also collect data on residents' self-reported attentional failures, MVCs, near-miss MVCs, and percutaneous injuries using the instruments we previously developed for use in our national cohort study. Any reported MVCs and percutaneous injuries will be validated by the collection of objective data (e.g. police reports, repair bills, etc. for MVCs), as was done in our cohort study.(1;4) When MVCs occur on the commute to and from work, we will also have drive diary data available. We believe that collecting MVC and percutaneous data is important given their implications for resident safety, but with 300 anticipated subjects in the study, and the relative infrequency of these occupational injuries,(1;4) we will have power to detect an effect of the intervention on these outcomes only if they are reduced more than two-fold. As such, analysis of these outcomes will be considered exploratory.

1.5.6.2 Educational Measures

As part of the study, participants will have the option of enrolling in an online educational platform entitled OPENPediatrics. OPENPediatrics is a free, open access, peer-reviewed, digital learning platform that utilizes the latest in innovative technology to provide robust continuing medical education. OPENPediatrics is sponsored through Boston Children's Hospital and IBM and located at Boston Children's Hospital (Website: <http://openpediatrics.org>). Through a feature entitled the Learning Pathways, participants will have access to the ROSTERS curriculum, or a similar ICU learning curriculum approved by each participant's hospital. This curriculum is comprised of 18 lessons by educational experts. Each lesson begins with a pre-test followed by a didactic or procedural demonstration video and concludes with a post-test. This unique format will allow for asynchronous learning, so that participants can complete their educational lessons outside the hospital and apply their knowledge during on-duty hours. OPENPediatrics' robust analytics will allow research staff to track each participant's submissions as they progress through the curriculum. Pre-test and post-test scores as well as duration in each module will allow researchers to note the educational gains made throughout the curriculum, and compare each participant's results in the control and Sleep and Circadian Science-based (SCS) intervention arms. A vigorous set of security measures will allow the analytic data from the application to be securely passed from the application to the data collection program, Cognos. As standard practice for the OPENPediatrics data storage procedures this data will be stored on IBM's secure servers, and IBM's analytic department will control access to this data. All residents in the unit will have access to the platform so no delineation between non subject residents and subject residents can be made by anyone except each site coordinator who will maintain the only identified list of subjects for the site. Resident data specific to each site will be sent from OPENPediatrics to each site coordinator; the site coordinator will then delete all data associated with non-subject residents. These measures are being taken so only site coordinators have knowledge of which data sets are associated with resident subjects. The team will work with the site PI to de-identify the data by removing the user's name/email. The data will only be stored on password-protected computers. Data will only be reported as de-identified, aggregated data.

On their end-of-rotation surveys, they will report their impressions of their educational experience.

1.5.6.3 Collection of Salivary Samples for Subsequent Genetic Analyses

In light of the emerging science exploring the genetic predictors of susceptibility to sleep loss and circadian misalignment, salivary samples will be collected to measure genetic modifiers of the *SCS intervention's* effects. Unfortunately, the limited number of subjects (~300) being studied in this proposed trial precludes conducting genome-wide association studies to determine what genes may convey an increased risk of fatigue-related error, and as yet, no candidate gene has been independently verified to convey altered vulnerability to the performance-impairment associated with sleep deprivation. However, given that this study will gather unprecedented data on sleep, performance, and safety, and the likelihood that one or more candidate genes will be verified in the near future, we will collect samples and analyze the DNA of all participants who agree to participate in a future genetic evaluation. These specimens will then be available at a later time to evaluate whether candidate genes verified to affect vulnerability to sleep loss or of making an error that leads to an AE.

1.6 SAFETY ASSESSMENTS

1.6.1 Patient Safety

The study will be looking for the occurrence of adverse events that occur in ICU care; some are preventable, and some are not. Data on adverse events will be systematically collected and reviewed by the DSMB after each 8 month data collection period. Rates of adverse events will be compared and the DSMB will subsequently make periodic recommendations on whether to continue, modify, or terminate the study. From prior studies, we have found that the cause of detected adverse events in hospitals cannot in most cases be reliably assigned on a case by case basis (e.g., was acquisition of a catheter-related bloodstream infection due to a resident's work schedule? A nurse error? Another cause?), so we anticipate that there will not be discrete, individual adverse events that would modify an assessment of the safety of the intervention or traditional work schedule's risks; rather, we expect that through epidemiologic methods, we will obtain useful data on the safety of the intervention vs. traditional work schedules, and act as needed. However, if there are discrete events that clinical staff or study investigators believe are attributable to either the intervention or traditional work schedule, these events will be brought to the attention of the DSMB for review and action as needed.

1.6.2 Resident Safety

As part of this study, we will ask resident subjects questions about depression, including questions about suicidal thoughts and plans, motor vehicle incidents, drowsy driving, including falling asleep at the wheel, and occupational exposures. The Data Coordinating Center for the study reviews survey responses, and if responses indicate suicidality, 3 or more occupational exposure reports, and/or motor vehicle crashes in which the damage was >\$1000 and/or drowsiness was reported as a factor, the study principle investigator will be asked to follow up with the resident subject. Near misses will not be followed up on. Additionally, initial reports of falling asleep at the wheel will trigger a follow up with by each site's research study coordinator; 3 or more responses of falling asleep while driving will trigger a follow up by each site's principle investigator. Specifically in regards to questions concerning suicide, if resident

subjects respond to the question “Over the past two weeks, how often have you thought about or wanted to commit suicide?” with “Some of the time,” “Most of the time,” or “All of the time,” regardless of whether they respond “Yes” or “No” to “Do you have a plan?”, the following message will appear on the form: “Your response to the previous questions causes us to be concerned for your welfare. All reports of suicide ideation will be reported to your site PI, who will then initiate your institution’s protocols for timely intervention and action, in compliance with their organizational rules and standards.” These criteria were discussed and decided on by the Clinical Coordinating Center, Steering Committee, and voted on and approved by the Data Safety Monitoring Board for this protocol.

1.7 STATISTICAL CONSIDERATIONS

1.7.1 Outcomes and Statistical Analyses

We will compare resident-related (Specific Aim 1) and total (Specific Aim 2) rates of harmful medical errors (preventable adverse events) on the two schedules. As a secondary measure, rates of non-harmful serious medical errors (i.e., near misses) will also be compared. In an intention-to-treat analysis, rates will be compared by schedule using Poisson models with compound symmetric working correlation and robust standard errors to account for both overdispersion and clustering by clinical center (15), and the number of patient-days at risk in each center and period included as so-called offset. The models will control for period effects and will be used to assess treatment-period interaction, a standard check with crossover trials(16).

In addition, actigraphy and sleep diaries will be used to ascertain the minimum and mean number of hours of sleep obtained per night, total sleep time, wake after sleep onset (WASO; minutes), and sleep efficiency. We will also compare performance based on results captured by the Psychomotor Vigilance Test (PVT). Specifically, we will compare the the numbers of lapses in vigilance, defined as a reaction time >500 ms, on the PVT. This Intention-to-treat comparison will be made using linear mixed models for repeated measures, with nested random effects to account for clustering within clinical center and residents¹². Outcomes will be normalized as necessary; generalized linear mixed models appropriate for other outcome distributions, and/or bootstrap standard errors will be used if adequate normalization cannot be achieved. In preliminary analyses, we will assess the comparability of the residents in the intervention and control periods in terms of age, gender, post-graduate year (PGY2 vs PGY3), as well as other potential confounders of the intervention. If imbalances are found, we will conduct sensitivity analyses in which we flexibly adjust for the potential confounders.

1.7.2 Sample Size and Minimum Detectable Effects

Based on the Intern Sleep and Patient Safety Study, during which 2,203 patient-days were accrued under both schedules over a total of 8.5 months at a single center with 2 ICUs totaling

Serious medical errors	Resident-related rate per 1000 patient-days	MD-RRR with Scale Factor of 1.0 (2.0)	Unit rate per 1000 patient-days	MD-RRR with Scale Factor of 1.0 (2.0)
overall	136.0	8.0% (11.2%)	193.2	6.7% (9.4%)
intercepted	70.3	11.0% (15.5%)	95.1	9.5% (13.3%)
non-intercepted	44.8	13.8% (19.2%)	59.5	11.9% (16.7%)
Preventable AEs	20.9	19.8% (27.5%)	38.6	14.8% (20.6%)

Figure 3, power table. Minimum detectable relative rate reductions (MD-RRRs) detectable with 90 percent power in two-sided tests (with alpha of 5%) for serious medical errors, by sub-type of error, using Poisson models. The primary outcomes of interest, resident-related and total preventable AEs, are bolded.

20 beds, we estimate that approximately 46,080 patient-days will be accrued across the six centers in this study, each contributing an observation period of 8 months on each

schedule, with an average census of 16 patients, or 80% of an average 20 beds. Assuming that the baseline error rates per-patient day on the standard schedule are the same as those observed in the Intern Sleep and Patient Safety Study, the new sample will provide 90% power to detect relative rate reductions (MD-RRRs) on the sleep and circadian science-based (SCS) intervention schedule as shown in Figure 3. Estimates are shown first assuming a scale factor of 1.0, corresponding to a Poisson distribution, while conservative estimates assuming an over-dispersed Poisson distribution with a scale factor of 2.0, are shown in parentheses. For overall serious medical errors, we will have 90% power to detect reductions in both resident-related and unit error rates of 7-11%; MD-RRRs for intercepted and non-intercepted medical errors will be between 9.5 and 19%. Even for the least frequent outcome but that of greatest interest, resident-related preventable AEs, we will have 90% power to detect a relative reduction of 19.8% if the distribution is Poisson, and 27.5% under our conservative assumptions about over-dispersion. The actual reductions seen in our preliminary study were larger than these thresholds in each sub-category of resident-related serious errors, including resident-related preventable adverse events. Thus, we expect to be adequately powered to draw definitive conclusions regarding the effectiveness of the *SCS schedule* intervention. In assessing interaction/period interactions, MD-RRRs will be fourfold larger than the main intervention effects. However, because residents will participate in at most one period, the potential for carryover effects is much smaller than in most crossover studies.

In addition, for sleep and work hours as well as PVT results, we estimate the expected sample of 300 residents will provide 90% power in 2-sided tests with alpha of 5% to detect standardized between-group differences of 0.30 to 0.37 standard deviations of the outcome, depending on the design effect

Outcome	MDE
Sleep hours (weekly)	1.75 / 1.92 / 2.21
Work hours (weekly)	1.39 / 1.53 / 1.76
Standardized units	0.30 / 0.32 / 0.37

Figure 4, minimum effects on resident outcomes detectable with 90% power in two-sided 5% tests, with design effects of 1.25/1.5/2.0.

due to clustering within centers and residents; calculations are shown in Figure 4 for minimum detectable effects (MDEs) for sleep and work hours, based on standard deviations observed for sleep and work hours observed in the ICU pilot study conducted at Brigham and Women’s Hospital. Because this pilot study did not collect data on other sleep outcomes (e.g. WASO, sleep efficiency) or the performance outcomes

(PVT), the standardized units are also shown in Figure 4. These calculations show that the study will be powered to detect small-to-moderate intervention effects on these outcomes, even if the design effect is as large as 2.

1.8 DATA COLLECTION AND QUALITY ASSURANCE

1.8.1 Data Acquisition and Transmission

The DCC will develop a front-end component for data entry and transmission. Data would be entered at remote sites on secure mobile computing devices and transmitted a minimum of once a day via secure transfer. Data received will be automatically imported into SQL tables and integrated into our standard data system. Data will be available for review/updating via the standard study website within 24-48 business hours. The DCC will create and maintain a comprehensive programmer's guide for all the data systems it provides.

1.8.2 Data Collection and Editing

Capturing data electronically will reduce the risk of missing data. Furthermore, edits checks may be built into the instruments to flag out of range or inconsistent data. Further custom edit checks will be written and run on data received at the DCC. Each hour, the cumulative study data is subjected to these custom edits to ensure completeness, consistency and validity of the data. The results of the error-checking procedures are posted to the study website, which the study staff will check daily to both confirm that the DCC has successfully received all of the transmitted forms and to address errors that have been detected by the edit system. The Project Manager and other Clinical Coordinating Center (CCC) staff will be responsible for checking the daily data edits and working in conjunction with the sites to address them. This data entry/data editing process is monitored by a number of standard monitoring reports that will be available on the website. An audit trail is maintained which includes the date of change, time of change, description of data change, and the study ID of the person making the change.

The DCC will also serve as the Reading Center for the actigraphy and PVT datasets. DCC staff will perform an initial review of the files upon receipt and report any issues to the clinical site staff; later DCC staff will clean and merge the device data with the form data.

The DCC will prepare comprehensive 'clean' datasets for analysis, providing the analysis-ready files to the CCC and others as necessary, for statistical analysis purposes. The DCC will also ensure that any entity receiving the dataset will have a Data Use Agreement on file, signed by the appropriate institutional authority. The DCC will also be responsible for preparing a public release dataset to be housed within NHLBI's BioLINCC (or a comparable public data repository) no later than 3 years after the end of the trial or 2 years after the main paper has been published, whichever comes first.

1.8.3 Data Management and Study Progress

The study website which includes a number of data management features and reports to enable clinical sites and study investigators to monitor data collection and study progress. Data Management features include a data inventory, lists of missing forms and queries by participant ID, and tools to resolve queries and update data via the website. Reports can be custom-designed to meet study needs and could include:

- Enrollment in aggregate and by site
- Demographics in aggregate and by site
- Early Discontinuation in aggregate and by site

1.8.4 Staff Training

To ensure inter-rater reliability, the physician observers and research nurses will undergo training in the detection of medical errors and adverse events prior to observing residents. The training will include evaluation of test cases designed to calibrate the observers' assessments. At least twice during each 8 month period of data collection, for each wave of sites, the DCC will examine the rates of events by observer at each of the sites to determine if there is significant variability. Re-training of physician observers will occur as needed to ensure consistent reporting of suspected medical errors across staff and sites. Documentation of the analyses of event rates as well as the staff training will be maintained by the DCC. Staff will also be instructed on procedures for entering data into electronic data collection forms and transmitting these data to the DCC. Lastly, staff will be trained in the operation of the actigraphs as well as administration of the PVT tests.

1.9 PARTICIPANT RIGHTS AND CONFIDENTIALITY

1.9.1 Institutional Review Board (IRB) Review

This protocol and informed consent documents, and any subsequent modifications, will be reviewed and approved by the IRB or ethics committee responsible for oversight of each of the clinical sites, as well as the clinical and data coordinating centers.

1.9.2 Informed Consent Forms

Informed Consent documents will be maintained at individual sites and coordinators must ensure that they are using an up-to-date, IRB approved version of the consent form. A signed Informed Consent form will be obtained from each participant. The Informed Consent will describe the purpose of the study, the procedures to be followed, and the risks and benefits of participation and must comply with the requirements of the study site's Institutional Review Board. A copy of the Informed Consent will be given to each participant and provision of the copy will be documented in the study participant's record. The DCC will ensure that all clinical site informed consents are consistent and include required elements.

1.9.3 Participant Confidentiality

1.9.3.1 Clinical Sites

In order to protect confidentiality of the research participants as well as the patients they treat, both will be assigned a unique study identification number, which will be used to refer to them on all study forms. The list of codes linking resident-subjects' and patients' names and study IDs will be kept by each site PI on a separate password protected computer in a locked office at that site. Each site PI will be responsible for ensuring the security of these data. These identifying data will not be transmitted outside of the originating institution. Risk to patient confidentiality will likewise be minimized. All information will be de-identified at the point of data analysis.

1.9.3.2 Data Coordinating Center

The DCC follows standard operating procedures (SOPs) for computer system security to ensure the confidentiality and validity of study data. The SOPs are designed to prevent unauthorized access and limit authorized access to our computer systems and are in compliance with established standards for Information Technology Security. Our network is privately maintained, hardware fire-walled and none of the workstations or database servers can be directly addressed from outside the Local Area Network. Study website and database access requires a network domain account with appropriate account-specific permission on the database. All requests for new accounts and access to the database must be documented by a System Access Request Form signed by the project director.

1.10 COMMITTEES

1.10.1 Steering Committee

The Steering Committee will be responsible for all decisions concerning the scientific and technical conduct of the study. It will appoint the analysis and publications committee and writing groups, ensuring that information from the study is disseminated in the scientific literature and at scientific meetings. The committee will be chaired by Dr. Czeisler and will include the lead site investigator from the clinical and data coordinating center and each of the clinical sites. The Steering Committee will have one in-person meeting on an annual basis, and will meet by teleconference on at least a bi-monthly basis. The Steering Committee consists of the following members:

Charles A. Czeisler, PhD, MD	Chair, PI, CCC, Brigham and Women's Hospital
Christopher P. Landrigan, MD, MPH	PI, CCC, Brigham and Women's Hospital
Katie L. Stone, PhD	PI, DCC, California Pacific Medical Center
Susan Redline, MD, MPH	Chair, Sleep Research Network
Ken Wright, PhD	PI, University of Colorado
Jeffrey Segar, MD	PI, University of Iowa
John McGuire, MD	PI, Seattle Children's Hospital
Pearl Yu, MD	PI, University of Virginia
Sue Poynter, MD	PI, University of Cincinnati
Phyllis Zee, MD, PhD	PI,
Robert Smith, PhD	Project Scientist, NHLBI

1.10.2 Executive Committee

An Executive Subgroup of the Steering Committee will be responsible for decisions that require attention between Steering Committee Meetings and for major financial, administrative and operational decisions. The Executive Committee will meet via teleconference at least monthly and will consist of the following members:

Charles A. Czeisler, PhD, MD	PI, CCC, Brigham and Women's Hospital
Christopher P. Landrigan, MD, MPH	PI, CCC, Brigham and Women's Hospital
Katie L. Stone, PhD	PI, DCC, California Pacific Medical Center
Robert Smith, PhD	Project Scientist, NHLBI

1.10.3 Principal Planning Group

A planning group comprised of the Principal Investigators and project staff of both the CCC and DCC will be responsible for the development of study documents, including the forms, protocol and operations manual, as well as the day-to-day management of the trial. The Principal Planning Group will meet via teleconference at least monthly and will consist of the following members:

Charles A. Czeisler, PhD, MD	PI, CCC, Brigham and Women's Hospital
Christopher P. Landrigan, MD, MPH	PI, CCC, Brigham and Women's Hospital
Conor O'Brien	CCC, Brigham and Women's Hospital
Katie L. Stone, PhD	PI, DCC, California Pacific Medical Center
Dana R. Kriesel, MPH	PD, DCC, California Pacific Medical Center

1.10.4 Working Groups

Members of the Steering Committee will form working groups to manage and oversee specific aspects of the trial. These include: (1) Data Management and Data Quality; (2) Patient Safety and PICU Quality Outcomes; (3) Sleep, Performance and Health Outcomes; and (4) Education Outcomes. Working groups will meet on an as needed basis.

1.10.5 Data and Safety Monitoring Board

To monitor the study for the possibility that the intervention schedule has an adverse effect on safety, a multidisciplinary Data and Safety Monitoring Board (DSMB) comprised of financially disinterested members was appointed by NHLBI, with guidance from DCC. The board is comprised of five members with expertise in pediatric intensive care, pediatric critical care, sleep medicine, clinical trial design and biostatistics, bioethics, healthcare quality and outcomes research. The DSMB will monitor the quality and integrity of the data emerging from the proposed study; assess the adequacy of recruitment, compliance, follow-up and other aspects of study execution; and review interim analyses of the major outcomes of the trial to identify safety issues and make periodic recommendations on whether to continue, modify, or terminate the study. The DSMB will be an advisory board to NHLBI and the Steering Committee. The DSMB will work under a Charter that will be developed by the DCC, working in tandem with NHLBI. The DCC will support the DSMB by preparing interim reports for review at DSMB meetings; and by organizing scheduled and ad hoc meetings of the DSMB as needed. Please see the DSMB Charter for more details.

1.11 CONFLICT OF INTEREST

The DCC will be responsible for surveying the key personnel at each study site on an annual basis regarding any conflicts of interest that may have arisen. The Executive Committee will review the results of these annual surveys and determine if any action is necessary.

1.12 REFERENCES

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