Healing Environments for Critically Ill Children: Development of a multidisciplinary and integrated approach to sleep, sedation, delirium and early mobilization

by

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ABSTRACT

Pediatric Intensive Care Unit mortality rates have decreased significantly in the last decade, but the proportion of children surviving with significant functional morbidity is rising.\textsuperscript{1-4} For decades, hospital routines have been in place that disrupt normal sleep-wake patterns, which may have negative effects on the developing brain. Sleep disturbances during childhood negatively impact learning, memory, and psychological well-being.\textsuperscript{5-7} During critical illness, children are exposed to both intrinsic and extrinsic factors that disturb sleep, potentially increasing the risk of delirium and post-intensive care syndrome.\textsuperscript{8-11} Intubated children frequently are heavily sedated to prevent inadvertent extubation or other complications, leading a culture of immobility in the pediatric critical care setting.\textsuperscript{12,13} Furthermore, acute rehabilitation may be delayed to the perception that a child is too critically ill to engage in early mobilization activities, further fueling the cycle of immobility and increasing the risk of intensive care unit-acquired weakness and potentially impacting quality of life after discharge. While optimizing sedation approaches, sleep promotion, delirium prevention and early mobilization individually is a viable option, integrating these components to create healing environments for children recovering from critical illness is a practical approach to optimize both short and long-term outcomes.

The work described in this dissertation systematically explores current PICU practice and clinician perceptions in each of these areas, and characterizes temporal sleep and activity patterns of critically ill children admitted to the PICU through hospital discharge. The dissertation concludes by demonstrating the safety and feasibility of a multicomponent, multidisciplinary early mobilization program which integrates titrated
sedation, sleep promotion, and delirium prevention. The overarching goal of my research is to create a paradigm shift in PICU care prioritizing minimal but effective sedation with sleep promotion to prevent delirium and facilitate early mobilization through multidisciplinary collaboration. I hope that transforming PICU culture to liberate the critically ill child from these iatrogenic risk factors will improve both short and long-term outcomes for children undergoing active neurocognitive development.

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INTRODUCTION

Over 250,000 children are admitted to the Pediatric Intensive Care Unit (PICU) each year. The modern PICU cares for infants and children from 1 day of age through adulthood, with a wide range of diagnoses encompassing cardiac and respiratory disease, trauma, and major surgery including transplants, sepsis and severe burns. While PICU mortality rates have decreased significantly in the last decade due to advanced medical technology, the proportion of children surviving with significant functional morbidity is rising, heightening awareness about modifiable risk factors impacting PICU outcomes. Children’s experiences in the PICU are affected by multiple exposures that can be, but often are not, optimized in the face of critical illness, leading to iatrogenic harm. Minimizing the exposures that increase harm can be achieved by sleep promotion, sedation optimization, delirium prevention and management and early mobilization.

With considerable heterogeneity in ages, development and diagnoses in the PICU, the implications of sleep disturbances on the developing brain during critical illness are unknown. Sleep needs are in a constant state of change as a child grows, reflecting neurologic maturation. The PICU environment is typically noisy with brightly lit environments where care providers make multiple interventions throughout the day and night for the benefit of a child’s recovery. In adult studies, frequent peaks in noise lead to arousals from sleep and adversely affect cardiovascular function. Exposure to natural light during the day and minimizing light exposure at night are essential for regulation of melatonin secretion and optimization of the sleep-wake cycle. However, it is often assumed that constant noise and bright lights are simply an unfortunate consequence of ICU care that cannot be remedied. For staffing convenience, often baths are given and
weights are obtained in the middle of the night. Because of a lack of education about the sleep process and the physical and psychological benefits of sleep, hospital routines have been in place for years that disrupt sleep in critically ill children.

Intubated children are often heavily sedated for comfort and safety to prevent inadvertent extubation or decannulation of catheters. Opioids and benzodiazepines, the most common sedative-analgesic combination used in children, have both been shown to decrease slow-wave and REM sleep in adults. Doses are often increased to improve the care provider’s subjective assessment of the patient’s sleep, fueling tolerance and dependence and potentially leading to further agitation and deterioration of sleep quality. Systematic approaches to sedation in the PICU have not shown improvement in PICU outcomes. Thus, the role of sleep-wake homeostasis in the PICU must be investigated to develop targets for early intervention to improve outcomes and create healing environments for critically ill children.

Sleep disturbance is a major risk factor for the development of delirium, and left untreated, delirium during critical illness is associated with worse functional outcome, longer hospitalization, and higher mortality rates. Delirium is an acute neurologic dysfunction characterized by disturbances in attention, alertness, and cognition that develop rapidly and fluctuate throughout the day. Interest in pediatric delirium has grown over the last five years, with a recent international study demonstrating a point prevalence of 38% among children in the PICU greater than six days. Like in adults, the cognitive consequences of delirium in children can last well after the hospitalization and may impact the child’s educational progress.

In 2010, the concept of the ‘ABCDE’ bundle was described, which has now evolved
to the ‘ABCDEF’ bundle (Assess, prevent and manage pain, Both spontaneous awakening and breathing trials, Choice of Sedation, Delirium monitoring/management, Early exercise/mobility, Family engagement and empowerment). The ABCDEF bundle is a multicomponent approach to “liberate” the mechanically ventilated ICU patient through organizational change to promote culture change. In addition to addressing sedation optimization (C= Choice of sedation) and delirium prevention and management (D), the ABCDEF bundle integrates early mobility as a key component of ICU liberation. Early mobilization in the adult ICU is associated with improved functional outcomes, less days on the ventilator, and decreased length of ICU and hospital stay. The concept of PICU Liberation and early mobilization has emerged just in recent years. Given the positive impact of activity on sleep and circadian rhythms, early mobilization in the PICU could play an important role in maintaining normal sleep-wake patterns and decrease the incidence of ICU-acquired weakness to improve short and long-term functional outcomes.

The inspiration for the work described in this dissertation came in 2010 when I was a pediatric critical care fellow caring for children in the midst of a winter with a high burden of respiratory infections and mechanically ventilated patients. Universally all of our intubated patients were on opioid and benzodiazepine infusions, with escalating doses each day. The word “sleep” was used synonymously on rounds with “sedation”, and all of these patients were in physical restraints for safety due to intermittent agitation, which may have been what we now know as delirium. Given the vital importance of sleep for the developing brain, I wanted to learn more about whether these children were experiencing natural, restorative sleep, and if sleep disturbances due to the chaotic PICU environment and pharmacologic therapies could be contributing to a vicious cycle. Exploring the literature,
I found that sleep in critically ill children was a severely underdeveloped area of research.

In this dissertation, I present the work that progressively developed into a multidisciplinary and integrated approach to sleep, sedation, delirium and early mobilization. Each chapter describes a key step in building the foundation for a research program that focuses on creating healing environments for critically ill children to optimize short and long-term functional outcomes.

Chapter One is a synthesis of the literature surrounding sleep in critically ill children. Chapter Two presents the results of an international survey of sedation, sleep promotion, and delirium screening practices in the care of mechanically ventilated children, highlighting significant heterogeneity in practice and a paucity of sleep promotion and delirium screening practices worldwide in 2012. In Chapter Three, the results of an observational study are described characterizing temporal patterns in the sleep EEG power spectrum in PICU patients, which demonstrates a lack of circadian and ultradian variability compared to healthy controls. Chapter Four describes data on activity monitoring in PICU patients to estimate sleep-wake patterns in children after major surgery. In Chapter Five, we surveyed nurses about their perception of the PICU environment before and after the transition to a new building with all single-patient rooms to understand how it impacts children’s care as well as nurses’ work satisfaction and well-being. Chapter Six builds on the association between sleep and delirium and investigates barriers to delirium screening through a survey of nursing staff. Finally, Chapter Seven integrates the work described in the previous chapters and culminates with a multidisciplinary, multicomponent quality improvement study to demonstrate the safety and feasibility of an early mobilization program for all critically ill children admitted to the PICU.
CHAPTER 1

Sleep of Critically Ill Children in the Pediatric Intensive Care Unit: A systematic review\textsuperscript{30}

(Reprinted with permission from Sleep Medicine Reviews)
INTRODUCTION

Approximately 250,000 children are admitted to the Pediatric Intensive Care Unit (PICU) each year in the United States. Critical illnesses in children encompass a range of medical and surgical diagnoses, such as multi-system organ failure requiring extracorporeal support, complex congenital heart disease, and severe trauma. The modern PICU admits all critically ill infants and children ages 0-18 with the exception of critically ill neonates, who are admitted to the Neonatal Intensive Care Unit (NICU). As a result, the PICU provides care for a heterogeneous age range of patients at vastly different developmental stages and biological needs. Thus, during any given shift over a 24 hour period, physicians and nurses in the PICU may be concurrently responsible for the care of a one month old infant and a 12-year old adolescent. Admission to the PICU is a stressful experience for children who are going through active neurocognitive development, and sleep disturbances are often an unavoidable result of the critical illness and associated management.

Although the importance of sleep in the intensive care unit setting has become a topic of significant research interest in recent years, there is a paucity of scientific evidence investigating sleep as a modulator of outcomes in critically ill children. Studies that have used polysomnography in adults admitted to the ICU have demonstrated a decrease in sleep efficiency, an increase in arousal frequency, and a decrease or absence of slow wave sleep (SWS) and rapid eye movement (REM) sleep. Furthermore, poor sleep quality and sleep onset and maintenance insomnia are the most frequent complaints noted by adult survivors of critical illness – impairments that persist even after discharge from the ICU. When a child becomes critically ill, admission to the PICU brings with it a multitude of
risk factors for disruption of the normal rhythm of the sleep-wake cycle, including a chaotic environment, administration of centrally acting medications, pain associated with the underlying illness, interruptions for nursing care, and invasive medical interventions (Figure 1.1). The resulting disruption in sleep continuity and reduction in sleep duration can interfere with a myriad of fundamental physiologic processes that, in turn, can lead to delirium, impaired immunity, catabolism and respiratory compromise - undesirable effects when a child is critically ill and recovery and healing are the goal.\textsuperscript{31,37-39} Despite obvious similarities between the pediatric and adult ICU environments, key differences exist in the exposures experienced by the critically ill child and adult. Moreover, across the age spectrum, there is substantial biological variability in normal sleep-wake behavior which may modify the detrimental impact of the ICU environment.

Figure 1.1: Proposed causal pathway for changes in sleep behavior as a modulator of outcomes in critically ill children

It is well known that sleep needs are in a constant state of change as a child matures, reflecting neurologic maturation. Newborns typically sleep up to 18 hours per day on an
irregular schedule, with periods of wakefulness that are limited to one to three hours. A newborn’s sleep cycle ranges from 50 to 60 minutes and is comprised of an equal proportion of REM and non-REM (NREM) sleep. Over the first twelve months of life, sleep becomes consolidated in infants, and by five years of age sleep patterns stabilize to one continuous period of sleep at night.4-6 Healthy children between 3 to 12 years old sleep between nine to ten hours each night on average, and spend a greater proportion of the night in slow wave sleep than adults, from 20-38% of total sleep time.5,7,8

To understand key factors that disrupt the normal sleep-wake cycle in children admitted to the PICU, it is imperative to recognize that there are several features of critical care in children that are distinct from adults. Perhaps one of the most challenging components of pediatric critical care is sedation of mechanically ventilated children. Mechanically ventilated children universally receive sedative and analgesic drugs for pain and anxiety associated with invasive instrumentation, the most common being the endotracheal tube. The inability to communicate and the developmental limitations in understanding the need for ICU interventions compounds the challenges involved in adequately sedating children to maintain safety and prevent inadvertent extubation or decannulation of catheters.40-42 Common medications used for sedation include opioids, benzodiazepines, ketamine, barbiturates and alpha-agonists such as dexmedetomidine and clonidine. Often these medications are used in combinations of two or more classes, the most common combination consisting of an opioid and a benzodiazepine after the initiation of mechanical ventilation. Opioids and benzodiazepines have been shown to decrease slow wave and REM sleep in adults.17,18 Paradoxically, sedative and hypnotic medications doses are often increased in critically ill children to improve the subjective assessment of sedation.
and sleep, leading to further agitation and deterioration of sleep quality. In a study of “difficult to sedate”, mechanically ventilated children in a tertiary care PICU (n=47), over 50% of these children received four or more distinct sedative or analgesic agents simultaneously highlighting the challenge of balancing patient comfort and medication side effects. Indeed, excessive sedation is a risk in the critically ill child given the efforts that are usually made to help the patient “sleep” and maintain comfort and safety. Part of the difficulty in optimizing the use of centrally acting medications in critically ill children is the use of subjective measures to assess sedation such as the COMFORT scale, the State Behavioral Scale (SBS), and the Richmond Agitation and Sedation Scale (RASS). While helpful to some degree, these scoring systems are subjective and rely on the nurse’s assessment of patient comfort and sedation. Negative consequences of the escalating doses of sedative medications include lengthened time to extubation, withdrawal syndromes, and need for detoxification from sedatives due to pharmacological dependence. The addition of neuromuscular blockade as an adjunct to the sedation regimen adds an additional layer of complexity to the assessment of sedation and potentially compounds the problem of achieving adequate sleep quality in the ICU. Neuromuscular blockade diminishes the ability of care providers to use physical movement as an indicator of sleep state, and may lead to oversedation in an effort to ensure that the child is amnestic while receiving muscle relaxant. The role of impaired PICU sleep quantity and quality in escalating sedative needs requires further evaluation.

Previous research on sleep in the PICU has relied predominantly upon subjective assessments. As a result, assessment of sleep quality and quantity in the PICU remains an area for much needed research. An obvious challenge in characterizing sleep in the ICU
results from the need to provide life-saving interventions and care for the critical illness that can interfere and confound the assessment of sleep. Interestingly, recommendations by the Society for Critical Care Medicine guidelines on sedation monitoring suggest that sleep assessment be a part of routine care. Both subjective and objective sleep assessment tools are available for use in the ICU. Techniques for objectively characterizing sleep in the ICU include polysomnography, actigraphy, and bispectral index monitoring. There are also subjective methods that are based on observations of patient’s behavioral state.

Due to a lack of general awareness about the physical and psychological significance of sleep, hospital routines have been in place for decades that disrupt sleep continuity in the adult and pediatric ICU. Interestingly, many neonatal intensive care units nationally have adopted protocols to minimize sleep disruption, but neonates have distinct sleep physiology compared to children and adults, and many neonates do not require sedatives while mechanically ventilated. Lack of adequate sleep duration and quality has a known association with delirium, and the vast majority of PICUs internationally do not have protocols in place for sleep promotion and optimization. Given the limited information on sleep in critically ill children, the objective of the current study was to: (a) summarize the current evidence base; (b) highlight the challenges of sleep research in the PICU; and (c) demonstrate avenues for future research on sleep as a potential modulator of outcomes in critically ill children.

METHODS

Criteria for Selecting Studies

All prospective studies investigating sleep in children admitted to the pediatric intensive care unit (ages 1 month-18 years, inclusive) were included. Broad criteria for
inclusion were employed to capture the entire breadth of sleep-related studies performed in the PICU environment, given the heterogeneous methodologies used and research questions posed. There were no exclusions for neurologic injuries. Studies in neonates were excluded because classification and evaluation of sleep in newborns is performed utilizing different criteria than in children, and the neonatal intensive care unit environment varies significantly from that of the PICU. Many newborns in the NICU are in incubators, and most of these patients do not require high doses of sedative medications to maintain invasive instrumentation such as the endotracheal tube and intravenous or intra-arterial catheters.

**Literature Search Methodology**

To identify relevant articles, the MEDLINE and EMBASE databases were searched. The search strategy focused on two main concepts: “sleep” and “pediatric intensive care unit”. There were no study period restrictions, and studies were limited to those performed in human subjects. The databases were last searched on August 20th, 2012. The search strategy for MEDLINE was as follows: (("sleep"[MeSH Terms] OR "sleep"[All Fields] OR "sleeping"[All Fields]) AND ("Intensive Care Units"[Mesh] OR "Intensive Care Units, Pediatric"[MeSH] OR "Intensive Care Units, Neonatal"[MeSH] OR "intensive care units"[All Fields] OR "intensive care unit"[All Fields] OR "pediatric intensive care units"[All Fields] OR "pediatric intensive care unit"[All Fields] OR "neonatal intensive care units"[All Fields] OR "neonatal intensive care unit"[All Fields] OR "critical care"[tw] OR "Burn Units"[Mesh] OR "burn units"[All Fields] OR "burn unit"[All Fields]). For the EMBASE database the following search approach was utilized: ("sleep'/exp OR 'sleeping'/exp OR sleep OR sleeping AND ("intensive care units'/exp OR
'intensive care unit'/exp OR 'burn units'/exp OR 'burn unit'/exp OR 'pediatric intensive care units' OR 'pediatric intensive care unit'/exp OR 'neonatal intensive care units' OR 'neonatal intensive care unit' OR 'critical care units' OR 'critical care unit' OR 'newborn intensive care'/exp OR 'newborn intensive care'). A total of 3,153 articles were identified and title and abstract screening yielded 141 articles for full-text review. Furthermore, reference lists of the included studies, as well as review articles, were also examined to identify additional studies for inclusion.

RESULTS

Nine studies of sleep in children admitted to the PICU were identified and included in the current review (Table 1.1).\textsuperscript{4,40,42,44-49} Seven of the published studies utilized PSG for sleep measurement, although four resulted from the same randomized-controlled trial.\textsuperscript{40,42,45-49} Two studies used the Patient Sleep Behavior Observation Tool (PSBOT) as the primary method of sleep measurement.\textsuperscript{4,44} Because of the significant heterogeneity in research objective, patient population (e.g., age, illness), and methodology among the nine studies identified, a quantitative synthesis of the published findings was not possible. Thus, in the following sections, available studies have been categorized by the method used for assessing sleep and summarized by specific patient subgroups. The subgroups focused on by the included studies were children with severe burns admitted to the PICU and mechanically ventilated children.
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<td>Al-Samsam &amp; Cullen, 2005&lt;sup&gt;40&lt;/sup&gt;</td>
<td>Cross-sectional</td>
<td>11</td>
<td>3-21 mo</td>
<td>Intubated children on sedatives</td>
<td>24 hour PSG</td>
<td>• ↓ REM sleep &lt;br&gt; • No diurnal variation in TST or sleep stages</td>
</tr>
<tr>
<td>Armour, Gottschlich et al, 2008, 2009, 2011*&lt;sup&gt;46-49&lt;/sup&gt;</td>
<td>Randomized Crossover Study</td>
<td>40</td>
<td>3-18 years</td>
<td>PICU patients with severe burns randomized to zolpidem or haloperidol</td>
<td>Nocturnal PSG (22:00-07:00) for two 3-day periods in the 7-20 days postburn injury</td>
<td>• ↑ Wakefulness on control and treatment nights  &lt;br&gt; • ↓ REM sleep  &lt;br&gt; • Zolpidem: ↑ stage 3 and REM sleep  &lt;br&gt; Haloperidol: ↓ sleep latency and ↑ TST &amp; N2 sleep  &lt;br&gt; Zolpidem + Haloperidol: ↑ sleep continuity  &lt;br&gt; Ketamine: ↓ REM sleep</td>
</tr>
<tr>
<td>Carno et al., 2004&lt;sup&gt;52&lt;/sup&gt;</td>
<td>Cross-sectional</td>
<td>2</td>
<td>3 years</td>
<td>PICU patients on sedation and neuromuscular blockade after laryngotraceoplasty</td>
<td>PSG for 96 hours beginning 2 hours after surgery</td>
<td>• ↑ Stage 1 and 2 sleep and ↓ slow wave sleep</td>
</tr>
<tr>
<td>Cureton-Lane and Fontaine, 1997&lt;sup&gt;44&lt;/sup&gt;</td>
<td>Cross-sectional</td>
<td>9</td>
<td>15 mo-10.5 years</td>
<td>Children in the PICU for at least 24 hours</td>
<td>PSBOT for a 10 hour nighttime period</td>
<td>• Frequent awakenings  &lt;br&gt; • Mean length of nighttime sleep less than at home  &lt;br&gt; • ↑ Noise levels associated with wakefulness  &lt;br&gt; • Abrupt changes in noise increased arousals  &lt;br&gt; • ↑ Light levels and caregiver contact correlated with wakefulness</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Age</td>
<td>Setting</td>
<td>Methodology</td>
<td>Findings</td>
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<td>Corser et al., 1996</td>
<td>Cross-sectional</td>
<td>12</td>
<td>13 mo-35 mo PICU patients</td>
<td>PSBOT for 12-hour Nighttime Period Sleep Follow-up Interview Guide</td>
<td>• Arousals after sleep onset more than home baseline</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Benzodiazepines: ↑TST</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>• No correlation between time to return to pre-illness sleep pattern and PRISM score, ICU, or hospital length of stay</td>
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<tr>
<td>Gottschlich et al., 1994</td>
<td>Cross-sectional</td>
<td>11</td>
<td>1.4-16 years PICU patients with burns</td>
<td>Biweekly 24-hour PSG measurements through discharge</td>
<td>• Mean TST over 24-hour period of 10.5 hours</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Absence of stage 3/4 in 40% of PSG periods</td>
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<td>• ↑ Stage 1 early in hospitalization</td>
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<td></td>
<td>• Progressive ↓ Stage 2 and ↑ Stage 3 and REM sleep with recovery</td>
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<td></td>
<td></td>
<td>• Normalization of sleep associated with clinical improvement</td>
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Table 1.1 (cont)
Polysomnography in Children Admitted to the PICU with Severe Burns

Studies have demonstrated that severe thermal injury has detrimental effects on sleep quality and quantity, and animal studies suggest that disruption of sleep continuity in the presence of severe burns may contribute to delayed wound healing and poor pain tolerance. Data from subjective assessments and objective measurements with actigraphy have also shown poor sleep quality in adult burn patients in the hospital. Gottschlich and colleagues have previously summarized the entirety of PICU sleep literature in burned children. The first study on sleep in critically ill children was published in 1994 and included children with burn injury that involved greater than 20% BSA admitted to the ICU with an endotracheal tube. Using biweekly 24-hour eight-channel polysomnography in 11 children enrolled over 16 months, the observed total sleep time was, on average, 10.5 hours of sleep time/patient/24 hour period, which did not change significantly as days post-burn increased. Of the 43 sleep studies performed, 40% showed no evidence of slow wave sleep, and 19% demonstrated complete absence of REM sleep. Interestingly, slow wave and REM sleep percentages increased over the course of the hospital stay concomitant with a decrease in stage 1 and 2 sleep. Although the aforementioned findings confirm the disturbance of sleep in burn patients admitted to the PICU, the clinical implications for recovery after thermal injury and overall ICU stay remains to be determined.

Four of the identified manuscripts for the current review resulted from the same prospective, randomized controlled crossover study investigating the effects of two sleep-inducing medications in 40 pediatric acute burn patients admitted to the PICU. The overarching objective was to evaluate the effects of zolpidem, a non-benzodiazepine short-
acting hypnotic, and haloperidol, an antipsychotic agent frequently used to treat delirium in the adult ICU setting, on sleep in children ages 3-18 admitted within seven days with burns that covered greater than 20% body surface area. Children were randomized to zolpidem or haloperidol in the second week post-burn for two nights, and crossed over to the other drug for two nights in the third week post-burn. Each subject had a control night on the night prior to administration of each drug. Nocturnal polysomnography was performed for three nights for each of medications from 9:30 p.m. to 7 a.m., resulting in six nighttime PSG recordings per subject. All medications administered within 72 hours of the PSG periods were recorded. Sleep variables used for analysis were time in sleep stage, number of awakenings and longest periods of wake and sleep. Thirteen of the forty patients enrolled were mechanically ventilated and the mean BSA burned was 50% (SD: 2.9%). Study subjects underwent anywhere from 2 to 21 surgical procedures during their hospitalization and 65% of subjects had inhalational injury. A majority of patients (82%) were receiving midazolam, while 42% and 44% were on methadone and morphine, respectively. Results from the control nights demonstrated a mean number of awakenings was 24.9 events/hr (SD: 10.3), with an average total sleep time of 4.2 hours (SD: 0.2 hours). At baseline, a five-fold increase in the proportion of time spent in stage 1 sleep was noted as compared to published normal values (13.1% vs. 2.8%). The greatest reduction was observed in the percentage of slow wave sleep, with an average 1.6% (SD: 2.5) on control nights in burned children compared to 21% in normal children. REM sleep amount was also reduced at 5.25% (SD: 5.0%). Zolpidem increased the number of awakenings compared to control nights (28.8 vs. 24.9 events/hr, p=0.03), whereas haloperidol had no significant effect on awakenings (p=0.72). Total sleep time was not statistically
significantly improved by zolpidem, with only a 12% increase, while children receiving haloperidol had an average of 23% higher total sleep than controls (p=0.02). Neither zolpidem or haloperidol had a significant effect on the average time spent in stage 1 sleep or REM sleep, but zolpidem was noted to increase the percentages of slow wave and REM sleep compared to controls (0.81 vs. 0.62 hrs., p=0.02). The overarching inference was that sleep duration and architecture are significantly affected among pediatric burn patients and that accelerated drug metabolism in burn patients may have had an effect on the outcome of the interventions, necessitating inclusion of pharmacokinetic parameters in future studies.

In a secondary analysis from the same randomized crossover trial, the correlation between the burn care provider’s subjective evaluation of sleep quality with simultaneous polysomnographic data was evaluated. Trained field observers carried out sleep assessments with concurrent polysomnographic recordings, and recorded their observations every 15 minutes over each nine hour nighttime period. The observers classified the subjects as “awake”, “drowsy” or “asleep”, based on behavioral characteristics such as eye closure, vital sign changes, and body movement. Sedation scores were not monitored in order avoid waking the patients. Sleep study epochs were analyzed in 2-minute and 10-minute intervals, and categorized as sleep, wakefulness or a combination of both. In order to be classified as sleep, all the epochs in the 2-minute and 10-minute intervals must be designated as either stage 1, 2, slow wave or REM sleep. The percentage of polysomnographic intervals rated as awake, asleep or mixed were calculated and averaged for all 40 patients. A secondary classification to facilitate statistical analysis was comprised of asleep (for all contiguous epochs) and not asleep (either mixed or awake).
Correlation of visual observation and polysomnography showed a poor agreement, with a kappa statistic of 0.21. Children judged to be asleep by visual assessment were awake by polysomnography 56.3% of the time. The sensitivity and specificity of visual assessment of sleep state were 97% and 28%, respectively. Administration of zolpidem or haloperidol did not improve the intraclass correlation between subjective and objective measurements. Patients on ventilators were noted to have a larger amount of wake time compared to non-ventilated patients (p=0.001), and mechanical ventilation altered the level agreement between subjective and objective measures (p<0.05), although the direction of the association was not reported.

A third subanalysis of data collected from the randomized crossover study investigated the effect of ketamine administration on the quantity and quality of sleep in the pediatric burn patient.\(^ {48}\) Patients were grouped retrospectively into those who received ketamine on their first control day/night (a period of 30 hours beginning at midnight the day of the control PSG) and those who did not. Twenty-three of 40 patients received ketamine during the study period, and demographics including age, percentage of body surface area burned, sex, length of stay and mortality were similar between the ketamine and non-ketamine groups. Ketamine administration was associated with reduced REM sleep when compared to the non-ketamine group (4.54% vs. 1.66%, p=0.04). Ketamine had no effect on nocturnal total sleep time, frequency of awakenings, or the percentages of stages 1, 2, or slow wave sleep.

Finally, Gottschlich et al. evaluated the association between hormonal abnormalities and sleep stage distribution post-burn, as well as the effects of zolpidem and haloperidol on measures of endocrine function in these subjects.\(^ {49}\) At 6:00 a.m. on each
study day, epinephrine, norepinephrine, and serotonin levels were measured, along with dehydroepiandrosterone (DHEA), growth hormone (GH), melatonin and cortisol. DHEA was the only hormone significantly affected by haloperidol or zolpidem. Serum levels of DHEA were higher than in the control group (p<0.03) but still below normal, and increases in DHEA were not associated with increases in slow wave or REM sleep. There was a significant inverse correlation between the amount of REM sleep and epinephrine levels (r=-0.34, p=0.004). Those subjects who had at least 2.5% REM sleep demonstrated reduced epinephrine levels, and groups with negligible REM had elevated concentrations of epinephrine. The same inverse association also existed between REM sleep percentage and norepinephrine, with subjects who experienced greater than 10% REM having normal norepinephrine levels compared to increased levels in those with <10% REM. Serotonin had a positive correlation with slow wave (r=0.24, p=0.01) and REM sleep (r=0.48, p=0.01). No significant associations were noted between GH, melatonin, or cortisol and slow wave sleep.

Polysomnography in Mechanical Ventilated Children

While the studies by Gottschlich and colleagues included a proportion of mechanically ventilated patients, two separate studies have focused on sleep in mechanically ventilated children using polysomnography. In a 2004 feasibility study of polysomnography in children receiving neuromuscular blockade, recordings were obtained for four days in two children following laryngotraceoplasty. These post-operative patients were chosen due to their uniform need for immobility after repair and the difficulty in subjective assessment of sleep in children receiving neuromuscular blockade. Both subjects’ had a greater proportion of sleep during the daytime, and their
sleep became more consolidated by day 4. There was a marked decrease of SWS and a pronounced shift to stages 1 and 2. REM sleep could not be documented due to neuromuscular blockade and resulting inability to record any eye movement and muscle activity data. There was significant variability in sedative and neuromuscular blockade dosing which may explain the lack of correlations between dose of drug of administered and sleep.

Al-Samsam and colleagues conducted 24-hour polysomnography, noise monitoring, and logging of staff interventions in infants from 3-21 months of age. No interventions were made on medical management including sedative medications, and staff interventions were logged by the interveners on a bedside log, categorized as mildly, moderately or severely intrusive. Data collected by polysomnography were manually scored in 30-second epochs as quiet sleep, active sleep, wake or indeterminate using criteria for infants. Sixty percent of subjects were post-operative cardiac surgery patients, and all were mechanically ventilated and sedated with morphine and midazolam infusions. Chlortal hydrate and trimetrazine were also used in all patients, and four patients were receiving dopamine. Active sleep was reduced to a mean of 3.0% (SD: 4.0%), although the 24-hour total sleep time was longer than expected for age, at 19 hours (SD: 2.6 hours). The average frequency of wake episodes per night was 40 (SD: 20), and the average of the longest sustained sleep period was 194 minutes (SD: 79 minutes). No statistically significant differences in percentages of total sleep time, wake, quiet or active sleep were present between daytime and nighttime, and the mean ratio of day/night total sleep time was 1.56 (SD: 2.3). Noise levels were ≥75 dB (A) for 19% of the nights, with minimum 24-hour Leq level of 48 dB (A). With regard to staff interventions, medical staff was in
contact with subjects for a mean duration of 240±90 minutes in a 24-hour period. Nighttime severely intrusive interventions were associated with wake states 88±13% of the time.

Studies on Subjective Assessments of Sleep in the PICU

Two studies utilized observation of sleep state as the primary method of sleep measurement in the PICU. Both of these measured sleep with the Patient Sleep Behavior Observation Tool (PSBOT), which was developed in 1968 by Echols as part of a master’s thesis (Catholic University of America, Washington, DC). The PSBOT is an instrument which describes four tiers of cortical vigilance, identifying patient behaviors in each category. These tiers include awake, drowsy, paradoxical (REM) and orthodox (NREM) sleep. Using polysomnography, validity and reliability has been demonstrated for sleep latency, midsleep awakenings and waking after sleep onset when PSBOT is used for evaluation every five minutes. Corser and colleagues examined the sleep of twelve 1-2 year old children during and after PICU admission, as well as environmental stimuli with sound and light measurement. The study recruited subjects from a limited age group to minimize the potential confounding effects of psychosocial, cognitive and neurological development. In addition to the PSBOT which was performed for one 12-hour nighttime period every five minutes with light and sound monitoring, the Caregiver Activity Rating Scale (CARS) was developed to measure caregiver actions during the study period. The Sleep History Interview Guide and Sleep Follow-up Interview Guide were used to elicit sleep patterns before admission and after hospital discharge, respectively, and follow-up interviews were conducted weekly with parents for a six week period. Mean sleep time for children in the PICU was 436 minutes (SD: 167 minutes), and children awoke a mean of 9 times per 12-hour night (SD: 4.4). Sleep periods averaged 52 minutes and benzodiazepine
use was associated with increased total sleep time (p=0.045). A negative correlation was noted between individual sleep state observations and noise, light, caregiver activity and pain (all p<0.05). Return to pre-illness total sleep time occurred at an average of 3.5 weeks (SD: 2.2), and the number of awakenings after discharge returned to baseline at 3.6 weeks (SD: 1.8). There was no association between time to return to baseline sleep patterns and extent of sleep change, disease severity or length of PICU stay or hospital stay.

One year after publication of the above study, Cureton-Lane and colleagues observed nine children from 15 months to 10 years of age admitted to the PICU for at least 24 hours. The PSBOT was used for one 10-hour period, with simultaneous light and sound monitoring. The technician/staff member performing the PSBOT also recorded interactions between healthcare workers and the subject, as well as information about sources of noise and parental activities likely to influence variables. Mean total sleep time in that study was 4.7 hours (SD: 0.5 hours) over the 10 hour period observed, with a mean length of sleep episode of 27.6 minutes (SD: 25.9 minutes). Average number of awakenings was 9.8 per night (SD: 2.5). Noise levels averaged 55.1 dB (A) (SD: 6.8), and descriptions of noise exposures included frequent sharp elevations due to ventilators, cardiac monitors, oximeters, IV pumps, and staff conversations. Light levels, measured in foot candles, did vary distinctly according to the time of night, and remained low until 6 a.m. Caregivers were in direct contact with subjects 13.4 % (SD: 34.2) of all 5-minute observation points, and 22.5 % (SD: 41.2) of the time between observations. PRISM score, a measure of severity of illness and risk of mortality for PICU patients, was low or moderate for all subjects, due to exclusion of severely ill PICU patients in the convenience sample. Associations between sleep and metrics of noise, light, caregiver contact, parental
presence and PRISM score indicated that noise (p<0.001), light (p<0.02), and caregiver contact (p<0.001) were predictive of sleep state.

DISCUSSION

In the characterization of sleep in critically ill children admitted to the PICU, it is important to note the complexity of sleep assessment in an environment with a multitude of confounding variables that include the age, nature of the critical illness, invasive instrumentation such as the endotracheal tube, mechanical ventilation, noise, light, staff interventions and medications. Each child admitted to the PICU has a unique sleep environment considering all the factors that are associated with the child’s illness. In the current study, nine publications were reviewed on sleep-related measurement in the PICU setting, resulting from six unique studies. The included studies assessed sleep in a wide range of ages, 3 months to 18 years, which is a major source of heterogeneity given the changes in sleep architecture that occur in development from infancy to adolescence. All of the included studies excluded children with neurologic disorders such as traumatic brain injury or baseline severe neurologic deficits. The effects of traumatic brain injury represent a fertile area for additional research given evidence that children and adults with traumatic brain injury demonstrate sleep disturbances after discharge from the hospital. Specific sites of neurologic injury may impact the sleep-wake cycle differentially, with resultant consequences for short and long-term prognosis. In addition, all but one study excluded patients who required neuromuscular blockade. Although exclusion criteria were consistently imposed on all of the included studies, six varied considerably with regards to inclusion criteria with only two focusing solely on children undergoing mechanical
ventilation, while the remainder included both spontaneously breathing and mechanically ventilated patients. There was also significant heterogeneity with regards to inclusion of children who had recently undergone surgery, which may play an important role when pain from the surgical intervention is factored into analgesic requirements.

Five of the included publications resulted from two studies focusing on sleep in children with severe burns admitted to the PICU. In addition to the physical, environmental and pharmacologic factors that contribute to sleep disturbances in critically ill children admitted to the PICU, the child with severe burns has experienced a major traumatic event that can have significant implications for the child’s stress response in the acute and chronic phase of the injury. These children have been shown to meet criteria for post-traumatic stress disorder soon after the injury that can extend months to years later. Much of the psychological distress is due to pain associated with the injury, but fear and anxiety may be difficult for medical providers to distinguish from pain, particularly in younger children. As a result, children with severe burns are potentially at the highest risk for sleep disturbances in the PICU.

Perhaps one of the most interesting factors common to all studies that included polysomnography was the use of historical controls, normative age-based sleep stage and duration data for analysis of the sleep parameters observed in the PICU. Overall, these studies demonstrated that children in the PICU experience changes in sleep-wake behavior.

**Mechanical Ventilation and Sedation**

Children requiring mechanical ventilation in the PICU are the most critically ill patients and have the longest hospital length of stay, morbidity and mortality. Therefore, when considering sleep in the PICU, a special focus must be made on this vulnerable
population. Many adult studies have focused on the effects of mechanical ventilation on sleep using polysomnography, demonstrating marked differences between the mechanically ventilated and spontaneously breathing patients.\textsuperscript{31,62} As mechanically ventilated patients spend a disproportionate amount of time in stage 1 sleep compared to the spontaneously breathing patient it is important to note that mechanically ventilated patients have the influence of an endotracheal or tracheostomy tube in addition to the other interventions (e.g., sedative medications, pulmonary toilet) from care providers.\textsuperscript{36,37} As a result, it is difficult to assess the true interplay between mechanical ventilation and sleep in the critically ill.

Mechanical ventilation modes may also have an effect on sleep. The irregularities in respiration and heart rate and the accompanying paralysis of respiratory muscles excepting the diaphragm during REM sleep may further influence mechanical ventilation and patient-ventilator synchrony.\textsuperscript{31} Studies in adults have demonstrated that sleep fragmentation is more frequent with pressure support ventilation, and sleep efficiency is higher with assist control ventilation.\textsuperscript{34,62} Mechanically ventilated patients demonstrate more disruption of the natural diurnal fluctuation of 6-sulfatoxymelatonin and a decrease in excretion of the metabolite when compared to the spontaneously breathing patient.\textsuperscript{63} Circadian fluctuation of melatonin can be completely abolished, but may not correspond to the level of sedation measured by a BIS monitor or sedation agitation scale, suggesting that sedative medications may play a greater role in circadian rhythmicity.\textsuperscript{64}

Although the effects of sedative and analgesic medications on sedation depth have been given much attention, little is known of their effects on sleep in the critically ill population, particularly in children.\textsuperscript{65} For example, benzodiazepines are known to increase
sleep efficiency and duration while decreasing sleep latency and awakenings. Yet, benzodiazepines have been observed to decrease and suppress REM and slow wave sleep, the most restorative components of the sleep cycle. In addition, benzodiazepines decrease EEG frequency and amplitude at high doses and increase cortical EEG frequency at low doses. The definition of high and low doses of these medications in children is complex given the plasticity of the developing brain and the wide range of ages and doses used in these critically ill children. Continuously changing dosing regimens add another confounding factor to the influence of mechanical ventilation, sedation and environmental stimuli on sleep architecture in the critically ill child.

Before strategies to improve sleep quality can begin in critically ill children, pediatric intensivists must begin to understand the physiology of normal sleep and the effect of sedative management on sleep. The majority of children in the ICU setting who require sedation are intubated; therefore a clear distinction between sleep and sedation becomes important. Sedation can be a form of augmented or artificial sleep, but it can also be used to define a patient’s level of unresponsiveness, or level of sedation, a complex interplay.

Challenges in PICU Sleep Research

Given the data summarized and the growing evidence for the role of sleep as a potential modulator of outcomes in critically ill adults, there is a great need for increased sleep research in the PICU, where each patient is undergoing active neurocognitive development. The call for increased research is not without significant challenges. First, there is the challenge of measuring sleep in a complex and uncontrolled environment. In addition to varying ages and developmental levels, the potential confounding of each
child’s individual illness, severity, medication exposures and external environment need to be adequately considered. Though some of these factors (e.g., noise, light, and medications) can be measured and accounted for, it is the effect of the child’s critical illness on the sleep process that is unknown. Added to the complex and heterogeneous milieu of the critically ill child are the effects of various medications (e.g., sedatives) on the neurobiology of the sleep process. Objective measurement of sleep in the PICU setting is ideal, utilizing the gold standard of polysomnography, but this approach has several operational limitations. Equipment needed for polysomnography is expensive and cumbersome and may be viewed by care providers as interfering with care of critically ill children. Parents may be reluctant to consent to non-therapeutic assessments which involve application of additional diagnostic sensors. In addition, to understand the sleep process of a child in the PICU, more than 24 hours of continuous recordings are likely required given that sleep may occur any time during the day and total sleep time during the night may not necessarily reflect a child’s experience. Studies that require extended monitoring periods are challenging particularly because critical illness increases the risk of sensor loss leading to missing data. Actigraphy, an alternative and simpler option given its ease of implementation and non-invasive nature, has not been validated in the ICU population, and results can be affected by movement not initiated by the child, such as routine nursing care. Furthermore, actigraphy offers no information about sleep quality in a sedated child, which is a compelling question in this population.

Aside from implementation of the sleep assessment tools, specifically polysomnography, there are significant challenges in the analysis of the data obtained. The electroencephalogram of a critically ill child may be confounded by the derangements of
their critical illness, in addition to the neurologic effects of medications administered. Neuromuscular blockade limits polysomnography given the inability to record muscle activity. Children add the additional layer of variability in normative sleep depending on age. Given these factors, traditional sleep staging may not be appropriate in the critically ill population.

**Future Directions**

This review has synthesized the available body of evidence in sleep in critically ill children admitted to the PICU and highlighted many of the confounders and challenges associated with research in this patient population. The role of sleep as a possible modulator of outcomes in these children needs to be investigated in a systematic fashion in order to understand the complex neurobiology at play. Given that there are a limited number of objective assessment tools available for use in the PICU setting, it is imperative that these are implemented in a rigorous fashion to obtain the most valid information possible. Although polysomnography and specifically the sleep EEG may be affected by independent factors such as critical illness, the variables that may prove to be the most dependent are dose and duration of sedative and analgesic medications. If a critically ill child’s sleep is adversely affected by centrally acting medications and these medications are being perhaps utilized to induce sleep, there is a clear need for developing methods for sleep optimization in the PICU. The potential effects of decreased REM sleep on autonomic function, inflammation and immunity present multiple avenues of future investigation. Modalities that may help improve the sleep-wake cycle in the PICU may include non-invasive, non-pharmacologic approaches such as earplugs, noise reduction protocols, lighting optimization, and pharmacologic approaches including melatonin. Although these preventative and treatment approaches may be viewed as simple and
inexpensive to implement, there is a major culture change that must occur in the pediatric critical care community to maintain these approaches. Scientific and clinical evidence is imperative to demonstrate that optimizing sleep in critically ill children can reduce morbidity through decreases in sedative medications, neuroinflammation, and hospital length of stay. Characterizing sleep and understanding the biology of circadian rhythmicity in critically ill children are possible avenues for research, using EEG, actigraphy, and biomarkers, in addition to long-term follow-up of neurodevelopmental outcomes. Finding the optimal balance between analgesia, anxiolysis and sleep is integral to the care of critically ill children in the PICU.
CHAPTER 2

Sedation, Sleep Promotion, and Delirium Screening Practices in the Care of Mechanically Ventilated Children: A wake up call for the pediatric critical care community$^{14}$

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INTRODUCTION

Optimal sedation management is an integral component of the comprehensive medical care of a mechanically ventilated child. The heterogeneity in ages and diagnoses in the pediatric intensive care unit (PICU) can create particular challenges in sedation of intubated children, with a myriad of physiologic considerations for each sedative or analgesic medication administered in a given clinical situation. Adequate sedation and analgesia is required for the comfort and safety of the child, as well as to promote patient-ventilator synchrony. The frequent noise and bright lights of the PICU environment and the recurrent interventions by the medical care team add to the stressors that a child experiences when critically ill, and unlike adults, many children cannot cooperate with or understand the need for medical instrumentation and interventions. These factors combined with the development of physiologic tolerance often lead to a cycle of increasing sedative and analgesic medications to maintain a child’s comfort and safety and improve sleep.

Most medications used for sedation and analgesia in the PICU, commonly opioids and benzodiazepines, are known to decrease slow-wave sleep and rapid-eye movement sleep (REM sleep). In addition, benzodiazepines are a strong independent risk factor for the development of delirium, which is common in adults treated with these medications. ICU delirium increases morbidity and mortality in critically ill adults, and emerging evidence suggests that delirium may be clinically relevant in critically ill children. Normal sleep-wake homeostasis has a critical role in immunity and thermoregulation, as well as prevention of delirium and the development of a catabolic state, which may influence the rate of recovery from critical illness. In addition to the clinical variability within the PICU patient population itself, approaches to sedation and analgesia of mechanically
ventilated children vary across PICUs and pediatric intensivists. There is no universally accepted goal-directed approach to sedation of mechanically ventilated children. The sedative and analgesic medications available for use in the PICU can vary from hospital to hospital, and choice of specific medications may differ in different areas of the world. As care providers change over the course of a child’s PICU admission, variations in sedation goals and approaches may be introduced from both physicians and nurses. In addition to the pharmacologic management of sedation and analgesia, many non-pharmacologic adjunctive approaches have been described in adult and pediatric critical care literature, including sleep promotion and early delirium recognition. To characterize the current state of practice internationally, we designed a detailed survey to describe the experiences and approaches of pediatric intensivists with regard to sedative availability, preferences and strategies, PICU environment, sleep optimization, and delirium recognition and treatment. We hypothesized that there is significant variability in the approaches to sedation of the child requiring long-term mechanical ventilation, and predict that sleep promotion and delirium screening are not routinely practiced in PICUs internationally.
METHODS

On July 5, 2012, the World Federation of Pediatric Intensive and Critical Care Societies (WFPICCS) invited all member societies to send the electronic survey to their membership. The survey was administered by Survey Monkey (www.surveymonkey.com) and was also made available by a direct link from the WFPICCS internet homepage. In September 2012, a reminder was sent in the WFPICCS newsletter. All participants were informed that individual responses would remain anonymous and confidential. The survey closed to further responses on January 15, 2013. Survey questions and topics were developed by content experts in the fields of pediatric critical care medicine and pediatric anesthesiology, and the survey was pilot tested among multiple pediatric intensivists for feedback regarding question clarity and the survey interface. WFPICCS leadership and the Johns Hopkins Institutional Review Board approved the study and final survey for distribution.

The survey was in English and consisted of 40 questions divided into four sections by concept. The first section ascertained particular demographics, including the size and type of hospital, number of years the intensivist had been in practice, and if the institution had a fellowship training program. Respondents were also asked about the physical layout of their PICU. The second section asked about medications available in the PICU, whether any sedative or analgesic agents had restrictions, and their preferences in medication for children who they anticipated to require mechanical ventilation longer than 24 hours. The third section had questions regarding sedation protocols/algorithms used in their PICU and methods used for sedation assessment. The last section gathered information about PICU sleep promotion and delirium screening practices. Questions were closed-ended, multiple-
choice design, but many included an “other” option for a free-text response.

Data were analyzed with the statistical software package STATA version 11.0 (StataCorp LP, College Station, TX). Characteristics of respondents were summarized with frequencies and proportions for categorical variables and means and standard deviations for continuous variables. Medication preferences and availability were compared across intensivist demographics and other survey responses by using chi-square analysis.

RESULTS

Intensivist and PICU Demographics

Demographic data for intensivist respondents and the PICU settings are shown in Table 2.1. In total, 341 respondents participated in the electronic survey through the e-mail link or online invitation. The majority of attending physician respondents (81%) had more than five years of experience caring for critically ill

Table 2.1: Pediatric Intensivist and ICU demographics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of Respondents (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>184 (53)</td>
</tr>
<tr>
<td>Age in years</td>
<td></td>
</tr>
<tr>
<td>21-29</td>
<td>15 (4)</td>
</tr>
<tr>
<td>30-39</td>
<td>99 (29)</td>
</tr>
<tr>
<td>40-49</td>
<td>113 (33)</td>
</tr>
<tr>
<td>50-59</td>
<td>103 (30)</td>
</tr>
<tr>
<td>≥ 60</td>
<td>16 (5)</td>
</tr>
<tr>
<td>Care for both children and adults in ICU</td>
<td>45 (13)</td>
</tr>
<tr>
<td>Years of practice</td>
<td></td>
</tr>
<tr>
<td>0-5</td>
<td>65 (19)</td>
</tr>
<tr>
<td>6-10</td>
<td>79 (24)</td>
</tr>
<tr>
<td>11-15</td>
<td>58 (17)</td>
</tr>
<tr>
<td>16-20</td>
<td>45 (13)</td>
</tr>
<tr>
<td>&gt; 20</td>
<td>80 (23)</td>
</tr>
<tr>
<td>Position</td>
<td></td>
</tr>
<tr>
<td>Attending physician</td>
<td>223 (70)</td>
</tr>
<tr>
<td>Critical care nurse</td>
<td>67 (21)</td>
</tr>
<tr>
<td>Fellow</td>
<td>20 (6)</td>
</tr>
<tr>
<td>Nurse practitioner</td>
<td>8 (3)</td>
</tr>
<tr>
<td>Fellowship training program in PICU</td>
<td>186 (54)</td>
</tr>
<tr>
<td>No. of PICU beds</td>
<td>176 (67 ± 12.1)</td>
</tr>
<tr>
<td>Mechanically ventilated children</td>
<td></td>
</tr>
<tr>
<td>&lt; 20%</td>
<td>50 (15)</td>
</tr>
<tr>
<td>20-40%</td>
<td>145 (45)</td>
</tr>
<tr>
<td>41-70%</td>
<td>101 (31)</td>
</tr>
<tr>
<td>&gt; 70%</td>
<td>28 (9)</td>
</tr>
<tr>
<td>Practice setting</td>
<td></td>
</tr>
<tr>
<td>Academic/university</td>
<td>192 (56)</td>
</tr>
<tr>
<td>Private/community</td>
<td>39 (11)</td>
</tr>
<tr>
<td>Teaching hospital/nonuniversity</td>
<td>112 (33)</td>
</tr>
</tbody>
</table>

Figure 2.1: Continents represented by survey participants
children, and most respondents (56%) reported their primary practice setting as an academic university. Across the sample, the PICUs were reported to accommodate an average of 17.6 (SD, 12.1) critically ill children. As shown in Figure 2.1, North America was the continent with the largest proportion of respondents (70%), followed by Europe (14%) and Asia (9%).

**Sedation Monitoring of Mechanically Ventilated Children**

Written sedation protocols with treatment algorithms were in place in only 27% of the respondents’ PICUs, and of those, 52% of the sample reported that the protocols were physician-driven (Table 2.2). North American respondents reported a higher percentage of nursing-driven protocols (58%; p=0.02). A physician-driven protocol was defined as one

<table>
<thead>
<tr>
<th>Table 2.2: Pediatric Intensive Care Unit Sedation Scoring and Protocols</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Survey Item</strong></td>
</tr>
<tr>
<td>Presence of unit-wide written sedation protocol for all mechanically ventilated patients (n = 322 respondents)</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>Driver of unit sedation protocol if present (n = 84 respondents)</td>
</tr>
<tr>
<td>Nurses</td>
</tr>
<tr>
<td>Physicians</td>
</tr>
<tr>
<td>Combination</td>
</tr>
<tr>
<td>Unit-wide sedation scoring system used for mechanically ventilated patients (n = 310 respondents)</td>
</tr>
<tr>
<td>No scoring system</td>
</tr>
<tr>
<td>COMFORT</td>
</tr>
<tr>
<td>Richmond Agitation-Sedation Scale</td>
</tr>
<tr>
<td>State Behavioral Scale</td>
</tr>
<tr>
<td>Ramsay</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>Frequency of sedation scoring system use for daily patient care, i.e., goal setting on rounds (n = 220 respondents)</td>
</tr>
<tr>
<td>Always or usually</td>
</tr>
<tr>
<td>Frequency of bispectral index monitoring for depth of sedation (n = 317 respondents)</td>
</tr>
<tr>
<td>Always or usually</td>
</tr>
<tr>
<td>Level of satisfaction with the state of sedation practice in primary practice setting (n = 291 respondents)</td>
</tr>
<tr>
<td>Satisfied</td>
</tr>
<tr>
<td>Neutral</td>
</tr>
<tr>
<td>Dissatisfied</td>
</tr>
</tbody>
</table>
from which the physician directs all medication and dosing changes, in contrast to a nursing-driven protocol where the nurse has the ability to independently titrate medications to the desired level of sedation, within set limits as defined by an initial physician order.

Sedation scoring systems, defined as a tool utilized to assess depth of sedation and set patient-specific goals for sedation, were in place in 70% of the respondents’ PICUs, but only 42% stated that they were used as a routine part of daily rounds and patient-care goals. Eleven percent reported that although a sedation scoring system existed in their PICU, it was never used. Most commonly used sedation scoring scales included COMFORT (37%), State Behavioral Scale (SBS; 24%), and Ramsay (18%). While 72% reported that the bispectral index monitor (BIS) was not available in their unit, 4% reported consistent use of this modality for mechanically ventilated children.

**Sedative-Analgesic Medication Preference**

In response to a question regarding preferred initial sedative regimen for a child with primary respiratory failure, 72% of survey participants chose a combination of opioid and benzodiazepine, whereas 12% preferred an opioid alone, 8% preferred using an opioid with dexmedetomidine, and only 1% used a combination of benzodiazepine and dexmedetomidine. Less than 1% used dexmedetomidine alone when initiating a sedation regimen. Interestingly, 2% reported the routine use of propofol in the initial sedation regimen, and this was always in combination with an opioid and benzodiazepine. Similarly, 2% used ketamine routinely along with an opioid and benzodiazepine.

Most respondents (66%) preferred fentanyl as the opioid for analgesia during sedation, whereas 28% preferred morphine, although respondents from countries outside of North America demonstrated a more even preference in comparison—42% for fentanyl and
46% for morphine (Fig. 2.2; p<0.001). The majority (93%) chooses to administer opioid as a maintenance infusion when it is used as part of a sedation regimen. Midazolam was the

**Figure 2.2: Preferred opioid for analgesia in mechanically ventilated children (%)**: p<0.001 when comparing opioid preference between North America and all other countries.

**Figure 2.3: Preferred benzodiazepine for sedation in mechanically ventilated children (%)**: p<0.001 when comparing benzodiazepine preference between North America and all other countries.
benzodiazepine of choice for most respondents (86%; Fig. 2.3) followed by lorazepam (12%).

Similar to opioid administration, most intensivists initiate benzodiazepines as a maintenance infusion (80%), with equal proportions choosing scheduled interval dosing and as-needed dosing (10% each). Propofol and dexmedetomidine were the most commonly restricted drugs for sedation in PICUs. Of 246 respondents who have dexmedetomidine available at their institution, 25% stated they have either duration or indication restrictions.

**PICU Layout, Sleep Promotion, and Delirium Screening**

As shown in Figure 2.4, the majority of North American respondents (62%) reported that their PICU consists of all private rooms, in contrast to 11% for all other countries (p<0.001).

*Figure 2.4: Delirium screening, sleep promotion, and pediatric intensive care unit layout (%). p-value for comparison between North America and all other countries *p=0.01 **p <0.001*
Seventy-seven percent of all respondents reported that all patient rooms had windows, and 4% reported no windows in any of the patient rooms. A small proportion reported the presence of unit protocols to optimize noise (16%) and light exposure (9%) for sleep promotion. Of those surveyed, 78% had never observed earplug use in their PICU, and 65% had never observed use of eye masks. Of those who had observed eye mask or earplug use, 5% and less than 1%, respectively, reported consistent use for all mechanically ventilated children.

Seventy-one percent of respondents reported that their unit does not perform routine delirium screening, and only 2% reported that delirium screening is performed on every child at least once per shift. Of the respondents who reported frequent or occasional delirium screening, the only validated delirium screening tool reported was the Pediatric Confusion Assessment Method-ICU (pCAM-ICU, n=6). Multiple respondents listed withdrawal assessment tools such as the WAT-1, SOS (Sophia Observation withdrawal Symptoms scale) and Finnegan as their method of delirium screening. Four respondents reported that their PICU utilizes a unit-specific delirium screening tool.

**Free-text responses**

Fifty-four respondents provided detailed comments regarding sedation of mechanically ventilated children. One common theme was frustration over inconsistencies in sedation goals. Many intensivists voiced concerns that bedside nurses often want a child to be immobile, without any signs of awareness, leading to oversedation. Several expressed interest in pursuing delirium education due to concerns that agitated, critically ill children may be receiving additional doses of psychoactive medications instead of therapy for what may actually be undiagnosed delirium.
DISCUSSION

Our study is the first international survey to characterize sedation, sleep promotion, and delirium screening practices in the pediatric population. We found that despite the need for, and near universal application of, pharmacologic sedation in the PICU, a minority of programs have formalized methods of sedation assessment, drug choice and delivery, or therapeutic goal direction. Unlike the adult and neonatal ICUs, sleep promotion is exceedingly uncommon in the PICU. Finally, the interplay between sedation, sleep, and ICU delirium is not prioritized in PICU management, even though delirium prevention with nonpharmacologic behavioral interventions including sleep promotion has become a major therapeutic initiative in the care of critically ill adults. Thus, we found significant variation in practice, with many opportunities for future study and therapeutic intervention in a population undergoing active neurocognitive development.

Our finding that less than one-third of respondents utilize a standardized, unit-wide, written sedation protocol for mechanically ventilated children is different from that of a previous survey of PICU fellowship programs in which 66% reported the use of a written sedation policy. This difference is likely due to the survey questions themselves, as we defined the written sedation protocol to be a specific algorithm that is consistently used in the PICU, in contrast to a written sedation policy, which may be more general and used as a guideline. The current study was an international survey that encompassed teaching and non-teaching hospitals, whereas the previous study was limited to only American fellowship program directors with a 59% response rate. Nevertheless, we found that even in PICUs with fellowship programs, the minority (35%) utilized standardized sedation protocols, and
sub-group analysis demonstrated no significant difference in the use of sedation protocols 
(p=0.73) and sedation scoring (p=0.13) between private and university-based respondents.

A growing body of literature has demonstrated the benefit of standardized sedation 
treatment algorithms in critically ill adults. Sedation protocols in the adult ICU have been 
shown to decrease days of mechanical ventilation, reduce hospital length of stay, and 
promote earlier ambulation. Perhaps most importantly, it reduces the incidence and severity 
of delirium, a negative consequence of critical care.80-82 A small number of published studies 
suggest that these benefits extend to pediatrics, and a large multicenter randomized 
controlled trial is ongoing.83-85

Much to our surprise, we found that most intensivists do not utilize formalized 
methods of sedation assessment to guide drug choice and delivery, although several 
validated measures exist. The COMFORT score continues to be the most commonly used 
scoring system overall, although North American respondents report increased usage of the 
SBS and Richmond Agitation-Sedation Scale (RASS) compared to that in a previous U.S. 
survey.79 The SBS was designed and validated in 2006 to define the sedation-agitation 
continuum in critically ill infants and children to guide goal-directed therapy.86 RASS, the 
sedation scale most commonly used in critically ill adults, has not been validated in critically 
ill children.87

Even when respondents stated there was a specific sedation scoring system 
designated in their PICU, the majority do not consistently use them to set goals for sedation 
management on a day-to-day basis. This finding is concerning because sedation is not one-
size-fits-all. Rather, it requires titration to effect. Thus, the failure to measure the level of 
sedation and to actually use these measures to guide and titrate therapy may result in
oversedation or undersedation, both of which have the potential to produce significant patient morbidity and mortality. Within a complex team framework of nurses, residents, nurse practitioners, fellows, respiratory therapists, and attendings who provide and manage sedation, the use of a streamlined sedation scoring tool in conjunction with a goal-directed treatment algorithm is imperative to facilitate consistent communication and optimal therapy.

A small proportion of care providers utilize automated tools such as the BIS for bedside monitoring of sedation. Initially designed to decrease the incidence of intraoperative awareness during general anesthesia in adults, the BIS monitor uses an algorithmic analysis of the electroencephalogram (EEG) to provide a single, dimensionless number to guide titration of anesthetic agents. Because the algorithm of the BIS monitor is derived from adult EEG data and the EEG of children changes as the brain matures, it remains controversial whether BIS can be generalized to infants and children in the operating room and ICU settings.

We found substantial differences in how sedation is provided, particularly in regard to drug preferences and delivery. Although most providers choose a combination of opioid and benzodiazepine as their initial regimen for sedation and analgesia, many opt for opioid alone. Opioids are primarily analgesics that produce sedation and either euphoria or dysphoria as wanted or unwanted side effects. Opioid alone may be chosen by PICU providers because they are less likely to adversely affect hemodynamics and are perceived as short-acting, an erroneous notion given the increased context-sensitive half-life when administered as a continuous infusion. This is especially true for fentanyl, now the most commonly prescribed opioid in North American PICUs, supplanting morphine. Opioid
use as a primary sedative agent in the PICU warrants concern due to a lack of anxiolytic and amnestic properties at low doses, leading to dose escalation to achieve the desired level of sedation and increased risk of tolerance and withdrawal. In addition, the child receiving opioid as a primary sedative is exposed to an increased risk of all the adverse effects associated with both long-term and high-dose opioid use, including gastrointestinal dysmotility that may lead to feeding intolerance during a period when optimal nutrition is crucial.

Fentanyl may also be chosen in the PICU due its hepatic clearance, facilitating use in children who have renal insufficiency. Although data are limited, the choice of fentanyl over morphine in the PICU may also be influenced by morphine’s association with histamine release, which may concern care providers when potential hypotension is an undesirable risk. Morphine is the most inexpensive opioid available. Emerging evidence has shown that when used as an infusion it is more favorable than fentanyl with regard to need for dose escalation, incidence of withdrawal, and length of hospital stay. Opioid tolerance and withdrawal pose major challenges for all providers in the PICU, and the predilection for fentanyl may be a trend that needs further evaluation through a randomized controlled trial.

Midazolam is the benzodiazepine most commonly used for sedation in mechanically ventilated children. Benzodiazepines are GABA(A) agonists that are sedative/hypnotic/amnestic with little to no analgesic property. Midazolam has a short plasma half-life, rapid onset, and is amenable to titration as a continuous infusion. Although benzodiazepines provide the benefits of amnesia, anxiolysis, and sedation, one major disadvantage is the increased risk of delirium with prolonged administration.
guidelines for long-term sedation recommend lorazepam, based on high-grade evidence that lorazepam infusions require fewer dosage adjustments, require less time to achieve adequate sedation, and provide more predictability for awakening times and time to extubation compared to midazolam.\textsuperscript{80,100,101} Midazolam pharmacokinetics and pharmacodynamics have been shown to change with age, leading to significant inter-individual variability.\textsuperscript{92,102,103} To date, direct comparisons of midazolam and lorazepam have not been made in the PICU population, and data are limited on the use of diazepam in the ICU setting.\textsuperscript{104} Consistent with other ICU surveys, we found that diazepam is rarely used as a first-line sedative agent in mechanically ventilated children.\textsuperscript{79,104,105}

Dexmedetomidine, an alpha-2 adrenergic agonist with analgesic, sedative, and anxiolytic properties, has emerged over the last decade as an attractive option for sedation of critically ill children because of its favorable hemodynamic profile and preservation of respiratory function.\textsuperscript{106} Compared to all sedatives and analgesics available, dexmedetomidine has been shown to induce an EEG pattern with the most similarities to natural sleep.\textsuperscript{107-109} Most respondents did not report restrictions on the use of dexmedetomidine in their units, yet only 10\% include it as part of the initial regimen. Although the currently patent-protected dexmedetomidine is more expensive than the commonly used benzodiazepines, studies have demonstrated comparatively less cost because time to extubation and ICU and hospital length of stay are reduced.\textsuperscript{110} Dexmedetomidine has been associated with decreased opioid and benzodiazepine administration in critically ill children, as well as decreased inotropic support.\textsuperscript{111-113} Despite these favorable qualities, anecdotal evidence suggests that long-term use of dexmedetomidine infusions can result in physiologic tolerance, withdrawal, and adrenal
insufficiency.\textsuperscript{114-117} Therefore, additional study is warranted.

Our survey demonstrates a clear preference for continuous infusions over scheduled, intermittent dosing of sedatives and analgesics during mechanical ventilation. Continuous infusions are advantageous because they are titratable, maintain steady-state plasma drug levels, decrease line breaks and infection risk, and are less labor-intensive for a busy critical care nurse. Disadvantages include potential for oversedation from drug accumulation and, perhaps more important, an increased risk for tolerance and escalation of sedative and analgesic doses.\textsuperscript{118-120} Intermittent, scheduled dosing of sedative and analgesic medications in the appropriate target population may effectively provide many of the purported benefits of sedation interruption, while exposing a child to decreased overall doses of psychoactive medications.\textsuperscript{121,122} These benefits must be considered alongside with the potential increase in nursing workload necessary to care for an awake, critically ill child.\textsuperscript{123}

Finally, this study underlines an impending and critical need for sleep promotion and delirium screening in critically ill pediatric patients. Sedatives and analgesics are often increased to improve the subjective assessment of “sleep,” yet these very medications decrease restorative sleep, leading to a vicious cycle of sleep disturbances that manifest as agitation and delirium.\textsuperscript{31} A small number of studies that have objectively evaluated sleep in critically ill children have shown significant decreases in slow-wave sleep and REM sleep, which are integral to neuronal development in childhood.\textsuperscript{30} Despite the availability of proven, noninvasive, and inexpensive modalities such as earplugs and eye masks to decrease sleep interruptions during nighttime hours, such methods are rarely used in adult and pediatric ICU settings.\textsuperscript{77,124,125}

A minority of PICUs employ noise-reduction strategies to target WHO-
recommended levels of noise (<30 dBA Leq day and nighttime). Several studies have demonstrated that ICU noise levels are frequently greater than 50 dBA throughout a 24-hr period, with several intermittent peaks to >80 dBA.\textsuperscript{126,127} Private rooms provide some protection from general ICU noise and may improve the quality of patient sleep.\textsuperscript{128} Light levels are also integral to maintaining circadian rhythmicity during critical illness. Receiving exposure to natural light during the daytime and minimizing nighttime light exposure are necessary for hormonal regulation, specifically melatonin secretion, to optimize the sleep-wake cycle.\textsuperscript{12,13}

Delirium in critically ill children is emerging as an extremely important diagnosis that must be recognized by all pediatric intensivists.\textsuperscript{38,74,75,129,130} A combination of critical illness, sedative-analgesic medications, and sleep disruption place the mechanically ventilated child at increased risk for delirium. Consequences can include increased morbidity and mortality from prolonged intubation and weaning of medications. Despite the availability of validated tools for delirium screening and diagnosis, our study draws attention to a PICU culture that does not prioritize this important diagnostic consideration. The low prevalence of PICU delirium screening may be related to multiple factors, including knowledge gaps surrounding the importance of delirium in critically ill children, availability of resources to perform unit-wide screening, and accessibility of therapies for treatment of delirium. Several respondents listed withdrawal screening tools such as the SOS and WAT-1 as their method of delirium screening, highlighting the need for widespread delirium education. Under-recognition of delirium may also be secondary to the reluctance of intensivists to engage the pediatric neuropsychiatrist as yet another consultation team, whose recommendations for nonpharmacologic and pharmacologic
therapies may seem challenging for an already burdened patient, family and PICU team.

Most survey results were similar across respondents internationally, although there were some interesting differences. The preference for fentanyl as the first-line opioid is higher in North America compared to all other countries, which may be due to differences in cost considerations or simply PICU culture that has been propagated based on fentanyl’s purported advantages over morphine. North American respondents also reported a higher percentage of nursing-driven sedation protocols, which may reflect an increasing focus on nursing autonomy in patient care as a predictor of greater job satisfaction and improved patient care within a team framework.\textsuperscript{131-133}

The current study has some notable limitations. First, the respondents may not be representative of PICU practitioners internationally, as the 341 respondents are a small proportion of all intensivists caring for critically ill children. It is also possible that, as a result of “chain sampling,” several respondents work in the same PICU, which may lead to bias; other PICUs may not have been represented if no staff member received the survey link. Second, a respondent’s practice may differ significantly from others in their center, potentially decreasing generalizability. Additionally, there was a higher proportion of responses from North American intensivists, which may decrease the generalizability of data on the international level. Finally, another limitation stems from questions the survey did not ask. For example, issues such as sedation interruption, rotation, weaning practices, or use of neuromuscular blockade were not included in the survey. Nevertheless, our study delineates the international heterogeneity of practice and differing approaches to sedation, sleep, and delirium in critically ill children.
CONCLUSION

Despite the need for, and near universal application of, pharmacologic sedation in the PICU, only a minority of intensivists utilize formalized methods of sedation assessment, drug choice and delivery, or even therapeutic goal direction. This study highlights the heterogeneity in sedation practices among pediatric intensivists, as well as a paucity of sleep promotion and delirium screening in PICUs worldwide. Thus, numerous opportunities exist for future study and therapeutic intervention in a population undergoing active neurocognitive development.
CHAPTER 3

Temporal Characteristics of the Sleep EEG Power Spectrum in Critically Ill Children\textsuperscript{134}

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INTRODUCTION

During infancy, childhood and adolescence, the sleep experience evolves over time, reflecting ongoing neurologic maturation. Sleep plays an integral role in homeostasis of multiple organ systems, including the respiratory, cardiac, gastrointestinal, endocrine and neurologic systems. Critically ill children in the Pediatric Intensive Care Unit (PICU) are exposed to a multitude of risk factors for sleep disruption, during a time when the restorative benefits of sleep are of fundamental importance for neurocognitive development. In fact, a number of studies in children have shown that slow wave activity in the sleep electroencephalogram (EEG) is associated with high levels of synaptic density and activity, a vital component of neurologic maturation. Critically ill children are at higher risk for altered sleep-wake homeostasis resulting from not just the underlying illness but also from exposure to the PICU environment. In addition, centrally acting medications used for sedation in critically ill children are detrimental to the biology of sleep. Internationally, the most common combination of medications used for sedation of mechanically ventilated children is opioid and benzodiazepine. Thus, given the number of environmental and iatrogenic exposures in the PICU, the normal ultradian variability of sleep EEG activity is likely to be absent. However, empirical evidence on whether the temporal organization of sleep is indeed disrupted is lacking.

Sleep is traditionally assessed using visual inspection of the sleep EEG from polysomnography (PSG). Although conventional sleep staging is clinically useful for assessing sleep architecture, its use in characterizing sleep of patients admitted to the ICU is of limited value. The EEG of a critically ill child is confounded by the derangements induced by the critical illness and by the central effects of various
medications that are typically administered for sedation. Furthermore, neuromuscular blockade limits the use of PSG as muscle activity is pharmacologically inhibited. Children add an additional layer of variability in normative sleep depending on age. Given these factors, alternative methods for characterizing the sleep EEG in critically ill children are needed. Additionally, sleep may occur any time during the day or night while in the PICU, therefore assessment of a 24 hour period is necessary to capture the temporal characteristics of sleep in these patients. The objective of the current study was to characterize the sleep EEG in a sample of critically ill children without baseline neurologic disease. It was hypothesized that critically ill children will not demonstrate day-night organization of sleep and will lack the normal characteristics of the sleep EEG that are typical in healthy children.

METHODS

Study Sample

Children with respiratory failure requiring mechanical ventilation were recruited from the PICU of the Johns Hopkins Children’s Center. Each bed in the PICU is positioned adjacent to a window with adjustable shades. Patients were eligible for the study on the first day of mechanical ventilation if ventilator support was expected to continue for least 24 hours. Exclusion criteria included a history of sleep-disordered breathing (SDB), surgery within the last seven days, seizures, neurological injury and severe developmental delay. To rule out SDB, a detailed history was obtained from the parent(s) including a history of snoring. In addition, the medical record was reviewed for previous sleep studies and parents were asked to complete the Children’s Sleep Habits Questionnaire. Finally, patients were excluded if it was deemed that the monitoring would interfere with medical
care. Eligible patients underwent informed consent with a parent or legal guardian. To compare the data collected during critical illness, healthy age- and gender-matched children without central or obstructive sleep apnea (OSA) from the Tucson Children’s Assessment of Sleep Apnea (TuCASA) study were used. The TuCASA study is a community-based study aimed at assessing the prevalence of sleep apnea in children.\textsuperscript{145} OSA was defined if the respiratory disturbance index, using the 3\% desaturation criteria, was 1 or more events per hour of total sleep time. Hypopneas were scored if the magnitude of any ventilation signal decreased to below approximately 70\% of the baseline amplitude for at least 6 seconds or for 2 or more consecutive breaths. The study protocol was approved by the Institutional Review Board (IRB) on human subjects research of the Johns Hopkins University School of Medicine.

\textit{EEG Monitoring and Power Spectral Analysis}

The recording montage for the PICU patients included bilateral central and occipital EEG leads sampled at 125 Hz, right and left-sided electrooculograms (EOG) and submental electromyogram (EMG) using the Embla N7000 system (Embla, Denver, Colorado U.S.A.). The montage was accompanied by high-resolution video monitoring for assessing medical interventions (e.g., suctioning, dressing changes) and occurrence of movement or activity. The recording was continued for at least 24 hours and discontinued when the patient was extubated or at 72 hours after the initiation of data collection. Home nocturnal PSG for the healthy children in the TuCASA sample included central leads as well as bilateral EOG leads and chin EMG. Detailed methodology for the TuCASA cohort have been previously described.\textsuperscript{146} Power spectral analysis of EEG recordings from the PICU and age and gender-matched subjects was conducted using the fast Fourier transform (FFT)
in Matlab (Ver. R2014A, Matlab, Inc.). The FFT was conducted on an EEG record length of 5-s to obtain a frequency resolution of 0.2 Hz. The power content (expressed as μV^2) for each 30-s epoch of sleep was determined as the average power across the six 5-s segments of the EEG. The resulting spectral distribution from the FFT was categorized into the following frequency bands: δ (0.8 to 4.0 Hz); θ (4.1 to 8.0 Hz); α (8.1 to 13.0 Hz); β_1 (13.1 to 16.0 Hz); and β_2 (16.1 to 20.0 Hz). The power in each frequency bandwidth was expressed as absolute power in each 30-s epoch of sleep. Frequencies < 0.8 Hz were excluded to remove the effects of low-frequency artifacts (e.g., sweating and respiration).

**Statistical Analysis**

Data are summarized as means ± standard deviation or medians (interquartile range) as appropriate. Differences in mean nocturnal EEG power between the PICU patients and matched healthy children were tested using the Wilcoxon signed-rank test given the small sample size and skewed distribution of EEG spectral power. Matching was performed using the ccmatch command in Stata 12 (StatacorpLP; College Station, TX). The nocturnal period was defined as the time from sleep onset for healthy children, and the hours of 2200-0600 for the PICU patients. Given well-established temporal patterns in the EEG spectra during the night in healthy children, analyses were also undertaken to characterize temporal patterns of EEG spectral power for each frequency band using a Locally Weighted Scatterplot Smoothing (LOWESS) spline technique for both the PICU patients and healthy children. The LOWESS method depicts the association between two variables (i.e. EEG δ power activity vs. time) using a smoothing coefficient to provide a robust fit to the data without eliminating changes in slope over time. Statistical tests were
2-sided, and a p-value less than 0.05 was defined as statistically significant. All calculations were performed in Stata 12 (StatacorpLP; College Station, TX).

RESULTS

Eight critically ill PICU patients with respiratory failure (median age 8 years, range 6-16 years) underwent limited montage EEG monitoring. Each patient was receiving a continuous background infusion of both opioid and benzodiazepine at the time of enrollment and monitoring, with a goal State Behavioral Score between -1 and 1. Demographic data and diagnoses for the study sample are shown in Table 3.1. Two of the eight patients were receiving a low-dose infusion of one sympathomimetic agent for hemodynamic support. Patient D received dopamine at 5 mcg/kg/hr while Patient F received phenylephrine at 2 mcg/kg/hr during the 24-hr EEG recording period. Although the full 24-h period was recorded in all patients, only 18 hours were included in two patients due to clinical instability. However, EEG power spectral analysis included the recordings

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Morphine Dose (mg/kg/day)*</th>
<th>Midazolam Dose (mg/kg/day)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Female</td>
<td>5</td>
<td>Pneumonia with ARDS</td>
<td>2.4</td>
<td>0.1</td>
</tr>
<tr>
<td>B</td>
<td>Male</td>
<td>5</td>
<td>Pneumonia with ARDS</td>
<td>2.3</td>
<td>0.2</td>
</tr>
<tr>
<td>C</td>
<td>Male</td>
<td>6</td>
<td>CVID with ARDS</td>
<td>2.6</td>
<td>3.2</td>
</tr>
<tr>
<td>D</td>
<td>Female</td>
<td>7</td>
<td>Sepsis and ARDS</td>
<td>1.3</td>
<td>0.1</td>
</tr>
<tr>
<td>E</td>
<td>Male</td>
<td>9</td>
<td>HLH with ARDS</td>
<td>0.4</td>
<td>0.1</td>
</tr>
<tr>
<td>F</td>
<td>Female</td>
<td>13</td>
<td>MAS with ARDS</td>
<td>0.8</td>
<td>0.04</td>
</tr>
<tr>
<td>G</td>
<td>Female</td>
<td>15</td>
<td>Pneumonia with ARDS</td>
<td>3.4</td>
<td>0.4</td>
</tr>
<tr>
<td>H</td>
<td>Male</td>
<td>16</td>
<td>Sarcoma with ARDS</td>
<td>6.3</td>
<td>2.5</td>
</tr>
</tbody>
</table>

Opioid and benzodiazepine dose received during 24-h sleep EEG recording period in morphine and midazolam equivalents. ARDS, acute respiratory distress syndrome; CVID, common variable immunodeficiency; HLH, hemophagocytic lymphohistiocytosis; MAS, macrophage activation syndrome.
Table 3.2: Average EEG spectral power during nocturnal period, expressed as μV² (mean ± SD).

<table>
<thead>
<tr>
<th>EEG Frequency Band</th>
<th>Healthy Children</th>
<th>PICU Patients</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>δ (0.8–3.9 Hz)</td>
<td>203.1 ± 210.5</td>
<td>174.7 ± 201.5</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>θ (4.0–7.9 Hz)</td>
<td>30.7 ± 23.9</td>
<td>5.6 ± 13.1</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>α (8.0–11.9 Hz)</td>
<td>6.6 ± 4.9</td>
<td>1.6 ± 4.8</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>β₁ (12.0–15.9 Hz)</td>
<td>0.8 ± 1.1</td>
<td>0.6 ± 1.74</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>β₂ (16.0–20. Hz)</td>
<td>1.1 ± 2.4</td>
<td>1.2 ± 3.4</td>
<td>0.017</td>
</tr>
</tbody>
</table>

EEG data from the first eight consecutive nocturnal hours (10:00 PM – 6:00 AM) were analyzed for each PICU patient and compared to nocturnal EEG of an age and gender-matched healthy child. The average EEG power in each of the frequency bands (i.e., δ, θ, α, β₁, β₂) was lower in the PICU patients compared to healthy patients (Table 3.2). Furthermore, unlike healthy children, PICU patients did not demonstrate the characteristic temporal EEG patterns in δ or θ power spectral bands during the night as evident in the healthy children. As shown in Figure 3.1, healthy children demonstrated the typical ultradian pattern in EEG activity with an increase in δ power during NREM sleep.

Figure 3.1: Nocturnal EEG δ power in PICU patients and age and gender-matched healthy children.

Values plotted were derived using a Loess smoothing function.
particularly in the first third of the night. Moreover, healthy children demonstrated a
decline in overall EEG δ power over the course of the night, while PICU patients
demonstrate little variability as evidenced by their flattened profiles. Subject A’s profile
differed from the other PICU patients in that the baseline delta activity was maintained at
a high level throughout the recording period. All other patients had peaks in EEG δ power
well below 500 µV².

Alterations in the nocturnal EEG θ power profile (4–7 Hz) were similar to the
findings for δ power, with lack of an ultradian rhythm during the night (Figure 3.2).
Healthy children demonstrated the expected temporal variability in EEG θ power, which
gradually declined in the latter part of the night. In contrast, θ power in the EEG was at
very low levels and did not display temporal variability in PICU patients. Mean absolute θ
power in the EEG in the healthy children was 30.7 μV², while mean EEG θ power in PICU
patients was 5.6 μV² (p < 0.001). Given that critically ill children in the PICU may

Figure 3.2: Nocturnal EEG θ power in PICU patients and age and gender-matched
healthy children.
experience sleep during any part of the day or night, EEG δ and θ power were evaluated in the 6 children with complete 24-h data. As seen in Figure 3.3, there was evidence of oscillations in EEG δ power over the 24-h period for PICU patients, most obvious for Patient G. In contrast, with the exception of Patients A and E, most PICU patients did not demonstrate ultradian variability in EEG θ power (Figure 3.4). Mean EEG δ and θ power of PICU patients were compared between the day (07:00 through 19:00) and night (19:00 through 07:00) hours. Mean EEG δ power was higher during the day (237 ± 243 μV²) than night (211 ± 223 μV²; p < 0.001). Similarly, EEG θ power during the day was higher than the night (10 ± 31 vs. 8 ± 17 μV², p < 0.001). Among PICU patients, nocturnal δ and θ power was not associated with cumulative nocturnal morphine (p = 0.4 and 0.5, respectively) or midazolam equivalents (p = 0.6 and 0.3, respectively). There was also no significant association among the PICU patients between cumulative 24-h morphine and midazolam equivalents and mean 24-h δ and θ power.

Figure 3.3/3.4: Twenty-four hour EEG δ and θ power in PICU patients.
DISCUSSION

The results of this study demonstrate that, over a 24-hour period, there are significant differences in the EEG power spectra between critically ill and healthy children. Critically ill children have no day-night organization of sleep and exhibit decreases in slow wave activity (i.e., δ power) during the nighttime hours when compared to healthy children. Although sleep has previously been investigated in PICU patients, available studies have relied on subjective assessment with visual scoring of the polysomnogram. In a recent systematic review on sleep in critically ill children, nine studies were identified, with four resulting from the same randomized controlled trial. Of the studies which focused on critically ill children and utilized objective measurements of sleep, common findings included decreases in REM sleep and slow wave sleep, with evidence of frequent nocturnal arousals. The findings of the current study add to the existing body of evidence by providing insights regarding the temporal trends of sleep EEG power spectral activity in critically ill children without baseline neurologic disease who are admitted with respiratory failure.

Although the true function of sleep remains elusive, a great deal is now known regarding the physiologic effects and consequences of altered sleep including effects on protein synthesis, cellular and humoral immunity and increased catabolism. Much research has been devoted to characterizing sleep in the adult ICU. Yet, the negative impact of sleep disruption in the critically ill pediatric patient undergoing rapid advances in growth, cognition and behavior has not been well characterized. Infancy and childhood are marked by sleep as the predominant behavioral state, and sleep structure and organization are in a constant state of change, paralleling central nervous system (CNS)
growth and differentiation. However, the ontogeny of sleep may not only be a correlate of CNS development, but a reflection of the reciprocal interactions between brain plasticity and sleep. Indeed, natural sleep may play a dynamic role in brain development, laying the groundwork for future learning.

Healthy children demonstrate a well-characterized temporal pattern of slow wave activity (EEG δ-power) activity when asleep, with a significant concentration of δ power in the first NREM period, which generally occurs within the first two hours after sleep onset. Data from the age and gender-matched healthy children in this investigation demonstrate that consistent pattern. With increasing age, EEG δ power exhibits a steep decline across adolescence after reaching a peak in childhood, again reflecting the role of NREM sleep in brain function. Findings from the patient sample in the current investigation show that critically ill children demonstrate major differences in nocturnal EEG patterns when compared to normal children, despite demonstrating a behavioral state (eyes closed, resting state) that is characteristic of sleep. The observed differences including the lack of day-night organization among sedated, critically ill children may, in part, be related to use of sedative medications. Pharmacologic management of sedation and analgesia for intubated children in the PICU primarily consists of opioids and benzodiazepines. A recent international survey of pediatric intensivists determined that fentanyl is the most commonly used opioid, and midazolam is the most commonly used benzodiazepine. Although opioids increase total sleep time in healthy subjects, they decrease slow wave and REM sleep. Benzodiazepines also significantly suppress slow wave and REM sleep, and are known independent risk factors for the development of ICU delirium in adults. The risks of continuous sedative and analgesic exposure are
compounded by polypharmacy and environmental factors such as noise, light and patient care interventions, leading to further negative effects on sleep architecture. Additionally, sympathomimetic medications frequently used in the critically ill setting are known to decrease both REM and slow wave sleep.\textsuperscript{31,67}

Poor sleep quality is a risk factor for delirium, which can lead to a vicious cycle of increasing sedation to maintain safety and help the patient “sleep”. The results of our study challenge the general notion that children in the PICU are experiencing natural, restorative sleep.\textsuperscript{19} Lack of day-night cycles in conjunction with loss of natural sleep among PICU patients is an important area for future research. Simple non-pharmacologic interventions such as earplugs and eye masks at night, consistently opening shades to achieve sunlight exposure during the day and implementation of noise reduction protocols may go a long way to promote sleep and decrease sedation needs.\textsuperscript{19,124,156,157} Therefore, it is essential that future studies investigating sleep in the PICU include continuous noise and light measurements. Before pharmacologic interventions such as melatonin are considered, it is imperative to further characterize dim light melatonin onset (DLMO) in critically ill children to better delineate the underlying pathophysiology of altered sleep in the PICU. Furthermore, sleep-wake problems that begin in the PICU may persist long after discharge from the PICU and hospital into the home setting, a long-term consequence that deserves further investigation as it relates to neuropsychological outcomes.

There are several limitations in the current study. First, the use of healthy children as a comparison group for patients in the PICU may not be the most suitable given that healthy children were monitored only overnight and not for the extended period as the PICU sample. The second limitation is a small sample size and all of the children in the
PICU had respiratory failure. Therefore, the results of the current study may not be generalizable to pediatric patients with other causes of critical illness. The same sample size may also explain the lack of an association between δ and θ power with sedative medication doses among PICU patients. Third, the sample of healthy children from the TuCASA cohort likely had greater exposure to sunlight than the PICU patients, which was not measured. Fourth, differences in the platform used to record the EEG in the PICU patients (Embla™) and the TuCASA cohort (Compumedics™) may lead to quantitative differences in EEG power spectra between the two groups. Finally, the results presented herein need to be interpreted with the knowledge that there are unmeasurable confounders that may affect the EEG recordings, including the severity of critical illness and underlying neurobiologic activity of the patients.

In summary, critically ill children in the PICU demonstrate differences in the EEG including the lack of ultradian increase in slow wave activity during the nighttime hours. The importance of sleep during recovery from critical illness deserves continued attention, particularly for children who are undergoing active neurologic maturation when sleep plays a vital role in normal development. Furthermore, disruption in sleep architecture has implications for how children are cared for during the most acute phase of their illness. Future research must focus on the modifiable risk factors for sleep disturbances in the critically ill child, including sedative approaches and non-pharmacologic behavioral interventions to promote natural sleep during recovery.
CHAPTER 4

Day-night Activity Patterns in Pediatric Patients after Major Surgery
INTRODUCTION

Sleep plays an integral role in normal neurodevelopment, which is reflected by the constantly evolving sleep needs of infants and children as they grow. Children admitted to the hospital, and in particular the Pediatric Intensive Care Unit (PICU) are exposed to several factors that can lead to disruption of the normal sleep-wake cycle, including invasive medical interventions, pain, noise, light, interruptions for nursing cares, and the underlying illness itself. It is routine for children who undergo major surgery to be admitted to the PICU in the post-operative period, and the majority of these children are exposed to sedative and analgesic medications that are known to have negative effects on restorative sleep and circadian rhythms.

Actigraphy is a non-invasive, well-tolerated, reliable and objective method to assess 24-hour patterns of day-night activity over several days to weeks. Validated for sleep assessment in infants and children, this wristwatch-like device produces minute-to-minute activity counts to monitor activity patterns over the course of hospitalization. While the actigraph can distinguish sleep from wake using algorithms to quantify the reduced movement associated with sleep, a more robust assessment of differences in day and night activity patterns can be performed with raw motor activity data.

To date, there have been no studies describing objectively assessing day-night activity patterns in children in the hospital after major surgery. The primary objective of this study was to characterize the day-night activity patterns of infants and children after major surgery, and describe the evolution of these children’s activity patterns from the PICU until discharge from the hospital.
MATERIALS AND METHODS

In this prospective, observational study, children were eligible for inclusion if they were admitted to the Johns Hopkins Pediatric Intensive Care Unit (PICU) after major cardiac, orthopedic or urologic surgery. Informed consent was obtained on the day after surgery from the child’s parent or legally authorized representative, and assent was obtained from the child when age or developmentally appropriate, unless the child was mechanically ventilated and receiving sedatives. Patients were only excluded if they had evidence of seizure activity at the time of screening or a history of traumatic brain injury or ischemic or hemorrhagic stroke. The study was approved by the Johns Hopkins Institutional Review Board.

Instruments and Measures

Clinical Variables

Demographic and clinical data collected through daily chart review during the duration of actigraphy recording included age, gender, type of surgery (cardiac/orthopedic/urologic), length of PICU, floor and hospital length of stay, pediatric risk of mortality score (PRISM-3), intubation status, length of mechanical ventilation, and sedative-analgesic medication administration.

Actigraphy

After informed consent, an actigraphy watch (MicroMotionlogger, Ambulatory Monitoring, Inc) was placed on the child’s wrist or ankle on post-operative day #1, and remained in place until the day of discharge from the hospital. The MicroMotionlogger has been used widely to document rest-activity patterns in infants and children. Motion sensors inside the accelerometry device capture data on patient movement using the Zero Crossing
Mode, which is measured as the number of accelerations per minute. The devices used in this study are capable of collecting data for up to twelve weeks. If the child was intubated at the time of actigraphy initiation, data analysis began at the time of extubation. The Act Millenium software was used for initializing and downloading actigraph data, and data processing was performed using the ActionW 2.7 software.

**Data Analysis/Statistical Methods**

For subjects with complete 24-hour actigraphy data, we analyzed activity profiles represented by 1440 minute-level (24 hours) activity counts. A log (count+1) transformation was applied to ensure symmetry of activity count distributions. Transformed activity counts were averaged within two specific time periods: daytime (08:00-20:00) and nighttime (20:00-08:00). Day-night activity patterns were estimated using the daytime activity ratio (DAR), defined as the ratio of the average daytime activity to total 24-hour activity.

\[
\text{DAR} = \frac{\bar{y}_d}{\bar{y}_d + \bar{y}_n},
\]

where \(\bar{y}_d\) and \(\bar{y}_n\) are the average log activity counts (per minute) for an individual during the daytime and nighttime hours respectively. A DAR of 50% suggests that the level of activity was equally distributed between day and night periods, while a DAR of 100% indicates that all activity occurred during the daytime period.

We utilize a mixed effect model with random intercepts for each subject to account for the variation within subjects due to the subjects having multiple days of activity data recorded. We examined the fixed effects for the PICU, gender, age, race, Pediatric Risk of Mortality Score (PRISM), cohort, and the time spent intubated measured in minutes. Due to the distribution of time intubated being extremely skewed, we transformed it by taking the log (log[int. min. + 1]) to allow it to be less skewed in order to conform to the model.
assumptions. All analyses were done using the lme() function in the nlme (v. 3.1-131) package in R 3.4.2.  

RESULTS

Demographic and clinical characteristics of the patient sample are shown in Table 4.1. During the study period, 250 children were enrolled and 221 of these subjects met criteria for completion of the study with >24 hours of analyzable actigraphy data (n=2271 hospital days). Only six children dropped out of the study due to some discomfort wearing the watch.

Table 4.1. Baseline Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cardiac</th>
<th>Orthopedic</th>
<th>Urology</th>
<th>All patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>143 (64%)</td>
<td>64 (29%)</td>
<td>14 (6%)</td>
<td>221</td>
</tr>
<tr>
<td>Age in months, mean (SD)</td>
<td>61.1 (67.9)</td>
<td>148.5 (55.0)</td>
<td>58.3 (74.4)</td>
<td>86.2 (75.9)</td>
</tr>
<tr>
<td>Weight in kg, mean (SD)</td>
<td>20.5 (20.2)</td>
<td>35.7 (17.6)</td>
<td>18.7 (17.7)</td>
<td>24.8 (20.5)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>92 (64%)</td>
<td>23 (36%)</td>
<td>9 (64%)</td>
<td>124 (56%)</td>
</tr>
<tr>
<td>PRISM score, mean (SD)</td>
<td>7.9 (5.0)</td>
<td>5.9 (4.8)</td>
<td>2.6 (5.2)</td>
<td>7.0 (5.2)</td>
</tr>
<tr>
<td>PICU LOS, mean (days-SD)</td>
<td>9.0 (17.2)</td>
<td>7.3 (9.0)</td>
<td>10.8 (12.8)</td>
<td>8.6 (15.0)</td>
</tr>
<tr>
<td>Intubated at Admission, n (%)</td>
<td>70 (80%)</td>
<td>18 (21%)</td>
<td>0 (0%)</td>
<td>88 (40%)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>73 (51 %)</td>
<td>37 (58 %)</td>
<td>12 (86 %)</td>
<td>122 (55%)</td>
</tr>
<tr>
<td>Black</td>
<td>39 (27 %)</td>
<td>9 (14 %)</td>
<td>0 (0 %)</td>
<td>48 (22%)</td>
</tr>
<tr>
<td>Other</td>
<td>31 (22 %)</td>
<td>18 (28 %)</td>
<td>2 (14 %)</td>
<td>51 (23%)</td>
</tr>
</tbody>
</table>

LOS = length of stay; PRISM = pediatric risk of mortality score; PICU = pediatric intensive care unit.
When all patients (n=221) and hospital days were included (n=2271), median daytime activity represented 58% of total activity while in the hospital (Figure 4.1). The mean daytime activity ratio during 1346 PICU days was 0.559, while the average DAR on the floor was 0.608 over 905 days (p<0.0001). Children in the cardiology cohort had the highest mean DAR (58.2%) when compared to the orthopedic (57.5%) and urology cohorts (57.0%).

In order to determine if daytime and nighttime activity are different between the PICU and the floor settings, a mixed model with random intercept for each subject was fit

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>Standard Error</th>
<th>T-statistic</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PICU</td>
<td>-0.0530</td>
<td>0.0047</td>
<td>-11.341</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Gender (F)</td>
<td>0.0001</td>
<td>0.0067</td>
<td>0.086</td>
<td>0.9931</td>
</tr>
<tr>
<td>PRISM</td>
<td>0.0000</td>
<td>0.0007</td>
<td>-0.047</td>
<td>0.9628</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>-0.0081</td>
<td>0.0086</td>
<td>-0.941</td>
<td>0.3479</td>
</tr>
<tr>
<td>Other</td>
<td>0.0063</td>
<td>0.0081</td>
<td>0.775</td>
<td>0.4390</td>
</tr>
<tr>
<td>Age</td>
<td>0.0018</td>
<td>0.0006</td>
<td>2.732</td>
<td>0.0068</td>
</tr>
<tr>
<td>Cohort</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ortho</td>
<td>-0.0331</td>
<td>0.0091</td>
<td>-3.627</td>
<td>0.0004</td>
</tr>
<tr>
<td>Urology</td>
<td>-0.0495</td>
<td>0.0124</td>
<td>-3.977</td>
<td>0.0001</td>
</tr>
<tr>
<td>Time Intubated</td>
<td>-0.0025</td>
<td>0.0010</td>
<td>-2.569</td>
<td>0.0109</td>
</tr>
<tr>
<td>(log - scale)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
controlling for age, gender, surgical cohort, PRISM score, log of time intubated, and race (Table 4.2). PICU days were associated with a significantly lower DAR (5.3%, p<0.0001) compared to days when the subject was on the floor. Older children had increased DAR, with a 0.18% increase with each year of age.

After adjustment, the urology cohort demonstrated the lowest DAR when compared to both the cardiology and orthopedic cohorts (-4.95%, p=0.0001). The log intubation time was associated with the DAR. As an example, for each 20% increase in intubation time, the DAR decreases on average by 0.05, or 0.05%. Severity of illness at PICU admission was not associated with the DAR.

DISCUSSION

The results of this study confirm that children recovering from major surgery experience disturbances in day-night activity patterns both in the PICU and after transfer to the floor. In addition to being in the PICU location, duration of intubation and orthopedic or urologic surgery were predictors of lower DAR. These findings provide important insights into how children’s rest-activity cycles are distributed throughout the 24-hour period, suggesting that the hospital setting may be severely disruptive to the normal sleep-wake patterns.

In healthy children, activity is consolidated during the daytime hours. We found that even older children in our cohort had significant increases in nighttime activity, consistent with alterations in rest-activity patterns or sleep fragmentation. In lieu of using algorithms to distinguish sleep from wake, we quantified raw motor activity data to analyze the daytime activity ratio and characterize how sleep patterns may be altered in the hospital setting. Raw motor activity provides a quantitative measure that as a percentage (DAR) can be easily compared across subjects regardless of age, disease process, or
neuromuscular strength. Additionally, algorithmic sleep-wake categorization can underestimate the amount of wake time and overestimate the amount of time in sleep due to a state of bedrest or immobility in the ICU.\textsuperscript{159}

Day-night differences were indistinguishable in 38\% of our subjects (<50\%), which is consistent with adult literature utilizing actigraphy in the hospital setting. Most pronounced in the PICU but also present in the floor setting, nursing and physician interventions, light, and noise from alarms and voices are risk factors for sleep disturbances. In a study of patients hospitalized after traumatic brain injury, rest-activity cycles were consolidated on only 46.6\% of all hospital days, however a linear trend of improvement was observed over time.\textsuperscript{160} In our cohort of children without acute neurologic disease, the average DAR on the floor setting was slightly lower than that of the PICU setting, suggesting that sleep-wake patterns do improve over time, however whether this is a consequence of the environment, improvement in illness process, or both is not known.

There are several limitations to this study. First, it is a single-center cohort and may not be generalizable to other pediatric hospital settings. Secondly, we did not account for children’s other comorbidities such as neuromuscular weakness in assessment of the daytime activity ratio- however, utilizing this ratio measure facilitates the child being his or her own control. Third, our analysis did not include pain, sedative and anesthetic medications before or during the period of actigraphic analysis, which may play a significant role in activity patterns and sleep quality.
CONCLUSION

Children admitted to the PICU after major surgery experience disruptions in day-night activity patterns during their hospital stay which may likely reflect fragmented sleep-wake patterns. Given the potential impact of sleep disturbances on the developing brain and importance of sleep during recovery from surgery further research is needed to identify methods of optimizing sleep hygiene in the perioperative period.
CHAPTER 5

Nurses’ Perceptions of the Pediatric ICU Environment Before and After a Transition to Single-patient Rooms

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INTRODUCTION

Every year in the United States, over 250,000 children are admitted to the pediatric intensive care unit (PICU). The chaotic PICU environment, including constant sound and bright light, exposes critically ill children to multiple risk factors that can fragment sleep during their hospital stay. Sleep is a basic human need. Integral to normal neurodevelopment in a healthy child, sleep may play an even more important role in the recovery of children with critical illness. Several studies have demonstrated that both adult and pediatric ICU patients experience circadian rhythm disturbances and decreases in slow-wave sleep. Although there are multiple risk factors for sleep fragmentation in critically ill patients, the most modifiable is the external environment, as sound and light levels play a key role in sleep-wake homeostasis.

Disturbances in sleep continuity may be associated with an increased risk of delirium in patients admitted to the ICU. Critical illness implies the need for invasive medical instrumentation and frequent interruptions for nursing care and monitoring. However, modifying the external environment can help optimize the sleep experience and potentially decrease a child’s sedation needs during mechanical ventilation. A lack of natural sunlight and periodicity in light-dark exposure can lead to adverse effects on circadian rhythms and sleep architecture. Constant loud and sudden sounds interrupt sleep, increase sedation needs, and affect physiologic parameters such as heart rate and respiratory rate.

In addition to potential benefits for patients, modifying the external environment to promote sleep for patients may also have favorable effects on nursing stress and job satisfaction. Caring for critically ill children and their families has a strong emotional
impact. Nursing has been well-established as a stressful profession, and studies of ICU nurses have shown that work satisfaction and stress levels are strongly correlated\textsuperscript{170}. Higher light levels during the day, achieved with exposure to natural sunlight, is integral to human health\textsuperscript{171}. Outside of the healthcare environment, previous studies have demonstrated that the presence of windows and sunlight improves job satisfaction\textsuperscript{169,172}. Furthermore, sound levels in most ICUs are universally higher than those recommended by the World Health Organization\textsuperscript{30,126,166,173-176}. Noisy work environments in the both the PICU and adult ICUs contribute to higher heart rates, fatigue and annoyance among nurses\textsuperscript{168,177}.

Most PICUs internationally have a layout with multi-patient rooms, which, though convenient for workflow of daily patient care, may not be conducive for sleep continuity or the preservation of circadian rhythm\textsuperscript{19}. In the past two 2 decades, hospital designs have been shifting from multi-patient to single-patient room configurations. In the acute care setting, single-patient rooms are associated with lower rates of medical errors, increased control of room light and temperature, lower sound levels, and even decreased delirium prevalence\textsuperscript{178}. Moreover, patients and their families prefer the private-room design\textsuperscript{179}. Literature from pediatric ICUs have largely focused on neonatal ICU (NICU) design, while the heterogeneous population of the PICU (ages 0-21) and impact of PICU design have not been investigated\textsuperscript{29-31}. Compounding the challenges of caring for critically ill children are the vastly different neurodevelopmental needs of PICU patients. The same nurse, for example, may be assigned to care for both a one-month-old infant and a sixteen-year-old adolescent on the same shift.

The primary objective of the current study was to examine changes in nursing
perceptions about the PICU environment with the transition from an ICU with multi-patient rooms to one with single-patient rooms. Specifically, we sought to examine the effect of having all private rooms on a nurse’s ability to control the external environment in a way that optimizes sleep for critically ill children and the effect of this change in environment on the nurses’ perception of their own personal work experience. We hypothesized that a private-room setting would improve a nurse’s ability to control the external environment in ways that would promote sleep in patients, decrease nursing stress and enhancing the overall work experience.

METHODS

A cross-sectional survey study was conducted during a transition of the PICU from multi-patient to single-patient rooms. The original PICU was a 32-bed unit that had four private rooms and four semi-private rooms; the remainder of the unit consisted of several beds in larger rooms. All of the private rooms and semi-private rooms had one window with shades, whereas the large multi-bed rooms had one window for four beds. Nurses’ stations were located in open spaces within the patient-care areas. The current PICU is a 40-bed unit with all private rooms and a window in each room. Each room includes lighting on dimmer switches and a movable boom which enables the patient to be positioned in any direction (facing window, nurses’ station or wall). There is also a sliding door which can be incrementally opened, whereas in the original PICU the door was either closed or open completely.

After receiving approval from the Institutional Review Board, we electronically mailed a survey to all PICU nurses 12 weeks before and 12 weeks after the PICU transition. We informed all participants that individual responses would remain confidential and
assigned respondents a numeric identifier to allow pre-post survey matching. To minimize reporting bias, we did not inform respondents about the follow-up survey at the time of the first survey. The survey was pilot tested among a committee of nurses in the PICU for feedback regarding question clarity and the survey interface. The final survey consisted of 20 questions that were divided into perceptions of the PICU sound and lighting environment for patient care and perceptions of the environment for the nurses' personal work experience. Questions were closed-ended, multiple-choice design measured on a 5-point Likert scale. Respondents were also asked to provide any specific comments or additional information in free-text form.

Statistical Analysis

Responses were collected in Survey Monkey. McNemar’s chi-square tests were used to compare responses to the questions regarding perceptions about the sleep environment and work experience before and after the move to the single-patient room layout. All tests were two-tailed, and a value of 0.05 or less was considered statistically significant. The data were analyzed with Stata 12 (StataCorp, College Station, TX).

RESULTS

Demographics

Demographic data of respondents are summarized in Table 5.1. Eighty-three percent of nurses (100/120) completed the pre-transition questionnaire, and of these respondents 90 completed the post-transition survey (75% overall response rate). The majority of the 90 respondents (63%) were 21-29 years old and 99% of the respondents (89/90) were female. Forty-three percent of nurses had 1 to 3 years of work experience in
the PICU, with 41% reporting greater than 3 years. The average percentages of the nurses’ work time spent on day shifts, night shifts, and administrative/education duties were 49%, 45%, and 6%, respectively.

**Table 5.1: Demographics of pediatric intensive care nurses who responded.**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>% of Nurses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Years of experience</td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
<td>16</td>
</tr>
<tr>
<td>1-3</td>
<td>43</td>
</tr>
<tr>
<td>4-6</td>
<td>11</td>
</tr>
<tr>
<td>7-10</td>
<td>11</td>
</tr>
<tr>
<td>&gt;10</td>
<td>19</td>
</tr>
<tr>
<td>Age range, y</td>
<td></td>
</tr>
<tr>
<td>21-29</td>
<td>63</td>
</tr>
<tr>
<td>30-39</td>
<td>18</td>
</tr>
<tr>
<td>40-49</td>
<td>16</td>
</tr>
<tr>
<td>50-59</td>
<td>3</td>
</tr>
</tbody>
</table>

**Perceptions of Sleep Environment: Sound and Light**

As shown in Table 5.2, nurses reported that a single-patient private room layout was overall more conducive to patients sleeping well at night and to promoting a normal sleep-wake cycle than was a multi-patient layout (p<0.001). More nurses agreed that they had increased control of light and sound for sleep promotion during both day and night (p<0.001) than they did with a multi-patient layout. However, in both the single- and multi-patient room settings, monitors and alarms were the greatest factor that affected sound levels during the day and night. Conversations between clinical staff were the second most commonly reported factor that affected sound exposure in both layouts, although it was cited less often after the move to single-patient rooms. With respect to light exposure, in both layouts the most important factors cited for increasing light at night were safety issues, followed by requirements of the charge nurse/unit culture to keep the lights on. Patient care
was also a persistent reason for increased light exposure at night in both PICU layouts.

**Nursing Perceptions of Annoyance and Stress**

Nurses were less annoyed by sound in the all-private room layout (79% vs. 33%; p<0.001; **Figure 5.1**). In addition, sound contributed less to the stress levels of nurses in

<table>
<thead>
<tr>
<th>Table 5.2: Nursing perceptions of the pediatric intensive care unit environment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unit</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Our current unit layout promotes a normal sleep-wake cycle</td>
</tr>
<tr>
<td>Agree</td>
</tr>
<tr>
<td>Disagree</td>
</tr>
<tr>
<td>Neutral</td>
</tr>
<tr>
<td>I am able to manipulate the unit’s environment to promote sleep</td>
</tr>
<tr>
<td>Agree</td>
</tr>
<tr>
<td>Disagree</td>
</tr>
<tr>
<td>Neutral</td>
</tr>
<tr>
<td>The factor that most affects <strong>daytime</strong> noise exposure for patients is</td>
</tr>
<tr>
<td>Monitors/alarms</td>
</tr>
<tr>
<td>Vocera®/overhead announcements</td>
</tr>
<tr>
<td>Visitors’ voices</td>
</tr>
<tr>
<td>Voices of clinical staff</td>
</tr>
<tr>
<td>Everyday maintenance activity</td>
</tr>
<tr>
<td>Other patients in the room</td>
</tr>
<tr>
<td>The factor that most affects <strong>nighttime</strong> noise exposure for patients is</td>
</tr>
<tr>
<td>Monitors/alarms</td>
</tr>
<tr>
<td>Vocera®/overhead announcements</td>
</tr>
<tr>
<td>Visitors’ voices</td>
</tr>
<tr>
<td>Voices of clinical staff</td>
</tr>
<tr>
<td>Everyday maintenance activity</td>
</tr>
<tr>
<td>Other patients in the room</td>
</tr>
<tr>
<td>I feel I have control over my patients’ exposure to light in the <strong>daytime</strong></td>
</tr>
<tr>
<td>Agree</td>
</tr>
<tr>
<td>Disagree</td>
</tr>
<tr>
<td>Neutral</td>
</tr>
<tr>
<td>I don’t work the day shift</td>
</tr>
<tr>
<td>I feel I have control over my patients’ exposure to light in the <strong>nighttime</strong></td>
</tr>
<tr>
<td>Agree</td>
</tr>
<tr>
<td>Disagree</td>
</tr>
<tr>
<td>Neutral</td>
</tr>
<tr>
<td>I don’t work the night shift</td>
</tr>
<tr>
<td>The factor that most affects <strong>nighttime</strong> light exposure for patients is</td>
</tr>
<tr>
<td>Charge nursing unit requirement to keep lights on</td>
</tr>
<tr>
<td>Inability to control shades/lack of windows</td>
</tr>
<tr>
<td>Safety issues (need to assess patient frequently)</td>
</tr>
<tr>
<td>Inability to dim lights</td>
</tr>
<tr>
<td>Visitors’ demands</td>
</tr>
<tr>
<td>Other patients in the room</td>
</tr>
<tr>
<td>* Patient care/nursing interventions</td>
</tr>
</tbody>
</table>

* Hands-free wireless communication device.
the single-patient room layout than in the open layout (90% vs. 44%; p<0.001) and fewer nurses desired a quieter unit after the move (89% vs. 27%; p<0.001). Finally, desire for
more sunlight exposure was significantly reduced after the move to the new layout (95% vs. 50%; p<0.001). Table 5.3 lists free-text responses from PICU nurses which summarize common themes that were present after the move to single-patient rooms.

**DISCUSSION**

In this cross-sectional survey study of PICU nurses, a change from multi-patient rooms to a single-patient room layout improved nurses' perceptions of the PICU environment for sleep promotion, particularly in regard to sound and lighting optimization. Additionally, nurses reported feeling significantly less stress and annoyance as a result of the PICU environment after a transition to the single-patient room layout. To our knowledge this is the first study to investigate the role of PICU architectural design on nursing perceptions of the patient care and work environment. In addition to results suggesting the single-patient room design has benefits for sleep promotion and decreasing nursing stress, we identified issues for ongoing improvement that must be addressed beyond a change in PICU design.

It is not surprising that monitors and alarms persisted in the single-patient room layout as the most important factor affecting sound levels in the PICU during the day and night, followed by clinical staff conversations. Private rooms provide a level of protection from general ICU sounds only. Although alarms are a necessary part of ICU care to anticipate and manage acute changes in a child’s clinical condition, a large body of evidence is mounting to support technological and institutional culture changes to minimize false alarms and alarm fatigue.\textsuperscript{180} Electronic sounds from intermittent alarms lead to the most arousals from sleep in studies of healthy volunteers in simulated ICU
environments. Therefore, quality improvement initiatives to individualize alarm thresholds and minimize false alarms are crucial to optimize the balance between patient safety and a healing ICU environment, while simultaneously decreasing nursing stress. Similarly, the institution of nighttime “quiet hours” both in patient rooms and general areas can change culture and minimize sound levels due to staff conversations, enabling adherence to WHO recommendations recommending no more than 30 dB at night. However, current evidence suggests that most PICUs internationally do not have either noise or light optimization protocols in place for sleep promotion.

Another important issue raised by the questionnaire was the struggle between optimizing patient safety and promoting sleep. Dimming lights in the rooms of the most critically ill children may not be feasible because staff need to make continual visual assessments of the patient and provide frequent care. Even with the ability to increase sunlight exposure during the day or dim lights at night, family and staff preferences can be major obstacles to lighting optimization. Nevertheless, the results of our study enabled physician and nursing leadership to identify areas for culture change and the need to create specific patient criteria for which noise and lighting protocols should be utilized.

Finally, transitioning to a single-patient layout improved PICU nurses’ perceptions of the work environment and decreased job stress. Mealer and colleagues found that 20-30% of adult ICU nurses had symptoms of post-traumatic stress disorder (PTSD) secondary to their work, significantly higher than the lifetime prevalence of 6.8% among the U.S. general population. PICU nurses spend their entire shift at the bedside of critically ill children, which has great psychological impact and increases the risk for secondary traumatic stress. In a study of pediatric acute care nurses, 21% of survey

80
respondents demonstrated strong PTSD symptoms which were also associated with comorbid symptoms of anxiety, depression and burnout.\textsuperscript{186} Younger ICU nurses (ages 20-29), the most highly represented demographic in our PICU, have reported higher job stress levels in previous studies than their older and more experienced colleagues.\textsuperscript{187,188} Therefore, the architectural design of an ICU where nurses care for critically ill pediatric patients may have important implications for nursing retention and wellness.\textsuperscript{189} Sound levels are known to increase stress and annoyance levels among nurses in the ICU environment.\textsuperscript{168,190} Sunlight exposure during the day optimizes circadian rhythms for nurses who are frequently transitioning between day- and night-shift, and also improves mood and energy.\textsuperscript{191} Thus, having the ability and control to minimize noise and increase their own sunlight exposure during the day was beneficial to nurses’ perceptions of the work environment.

There are limitations to this single-center study. First, perceptions of the environment may have been affected by anticipation and completion of the change. That is, it is possible that the new building and environment in general worsened perceptions of the old unit. Second, the ages and experience levels of the nurses who responded were very heterogeneous, although this heterogeneity is generalizable to the majority of adult and pediatric ICUs. Third, the survey that we disseminated was not a previously validated tool. Finally, we do not have quantitative sound and light level data to correlate the change in perceptions with actual changes in sound and light levels before and after the move.

In summary, a single-patient private room layout led to improved perceptions of the patient environment for sleep promotion and decreased stress levels among pediatric ICU nurses. As more ICUs shift their architectural designs to the single-patient room
model, it is important to continue to focus on issues that are not completely addressed by a new design. These issues include patient alarms, staff conversations, and the perception that an optimized sleep environment may detract from patient safety. Future quality improvement and research initiatives should systematically address methods to optimize sound and light in the ICU environment so that patients can benefit from optimized sleep continuity and staff can work in an ICU that promotes a healing environment.
CHAPTER 6

Identifying Barriers to Delirium Screening and Prevention in the Pediatric ICU: Evaluation of PICU Staff Knowledge

(Reprinted with permission from Journal of Pediatric Nursing)
BACKGROUND AND OBJECTIVES

Delirium in the pediatric intensive care unit (PICU) setting is often unrecognized and undertreated. As defined in the Diagnostic and Statistical Manual of Mental Disorders: Fifth Edition (DSM-5) delirium is a disturbance and change in attention and awareness from baseline, developed over a short time, with a fluctuating course. The change from baseline includes a disturbance in cognition, which is not better explained by another neurocognitive disorder. In adults, Intensive Care Unit (ICU) delirium is associated with increased hospital length of stay, morbidity and mortality. Due to heterogeneity in ages, development and diagnoses, delirium screening in critically ill children can be challenging. Despite validated tools for screening delirium in this population, few pediatric ICUs (PICUs) internationally perform screening.

Pediatric delirium has been more recently highlighted in literature, with the development and evolution of pediatric screening tools. Pediatric studies have shown that delirium is present in at least 30% of critically ill children and adolescents. There is limited data on pediatric patient outcome measures after delirium, but a few retrospective studies describe longer length of stay and similarities to an adult delirium course. However, many PICU’s internationally are still not screening for delirium. In a recent survey study characterizing international PICU practices, 71% of respondents reported that their unit does not perform routine delirium screening, and only 2% reported that delirium screening is performed on every child at least once per shift.

Knowledge of etiology and risk factors for delirium in adults is growing. One study by Ouimet in 2007 showed that hypertension, alcoholism, severity of illness score (APACHE II), and use of sedatives and analgesics to induce coma were independently
associated with the incidence of delirium. Another study by Aldemir in 2001 indicated that respiratory disease, infection, fever, anemia, hypotension and metabolic derangements were associated with incidence of delirium. While there are less documented investigations into risk factors for pediatric delirium, it could be assumed that similar risk factors might be indicated in delirium for the pediatric critically ill patient.

In order to tailor an educational intervention to facilitate consistent and reliable screening, it is important to determine current knowledge gaps and barriers to delirium screening and prevention. Our goal was to implement twice-daily delirium screening with the Pediatric Confusion Assessment Method-ICU (pCAM-ICU) in our large, tertiary-care PICU. The overall objective of this study was to determine current knowledge regarding delirium and its risk factors among PICU nurses prior to beginning targeted education. In adult literature, similar surveys have been done to evaluate knowledge and opinions about delirium screening. We hypothesized that prior to a targeted educational intervention, PICU nursing staff do not have an adequate knowledge base for accurate screening and diagnosis of delirium in critically ill children.

METHODS

A 17-item questionnaire was administered to all nurses in a 36-bed tertiary care PICU to assess current staff knowledge about pediatric delirium. The survey was sent to all PICU nursing staff, and responding to the survey was voluntary. Survey questions were formulated based on available evidence surrounding risk factors, screening methods, treatments, and diagnostic criteria for adult and pediatric delirium.

After the survey was piloted for feedback to PICU nursing leadership, the questionnaire was administered online to all PICU nurses before targeted education and
implementation of the pCAM-ICU tool. All participants were informed that individual responses would remain anonymous and confidential, and participation in the survey was considered consent to be involved in the study. The institutional review board approved the questionnaire and study. Data were summarized as the proportion answering correctly for each of the items.

RESULTS

Of the 143 nurses who received the survey link, 105 completed the survey (73.4%). The percentage of nurses who answered each question correctly ranged from 35% to 100%. Only one nurse scored 100%. The answers to each item are summarized in Table 6.1. Several concepts reviewed in the survey revealed a strong knowledge base. Out of 105 respondents, over 95% recognized that poor nutrition and dehydration increases the risk of delirium. Additionally, almost all nurses (103/105; 98%) confirmed that delirium does not always manifest as a hyperactive, confused state. All respondents correctly identified that altered sleep/wake cycles may be a symptom of delirium, and 91% recognized that delirium is characterized by fluctuations in orientation and disorientation.

Table 6.1: Survey answers

<table>
<thead>
<tr>
<th>Survey item</th>
<th>Correct</th>
<th>Incorrect</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Fluctuation between orientation and disorientation is not typical of delirium (FALSE)</td>
<td>96 (91.4%)</td>
<td>9 (8.5%)</td>
</tr>
<tr>
<td>2. Poor nutrition increases the risk of delirium (TRUE)</td>
<td>102 (97.1%)</td>
<td>3 (2.9%)</td>
</tr>
<tr>
<td>3. The GCS score is the best way to diagnose delirium in critically ill children (FALSE)</td>
<td>93 (88.6%)</td>
<td>12 (11.4%)</td>
</tr>
<tr>
<td>4. Hearing or vision impairment increases the risk of delirium (TRUE)</td>
<td>86 (81.9%)</td>
<td>19 (18.1%)</td>
</tr>
<tr>
<td>5. Delirium in children always manifests as a hyperactive, confused state (FALSE)</td>
<td>103 (98.1%)</td>
<td>2 (1.9%)</td>
</tr>
<tr>
<td>6. Benzodiazepines can be helpful in the treatment of delirium (FALSE)</td>
<td>65 (61.9%)</td>
<td>40 (38.1%)</td>
</tr>
<tr>
<td>7. Behavioral changes in the course of the day are typical of delirium (TRUE)</td>
<td>96 (91.4%)</td>
<td>8 (7.6%)</td>
</tr>
<tr>
<td>8. Patients with delirium will often experience perceptual disturbances (TRUE)</td>
<td>98 (93.3%)</td>
<td>6 (5.7%)</td>
</tr>
<tr>
<td>9. Altered sleep/wake cycle may be a symptom of delirium (TRUE)</td>
<td>104 (99%)</td>
<td>0</td>
</tr>
<tr>
<td>10. Symptoms of depression may mimic delirium (TRUE)</td>
<td>87 (82.9%)</td>
<td>17 (16.1%)</td>
</tr>
<tr>
<td>11. The greater the number of medications a patient is taking, the greater their risk of delirium (TRUE)</td>
<td>86 (81.9%)</td>
<td>18 (17.1%)</td>
</tr>
<tr>
<td>12. Delirium usually lasts several hours (FALSE)</td>
<td>59 (56.2%)</td>
<td>45 (42.8%)</td>
</tr>
<tr>
<td>13. A urinary catheter in situ reduces the risk of delirium (FALSE)</td>
<td>99 (85.7%)</td>
<td>14 (12.3%)</td>
</tr>
<tr>
<td>14. Gender has no effect on the development of delirium (FALSE)</td>
<td>37 (35.2%)</td>
<td>67 (63.8%)</td>
</tr>
<tr>
<td>15. Dehydration can be a risk factor for delirium (TRUE)</td>
<td>104 (99%)</td>
<td>0</td>
</tr>
<tr>
<td>16. Children generally do not remember being delirious (FALSE)</td>
<td>39 (37.1%)</td>
<td>65 (61.9%)</td>
</tr>
<tr>
<td>17. A family history of dementia predisposes a patient to delirium (FALSE)</td>
<td>72 (68.6%)</td>
<td>32 (30.4%)</td>
</tr>
</tbody>
</table>
In contrast, there were specific concepts that identified significant knowledge gaps and areas for education. Eleven percent of nurses (12/105) believed the Glasgow Coma Scale (GCS) is an appropriate method for delirium screening. Furthermore, 38% surveyed (40/105) answered that benzodiazepines are beneficial in the treatment of delirium. When questioned about the presence of a urinary catheter as a risk factor, thirteen percent (14/104) incorrectly answered that the presence of a catheter can reduce the risk of delirium. Forty-three percent incorrectly responded (45/104) that delirium usually lasts several hours. Sixty-three percent believe that gender has no effect on the development of delirium. Finally, the majority of respondents (62%) believed that children generally don’t remember being delirious.

DISCUSSION

The results of this survey demonstrate specific areas where there is a deficiency in knowledge about risk factors and treatment of pediatric delirium among PICU nursing staff. In a recent international survey of pediatric intensivists by our group, less than 2% of pediatric intensivists report consistent delirium screening in their PICU. When asked what forms of delirium screening tools were most commonly used, many listed pain and withdrawal assessment tools such as the Finnegan, WAT, and SOPHIA assessments. Therefore, targeted multidisciplinary educational interventions are critical to successfully implement delirium prevention and treatment programs in the PICU.

This survey highlighted several particularly concerning areas where PICU nursing staff knowledge was deficient about delirium. Lorazepam has been identified as an independent risk factor for delirium. However, thirty-eight percent of the nurses
surveyed believed that benzodiazepines were an effective treatment option for delirium. The GCS score is a neurological scale that gives a reliable, description of state of consciousness. Education about screening tools for delirium became an important focus after observing that eleven percent of our nurse respondents believed that the GCS was an appropriate method to screen for delirium. Presence of a foley catheter can be a functional restraint, increase risk of infections, and be a precipitating factor for delirium\textsuperscript{204}, however thirteen percent of nurses responded incorrectly that placement of a foley catheter can help reduce the incidence of delirium. Finally, several studies have found that both adult and pediatric patients have memories of their delirious state after discharge from the ICU, which can have long-term psychological sequelae\textsuperscript{205-208}. We identified the importance of education surrounding potential long-term effects of delirium, as 37% of nursing staff believed that children don’t remember being delirious. The misconception that delirium isn’t remembered may lead to decreased urgency and emphasis in prevention and treatment.

Many publications have demonstrated that prior to implementation of a protocolized screening program, the nursing or physician staff may use simple observation to diagnose delirium.\textsuperscript{203,209} Given that delirium has a waxing and waning course, the bedside nurse is the ideal front line provider to evaluate presence or absence of delirium. Knowledge about the importance of delirium screening and the ability to accurately perform a rapid and efficient delirium assessment that is uniform in the PICU is vitally important to patient care. Barriers to evaluation include lack of education, concern about the time involved, or complicated nature of the assessment tool. Another barrier which should also be considered when implementing new screening is the investment of the
physician team. Physicians are more likely to take notice and act upon a new diagnosis of delirium when a known assessment tool is used on a regular basis, validating the nursing efforts to screen.

There are notable limitations to this study. First, given the survey was administered only to nursing staff in a single-center, it is possible that the results are not generalizable to nurses in other PICUs. In addition, although the respondents represented a wide range of education and experience levels with critically ill children, there is also the potential for selection bias if the non-responders were different from the responders in years of experience or knowledge of delirium.

CONCLUSIONS

Pediatric delirium is a significant issue for the critically ill child, with a need for close monitoring, recognition, and treatment. Our study highlighted areas for which targeted education needed to be done. Prior to implementation of unit-wide delirium screening, it was determined that the staff required further education regarding the importance, risk factors, and treatments for pediatric delirium. Furthermore, the results obtained may be considered applicable to most pediatric critical care units who employ staff with a wide variation of experience and education. It is likely that most critical care units, whether pediatric or adult, will have similar deficits in knowledge without targeted education for the staff about how to diagnose delirium, appropriate screening and associated risk factors.
CHAPTER 7

PICU Up!: Impact of a quality improvement program to promote early mobilization in critically ill children

(Reprinted with permission from Pediatric Critical Care Medicine)
INTRODUCTION

The central focus of care in the pediatric intensive care unit (PICU) is on resuscitation, stabilization, management of critical disease processes, and reversal of organ failure. As a result, children are often sedated, restrained, and confined to bed for prolonged periods due to perceived benefits of safety, comfort, and hemodynamic stability. A culture of immobility may have several short- and long-term implications for critically ill children and their families, negatively affecting circadian rhythms and potentially increasing the risk of delirium. Ineffective positioning and limited mobility contribute to a high incidence of pressure ulcers in both infants and children. Moreover, children who survive their illness can experience residual perceptual-motor, psychiatric, and behavior problems as sequelae of critical illness.

Data from adult ICUs demonstrate that structured and interdisciplinary approaches to early mobilization are associated with reduced intensive care and hospital LOS, improved muscle strength and self-perception of functional status, and decreased sedation, delirium, and length of mechanical ventilation. Although pediatric literature regarding early mobilization practices is just emerging, available data indicate that early mobilization activities for the critically ill child are likely safe and feasible and may have short and long-term benefits.

The overall objective of this quality improvement (QI) project was to evaluate a structured and interdisciplinary early rehabilitation and progressive mobility protocol, “PICU Up!,” for all critically ill children in a large, academic, tertiary-care PICU. Previously, the referral of children for therapy and mobilization was at the discretion of the medical providers without standardization or guidelines. The goals of PICU Up! were to
provide a standardized, evidence-based, interdisciplinary mechanism to increase each child’s activity level safely while simultaneously initiating and promoting a culture of mobility.

**MATERIALS AND METHODS**

**Overview of Project Setting, Design and Patients**

The PICU Up! Initiative was developed using an established and structured QI framework (described below in “Quality Improvement Process”) and evaluated using a pre-post design. The setting was the Johns Hopkins PICU, a 40-bed academic, tertiary care, combined medical-surgical unit with single-patient rooms that provides care for children from ages 1 day to 21 years. Registered nurse-to-patient ratios are 1:1 or 1:2 depending on patient acuity. Pediatric occupational therapist (OT), physical therapist (PT), and speech/language pathologist consultations and treatments are available when ordered by a medical provider. The PT and OT staff who care for children in the PICU also staff other units in the hospital. PICU Up! was implemented without any additional personnel or equipment resources.

A non-probability, convenience sampling strategy was used for program evaluation. Inclusion criteria were children aged 1 day to 17 years who required PICU admission for 3 or more days. Exclusion criteria included ECMO, open chest or abdomen, unstable fractures, or medical orders specifying alternate activities. Charts of the first consecutive 100 children who met inclusion criteria were reviewed retrospectively both before (July-August 2014) and after (July-August 2015) implementation of the mobility protocol. PICU Up! was implemented in March-May 2015. This QI project was reviewed and approved by the Johns Hopkins Institutional Review Board.
Quality Improvement Process

The structured QI model (22) used for the PICU Up! initiative aimed to create a change in practice through the “4 Es” approach: engage, educate, execute and evaluate. To achieve this, a collaborative interdisciplinary QI team, the PICU Up! Working Group, was created. Participation in the PICU Up! Working Group was open to all interested PICU staff. Active participants included at least one champion from each of the following groups: physicians, nurse practitioners, nursing, OT, PT, child life specialists, speech language pathology, respiratory therapy, and rehabilitation medicine. This core group of individuals met together on a weekly basis over one year to plan (engage and educate) the QI project prior to its execution and evaluation.

First, champions from the interdisciplinary team conducted focus groups with all stakeholders from their respective disciplines to present the problem and identify PICU-based facilitators and barriers to early mobilization. Second, the group worked together to develop guidelines for mobilization in the PICU based on the feedback provided from the focus groups and prior literature regarding early mobilization (14,22). Third, educational resources were developed for all PICU staff (“Staff Educational Resources”, below). Finally, the interdisciplinary team determined valid and feasible outcome measures based on previously published adult early mobilization QI studies to evaluate performance.

The PICU Up! Program

Components of PICU Up! included a tiered activity plan based on clinical parameters and exclusion criteria (Table 7.1). A foundation of PICU Up! was implementation of sleep hygiene promotion and routine delirium screening for all children. Each activity level was
connected with a set of interventions, written to promote individualization based on the child’s unique needs. Also included were criteria for pausing activity and reassessing the child before continuing the activity (Table 7.2).

**Table 7.1: PICU Up! levels and activities**

<table>
<thead>
<tr>
<th>PICU Up! Level</th>
<th>Parameters for Inclusion</th>
<th>Activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1</td>
<td>Intubated with FiO₂ &gt; 60% or Intubated with PEEP &gt; 8 or Intubated difficult airway or New tracheostomy or Acute neurologic event or Sedated and SBS –3 to –2 or Vasopressor other than milrinone</td>
<td>Lights on/shades up by 09:00 Bed/bath/weight by 23:00 Lights dimmed/out by 23:00 Increase lighting as needed for cares/interventions Television limited to 30 min at a time and a goal of &lt; 2 hr/d for children &gt; 2 yr old Head of bed elevated ≥ 30° Turn every 2 hr during the day and every 4 hr at night Positioned in developmentally supportive position or as recommended by OT/PT OT consult by PICU day 3 PT consult as needed</td>
</tr>
<tr>
<td>Level 2</td>
<td>Intubated or tracheostomy with FiO₂ ≤ 60% +/- PEEP ≤ 8 and SBS –1 to +3 or Noninvasive support with FiO₂ &gt; 60% or Dialysis/renal replacement therapy or Femoral access</td>
<td>Level 1 activities plus Positive touch for infants/toddlers Sitting up in bed TID Team to consider OOB to chair +/- or ambulation OT/PT consult by PICU day 3 Assess for difficulty with communication or phonation and consult SLP Assess for swallowing readiness in high risk children and consult SLP Assess need for daily schedule Preschool Confusion Assessment Method-ICU or Pediatric Confusion Assessment Method-ICU BID</td>
</tr>
<tr>
<td>Level 3</td>
<td>Noninvasive pulmonary support with FiO₂ ≤ 60% or Baseline pulmonary support or External ventricular drain cleared by neurosurgery and SBS –1 to +3</td>
<td>Level 1 and 2 plus OOB to chair TID or sitting up in bed TID if appropriate chair is not available Ambulate BID if trunk control present</td>
</tr>
</tbody>
</table>

BID = twice a day, OOB = out of bed, OT = occupational therapist, PEEP = positive end-expiratory pressure, PT = physical therapist, SBS = State Behavioral Scale, SLP = speech language pathology, TID = three times a day.
It was determined that each child’s activity level would be discussed and established during morning rounds, with the bedside nurse reporting the PICU Up! level (1, 2 or 3) based on the established criteria (Table 7.1). The interdisciplinary team caring for the patient considered the activity level and activity goal for the day during rounds. The bedside nurse recorded this information in the electronic record daily goals note, which was accessible to all providers, and assessed the appropriateness of the activity level throughout the day. Activities could be implemented by nursing and/or therapists based on their specific skills and the child’s needs. The PICU Up! levels were intended to provide guidelines for appropriate activities, with the option to perform more advanced activities (i.e. ambulation of an intubated patient) with interdisciplinary team discussion individualized to the child.

Staff Educational Resources

Educational resources were presented in meetings, presentations and online communications to ensure involvement of all PICU stakeholders. A formal written procedure was available to staff via the Johns Hopkins online policies portal. Formal educational materials included a required 10-minute online learning module about early

Table 7.2: Criteria to “Rest and Reassess”

<table>
<thead>
<tr>
<th>Change in heart rate, 20%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in blood pressure, 20%</td>
</tr>
<tr>
<td>Change in respiratory rate, 20%</td>
</tr>
<tr>
<td>Decrease arterial oxygen saturation, 15%</td>
</tr>
<tr>
<td>Increase Fio₂, 20%</td>
</tr>
<tr>
<td>Increase end-tidal CO₂, 20%</td>
</tr>
<tr>
<td>Ventilator asynchrony</td>
</tr>
<tr>
<td>Continuous/bilevel positive airway pressure asynchrony</td>
</tr>
<tr>
<td>Respiratory distress</td>
</tr>
<tr>
<td>New arrhythmia</td>
</tr>
<tr>
<td>Hemodynamic concerns</td>
</tr>
<tr>
<td>Change in mental status</td>
</tr>
<tr>
<td>Concern for airway device, vascular access, or external ventricular drain integrity</td>
</tr>
<tr>
<td>Behavior interfering with safe activity</td>
</tr>
</tbody>
</table>

Vital sign changes based on baseline value prior to activity initiation.
rehabilitation in critically ill patients, including a brief overview of relevant adult and pediatric literature. The module then transitioned into interactive case-based scenarios to illustrate application of the PICU Up! criteria. Because we identified a simultaneous need for pediatric delirium education among the staff, a parallel educational module for pediatric delirium utilizing the same interactive cases was developed. A pocket card that summarized the levels and activities was distributed to all staff members.

**PICU Outcome Measures**

Early mobilization was defined by the team as any passive or active activity that occurred within the first 3 days of PICU admission and was intended to maintain or restore musculoskeletal strength and function. At our institution, both PT and OT must be formally consulted by physicians or nurse practitioners to work with patients. PTs facilitate ambulation and mobility, while splinting, range of motion, seating, and positioning are the purview of OTs, with PT collaboration as needed. The primary outcome measures were 1) the proportion of patients with OT and/or PT consultations by PICU Day 3 and 2) the number and types of mobilization activities performed by PICU Day 3. Activities were categorized as in-bed therapies or mobility therapies. In-bed therapies included passive range of motion, active range of motion, and active or passive bed positioning. Mobility activities included sitting at edge of bed, sit to stand, transfer, pre-gait activities, mobility device, ambulation, and play. Secondary outcome measures were 1) the number of times and reasons that activities were stopped, 2) barriers to activities, and 3) mobilization-related adverse events, including inadvertent extubation or line removal. Data for all outcome measures, including mobilization activities, adverse events and barriers were collected for each day of PICU admission in all patients. After implementation, a Likert-
style four-question, voluntary and anonymous response questionnaire was sent to the entire PICU staff to collect general feedback about PICU Up! and ongoing barriers to mobilizing the critically ill child.

**Statistical Analysis**

Data were summarized as proportions for categorical variables and median and interquartile range for continuous variables. Unadjusted comparisons before and after implementation of PICU Up! were performed by using chi-square analysis, Fisher’s exact test, and Wilcoxon rank-sum test, as appropriate. All data were analyzed with the statistical software package STATA version 11.0 (StataCorp LP, College Station, TX).

**RESULTS**

**Patient Characteristics** Data was collected from 100 children who met inclusion criteria in the pre-implementation group (675 PICU days) and 100 children in the post-implementation group (737 PICU days). Characteristics of the pre- and post-implementation groups are summarized in Table 7.3. The groups were similar with regard to age, weight, PICU admission diagnoses, and Pediatric Risk of Mortality (PRISM) scores. The PICU Up! level did not differ between pre- and post-implementation groups at PICU day 3 ($p= 0.79$).

**Occupational and Physical Therapy Consultations**

OT consultations increased significantly from the pre- to post-implementation phase by PICU day 3 (44% vs 59%; $p=0.034$). The number of PT consultations by PICU day 3 increased but did not reach significance (54% vs. 66%; $p= 0.08$).
Activities

There was no difference in the participation in at least one mobility activity prior to and after PICU UP on PICU Day 3, while the proportion of children receiving in-bed activities increased significantly from 50% to 93% (Table 7.4; p=0.001). There was an increase in the number of children who transitioned from sit to stand (14% vs. 33%; p= 0.002) and the number of children who ambulated. (11% vs. 24%; p = 0.016). Three children were orally intubated at the time of ambulation after PICU Up! implementation. Before PICU Up! implementation, no children with endotracheal tubes ambulated.

Fifty-six percent and 53% of the study sample remained in the PICU for 5 or more days in the pre- and post-implementation phases, respectively. After implementation of PICU Up!, this group had increased passive range of motion (2% vs. 12%; p = 0.037) and
passive bed positioning, (29% vs. 49%; \( p = 0.028 \)) in the 24 hours prior to PICU discharge. There was also an increase in active bed positioning (head of bed elevation >90%) in the post-implementation phase (18% vs. 45%; \( p = 0.002 \)), and more children were reported to have at least one bed activity (52% vs. 94%; \( p < 0.001 \)).

**Table 7.4: Early mobilization activities- First 3 days after PICU admission**

<table>
<thead>
<tr>
<th>Activity (No. of Children Participating in That Activity)</th>
<th>Preimplementation ( n = 100 )</th>
<th>Postimplementation ( n = 100 )</th>
<th>( p^* )</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-bed activities, ( n )</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Passive range of motion</td>
<td>13</td>
<td>17</td>
<td>0.43</td>
</tr>
<tr>
<td>Passive bed positioning</td>
<td>41</td>
<td>47</td>
<td>0.39</td>
</tr>
<tr>
<td>Splinting</td>
<td>3</td>
<td>9</td>
<td>0.08</td>
</tr>
<tr>
<td>Active range of motion</td>
<td>2 (2)</td>
<td>2 (1)</td>
<td>0.99</td>
</tr>
<tr>
<td>Active bed positioning</td>
<td>26</td>
<td>57</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>At least one bed activity</td>
<td>70</td>
<td>98</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Mobility activities, ( n )</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sit edge of bed</td>
<td>6</td>
<td>11</td>
<td>0.20</td>
</tr>
<tr>
<td>Sit to stand</td>
<td>24</td>
<td>30</td>
<td>0.34</td>
</tr>
<tr>
<td>Transfer</td>
<td>48</td>
<td>46</td>
<td>0.77</td>
</tr>
<tr>
<td>Ambulate</td>
<td>15</td>
<td>27</td>
<td>0.04*</td>
</tr>
<tr>
<td>Play</td>
<td>6</td>
<td>3</td>
<td>0.78</td>
</tr>
<tr>
<td>Other</td>
<td>5</td>
<td>3</td>
<td>0.31</td>
</tr>
<tr>
<td>At least one mobility activity</td>
<td>63</td>
<td>76</td>
<td>0.05*</td>
</tr>
</tbody>
</table>

*Descriptive, Fisher exact, and chi-square tests used for analysis, as appropriate.
*Statistically significant.

**Barriers to Activities and Adverse Events**

Barriers to activities before and after PICU Up! implementation in the first 3 days of PICU admission are shown in **Table 7.5**. Pre-implementation, the most frequently reported barrier to early mobilization activities as documented by nursing and/ or therapists included procedures (\( n = 19 \)), patient condition (\( n = 10 \)), and bed rest orders (\( n = 3 \)). Post-implementation, the most frequently reported barrier was lack of equipment, specifically age and size-appropriate seating devices and positioning materials (\( n = 22 \)), which was reported only twice preimplementation. Procedures were less frequently reported as a barrier (\( n = 10 \)) after PICU Up! implementation and patient condition continued to be
reported with similar frequency \((n = 11)\). No adverse events related to mobility, including unplanned extubations or line displacements, were reported in either phase of the program. In addition, there were no documented events of aborting mobilization activities once they had been initiated for hemodynamic, respiratory, pain, behavior, or pain criteria.

**Table 7.5: Barriers to activities- First 3 days of PICU admission**

<table>
<thead>
<tr>
<th>No. of Times Barrier Reported</th>
<th>Preimplementation</th>
<th>Postimplementation</th>
<th>(p^*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child refused</td>
<td>0</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Parent refused</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Test/study/procedure/surgery</td>
<td>19</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Patient condition</td>
<td>10</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Equipment availability</td>
<td>2</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Bed rest order</td>
<td>3</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

*Fisher exact test used for analysis.

**Feedback from PICU Staff**

Ninety-five PICU staff responded to the post-implementation feedback questionnaire, and 58% of respondents were nurses. Most staff (95%) indicated that the PICU Up! levels were helpful in planning activities. Seventy-three percent reported that the pocket card was the most useful resource for daily use to increase knowledge regarding mobilization of the critically ill child, and 68% agreed that they had the support needed from team members to increase patient activity. Support from PTs and OTs was reported as a valuable personnel resource for mobilization. Barriers included not having adequate staff to mobilize the child while continuing to care for the other patients. Respondents also indicated that the medical team was not always sensitive to competing demands of the bedside caregivers when discussing mobilization.
DISCUSSION

Through a structured QI process, the PICU Up! Early Rehabilitation and Progressive Mobility Program established an interdisciplinary, multicomponent, and stratified intervention for critically ill children admitted to the PICU. Implementation of a bundled intervention to create a culture of mobility in the PICU was safe and feasible and facilitated the formal involvement of physical and occupational therapists in the care of critically ill children. Although PICU Up! led to increases in early mobilization activities of critically ill children, our QI initiative identified several areas for ongoing education and modification.

A structured and stratified approach to adult ICU rehabilitation has been shown to increase the success of mobility program implementation. In line with the adult literature, key factors that fostered a culture of mobility after PICU Up! implementation included 1) standardization of workflow, 2) facilitation of discussions regarding mobility goals during morning work rounds, and 3) identification of safe activities for each patient based on his/her acuity level and specific needs. Unlike the adult literature, data to support early rehabilitation in the PICU are limited to pilot studies, case series, and case reports. To our knowledge, this is the first report of a large-scale, multifaceted QI intervention aimed at promoting a culture of mobility in the PICU setting.

PICU Up! significantly increased the formal involvement of occupational and physical therapists in the care of critically ill children. These resources were determined to be the most valuable by all staff in creating a culture of PICU mobility. Like many adult and pediatric intensive care units nationally, our PICU does not have dedicated PT/OT staff, and because PTs and OTs care for children throughout the hospital, they must be
formally consulted by physicians or nurse practitioners to work with PICU patients. Therefore, prior to implementation, we observed that PT/OT consultations were commonly delayed for the most critically ill children. This observation is consistent with a recent Canadian survey in which physiotherapists identified the need for a physician order as the major barrier to PICU rehabilitation. Before PICU Up! implementation, even when PT/OT consults were ordered early, nurses and/or physicians often would turn away therapy staff because they perceived that the patient’s acuity was a contraindication to rehabilitation therapies. This was true particularly for intubated children. In addition to creating a framework for timely PT/OT consultation for all PICU patients, educating staff about the breadth of early mobilization activities and empowering PT/OT staff to advocate for therapy was crucial. Nurses also used PT/OT sessions to learn simple interventions from therapists that they could facilitate between sessions. Guidelines for stopping and reassessing children during therapy activities also enabled all staff involved to have a shared mental model.

The increase in OT consultations by PICU day 3 is consistent with prior pre-post implementation mobility studies investigating early activity in ICUs. Unlike programs demonstrating increased mobility activities as measured by billable PT units, we did not observe a significant increase in PT referrals by PICU day 3. However, more children ambulated, suggesting that PICU Up! facilitated a transition to early ambulation through streamlined workflow and discussions.

Like other pediatric studies, our large-scale QI intervention did not result in any mobilization-related adverse events, such as inadvertent extubation. There were also no reports of a child needing to terminate activities early due to a decline in physiologic...
status or behavior. This finding is likely related to the fact that we designed the mobility levels based on the physiologic and developmental level of each child.

Although PICU Up! led to an increase in mobilization activities on PICU day 3 for both intubated and non-intubated children, activities on the day before PICU discharge were not significantly different before and after program implementation. Even if children were designated as Level 3 on the day before discharge, a longer LOS may be associated with the patient being more sedated and/or debilitated, requiring additional recovery time and resources for mobilization. In this study, additional resources were not allotted for personnel or equipment, and, consistent with the adult literature, PICU staff indicated that lack of equipment was a deterrent to mobilizing patients. Equipment challenges are further magnified in the pediatric population because of the heterogeneous nature of patients’ heights and weights. Barriers reported in the staff survey were consistent with the chart review and supported the importance of appropriate equipment and personnel in mobilizing the child.

Finally, the exclusion criteria for PICU Up! were based on several factors. First, in order to ease the implementation phase, address safety concerns, and optimize acceptability of the program among staff, we chose to exclude ECMO patients in the initial PICU Up! rollout given the unique needs of this patient population. After the completion of this study, we have begun translating the PICU Up! principles to ECMO patients and are successfully increasing mobilization activities in this population. The PICU Up! criteria will be modified after a pilot phase with ECMO-specific activity guidelines developed in conjunction with the ECMO team. Second, post-surgical patients with specific orders outlining mobilization restrictions were excluded from the initial implementation, although
sleep hygiene and delirium screening were in place for all patients. The same applied for open chests and open abdomens. All in all, the vast majority of surgical patients were included in the PICU Up! program which was well-received by our surgeons.

This study had several important limitations. First, data collected from a convenience sample in a single academic pediatric hospital may limit the generalizability. Second, the retrospective nature of data collection is limited by the quality of documentation, specifically with regards to barriers. Third, only children who remained in the PICU for 3 or more days were included, limiting generalizability for short-stay patients. Fourth, we were unable to determine changes in delirium incidence given that delirium screening was not yet routine in the pre-implementation phase. Fifth, we did not measure the impact of PICU Up! implementation on resource utilization and workload, an important future direction for research given that most PICUs do not have dedicated PTs and OTs. Finally, data on sedative-analgesic dosing was not collected.

**CONCLUSION**

A multicomponent and interdisciplinary approach to early mobilization of children admitted to the PICU is safe and feasible. PICU Up! increased the formal involvement of PTs and OTs and increased early mobilization activities including ambulation, without adverse events. Promoting and maintaining a culture of mobility in the PICU creates a strong foundation to investigate the effects of early mobilization on functional outcomes in critically ill children to potentially improve short and long-term outcomes while providing a healing PICU environment.
CONCLUSIONS AND FUTURE DIRECTIONS

The work in this dissertation systematically examined the state of sedation, sleep promotion, and delirium screening practices internationally and identified major knowledge gaps in need of investigation to identify interventions to decrease iatrogenic harm and optimize functional outcomes in critically ill children. In two single-center, observational studies, we demonstrated that children admitted to the PICU for respiratory failure or post-surgical management experience severe disruptions in day-night activity patterns as shown by EEG and accelerometry. We determined ongoing barriers to sleep promotion despite optimization of the architectural modification to single-patient rooms through a single-center survey, and also investigated barriers to accurate and effective delirium screening and management through a single-center survey of PICU staff. Finally, we integrated sedation, sleep promotion, and delirium screening with early mobilization to create a multidisciplinary program, and tested the safety and feasibility of this program in a large, tertiary care PICU. This quality improvement demonstrated that a streamlined approach to early mobilization in the PICU is indeed safe and feasible, and increased the engagement of PT and OT early in the course of critical illness. The long-term goal of this research is to create a paradigm shift in the care of critically ill children internationally and facilitate a culture of mobility with minimal but effective sedation, attention to sleep hygiene, and consistent and accurate delirium screening.

Over the last five years, there has been heightened awareness and attention to outcomes of both adult and pediatric survivors of critical illness after discharge from the hospital. In 2010, the Society of Critical Care Medicine convened a conference of stakeholders involved in the care of intensive care unit survivors after discharge. At this
conference, the term post-intensive care syndrome (PICS) was agreed upon as the recommended term to define as new or worsening impairment in physical, cognitive or mental health status arising after critical illness and persisting beyond discharge from the acute care setting.235,236

Physical disability after ICU discharge is most commonly manifested as ICU-acquired neuromuscular weakness, described in greater than 25% of adult ICU survivors.237,238 Prolonged mechanical ventilation, sepsis, and prolonged bedrest are common risk factors. Psychiatric symptoms include depression, post-traumatic stress disorder (PTSD), and anxiety, affecting up to 62% of adult patients.239,240 Cognitive impairment is demonstrated by new or worsened deficits in global cognition or executive function, which can persist beyond one year after ICU discharge.241 These manifestations of PICS have significant impact on quality of life. In a recent study of adult ARDS survivors, nearly one-third of patients who were previously employed never returned to work across five years of follow-up.242

Although PICS was defined with the lens of adult survivors of critical illness, there is also increased focus on outcomes in pediatric ICU survivors. Our recent systematic review synthesized the available evidence focusing on morbidities in pediatric survivors of critical illness that fall within the construct of PICS in adults.25 We found that PICS-related morbidities impact a significant proportion of children discharged from PICUs, however, substantial heterogeneity in functional outcome assessment tools and patient populations studied limited the generalizability of the findings. Long-term functional outcomes are associated with use of mechanical ventilation, ventilator days, use of vasoactive medications, and PICU length of stay.243
The primary goal of critical care medicine will always be to resuscitate and stabilize patients in the face of severe illness. However, there are several aspects of the care we provide that we can change and optimize to create an environment that promotes the best outcomes possible for PICU survivors. This dissertation work has laid the foundation for several projects that will continue to help us understand how the care we provide critically ill infants and children and their families impacts our patients both in the short and long-term.

**Prevalence of Acute Rehabilitation for Kids in the PICU (PARK-PICU)**

Through the PICU Early Mobilization Study, we demonstrated that a multidisciplinary program with formal PT and OT involvement to facilitate PICU mobilization is safe and feasible. Although PICU Up! led to a modest increase in PT/OT consultations within the first 72 hours of admission, perhaps most impactful was the two-fold increase in mobilization activities per child. These data suggest that mobilization activities were being conducted by nursing and families even when therapists weren’t at the bedside, similar to data from a recent ARDSnet point prevalence study of adult patients with respiratory failure. Staff received the program very positively, and felt that PT/OT were the most valuable educational resource available to them. However, data from one large academic PICU may not be generalizable to all PICUs.

Adult point-prevalence studies have demonstrated that although physical and occupational therapy (PT/OT) involvement is predictive of achieving greater mobility levels and improved outcomes, physical and occupational therapy-provided mobility is infrequent. Yet, adult studies cannot simply be extrapolated to the PICU due to wide range of ages and development in this population. Before large-scale trials can be designed
to investigate the effects of early mobilization therapies on outcomes in critically ill infants and children, it is critical to understand the current state of PICU practice for early mobilization and rehabilitation.

Building on what we learned from PICU Up!, we designed the **PARK-PICU** study: **Prevalence of Acute Rehabilitation for Kids in the PICU.** PARK-PICU is a 2-day cross-sectional point prevalence study of PICUs in the United States. The overall objective of this national point prevalence study is to characterize the prevalence and characteristics of mobility as part of routine clinical care for critically ill children in the PICU. We hypothesize that PT/OT-provided mobilization activities are infrequent, with severity of critical illness and mechanical ventilation predicting a decrease in mobilization activities.

We are testing our hypothesis with the following aims:

**Specific Aim 1:** Determine the prevalence of mobilization activities facilitated by physical and occupational therapists for critically ill children admitted to PICUs in the United States.

**Specific Aim 2:** Determine the demographic and treatment-related barriers to the formal involvement of PT and OT in the care of critically ill children in the PICU.

**Specific Aim 3:** Determine the frequency and characterize the types of mobilization activities in the PICU and identify factors associated with mobility progression.

With the collaboration of the Pediatric Acute Lung Injury Network and Pediatric Neurocritical Care Research Group, PARK-PICU has enrolled 80 PICUs encompassing cardiac, medical-surgical, and neurointensive care units across the United States in 60 hospitals. We anticipate a sample size of >1500 over the two point prevalence days, which will provide rich information about the current landscape of PICU acute rehabilitation. Because rehabilitation staffing and practice varies from continent to continent to continent...
and even country to country, PARK-PICU is being conducted separately in Canada, Brazil and Europe, with over 75 sites already on board in the planning stages. PARK-PICU Asia is also in its initial planning stages.

**Families PICU Up!**

While the ‘ABCDE’ bundle was first introduced in 2010, it has been since been augmented to include ‘F’ for family engagement. There is perhaps no more crucial role for families to engage in ICU care than in the pediatric ICU. While the traditional role of parents and guardians is to be with their child at the bedside and discuss their child’s care with the medical team, in an era of patient and family-centered care it becomes even more critical for families to directly engage in their child’s progress. To facilitate a culture of mobility in the PICU, it is not only the staff who need to be educated, informed and engaged about the importance of sleep promotion, minimal sedation, delirium prevention and early mobilization. Family members play a key role in implementing practices to support a healing environment for their child. However, the stress of having a child that is critically ill in an unfamiliar and fast-paced environment can be overwhelming for families, leading to a feeling of being secluded and uninformed. Parents may want their child to be heavily sedated in order to ensure that their child does not remember a stressful time, or keep the lights off and the shades closed in the morning to “let them sleep”.

“Families PICU Up!” is a quality improvement study to investigate the role of a family-specific education and orientation program on family satisfaction and engagement in daily care activities. In this pre-post implementation study, we are surveying fifty families of critically ill children to characterize the barriers and facilitators to family engagement. Additionally, we are learning about what activities families feel comfortable
with, and which activities cause anxiety or concern. Based on this information, we will create a Families PICU Up! menu modeled after the work of the adult ICUs at Johns Hopkins. In addition, a multidisciplinary team comprised of physicians, child life specialists, nurses and patient services coordinators will create a PICU Family Orientation Program that includes an introduction to the family menu as well as education about the importance of sleep hygiene, delirium prevention, minimal but effective sedation and early mobility. The orientation on the family’s role in optimizing the PICU environment and how they can partner with the critical care team to advocate for their child. After a 3-month implementation phase, 50 families will be surveyed in the post-implementation phase to characterize how the Families PICU Up! program impacted their perceptions of inclusion and comfort in their child’s PICU care. The Families PICU Up! study will provide critical information to guide multicomponent programs incorporating families to facilitate PICU liberation.

A stepped-wedge cluster randomized trial of a multidisciplinary, multicomponent early mobilization intervention

We have developed a sustainable and low-cost strategy to facilitate early mobilization in the PICU setting, and the results from our large-scale, multidisciplinary PICU quality improvement (QI) initiative (PICU Up!) has demonstrated that a streamlined, multicomponent early mobilization program is safe and feasible. However, there are no clinical trials to date investigating the impact of PICU early mobilization programs on short and long-term outcomes. Therefore, we propose to conduct the first trial of its kind building on the foundation of work in this dissertation.

The overall objective of the proposed study is to establish that an interdisciplinary
multicomponent early mobilization program improves outcomes of critically ill children admitted to the PICU in a stepped wedge cluster randomized controlled trial. Our central hypothesis is that implementation of a multicomponent early mobilization program will increase the direct involvement of PT/OT early in PICU admission (first 72 hours) and translate to increase in mobilization activities, decreased sedative administration, and improved functional outcomes compared to usual care.

At the completion of this project, it is our expectation that we will have elucidated the effectiveness of a multicomponent early mobilization program with quantitative and qualitative outcome measures, in addition to identifying barriers and facilitators to widespread implementation in the pediatric critical care setting. A large-scale randomized controlled trial has not been conducted to demonstrate the impact of EM on short and long-term PICU outcomes, therefore it is imperative that the pediatric critical care community simultaneously identify effective methods for implementation of early mobilization interventions that are generalizable, pragmatic and efficacious. Goal-directed sedation, sleep hygiene and delirium prevention are key contributors to creating a healing environment in the ICU, and incorporating these interventions into an early mobilization program is practical and low-cost. The primary positive impact of our anticipated findings would be evidence-based verification that multidisciplinary, multicomponent approaches to early mobilization are feasible and generalizable, with important benefits for children recovering from critical illness.
BIBLIOGRAPHY


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earplugs during the night on the onset of delirium and sleep perception: a randomized controlled trial in intensive care patients. Crit Care 2012;16:R73.


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Brief Biography

Sapna Ravi Kudchadkar was born on October 25th, 1977 to Shailaja and Kananur Ravi in Warner Robins, GA. She grew up in Charleston, IL, where her father was employed with the United States Department of Agriculture. Dr. Kudchadkar attended Charleston High School followed by college at Washington University in St. Louis. She graduated from medical school at the University of Chicago and completed all of her clinical training at Johns Hopkins, including pediatric and anesthesiology residencies and pediatric critical care and pediatric anesthesiology fellowships.

After joining the faculty at The Johns Hopkins University School of Medicine, Dr. Kudchadkar is now an Associate Professor of Anesthesiology and Critical Care Medicine, Pediatrics and Physical Medicine and Rehabilitation. She is board certified in Pediatrics and Pediatric Critical Care Medicine by the American Board of Pediatrics, and board-certified in Anesthesiology and Pediatric Anesthesiology by the American Board of Anesthesiology. Dr. Kudchadkar directs the PICU Clinical Research Program and the PICU Up! Taskforce at Johns Hopkins, where her clinical practice covers all aspects of pediatric critical care and anesthesiology.

Dr. Kudchadkar’s research focus is the interplay of sedation, sleep, delirium and early mobilization on outcomes in critically ill children. She has received funding from the NIH, American Thoracic Society and Foundation for Anesthesia Education and Research. She has authored over 40 peer-reviewed articles as well as several invited editorials and chapters in the field.

Dr. Kudchadkar is married to Janardan “Raj” Kudchadkar and has two incredible children, Kishen and Asha.
CURRICULUM VITAE
The Johns Hopkins University School of Medicine

The Johns Hopkins University School of Medicine

(Signature) _____________________________   February 5th, 2018
(Typed Name) Sapna R. Kudchadkar, MD    Date of this version

DEMOGRAPHIC AND PERSONAL INFORMATION

Current Appointments
2011-18    Assistant Professor, Department of Anesthesiology & Critical Care Medicine,
    Johns Hopkins University School of Medicine
2018-    Associate Professor, Department of Anesthesiology & Critical Care Medicine,
    Johns Hopkins University School of Medicine
    Pediatric Intensivist
    Johns Hopkins Hospital
    Pediatric Anesthesiologist
    Johns Hopkins Hospital

2013-present    Department of Pediatrics, Johns Hopkins University School of Medicine
2017-present    Department of Physical Medicine & Rehabilitation, Johns Hopkins University
    School of Medicine

Personal Data
    Johns Hopkins Charlotte R. Bloomberg Children’s Center
    1800 Orleans Street, Suite 6318B
    Baltimore, MD 21205
    Tel  (410) 955-6412
    Fax  (410) 502-5312
    E-mail sapna@jhmi.edu

Education and Training
Undergraduate
1999    B.A., Washington University, St. Louis, MO; graduated magna cum laude

Doctoral/graduate
2003    M.D., University of Chicago Pritzker School of Medicine, Baltimore, MD
2011-present    Ph.D., Johns Hopkins University Bloomberg School of Public Health, Baltimore, MD;
    anticipated graduation October 2017

Postdoctoral
2003-2006    Residency, Pediatrics, Johns Hopkins Hospital, Baltimore, MD
2006-2009    Residency, Anesthesiology, Johns Hopkins Hospital, Baltimore, MD
2009-2011    Fellowship, Pediatric Anesthesiology and Pediatric Critical Care Medicine, Johns
    Hopkins Hospital, Baltimore, MD
Professional Experience
1997-1999  Research Assistant, Division of Reproductive Endocrinology, Washington University School of Medicine, St. Louis, MO
2011-present Assistant Professor, Department of Anesthesiology and Critical Care Medicine, Johns Hopkins University School of Medicine, Baltimore, MD
2014-2015 Co-director, Johns Hopkins Pediatric Critical Care Clinical Research Program, Baltimore, MD
2015-present Director, Johns Hopkins Pediatric Critical Care Clinical Research Program, Baltimore, MD
2016-present Associate Director, ACCM Clinical Research Core, Baltimore, MD

PUBLICATIONS

Original Research [OR]  (Total citations= 388; h-index= 9; Google scholar)


Guidelines/Protocols, Consensus Statement, Expert Opinion, Consortium Articles [GL]

Review Articles [RA]


Case Reports [CR]


Book Chapters, Monographs [BC]


**Other Publications**

**Invited Editorials [ED]**


5. **Kudchadkar SR.** Benzodiazepines and delirium in the young and old: truth be told or still not sold? Crit Care Med. 2017 Sep;45(9):1562-1564. PMID: 28816839

**Letters, Correspondence [LT]**


**Media Releases or Interviews [MR]**


Interviewed by Evelyn Zuberbuhler for WFPICCS newsletter on #PedsICU initiative and new Associate Editor position: http://www.wfpiccs.org/qa-with-sapna-kudchadkar-md/

Other Media [OM] (Videos, Websites, Blogs, Social Media, etc.)


2015 Kudchadkar SR. Social media: www.twitter.com/HopkinsPICU. Twitter account creator and manager for the Johns Hopkins PICU. Dissemination of content and announcements relevant to pediatric critical care medicine and PICU staff.

2015 Kudchadkar SR. Social media: www.twitter.com/PedsPainMed. Twitter account creator and manager for the Society for Pediatric Pain Medicine

FUNDING

EXTRAMURAL Funding
Research Extramural Funding – Current
1/31/16–1/31/18 Alterations in Temporal Sleep-Wake Patterns of Critically Ill Children
Outstanding Early Career Investigator Award
American Thoracic Society Foundation
$40,000
Role: PI, 75%-- The objective of this career development grant is to obtain pilot data for the development of an R01 proposal investigating the impact of the PICU environment and sedative medications on the sleep-delirium pathway.

7/1/17-6/30/18 Diagnosing ICU-acquired Weakness to Optimize Functional Outcomes in Critically Ill Children
Thomas Wilson Sanitarium Research Grant
$15,000
Role: PI, 3%--The objective of this study is to validate methods for diagnosis of critical illness polyneuropathy and myopathy in the PICU using surface EMG and ultrasound.

7/1/17-6/30/19 RESTORE resilience (R2) in Critically Ill Children
R21HD093369/NIH(NICHD)
$70,410
Role: MPI, 3%- The overall objective of this study is to pilot-test the effect of a 7-item individualized circadian rhythm-restoring bundle on the critically ill child’s circadian activity pattern.

Research Extramural Funding – Previous
6/1/10-6/1/11 The Impact of Pain and Pain Management on Sleep in Mechanically Ventilated, Critically Ill Children
RFG-02/15/2010-Kudchadkar (Sapna)
$75,000
Role: PI, 75%-- In this study, polysomnography was used to characterize sleep disturbances in the PICU and develop analysis techniques for EEG in mechanically ventilated, critically ill children

7/1/11–6/30/13 Impact of Opioids and Sedatives on Sleep in Intubated Children
L40 HL110231-01
National Institutes of Health/NHLBI
Role: PI, 75%-- Loan repayment support during period of clinical research training.

2/1/13–2/1/14 Measuring and Optimizing Sleep in Mechanically Ventilated, Critically Ill Children
Sleep Services of America/Sleep Research Training Advancement Award
$50,000
Role: PI, 10%-- The objective of this study was to measure sleep fragmentation in children after major surgery using actigraphy in the PICU
and after transfer to the floor to determine the circadian activity ratio (CAR) of children admitted to the hospital.

1/1/15–05/31/17 The Role of Sleep Disturbances on Neuroinflammation in the Developing Brain Society for Anesthesia and Sleep Medicine $20,000 Role: PI, 10%-- This study investigated associations between sleep fragmentation and both short- and long-term neuroinflammation in a neonatal rabbit model.

4/1/15–8/30/17 Intravenous Clonidine for Infants and Children Who Are Mechanically Ventilated: A Dose-finding Study Thomas Wilson Sanitarium Research Grant $50,000 PI: Estelle Gauda/Sapna Kudchadkar Role: Co-PI, 5%-- In this pilot study, we are comparing the effectiveness of intravenous clonidine to that of dexmedetomidine for use as a sedative in infants admitted to the PICU, in addition to obtaining plasma clonidine levels to guide dosing for a large-scale therapeutic intervention.

Educational Extramural Funding – Previous
9/1/16–9/9/17 Impact of a Targeted Educational Program for Delirium Screening and Prevention in Critically Ill Children American Academy of Pediatrics Section on Critical Care $3,000 Role: PI/Mentor (Sean Barnes, MD, awardee), 2%--The objective of this proposal is to investigate the effectiveness of an online learning module about pediatric delirium for PICU staff that incorporates the psCAM-ICU (preschool confusion assessment method-ICU).

INTRAMURAL Funding
Research Intramural Funding – Previous
7/1/11–6/30/13 Sleep, Sedation, and Delirium in the Pediatric Intensive Care Unit 5KL2RR025006 NIH/NCRR KL2/Johns Hopkins Clinical Research Scholars Award $80,000/year Role: PI, 75%-- This grant provided funding for clinical research training through the Johns Hopkins Bloomberg School of Public Health and the Graduate Training Program in Clinical Investigation Ph.D. track to provide the foundation for ongoing research and new projects in pediatric anesthesia and critical care medicine.

7/1/13–6/30/16 Sommer Scholar Award for PhD Candidates Johns Hopkins University Bloomberg School of Public Health/Sommer Scholar Fund Role: PI, 75%-- This grant provided ongoing funding for PhD coursework through the GTPCI program.

7/1/16–6/30/18 Alterations in Temporal Sleep-Wake Patterns of Critically Ill Children Ross Physician Scientist Endowment
Johns Hopkins Clinician Scientist Award
$80,000/year
Role: PI, 75%-- The objective of this career development grant is to obtain pilot data for the development of an R01 proposal investigating the impact of the PICU environment and sedative medications on the sleep-delirium pathway.

System Innovation or Quality Improvement Intramural Funding – Previous
4/1/15–3/30/17 Cycled Lighting in the Neonatal Intensive Care Unit
Dorothy Evans Lyne Fund for Collaborative Nursing Research/JHU
$10,000
Role: Co-I, 5%-- The objective of this study was to investigate the impact of a cycled lighting protocol on sleep-wake patterns in critically ill neonates.

CLINICAL ACTIVITIES

Clinical Focus
As a pediatric intensivist and anesthesiologist, I am devoted in my clinical practice to the care of critically ill children in the pediatric intensive care unit and to the perioperative care of children undergoing surgery, including general anesthesia. I am dedicated to improving PICU and pediatric anesthesia care through a multidisciplinary approach to ICU liberation, with special emphasis on optimizing sleep and sedation, preventing delirium, and increasing early rehabilitation. As the Director of the PICU Clinical Research Program and creator of the “PICU Up!” initiative, I am focused on translating the complementary knowledge obtained from translational, human subject, and quality improvement studies to advance care of the pediatric patient.

Certification

Medical, other state/government licensure
2009-present Maryland Medical License, D69587

Boards, other specialty certification
10/06 Diplomate, American Board of Pediatrics (#669241)
10/10 Diplomate, American Board of Anesthesiology
10/12 Pediatric Critical Care Board Certification, American Board of Pediatrics
10/14 Pediatric Anesthesiology Board Certification, American Board of Anesthesiology

Clinical (Service) Responsibilities
2011-present Attending Physician, Pediatric Intensive Care Unit (40 beds), 6-7 weeks/year and 25 in-house calls/year
2011-present Attending Physician, Pediatric Anesthesiology/operating room, 1-2 days/week

Clinical Productivity
My targeted clinical effort assignment is 25%, with my actual clinical effort averaging 35-40% over the last three years.

- **PICU**: Approximately 2,500 patients between the ages of 1 day and 22 years are admitted annually to the Johns Hopkins PICU. As PICU faculty, I supervise and direct teams of
residents, fellows, medical students, and nurse practitioners in the care of critically ill pediatric patients with life-threatening medical and surgical conditions. My responsibilities also include medical direction for pediatric critical care transport. I also provide consultation, direction, and airway management for pediatric traumas and oversee pediatric rapid response team activations and medical emergencies throughout the hospital.

- **Pediatric Anesthesia:** In my role as a pediatric anesthesiologist, I supervise and direct residents, fellows, medical students, and nurse anesthetists in the provision of general anesthesia in the operating room and remote locations, including the cardiac catheterization lab, MRI, and interventional radiology.

**Clinical Program Building / Leadership**

2013–present  
Collaborated with Nick Dalesio, MD, (Chair, Pediatric DART program) as a co-chair in planning and implementing the Pediatric Difficult Airway Program, which subsequently led to development of the Pediatric Airway Consultation Service.

2013–present  
Developed and implemented the PICU Up! Early Mobilization Program in collaboration with the PICU Up! Working Group, a multidisciplinary taskforce I created to initiate the quality improvement process and promote acute rehabilitation for all critically ill children admitted to the PICU. The PICU Clinical Program impacts approximately 2,500 children per year in the Johns Hopkins PICU, and is a direct conduit to the physical and occupational therapy program (see System Innovation section). In addition, we created a streamlined process for the diagnosis and treatment of pediatric delirium using the pediatric CAM-ICU. Under my leadership, the PICU Up! Working Group was nominated for and awarded the 2016 Johns Hopkins Health System Clinical Teamwork & Collaboration Award.

**Clinical Demonstration Activities to external audience, on or off campus**

2016–present  
Johns Hopkins Health Care Solutions, PICU Up! Train the Trainer Program. Through this program, physicians, therapists, and nurses have the opportunity to be trained in group sessions on specific early mobilization interventions. I am the Director of this program and we currently have three tertiary-care children’s hospitals scheduled for training sessions either at Johns Hopkins or at their own sites in the next 12 months. PICU Up! has been adapted in Scotland and Brazil, with multiple other institutions currently developing their programs in Europe and Asia in addition to North America.

**EDUCATIONAL ACTIVITIES**

My educational focus includes the topics of ICU liberation for the pediatric population, specifically pediatric sedation, sleep promotion, pediatric delirium, and early rehabilitation. I am also passionate about difficult airway management as it relates to the pediatric patient. Finally, a major educational focus is clinical research design, biostatistics, and ethics in human subjects research.

**Teaching**

**Classroom instruction for clinical trainees**

2011–present  
Resident lecture for pediatric, anesthesiology, and emergency medicine residents during PICU rotation, lecture ~2X/month

2011–present  
“Sedation and Airway Management in the PICU: Practical Applications”- PICU fellow annual orientation and quarterly lecture series

2011–present  
“Scoliosis and the Pediatric Patient: Anesthetic Considerations”- Pedi-20 lecture series, ~5X/year
2011–present PICU fellow lecture series- core topics: ~8X/year
2012–present Anesthesia Resident College Day - One-day lecture and workshops ~ 6X/year (intraosseous access, standardized patient interviews, resuscitation)
2015–present Biostatistics and Epidemiology for PICU Fellows: Designed and implemented an educational curriculum around core biostatistics and epidemiology concepts including, evidence-based medicine. I facilitate and/or teach 10 sessions per year.

Classroom instruction for Johns Hopkins University students
2013–2015 Instructor, Clinical Epidemiology- Johns Hopkins University School of Medicine
2014–2016 Faculty Preceptor, Semester Medical Tutorials- Johns Hopkins University School of Medicine
2015–present Course Leader, Introduction to Clinical Research (ME.800.274), Cell and Molecular Medicine Graduate Program/Johns Hopkins ICTR
2015–present Lecturer, Professional Goals and Objectives- JHSPH GTPCI Program
2017 Lecturer, Neuromuscular Blockade and Local Anesthetics- JHUSOM 1st year medical students

Clinical instruction
2011-present Pediatric Resident Clinical Rotation, supervise/teach residents (pediatrics, anesthesiology, adult emergency medicine) during PICU rotation (~4 residents per month)
2011-present Pediatric Critical Care Fellows, supervise/teach subspecialty fellows during clinical service in PICU (~3 fellows/week)
2011-present Pediatric Anesthesia Fellows, supervise/teach in the operating room
2012-present Transition to Wards: Clinical Skills, 2nd year medical student instruction/mentoring in the history and physical

Workshops / seminars
JHMI/Regional
2011-2015 Speaker, Sadie Abell Annual Senior PICU fellow boot camp: Advanced Airway Workshop
2014-2015 Speaker and Organizer, Johns Hopkins Annual Pediatric Multidisciplinary Airway Workshop

National
2017 Organizer and Faculty, Research Workshop, 2017 Society for Pediatric Pain Medicine Annual Meeting; Houston, TX

Mentoring
Pre-doctoral Advisees /Mentees
2015-present Anisha Nadkarni, MD [medical student], currently combined pediatrics-anesthesia resident at Johns Hopkins; mentored research investigating sleep-wake patterns in post-op PICU patients while she was in medical school. Manuscript in submission.
2017-present  Ruchit Patel [undergraduate student], current sophomore at Johns Hopkins University. Mentoring research project qualitatively assessing the sustainability of early mobilization programs in the PICU. Awarded a Provost’s Undergraduate Research Award (PURA) 11/17.

Post-doctoral Advisees /Mentees
2011-2013  Othman Aljohani, MBBS [Research Fellow], currently 1st year pediatric cardiology fellow at UC San Diego; mentored his research in determining sleep quality of postoperative pediatric cardiac surgery patients with actigraphy. Two oral presentations at World Pediatric Critical Care Congress in Istanbul, Turkey (2012). Co-author on OR 2.

2013-2014  Ebaa Jastaniah, MBBS, MPH [Research Fellow], currently 3rd year pediatric resident at Tufts University, Boston, MA. Investigated role of environment, opioids, and sedatives on sleep patterns in the PICU. Oral presentation at AAP 2016 in San Diego, CA. Co-author on OR 9.

2013-2015  Melanie Cooper, DO [PICU Fellow], currently PICU attending at Pediatrics Medical Group, Spokane, WA. Investigated barriers to delirium screening in the PICU. Co-author on OR 8.

2013-present  Beth Wieczorek, NP, DNP [PICU nurse practitioner]. Developed and implemented a systematic approach to early mobilization for critically ill children. Co-author on OR 5, 10; GL 1.

2015-present  Sean Barnes, MD, MBA [PICU/Pediatric Anesthesia fellow]; Mentoring research in risk factors for delirium in the PICU and strategies for delirium education. Awarded AAP Section on Critical Care Small Projects Grant and American Thoracic Society Travel Award (2016). Co-author on OR 12; RA 4; ED 3; LT 3.

2015-present  Nehal Shata, MBBS [Research Fellow]; currently 1st year pediatric resident at McGill University. Investigated sleep-wake patterns in postoperative patients and worked on PICU Up! QI. Abstract presentation at PICC 2016 in Toronto, Co-author on OR 10.

2015-present  Sarah Bertrand, PhD [Postdoctoral Fellow]; currently 2nd year on multi-institutional T32 for sleep research; mentoring her translational research on sleep fragmentation-induced neuroinflammation in a pediatric rabbit model.

2015-present  Elizabeth Herrup, MD [PICU fellow]; Mentoring research on post-intensive care syndrome in PICU patients. Co-author on OR 15.

2016-present  Meghan Shackelford, CRNP [PICU nurse practitioner]; Current Armstrong Institute Leadership Academy Fellow. Mentoring QI work on sedation scoring in mechanically ventilated PICU patients.

2017-present  Alex Parra [Pediatric Physical Therapy Resident]; Mentoring research validating use of surface EMG in pediatric critical illness to diagnose critical illness polyneuropathy and myopathy. Awarded Thomas Wilson Sanitarium Grant.

Thesis committees
2015  Beth Wieczorek, DNP; “Impact of an Early Mobilization Program for Critically Ill Children,” Research Mentor

2016  Shinya Mura, MPH “Barriers to Early Mobilization in Critically Ill Children” Capstone Research Mentor

2017  Marjorie Birdsong, RN, “Prevention of Pressure Ulcers in Critically Ill Children” DNP Research Mentor
Educational Program Building / Leadership
2015  Designed two myLearning modules in collaboration with Hopkins myLearning on Pediatric Delirium and PICU Early Mobilization. These modules are taken by all PICU staff and are now being disseminated nationally through a collaboration with Johns Hopkins Health Care Solutions and the Armstrong Institute.

RESEARCH ACTIVITIES
Research Focus
My primary research focus is the role of sleep disturbances as modulator of outcomes in critically ill children, and the effects of sedation optimization, delirium prevention, and early rehabilitation in the management of children in the PICU. My current projects as PI include investigations of sleep in mechanically ventilated children using quantitative techniques and describing the evolution of sleep-wake cycles after critical illness as evidenced by long-term actigraphic monitoring. Additionally, I conduct translational work to study the role of sleep fragmentation on neuroinflammation in a neonatal rabbit model. Finally, I am the Lead PI for the international PARK-PICU (Prevalence of Acute Rehab for Kids in the PICU) study, which includes >130 sites in the US, Canada, Brazil, Europe and Asia. I have methodological expertise in clinical trials and statistical expertise in the time-series analysis of bio-signal data including accelerometry and electroencephalography (EEG). I have devoted my career as a clinician-scientist to advancing science in pediatric critical care through rigorous clinical research.

Research Program Building / Leadership
2015–present  Director, Pediatric Critical Care Clinical Research Program. I am responsible for oversight of all human subjects research conducted in the Johns Hopkins PICU. I also act as a resource for PIs conducting this research to ensure that studies are implemented smoothly and that multicenter trial requirements are being met. My roles include a) increasing participation of the Johns Hopkins PICU in national collaborative network studies (i.e., PALISI, CPPCRN, PNCRG); b) guiding fellows and faculty in study methodology and statistical analysis approaches and securing specific resources; c) centralizing screening for sponsored and non-sponsored single and multicenter studies; d) hiring and supervising full-time clinical research coordinator and pediatric research nurse.

2016–present  Associate Director, ACCM Clinical Research Core (CRC). Work in close collaboration with Dr. Nauder Faraday (Director) to create and maintain infrastructure for clinical research in the Department of Anesthesiology & Critical Care Medicine. Allocate resources (coordinator support, statistical support, database management) of ACCM CRC staff after review of applications from ACCM faculty and fellows. Work closely with ACCM Grants Management to streamline financing of studies and staff salaries while providing needed support for ACCM faculty seeking pilot funding for new studies or preliminary data.

Inventions, Patents, Copyrights

SYSTEM INNOVATION AND QUALITY IMPROVEMENT ACTIVITIES

System Innovation Focus
My system innovation focus is multicomponent approaches to early mobilization for the critically ill child. Through the PICU Up! Working Group at Johns Hopkins, I have led a multidisciplinary team of PICU staff in creating a standardized and streamlined approach to early mobilization and progressive rehabilitation for all PICU patients, changing the traditional paradigm of immobility and sedation to a culture of mobility. As such, improving family engagement to create healing environments in the PICU with augmentation of patient communication is a natural progression of this work.

System Innovation and Quality Improvement efforts within JHMI:
2013-present Chair (10%); PICU Up! Early Mobilization Initiative, Johns Hopkins PICU. In this QI project, data were collected and analyzed from July to August 2014 (preimplementation phase) and July to August 2015 (post-implementation). The study sample included 200 children aged 1 day through 17 years who were admitted to the PICU and had a length of stay of at least 3 days. PICU Up! implementation led to an increase in occupational therapy consultations (44% vs 59%; p=0.034) and physical therapy consultations (54% vs. 66%; p=0.08) by PICU day 3. The median number of mobilizations per patient by PICU day 3 increased from 3 to 6 (p<0.001). More children engaged in mobilization activities after the PICU Up! intervention by PICU day 3, including active bed positioning (p<0.001) and ambulation (p=0.04). No adverse events occurred as a result of early mobilization activities. In summary, implementation of a structured and stratified early mobilization program in the PICU was feasible and resulted in no adverse events. PICU Up! increased physical therapy and occupational therapy involvement in the children’s care and increased early mobilization activities, including ambulation.

System Innovation and Quality Improvement efforts outside of JHMI:
2016–present Site Lead, 3%; SCCM Peds ICU Liberation Initiative. This national quality improvement collaborative, which includes the Johns Hopkins PICU, aims to implement the ABCDEF bundle as part of a multisite quality improvement initiative. The ABCDEF bundle is a multimodal approach for liberating the ICU patient that incorporates analgesia (A), ventilator weaning (B), sedation coordination (C), delirium prevention (D), early mobilization (E), and family engagement (F). This collaborative has completed the baseline data collection phase, and is in the midst of rolling out subsequent components of the bundle with post-implementation data collection.

2015–present Pediatric ICU Social Media Initiative. As the Social Media ambassador for the American Academy of Pediatrics Section on Critical Care, I have led an initiative for system innovation in social media use within the pediatric critical care, anesthesiology, and pain medicine communities. Through the creation of #PedsICU, #PedsAnes, and #PedsPain, I am creating an international online community for research collaboration, dissemination, and education. My work to build these social media communities in medicine has led to over 20 million impressions since January 2016 for #PedsICU. I currently have ~2200 Twitter followers on my personal professional account, and the @HopkinsPICU and @PICU_Up! pages that I manage have 1000 followers each and are growing.
Based on my success with these social media initiatives and history of scholarly productivity in research, I was asked to be the Associate Editor of *Pediatric Critical Care Medicine* (PCCM) in February 2017. PCCM is the specialty’s primary journal and is the official pediatric journal of the Society of Critical Care Medicine and of the World Federation of Pediatric and Intensive Critical Care Societies. Since I have started in this role, PCCM has tripled its Twitter followers (700→>2000) and the number of unique visitors to the PCCM web page per month has doubled.

**System Innovation and Quality Improvement Program Building/Leadership:**

2016–present Leading collaboration with Johns Hopkins Health Care Solutions and the Armstrong Institute to provide early rehabilitation quality improvement tools to other institutions internationally, including online modules and bedside tools.

https://www.johnshopkinssolutions.com/solution/picu-up/

**ORGANIZATIONAL ACTIVITIES**

**Institutional Administrative Appointments**

2014-present Director of the Johns Hopkins PICU Clinical Research Program
2015-present Associate Fellowship Director (Research), PICU Fellowship Program
2013-present Pediatrics-Anesthesia Combined Training Liaison
2013-2016 Co-Chair, Pediatric Difficult Airway Taskforce
2013-present Director: PICU UP! Early Mobilization Team
2015-present Johns Hopkins Faculty Senate: Departmental Representative
2016-present Associate Director, ACCM Clinical Research Core
2016-present Johns Hopkins Anesthesia & Analgesia Pharmacy Specialty Panel
2017-present ACCM Research Committee, Co-chair ACCM Resident Research

**Editorial Board Appointments**

2017-present Associate Editor, *Pediatric Critical Care Medicine*

**Journal peer review activities**

2012-present *Pediatric Critical Care Medicine*
2012-present *Sleep*
2014-present *Journal of Clinical Anesthesia*
2014-present *Lancet Neurology*
2015-present *Pediatrics*
2015-present *Pediatric Drugs*
2015-present *Pediatric Transplantation*
2015-present *Journal of Neurotrauma*
2016-present *Critical Care Nurse*
2016-present *Hospital Medicine*
2016-present *Critical Care Medicine*
2016-present *Journal of Intensive Care Medicine*
2017-present *Patient Centered Outcomes Institute (PCORI)*

**Review groups/Study Sections**

03/2017 Ad hoc reviewer, National Institutes of Health NINDS/NSD-K Study Section
Professional Societies
2009-present Society of Critical Care Medicine
  - Pediatric section member
  - ICU Liberation Task Force
  - Chair Elect, Social Media Task Force
2009-present Society of Pediatric Anesthesia
  - Education Committee Member
  - Research Committee Member
2010-present American Academy of Pediatrics
  - Social Media Ambassador, Section on Critical Care (Appointed)
2011-present American Thoracic Society
  - Sleep & Respiratory Neurobiology Assembly Member
2012-present American Delirium Society
  - Research Committee Member (Appointed)
2014-present Society for Pediatric Pain Medicine
  - Chair, Research Committee

Conference Organizer
JHMI/Regional
11/14 Johns Hopkins Multidisciplinary Pediatric Airway Course, Conference Organizing Committee
11/16, 11/17 Johns Hopkins Critical Care Rehabilitation Conference, Chair and Organizer for Pediatric Critical Care Track
10/18 2018 Pediatric Critical Care Colloquium, Activity Co-Director.

Session Chair/Facilitator
JHMI/Regional
12/15 Co-chair, ACCM Research Day, Baltimore, MD
National
1/17 Session Chair, Society for Critical Care Medicine Annual Meeting, “From Toxic to Healing PICU Environments,” Honolulu, HI
5/16 Thematic Poster Session Facilitator, American Thoracic Society Meeting
4/17 Session Chair, Society for Pediatric Pain Medicine Annual Meeting, “Pediatric Pain Research: Year in Review,” Austin, TX
5/16, 5/17 Thematic Poster Session Facilitator, American Thoracic Society Meeting
2/18 Session Chair, Society of Critical Care Medicine Annual Congress, “Social Media in Critical Care,” San Antonio, TX
International
6/16 Session Chair, World Pediatric Intensive and Critical Care Societies Congress, “PICU Outcomes and Rehabilitation,” Toronto, Canada
6/18 Session Chair, World Pediatric Intensive and Critical Care Societies Congress, “Delirium in the PICU,” Singapore

Awards and Honors
1999 William Greenleaf Eliot Distinguished Leadership and Service Award, Washington University in St. Louis
2001 Soros Foundation Open Society Fellowship Award
2003 American College of Physicians (ACP) National Medical Student Poster Winner
2003 American Medical Women’s Association Leadership Award
2010 Foundation for Anesthesia Education and Research (FAER) Research Fellowship Grant
2010 Best Poster- 12th Annual Anesthesiology and Critical Care Medicine (ACCM) Research Day
2011 American Thoracic Society Fellow Travel Award
2011 Johns Hopkins KL2 Clinical Research Scholars Award
2011 NIH Extramural Pediatric Loan Repayment Program (LRP) Award
2013 Alfred Sommer Scholar Award-Graduate Training Program in Clinical Investigation, Johns Hopkins Bloomberg School of Public Health
2015 Ross Physician Scientist Endowment Award
2016 American Thoracic Society Outstanding Early Career Investigator Recognition Award
2016 Johns Hopkins Health System Clinical Teamwork and Collaboration Award
2017 Baltimore Magazine “Top Doctor” in Pediatric Anesthesiology

Invited Talks
JHMI/Regional
4/12 Speaker at Pediatric Resident Case Conference, “Pediatric Anesthesia Pearls: IV access,” Baltimore, MD
10/12 Speaker at Pediatric Critical Care Lecture Series for Visiting Professor Dr. Pat Kochanek, “Sleep in the Pediatric Intensive Care Unit,” Baltimore, MD
11/12 Speaker at PICU Research Series for Visiting Professor Dr. Carol Nicholson (NIH), “Sleep Research in Pediatric Critical Care,” Baltimore, MD
3/13 Keynote Speaker, Johns Hopkins Delirium Consortium, “Diagnosis and Management of Delirium in the Pediatric ICU,” Baltimore, MD
3/13 Guest Speaker for Pediatric Cardiology Faculty, “Sleep-Wake Cycles of Children after Cardiac Surgery,” Baltimore, MD
10/13 Keynote speaker for Johns Hopkins Sleep Medicine Lecture Series, “Characterizing Sleep in the PICU: Applications of the Fast Fourier Transform,” Baltimore, MD
4/14 Guest speaker for Johns Hopkins Pediatric Pulmonary Divisional Conference, “Sleep Disturbances in the PICU,” Baltimore, MD
8/14 Speaker for JHH Bench-to-Bedside Research Training Course, “Hypothesis and Rationale Building in Clinical Research,” Baltimore, MD
10/14 Speaker at Johns Hopkins Critical Care Rehabilitation Conference, “The PICU UP! Early Mobilization Initiative,” Baltimore, MD
11/14 Speaker for Johns Hopkins Neurocritical Care Seminar, “To Sleep or Not to Sleep in the PICU: Characterizing the Sleep EEG in Critically Ill Children,” Baltimore, MD
4/15 Speaker for Johns Hopkins Sleep Medicine Seminar, “Sleep, Critical Illness and the Developing Brain,” Baltimore, MD
11/15 Speaker at Johns Hopkins Critical Care Rehabilitation Conference, “Pediatric ICU Mobility: Case Studies,” Baltimore, MD
4/16 Speaker at JHU Anesthesiology & Critical Care Medicine Grand Rounds, “Sedation, Sleep, Delirium and the Critically Ill Child: We DID start the fire!” Baltimore, MD
6/16 Speaker at JHSPH Centennial Celebration introducing guest of honor Michael Bloomberg, Baltimore, MD
3/16   Grand Rounds Speaker at University of Maryland Department of Pediatrics, “Sleep, Sedation, Delirium and the Hospitalized Child,” Baltimore, MD
11/16  Speaker at Johns Hopkins Critical Care Rehabilitation Conference, “PICU Early Mobilization: Where we’ve come and where we’re headed,” Baltimore, MD
4/17   Speaker for Johns Hopkins Sleep Research Seminar, “Sleep and the Inpatient: More than meets the eye?” Baltimore, MD
6/17   Speaker for ACCM 39th Biennial Meeting, “Lessons Learned from PICU Up!: Successfully Educating Patients, Families and Colleagues to Implement a Paradigm Changing Program” Baltimore, MD
10/17  Speaker for ACCM Discovery Rounds, “The Quest to Liberate the Critically Ill Child” Baltimore, MD

National
2/12   Problem Based Learning Discussion, Society of Pediatric Anesthesia Annual Conference, “Factor VII deficiency and Craniofacial Reconstruction,” Tampa, FL
2/12   Speaker on panel discussion, Society of Pediatric Anesthesia Annual Conference, “Trends in Pediatric Anesthesia,” Tampa, FL
2/14   Speaker at University of Pennsylvania Anesthesia Research Seminar, “To Sleep or Not to Sleep in the Pediatric ICU,” Philadelphia, PA
4/15   Guest Speaker at Children’s National Medical Center PICU Research Series, “Sedation, Sleep, and Delirium: Friends or Foes?” Washington, DC
10/15  Invited talk at Society for Anesthesia and Sleep Medicine, “Sleep and Neuroinflammation in the Developing Brain,” San Diego, CA
2/16   Grand Rounds Speaker at St. Joseph’s Medical Center, “PICU Up!: Early Mobilization and the Critically Ill Child,” Paterson, NJ
2/16   Grand Rounds Speaker at Cornell University Department of Pediatrics, “Sleep and Hospitalized Children—Paradox?” New York, NY
5/16   Speaker for Postgraduate Course at American Thoracic Society Meeting, “Sleep, Critical Illness and the Developing Brain,” San Francisco, CA
6/16   Speaker for keynote panel at American Delirium Society Meeting, “Pediatric Delirium: Year in Review,” Nashville, TN
6/16   Grand Rounds Speaker at Medical College of Wisconsin Departments of Physical Medicine & Rehab and Pediatrics, “PICU Up!: Promoting a Culture of Mobility for Critically Ill Children,” Milwaukee, WI
9/16   Speaker at Pediatric Neurocritical Care Research Group Meeting, “Sleep Disturbances in Traumatic Brain Injury,” Washington, DC
11/16  Speaker at Annual Pediatric Critical Care Colloquium, “Early Mobilization in the PICU: But first a good night’s sleep!” New York, NY
1/17   Speaker at Society for Critical Care Medicine Congress, “Sleep, Delirium, and the ABCDEF Bundle”
1/17 Speaker at Society for Critical Care Medicine Congress and Session Chair, “From Toxic to Healing PICU Environments—Sleep Promotion in the PICU,” Honolulu, HI
3/17 Speaker at the Northwell Health ABCDEF Bundle Collaborative Meeting, “PICU Up! and the ABCDEF Bundle,” Lake Success, NY (web conferencing)
4/17 Grand Rounds Speaker at SUNY Stonybrook Department of Pediatrics, “Promoting a Culture of Mobility for Critically Ill Children,” Stonybrook, NY
4/17 Grand Rounds Speaker at University of Virginia Department of Pediatrics, “To Sleep or not to Sleep in the PICU,” Charlottesville, VA
5/17 Grand Rounds Speaker at Nationwide Children’s Hospital Department of Anesthesia, “Delirium: We did start the fire,” Columbus, OH
9/17 Keynote Speaker, Richard and Coral A. Tegley Memorial Lecture, LLUCH Pediatric Critical Care Symposium, “PICU UP! Teaming up and Transforming to a Culture of Mobility for the Critically Ill Child,” Loma Linda, California
12/17 Grand Rounds Speaker at Emory University Department of Pediatrics, Children’s Healthcare of Atlanta: Children’s at Egleston
12/17 Grand Rounds Speaker at Emory University Department of Pediatrics, Children’s Healthcare of Atlanta: Children’s at Scottish Rite
1/11/18 Grand Rounds Speaker at Case Western University/Rainbow Babies and Children’s Hospital, Cleveland, OH

Upcoming
2/23/18 Keynote Speaker at the Society for Critical Care Medicine Current Concepts in Pediatric Critical Care Course, San Antonio, TX “Sleep Hygiene in the PICU”
3/1/18 Grand Rounds Speaker at University of Iowa Department of Pediatrics, Iowa City, IA
3/19/18 Grand Rounds Speaker at Connecticut Children’s Medical Center, Hartford, CT
4/5/18 Grand Rounds Speaker at Children’s Hospital of Philadelphia/University of Pennsylvania, Philadelphia, PA
10/12/18 Speaker, 32nd Annual Meeting of the Society for Pediatric Anesthesia, San Francisco, CA “Progress Mobility in the Perioperative Period”

International
6/16 Speaker at World Pediatric Intensive and Critical Care (PICC) Congress, “Early Rehabilitation in the PICU: Practical Applications,” Toronto, Canada
6/16 Speaker at World Pediatric Intensive and Critical Care (PICC) Congress “ABCDE in the PICU: Ready for prime-time?” Toronto, Canada

Upcoming
6/18 Speaker at pre-conference workshop; World Pediatric Intensive and Critical Care (PICC) Congress, “Current Concepts in Pediatric Sedation Outside the Operating Room” Singapore
6/18 Speaker at World Pediatric Intensive and Critical Care (PICC) Congress, “Optimizing outcomes with PICU Rehabilitation” Singapore
6/18 Speaker and Session Chair at World Pediatric Intensive and Critical Care (PICC) Congress, “Social Media Use in Pediatric Critical Care” Singapore