SLEEP IN ADOLESCENT TRANSPLANT RECIPIENTS: A SOCIOECOLOGICAL SYSTEMS APPROACH

by

ANA M. GUTIERREZ-COLINA

(Under the Direction of Ronald L. Blount)

ABSTRACT

Objective: This investigation aimed first, to examine sleep quality in a sample of adolescent transplant recipients using a socioecological systems framework, and second, to evaluate sociocultural factors as markers of ecological risk. *Method*: Seventy-one adolescents (M = 16.49 years; SD = 1.62) with a solid organ transplant and their caregivers completed self- and proxy-report measures. *Results*: Adolescent transplant recipients have significantly more problems on certain domains of sleep quality compared to healthy peers. Better sleep quality was significantly associated with better psychosocial functioning, quality of life, fewer barriers to adherence, and greater medication adherence. Sleep quality was also a significant unique predictor of quality of life and barriers to adherence. Race significantly moderated the association between sleep and adolescent depressive symptoms. Sleep quality was not correlated with any of the micro- or macro-level factors examined. *Discussion*: Adolescent transplant recipients are at increased risk for experiencing poor sleep. Lower sleep quality in this population appears to be linked to various patient-level outcomes. Those from minority backgrounds are particularly vulnerable to the risks associated with disruptions in sleep. Sleep is an important modifiable factor that may contribute to adaptation and adjustment among adolescent transplant recipients.

INDEX WORDS: Sleep, Transplantation, Psychosocial Functioning, Socioecological Systems

SLEEP IN ADOLESCENT TRANSPLANT RECIPIENTS: A SOCIOECOLOGICAL SYSTEMS APPROACH

by

ANA M. GUTIERREZ-COLINA

B.A., University of Pennsylvania, 2009

M.S., University of Georgia, 2014

A Dissertation Submitted to the Graduate Faculty of The University of Georgia in Partial Fulfillment of the Requirements for the Degree

DOCTOR OF PHILOSOPHY

ATHENS, GEORGIA

2018

SLEEP IN ADOLESCENT TRANSPLANT RECIPIENTS: A SOCIOECOLOGICAL SYSTEMS APPROACH

by

ANA M. GUTIERREZ-COLINA

Major Professor:	Ronald L. Blount
Committee:	Anne E. Shaffer
	Cynthia M. Suveg

Electronic Version Approved:

Suzanne Barbour
Dean of the Graduate School
The University of Georgia
August 2018

DEDICATION

This dissertation is dedicated to all of those who have guided, challenged, and inspired me along the way, especially my parents, Javier and Lourdes, my sister, Lourdes, and my partner in life, Avner.

ACKNOWLEDGEMENTS

This investigation would not have been possible without the support and generosity of many individuals and institutions. Most notably, I would like to express my most sincere gratitude to my research advisor, Dr. Ronald L. Blount, for his unwavering support and guidance. His dedication to mentorship has profoundly shaped my development as a pediatric psychologist and as an individual. I would also like to deeply thank my committee members, Dr. Anne E. Shaffer and Dr. Cynthia M. Suveg, for their generous time, their thought-provoking feedback and their valuable guidance throughout graduate school. In addition, this work would not have been possible without the involvement of collaborators and families at Children's Healthcare of Atlanta, as well as the graduate and undergraduate members of the Pediatric Psychology Lab at the University of Georgia. Last but not least, I would like to acknowledge the funding sources that have generously supported this research through their grants.

TABLE OF CONTENTS

Page

CHAPTER

CHAPTER 1

INTRODUCTION

Sleep is a fundamental human need that plays a vital role in the mental and physical health of children. Despite the apparent lack of overt behaviors, sleep is a highly active physiological state of reversible unconsciousness, critical for brain development, arousal regulation, reparative processes, and optimal health (Colten & Altevogt, 2006). Early in development, sleep is the primary activity of infants who spend almost 80% of their time asleep (Colten & Altevogt, 2006). As children age, their sleep architecture changes and their sleep needs decrease as a result of both changing physiologic demands and cultural variables. Among adolescents, developmental changes precipitated by puberty lead to altered sleep patterns with shifts towards later sleep onset and later wake times. Despite reduced sleep demands with increasing age, the need for sleep remains a critical aspect of physical and emotional well-being throughout the lifespan.

The importance of sleep on child development and adjustment has been increasingly recognized in the field of child and pediatric psychology, with the last two decades demonstrating an exponential growth in the number of scientific articles dedicated to sleep in childhood (Beebe, 2016). With the surge in somnology research, it has become increasingly evident that juvenile sleep problems are common and frequently underrecognized, with about 15 million American youth affected by inadequate sleep (Smaldone, Honig, & Byrne, 2007). During childhood, approximately 20-30% of healthy children experience recurrent sleep difficulties (Davis, Parker, & Montgomery, 2004). As children get older and enter adolescence, natural

changes in sleep patterns, along with increased academic demands and access to technology, can result in misaligned biological circadian rhythms and clock time, leading to even greater risk for sleep problems. Sleep loss becomes increasingly worse over the course of adolescence (Wolfson & Carskado, 2003; Howell, Jahrig, & Powell, 2004). In the United States (US), sleep deprivation among teens has become an epidemic with approximately 87% of high school students getting suboptimal sleep (National Sleep Foundation, 2006). According to the National Sleep Foundation, teens need between 8 and 10 hours of sleep each night for optimal functioning, but only 15% of adolescents in the US get at least 8.5 hours of sleep on school nights (National Sleep Foundation, 2017). Changes in cultural and societal norms (Jenni & O'Connor, 2005) are likely responsible, at least in part, for the steady decline in children's total sleep duration over the past few decades (Dollman, Ridley, Olds, & Lowe, 2007; Matricciani, Olds, Blunden, Rigney, & Williams, 2012). Taken together, these data highlight the troublesome fact that children and adolescents are not getting the recommended amount of sleep they need for optimal functioning (National Sleep Foundation, 2008).

Among children with special developmental or medical needs, sleep problems are even more prevalent than among healthy children (Boergers & Koinis-Mitchell, 2010), with rate estimates as high as 80% (Liu, Hubbard, Fabes, & Adam, 2006). Comorbid sleep problems have been documented across a wide range of pediatric medical conditions, including cancer, diabetes, asthma, spina bifida, and obesity (Beebe, 2016). The extent to which these findings can be generalized to solid organ transplant populations, however, is unknown. A wide variety of factors related to disease-specific processes, such as pain, nocturnal exacerbation of symptoms, and disease-related disruptions in brain function, along with factors related to illness management, including the timing of drug administration, medication side-effects, and altered

family dynamics due to hospitalizations represent some of the pathways by which children's sleep can be disrupted among chronically ill children (Valrie, Gil, Redding-Lallinger, & Daeschner, 2007). The confluence of disease-specific processes and illness management factors makes pediatric transplant recipients particularly vulnerable to disruptions in sleep.

Limited research has examined sleep disturbances in pediatric transplantation, with only preliminary data on children with a liver transplant indicating that sleep problems are prevalent in this population. Approximately 25% of children who have received a liver transplant exhibit clinically significant symptoms of sleep problems (Fredericks, Dore-Stites, Calderon, Well, Eder, Magee, & Lopez, 2012). No research to date has examined the prevalence of sleep disturbances among children with kidney or heart transplantation despite sharing many of the same risk factors that affect liver transplant recipients. Some empirical data, however, supports the hypotheses that sleep problems may also be common among kidney and heart transplant recipients. Prior to heart transplantation, patients with end-stage heart disease have been found to be at risk for poor sleep quality (Zambroski, Moser, Bhat & Ziegler, 2005), suggesting that some of these sleep problems may persist following transplantation. Similarly, findings in the pediatric nephrology literature have demonstrated that among pediatric patients undergoing dialysis, a common treatment for children prior to kidney transplantation, sleep disturbances are very common (80%) (Davis, Baron, O'Riordan & Rosen, 2005), suggesting that kidney transplant recipients may continue to be at increased risk for sleep problems following transplantation.

The deleterious repercussions of sleep disturbances have been widely documented across nearly every aspect of functioning in healthy children. Scant research, however, has examined sleep-related outcomes among chronically ill children, with practically nonexistent research on

pediatric transplantation. Given the potential implications of disruptions in sleep and the need to identify modifiable factors that may promote better adaptation to living with a medical condition, researchers have called for greater emphasis on sleep among chronically ill children (Koinis-Mitchell, Craig, Esteban, & Klein, 2012). This investigation will answer this call by examining sleep quality in a sample of adolescent transplant recipients, a pediatric population known to be at increased risk for a wide variety health, psychosocial and cognitive difficulties (Eaton et al., 2017). A socioecological systems framework adapted for pediatric populations will be used as a comprehensive conceptual model to integrate and organize empirical findings related to sleep (El-Sheikh & Sadeh, 2015; Pai & Drotar, 2010). According to this model, variables can be categorized into four different systems based on how proximal or distal they are from the patient. Variables in each of these systems may influence or be influenced by sleep. Patient-level variables are those closest or directly experienced by the patient, including variables such as emotional functioning, quality of life, or morbidity. Micro-level variables are those that affect the immediate circle of the child, such as family functioning or parent emotional well-being. Meso-level factors are related to the child's community or school. Lastly, macro-level variables are the most distal from the patient and include larger system dimensions such as public health, healthcare costs, socioeconomic variables, or cultural values. This conceptual model will be used to review the empirical literature on sleep disruptions and how they relate to multiple levels of analysis (patient-, micro-, and macro-level variables) relevant to the research questions addressed in this study.

Sleep and Patient-level Factors

Disturbances in sleep have been associated to a wide array of adverse psychosocial and health outcomes in children. The bidirectional relation between sleep and mood regulation

specifically has been well established in the literature. Among healthy adolescents, experimental restrictions in sleep duration have been associated with increased emotion dysregulation, including greater symptoms of anxiety, tension, irritability, hostility and confusion as reported by both adolescents and their parents (Baum et al., 2014). Studies with younger children demonstrate similar results, with sleep loss leading to less positive affective responses and greater difficulties in emotion regulation (Vriend et al., 2013). Further, persistent sleep problems have been associated to a 16-fold risk of having clinical or subclinical psychosocial concerns 4 years later, including aggression, social and attention problems, anxiety and depressed mood (Simola, Luikkonen, Pitkaranta, Pirinen, & Aronen, 2012). In a population-based study of mixed illness groups, chronically ill children were shown to have more sleep disturbances and greater emotional problems than healthy children (Hysing, Sivertsen, Stormark, Elgen, & Lundervold, 2009). However, the differences in sleep became non-significant when adjusting for emotional problems. The extent to which sleep disturbances may be related to psychosocial functioning among transplant recipients has not been examined despite the documented risk for emotional problems in this population (Eaton et al., 2017), and the many disease-specific and illness-related factors that may affect their ability to obtain adequate sleep.

The relation between sleep and health is especially important among chronically ill children. Pediatric transplant recipients, who have highly suppressed immune systems as a result of the immunosuppressant medications they take to management of their condition, may be particularly affected by disruptions in sleep because sleep plays a central role in maintaining adequate immune responsiveness (Besedovsky, Lange, & Born, 2012). Epidemiologic data in adult populations corroborates the adverse effect of sleep disturbances on the incidence of physical illness (Gangwisch et al., 2007), immune function (Besedovky et al., 2012), disease

activity (Wolfe, Michaud, & Li, 2006), medication adherence (Saberi, Neilands, & Johnson, 2011; Phillips et al., 2005), obesity (Jean-Louis et al., 2014), and mortality (Shankar, Koh, Yuan, Lee, & Yu, 2008). In healthy children, sleep deprivation is a risk factor for greater frequency of health complaints (Paiva, Gaspar, & Matos, 2015; Smaldone et al., 2007), and in pediatric populations, sleep-related variables have been related to medication adherence (Bullington et al., 2007). The importance of sleep in the context of adherence has also been stressed in the literature as an important area of future research (Boergers & Koinis-Mitchell, 2010). Although no investigation to date has examined associations between sleep, barriers to adherence and medication nonadherence in transplant recipients, this area of study is particularly critical given the negative consequences associated with medication non-adherence (Fredericks, Lopez, Magee, Sheck, & Opipari-Arrigan, 2007), and the need to identify risk factors that can be targeted in adherence interventions.

Health-related quality of life encompasses many of the physical and psychosocial domains of functioning discussed thus far, and is a commonly used approach to health outcome measurement in pediatric research. The association between sleep and quality of life among chronically ill children has received greater attention in the last few decades, highlighting the increased interest that these constructs have spurred in the field of pediatrics. In a study of children undergoing treatment for acute lymphoblastic leukemia (ALL), for example, impaired sleep was associated with lower quality of life (van Litsenburg et al., 2011). Among children with a liver transplant, one study found that sleep disturbances similarly predict lower psychosocial, physical and overall quality of life (Fredericks et al., 2012). Whether similar relations exist among children with kidney and heart transplantation is yet to be examined in the literature. Given that quality of life has been increasingly recognized as an important

multidimensional outcome measure that appeals to experts across disciplines, a better understanding of the relation between sleep quality and quality of life among transplant recipients may serve as a bridge to foster multidisciplinary collaborations.

Sleep and Micro-level Factors

Sleep difficulties have rippling effects that affect not only patients but also the families and social circles where they develop. Most research in this area, although sparse, has been conducted with the parents of children experiencing sleep problems. Inadequate sleep in healthy children has been associated with significant parental and family burden. Data from the 2003 National Survey of Children's Health, for example, showed that children getting inadequate amounts of sleep were more likely to experience greater family conflict, and have parents with worse emotional functioning and poorer physical health (Smaldone et al., 2007). Behavioral interventions designed to address sleep problems in young children have been found to improve parents' sleep quality and family well-being (Eckerberg, 2004), providing support for the connection between sleep disturbances and micro-level outcomes. Increased marital conflict has also been associated with disruptions in the quantity and quality of children's sleep (El-Sheikh, Buckhalft, Mize, & Acebo, 2006), highlighting that family dynamics may not only be influenced by but also influence children's sleep. Among chronically ill children, poor sleep quality has been linked to worse parent quality of life (Fagnano, Bayer, Isensee, Hernandez, & Halterman, 2011), suggesting that sleep difficulties in pediatric populations might negatively affect parental functioning. These findings have been replicated among pediatric liver transplant recipients, with a recent study demonstrating that disruptions in sleep are linked to lower parent and family quality of life (Andersen, Dore-Stites, Gleit, Lopez, & Fredericks, 2014). Given the burden associated with caring for a chronically ill child and the increased risk for emotional distress

documented among the caregivers of pediatric transplant recipients (Cousino, Rea, Schumacher, Magee, & Fredericks, 2017), broadening our understanding of the connections between sleep and micro-level variables in children with a transplant might provide novel avenues to improve the well-being of families and caregivers.

Sleep and Macro-level Factors

The Institute for Healthcare Improvement (IHI) has called for new ways to improve the health of individuals and populations while reducing the cost of health care per capita (Orszag & Emanuel, 2010). In response to this call, the cost of sleep disruption and sleep deprivation has emerged as an area of future promise. Each year billions of dollars are spent on the direct and indirect costs of sleep loss and sleep disturbances (Colten & Altevogt, 2006). These costs include expenditures related to doctor visits, emergency room visits, hospitalizations, medications, loss of productivity, absenteeism, mortality and accidents (Colten & Altevogt, 2006).

Although no studies to date have examined the impact of sleep disturbances on pediatric health-care utilization, limited data exists in the adult literature. A community-based study of over 6,000 adults, for example, demonstrated significant associations between sleep disturbances and healthcare utilization (Kapur et al., 2002), leading authors to conclude that sleep disturbances are an under-recognized public health concern and constitute a substantial financial burden to the healthcare system. Daley and colleagues (2009) replicated these findings and further demonstrated that the largest proportion of healthcare expenses were related to work absences and reduced productivity. Additional research studies are needed to evaluate whether sleep problems among chronically ill children are linked to greater healthcare utilization and healthcare costs.

The Role of Sociocultural Factors in Sleep

In addition to the macro-level factors previously discussed, the influence of other macro-level variables, such as sociocultural factors, has been examined as potential moderators of the effects of sleep on children's functioning. Research with healthy children has demonstrated that factors such as race (Villaneuva, Buchanan, Yee, & Grunstein, 2005), socioeconomic status (SES; Spilsbury et al., 2006), and parent education (Buckhalt, El-Sheikh, Keller, & Kelly, 2009) can positively or negatively influence the effects of sleep deprivation. In a study of healthy African American (AA) and European American (EA) children, race and SES were found to moderate the association between children's sleep and internalizing symptoms (El-Sheikh, Kelly, Buckhalt, & Hinnant, 2010). Specifically, AA children demonstrated significantly more internalizing symptoms when their sleep was disrupted compared to EA children. The authors of this study also found that although children from lower and higher SES backgrounds had similar levels of internalizing symptoms when they had quality sleep, children from lower SES demonstrated more internalizing symptoms when sleep was disrupted, suggesting that optimal sleep is important for children's well-being, particularly in the context of ecological risk. Although the literature on the influence of sociocultural factors on children's sleep is limited, particularly among the chronically ill, evidence suggests that the link between sleep and illness is especially important in diverse populations (Boergers & Koinis-Mitchell, 2010). Recognizing the importance of this topic, Boergers & Koinis-Mitchell (2010) have called for greater consideration of culture within the context of sleep and chronic illness.

The Current Study

Guided by the existing body of literature, the current study adopted a socioecological systems model to better understand the role of sleep at multiple levels of analysis, including patient-level, micro-level, and macro-level systems (Figure 1). This study is the first to document sleep functioning and to evaluate sociocultural factors as markers of ecological risk in a sample of heart, kidney and liver pediatric transplant recipients. More specifically, the following hypotheses were explored: 1) Adolescent transplant recipients will exhibit significantly lower levels of sleep quality compared to healthy peers, 2) sleep quality will be related to patient-level variables (i.e., emotional functioning, quality of life, barriers to adherence, and medication adherence), micro-level variables (i.e., parent emotional functioning and family functioning), and macro-level variables (i.e., healthcare costs and healthcare utilization), and 3) sociocultural factors (i.e., race and SES) will moderate the associations between sleep and patient emotional functioning, such that children from minority and lower SES backgrounds will exhibit worse emotional functioning compared to those from majority and higher SES backgrounds when sleep is disrupted.

CHAPTER 2

METHOD

Participants

Participants included 71 AYAs between the ages of 12 and 18 who had received a solid organ transplant (heart, liver or kidney) and their parent or caregiver. All participants were recruited at a large tertiary-care pediatric hospital during routine follow-up medical appointments. Predefined inclusion criteria were as follow: 1) AYAs had received a heart, liver or kidney organ transplant more than 6 months prior to study enrollment, 2) AYAs were at least 12 year of age, and 3) AYAs and their caregivers spoke English fluently. Patients identified as having developmental delay by either the medical team or the caregiver were excluded from the study.

Procedure

Eligible participants were approached by a trained member of the research team during routine medical appointments in the hospital's transplant service. Once in the exam room, potential participants were given a brief summary of the study and invited to participate. All research questions were answered and interested families provided informed consent, assent, and Health Insurance Portability and Accountability Act (HIPPA) release prior to participating in the study. Participants independently completed paper and pencil self-report and/or parent-proxy report measures. A gift card was provided to each participant as an incentive for completing all study measures. Families who declined to participate were asked to complete an anonymous demographic questionnaire to assess for significant differences between those who agreed to

participate and those who declined. Procedures for this study were in full HIPAA compliance and approved by the Institutional Review Boards of participating institutions.

Measures

Medical and sociodemographic data

All participants completed a brief questionnaire to assess basic demographic and health information including participant's age, race, gender, household income, caregiver highest level of education, caregiver marital status, and transplant type. Medical data including time since transplantation was extracted retrospectively via medical chart review.

Sleep

Adolescent Sleep Wake Scale (ASWS; LeBourgeois, Cortesi, Wolfson, & Harsh, 2005). The ASWS is a 28-item self-report measure used to assess sleep quality in adolescent populations. Participants are asked to indicate on a 6-point scale ranging from *always* to *never* how often a particular sleep behavior has occurred over the past month. The ASWS is comprised of 5 different subscales each assessing a different dimension of sleep including going to bed, sleep onset, sleep maintenance, sleep re-initiation, and return to wakefulness. Only the Falling asleep, Maintaining sleep, and Returning to wakefulness subscales were used in this study. To calculate mean subscale scores, pertinent questions were reverse scored and the items comprising each subscale were summed and averaged. Scores range from 1 to 6, with higher scores indicating better sleep quality. Previously published normative scores for the ASWS were used to compare sleep quality in this sample to scores of healthy peers (Murray, Murphy, Palermo, & Clarke, 2012). The ASWS has been categorized as "approaching well-established" using evidence-based assessment criteria (Lewandowski, Toliver-Sokol, & Palermo, 2011). In the

current study, internal consistency reliability for the ASWS was α = .76 (Falling asleep), α = .72 (Maintaining sleep), α = .79 (Returning to wakefulness), and α = .74 (Total).

Psychosocial functioning

Behavior Assessment System for Children – 2nd Edition Parent Report Scales (BASC-2-SRP; Reynolds & Kamphaus, 2004). The BASC-SRP is a self-report, multidimensional measure used to assess children's emotional and behavioral problems. Participants use a 4-point Likert scale ranging from *never* to *almost always* to rate how frequently a certain behavior occurs. Individual items for each of the 13 subscales are added to calculate age-normed *T*-scores. BASC *T*-scores between 60-69 indicate "at-risk" levels for internalizing, externalizing, and behavioral problems. Similarly, *T*-scores that are ≥ 70 indicate the presence of clinically significant problems. Only the Depression and Anxiety subscales were used in this study. Internal consistency and convergent validity for the BASC has been demonstrated in the literature (Reynolds & Kamphaus, 2004). In the current study, Cronbach's alphas for the Depression and Anxiety subscales were α = .90 and α = .84, respectively.

Health-related quality of life

Pediatric Quality of Life Inventory, Generic Core Scales, Version 4.0 (PedsQL; Varni, Seid, & Kurtin, 2001). The PedsQL is a 23-item self- and proxy-report measure used to assess health-related quality of life in pediatric populations and health children. Participants use a 5-point Likert scale ranging from *never* to *almost always* to rate how frequently different problems have occurred over the previous month. The PedsQL is comprised of four different subscales including Social Functioning, School Functioning, Emotional Functioning, and Physical Health. Scores from the Social, School, and Emotional Functioning subscales are averaged to constitute the Psychosocial Functioning composite score. An overall quality of life score can be obtained

by averaging all individual subscale scores. Subscale and composite scores can range from 0 to 100, with higher scores indicating better quality of life. Internal consistency reliability and construct validity for the PedsQL have been empirically demonstrated in the literature (Varni et al., 2001). In the current study, Cronbach's alphas ranged from .83 to .89.

Barriers to Adherence

Adolescent Medication Barriers Scale (AMBS; Simons & Blount, 2007). The AMBS is a multidimensional 17-item self-report measure used to assess barriers to medication adherence in adolescent populations. Participants use a 5-point Likert scale ranging from *strongly disagree* to *strongly agree* to indicate how much different barriers interfere with their ability to take medications as prescribed. Barriers to adherence are classified into 3 different factor-analytically derived subscales including Regimen Adaptation/Cognitive Issues, Disease Frustration/Adolescent Issues, and Ingestion Issues. The psychometric properties for the AMBS have been demonstrated to be robust in the literature. Criterion-related validity has been shown to be strong with adherent adolescents reporting significantly fewer barriers compared to nonadherent adolescents (Simons & Blount, 2007). In the current study, Cronbach's alphas for the Total Barriers score and each of the 3 AMBS subscales were $\alpha = .91$ (Total), $\alpha = .82$ (Disease Frustration/Adolescent Issues), $\alpha = .77$ (Ingestion Issues), and $\alpha = .60$ (Regimen Adaptation/Cognitive Issues).

Medication Adherence

The Medication Adherence Measure (MAM; Zelikovsky & Schast, 2008; Zelikovsky, Schast, Palmer, & Meyers, 2008). The MAM is a semi-structured interview used to assess medication adherence over the previous 7 days. Adolescents are independently interviewed and report on the names and dosages of prescribed medications that they are taking, as well as the

number of prescribed medications that the adolescent missed, took late, or took on time. They also rate on a scale of 0 to 10 how adherent they have been to their medical regimen overall. Only the overall rating scale was used in this study. The MAM has been shown to have adequate predictive validity as indicated by empirical data documenting significant associations between MAM-reported nonadherence, clinical outcomes and barriers to adherence (Simons et al., 2010; Zelikovsky et al., 2008). The MAM has also been shown to have adequate convergent validity (Dobbels et al., 2010). Given the highly skewed nature of the data, this variable was dichotomized by patients who reported perfect adherence (coded as "0") versus those who endorsed less than perfect adherence (coded as "1"). Forty-four percent of the adolescents were in the first group, and the remaining (56%) were in the second group.

Parent Emotional Functioning

Brief Symptom Inventory (BSI-18; Derogatis, 2001). The BSI-18 is an 18-item self-report measure of overall psychological functioning and distress in adults. Participants are asked to endorse how much a particular symptom bothered them in the past 7 days. Possible answers are provided using a Likert-scale ranging from *not at all* to *extremely often*. The BSI-18 is comprised of three different subscales including Depression, Anxiety and Somatization, all of which yield the Global Symptom Inventory (GSI) summary score. Raw scores are converted to *T*-scores derived from a normative sample. GSI scores ≥ 63 are indicative of clinically significant levels of emotional distress (Derogatis, 2001). The validity of the BSI-18 has been empirically demonstrated with strong positive correlations with the Symptom Checklist-90-Revised, the original scale used to develop BSI-18 (Recklitis & Rodriguez, 2007). Internal consistency for the BSI total and subscale scores was $\alpha = .84$ (Depression), $\alpha = .86$ (Anxiety), $\alpha = .89$ (Somatization), and $\alpha = .94$ (GSI).

Family Functioning

Family Adaptability and Cohesion Evaluation Scale IV (FACES-IV; Olson et al., 2006). The FACES-IV is a 43-item inventory developed to assess two different dimensions of family functioning, including Family Cohesion and Flexibility from the Circumplex Model of Marital and Family Systems. These two dimensions are comprised of six different family scales, including Balanced Cohesion, Balanced Flexibility, Disengaged, Enmeshed, Rigid, and Chaotic. Only the Balanced Flexibility and Balanced Cohesion subscales were used in this study. Participants endorse how much they agree with various descriptions of family functioning using a 5-point Likert scale. The FACES-IV has demonstrated good levels of reliability and validity (Olson et al., 2006). In the current study, Cronbach's alphas for the Balanced Flexibility and Balanced Cohesion subscales were $\alpha = .87$ and $\alpha = .92$, respectively.

Healthcare Costs and Utilization

Healthcare Cost and Utilization Questionnaire. A healthcare cost and utilization questionnaire was developed for this study to assess the financial loss families incurred related to patients' healthcare over the previous 6 months, as well as how much each patient utilized the healthcare system during the previous 6 months. This questionnaire assessed a variety of domains including how much work caregivers had to miss due to their child's illness, how much school adolescents missed due to their health, out-of-pocket expenses related to the patient's medical condition, lost wages, number of times patients attended medical appointments, had lab work, were hospitalized and went to the emergency room.

Data Analytic Plan

All data analyses were conducted using IBM SPSS Statistics, Version 22. Descriptive statistics including means, standard deviations (*SD*) and ranges were calculated for all

demographic and study variables. External validity was examined by comparing the demographic characteristics of those families who agreed to participate to those who declined. *T*-scores were calculated for pertinent measures and one-sample *t*-test analyses were used to compare the current sample to normative data. Cohen's *d* (Cohen, 1992) was the effect size calculated for all *t*-test results. Group differences in sleep quality across organ groups were tested using ANOVA. A *p*-value of $< .05$ was considered statistically significant for results involving hypothesis testing. Correlational analyses were conducted to examine associations between study variables and demographic factors. Demographic variables that were not continuous or ordinal were dichotomized prior to conducting correlational analyses.

Guided by prior literature (Bemis et al., 2015), a cumulative SES factor was calculated using the following variables: household income, marital status, and caregiver education level. Each of these variables was dichotomized such that families received either a 0 or a 1 depending on their level of risk: annual household incomes $\leq$ \$50,000 were coded as 1 versus incomes > \$ 50,000 which were coded as 0; single or divorced caregiver status was coded as 1 versus partnered status which was coded as 0; and caregiver education level $\leq 12^{th}$ grade was coded as 1 versus $>12^{th}$ grade which was coded as 0. The cutoff for annual household income was chosen to approximate families above and below the median income for US families, which was \$53,718 based on the 2014 US Census data. The cutoff for caregiver education was chosen following previously published recommendations (Brody et al., 2013; Bona et al., 2014). The cumulative SES factor, which ranged from 0 to 3, was calculated by summing scores across each one of the variables described.

Primary Analyses

Correlational analyses were conducted to examine associations between sleep quality and patient-level, micro-level and macro-level variables. Hierarchical multiple regression analyses were conducted to examine sleep quality as a cross-sectional predictor of patient-level variables after controlling for the effects of pertinent study variables as determined in preliminary analyses. Significant correlations between study variables were used to guide the entry of variables in the regression analyses. Baron and Kenny's (1986) criteria for testing moderation was used to examine the moderating effect of race and SES on the hypothesized association between sleep quality and patient emotional functioning. The recommendations by Holmbeck (2002) were followed when significant moderation effects were found to examine the simple interaction effects of race and SES. The procedures of Hayes and Matthes' (2009) macro (http://afhayes.com/spss-sas-and-mplus-macros-and-code.html) were used to probe significant interactions.

Power Analysis

G*Power (Faul, Erdfelder, Lang, & Buchner, 2009) was used to determine sample sizes needed to detect medium effect sizes (Cohen, 1992) for all planned analyses. For 2-tailed, one-sample *t*-tests examining differences between sample and norm means, a sample size of 64 is needed to detect effects (power = .80, α = .05, and effect size = .50). For Pearson product-moment correlational analyses, a sample of 84 is needed to achieve adequate power (power = .80, α = .05, and effect size = .30). For regression analyses including up to four predictors, a sample size of 68 participants is needed to detect effects (power = .80, α = .05, and effect size = .15).

CHAPTER 3

RESULTS

Participants

Of the 71 AYAs included in this study, 28 were female (39.4%) and 43 were male (60.6%). They ranged in age from 12 to 18 years (M = 16.49 years; SD = 1.62). Twenty-one of the adolescents enrolled in the study received a heart transplant (29.6%), 25 (35.2%) received a liver transplant, and 25 (35.2%) received a kidney transplant. On average, adolescents had received their transplant 8.03 years prior to enrollment in the study (SD = 5.68). Approximately half of the participants were Caucasian (n = 37; 52.1%), followed by African American (n = 19; 26.8%), Asian (n = 6; 8.5%), biracial (n = 6; 8.5%), and Hispanic (n = 3; 4.2%). Participating parents/caregivers included 58 (90.6%) females and 6 (9.4%) males. The mean age for caregivers was 45.58 years (SD = 8.33; range = 33-73 years). The majority of caregivers were biological parents (n = 54; 84.4%), 11.1% were legal guardians (n = 6), 1.6% were step-parents (n = 1), and 4.7% were grandparents (n = 3). A detailed description of additional demographics is presented in Table 1.

Comparison of participating families versus those who declined. Twelve of the families approached for participation in this study declined due to lack of interest. To assess external validity, one-way ANOVA and χ^2 tests were conducted to compare families who agreed to participate to those who declined in terms of patient's age, gender, race, organ type, caregiver

education level, and annual household income. There were no significant differences between the two groups in regards to transplant type, gender, race, age, or family income.

Preliminary Analyses

Bivariate correlations revealed significant associations on the following study variables based on medical and demographic factors: Child race was significantly associated with scores on the ASWS Falling asleep (r = .28, $p \leq .05$) and Total barriers to adherence (r = -.26, $p \leq .05$) subscales, such that those from non-minority backgrounds reported better sleep quality and less barriers to adherence. Child gender was significantly related to health-related quality of life (r = .32, $p \leq .01$), with females having significantly worse quality of life than males. Older age was also associated with more overall barriers to adherence (r = .24, $p \leq .05$). Significant demographic variables were used as covariates in subsequent regression analyses to statistically control for their effects on the variables of interest. Significant correlations between study variables were also used to guide the entry of variables in the regression analyses (Table 2).

Primary Analyses

Sleep in Adolescent Transplant Recipients

T-test analyses were conducted to compare sleep quality scores in the current sample to published scores for healthy adolescents (Murray et al., 2012). Results revealed that adolescents with a solid organ transplant have, on average, significantly more difficulty falling asleep than healthy peers (Table 3). No significant differences were found for this subscale across organ groups. Approximately 42% of the current sample endorsed experiencing difficulty falling asleep *Quite often, Almost Always* or *Always*. Differences on the maintaining sleep subscale were trending in the expected direction but did not reach significance. However, adolescents with heart transplants (M = 3.9; SD = 1.03) had significantly more difficulties maintaining sleep than

those with liver (M = 4.65; SD = 0.73) or kidney (M = 4.77; SD = 0.93) transplants (F[2,66] = 5.94, p = .004). Therefore, additional t-test analyses were conducted to separately compare heart transplant recipients to norms. Results revealed significant differences between heart transplant recipients and healthy peers, such that heart transplant recipients endorsed significantly more problems maintaining sleep than their healthy counterparts (t [19] = -3.39, $p \leq .01$). Overall, slightly over 22% of the total participant sample reported having difficulties maintaining sleep *Quite often* to *Always.* No significant differences were found between adolescents with a transplant and healthy peers on their ability to return to wakefulness, but about 65% of adolescents in this study reported that their problems returning to wakefulness ranged from *Quite often* to *Always*. There were no differences across organ groups on this domain of sleep quality.

Sleep in Adolescent Transplant Recipients and Patient-Level Variables

Sleep Quality and Patient-level Variables

Correlational analyses revealed that all domains of sleep quality, including Falling asleep, Maintaining sleep, Returning to wakefulness and Overall sleep quality were significantly and negatively related to adolescent psychosocial functioning. Specifically, adolescents who endorsed poorer sleep quality also reported higher symptoms of anxiety and depression (Table 4). Consistent with these results, all domains of sleep quality were positively related to health-related quality of life across all domains, with adolescents who reported higher levels of sleep quality also endorsing better Physical, Psychosocial and Total quality of life (Table 4).

As shown in Table 4, all sleep quality subscale scores, with the exception of the Returning to wakefulness subscale, were significantly associated with Total adherence barriers, as well as barriers related to Disease Frustration/Adolescent Issues, Regimen Adaptation/Cognitive Issues, and Ingestion Issues. Specifically, adolescents who endorsed lower

sleep quality also endorsed more barriers to adherence. The Returning to wakefulness subscale was associated with the Ingestion Issues barriers subscale only (Table 4). Consistent with these results, lower scores on the Falling asleep and Overall sleep quality subscales were related to less adherence on the MAM. No significant associations were found between the Maintaining sleep and Returning to wakefulness subscale scores and the MAM adherence variable.

Is Sleep a Predictor of Patient-level Variables?

Multicollinearity diagnostic analyses were performed for all regression analyses and no multicollinearity issues were detected (VIF ≤ 2 and Tolerance $\geq .5$). Hierarchical regression analyses for adolescent quality of life are presented in Table 5. Given that Depressive and Anxiety symptoms were highly correlated ($r = .62$, $p \leq .01$), a composite internalizing symptoms variable was calculated by averaging the T-scores of each subscale in order to avoid entering potentially multicollinear variables. Child gender was entered in step 1, emerging as a statistically significant predictor and accounting for 10% of the variance in overall quality of life. Adolescent internalizing symptoms was entered in the second step of the model and emerged as a significant predictor. This model accounted for 51% of the variance in adolescent quality of life. Overall sleep quality was entered in the last step of the model and emerged as a significant predictor, contributing an additional 5% of the variance in the prediction of adolescent quality of life. Child gender and internalizing symptoms remained significant predictors in step 3. The final model accounted for a total of 56% of the variance in overall quality of life.

In predicting adolescent barriers to adherence, patient age and race were entered in step one, predicting 12% of the variance (Table 6). Both child race and child age emerged as significant predictors. Adolescent internalizing symptoms was added in the second step of the model, emerging as a significant predictor. Child age, but not child race, remained as a

significant predictor, with this model predicting 30% of the variance in Total barriers . Overall sleep quality was entered in the third step of the model and emerged as a significant predictor, contributing an additional 7% of the variance in the prediction of barriers to adherence. All predictors were significant in the final model, which accounted for a total of 37% of the variance.

Logistic regression analyses were conducted to examine sleep quality as a unique predictor of medication adherence above and beyond barriers to adherence (Table 7). The AMBS Total subscale was entered in the first step of the model. The Wald criterion revealed that barriers to adherence made a significant contribution to the prediction of medication nonadherence (Wald = 5.59, $p \leq .05$). A test of this model against a constant only model was statistically significant, indicating that the predictor reliably distinguished between adolescents who reported perfect adherence and those who did not ($\chi^2 = 6.43$, $p \leq .05$, df = 1). This model accounted for approximately 14% of variance. Overall sleep quality was entered in the second step of the model. The standardized coefficient for the sleep quality variable was not significant, indicating that sleep did not improve the model's ability to distinguish between those who had perfect adherence and those who did not. The final model accounted for approximately 18% of the variance in medication adherence, which was not a statistically significant increment from the first model, which only included barriers to adherence. Detailed information about odds ratios (i.e., Exp[B]) are presented in Table 7.

Sleep in Adolescent Transplant Recipients and Micro-Level Variables

Correlations between Sleep Quality and Micro-Level Variables

No significant associations were found between domains of sleep quality and scores on any of the BSI (Depression, Anxiety, Somatization, Global) and FACES (Cohesion, Flexibility) subscales (Table 8).

Sleep in Adolescent Transplant Recipients and Macro-Level variables

Correlations between Sleep Quality and Macro-Level Variables

No significant associations were found between domains of sleep quality and any of the healthcare-related costs (out-of-pocket medical expenses, loss wages, missed days of work and school) or healthcare utilization (medical appointments, hospitalizations, lab work, emergency room visits) domains assessed (Table 9).

Sleep in Adolescent Transplant Recipients and the Role of Sociocultural Factors

Does Race Moderate the Association Between Sleep Quality and Emotional Functioning?

Hierarchical linear regression analyses were conducted to examine the moderating effect of race on the relationship between sleep quality and both depressive and anxiety symptoms (Table 10). Predictors were mean centered prior to conducting analyses. Child race was entered in Step 1 of the regression models, overall sleep quality was entered in Step 2, and the interaction of race and sleep quality was entered in Step 3. The first model examined evaluated the moderating effect of race on the association between sleep quality and depressive symptoms. In the first step of this model, race did not emerge as a significant predictor. In the second step, sleep quality was found to be a significant predictor of adolescent depressive symptoms, accounting for 29% of the variance. The interaction between sleep quality and race entered on the third step was significant and contributed an additional 5% of the variance predicting adolescent depressive symptoms. The final model accounted for a total of 34% of the variance in adolescent depressive symptoms. Following the recommendations by Holmbeck (2002), additional analyses were conducted to examine the simple effects of the interaction for adolescents from minority and non-minority backgrounds. The PROCESS macro for SPSS and procedures recommended by Hayes (2013) were followed. Results indicated that the slope was

not significant for adolescents from non-minority backgrounds (t[65] = -1.94, $p > .05$), but significant for adolescents from minority backgrounds (t[65] = -5.09, $p \leq .001$). Figure 2 depicts this interaction. For non-minority adolescents, similar levels of depressive symptoms were reported at low and high levels of sleep quality. For minority adolescents, on the other hand, depressive symptoms were significantly higher for those with worse sleep quality compared to those with better sleep quality.

Race was not found to be a significant moderator of the association between sleep quality and anxiety symptoms.

Do SES Moderate the Association Between Sleep Quality and Emotional Functioning?

A second set of regression analyses was conducted to evaluate SES as a moderator of the association between sleep quality and both depressive and anxiety symptoms. In Step 1 of the regression model, SES was entered. Overall sleep quality was entered in Step 2, and the interaction of SES and sleep quality was entered in Step 3. Results revealed that SES did not emerge as a significant moderator of the association between sleep quality and depressive symptoms, nor between sleep quality and anxiety symptoms.

CHAPTER 4

DISCUSSION

The importance of sleep on the adjustment and psychosocial well-being of chronically ill children has been increasingly recognized in the field of pediatric psychology (Beebe, 2016), with recent work emphasizing the value of considering sociocultural variables as potential moderators of the connection between sleep and children's functioning (Boergers et al., 2010). Much more limited attention has been devoted to the link between sleep and more distal variables such as family functioning or healthcare utilization. This study sought to build upon the existing body of literature by evaluating sleep quality in a diverse group of adolescent transplant recipients and by adopting a socioecological systems framework in the investigation of proximal and distal factors associated with sleep, with particular emphasis placed on the moderating role of race and SES.

Partially consistent with the study's hypothesis, adolescent transplant recipients endorsed significantly more problems on some domains of sleep quality compared to healthy peers. Specifically, adolescents in the current sample reported significantly more difficulties falling asleep, indicating more prominent problems with sleep onset compared to norms. Although total amount of sleep was not directly measured in the current study, increased sleep onset latency at bedtime suggests that this patient population may obtain even lower amounts of sleep than their healthy counterparts - a group shown to obtain insufficient sleep according to NSF guidelines for optimal functioning (National Sleep Foundation, 2017). The prevalence of adolescents who endorsed experiencing sleep onset problems at least *quite often* is consistent with previous reports in adolescent liver transplant recipients (Fredericks et al., 2012). A number of key factors

may be contributing to teens' difficulties falling asleep, including stressors related to having a chronic medical condition, strict medication-taking schedules, or the immunosuppressant drugs they are required to take to prevent organ rejection. Steroids and tacrolimus, for example, are two commonly prescribed immunosuppressant medications that have been associated with sleep disturbances and insomnia (Kemper, Sparta, Laube, Miozzari, & Neuhaus, 2003; Turner & Elson, 1993), and which may negatively affect teens' ability to fall asleep. Overall, adolescent transplant recipients experiencing sleep onset difficulties would likely benefit from information about the potential sleep-related side effects of their medication regimen, psychoeducation about sleep hygiene, and ongoing clinical assessment and monitoring of the potential contributors to sleep-related symptomology.

Although trending in the expected direction, no significant differences were found between liver and kidney transplant recipients and healthy peers on the sleep maintenance subscale, indicating that liver and kidney transplant recipients had no more difficulty staying asleep than their healthy counterparts. Conversely, adolescents with a heart transplant endorsed significantly more problems staying asleep compared to both healthy peers and other transplant recipients. These findings highlight the particular vulnerabilities that heart transplant recipients may have to experience sleep problems. Prior to heart transplantation, patients with end-stage heart disease have been found to be particularly vulnerable to poor sleep quality and sleep-disordered breathing (Lofaso, Verschueren, Rande, Harf, & Goldenberg, 1994; Zambroski et al., 2005), suggesting that some of these difficulties may persist following transplantation. Despite reported accounts of overall improvements in sleep post-transplant in adults (Fisher, Lake, Reutzel, & Emery, 1994), ongoing monitoring of sleep and sleep-related difficulties may be particularly important following pediatric heart transplantation.

With regards to adolescents' capacity to return to wakefulness, participants in the current study did not demonstrate significantly more challenges than healthy peers in this domain of sleep quality. A high percentage of the sample (65%), however, endorsed having difficulty returning to wakefulness *Quite often, Almost always,* or *Always*, suggesting that despite the lack of overall significant differences with healthy norms, a large portion of adolescent transplant recipients experience challenges in this domain of sleep. It is possible that difficulties with sleep onset are limiting the amount of nightly sleep that adolescents obtain, which could directly influence their ability to feel refreshed and rested in the morning. Although not the focus of this investigation, symptoms of fatigue, sleepiness, and drowsiness after waking can have important implications for some of the developmental tasks characteristic of this developmental period, such as academic learning (El-Sheikh et al., 2007). Given that difficulties in this domain of functioning may be particularly impactful among transplant recipients who may regularly miss school due to routine medical appointments, lab draws, and hospitalizations, special attention should be paid to the potential role of daytime fatigue and sleepiness on adolescents' academic performance.

Associations between sleep quality and patient-level factors were consistent with study hypothesis. Adolescents who experienced poorer sleep quality also endorsed significantly more symptoms of depression and anxiety. Previous experimental work on healthy adolescents has demonstrated that shortened sleep is causally related to worsened mood, decreased ability to regulate negative emotions (Baum et al., 2014), and reduced self-ratings of positive affect (Dagys et al., 2012). Identifying modifiable factors potentially related to emotion regulation in adolescent transplant recipients is particularly salient not only because adolescence has been linked to increased psychopathology (Walker, 2002) and emotional reactivity (Dahl & Gunnar,

2009), but also because of the increased rates of psychosocial difficulties documented in this patient population (Eaton et al., 2017). Although sleep alone is certainly not exclusively responsible for the higher prevalence of mood difficulties observed among transplant recipients, it may be a nonspecific stressor (Steinberg & Avenevoli, 2000) capable of accentuating existing vulnerabilities in this population. Patients on certain types of immunosuppressant medications, for example, are at increased risk for emotion regulation difficulties (Pretorius, 2004), which could be exacerbated by poor sleep. For adolescents facing the stressors and challenges that come with living with a transplant (e.g., shortened lifespan, frequent medical appointments, possible need for an additional transplant), this combination of vulnerabilities may be particularly detrimental. Given that sleep is one of the modifiable factors experimentally linked to poor emotion regulation (Baum et al., 2014), psychologists working as part of pediatric transplant teams should routinely assess and, when needed, target this area of functioning that could facilitate adjustment and promote the well-being in this patient population, particularly those at risk for poor emotion regulation.

Given the complex and bidirectional relation between sleep and internalizing symptoms, clinicians working with transplant recipients should also consider the possibility that increased anxiety and depressive symptoms, particularly those surrounding disease-specific factors (e.g., the possibility of re-transplantation, organ rejection) and illness management variables (e.g., worries related to taking medications, treatment-related weight gain), are negatively affecting adolescents' ability to obtain adequate sleep. Increased rumination, for instance, is one of the hallmark symptoms of both anxiety and depression, which may challenge adolescents' ability to fall asleep. Therefore, attention to the role of internalizing symptoms on sleep disruption is also an important avenue to successfully guide intervention recommendations. If difficulties falling

asleep are primarily linked to ruminative thought patterns, rather than use of technology at night or medications side effects, treatment recommendations would likely focus on addressing the mood symptomatology that is negatively affecting adolescents' ability to obtain quality sleep. In this manner, assessment of sleep problems may not only promote patient well-being by indirectly improving sleep but also by addressing the underlying emotional difficulties affecting adolescents.

In line with this pattern of results, poor sleep quality in each aspect assessed was consistently associated with lower levels of health-related quality of life across all domains, including physical, psychosocial, and overall functioning. These findings are consistent with past work demonstrating links between sleep and quality of life among liver transplant recipients (Fredericks et al., 2012) and suggest that kidney and heart transplant patients are also at increased risk for experiencing lower quality of life in the context of poor sleep. To evaluate overall sleep quality as a unique predictor of quality of life after accounting for the effect of internalizing symptoms, regression analyses were conducted. As hypothesized, results revealed that while internalizing symptoms accounted for a significant portion of the variance in quality of life, sleep quality explained significant additional variance and was a significant unique predictor of quality of life. These findings highlight the potential role that adequate sleep may have in the promotion of patient well-being above and beyond internalizing symptoms – an undoubtedly important component of quality of life. Targeting a readily modifiable factor such as sleep in pediatric transplant recipients may help ameliorate the well-established pattern of impaired quality of life in this population.

Besides investigating emotional functioning and quality of life, this study builds upon past work by examining one of the potential key factors that may help explain, in part, the

documented link between sleep and adherence (Bullington et al., 2007). Consistent with study hypothesis, adolescent transplant recipients who reported better overall sleep quality also endorsed having fewer barriers to adherence, with the domains of sleep onset and sleep maintenance driving these associations. Past experimental studies have demonstrated that decreased sleep is related to decreased alertness, lower efficiency, more forgetfulness and more exhaustion (Baum et al., 2014) - all aspects that may directly influence and potentially mediate the relation between sleep quality and the Regimen Adaptation/Cognitive Issues subscale, which includes items such as "I don't realize when I run out of pills" or "I am not organized about when to take the medicine." Similarly, disruptions in sleep may be related to decreased ability to regulate emotions (Baum et al., 2014), which could be directly connected to adolescents' ability to cope with the frustration of having a medical condition or having to take medications, both aspects captured by items on the Disease Frustration/Adolescent Issues subscale (e.g., "I am tired of living with a medical condition"). Although maybe less intuitive, similar disruptions in emotion regulation and cognitive sharpness may challenge adolescents' ability to cope with ingestion-related barriers such as "I have to take too many pills" or "I get confused about how the medicine should be taken." Surprisingly, only barriers related to the Disease frustration/Adolescent issues subscale were associated with difficulties returning to wakefulness, suggesting that feeling alert in the morning may be particularly important for managing illness-related and medication-related frustration.

To build upon these findings, regression analyses were conducted to both identify unique predictors and evaluate, for the first time, whether sleep quality explains additional variance in the prediction of barriers to adherence above and beyond age, race, and internalizing symptoms. Although internalizing symptoms have been previously shown to be positively related to barriers

to adherence in the pediatric transplant population (King et al., 2014), it remained unclear whether poor sleep exerts its influence on barriers to adherence through children's internalizing symptoms exclusively, or whether the construct of sleep quality served as an important additional predictor of barriers even after accounting for internalizing symptoms. Consistent with study hypothesis, results revealed that sleep quality remained a significant predictor of barriers after controlling for relevant variables, including internalizing symptoms. These findings suggest that targeting poor sleep, particularly as it pertains to sleep onset and sleep maintenance, may not only ameliorate potential difficulties with emotional regulation and internalizing symptoms, but also decrease the likelihood that transplant recipients will experience barriers that may challenge their ability to adhere to their prescribed medication regimen.

In addition to the significant associations found between sleep quality and barriers to adherence, findings in the present study replicated previous research (Bullington et al., 2007) demonstrating a significant connection between certain domains of sleep quality and medication adherence. In the current investigation, adolescents who reported having better sleep quality overall or fewer difficulties with sleep onset, also endorsed significantly less problems with medication nonadherence. This was not the case for the maintaining sleep and returning to wakefulness domains. It is possible that the sleep schedule of adolescents with sleep onset difficulties is less predictable (e.g., naps, getting up late), which may interfere with their ability to stick to a consistent and rigorous medication schedule. A teen who has difficulty falling asleep at night, for example, may wake up significantly later on weekends in order to catch up on missed sleep. This lack of consistent wake times could interfere with teens' ability to take medications on time. Further, as discussed above, sleep may also interfere with medication-taking by making barriers to adherence more salient or more likely to occur. To evaluate the

question of whether sleep quality is a unique predictor of adherence and also whether it explains significant variance after accounting for the effects of barriers on medication adherence, regression analyses were conducted. Findings were inconsistent with hypothesized results and revealed that sleep quality did not account for significant additional variance in the prediction of medication adherence after accounting for barriers. Thus, it appears that sleep quality may be exerting its influence on adherence via barriers. Future research is needed to examine barriers as a potential mediator of the relation between sleep and adherence, as well as to evaluate whether targeting sleep difficulties indirectly improves adherence by decreasing barriers.

The lack of significant findings between sleep and micro-level variables was unexpected. Although research in this area is sparse, a number of studies have found significant associations between sleep and micro-level variables, including family burden, family conflict, and family well-being (Eckerberg, 2004; Smaldone et al., 2007). It is possible that the current findings do not replicate results from previous studies due to the different constructs examined. Namely, family cohesion and flexibility, rather than family conflict and burden were assessed in the current study to capture aspects of family functioning. One potential explanation is that family cohesion and flexibility are more stable family characteristics unlikely to affect or be affected by the quality of adolescents' sleep or the potential ramifications that poor sleep might have on adolescents' functioning (e.g., increased emotional dysregulation, greater fatigue, more forgetfulness). Family conflict and parent burden, on the other hand, may be more context-dependent variables, and thus, more easily influenced by adolescent's sleep quality.

A lack of significant associations was also found between adolescent sleep quality and parent psychosocial functioning, which was inconsistent with previous work demonstrating significant associations between sleep and parent quality of life (Fagnano et al., 2011). It is

possible that examination of slightly different constructs is also responsible for the lack of consistent findings in this scenario. Sleep quality may influence parents' functioning on a more global level that is captured by measures that assess a combination of domains of functioning, such quality of life. Conversely, the influence of sleep on more specific domains of functioning, such as emotional functioning, may not be as strong, leading to a lack of significant associations between those constructs. It is also possible that because the age of participants used in past research was significantly younger (4-10 years; Fagnano et al., 2011) or included a much wider age range (2-17 years; Andersen et al., 2014) compared to participants in the current study, previous findings are not generalizable to teens. Younger children may rely more heavily on parents when their sleep is disrupted compared to older teens, who are more likely to regulate their sleep patterns independently. This would explain differential findings and the more limited role that adolescent sleep quality may have on parents' emotional functioning. An alternative possibility is that as teens become increasingly more independent and seek greater individuation from their caregivers, they are less vulnerable to the influences of their parents' psychosocial functioning, which may be more salient for younger children who heavily rely on parental figures for sleep. Additional research is needed to elucidate whether discrepancies in findings are due to changing developmental needs and trajectories as children get older, underlying differences in the constructs examined, or peculiarities of the current sample.

With regard to macro-level factors, a lack of significant findings between sleep and more distal variables was not completely unexpected given both the limitations of the measures used to capture aspects of healthcare utilization and healthcare costs, and also the mostly exploratory nature of the analyses. Although preliminary data in the adult literature suggests that sleep disturbances are related to healthcare use (Kapur et al., 2002), the use of indirect measures of

healthcare utilization (e.g., measures of chronic disease status empirically shown to correlate with hospitalizations, ambulatory visits, mortality, etc.) in those studies limits our ability to compare those results with data in the current study, which exclusively relied on parents' direct reports of healthcare utilization for their children. Significant findings in the adult literature may also be driven by the accumulated effect of sleep problems and stress overtime. Consistent with cumulative models of risk (Rutter, 1983), the higher the number of sleep-related risks accumulated overtime, the more likely an individual will be to suffer the physical and mental consequences that lead to higher healthcare utilization and costs. Pediatric populations, unlike adults, might not have been exposed to the stressors associated with sleep problems long enough to incur higher healthcare costs and utilization. It is equally important to note that the significant shortcomings of the measures used in the current study to assess macro-level variables, as indicated below, may also be partially responsible for the lack of significant findings. While present results should be interpreted with considerable caution, it is the hope that these findings will be a preliminary step in the future exploration of sleep and more distal system-wide variables in chronically ill populations.

Lastly, moderation analyses were conducted to evaluate whether poor sleep quality is particularly salient in the context of ecological risk. Consistent with study hypothesis, results revealed that race was a significant moderator of the association between sleep and depressive symptoms, such that among adolescents who endorsed lower levels of sleep quality, those who were from minority backgrounds experienced the highest levels of depressive symptoms. Conversely, when sleep was not disrupted, those from minority and non-minority backgrounds experienced similar levels of depressive symptoms. These findings replicate past studies examining the moderating role of race on the relation between sleep and internalizing symptoms

in healthy children (El-Sheikh et al., 2010), and suggest that adolescent transplant recipients who experience poor sleep quality are at increased risk for concurrent depressive symptoms. Consistent with work on health disparities, these results highlight both the importance of considering contextual factors (Boyce et al., 1998), and the notion that certain populations may be more negatively affected by stressors (Foundation for Child Development, 2010). Although the actual pathways that produced significant moderation were not examined, there are a number of possible mechanisms. First, given that contextual risk has been linked to poorer emotion regulation (Walton & Flouri, 2010), and that poor sleep has been associated with decreased ability to regulate negative emotions (Baum et al., 2014), it is possible that those from minority backgrounds are more negatively affected by disruptions in sleep because the emotion regulation processes affected by poor sleep would exacerbate pre-existing difficulties with emotion regulation. Second, poor sleep may affect those from minority backgrounds to a greater extent because of the theoretical higher number of chronic stressors that they have, which may become more difficult to manage when sleep disrupts emotion regulation processes. Third, minorities experiencing poor sleep may also be exposed to other environmental stressors not accounted for in the study, which might contribute to higher levels of depressive symptoms. Although these are just a few of the possible mechanisms, further research is needed to elucidate the connection between race, sleep and depressive symptoms.

Unlike the moderation results for depression, race was not found to be a significant moderator of the association between sleep and anxiety symptoms. Previous work evaluating the moderating role of race used a composite score including anxiety, self-esteem, and depression to jointly capture internalizing symptoms, therefore making it challenging to compare the current results with previous findings. It is possible that the significant moderating role of race on the

relation between sleep and internalizing symptoms previously found was driven by depressive symptoms and not anxiety. Future research is needed to clarify discrepancies in findings.

The lack of significant results using SES as a moderator was surprising and somewhat inconsistent with previous studies documenting the moderating role of SES on the relationship between sleep and internalizing symptoms in healthy children (El-Sheikh et al., 2010). It is worth noting that previous research examining this question only found significant moderating effects for SES when parent-report of child internalizing symptoms was used. Similar moderating effects were not found for child-reported internalizing symptoms, which is aligned with results in the current study. Further, the previous study examining this question was conducted among third and fifth graders, a significantly younger age range than the adolescents included in this study. It is possible that different patterns of interactions may be present at different stages of development. Future research is needed to examine how associations between sleep and adjustment develop and change over time.

A number of limitations limit the conclusions that can be drawn from the current investigation. First, the cross-sectional design of the study limits the types of inferences that can be drawn from the data. Sleep can function as a symptom and a stressor, and as such, the associations reported in this investigation likely reflect complex and bidirectional relations, not fully captured in this study. Future longitudinal and experimental methodologies are needed to assess the influence of sleep, as a nonspecific stressor, on factors both proximal and distal to the child. Further, although sleep was independently examined across three different levels of analyses in this investigation, interactive and dynamic relations likely characterize the associations among these variables. Future research and theory is needed to guide our understanding of the complexities inherent in the study of sleep, how sleep changes over time

and evolves throughout development, and how it affects and is affected by variables across multi-level systems. Second, only subjective self-report measures of sleep quality and adherence were obtained in the current study. The use of objective data, such as actigraphy, polysonmography, and immunosuppressant serum levels, will be a vital aspect of future research to more comprehensively capture accurate levels of sleep functioning and adherence. Third, the measure used to assess healthcare costs and utilization had significant limitations and has not been validated. Although not without its own challenges and limitations, the use of more objective measures, such as hospital records of healthcare-related expenditures or healthcare use, is likely a more fruitful and reliable avenue to examine the potential role of sleep disturbances on healthcare utilization and costs in future studies. Fourth, minority participants in this study were grouped together to obtain adequate statistical power. However, minority teens represented a variety of races and ethnicities. As a result, the existence of potential racial differences in the relations examined could not be evaluated in this study. Finally, while the sample was diverse in terms of organ type, race, and SES, all participants were recruited from a single transplant center, which may limit the generalizability of these findings. Future multi-site collaborations will help address concerns surrounding external validity, and will provide greater statistical power to detect significant findings by increasing sample size.

Despite these limitations, the present study made significant contributions and is novel in a number of ways. First, this investigation builds upon the existing body of literature by evaluating sleep patterns in a diverse group of adolescent transplant recipients and documenting domains of sleep that are significantly more impaired compared to norms. Second, this investigation is also the first to adopt a socioecological systems framework to examine the proximal and distal connections between sleep and various factors at multiple-levels of analyses.

The strong associations found between sleep and patient-level variables suggest that when sleep functions as a stressor, it may be a readily modifiable target of intervention that can positively affect adaptation, functioning, barriers, and adherence among adolescent transplant recipients. These findings stress the importance of routine sleep assessment in outpatient clinical settings, particularly among heart transplant patients, and also highlight that sleep assessment may not only aid in the identification of sleep as a pathway of risk for poor adaptation (El- Sheikh et al., 2006), but also alert clinicians of the potential underlying difficulties that may be manifesting as sleep problems (e.g., depressive symptoms, anxiety symptoms). Third, this investigation demonstrates that the negative outcomes associated with disruptions in sleep, a fundamental system of biological regulation, appear to be exacerbated in the context of ecological risks, specifically minority status. Consequently, particular attention should be paid to the assessment of sleep difficulties in this vulnerable group of transplant recipients. Clinical interventions and recommendations should be tailored to the specific needs of each patient in order to maximize their relevance, effectiveness and impact. Lastly, this study highlights the need for theory development in order to guide the exploration of the complex, dynamic and interactive relations that characterize the associations between sleep and variables across multi-level systems.

REFERENCES

Andersen, M. N., Dore-Stites, D., Gleit, R., Lopez, M. J., & Fredericks, E. M. (2014). A pilot study of the association between sleep disturbance in children with liver transplants and parent and family health-related quality of life. *Journal of Pediatric Psychology, 39,* 735-742. doi: 10.1093/jpepsy/jsu037.

Baron, R. M., & Kenny, D. A. (1986). The moderator–mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology, 51*(6), 1173. doi: 10.1037/0022-3514.51.6.1173

Baum, K. T., Desai, A., Field, J., Miller, L. E., Rausch, J., & Beebe, D. W. (2014). Sleep restriction worsens mood and emotion regulation in adolescents. *Journal of Child Psychology and Psychiatry, 55*(2), 180-190. doi: 10.1111/jcpp.12125

Beebe, D. W. (2016). Sleep Problems as Consequence, Contributor, and Comorbidity: Introduction to the Special Issue on Sleep, Published in Coordination With Special Issues in Clinical Practice in Pediatric Psychology and Journal of Developmental and Behavioral Pediatrics. *Journal of Pediatric Psychology, 41,* 583-587. doi:10.1093/jpepsy/jsw037

Bemis, H., Yarboi, J., Gerhardt, C. A., Vannatta, K., Desjardins, L., Murphy, L. K., ... & Compas, B. E. (2015). Childhood cancer in context: sociodemographic factors, stress, and psychological distress among mothers and children. *Journal of Pediatric Psychology, 40*(8), 733-743. doi: 10.1093/jpepsy/jsv024

Besedovsky, L., Lange, T., & Born, J. (2012). Sleep and immune function. *Pflügers Archive-European Journal of Physiology, 463*(1), 121-137. doi: 10.1007/s00424-011-1044-0

Boergers, J., & Koinis-Mitchell, D. (2010). Sleep and culture in children with medical conditions. *Journal of Pediatric Psychology, 35*, 915-926. doi: dx.doi.org/10.1093/jpepsy/jsq016

Bona, K., Dussel, V., Orellana, L., Kang, T., Geyer, R., Feudtner, C., & Wolfe, J. (2014). Economic impact of advanced pediatric cancer on families. *Journal of Pain and Symptom Management, 47*, 594-603. doi: 10.1016/j.jpainsymman.2013.04.003.

Boyce, T., Frank, E., Jensen, P., Kessler, R., Nelson, C., & Steinberg, L. (1998). The role of context in the development of psychopathology. *Development and Psychopathology, 10,* 143-164.

Brody, G. H., Yu, T., Chen, E., Miller, G. E., Kogan, S. M., & Beach, S. R. (2013). Is resilience only skin deep? Rural African Americans' socioeconomic status–related risk and competence in preadolescence and psychological adjustment and allostatic load at age 19. *Psychological Science,* 24, I1285-1293. doi: 10.1177/0956797612471954

Buckhalt, J. A., El- Sheikh, M., Keller, P. S., & Kelly, R. J. (2009). Concurrent and longitudinal relations between children's sleep and cognitive functioning: The moderating role of parent education. *Child Development, 80*(3), 875-892. doi: 10.1111/j.1467-8624.2009.01303.x

Bullington, P., Pawola, L., Walker, R., Valenta, A., Briars, L., & John, E. (2007). Identification of medication non- adherence factors in adolescent transplant patients: The patient's viewpoint. *Pediatric Transplantation, 11*(8), 914-921. doi: 10.1111/j.1399-3046.2007.00765.x

Cohen, J. (1992), A power primer. *Psychology Bulletin, 112*, 155-159. doi: 10.1037/0033-2909.112.1.155

Colten, H. R., & Altevogt, B. M. (Eds.). (2006). *Sleep Disorders and Sleep Deprivation: An Unmet Public Health Problem*. National Academies Press.

Cousino, M. K., Rea, K. E., Schumacher, K. R., Magee, J. C., & Fredericks, E. M. (2017). A systematic review of parent and family functioning in pediatric solid organ transplant populations. *Pediatric Transplantation.* Advance online publication. doi: 10.1111/petr.12900

Dagys, N., McGlinchey, E. L., Talbot, L. S., Kaplan, K. A., Dahl, R. E., & Harvey, A. G. (2012). Double trouble? The effects of sleep deprivation and chronotype on adolescent affect. *Journal of Child Psychology and Psychiatry, 53*, 660-667. doi: 10.1111/j.1469-7610.2011.02502.x

Dahl, R.E., & Gunnar, M.R. (2009). Heightened stress responsiveness and emotional reactivity during pubertal maturation: Implications for psychopathology. *Development and Psychopathology, 21*, 1–6. doi: 10.1017/S0954579409000017

Daley, M., Morin, C. M., LeBlanc, M., Gregoire, J. P., & Savard, J. (2009). The economic burden of insomnia: direct and indirect costs for individuals with insomnia syndrome, insomnia symptoms, and good sleepers. *Sleep, 32*(1), 55-64.

Davis, I. D., Baron, J., O'Riordan, M. A., & Rosen, C. L. (2005). Sleep disturbances in pediatric dialysis patients. *Pediatric Nephrology*, *20*(1), 69-75. doi: 10.1007/s00467-004-1700-0

Davis, K. F., Parker, K. P., & Montgomery, G. L. (2004). Sleep in infants and young children: Part two: Common sleep problems. *Journal of Pediatric Health Care, 18*, 130–137. doi: 10.1016/S0891-5245(03)00150-0

Derogatis, L. R. (2001). *Brief symptom inventory 18*. Bloomington, MN: PsychCorp.

Dobbels, F., Ruppar, T., De Geest, S., Decorte, A., Damme- Lombaerts, V., & Fine, R. N. (2010). Adherence to the immunosuppressive regimen in pediatric kidney transplant recipients: a systematic review. *Pediatric Transplantation, 14*(5), 603-613. doi: 10.1111/j.1399-3046.2010.01299.x

Dollman, J., Ridley, K., Olds, T., & Lowe, E. (2007). Trends in the duration of school-day sleep among 10- to 15-year-old South Australians between 1985 and 2004. *Acta Paediatrica, 96*, 1011–1014. doi: 10.1111/j.1651-2227.2007.00278.x

Eaton, C. K., Gutierrez-Colina, A. M., Fredericks, E. M., Lee, J. L., Reed-Knight, B., Mee, L. L., LaMotte, J., & Blount, R. L. (2017). Organ Transplantation. In M. C. Roberts & R. Steele (Eds.). *Handbook of pediatric psychology* (5th ed.). New York: Guilford Press.

Eckerberg, B. (2004). Treatment of sleep problems in families with young children: Effects of treatment on family well-being. *Acta Paediatrica, 93*, 126–134. doi: 10.1111/j.1651-2227.2004.tb00686.x

El- Sheikh, M., Buckhalt, J. A., Cummings, E. M., & Keller, P. (2007). Sleep disruptions and emotional insecurity are pathways of risk for children. *Journal of Child Psychology and Psychiatry, 48*, 88-96. doi: 10.1111/j.1469-7610.2006.01604.x

El- Sheikh, M., Buckhalt, J. A., Mize, J., & Acebo, C. (2006). Marital conflict and disruption of children's sleep. *Child Development, 77*, 31-43. doi: 10.1111/j.1467-8624.2006.00854.x

El- Sheikh, M., Kelly, R. J., Buckhalt, J. A., & Benjamin Hinnant, J. (2010). Children's sleep and adjustment over time: The role of socioeconomic context. *Child Development, 81*, 870-883. doi: 10.1111/j.1467-8624.2010.01439.x.

El-Sheikh, M., & Sadeh, A. (2015). I. Sleep and development: introduction to the monograph.

Monographs of the Society for Research in Child Development, 80, 1-14. doi: 10.1111/mono.12141

Fagnano, M., Bayer, A. L., Isensee, C. A., Hernandez, T., & Halterman, J. S. (2011). Nocturnal asthma symptoms and poor sleep quality among urban school children with asthma. *Academic Pediatrics, 11*, 493-499. doi: 10.1016/j.acap.2011.05.006

Faul, F., Erdfelder, E., Buchner, A., & Lang, A. G. (2009). Statistical power analyses using G*Power 3.1: Tests for correlation and regression analyses. *Behavior Research Methods, 41*, 1149–1160. doi:10.3758/BRM.41.4.1149.

Fisher, D. C., Lake, K. D., Reutzel, T. J., & Emery, R. W. (1994). Changes in health-related quality of life and depression in heart transplant recipients. *The Journal of Heart and Lung Transplantation, 14*, 373-381.

Foundation for Child Development. (2010). Racial-ethnic inequality in child well-being from 1985-2004: Gaps narrowing, but persist. In D. J. Hernandez, & S. E. Macartney, FCD Policy Brief, Child well-being index (CWI), #9. Retrieved May 1, 2017, from https://www.fcd-us.org/racial-ethnic-inequality-in-child-well-being from-1985-2004-gaps-narrowing-but-persist/

Fredericks, E. M., Dore- Stites, D., Calderon, S. Y., Well, A., Eder, S. J., Magee, J. C., & Lopez, M. J. (2012). Relationship between sleep problems and health- related quality of life among pediatric liver transplant recipients. *Liver Transplantation, 18*, 707-715. doi: 10.1002/lt.23415

Fredericks, E. M., Lopez, M. J., Magee, J. C., Shieck, V., & Opipari- Arrigan, L. (2007). Psychological functioning, nonadherence and health outcomes after pediatric liver

transplantation. *American Journal of Transplantation, 7*(8), 1974-1983. doi: 10.1111/j.16006143.2007.01878.x

Gangwisch, J. E., Heymsfield, S. B., Boden-Albala, B., Buijs, R. M., Kreier, F., Pickering, T. G., ... & Malaspina, D. (2007). Sleep du-ration as a risk factor for diabetes incidence in a large US sample. *Sleep, 30,* 1667-1673. doi: 10.1093/sleep/30.12.1667

Hayes, AF. *Introduction to Mediation, Moderation, and Conditional Process Analysis.* New York, NY: The Guilford Press, 2013.

Hayes, A. F., & Matthes, J. (2009). Computational procedures for probing interactions in OLS and logistic regression: SPSS and SAS implementations. *Behavior Research Methods, 41*(3), 924-936. doi: 10.3758/BRM.41.3.924

Holmbeck, G. N. (2002). Post-hoc probing of significant moderational and mediational effects in studies of pediatric populations. *Journal of Pediatric Psychology, 27*(1), 87-96. doi: 10.1093/jpepsy/27.1.87

Howell, A. J., Jahrig, J. C., & Powell, R.A. (2004). Sleep quality, sleep propensity and academic performance. *Perceptual and Motor Skills, 99,* 525–535. doi: 10.2466/PMS.99.5.525-535

Hysing, M., Sivertsen, B., Stormark, K. M., Elgen, I., & Lundervold, A. J. (2009). Sleep in children with chronic illness, and the relation to emotional and behavioral problems—a population-based study. *Journal of Pediatric Psychology, 34*(6), 665-670. doi: 10.1093/jpepsy/jsn095

Jean-Louis, G., Williams, N. J., Sarpong, D., Pandey, A., Youngstedt, S., Zizi, F., & Ogedegbe, G. (2014). Associations between inadequate sleep and obesity in the US adult population: analysis of the national health interview survey (1977–2009). *BMC Public Health, 14*(1), 290-299. doi: 10.1186/1471-2458-14-290

Jenni, O. G., & O'Connor, B. B. (2005). Children's sleep: an interplay between culture and biology. *Pediatrics, 115,* 204-216. doi: 10.1542/peds.2004-0815B

Kapur, C., Redline, S., Nieto, J., Young, T., Newman, A., & Henderson. (2002). The relationship between chronically disrupted sleep and healthcare use. *Sleep*, *25*(3), 289-296.

Kemper, M. J., Spartà, G., Laube, G. F., Miozzari, M., & Neuhaus, T. J. (2003). Neuropsychologic side- effects of tacrolimus in pediatric renal transplantation. *Clinical Transplantation, 17,* 130-134. doi: 10.1034/j.1399-0012.2003.00028.x

King, M. L. M., Mee, L. L., Gutiérrez-Colina, A. M., Eaton, C. K., Lee, J. L., & Blount, R. L. (2014). Emotional functioning, barriers, and medication adherence in pediatric transplant recipients. *Journal of Pediatric Psychology*, *39*(3), 283-293. doi: 10.1093/jpepsy/jst074

Koinis-Mitchell, D., Craig, T., Esteban, C. A., & Klein, R. B. (2012). Sleep and allergic disease: a summary of the literature and future directions for research. *Journal of Allergy and Clinical Immunology*, *130*(6), 1275-1281. doi: 10.1016/j.jaci.2012.06.026

LeBourgeois, M. K., Giannotti, F., Cortesi, F., Wolfson, A. R., & Harsh, J. (2005). The relationship between reported sleep quality and sleep hygiene in Italian and American adolescents. *Pediatrics, 115,* 257-265. doi: 10.1542/peds.2004-0815H

Lewandowski, A. S., Toliver-Sokol, M., & Palermo, T. M. (2011). Evidence-based review of subjective pediatric sleep measures. *Journal of Pediatric Psychology*, *36*(7), 780-793. doi: 10.1093/jpepsy/jsq119

Liu, X., Hubbard, J. A., Fabes, R. A., & Adam, J. B. (2006). Sleep disturbances and correlates of children with autism spectrum disorders. *Child Psychiatry and Human Development*, *37*(2), 179-191. doi: 10.1007/s10578-006-0028-3

Lofaso, F., Verschueren, P., Rande, J. L. D., Harf, A., & Goldenberg, F. (1994). Prevalence of sleep-disordered breathing in patients on a heart transplant waiting list. *Chest, 106*, 1689-1694. doi: 10.1378/chest.106.6.1689

Matricciani, L., Olds, T. S., Blunden, S., Rigney, G., & Williams, M. T. (2012). Never enough sleep: A brief history of sleep recommendations for children. *Pediatrics, 129*, 548–556. doi: 10.1542/peds.2011-2039

Murray, C. B., Murphy, L. K., Palermo, T. M., & Clarke, G. M. (2012). Pain and sleep–wake disturbances in adolescents with depressive disorders. *Journal of Clinical Child & Adolescent Psychology*, *41*, 482-490. doi: 10.1080/15374416.2012.658613.

National Sleep Foundation. (2006). 2006 Sleep in America poll. Washington, DC: National Sleep Foundation.

National Sleep Foundation. (2008). 2008 Sleep in America poll. Washington, DC: National Sleep Foundation.

National Sleep Foundation. (2017). Teens and sleep. Washington, DC: National Sleep Foundation.

Olson, D. H., Gorall, D. M., & Tiesel, J. W. (2006). FACES IV. *Development and Validation.* Minneapolis, MN: Life Innovations.

Orszag, P. R., & Emanuel, E. J. (2010) Health care reform and cost control. *New England Journal of Medicine,* 363, 601-603. doi: 10.1056/NEJMp1006571

Pai, A. L., & Drotar, D. (2009). Treatment adherence impact: the systematic assessment and quantification of the impact of treatment adherence on pediatric medical and psychological outcomes. *Journal of pediatric psychology*, *35*(4), 383-393.

Paiva, T., Gaspar, T., & Matos, M. G. (2015). Sleep deprivation in adolescents: correlations with health complaints and health-related quality of life. *Sleep Medicine, 16,* 521-527.

Phillips, K. D., Moneyham, L., Murdaugh, C., Boyd, M. R., Tavakoli, A., Jackson, K., & Vyavaharkar, M. (2005). Sleep disturbance and depression as barriers to adherence. *Clinical Nursing Research, 14*(3), 273-293. doi: 10.1177/1054773805275122

Pretorius, E. (2004). Corticosteroids, depression and the role of serotonin. *Reviews in the Neurosciences, 15*(2), 109-116. doi: 10.1515/REVNEURO.2004.15.2.109

Recklitis, C. J., & Rodriguez, P. (2007). Screening childhood cancer survivors with the Brief Symptom Inventory- 18: Classification agreement with the symptom checklist- 90-revised. *Psycho- Oncology, 16,* 429-436. doi: 10.1002/pon.1069

Reynolds, C. R., & Kamphaus, R. W. (2004). *BASC-2: Behavior Assessment System for Children 2nd Edition Manual.* Circle Pines, MN: AGS Publishing.

Rutter, M. (1983). Statistical and personal interactions: Facets and perspectives. In D. Magnusson & V. Allen (Eds.*), Human development: An interactional perspective* (pp. 295–319). New York, NY: Academic Press.

Saberi, P., Neilands, T. B., & Johnson, M. O. (2011). Quality of sleep: associations with antiretroviral nonadherence. *AIDS patient care and STDs, 25*(9), 517-524. doi: 10.1089/apc.2010.0375

Shankar, A., Koh, W. P., Yuan, J. M., Lee, H. P., & Mimi, C. Y. (2008). Sleep duration and coronary heart disease mortality among Chinese adults in Singapore: a population-based cohort study. *American Journal of Epidemiology, 168*(12), 1367-1373. doi: 10.1093/aje/kwn281

Simola, P., Liukkonen, K., Pitkäranta, A., Pirinen, T., & Aronen, E. T. (2012). Psychosocial and somatic outcomes of sleep problems in children: a 4- year follow- up study. *Child: Care, Health and Development*, *40*(1), 60-67. doi: 10.1111/j.1365-2214.2012.01412.x

Simons, L. E., & Blount, R. L. (2007). Identifying barriers to medication adherence in adolescent transplant recipients. *Journal of Pediatric Psychology*, *32*(7), 831-844. doi: 10.1093/jpepsy/jsm030

Simons, L. E., McCormick, M. L., Devine, K., & Blount, R. L. (2010). Medication barriers predict adolescent transplant recipients' adherence and clinical outcomes at 18-month follow-up. *Journal of Pediatric Psychology*, *35*(9), 1038-1048. doi:10.1093/jpepsy/jsq025

Smaldone, A., Honig, J. C., & Byrne, M. W. (2007). Sleepless in America: inadequate sleep and relationships to health and well-being of our nation's children. *Pediatrics*, *119*, S29-S37. doi: 10.1542/peds.2006-2089F

Spilsbury, J. C., Storfer-Isser, A., Kirchner, H. L., Nelson, L., Rosen, C. L., Drotar, D., & Redline, S. (2006). Neighborhood disadvantage as a risk factor for pediatric obstructive sleep apnea. *The Journal of Pediatrics*, *149*, 342-347. doi: 10.1016/j.jpeds.2006.04.061

Steinberg, L., & Avenevoli, S. (2000). The role of context in the development of psychopathology: A conceptual framework and some speculative propositions. *Child Development*, *71*, 66-74.

Turner, R., & Elson, E. (1993). Sleep disorders. Steroids cause sleep disturbance. *BMJ: British Medical Journal*, *306*, 1477-1478. doi: 10.1136/bmj.306.6890.1477-d

Valrie, C. R., Gil, K. M., Redding-Lallinger, R., & Daeschner, C. (2007). Brief report: sleep in children with sickle cell disease: an analysis of daily diaries utilizing multilevel models. *Journal of Pediatric Psychology*, *32*(7), 857-861. doi: 10.1093/jpepsy/jsm016

van Litsenburg, R. R., Huisman, J., Hoogerbrugge, P. M., Egeler, R. M., Kaspers, G. J., & Gemke, R. J. (2011). Impaired sleep affects quality of life in children during maintenance treatment for acute lymphoblastic leukemia: an exploratory study. *Health and Quality of Life Outcomes*, *9*(1), 25-31. doi: 10.1186/1477-7525-9-25

Varni, J. W., Seid, M., & Kurtin, P. S. (2001). PedsQL™ 4.0: Reliability and validity of the Pediatric Quality of Life Inventory™ Version 4.0 Generic Core Scales in healthy and patient populations. *Medical Care*, *39*, 800-812. doi: 10.1097/00005650-200108000-00006

Villaneuva, A. T. C., Buchanan, P. R., Yee, B. J., & Grunstein, R. R. (2005). Ethnicity and obstructive sleep apnoea. *Sleep Medicine Reviews*, *9*, 419-436. doi:10.1016/j.smrv.2005.04.005

Vriend, J. L., Davidson, F. D., Corkum, P. V., Rusak, B., Chambers, C. T., & McLaughlin, E. N. (2013). Manipulating sleep duration alters emotional functioning and cognitive performance in children. *Journal of Pediatric Psychology*, *38*, 1058-1069.

Walton, A., & Flouri, E. (2010). Contextual risk, maternal parenting and adolescent externalizing behaviour problems: The role of emotion regulation. *Child: Care, Health and Development*, *36*(2), 275-284. doi: 10.1111/j.1365-2214.2009.01065.x.

Walker, E. F. (2002). Adolescent neurodevelopment and psychopathology. *Current Directions in Psychological Science*, *11*, 24-28. doi: 10.1111/1467-8721.00161

Wolfe, F., Michaud, K., & Li, T. (2006). Sleep disturbance in patients with rheumatoid arthritis: evaluation by medical outcomes study and visual analog sleep scales. *The Journal of Rheumatology, 33*(10), 1942-1951.

Wolfson, A. R., & Carskadon, M. A. (2003). Understanding adolescent's sleep patterns and school performance: a critical appraisal. *Sleep medicine reviews, 7*(6), 491-506.

Zambroski, C. H., Moser, D. K., Bhat, G., & Ziegler, C. (2005). Impact of symptom prevalence and symptom burden on quality of life in patients with heart failure. *European Journal of Cardiovascular Nursing, 4,* 198-206. doi: 10.1016/j.ejcnurse.2005.03.010

Zelikovsky, N., & Schast, A. P. (2008). Eliciting accurate reports of adherence in a clinical interview: Development of the medical adherence measure. *Pediatric Nursing, 34,* 141–146.

Zelikovsky, N., Schast, A.P., Palmer, J., & Meyers, K. E. (2008). Perceived barriers to adherence among adolescent renal transplant candidates. *Pediatric Transplantation, 12,* 300–308. doi: 10.1111/j.1399-3046.2007.00886.x

Table 1. *Demographic Information*

Factor	Frequency	%
Family income		
Less than $10,000	5	7.0
$10,000-24,999	10	14.1
$25,000-49,999	19	26.8
$50,000-74,999	11	15.5
$75,000-99,999	5	7.0
$100,000 or greater	16	22.5
Missing	5	7.0
Parent education level		
Less than high school diploma	3	4.2
High school diploma/GED	11	15.5
Some college	19	26.8
Associate's degree	5	7.0
Bachelor's degree	10	14.1
Advanced degree	13	18.3
Other/Missing	10	14.1
Caregiver marital status		
Married	45	63.4
Committed partnership	1	1.4
Single, never married	6	8.5
Divorced	11	15.5
Other/Missing	8	11.3

Note. $N = 71$

Table 2. *Correlates of Sleep and Patient-level Variables to Guide Regression Analyses*

Variable	2	3	4	5	6
1. ASWS Total Sleep Quality *M* = 4.01, *SD* = .76, Range: 1.68-5.78	-.52**	-.44**	.56**	-.46**	-.30*
2. BASC Depressive Symptoms *M* = 45.81, *SD* = 7.70, Range: 39.00-76.00	--	.62**	-.61**	.45**	.25
3. BASC Anxiety Symptoms *M* = 42.98, *SD* = 9.66, Range: 29.00-71.00	--	--	-.63**	.40**	.06
4. PedsQL Total Health-Related Quality of Life *M* = 74.28, *SD* = 17.63, Range: 26.56-100	--	--	--	-.44**	-.15
5. AMBS Total Barriers to Adherence *M* = 34.62, *SD* = 12.57, Range: 17.00-72.00	--	--	--	--	.32*
6. Medication Adherence *0=Perfect Adherence (56%), 1=Nonadherence (44%)*	--	--	--	--	--

Note. ASWS = Adolescent Sleep Wake Scale; BASC = Behavioral Assessment Scale for Children; PedsQL = Pediatric Quality of Life Inventory; AMBS = Adolescent Medication Barriers Scale; Pearson and Point-biseral correlations; * $p \leq .05$, ** $p \leq .01$

Table 3. *Sleep Quality in Transplant Recipients Compared to Norms*

	Transplant		*Normative*				
Variable	*M*	*SD*	*M*	*SD*	*t*	*p*	Cohen's *d*
Adolescent Sleep Wake Scale							
Falling asleep	4.09	0.90	4.48	0.80	-3.60	.001	0.46
Maintaining sleep	4.48	0.96	4.68	0.80	-1.76	.083	0.23
Returning to wakefulness	3.46	1.11	3.38	0.90	0.58	.563	0.10

Table 4. *Correlations Between Sleep Quality and Patient-level Variables*

	ASWS Falling Asleep	ASWS Maintaining Sleep	ASWS Returning to Wakefulness	ASWS Total
Emotional Functioning				
BASC Depression symptoms	-.46***	-.39***	-.35**	-.52***
BASC Anxiety symptoms	-.34**	-.37**	-.30*	-.44***
Quality of Life				
Physical functioning	.37**	.44***	.33**	.49***
Psychosocial functioning	.44***	.40***	.41***	.54***
Total	.45***	.44***	.41***	.56***
Barriers to Adherence				
Regimen adaptation/Cognitive issues	-.33**	-.42***	-.14	-.38**
Ingestion issues	-.35**	-.36*	-.10	-.34**
Disease frustration/Adolescent issues	-.45***	-.39***	-.27*	-.47***
Total	-.44***	-.43***	-.22	-.46***
Medication Adherence				
MAM	-.30*	-.24	-.16	-.28*

Note. ASWS = Adolescent Sleep Wake Scale; BASC = Behavioral Assessment Scale for Children; MAM = Medication Adherence Measure; $p \leq .05$, ** $p \leq .01$, *** $p \leq .001$

Table 5. *Hierarchical Regression of Adolescent Quality of Life*

Quality of Life	B[a]	SEB[b]	β[c]	R^2	Δ R^2	*F*
Step 1:				.09	.09**	7.80**
Gender	11.58	3.24	3.23**			
Step 2:				.50	.41***	34.23***
Gender	6.70	3.13	0.19*			
Internalizing Symptoms	-1.46	0.20	-0.65***			
Step 3:				.55	.05**	27.78***
Gender	6.48	3.01	0.18*			
Internalizing Symptoms	-1.15	0.22	-0.51***			
Overall Sleep Quality	6.25	2.23	0.27**			

Note. [a]B, unstandardized coefficients; [b]SEB, standard error of unstandardized coefficients; [c]β, standardized coefficients; * $p \leq .05$, ** $p \leq .01$, *** $p \leq .001$

Table 6. *Hierarchical Regression of Barriers to Adherence*

Barriers to Adherence	B[a]	SEB[b]	β[c]	R^2	Δ R^2	*F*
Step 1:				.14	.14**	5.15**
Age	2.05	0.89	0.27*			
Race	-6.94	2.87	-0.28**			
Step 2:				.30	.16***	9.16***
Age	1.73	0.81	0.22*			
Race	-4.83	2.66	-0.19**			
Internalizing Symptoms	0.66	0.17	0.41***			
Step 3:				.37	.07**	9.42***
Age	1.86	0.77	0.24*			
Race	-5.07	2.54	-0.20*			
Internalizing Symptoms	0.39	0.19	0.24*			
Overall Sleep Quality	-5.26	1.93	-0.32**			

Note. [a]B, unstandardized coefficients; [b]SEB, standard error of unstandardized coefficients; [c]β, standardized coefficients; * $p \leq .05$, ** $p \leq .01$, *** $p \leq .001$

Table 7. *Logistic Regression of Medication Adherence*

Medication Adherence	B[a]	SEB[b]	Wald[c]	Exp(B)[d]	*Nagelkerke* R^2	ΔR^2	χ^2
Step 1:					.14	.14*	6.43*
AMBS Total	0.06	0.02	5.59*	1.06			
Step 2:					.18	.04	8.43*
AMBS Total	0.04	0.03	2.73	1.04			
Overall Sleep Quality	-0.58	0.43	1.87	0.56			

Note. AMBS = Adolescent Medication Barriers Scale; [a]B, unstandardized coefficients; [b]SEB, standard error of unstandardized coefficients; [c]Wald, standardized coefficients; [d]Exp(B), odds ratio,
* $p \leq .05$

Table 8. *Correlations Between Sleep Quality and Micro-level Variables*

	ASWS Falling Asleep	ASWS Maintaining Sleep	ASWS Returning to Wakefulness	ASWS Total
Parent Emotional Functioning				
BSI Depression symptoms	-.15	-.20	.05	-.12
BSI Anxiety symptoms	-.15	-.20	.01	-.14
BSI Somatization	-.23	-.19	.01	-.17
BSI Global Symptoms	-.18	-.20	.01	-.15
Family Functioning				
FACES Cohesion	.13	.17	.07	.16
FACES Flexibility	.12	.16	.12	.18

Note. ASWS = Adolescent Sleep Wake Scale; BSI = Brief Symptom Inventory; FACES = Family Adaptability and Cohesion Evaluation Scale

Table 9. *Correlations Between Sleep Quality of Macro-level Variables*

	ASWS Falling Asleep	ASWS Maintaining Sleep	ASWS Returning to Wakefulness	ASWS Total
Healthcare Utilization				
Medical appointments	.22	.30	.32	.37
Hospitalizations	-.27	.04	-.20	-.20
Lab work	.02	.11	.06	.07
Emergency room visits	.09	.06	-.14	-.01
Healthcare-Related Costs				
Out-of-pocket expenses	.14	.08	-.01	.09
Loss wages	-.12	-.08	-.04	-.11
Missed days of work	-.01	-.02	-.02	-.06
Missed days of school	-.10	.03	-.04	-.05

Note. ASWS = Adolescent Sleep Wake Scale

Table 10. *Hierarchical Regression of Adolescent Depressive Symptoms*

Depressive Symptoms	B[a]	SEB[b]	β[c]	R^2	Δ R^2	*F*
Step 1:				.04	.04	2.76
Race	-3.04	1.83	-0.20			
Step 2:				.29	.25***	13.54***
Race	-2.43	1.59	-0.16			
Overall Sleep Quality	-5.08	1.05	-0.50***			
Step 3:				.34	.05*	11.17***
Race	-20.47	8.33	-1.34*			
Overall Sleep Quality	-7.31	1.44	-0.72***			
Race x Overall Sleep Quality	4.50	2.04	1.24*			

Note. [a]B, unstandardized coefficients; [b]SEB, standard error of unstandardized coefficients; [c]β, standardized coefficients; * $p \leq .05$, ** $p \leq .01$, *** $p \leq .001$

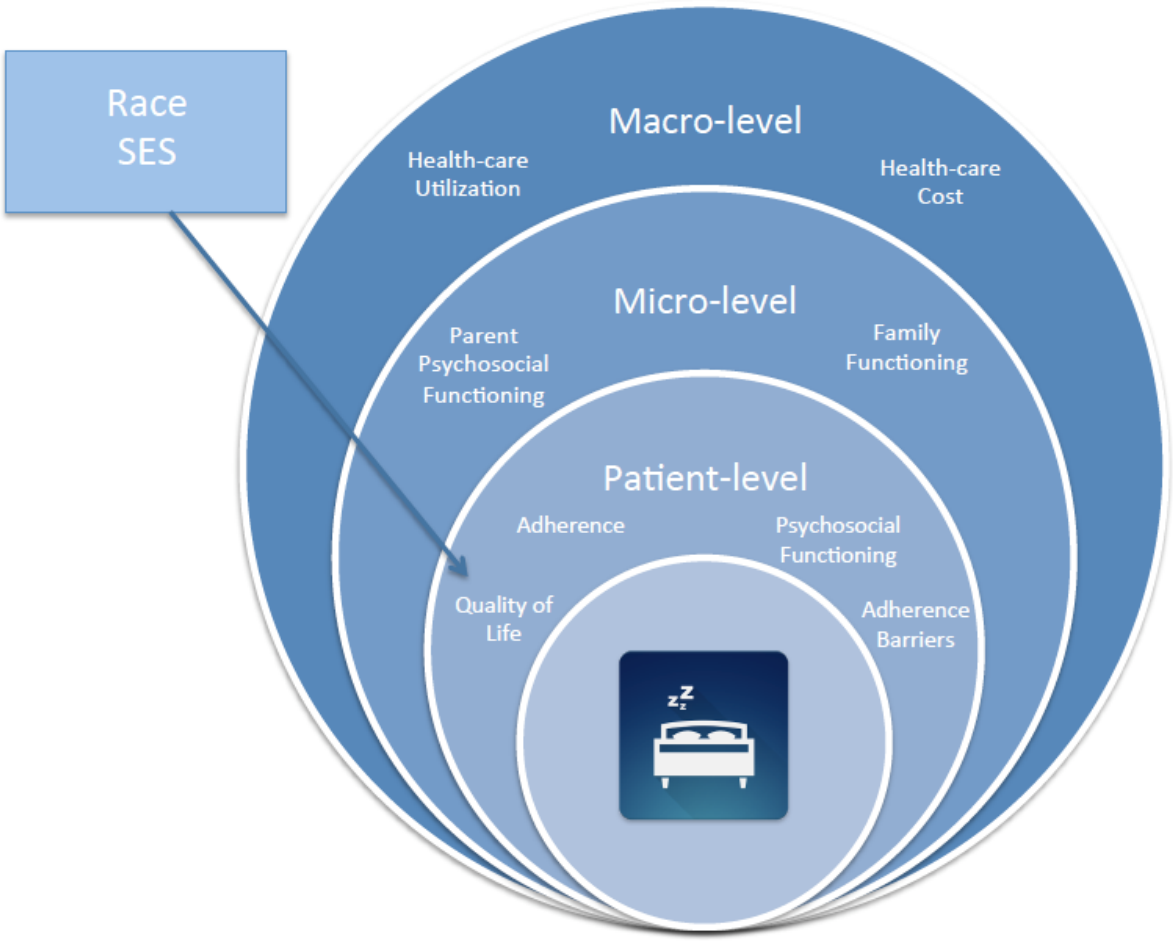

Figure 1: Socioecological System Factors Associated with Sleep

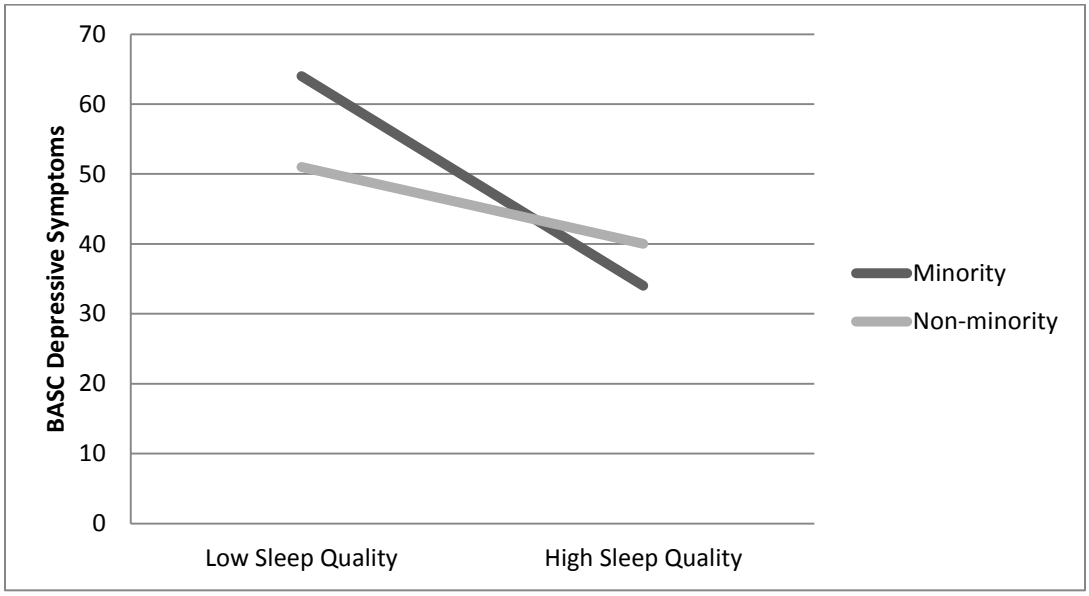

Figure 2. *Moderation of Sleep Quality and Depressive Symptoms by Race*