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Sleep Homeodynamics And Wellbeing In Asymptomatic Hiv-Seropositive African American Women

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SLEEP HOMEODYNAMICS AND WELLBEING IN ASYMPTOMATIC HIV-SEROPOSITIVE AFRICAN AMERICAN WOMEN

by

TABETHA LYNN GAYTON

DISSERTATION

Submitted to the Graduate School

of Wayne State University,

Detroit, Michigan

in partial fulfillment of the requirements

for the degree of

DOCTOR OF PHILOSOPHY

2013

MAJOR: NURSING

Approved by:

Advisor

Date

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DEDICATION

I would like to dedicate this dissertation to my amazing family.

To my parents, Van and Ellen...

You are my biggest champions and cheerleaders.

Over the years you have modeled excellence and perseverance.

Without your unconditional love and support none of this would have been possible.

And to my beautiful daughter, Jasmine...

You are my heart.

Thank you for your patience and understanding.

I love you!

ACKNOWLEDGEMENTS

This dissertation has been one of the most challenging, yet fulfilling projects of my life.

That being said, I wish to express my sincere gratitude to my Chair, Dr. Hossein N. Yarandi, for I could not have completed this tremendous effort without your guidance and support in my most difficult times.

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CHAPTER 1

INTRODUCTION

The Center for Disease Control (CDC) HIV/AIDS Surveillance Report 2011 (2013) estimates that African Americans, who make up 12-14% of the US population, now account for approximately half of the populace living with HIV and half of the upsurge of all new HIV diagnoses. Early in the epidemic, relatively few African American (AA) women contracted the disease, but today their prevalence rate (40.0 per 100,000) is alarmingly one of the highest of all groups. In fact, 64% of all new female infections identified themselves as African American, as compared to 17% Caucasian. While among other ethnicities and cultures infection has decreased significantly, HIV has been reported as the leading cause of death among AA women ages 25-34 years, third among those ages 35-44 years, and fourth among ages 45-54 years (CDC, 2008). There is no doubt that the disparity of HIV has affected AA women the hardest; HIV-related sleep disruption seems to be no different (Hand, Phillips, Sowell, Rojas, & Becker, 2003; Marion et al., 2009; Phillips, Sowell, et al., 2005). HIV-related sleep disruption places many AA women with HIV disease at risk for exacerbation of existing stressors, having assiduous ramifications on their health and wellbeing.

HIV-related sleep disruption is a well-documented debilitating phenomenon that dates back to the earliest clinical reports of HIV infection (Norman, Resnick, et al., 1988). Prevalence rates of sleep disruption range from 73 to 100% in those who are HIV-seropositive (Dreher, 2003; Hand et al., 2003). Individuals experiencing sleep disruption may complain of a greater delay in sleep onset, earlier morning awakenings, more frequent arousals during the night, reduced total sleep time, unrefreshing sleep, and a decreased feeling of wellbeing upon awakening (Edinger et al., 2004; Jean-Louis et al., 2012; Omonuwa, Goforth, Preud'homme, &

Krystal, 2009). Such disturbances have been reported early in the infection, during clinical latency or the asymptomatic phase of the disease progression (Chen et al., 2012; Robbins, Phillips, Dudgeon, & Hand, 2004). The asymptomatic phase is a long chronic period, just after an acute seroconversion, when the immune system gradually deteriorates but presents with little to no clinical signs and symptoms suspicious of HIV infection or immunocompromise. However, due to suspected changes in the central nervous system, sleep disturbances are likely to manifest throughout all phases of the disease, progressing to more than just minor aberrations (Hand et al., 2003; Reid & Dwyer, 2005). In fact, HIV-related sleep disruption has been reported to be of the more intense and distressful symptoms of HIV, leading to excessive daytime sleepiness, antiretroviral nonadherence, reduced neurocognitive functioning, increased comorbidity, untoward effects on one's quality of life and wellbeing, and eventually increased risk for all-cause mortality (Hudson, Kirksey, & Holzemer, 2004; Lee et al., 2012; Phillips, Sowell, et al., 2005; Robbins et al., 2004; Saberi, Neilands, & Johnson, 2011; Vance & Burrage, 2005; Webel et al., 2013).

Just as the course of disease progression in HIV may vary from individual to individual, it is expected that HIV-related sleep disruption may also differ. The dynamics of sleep in HIV disease are influenced by a myriad of physiological, psychological, and sociological factors (Phillips & Skelton, 2001). Antiretroviral medications, notably efavirenz, have been found to bear a certain risk for physiological side effects that are disruptive to sleep (Gallego et al., 2004; Nunez et al., 2001). And despite some conflicting evidence, $CD4^+$ lymphocyte cell count and HIV RNA viral load are explained by researchers to have a great impact on sleep quality, especially with the derangement of immune system functioning seen late in the progression of the disease (Ferreira & Ceolim, 2012; Lee, Portillo, & Miramontes, 2001; Okocha et al., 2009;

Robbins et al., 2004). Several investigators have focused on various psychological correlates, such as feelings of anxiety, stress, and depression, and their negative consequence to sleep among those infected (Jean-Louis et al., 2012; Marion et al., 2009; Mock, Phillips, & Sowell, 2002). Meanwhile, others have demonstrated differential effects of social engagement, such as social support on HIV-related sleep disturbance (Friedman et al., 2005; Vosvick et al., 2004). Remarkably, perceived social support has even been implicated in affecting one's ability to self-estimate sleep efficiency (Jackowska, Dockray, Hendrickx, & Steptoe, 2011).

Reports of distorted sleep physiology in response to HIV infection date back to the late 1980's (Darko et al., 1992; Norman & Chediak, 1992; Norman, Nay, & Cohn, 1988; Rothenberg, Zozula, Funesti, & McAuliffe, 1990). The HIV-diseased biological processes of the central nervous system (CNS) were postulated to cause the alterations in sleep architecture, even before HIV-immunosuppression could be detected (Norman, Shaukat, Nay, Cohn, & Resnick, 1987). The CNS involvement manifested as anomalies in the NREM/REM sleep periods. The most salient of these findings was a significant increase in NREM slow wave sleep (SWS), which extended late into the second half of the night, when normally it predominates in the first few hours of sleep and then tapers rapidly (Norman, Chediak, Kiel, & Cohn, 1990; Norman, Demirozu, & Chediak, 1990; Norman, Resnick, et al., 1988; White et al., 1995). Cytokine dysregulation, a direct physiologic effect of the HIV virus, has gained a recent spotlight as a major contributor to the disruption of sleep generation and sleep patterns (Foster et al., 2008). The HIV envelope glycoproteins and infected immune cells were found to induce altered secretion of various inflammatory cytokines, such as IL-1, TNF- α , & IL-6 (Gemma & Opp, 1999; Opp et al., 1996), which are known for their influence in the initiating, maintaining, and ending of sleep (Chrousos, 1995). The resulting cytokine imbalance (dysregulation) has been

highly correlated with the subjective complaints related to these pathophysiologic aberrations of sleep parameters (Norman, Chediak, Kiel, & Cohn, 1990; Norman, Chediak, Kiel, Gazeroglu, et al., 1990; Norman, Resnick, et al., 1988; Vgontzas et al., 1999).

As the scientific trends evolved, studies noted interleukin-6 (IL-6), a putative ‘sleep factor’, as elemental in sleep research given its apparent relation with sleep quality and its association with disorders of excessive daytime sleepiness (Bovbjerg, 2003; Morrow & Opp, 2005; Vgontzas & Chrousos, 2002; Vgontzas et al., 2005). IL-6 is an inflammatory cytokine ranging from 2-29 pg/mL and exhibiting a biphasic circadian pattern, having two nadirs (8am and 9pm) and two zeniths (about 7pm and 5am, Burgos et al., 2006; Vgontzas et al., 1999). Nevertheless, daytime IL-6 levels are sensitive, inversely influenced by the quantity and quality of the previous night’s sleep (Irwin, 2002; Mills et al., 2007; Vgontzas, Zoumakis, et al., 2002). Generally, lower IL-6 levels are associated with better sleep and a good sense of wellbeing the next day, and higher IL-6 levels are associated with poor or disrupted sleep and an increase in SWS the second half of the next night (Vgontzas & Chrousos, 2002; Vgontzas et al., 2003). Data from studies on disorders of excessive daytime sleepiness, exogenous administration, and experimentally induced hypersecretion of IL-6 (via sleep-deprivation) concurrently reflect its homeostatic drive for sleep and its direct action on CNS sleep mechanisms (Friedman et al., 2005; Mills et al., 2007; Vgontzas et al., 2005). Therefore, the dramatic increase in IL-6 levels seen in past HIV studies appropriately fits amid the complaints of poor sleep and the CNS-related alterations in sleep architecture (Breen et al., 1990; Honda et al., 1990).

IL-6 is also known as a pleiotropic cytokine with its wide variety of biological effects causing ‘sickness manifestations’ that may also affect sleep, including symptoms of anorexia, fatigue, somnolence, fever, malaise, listlessness, and hyperalgesia to name a few (Breen et al.,

1990; Chrousos, 1995; Vgontzas et al., 1999; Vollmer-Conna et al., 2004). Average IL-6 plasma levels correspond with overall health outcomes and general wellbeing; with inflammatory conditions, immune-related diseases, and chronic pain syndromes negatively influencing its overall secretion (Friedman et al., 2005; Vgontzas et al., 2003). Prolonged dysregulation or shifts in the IL-6 circadian rhythm are consistent with reports of increased morbidity and mortality (Bovbjerg, 2003; Mills et al., 2007). Consequently, daytime dysfunction, viral replication, and inappropriate apoptosis seen in HIV is congruent with data suggesting that IL-6 is a highly valuable predictor of morbidity and mortality in HIV disease (Fumaz et al., 2012; Míguez, Rosenberg, Burbano-Levy, Carmona, & Malow, 2012).

Research has played a vital role in the formation of treatment modalities for HIV. HIV care has evolved from an acute medically-based treatment model to a more holistic chronic-illness approach, which demands investigations into the integrative factors which influence the promotion of health, quality of life, and wellbeing (Mock et al., 2002). The World Health Organization (WHO) defined health as “a state of complete physical, mental, and social wellbeing and not merely the absence of disease or infirmity” (<http://www.who.int/about/definition/en/print.html>). Quality of life is a broad concept often used to portray all aspects of an individual’s wellbeing. It has also been described as a dynamic, multidimensional reflection of the internal satisfaction or happiness with how life is going compared to some aplombed conjecture of how life should be (Cella & Tulsy, 1990; Lutgendorf, Antoni, Schneiderman, & Fletcher, 1994). Thus, quality of life is the degree to which an individual perceives that life is worth living. Within the past decade, the measurement of quality of life has grown in recognition as a critical outcome measure in research, used to determine whether or not an individual is living better not just longer (Hays et al., 2000). This becomes particularly relevant when

assessing the burden incurred from chronic illnesses, especially those with a debilitating course and aggressive treatment modalities, such as HIV. HIV is a chronic disease haunted by an uncertain trajectory of life-threatening physical decline, a lifestyle full of stigma and redress, and an ever increasing reliance on healthcare services and medical adeptness (Lutendorf et al., 1994). Such burdens tend to challenge every aspect of an individual's life and wellbeing. So, whether it is viewed from the looking-glass of a philosopher captivated in the nature of human existence (Faden & LePlège, 1992), an ethicist concerned for the sanctity of life and social utility (Edlund & Tancredi, 1985), an economist interested in the efficient allocation of resources needed to achieve goals (Grabowski & Hansen, 1990), a physician focused on disease-related variables (Pearlman & Uhlmann, 1988), or a nurse keeping in a holistic approach (Ferrans, 1990), quality of life has established priority in HIV care and remains a key element in HIV research (Phillips, Mock, Bopp, Dudgeon, & Hand, 2006).

An association between sleep quality and quality of life was found in HIV-seropositive African American women, when "good" sleepers reported significantly higher levels of quality of life (Phillips, Sowell, et al., 2005). Sleep, which was originally depicted as a passive, dormant part of our daily life, has since been recognized as a very active and dynamic time of growth, healing, and rejuvenation for many body systems (National Institute of Neurological Disorders and Stroke [NINDS], 2007; Wilson; 2010). In fact, chronic disruptions in this time of healing and rejuvenation are now recognized as major risk factors for all-cause mortality (Alvarez & Ayas, 2004, Reid & Dwyer, 2005, Webel et al., 2013). Therefore, sleep should not be perceived as a luxury, but as a basic need that must be satisfied in order to lead an optimal, healthy, and productive life (Alvarez & Ayas, 2004; Edéll-Gustafsson & Ek, 1992). As such, health maintenance is consistent with the science of nursing; it creates a great opportunity for nurse

researchers to explore the interplay of biophysical research on the nature of sleep, health, and wellness.

Statement of Problem

With the demographical shifts, African American women of childbearing age have now emerged as one of the fastest growing HIV populations today, and confirmed that HIV exhibits differential patterns of influence on different groups of people. Despite the gender and racial differences known to influence the hormonal and metabolic effects of HIV and HIV treatments (Cargill & Stone, 2005), surprisingly, this relevant group (AA women) remains a vulnerable and underrepresented population in the sleep literature. With no published works found to describe objective assessments of sleep parameters and relatively few subjective assessments, sleep researchers have only an elusive idea of what HIV-related sleep disruption looks like specific to HIV-seropositive AA women. With sparse data, development of sleep-related treatment modalities specific to the needs of young minority women becomes a guessing game; incoherent, unfounded in research, and lacking a scientific foundational base. Additionally, with the majority of the research still focusing primarily on men, there remains paucity as to the various impacts of HIV-related sleep disruption on AA women's wellbeing.

Statement of Purpose

The purpose of this pilot study was to examine the dynamics of HIV-related sleep disruption and wellbeing in asymptomatic HIV-seropositive AA women of childbearing age within the context of a holistic, theoretical substruction from Myra Levine's Conservation Model (1967). The rationale for the proposed study was to provide a foundation of both the objective and subjective experience of HIV-related sleep disruption, which as a stressor can affect wellbeing in HIV-seropositive AA women.

Specific Aims and Research Questions

The specific aims and research questions in this study are as follows:

Specific Aim 1: To describe sleep homeodynamics of HIV-related sleep disruption in asymptomatic HIV-seropositive African American women of childbearing age, as evidenced by sleep/wake rhythm, sleep quality, daytime sleepiness, and interleukin-6 rhythm.

Research Question 1(A): What are the characteristics of the sleep/wake rhythm, as measured by actigraphic estimates of sleep/wake minutes, sleep/wake episodes, minutes before sleep onset, sleep percentage, sleep efficiency, sleep fragmentation index, activity mean, activity index, and acceleration index?

Research Question 1(B): What is the perception of sleep quality, as measured by the Pittsburgh Sleep Quality Index (PSQI) and the Subjective Sleep Quality Questionnaire (SSQ)?

Research Question 1(C): What is the perception of daytime sleepiness, as measured by the Epworth Sleepiness Scale (ESS) and the Stanford Sleepiness Scale (SSS)?

Research Question 1(D): What are the characteristics of the interleukin-6 rhythm, as measured by four time-specific plasma interleukin-6 levels?

Specific Aim 2: To describe wellbeing in asymptomatic HIV-seropositive African American women of childbearing age experiencing HIV-related sleep disruption, as evidenced by quality of life.

Research Question 2: What is the perception of quality of life, as measured by the Quality of Life Index (QLI) and the Quality of Life Visual Analogue Scale (VAS-Q)?

Specific Aim 3: To determine the relationship between variables of sleep homeodynamics and wellbeing in asymptomatic HIV-seropositive African American women of childbearing age experiencing HIV-related sleep disruption.

Research Question 3(A): What is the strength and direction of the correlation between the sleep/wake rhythm and wellbeing, as measured by sleep efficiency and the Quality of Life Visual Analogue Scale (VAS-Q)?

Research Question 3(B): What is the strength and direction of the correlation between sleep quality and wellbeing, as measured by the Subjective Sleep Quality Questionnaire (SSQ) and the Quality of Life Visual Analogue Scale (VAS-Q)?

Research Question 3(C): What is the strength and direction of the correlation between daytime sleepiness and wellbeing, as measured by the Stanford Sleepiness Scale (SSS) and the Quality of Life Visual Analogue Scale (VAS-Q)?

Research Question 3(D): What is the strength and direction of the correlation between the interleukin-6 rhythm and wellbeing, as measured by the average interleukin-6 level and the Quality of Life Visual Analogue Scale (VAS-Q)?

Specific Aim 4: To determine the agreement between the quality of life measurements in asymptomatic HIV-seropositive African American women of childbearing age experiencing HIV-related sleep disruption.

Research Question 4: What is the agreement between the Quality of Life Index (QLI) and the Quality of Life Visual Analogue Scale (VAS-Q)?

Significance

One of the major challenges in HIV care, besides viral suppression, is effective symptom management in order to maintain an optimal state of health and quality of life (Hudson et al.,

2004). Although many acquiesce to the significance of this phenomenon, there remains no standard criterion for the diagnosis or management of HIV-related sleep disruption. In fact, a recent study demonstrated the significant impact of underdiagnosed HIV-related sleep disorders on quality of life and daytime functioning (Gamaldo et al., 2013). Despite the growing body of sleep literature considering IL-6, as a biological marker of health and wellbeing (Friedman et al., 2005), the connection with IL-6 remains scarce in the HIV-related sleep research literature. Elevated IL-6 plasma levels have undoubtedly been seen in HIV infection, with HIV envelope glycoproteins and infected monocytes being the primary source of HIV-induced IL-6 hypersecretion (Breen et al., 1990; Honda et al., 1990). By considering IL-6 as a common link between HIV-related sleep disruption, progression of disease, and quality of life, this pilot study will contribute substantially to mainstream biobehavioral research by describing a key biological measure inherent in the nature of health and wellbeing seen in HIV disease. Such inquiry responds to the growing interest into the many facets that may prevent or delay the damaging nature of HIV infection, and to the call for integrative studies that combine influences on health across multiple domains.

HIV-sleep literature has followed a gender and ethnicity trend dictated by the evolution of national incidence rates, starting with the classics, whose primary focus was on homosexual Caucasian men. As with most chronic diseases of premature mortality, HIV is known to exhibit differential patterns of impact across racial/ethnic and gender groups (Míguez et al., 2012). This current study wishes to contribute to the progression of the literature by exploring HIV-related sleep disruption in one of the most clinically relevant HIV populations today, asymptomatic African American women of childbearing age. The Healthy People 2020 public health goals, sponsored by the United States Department of Health and Human Services

(<http://www.healthypeople.gov/2020/about/>), renewed their focus on exploring ways to improve quality of life and to eliminate health disparities among divergent segments of the population. The 10-year agenda for improving the Nation's health continues to target HIV as it has done in the past, however, several new focus areas have been added, sleep health being one of them. The goal to increase the awareness and treatment of poor sleep health, acknowledges sleep as a basic requirement and a critical determinant of health and wellbeing. Having emerged as a major subgroup and incurred such a disproportionate burden related to HIV infection, each piece of research regarding AA women becomes imperative in meeting the goals put forth. Characterizing the various features of sleep homeodynamics and wellbeing in HIV-seropositive AA women will add a more accurate assessment of sleep health in this population and potential clarification to the understanding of the conundrum of group differences found in people at risk for negative health outcomes.

Significance to Nursing

Nursing's social mandate is to pursue the enhancement of health, quality of life, and wellbeing, and its domain of inquiry should be reflective of its nature of service and social accountability (Parse, 2006). Nursing's holistic nature is found within its unique process, manifested by complexity and integration that generates wellbeing through health promotion (Reed, 1995). A commitment to the development of nursing knowledge aims to explain the relationships between and among concepts specific to nursing, and provide the grounds for designing interventions congruent within nursing's nature (Fawcett, 1991). HIV has been and continues to be one of the leading health concerns in today's society. The noxious insult of HIV-related sleep disruption, which only serves to exaggerate the progression of disease and ravage quality of life, demands further scientific inquiry. The goal is to advance nursing knowledge by

providing an extended understanding of the complexity of HIV-related sleep disruption experienced by HIV-seropositive AA women. Such inquiry will document key biological measures along with various psychosociobehavioral factors to join a growing literature that is mapping diverse pathways to be utilized in the formulation of innovative health-promoting interventions in this population.

Even though early nurse theorists laid the groundwork for the inclusion of sleep research in their conceptual frameworks, the literature fails to depict much advancement of nursing science in this area (Mornhinweg & Voignier, 1996). A commitment to the development of nursing science includes examining explicit exemplars guided by a nursing conceptual framework, in order to establish the underlying validity of the framework (Fawcett, 1999; Silva, 1986). With a program of study that is focused on the advancement of nursing science in the area of sleep research through the application and testing of Levine's Conservation Model, this pilot study serves as a preliminary investigation for the utilization of the Conservation Model as an organizing framework for examining HIV-related sleep disruption and wellbeing in asymptomatic HIV-seropositive AA women.

CHAPTER 2

THEORETICAL FRAMEWORK

Myra Levine (1967), developed the Conservation Model as a “generalization of nursing” in order to provide the “whys” of nursing activities. Levine characterized the conceptual model, more specifically, as an interaction model of the complex relationship between an ever-changing person and the ever-changing environment. With a unique focus on conservation or the “keeping together” of a person’s wholeness, Levine recognized the process of adaptation as the essential component in defining one’s lifecourse, in that it bridges the gap between the person and the environment (Levine, 1967, 1969).

Threats are experienced from the internal and external environments with which the person is connected. This can cause perturbation in the homeostasis (static state) and/or homeorhesis (stabilized flow) of various systems within the person. Consequently, an adaptation process of integrative organismic responses, such as fight or flight, inflammatory or immune, stress, and perceptual awareness, is evoked. Conservation is the natural law governing the self-sustaining conditions and the cascade of adaptive changes initiated by the assiduous encroachment of noxious influences, which may arise. Survival depends on the frugal use of resources in effort to spare one’s integrity from these life-threatening implications. Making the ultimate purpose of conservation; be it conservation of energy, structural integrity, personal integrity, and/or social integrity, to defend the system for which it functions. If the person can retain integrity while faced with the dynamic exchange of threatening realities of the environment, then adaptation is said to be successful. Environmental congruency, integrity, health, and wholeness (all of which are used interchangeably) are maintained (Levine, 1969, 1989, 1991, 1996).

Levine presented the Conservation Model to provide a unifying structure for understanding the person as an active holistic being with an enduring concern to pursue wholeness and integrity. Wholeness is achieved through the life process of adaptation and safeguarded by the essence of conservation. Life testifies to the ever-present nature of this biological wisdom that seeks, sorts, selects, and acts on behalf of communal wellbeing (Levine, 1967, 1969, 1971). An initial linear sketch of a scholarly interpretation of this dynamic and fluid person-environment interaction has been constructed in Figure 2.1.

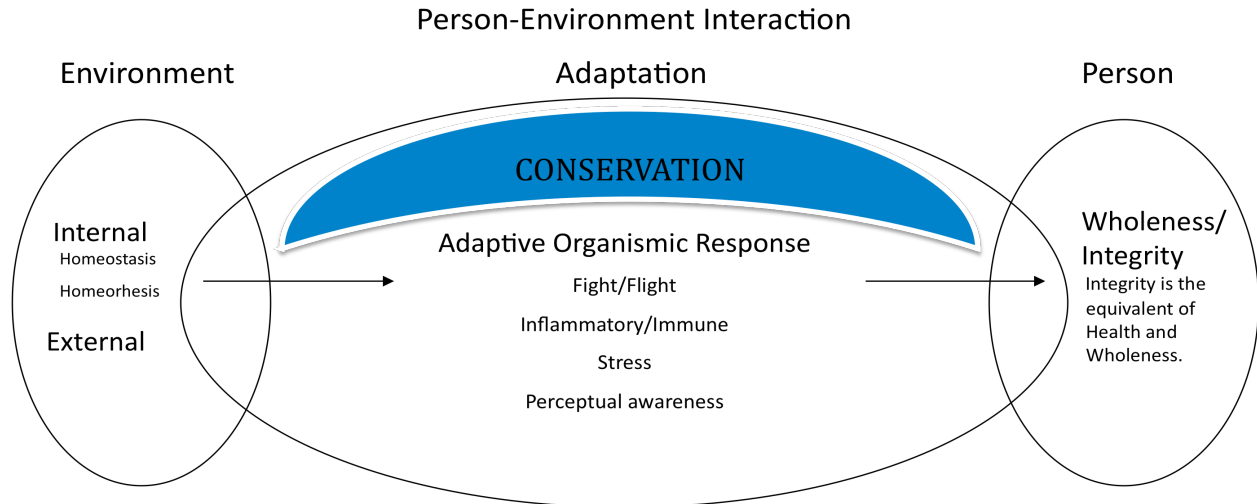


Figure 1. A linear sketch of Levine's interaction model between person and environment.

Conceptual Level Concepts

Conservation. Levine conceptualized conservation as the “keeping together” function or guardian activity over the achievement of adaptation that defends and protects an individual’s wholeness. Conservation is a consequence of numerous, synchronized feedback systems which interact and enable the adjustment and stabilizing of living organisms. More specifically,

conservation is the fundamental biological ability to weigh the resources against the demands and allow the body to thrive with the most economic, frugal, and energy-sparing use of resources needed for effective functioning. This sparing (conserving) of the individual's expense, Levine described, is of crucial importance to defend, sustain, maintain, define, and reclaim the person's health and wholeness. Conservation is the process of successful adaption; which assumes unity and integrity (Levine, 1967, 1989, 1991).

To Levine, the concept of conservation breaks down into four dimensions, which she called "the principles of conservation". There is conservation of energy, structural integrity, personal integrity, and social integrity. Each conservation principle is constant, in that the process cannot be turned on and off, and that it begins with birth and does not end until death. Each principle may be examined separately in order to focus on discrete issues. However, when speaking of the integrity of the whole person, the influences of all four principles must be acknowledged (Levine, 1969, 1991). An illustration of Levine's Conservation Model has been constructed at a conceptual level in Figure 2.2.

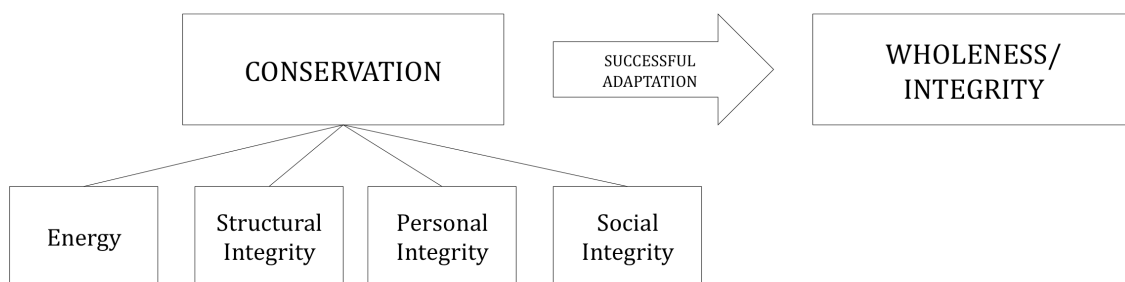


Figure 2. An illustration of the conceptual level of Levine's Conservation Model.

Energy. Energy is the provenance of life; a life source if you will. For life is dependent on the production, exchange, and expenditure of energy. Energy is not directly observable, but the consequences of it can be quantified, predicted, and, thus, managed (Levine, 1991, p. 7). The resources of energy are finite. When energy is exhausted, so is the ability to adapt. Therefore, energy should be spent carefully, with priority given to life-sustaining activities. In other words, one's energy consumption related to body functions, repair, and healing should never outweigh one's energy potential gained from proper rest, nutrition, and exercise. Conservation of energy expresses that the use of energy should be only for as long as it is needed. Not limited to minimal activity, conservation of energy also means the proper disbursement of energy expense for life to flourish. The rationale is a natural defense to maintain sufficient resources necessary for free participation in an active life, which is essential to the wholeness of the individual (Levine, 1967, 1971, 1991).

Structural Integrity. Structural integrity refers to the wholeness of a person's structure and function, or the architectural balance which allows the body to move and choose activities freely. Structural integrity is maintained and restored by preventing physical breakdown and promoting timely repair and healing when needed. If the remarkable design of biological structures determines optimum function, then with structural changes comes debilitation or restriction of function. Conservation of structural integrity is the body's defense against the insult of environmental hazards, which emphasizes biological priority, as well as, the most economical and restorative expense of healing efforts. The rationales behind conservation of structural integrity is to minimize the functional tissue that is sacrificed due to trauma or disease and/or limit the aberration of the adjacent structures (Levine, 1967, 1971, 1991).

Personal Integrity. Personal integrity refers to the wholeness of a person's self-identity as a unique and cherished personhood. The knowledge of such an inner, most-private self conveys much more than just physical realities. It conveys an awareness of self-worth, self-respect, being intact, independent, and always unique. Realizations of a person's own self-definition is fundamental to the acceptance, confidence, security, and cultivation of self. Loss of personal validity can have a tremendous impact on the life experience, for the sense of self is indelibly written on every choice. Conservation of personal integrity is the recognition of the value of privacy, independence, and the secret knowledge of inner-self, which defines the person. The rationale behind conservation of personal integrity is to minimize vulnerability of dependence, loss of freedom, and loss of self, all of which only produce anxiety, low self-esteem, and a negative influence on every choice a person makes (Levine 1967, 1989, 1991, 1996).

Social Integrity. Social Integrity is the wholeness of the person's interactions as a social being, for the essence of humanity is seen in the reflection from others. Each person is affected by the dynamics of an interwoven social context, including their family, friends, workplace, community, religion, education, culture, and ethnic heritage. Social norms mediate the specific interactions, roles, and lifestyles in which the individual chooses to participate. Conservation of social integrity involves the recognition of the need for definition of self that extends far beyond the individual. The rationale behind conservation of social integrity is that a satisfying and fulfilled life depends on the ability to develop behaviors that allow for participation and acceptance in many social relationships and settings (Levine, 1967, 1989, 1991, 1996).

Wholeness. "Wholeness emphasizes a sound, organic, progressive mutuality between the diversified functions and parts within an entirety, the boundaries of which are open and fluid" (Erikson, 1968, as cited by Levine, 1996). Wholeness speaks to the universal idea of completion

and the longing for unity. Wholeness accounts for the multi-dimensions of the complete and total person as a bio-psycho-social-spiritual being. Wholeness, a function of the harmonious interaction between the internal environment and the external environment, is what each individual cherishes and defends throughout the entire life process. It represents the uninterrupted continuity of energy, structural integrity, personal integrity, and social integrity. Wholeness is integrity, and infers health, healing, and wellbeing. Because such terms are known to stem from the Anglo-Saxon word for “whole”, they are commonly used interchangeably within Levine’s writings. Wholeness is maintained and reclaimed through conservation, which is a process of successful adaptation (Levine, 1969, 1989, 1991, 1996).

Substruction of the Theoretical Framework

The Sleep Conservation Model represents a vertical descent or a substruction of a less-abstract form of the Conservation Model described above. The Sleep Conservation Model is the theoretical framework or the middle range theory guiding the present study. The components of the Sleep Conservation Model include theoretical concepts, theoretical variables, and relational propositions.

Theoretical Level Concepts

The theoretical concepts of the Sleep Conservation Model represent a vertical descent or a substruction of a less-abstract form of the conceptual concepts of the Conservation Model. An illustration of the substruction to the theoretical concepts of the Sleep Conservation Model has been provided in Figure 2.3. Note, the causal arrow of successful adaptation at the conceptual level has been modified to a dotted line in the theoretical model to denote a possible relationship between conservation of sleep and wellbeing. The reason for the modification is that there is not enough data in this field to establish or test cause and effect. Therefore, the goal of this

preliminary project was to provide base-level data toward identifying relationships between the study variables. Cause and effect will be tested in future higher-level studies in this program of research.

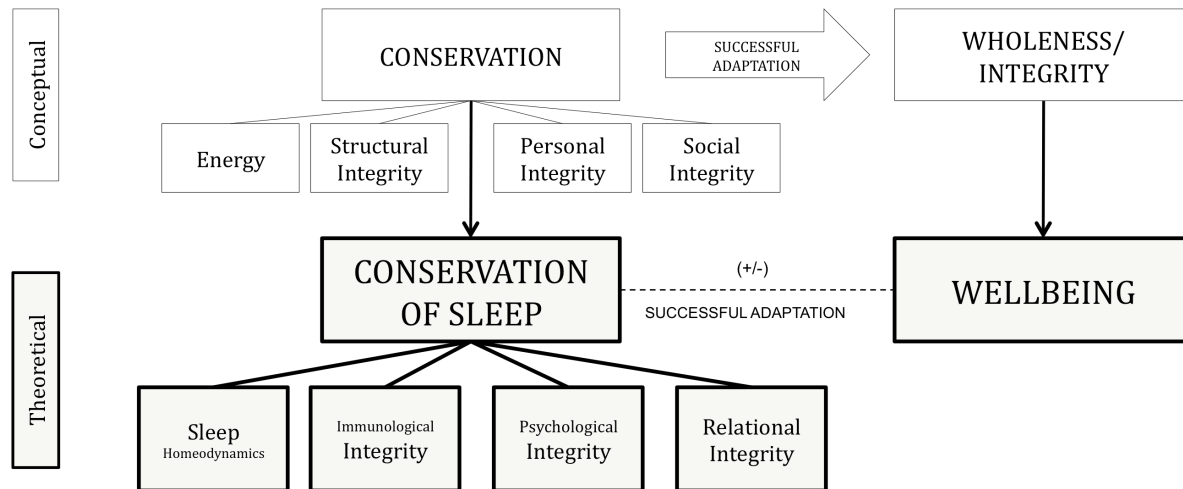


Figure 3. An illustration of the first substructure to the theoretical concepts of the Sleep Conservation Model .

Conservation of Sleep. Conservation of sleep is the guardian activity required for the maintenance and restoration of one's physical, mental, and emotional wellbeing. Conservation of sleep governs over the biological processes of adaptation, in order to achieve the adequate quantity and quality of sleep, necessary to defend and protect the individual's wellbeing. It is a consequence of many feedback systems of the hypothalamic-pituitary-adrenal axis, cytokines, hormones, and circadian effects allowing for the frugal or energy-sparing adjustments that facilitate and stabilize sleep (Vgontzas & Chrousos, 2002). Conservation of sleep allows for the sparing of an individual's expense of sleep homeodynamics, immunological integrity, psychological integrity, and relational integrity. This sparing of expense is of crucial importance

to defend, sustain, maintain, define, and reclaim the person's adaptive wellbeing. Conservation of sleep is the process of successful adaptation; which assumes wellbeing.

Sleep Homeodynamics. Sleep homeodynamics refers to processes, or biofields of change or activities, which are in constant interaction with each other, in order to self-regulate the energy source sleep. Biofields, such as sleep-wake behaviors and IL-6 production/secretion, manifest objective patterns or rhythms from sleep-related energy interactions, which become quantifiable measures of sleep energy (Rubik, 2002; Schaefer, 1991). Biofields, such as sleep quality and daytime sleepiness, manifest subjective patterns or rhythms from sleep-related energy interactions, which also become quantifiable measures of sleep energy. Sleep conservation related to sleep homeodynamics is successful adaptation towards achieving sleep homeorhesis.

Immunological Integrity. Immunological integrity refers to an unimpaired condition or free movement through the cascading activities of cells involved in the innate and adaptive subdivisions of the immune system. An intact or uninterrupted immune system is essential to the body's defense against the hazards in the environment, and to the healing processes necessary to overcome insult and injury (Levine, 1991). Sleep conservation related to immunological integrity recognizes the need for adequate sleep to allow the body to rebuild the immune system and combat infection effectively, which are indicators of successful adaptation (Bryant, Trinder, & Curtis, 2004).

Psychological Integrity. Psychological integrity refers to stable or unimpaired cognitive evaluation and the well adjustment of ongoing emotional reactions. Alterations or interruptions in one's affect and/or judgment of life satisfaction, compromise the mind's defense against the stressors of life, creating a catalyst for anxiety, stress, and depression (Levine, 1996; Nathawat,

1996). Sleep conservation related to psychological integrity recognizes the need for adequate sleep to allow for the restoration and rebalancing of emotion and reason, necessary for inner peace and a productive lifestyle (Gorman, 2004).

Relational Integrity. Relational integrity refers to adequate or unimpaired perception of social support gained from both emotional (non-tangible) and instrumental (tangible) support of earlier and present-day relationships. Disruption or interference in the consanguinity of supportive feedback and/or behaviors from significant relationships affects a person's sense of acceptance, and ultimately, the ability to cope or respond to stress successfully (Sarason & Sarason, 1994; Young, 2006). Sleep conservation related to relational integrity recognizes the need for adequate sleep to reduce irritability, crankiness, and preventable frustration (NINDS, n.d.), all of which are major threats to social interaction and the perception of social support.

Wellbeing. Wellbeing is a sense or awareness of the internal feelings of satisfaction or dissatisfaction with how life is going. Wellbeing is multidimensional and encompasses aspects related to physical, psychological, and social status. Myra Levine (1991) describes wellbeing as the end product of successful adaptation. Levine asserts that wellbeing depends on every activity respecting the structural wholeness of the individual (1996, p. 10), and the pursuit of health offers the promise of wellbeing (p. 3). A "good" sense of wellbeing is what one cherishes and strives for throughout life (Levine, 1991).

Theoretical Level Variables

Within the theoretical level there is a further descent to measurable theoretical variables, which are used to define the theoretical concepts of this study. The theoretical variables are even less abstract than the theoretical concepts, and from these variables analyses were done according to the study-specific aims. The variables chosen to represent the concepts were based

on their significance in the literature; especially those with consequence in both the sleep and HIV literature. An illustration of the substruction to the theoretical variables of the Sleep Conservation Model has been provided in Figure 2.4.

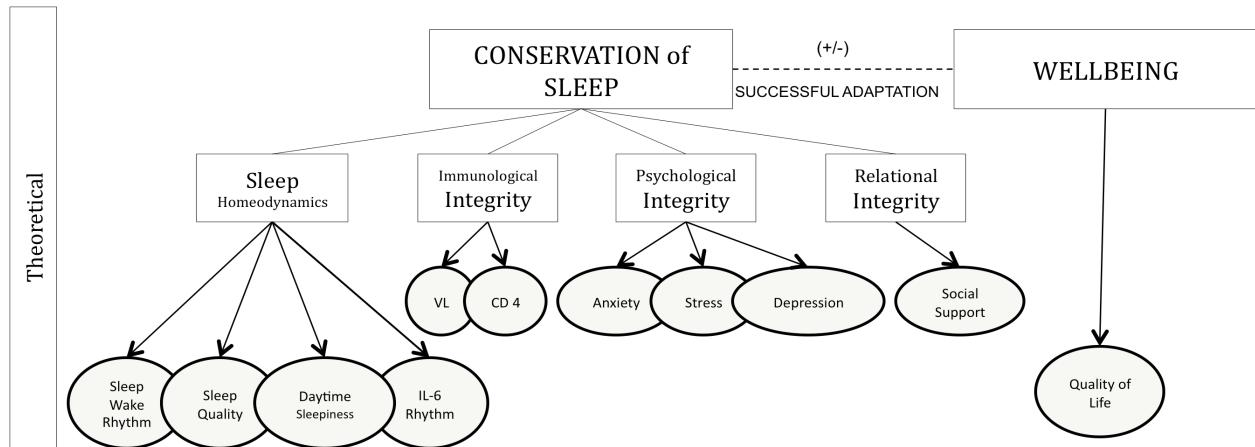


Figure 4. An illustration of the substruction to the theoretical variables of the Sleep Conservation Model.

Sleep Homeodynamics. The phenomenon known as sleep homeodynamics encompasses quantifiable manifestations of multiple processes or biofields of change or activity which are in constant interaction with each other, in order to self-regulate sleep. The manifestations of interest in this study are expressed as the sleep/wake rhythm, sleep quality, daytime sleepiness, and the interleukin-6 (IL-6) rhythm.

Immunological Integrity. The phenomenon known as immunological integrity encompasses quantifiable manifestations of an intact or freely moving system of cascading cells involved in the body's defense against physical hazards of the environment (internal and external). The variable set of immunological consequence in this study is expressed as CD4⁺ lymphocyte cell count and HIV RNA viral load.

Psychological Integrity. The phenomenon known as psychological integrity encompasses quantifiable manifestations of unimpaired cognitive evaluations and the well adjustment of ongoing emotional reactions involved in the mind's defense (ability to cope or respond successfully) against the psychological hazards of the environment (stressors of life). The variable set of psychological consequence might include variables such as anxiety, stress, depression, coping, and hopefulness; nonetheless, this theoretical concept requires further development and will not be addressed in this study.

Relational Integrity. The phenomenon known as relational integrity encompasses quantifiable manifestations of adequate or unimpaired emotional (non-tangible) and instrumental (tangible) social support of both earlier and present-day relationships that are involved in the mind's defense (sense of acceptance, self-worth, or belonging) against the sociological hazards of the environment (social conflicts). The variable set of relational consequence might include the variable social support; nonetheless, this theoretical concept requires further development and will not be addressed in this study.

Wellbeing. The phenomenon known as wellbeing encompasses quantifiable manifestations of the sense or awareness of the internal feelings of satisfaction or dissatisfaction with how life is going compared to some self-actualized idea of how life should be. Wellbeing is multidimensional and takes into account the influences of a physical, psychological, social, and spiritual nature. In this study, wellbeing is expressed as quality of life.

Relational Propositions of the Sleep Conservation Model

The Sleep Conservation Model is also horizontally congruent with Levine's Conservation Model, in that the primary and secondary relational propositions flow from that of the conceptual level. Study Proposition: The phenomenon known as conservation of sleep is a process of

adaptation that occurs in effort to maintain and/or restore sleep homeodynamics, immunological integrity, psychological integrity, and relational integrity, which assumes wellbeing.

Primary Relational Proposition. The primary relational proposition of the Sleep Conservation Model is a substitutive relationship of three concepts; where if concept X (conservation of sleep) occurs, the other concept Y (wellbeing) will occur. However, if some similar concept S (successful adaptation) occurs, the second concept Y (wellbeing) also will occur. Simply stated as:

If X, but also if S, then Y.

Conservation of sleep or successful adaptation is related to wellbeing.

Because conservation of sleep influences four very specific concepts: X1 (sleep homeodynamics), X2 (immunological integrity), X3 (psychological integrity), and 4X (relational integrity), the primary relational proposition can be more specifically stated as:

If [X1 + X2 + X3 + X4], but also if S, then Y.

Conservation of sleep as it relates to sleep homeodynamics, immunological integrity, psychological integrity, and relational integrity or successful adaptation is related to wellbeing.

The concept map of the primary relational proposition of the Sleep Conservation Model is shown below in Figure 2.5.

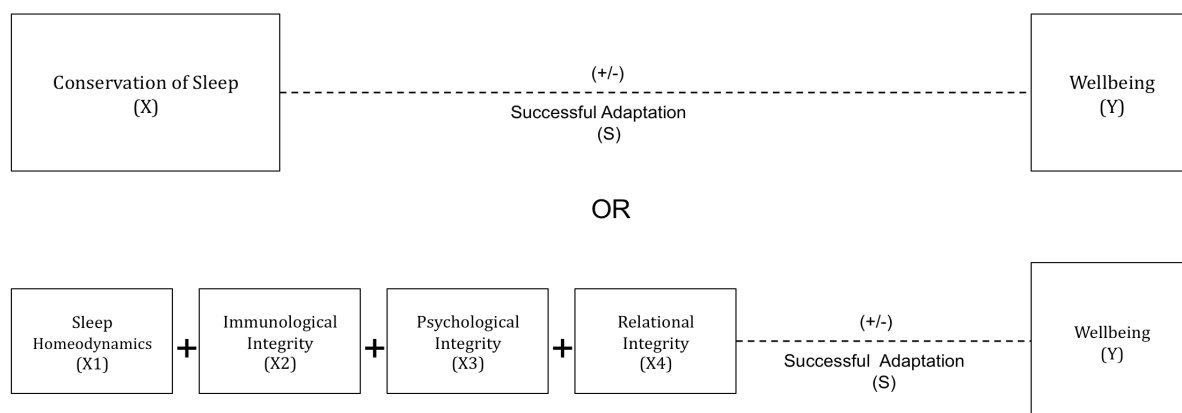


Figure 5. A concept map of the primary relational proposition of the Sleep Conservation Model.

Secondary Relational Propositions. The secondary relational propositions of the Sleep Conservation Model are symmetrical relationships between the aforementioned four concepts influenced by the conservation of sleep: X1 (sleep homeodynamics), X2 (immunological integrity), X3 (psychological integrity), and X4 (relational integrity). Simply stated as:

X1 is related to X2; and X2 is related to X1

X2 is related to X3; and X3 is related to X2

X3 is related to X4; and X4 is related to X3

X1 is related to X3; and X3 is related to X1

X1 is related to X4; and X4 is related to X1

X2 is related to X4; and X4 is related to X2

Sleep homeodynamics, immunological integrity, psychological integrity, and relational integrity all have a reciprocal relationship with each other.

The concept map of the secondary relational propositions of the Sleep Conservation Model is shown below in Figure 2.6.

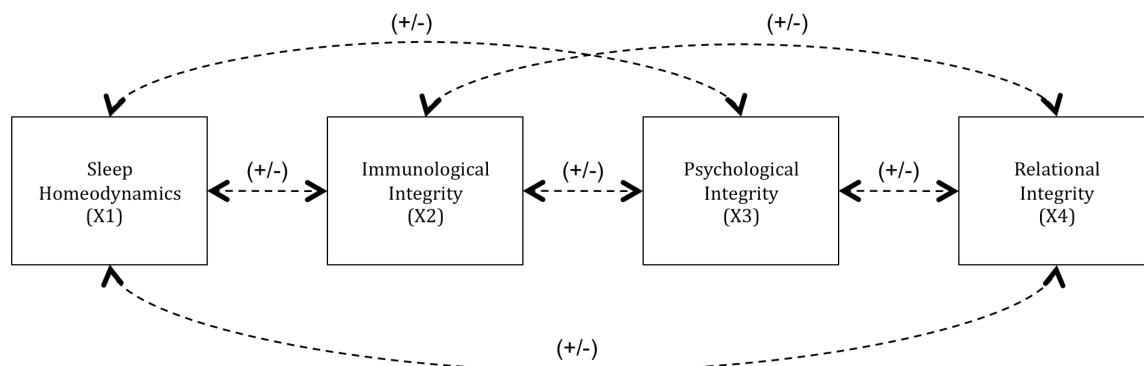
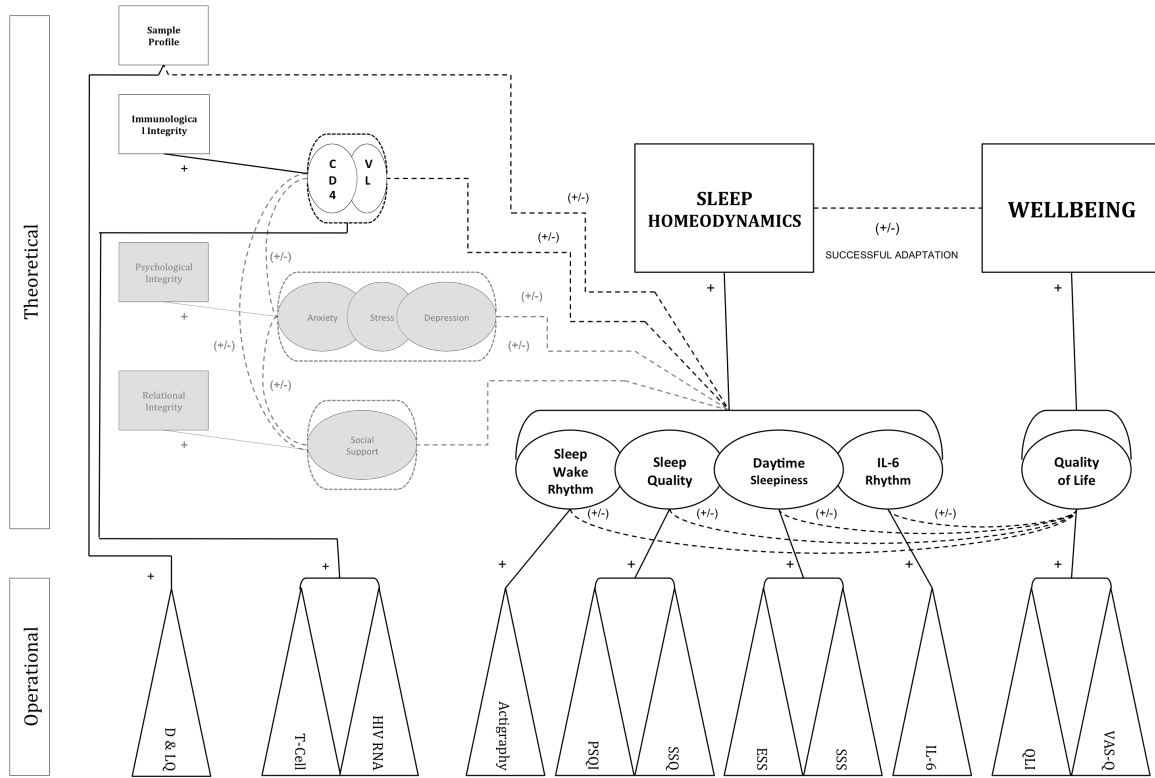


Figure 6. A concept map of the secondary relational propositions of the Sleep Conservation Model.

Operational Level of the Substruction

From the theoretical level, there was one final vertical descent or substruction to the operational level variables which are the specific instruments used in the measurement of the theoretical variables in the present study. An illustration of the substruction to the operational level from the Sleep Conservation Model has been substructured in Figure 2.7. The operational variables of this study are discussed in detail in the “Study Variables and Measurements” section of Chapter 4. Note, the arrangement of the theoretical level concepts and variables in Figure 2.7 have been modified to help distinguish what was and was not examined in this present study. Psychological integrity and relational integrity were grayed out in Figure 2.7, as they were the theoretical concepts excluded from this study and require further development that will be forthcoming within my program of research. As will the testing of the various relational propositions of this model.



Sleep Homeodynamics and Wellbeing in Asymptomatic HIV-Seropositive African American Women.

Concepts/variables and relationships included in this study are in white and black.
 Concepts/variables and relationships not included in this study are grayed out.

CHAPTER 3

LITERATURE REVIEW

The goal of the current study was to extend the understanding of disrupted sleep homeodynamics among asymptomatic HIV-seropositive African American women as it relates to their immunological integrity and their experience of wellbeing. The following literature review provides a systematic overview of the relevant empirical research related to the study variables explored: CD4⁺ cell count, HIV viral load, sleep/wake rhythm, sleep quality, daytime sleepiness, interleukin-6 rhythm, and quality of life.

Study Variables

CD4⁺ Cell Count and HIV Viral Load

HIV infection sets the context for this inquiry, along with the unique challenges and vulnerabilities it creates as a result of the derangement of the immune system. HIV disease is a continuum of progressive immunologic damage that begins with a chronic asymptomatic state and over time evolves to an ever-increasing symptomatic quandary of susceptibility to opportunistic infections, neoplasms, wasting, acquired immunodeficiency syndrome (AIDS), and eventually death (Osmond, 1998). A deteriorating CD4⁺ lymphocyte cell count and a propagating HIV RNA viral load are indicators of the natural history or progression of the disease (Cohen, Ferrans, Vizgirda, Kunkle, & Cloninger, 1996). Because the virus targets and kills CD4⁺ lymphocytes in particular, it has become the hallmark laboratory marker used to assess the level of immunosuppression and susceptibility to specific HIV-related conditions (Call et al., 2000, Honda et al., 1990; Osmond, 1998; Phillips et al., 1994). Depending on the laboratory, normal CD4⁺ lymphocyte cell counts, also known as T-helper cell counts, range from 500 cells/mm³ to 1000 cells/mm³. The HIV RNA viral load has also become an important

laboratory marker in assessing the extent of viral proliferation, related symptomology, and effectiveness of antiviral therapies in controlling viral replication. Since there is no true normal range for the virus, the objective of treatment is undetectable levels less than 20 copies/mL, depending on the type and sensitivity of the test. In general, the lower the CD4⁺ cell count and the higher the HIV viral load, the more likely an individual is to experience HIV-related symptomologies and opportunistic infections (Osmond, 1998). These aversive events, ultimately, become disruptive and incompatible with normal restorative sleep profiles (Robbins et al., 2004).

Numerous historical studies found an inverse relationship between the frequency of sleep complaints and CD4⁺ cell counts, suggesting that sleep disturbances increase as the disease progresses and the immune system deteriorates (Brown et al., 1991; Nuñez et al., 2001; Wheatley & Smith, 1994; Rothenberg et al., 1990). Funesti and coworkers (1991) found that CD4⁺ counts had an intense relationship with both sleep onset and sleep maintenance problems in asymptomatic subjects with sleep complaints. White and colleagues (1995) found a specific architectural correlation related to CD4⁺ counts; uniquely, those with a CD4⁺ greater than 400 cells/mm³ demonstrated a significant increase in SWS in the middle and final third of the night, along with significantly fewer awakenings during the night when compared to controls. The length of time infected and antiviral medications were of no consequence in White's study. Lee's cohort (2001) duplicated the inverse relationship between CD4⁺ cell count and the number of awakenings throughout the night, but found nothing significant with sleep efficiency or with daytime activity in this study. Later, Lee and associates (2012) were able to establish a relationship between short sleep (< 6 hours) and lower CD4⁺ counts. In a pediatric trial, both decreasing CD4⁺ counts and increasing viral loads were associated with increased nocturnal sleep, daytime sleep, and overall total 24-hour sleep time (Okocha et al., 2009).

Sleep disruptions of varying kinds have been demonstrated in multiple age groups and stages of HIV disease, but the advanced stage of the infection, in particular, tends to elicit significant increases in the frequency and intensity of the disruptions (Darko et al., 1992, Möeller et al., 1991; Okocha et al., 2009; Reid & Dwyer, 2005). As a result, those with progressive disease were found to have a tendency to use sleep medications more often than not (Möeller et al., 1991). It is important to note that not only have studies shown immune status to have profound effects on sleep, but the data has also demonstrated that sleep disturbance can further impair immune functioning beyond the damage caused by the virus (Moldofsky, Lue, Eisen, Keyston, & Gorczynski, 1986; Wheatley & Smith, 1994). This downward spiral between cause and consequence supports a reciprocal link between sleep regulating hormones and immune cells (Darko et al., 1992).

To the contrary, several investigators found no correlation between sleep measures and CD4⁺ cell counts (Cohen et al., 1996; Cruess et al., 2003; Rubinstein & Selwyn, 1998; Nokes & Kendrew, 2001, Saberi et al., 2011). Saberi and researchers (2011) analyzed data from a sample of 2845 HIV-positive adults, and although they found no correlation with CD4⁺, every tenfold increase in viral load was independently related to a pattern of heightened sleep problems. In a Brazil study, most subjects who described a good experience in quality of sleep were those with undetectable viral loads (Ferreira & Ceolim, 2012).

Sleep/Wake Rhythm

Polysomnography Studies. Initial scientific and clinical investigations into sleep disruption experienced in HIV disease began in the late 1980's, soon after researchers had isolated the human immunodeficiency virus in the cerebrospinal fluid. This confirmed that HIV infects the CNS, and thus, the sleep-regulating mechanisms located therein (Norman, Chediak,

Kiel, & Cohn, 1990). Focus was placed on laboratory-based analyses of sleep physiology through the use of polysomnography. Polysomnography (PSG), the gold standard of sleep assessment, allowed for the objective exploration into the circadian rhythm of sleep and its dynamic architecture. Alterations in nocturnal architectural patterns demonstrated the subtle CNS manifestations postulated to be directly related to HIV infection and altered immune responses (Reid & Dwyer, 2005).

Dr. Suzan Norman and her colleagues were of the first to pioneer evaluations into distorted sleep physiology related to HIV infection. Focus was initially placed on the associated sleep changes experienced during the asymptomatic phase of the illness. Preliminary studies of asymptomatic homosexual men demonstrated various architectural changes, such as decreased sleep efficiency and increases in sleep fragmentation and the amount of SWS pathologically shifting to the second half of the night (Norman et al., 1987; Norman, Resnick, et al., 1988). Trials using similar samples were able to reaffirm the SWS anomaly, noting that persistent SWS occurring in the later sleep cycles may be a physiological feature consistent with early HIV infection (Norman et al., 1989; Norman, Chediak, Freeman, et al., 1992; Norman, Chediak, Kiel, & Cohn, 1990; Norman, Chediak, Kiel, Gazeroglu, et al., 1990; Norman, Nay, et al., 1988). Findings excluded the influences of azidothymidine (AZT) antiretroviral medication use, anxiety, and depression (Norman, Chediak, Kiel, Gazeroglu, et al., 1990). Also noteworthy, PSG-derived sleep measures were found to lack correlation with subjective sleep complaints (Norman, Chediak, Freeman, et al., 1992).

Animal models using domestic cats infected with feline immunodeficiency virus (FIV) demonstrated similar abnormalities to those seen in HIV-seropositive humans, including the increased SWS structures appearing throughout the latter parts of the night (Prospero-Garcia et

al., 1994). Researchers concluded that FIV mimics HIV in its invasion of the CNS, producing sleep alterations that are apparently reflective of changes in immune system functioning soon after infection (Darko, Mitler, & Henriksen, 1995; Prospero-Garcia et al., 1994). Such findings were somewhat challenged by Ferini-Stambi and associates (1995), who found that asymptomatic HIV-infected men had difficulty achieving deeper levels of sleep as evidenced by a reduced percentage of SWS compared to matched controls. Seemingly dependent on severe immune dysregulation, such a reduction in SWS had previously only been reported in patients in advanced stages of their HIV disease progression (Norman & Chediak, 1992; Wiegand et al., 1991). Ferini-Stambi's group specifically explored the microstructures of sleep, and found a significant difference in the rate of cyclic alternating pattern (CAP) cycles in 9 asymptomatic seropositive men without sleep complaints as compared to 9 age-matched seronegative counterparts. Thus, suggesting dynamic HIV-related alterations in fine sleep stability even prior to sleep complaints or PSG detection. Additional abnormalities seen in other studies, enrolling asymptomatic males, included alpha-intrusions and altered NREM/REM patterns, such as increased number of REM periods and decreased total REM percentage (Norman, Chediak, Kiel, Gazeroglu, et al., 1990; Norman et al., 1989). When compared to published normative data, HIV⁺ subjects demonstrated increases in the number of awakenings, stage 1 shifts, alpha-NREM anomalies, total percent of SWS attributed to its presence in the second half of the night, and number of REM periods. HIV-subjects also demonstrated decreased stage 2 sleep, sleep latency, and average REM durations (Norman Chediak, Freeman, et al., 1992; Norman, Chediak, Kiel, & Cohn, 1990). In contrast, however, White and co-investigators (1995) evaluated 23 asymptomatic seropositive and 13 seronegative men, finding only a significant difference in REM latency between the groups.

Evaluations of symptomatic stages of the illness, including AIDS, demonstrated an exacerbation of fragmented sleep and markedly reduced percentage of both REM and SWS (Norman & Chediak, 1992; Norman, Nay, et al., 1988). Kubicki and fellows (1988) evaluated a small group of AIDS patients who demonstrated consistent findings, including a reduced total sleep time, more time awake in stage 1, and less SWS and REM sleep. Additionally, they found increases in REM latency, SWS latency, and length of NREM period; and decreases in percentage of stage 2 sleep, K complexes, and extremely low sleep spindle density. Results were confirmed in a later study with a much larger sample of AIDS patients (Kubicki et al., 1989). Wiegand and researchers (1991) also reported comparable findings of longer sleep latency, reduced total sleep time, reduced sleep efficiency, increased awake time, and more stage 1 and stage 2 than deeper sleep stages in symptomatic HIV patients. However, they did not find a significant difference in percentage of REM sleep, REM density, or SWS when compared to healthy matched controls.

Wrist Actigraphy Studies. Following the hallmark PSG studies, measurement of HIV-sleep profiles progressed to a more feasible and subject-friendly method of assessment via wrist actigraphy. Although actigraphy does not allow for the precise assessment of sleep architecture or sleep stages, it is another valid option to objectively explore the circadian nature of sleep and activity patterns with minimal restrictions on normal routines. As a result, investigators have been able to monitor sleep-wake activity rhythms in virtually any sample and environment. By scoring the data, researchers are able to estimate a variety of sleep-wake variables related to nocturnal sleep patterns and daytime functioning.

Lee, Portillo, & Miramontes (2001) used wrist actigraphy to describe sleep and activity patterns in relation to HIV status and fatigue. This was one of the first HIV-actigraphic studies

published, and its sample included 100 women of mixed ethnicity in various stages of their illness. Sleep, in terms of total sleep time (6.5 hours \pm 1.95) and sleep efficiency (74.7%), was poor; resulting in more frequent naps (45%) in comparison to previous reports of healthy women in the community. However, women with high fatigue demonstrated more difficulty falling asleep, more nocturnal awakenings, and poorer daytime functioning compared to those with low fatigue. Phillips & Skelton (2001) were of the first to objectively test the significance of an HIV-related sleep disruption intervention (a 5-week course of acupuncture) in 21 HIV⁺ men and women using actigraphy. Post-intervention results demonstrated significant improvement in total sleep time, sleep latency, number of awakenings, number of minutes spent awake, sleep percentage, wake percentage, and sleep ratio. Hudson, Portillo, & Lee (2008) also made use of actigraphic data to pilot test a tailored sleep promotion intervention in 30 women recruited from Lee's 2001 study. This sub-group showed post-intervention improvement with a significant decrease in the percentage of nappers. When separated out, poor sleepers were the only ones to demonstrate significant improvement in their post-intervention actigraphic measurements of initiation insomnia and maintenance insomnia. Actigraphic methodologies were also successful in evaluating sleep characteristics in HIV-infected children. Unlike adult assessments, Foster and investigators found that overall, HIV-infected children slept more and longer than controls (Foster et al., 2007), and that children with viremia had an even higher increase in sleep duration and sleep efficiency relative to HIV-infected children with undetectable viral loads and controls (Foster et al., 2008).

More recently, Lee and coworkers (2012) utilized actigraphic estimates of nocturnal sleep time, wake after sleep onset, and daytime sleep to characterize specific types of sleep problems in 290 adult men and women with HIV. Nearly half (45%) of the sample slept less than 6 hours

per night (mean 6.2 hours \pm 1.6) and over half (56%) demonstrated fragmented sleep throughout the night. Results supported the need for continued efforts to improve both sleep initiation and sleep maintenance difficulties in the majority of adults living with HIV/AIDS, regardless of clinical and demographic profiles. Chen and partners (2012) employed a dual qualitative and biomedical approach to examine HIV-related sleep disturbance in a subgroup of 9 Chinese women from a larger parent-study in Shanghai. Although the study did not report actigraphic sleep time, collectively, participants cognitively set aside less than 7.5 hours for sleep (from the time they laid down until they got up). Those who demonstrated fragmented sleep showed increased daytime sleep, as evidenced by longer nap times (average 3.15 hours). Objective data also implied that these women maintained the normal activity levels of their healthy counterparts. In a sample of eight HIV⁺ men and women of varying ethnicities, Taibi, Price, and Voss (2012) described comparable actigraphic outcomes (mean total sleep time = 6.1 \pm 1.6 hours and sleep efficiency = 72.4 \pm 12.6%) first reported by Lee's group more than 10 years prior (Lee et al., 2001). Wake time in bed averaged 142.2 minutes (2.37 hours), however, data showed lack of napping as participants were engaged in a program of activities throughout the day. In this study, objective sleep data presented more severe than the subjective data reported on sleep diaries, again corroborating the objective-subjective sleep measure discrepancies seen in prior studies (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989; Norman, Chediak, Freeman, et al., 1992). Gamaldo and investigators (2013) conducted a comparative multi-method assessment of sleep, function and HIV in an all-Black male sample (25 HIV-positive and 19 HIV-negative). Similar actigraphic measures included sleep times less than 6 hours and sleep efficiencies less than 70%. Sleep latency periods, however, were longer in the HIV⁺ group and were correlated

with lower quality of life scores. The difference between sleep latency scores was statistically significant until they were adjusted for education and trait anxiety.

Conclusion. A review of each of the 13 classic PSG studies found clear abnormalities in nocturnal sleep physiology, which suggests that CNS sleep-structure distortion is one of the earliest and most consistent signs of HIV infection (White et al., 1995). The attenuations in sleep architecture varied with the progression of disease; however, severe destruction of sleep structures was only evident in the late-stages of AIDS. Wrist actigraphy studies were supportive, in that they provided additional objective findings of distorted sleep-wake patterns, consistent with that of HIV-related CNS sleep disruption. The use of wrist actigraphy made way for feasible evaluation of sleep intervention and the exploration of more diverse populations, including children. Progressively, researchers have tried to exclude known primary sleep disorders, first night effect, medications, drug use, anxiety, depression, and other psychopathologies as major contributors of the aberrations seen in HIV. Based on the studies reviewed, it is probable that the decay of healthy sleep profiles associated with early HIV infection could be primarily pathophysiological in origin with few psychosocial causes, except perhaps for the frequent arousals which are also seen as sequelae of stress and anxiety (Darko et al., 1995; Norman, Resnick, et al., 1988).

Many of the objective sleep studies reviewed were wrought with limitations. PSG studies are extremely costly and usually very limited in the number of nights available for data collection, making longitudinal studies almost nonexistent. Sleep-laboratories are endowed with foreign conditions, which tend to facilitate a false representation of typical sleep patterns. Type II errors are notable in studies with such small sample sizes. Very few of these studies used controls with a sufficient number of participants or matched variables in each group.

Methodologies were highly selective and controlled, thus, limited in their consideration of various lifestyles and environmental confounders. Documentation or potential exclusion of preexisting sleep conditions prior to HIV infection was lacking, and normative data used for comparisons were from results published over 15 years prior, before a diagnosis of HIV even existed. Lastly, the many variations in definitions, methodologies, and sub-populations utilized in these inquiries may account for some of the conflicting results reported between studies.

Sleep Quality

Manifestations of HIV-related sleep disruption were not only observed through objective measures of the sleep/wake rhythm, but interest quickly grew in the subjective experience of sleep quality as well. Participants clearly articulated a noticeable change in sleep for the worse with their diagnosis (Portillo, Tom, Lee, & Miramontes, 2003). Poor sleep quality was found to include any self-reports of difficulty initiating sleep, difficulty maintaining sleep, waking up too early, and sleep that was chronically nonrestorative, poor in quality and/or quantity (Edinger et al., 2004; Phillips & Branson, 2009). Once subjects equated the experience of a good night's rest to a sense of normalcy and a happier life, quality of sleep soon proved to be just as important as the quantity and physiology of sleep (Nokes & Kendrew, 2001; Portillo et al., 2003). As a result, HIV-sleep researchers over the past several years have focused much of their attention on the self-reported experiences of disrupted sleep quality.

Historically, disturbances in sleep quality has been a common complication associated with HIV infection, and to the trained professional eye, a potential predictor of the disease (Cohen et al., 1996; Nokes & Kendrew, 1996; Nokes, Chidekel, & Kendrew, 1999; Norman, Chediak, Kiel, & Cohn, 1990; Norman, Chediak, Freeman, et al., 1992; Ragsdale & Morrow, 1990; Reid & Dwyer, 2005; Rubinstein & Selwyn, 1998; Saberi et al., 2011). While the general

population has demonstrated anywhere from 10% to 40% prevalence of poor sleep quality, this remains significantly lower than that reported in the context of HIV disease (Lee et al., 2001; Omonuwa et al., 2009; Reid & Dwyer, 2005). In fact, reports of HIV-related sleep quality disturbances have surpassed those of other chronic diseases, such as cancer and renal failure (Lee et al., 2001; Rubinstein & Selwyn, 1998). Despite the high prevalence, most subjects reported little or no use of sleeping aids, and physician-guided intervention was almost nonexistent (Gamaldo et al., 2013; Phillips & Sowell, 2005; Robbins et al., 2004).

In 1992, Norman, Chediak, Freeman, and other partners proposed that HIV-seropositive individuals had a greater perception of sleep disturbance and a significant increase in sleep-related complaints than their seronegative counterparts. Supporting such claims, Lee, Portillo, & Miramontes (2001) and Nokes & Kendrew (2001) established PSQI scores of 9.9 (SD = 4.4) and 10 (SD = 5), respectively. Hand and partners (2003) found that 100% of their African American sample experienced some type of sleep disturbance, and their PSQI group mean was 12.4 (SD = 3.9). Age and gender were not shown to be factors in this study. Robbins and associates (2004) and Phillips and associates (2006), independently, confirmed that 100% of their samples self-reported poor sleep quality with PSQI means remaining stable at 12.3 (SD = 3.9). More recently, Salahuddin and comrades (2009) reported an 80% prevalence of substantial sleep complaints in a sample of 128 participants, most of which were African American men at varying stages of HIV disease. Their PSQI group mean was 9.4 (SD = 4.4). Lee and colleagues (2012) reported an average PSQI of 7.7 (SD = 3.8) in short sleepers (those routinely sleeping < 6 hours). Wibbeler and researchers (2012) compared sleep quality in 180 infected subjects against 120 controls, finding increased prevalence rates (63.9% vs. 21.0%) and increased scores (8.0 ± 4.4 vs. 4.1 ± 2.5) in the infected group. In Brazil, however, participants (N=122) reported a lower prevalence

of poor sleep quality (46.7%); their mean PSQI score was 6.1 (SD = 4.1) and the median was 5.0 (Ferreira & Ceolim, 2012). Discordantly, comparable sleep quality scores between HIV and non-HIV groups have been observed in a few studies (Crum-Cianflone et al., 2012; Vance & Burrage, 2005; White et al., 1995).

Hypotheses of a direct connection with immune function led some investigators to explore poor sleep quality early in the asymptomatic phase of HIV disease, while others focused more of their attention on its ubiquitous nature throughout the symptomatic phases. Although disturbances in sleep quality have been clearly described in each phase since the early '90s, the underlying pathophysiology of the disturbances remains unclear and the data regarding the association between sleep quality and the phase of illness inconsistent. (Reid & Dwyer, 2005). To further explore possible causal factors, qualitative interviews conveying noticeable changes in sleep quality with HIV infection, exposed issues of subsequent health problems, decreased productivity, increased psychosocial problems, addictions, and accidental deaths (Nokes & Kendrew, 2001; Portillo et al., 2003; vanServellen, Sarna, & Jablonski, 1998). Researchers noted that such changes in sleep quality were generally entwined with numerous disease-specific and non-disease-related correlates of influence including immunological, neurological and cognitive dysfunction, opportunistic infections, psychosocial circumstances, environment, lifestyle choices, and side effects of the various treatments (Hand et al., 2003; Hand, Phillips, & Dudgeon, 2006; Robbins et al., 2004; Vosvick et al, 2004).

In an exploratory study by Nokes and Kendrew (2001), 58 subject's sleep quality was linked to employment status, general wellbeing, trait anxiety, sleeping arrangements, addictive substances (cigarettes, caffeine, marijuana, and alcohol), symptom severity, depressive symptoms, daytime sleepiness, functional status, state anxiety, length of time living with HIV,

and antiretroviral medications. Of that list, depressive symptoms, daytime sleepiness, symptom severity, state anxiety, and functional status, collectively, explained 43% of the variance found in sleep quality ($F= 7.93$, $p= .000$). Moreover, worst sleep was correlated with a noisy bedroom, impaired functional status, and a longer duration of HIV disease. No relationships were found related to age, intravenous drug use, AIDS diagnosis, $CD4^+$ cell count, or HIV viral load. Several studies explored HIV-related fatigue and its association with sleep quality (Marion et al., 2009; Phillips et al, 2004; Robbins et al., 2004). Lee's cohort (2001) demonstrated that high levels of fatigue, depression, poor sleep quality, and poor daytime functioning were all associated. Robbins and fellows (2004) concluded HIV symptoms, total pain, fatigue, depression, state anxiety, and number of adults in the household were related to sleep quality.

Through time, investigators continued to examine correlates such as pain (Phillips & Skelton, 2001; Vosvick, et al., 2004), existential wellbeing and total spiritual wellbeing (Phillips et al., 2006), number of HIV symptoms and poor adherence with antiretroviral therapy (Minarik, Portillo, & Lee, 2007; Phillips, Moneyham, et al., 2005; Saberi et al., 2011), lack of employment (Phillips, Sowell et al., 2005), viral load and $CD4^+$ cell count (Ferreira & Ceolim, 2012; Okocha, et al, 2009), cognitive impairment (Gallego et al, 2004; Hand et al., 2003), caffeine intake (Dreher, 2003), living space (Nokes & Kendrew, 2001), sexual quality of life (Rose, Peake, Ennis, Pereira, & Antoni, 2005), social support (Vosvick et al., 2004), maintenance of risk behaviors (Ferreira & Ceolim, 2012), and various sleep-related behaviors (Hudson et al., 2008), just to name a few. Given the dominance of anxiety, stress, and depression experienced in HIV disease, numerous studies supported the significant impact psychological correlates have on sleep quality (Jean-Louis et al., 2012; Junqueira, Bellucci, Rossini, & Reimao, 2008; Lee et al., 2001; Mello, Segurado, & Malbergier, 2010; Mock et al., 2002; Nokes & Kendrew, 2001;

Phillips, Moneyham, et al., 2005; Robbins et al., 2004). Cruess and researchers (2003) concluded that sleep quality was the mediator between psychological distress and immune status.

A few studies have explored the use of antiretroviral therapy (ART) as it relates to sleep quality in HIV disease. Despite the fact that insomnia is almost always listed as an adverse effect of most drugs, early studies seem less than supportive (Möeller et al., 1991; Rubenstein & Selwyn, 1998; Wheatley & Smith, 1994). In 2001, Nokes' group found that antiretroviral therapy did correlate significantly with poor sleep quality. Seventy-two percent of their sample reported zidovudine, didanosine, zalcitabine, stavudine, or lamivudine use. Nuñez and associates (2001) demonstrated a significant difference in sleep quality when comparing 51 patients receiving efavirenz to case-controls. Elevated plasma levels were associated with extended abnormal dreams, increased awakenings, and trouble falling asleep. An efavirenz plasma level over 3.5 ug/mL was found to be an independent predictor of poor sleep quality. Gallego and partners (2004) also supported efavirenz-related sleep quality disruptions via PSQI data. A recent study noted the contrary, with no associations with HAART use or long-term efavirenz use found (Crum-Cianflone et al, 2012).

Conclusion. In summary, the exploration of such a complex and subjective experience has led to some elusiveness throughout the literature. Authors made reference to a wide array of terminology, such as insomnia, dysfunctional sleep, distorted sleep, nonrestorative sleep, or simply just poor sleep. Methodologies and working definitions were incoherent between studies. For example, progression of disease, which can be defined in terms of CD4⁺ cell count, CDC staging, or by WHO staging varied by study. Together with small sample sizes, data seemed inconsistent making it hard to draw firm conclusions. However, regardless of the terms or definitions used, one can agree that sleep quality is dynamic, highly individual, and influenced

by a multitude of physiological, psychological, psychosocial, and pharmacological factors (Phillips & Skelton, 2001).

Daytime Sleepiness

HIV-related sleep disruption often manifests in the daytime as a functional impairment known as excessive daytime sleepiness (Darko et al., 1995; Nokes & Kendrew, 2001; Wibbeler et al., 2012). Daytime sleepiness can have a profound effect on an individual's important activities of daily living, such as self-care practices, work performance, and interpersonal relationships (Lee et al., 2001; Nokes & Kendrew, 2001; Perkins et al., 1995; Wheatley & Smith, 1994). Even modest levels of sleepiness have been noted to have substantial adverse influences on everyday life (Briones et al., 1996). Subjectively, one might express the experience in terms of drowsiness, lethargy, tiredness, somnolence, malaise, and/or fatigue. Such dysfunction usually entails physiological and psychological components that tend to translate into a propensity toward excessive daytime napping, reduced cognition and reflexes, irritability, curtailed social activities, depression, and even exaggerated perceptions of illness (Hand et al., 2006; Wheatley & Smith, 1994). Given the important role that each of these may play in terms of general health and quality of life, the research on the prominence of excessive daytime sleepiness associated with HIV disease remains particularly modest in quantity. (Lee, Portillo, & Miramontes, 1999; Wheatley & Smith, 1994).

Increased rates of daytime sleepiness, secondary to HIV-related sleep disruption, have readily been found in HIV-infected patients upon assessment and even reported as a typical presenting symptom of HIV infection (Aldrich et al., 1988; Epstein et al., 1995; Hand et al., 2006). More than just a physiological or behavioral propensity to fall asleep, sleepiness has been further described as an encompassing phenomenological experience of subjective feelings

associated with alterations or imbalances in sleep/wake mechanisms (Shen, Barbera, & Shapiro, 2006). In a study conducted by Cohen and co-investigators (1996), HIV-positive women reported feeling very tired in the morning (40%) more than HIV-positive men (13.3%), yet no statistical difference was demonstrated in the number of naps between men and women. Interestingly, national polls, sponsored by the National Sleep Foundation (n.d.), support such findings that women generally are more likely than men to experience symptoms of sleep disruption, including daytime sleepiness. Subjects in symptomatic CDC stages III and IV have been noted to complain of sleeping more, napping more, and having diminished midmorning alertness (Nokes & Kendrew, 2001; Robbins et al., 2004). Lee and coworkers (2001) established that HIV-positive women with lower rhythm strength on wrist actigraphic assessment (indicative of irregularities in their sleep/activity patterns), perceived more daytime dysfunction and spent more time napping during the day as compared to those with higher rhythm strength (indicative of stable sleep/activity pattern). Salahuddin and researchers (2009) analyzed 128 HIV-positive individuals and found a high prevalence of sleep-related daytime dysfunction (42%) and feelings of excessive daytime sleepiness (55%). The sample mean on the Epworth Sleepiness Scale (ESS) was 11 (SD = 5.2), ten indicating pathology. Uniquely, Salahuddin's group also examined daytime sleepiness in context of fatigue, finding a significant correlation between the ESS and the HIV-Related Fatigue Scale (HRFS). In a multiple regression model, daytime sleepiness did not explain the association between stress and fatigue intensity, however, it did marginally explain the association between stress and fatigue-related impairment of functioning. In a controlled study, Wibbeler and associates (2012) demonstrated a significant increase in daytime sleepiness in HIV-infected participants (46.6%) versus the control group (19.4%). Mean ESS scores differed significantly as well, 9.4 (SD = 4.9) in the infected group and 6.5 (SD = 3.2) in

the non-infected group. They observed a trend where those with a significantly higher percentage of HAART intake and lower viral loads were more likely to report increased daytime sleepiness. Incongruously, Crum-Cianflone and colleagues (2012) detected no significant difference in ESS scores among a group of 193 early-treated HIV infected participants (7.5 ± 4.4) and 50 uninfected controls (6.6 ± 3.6). Gamaldo and co-investigators (2013) supported the lack of significance in an all-Black controlled study, however, ESS results were listed in a table and no discussion was provided related to ESS scores.

In summary, those experiencing HIV-related sleep disruption are also predisposed to experience excessive daytime sleepiness. Nonetheless, there seems to be some ambiguity in the HIV-sleep literature regarding the conceptual distinctions, particularly between fatigue and daytime sleepiness. The two are often used interchangeably, and there is no established consensus on what the universal experience of 'sleepiness' actually entails or what is considered to be 'excessive' sleepiness (Shen et al., 2006). Very few studies were found that assessed daytime sleepiness at length. The ESS was utilized the most, however, some described sleepiness within the context of their assessment of sleep quality via PSQI, and others may have simply misclassified it or included it in with fatigue.

For clarification purposes, it is this investigator's scholarly opinion that daytime sleepiness is a manifestation of sleep disruption, contradistinguished from fatigue. Fatigue denotes a much broader construct of HIV-symptomology related to the many infectious processes involved in HIV infection, which may or may not include sleep/wake alterations and an increased sleep propensity (Shen et al., 2006; Vgontaz et al, 2002). This may explain why Lee and colleagues (2001) found that fatigue was not associated with total sleep time at night, circadian rhythm parameters, or napping behaviors during the day. Likewise, Mock and fellows

(2002) found that sleep dysfunction accounted little for the variation in fatigue, and thus, hypothesized physiological and pathophysiological processes of the disease instead.

IL-6 Rhythm.

Interleukin-6 (IL-6) is an inflammatory cytokine produced by many different cells in the body, such as T-lymphocyte cells, monocytes, macrophages, osteoblasts, bone marrow stromal cells, intestinal epithelial cells, and cells of the testis, pituitary, endometrial, and vascular smooth muscle (Babakhanian, 1995; Papanicolaou, Wilder, Manolagas, & Chrousos, 1998). IL-6 is a pleiotropic cytokine, in that the immune system uses it to communicate and orchestrate specific responses related to inflammatory, endocrine, neurologic, and metabolic functioning (Babakhanian, 1995; Kishimoto & Hirano, 1988; Papanicolaou et al., 1998; Späth-Schwalbe et al., 1998; Vgontzas et al., 2005). As a result, IL-6 plays a role in a broad array of biological activities: stimulates the secretion of growth hormone, inhibits thyroid-stimulating hormone secretions, suppresses serum lipid concentrations, plays a central role in the pathogenesis of osteoporosis related to bone resorption conditions, stimulates energy mobilization which leads to increased body temperature and resting metabolic rates, inhibits secretion of TNF α and IL-1, synergistic with glucocorticoids activates the production of acute phase reactants from the liver (C-reactive protein, haptoglobin, fibrinogen), stimulates the hypothalamic-pituitary-adrenal axis (HPA), activates B-cell differentiation and maturation, activates T-cell proliferation and differentiation, and helps control various inflammatory, stress, and immune responses (Chrousos, 1995; Kishimoto & Hirano, 1988; Papanicolaou et al., 1998). IL-6 normally circulates in the blood at levels ranging from 5 to 15 pg/mL (Honda et al., 1990). Honda and comrades (1990) described these values as being reflective of the minimal activation required for normal-everyday functioning of the immune system, absent of major injury, sickness, or stress. Secretion of IL-6

is positively influenced by body mass index, catecholamines, IL-1, and TNF α ; and negatively influenced by glucocorticoids, estrogen, and androgen (Chrousos, 1995; Papanicolaou et al., 1998). Elevated levels of IL-6 are seen in many severe inflammatory, infectious, stressful, and traumatic states, such as pain, obesity, major depression, chronic insomnia, nightshift workers, steroid withdrawal syndrome, alcoholism, rheumatoid arthritis, and systemic erythematous lupus (Alesci et al., 2005; Bovbjerg, 2003; Chrousos, 1995; Friedman et al., 2005; Krueger et al., 1995, Papanicolaou et al., 1998; Redwine, Dang, Hall, & Irwin, 2003; Vgontzas et al., 2003; Vgontzas et al., 2002). Overproduction may contribute to illness by causing reciprocal sickness behaviors including symptoms of anorexia, fatigue, somnolence, inability to concentrate, sleepiness, fever, decreased motivation, joint and muscle pain, malaise, headaches, listlessness, social withdrawal, and hyperalgesia (Alesci et al., 2005; Breen et al., 1990; Chrousos, 1995; Dantzer, 2004; Papanicolaou et al., 1998; Vgontzas et al., 1999; Vollmer-Conna et al., 2004). With such a bi-directional relationship, it is not hard to understand how average IL-6 plasma levels correspond with overall health outcomes and general wellbeing (Friedman et al., 2005; Vgontzas et al., 2003).

In addition to all the immunomodulating of the complex networks listed above, IL-6 has shown to be a somnogenic cytokine, a putative 'sleep factor', elemental in sleep research because of its apparent association with sleep architecture, sleep quality, and disorders of excessive daytime sleepiness (Bovbjerg, 2003; Vgontzas et al., 2005; Vgontzas & Chrousos, 2002). Along with other somnogenic cytokines, namely IL-1 and TNF α , IL-6 plays a major role in the neural-biochemical interactions of the central nervous system responsible for the regulation of sleep (Chrousos, 1995; Gemma & Opp et al., 1999; Opp et al., 1996; Redwine et al., 2003; Redwine, Hauger, Gillin, & Irwin, 2000). Investigators have described both a

circadian rhythm and a homeostatic component in the IL-6 signaling related to sleep (Krueger et al., 1998; Opp et al., 1996; Vgontzas et al., 1999). Generally, increasing levels of IL-6 correspond with sleep onset, and tend to peak sometime in the latter part of normal sleep (Bauer et al., 1994; Friedman et al., 2005; Redwine et al., 2000). Daytime levels, which are inversely influenced by the previous night's sleep, normally decrease and tend to be influenced by daily temporal patterns of sleepiness (Friedman et al., 2005; Irwin, 2002; Mills et al., 2007; Vgontzas et al., 2005; Vgontzas et al., 2002). In fact, lower daytime IL-6 concentrations are reflective of better sleep the night before and a good sense of wellbeing upon awakening (Miller, Cohen, & Ritchey, 2002; Späth-Schwalbe et al., 1998; Vgontzas et al., 1999, 2003; Vgontzas & Chrousos, 2002). Extensive investigations into IL-6 levels throughout the day have revealed a naturally occurring biphasic circadian rhythm with two nadirs (troughs) around 0800 and 2100 hours and two zeniths (peaks) approximately 1900 and 0500 hours (Honda et al., 1990; Vgontzas et al., 1999). The 0500 zenith has been noted to be the stronger of the two peaks (Vgontzas et al., 1999, 2005). Another source reported a similar circadian periodicity in healthy individuals with a primary zenith during the night between 0100 and 0500 hours, a nadir in the morning between 0800 and 1000, and a secondary zenith between 1700 and 1900 hours (Alesci et al., 2005).

Poor or disrupted sleep is known to result in a subsequent elevation of daytime IL-6 levels (Irwin, 2001; Miller et al., 2002; Redwine et al., 2003; Shearer et al., 2001; Vgontzas et al., 1999, 2002, 2003). Data from experimentally-induced hypersecretion of IL-6 (by either exogenous administration or sleep-deprivation studies) concurrently reflect that IL-6 has direct effects on sleep progression through feedback mechanisms of the HPA axis, which are thought to trigger the restorative homeostatic drive for sleep (Bollinger et al., 2009; Friedman et al., 2005; Mills et al., 2007; Shearer et al., 2001; Späth-Schwalbe et al., 1998; Vgontzas et al., 1999, 2005).

Participants experienced an ensuing somnolence, mental and physical weariness with a propensity for sleep during the day, delays or shifts in their IL-6 rhythm zeniths (from nighttime to daytime), and architectural changes, such as prolonged sleep latency, deeper sleep, decreased REM, and shifted SWS into the second half of the following night (Miller et al., 2002; Redwine et al., 2003; Späth-Schwalbe et al., 1998; Vgontzas et al., 1999, 2002, 2003). Interestingly, those naturally prone to increased SWS, exhibited an inherent ability to tolerate sleep loss, seemingly protective against IL-6 hypersecretion (Papanicolaou et al., 1998; Shearer et al., 2001; Vgontzas et al., 1999). Progressive age-related increases in IL-6 secretion explained the dawdling decreases in the quantity and quality of sleep, as well as other common ailments associated with aging (Okun et al., 2011; Vgontzas et al., 2003). Regardless of the reason, a prolonged imbalance (dysregulation) or shift in the IL-6 circadian rhythm are consistent with reports of pronounced sleep problems and increased morbidity, disability, and mortality (Bovbjerg, 2003; Friedman et al., 2005; Mills et al., 2007).

Animal studies have demonstrated evidence consistent with human studies, which hypothesize that IL-6 possesses sleep modulatory properties. Guan, Omori, Vgontzas, Bixler, and Fang (2003) induced total sleep deprivation in adult male rats, finding a 10% to 26% increase in IL-6 levels by the 6th hour of sleep loss compared to that of controls. While controlling for other stressors, Hu and colleagues (2003) found similar results in mice with 36 hours of sleep deprivation. Hogan and investigators (2003) utilized exogenous administration of IL-6 in albino male rats, which evoked dose-dependent NREM alterations. Morrow and Opp (2005) also confirmed a general role in sleep physiology by using advanced IL-6 knockout mice, genetically altered for IL-6 gene deletion. These sleep-deprived mice lacking the expression of

IL-6 spent more time in REM sleep and took 6 hours longer to obtain the same amount of NREM sleep than their controls.

In 1987, Dr. Norman's group first suggested that changes in cytokine concentrations during HIV infection played a pivotal role in the alterations of sleep-wake behaviors that were observed. Several studies found the expression of somnogenic cytokines, like IL-6, greatly amplified due to immune dysfunction during the viral challenge and in phase with the altered sleep-wake rhythms (Babakhanian, 1995; Foster et al., 2008; Krueger et al., 1995; Kubicki et al., 1989; Norman, Chediak, Kiel, & Cohn, 1990; White et al., 1995). Honda and group (1990) found mean IL-6 levels of 55.5 pg/mL in a group of asymptomatic HIV-seropositive carriers. This was significantly higher than the 9.5 pg/mL exhibited by healthy age-matched controls. Data from in vitro studies led them to propose the continuous stimulation of infected monocytes and macrophages as the likely source of elevated serum IL-6 levels. Breen and partners (1990) found circulating plasma levels of IL-6 in HIV-infected donors to be 16-fold higher (mean 1.3 U/mL) as compared to that of healthy donors (mean 0.08 U/mL, $p \leq 0.005$). In a twenty-four hour culture, with no exogenous stimulation from IL-6 activators, isolated donor cells exhibited a 10-fold increase from HIV-infected donors (2.5 U/mL) compared with controls (0.22 U/mL, $p < 0.025$). Furthermore, fractionation of the isolated blood into groups prior to the 24-hour culture helped to identify the cell-type responsible for the increased IL-6 secretions. The monocytes/macrophage fraction was found to account for the majority of the IL-6 secreted in vitro. Animal models confirmed cytokine dysregulation as instrumental in sleep pathology throughout the course of HIV infection. Opp and coworkers (1996) used exogenous administration of HIV-envelope glycoprotein 120 (gp120) in rats to induce altered synthesis and secretion of various somnogenic cytokines, and thus, alter sleep. Sleep-wake behaviors were

unremarkable at low doses (20ng of gp120). However, larger doses of 100ng and 500ng produced hallmark responses seen in elevated cytokine levels, including fragmented sleep, stage 1 shifts, and increased NREM sleep (equivalent to SWS in human studies). Gemma and Opp (1999) replicated these findings in another rat study, except they established that the HIV-envelope gp160 and gp41 could produce the characteristic sleep patterns associated with cytokine dysregulation.

Honda's group (1990) also noted that as HIV-disease progressed to symptomatic stages like AIDS-related complex (ARC) and AIDS, so did IL-6 levels (106.8 pg/mL and 283 pg/mL, respectively). Data suggested that IL-6 levels associated with the degree or stage of HIV-induced illness may be a consequence of an immune interaction that appears to favor immune pathogenesis, where infected mononuclear phagocytic cells (monocytes and macrophages) are continuously stimulated to secrete IL-6, produce large quantities of the HIV virus (viral replication), and serve as a reservoir for the virus. IL-6 and viral copies affect the function of T- and B-cells, as well as many other cell types favoring immune abnormalities (Honda et al., 1990). Since then, Foster and colleagues (2007) found greater cytokine dysregulation and significantly higher percentage of T-cell activation in HIV-infected children with higher viral loads >400 copies/mL (viremia) compared to those with undetectable viral loads <400 copies/mL or controls. In a subsequent study led by Foster (2008), children with viremia demonstrated enhanced alterations in sleep patterns and an increased mean plasma IL-6/IL-1 β ratio (1.3, ln) compared to controls (-1.7, ln, $p = 0.003$). Kinoshita and Taguchi (2008) provided a technical explanation of the mechanism underlying viral replication. They described IL-6 transcription factor (NF-IL6), also known as an IL-6 promoter, as a natural inhibitor of APOBEC3G, an antiviral cytidine deaminase. The resulting inhibition of APOBEC3G, which

normally blocks HIV-1 reverse transcriptions, permits the uninhibited activation of T-cells, a crucial step in allowing HIV viral replication to proceed.

Recent studies have been able to duplicate the association between IL-6 levels and CD4⁺ counts and viral burden (Bastard et al., 2012; Míguez, Rosenberg, Burbano-Levy, Carmona, & Malow, 2012). Bastard and researchers (2012) found 122 immunologically stable subjects (80.3% men) with an IL-6 range of 0.15-5.46 pg/mL and a median of 0.685pg/mL. IL-6 levels correlated with nadir CD4⁺ level and HIV viral load, the threshold value for increased IL-6 level was 31 HIV copies/mL. Míguez and colleagues (2012) contended that lower IL-6 levels were associated with smokers compared to nonsmokers, HAART-treated individuals compared to non-treated, and hazardous alcohol users compared to nonhazardous users. Gender differences were also noted with African American participants having lower levels of IL-6. Fumaz and coworkers (2012) noted a mean plasma IL-6 level of 7.0 pg/mL in 50 subjects (88% men), when they found a strong correlation between IL-6 and stress. Additional studies regarding IL-6 levels in HIV-infected individuals were related to BMI and obesity (Koethe et al., 2013), omega-3 fatty acid therapy in hypertriglyceridemic HIV patients (Metkus et al., 2013), Hepatitis C virus and liver fibrosis (Fuster et al., 2013), and lastly, McDonald and partners (2013) who emphasized that IL-6 levels are important predictors of all-cause mortality.

In summary, research efforts that specifically seek to understand IL-6, an inherent biomarker of health and wellbeing, as a common variable between HIV-related sleep disruption, disease progression, and quality of life are lacking. Most had very small sample sizes and relied on single-point measurements of IL-6, which consequently undermines its periodicity in phase with sleep-wake rhythms. Additionally, many studies fail to mention consideration of potential confounders related to gender, body composition, and other biological or pathological

abnormalities. In an attempt to simplify the feedback loop hypothesized above, HIV infects the central nervous system and immune competent cells causing cytokine dysregulation. The dysregulation of somnogenic cytokines disrupts sleep-wake behaviors and promotes viral replication. The resulting sleep disruption and increased viremia, not only affects daytime functioning, increased morbidity, and quality of life, but also leads right back to further cytokine dysregulation. Thus, the interplay between cause and consequence continues.

Quality of Life.

Quality of life has evolved into a critical outcome measure that gives researchers an indication of an individual's subjective perception of their overall state of health and wellbeing. Health is an impliable factor of wellbeing, contributing not only to the quantity of life expectancy but also to the quality of life tolerability (Cella & Tulsy, 1990; O'Keefe & Wood, 1996). Since 1946, the WHO has defined health as "a state of complete physical, mental, and social wellbeing and not merely the absence of disease or infirmity" (<http://www.who.int/about/definition/en/print.html>). However, with no real consensus as to the precise meaning or conceptual boundaries for these terms, quality of life and wellbeing are often used interchangeably and synonymously with health. Traditionally, quality of life was thought of as "a vague and ethereal entity, something that many people talk about, but which nobody very clearly knows what to do about" (Campbell, Converse, & Rodgers, 1976). It has also been described as a fluid or dynamic multidimensional reflection of the internal satisfaction or happiness with how life is going compared to some aplombed conjecture of how life should be (Cella & Tulsy, 1990; Lutgendorf et al., 1994). Health status, general functional abilities, income, freedom, environment are just a few important factors that may influence one's quality of life (Briones et al., 1996; O'Keefe & Wood, 1996).

HIV is a chronic disease thwart with a relapsing and remitting nature, a hauntingly uncertain trajectory of life-threatening physical decline, a lifestyle full of stigma and redress, and an ever-increasing reliance on innovative healthcare and medical adeptness. Highly active antiretroviral therapy (HAART) and an improved ability to monitor the effectiveness of treatment with HIV viral loads and CD4⁺ cell counts has led to a significant decrease in the traditional clinical outcomes of HIV disease (Call et al., 2000). Subsequently, the emerging goal of HIV care not only seeks to postpone these fatal outcomes, but vies to balance the prolongation of life in a manner consistent with optimal productivity and normalizing quality of life as much as possible (Davis, 2004; Lutendorf et al., 1994); thus, shifting the focus of HIV care to more of a ‘patient-based’ set of outcome measures, particularly those related to adherence, tolerability, and quality of life (Call et al., 2000). The measurement of quality of life helps to weigh the burden incurred from the debilitating course of HIV and its associated sequelae, assess the effectiveness of various treatments, gauge the durability of the therapeutic net benefit against the risk of common side effects experienced, and track the perception of health and wellbeing over time (Hays et al., 2000; Revicki, Wu, & Murray, 1995).

Early on, researchers were able to establish that HIV/AIDS greatly affects one’s quality of life. In Philadelphia, 90 participants diagnosed with AIDS responded to a mail-in survey conducted by Ellerlman (1989). They reported a mean score of 6.8 on the standardized Spitzer’s Quality of Life Index, which was significantly lower than that reported by cancer (7.1) and other chronically ill patients (7.3). Lutendorf and researchers (1994) found that even in asymptomatic HIV-positive men, just the knowledge and perceived implications of their serostatus was enough to permeate their awareness, behaviors, and sense of wellbeing. Asymptomatic disease, however, demonstrated less diminution in quality of life than later stages in the progression of disease

(Ragsdale & Morrow, 1990; O'Keefe & Wood, 1996; Lubeck & Fries, 1997). Many found a general trend, such that, as HIV disease progresses, health declines, associated symptoms arise, and quality of life becomes poorer (Bing et al., 2000; Hand et al., 2006; Hays et al., 2000; Kohli, Sane, Kumar, Paranjape, & Mehendale, 2005; Lubeck & Fries, 1992; Phillips, Sowell, Rush, & Murdaugh, 2001; Wu et al., 1991).

Investigators were first interested in establishing generic quality of life instruments as valid and reliable within the HIV population. Common instruments included, but were not limited to the Quality of Life Index, Quality of Well-being Scale, Sickness Impact Profile, and multiple versions of the Medical Outcomes Survey (MOS). As such outcome measures became more integrated within HIV research, various disease-specific and health-related quality of life measures were developed and validated, including the Medical Outcomes Survey disease-specific modified version (MOS-HIV), the HIV/AIDS Targeted Quality of Life Instrument (HAT-QoL), and the Functional Assessment of HIV Quality of Life Instrument (FAHI). Both generic and disease-specific measures took a deeper look into specific biomarkers of disease severity, such as symptomology, HIV viral load, and CD4⁺ cell count, as surrogate outcome measures of quality of life (Call et al, 2000; Weinfurt, Willke, Glick, Freimuth, & Schulman, 2000). In a sample of 2295 homosexual men, Bing and coworkers (2000) found that having even one HIV-related symptom was enough to significantly decrease quality of life scores per the SF-36. Hays and partners (2000), with an even larger sample, further concluded that symptoms may provide more insight into the effects of HIV disease progression on wellbeing than clinical staging or CD4⁺ cell counts. This had significant ramifications related to HIV care, making early detection and prevention of the symptomatic phase of great importance. Gill and co-investigators (2002) focused on viral loads and CD4⁺ cell counts in response to HAART. Besides the usual

findings of lower viral loads and higher CD4⁺ cell counts being associated with superior quality of life, they added that viral loads needed to be suppressed to undetectable levels in order to see significant improvements. Even though HAART had its own problems with quality of life, they also found that those who were adherent in the long run were able to experience improvements that outweighed the side effects. Hudson, Kirksey, and Holzmer (2004) endorsed symptomology as contributing the most to the variance seen in quality of life measures in their sample. Burgoyne & Tan (2008) agreed that advances in HAART are responsible for the decreases in morbidity and mortality, yet adherence issues, tolerability, and toxicity have continued to erode quality of life. Quality of life scores being relatively stable suggested that, in spite of viral suppression and immunological repletion, the lived experiences of HIV-related symptoms and/or HAART-related side effects are actually most responsible for the variance in the quality of life.

McDonnell and associates (2000) recognized a noticeable lack in research related to the quality of life in women living with HIV. A sample of 287 inner-city HIV⁺ women yielded a profile description of African American women (94%), mean age 33 years old, high school nongraduate (55%), never been married (63%), with heterosexual contact as the mode of transmission (46%). Per MOS-HIV scores, this sample was consistent with that of other HIV-positive female samples from previous validation studies. However, even after adjusting for symptomatic status, their scores were notably lower than that recorded from their higher socioeconomically profiled HIV-positive male counterparts whose mode of transmission was homosexual contact. Another study, which interviewed 3,778 HIV-positive adults for an ongoing CDC supplemental behavioral surveillance study, demonstrated that increased age, female, African American or Hispanic ethnicity, lower education, lower income, and no private health insurance were all significantly associated with lower quality of life scores (Campsmith,

Nakashima, & Davidson, 2003). Hays and partners (2000), however, had already explained that an association with socioeconomic status is not surprising, in that it is reflective of the potential role that accomplishment, productivity, and access to healthcare may play in the promotion of wellbeing. Kohli's group (2005) reinforced the differences in sociodemographics with respect to quality of life in a mixed sample of 100 HIV-infected individuals from India. Lower societal status and poor health seeking behaviors among the women in India were suggested as the reasons for the observed differences seen in the quality of life scores.

Many psychosocial variables have been associated with quality of life, especially given high rates of sexual and physical violence, inadequate social support, and the tremendous concerns regarding stigma, discrimination, and hopelessness (Andrinopoulos, et al., 2011; Gielen, McDonnell, Wu, O'Campo, & Faden, 2001). Sherbourne and staff (2000) reported subjects with probable mood disorders had significantly lower quality of life scores, and heavy drinking and drug use were not associated. Gielen and associates (2001) found that women with more social support resources and self-care behaviors, such as adequate sleep and exercise, reported better mental health and overall quality of life. Yang, Chen, Kuo, and Wang (2003) revealed that higher quality of life was associated with less mood disturbance, reduced physical-symptom distress, and higher levels of social support. The mean QLI score for their sample in Taiwan was 18.50 (SD = 4.30, range = 5.67-29.36). In adolescent and young adult women studies, researchers recommended interventions that effectively decrease stigma and depression, increase social support and illness acceptance, and likely improve their wellbeing and quality of life (Andrinopoulos et al., 2011). Armon & Lichtenstein (2012) explored coping and found it associated with both the mental and physical subscales of the MOS-HIV.

A growing body of knowledge demonstrates that sleep impacts an individual's general health and wellbeing. Many studies attest to the intrusive nature of HIV-related sleep disruption contributing to a waning quality of life and wellbeing (Cohen et al., 1996; Morin, 1993; Nokes et al., 1999; Nokes & Kendrew, 1996, 2001; Vosvick et al., 2004). Briones and fellows (1996) found that sleepiness accounted for 6% of the variance in the measurement of wellbeing in a generally healthy sample without severe chronic medical or psychiatric illnesses. Davis (2004) concurred, describing sleep disturbances as one of the most common clinical symptoms affecting the quality of life in HIV-positive patients. Dreher (2003) found that by simply decreasing the caffeine intake, the experimental group experienced a 35% sleep improvement and a subsequent 7% improvement in perceived wellbeing. Interestingly, the sample, fairly stable Caucasian HIV-positive males, consumed 2.4 times more caffeine (476mg/day) a day than that of the National US consumption average (200mg/day). This supported the fact that to a degree, sleep has an underlying effect on wellbeing in HIV disease. Phillips, Sowell, and researchers (2005) undertook an important descriptive study with a sample of 144 AA HIV-positive females recruited from 12 southern US clinics. In this sample, there was an increased prevalence of poor sleep quality, with poor sleepers reporting decreased quality of life. Asymptomatic poor sleepers scored lower on the mental component of the quality of life scale, and symptomatic poor sleepers scored lower on the physical component. Of importance, sleep quality explained more of the variance on quality of life in a regression model than the stage of illness. Sleep quality accounted for 20% of the variance in the mental component of the quality of life score, while stage of illness accounted for 14% of variance in the physical component. They concluded that improving sleep quality might improve quality of life, especially mental quality of life, which in turn means better adherence, healthier choices, improved self-care, and more health-promoting behaviors.

Phillips' group (2006), in a subsequent study, presented evidence that spiritual wellbeing was not only tied into mental and physical health, but sleep quality as well.

In summary, HIV-related sleep disturbances are undoubtedly associated with poor quality of life and a lower sense of wellbeing. There is a lack of coherence related to the various working definitions and the many measures of quality of life available, thus complicating the efforts of comparative analysis and drawing firm conclusions beyond that which was already stated. Quality of life has been measured using unidimensional, multidimensional, global, modular, generic, and disease-specific instruments. The choice of instrument may be affected by many factors, such as the lens through which one is viewing quality of life, form of data collection, investigator preference, and participant burden. Regardless of the many constraints and methodological issues to consider, interest in the area of quality of life in HIV research continues to escalate and has led to a proliferation of consequential studies. Perhaps future investigation into quality of life issues would benefit from the use of conceptual theories and mid-range theories as frameworks to actually guide the intricate methodological details of the research, instead of just making mention of the studies theoretical underpinnings. Theory-driven research may provide a much better structure from which to organize and synthesize conclusions.

CHAPTER 4

METHODOLOGY

Methods for measuring sleep disruption in asymptomatic HIV-seropositive AA women were initially assessed by this investigator via a small feasibility study (Protocol Number 080907M1F), which was approved by the Wayne State University Human Investigation Committee (HIC) and completed as a master's project in the winter semester, 2008. The feasibility study specifically looked for any technical and operational issues that might arise with such a biophysical protocol, as well as the level of difficulty or participant burden related to the population of interest. Findings of the feasibility study were used to revise and expand the methodology proposed in this dissertation project. After all the prerequisites for the dissertation project were met, a letter of amendment, revised informed consent form, and expanded protocol 080907M1F were submitted to the HIC for approval. This amended the HIC approval from the master's project NUR7998MRP029 to the dissertation project NUR9995DRP20. This chapter presents the study design, variables, protocol, and methods for the dissertation project.

Research Design

A descriptive, correlational study design was used to examine the dynamics of HIV-related sleep disruption and wellbeing experienced in asymptomatic HIV-seropositive African American women of childbearing age. This biophysical monitoring protocol had a cross-sectional study period of four days. The variables of interest were organized within the framework of the Sleep Conservation Model substructured from Levine's Conservation Model. The study utilized multiple quantitative techniques, including an objective device (wrist actigraph), chart abstraction, questionnaires, visual analogue scales, and biological specimens to

measure the variables of the sleep/wake rhythm, sleep quality, daytime sleepiness, the IL-6 rhythm, and quality of life in this sample.

Sample Inclusion/Exclusion Criteria

A purposeful sample of twenty asymptomatic HIV-seropositive African American women of childbearing age, experiencing HIV-related sleep disruption was recruited for this preliminary study. To be eligible, the potential subjects had to meet the following criteria:

- Gender: Female
- Race: African American
- Age: 18-40 years
- Documentation of current asymptomatic phase of HIV-1 infection
- Experiencing HIV-related sleep disruption

Limited by design, the aforementioned eligibility criteria were set to control for any sleep differences due to gender, race, age, and progression of disease. To further ensure that the sleep disruption was related to the purpose of this study, potential participants presenting with any of the following, either by self-report or upon review of the medical records, were excluded from the study:

- Diagnosis or symptoms of a primary sleep disorder (i.e. narcolepsy, primary insomnia, primary hypersomnia)
- Diagnosis or symptoms of a secondary sleep disorder not related to HIV (severe pain, sleep apnea, restless leg syndrome)
- Sleep disruption prior to HIV exposure
- Formal treatment for sleep disorders of any kind

- Diagnosis of a cognitive impairment (mental retardation, dementia, memory impairment)
- Diagnosis of a major inflammatory disease (rheumatoid arthritis, inflammatory heart disease, systemic lupus erythematosus)
- Pregnancy
- BMI calculation ≥ 30
- Average pain severity rating ≥ 7
- Diagnosis of a major psychiatric disorder (panic disorder, post-traumatic stress disorder, major depression)
- Night-shift work
- Any condition or illness, which in the opinion of the investigator, would interfere with patient safety or compliance to the study protocol

Setting

Participants for this study were recruited from Wayne State University Physician Group Infectious Diseases Clinic (ID Clinic) located at 3750 Woodward Ave. Detroit, Michigan. At the time, the ID Clinic served a 73% African American demographic and 83% of the females were African American. The clinic was equipped to treat most infectious diseases, however, the primary focus was HIV care. Patients of the clinic were educated on various types of research; and many had participated in government sponsored network trials [Community Programs for Clinical Research on AIDS (CPCRA), International Network for Strategic Initiatives in Global HIV Trials (INSIGHT), and AIDS Clinical Trials Group (ACTG)], pharmaceutical studies (Pfizer, GlaxoSmithKline, and Boehringer Ingelheim), and various local provider-driven studies. This setting was also ideal in that, as an employee of the WSU ID Research Department, the

Principal Investigator (PI) was able to establish a comfortable and trusting work-relationship of eight years with staff and patients of the ID Clinic alike.

Recruitment

A list of potential participants was generated from an eligibility query of the ID Clinic's HIV/AIDS Program database. The program database was originally designed in 1994 to provide an aggregate of demographic and clinical data for grant reporting purposes. Over time, the database grew in size and complexity, and was now stored on a secured WSU School of Medicine server, managed by the Medical School Information Services Group (MSIS). The database was able to measure and closely monitor outcome objectives in order to ensure continued excellence in patient care and service delivery, as well as meet grantor requirements for data reporting. The database included data fields for demographic information, encounter data, diagnoses, hospitalizations, laboratory results, vital statistics, psychosocial data, immunization history, medication history, genotypes, clinical trials, and special research. The query request prompted a database search for all subjects who met the gender, race, age, and category of disease requirements listed in the eligibility criteria of this study. A query report was provided to the investigator listing one hundred potential participants meeting the inclusion criteria along with other pertinent information such as medical record number, ID physician, last CD4⁺ cell count and draw date, and date of last clinic visit. Once participant interest was established and their primary ID physician had given consent for participation in the study, the patient was able to start the research process beginning with informed consent as described below. A unique personal identification number (PID) was then assigned to each informed participant for identification purposes of all study-related documents, including source documents, laboratory requisitions, and questionnaires. The PID ensured confidentiality of

protected health information. The PIDs for this study followed the pattern SC001, SC002, SC003, and so on.

Informed Consent

Following HIC approval, the informed consent form was reviewed in detail with each interested participant to ensure full disclosure of the nature, objectives, and procedures of the study, as well as any anticipated risk, although minimal risk was associated with the study. Special attention was given to the fact that participation in the study was voluntary; meaning one could withdraw from the study at any point. Ample time was set aside for questions and concerns. Once full awareness was confirmed, the investigator obtained documented consent from each participant prior to any study-related data collection. Consent was documented by the participant's dated signature on a consent form along with the dated signature of the investigator conducting the consent discussion. A copy of the signed consent form was given to the participant.

Study Variables and Measurements

This section discusses the variables used to sketch a sample profile, as well as each of the major study variables explored in this study. The study variables examined were the CD4⁺ cell count, HIV RNA viral load, sleep/wake rhythm, sleep quality, daytime sleepiness, the IL-6 rhythm, and quality of life. A study definition for the study variables will be provided, along with a discussion of the instruments used to measure each of these variables. Copies of the instruments can be found in the appendices.

Study Variables and Measurements

Sample Profile

Demographic and Lifestyle Questionnaire. Distinctive characteristics of the participants were collected in order to provide a profile summary of the sample of interest. The sample profile includes a description of the general demographic profile, medical profile, lifestyle profile, and sleep environmental profile obtained via chart abstraction of the participant's ID medical chart and the Demographic and Lifestyle Questionnaire. The Demographic and Lifestyle Questionnaire is an investigator-developed questionnaire that includes a combination of 30 forced-choice and fill-in response items. General demographic characteristics include age, marital status, religious affiliation, level of education, employment status, and income range. The medical profile consists of a general medical profile, HIV profile, and ART profile. General medical variables include body mass index (BMI), average pain level, menstrual cycle phase, and medication allergies. HIV disease variables include date of HIV diagnosis, mode of transmission, lowest CD4⁺ cell count, and highest HIV RNA viral load. ART variables include total time on ART, current ART use, current ART regimen, and the CNS penetration effectiveness score (CPE) of the current ART regimen. The lifestyle variables include various dietary sways (caffeine intake, time of last meal and liquids for the day), recreational medication use (alcohol, tobacco, and marijuana), and exercise habits. Lastly, the sleep variables include data on various sleeping habits, use of sleep aids or medications, and environmental sleep settings and preferences. Each of these characteristics or behaviors have been linked with or known to modify sleep and/or plasma IL-6 levels in the literature, and thus, were accounted for in this study.

CD4⁺ Cell Count/HIV Viral Load

CD4⁺ Cell Count. The CD4⁺ cell count in this study is the amount of T-helper lymphocyte cells expressing a surface protein CD4, which activates and helps determine the type

of immune response the body will make against a particular pathogen. The CD4⁺ cell count is an indication of the strength of the immune system and was obtained by the most recent documentation of a T-cell lymphocyte subpopulation from the medical chart. The CD4⁺ cell count is expressed in cubic millimeters. Rationale for this measure was to account for the strength of the immune system in defending the body, which may influence the likelihood of experiencing opportunistic infections (candidiasis, pneumocystis carinii pneumonia, herpes zoster) and HIV symptomologies (unexplained diarrhea, seborrheic dermatitis, papular pruritic eruptions) that have been found to create annoyances, disrupting sleep.

HIV RNA Viral Load. The HIV RNA viral load in this study is the amount of HIV viral copies or genetic material (RNA) present in the blood. The viral load is an indication of the strength of the HIV disease and was obtained by the most recent documentation of an ultrasensitive HIV-RNA by PCR from the medical chart. The HIV viral load is expressed in RNA copies per milliliter. Rationale for this measure was to account for the accretion of the virus in dismantling the body, which may influence the likelihood of experiencing HIV-symptomologies and the dysregulation of IL-6, both of which have been found to distort and abrogate normal sleep.

Sleep/Wake Rhythm

The sleep/wake rhythm in this study is a circadian pattern of rest and activity of the body. Each 24-hour period of the sleep/wake rhythm was uniformly broken into two 12-hour segments, a sleep segment followed by a wake segment. Similar to Lee, Portillo, and Miramontes' study (2001), specific start and stop times for the sleep/wake segments were pre-set given that the protocol did not utilize a sleep log or sleep diary (due to a history of poor compliance) to help identify individualized sleep/wake segments. The sleep segment also referred to as "down" time,

was defined as 2100 to 0859 hours. The wake segment also referred to as “up” time, was defined as 0900 to 2059 hours. The objective experience of the sleep/wake rhythm was measured by a physiologic recording device, the MicroMini-Motionlogger® wrist actigraph. A picture of the wrist actigraph can be found in the appendices.

Wrist Actigraph. The MicroMini-Motionlogger® (Ambulatory Monitoring Inc., Ardsley, NY) is a small, waterproof, watch-like microprocessor that with minimal imposition is usually attached to the nondominant wrist to provide continuous, noninvasive monitoring of wrist motion. Per the Material Safety Data Sheet (MSDS) from Precision Control Design, Inc., this product is a non-significant risk device. However, temporary discomfort and mild irritation from skin contact are potential risks if the device is strapped too tight or does not fit properly. The actigraph sensor measures linear acceleration of wrist movement in one-minute intervals (epochs), translates the motion into a numeric representation (activity count), then aggregates and digitally stores the values at a constant interval or epoch, which can be displayed graphically. Muscle activity is usually frequent during wakeful hours and infrequent during sleep. So, the presence or absence of muscle activity is then used to estimate various objective sleep/wake behaviors. The actigraph requires a microinterface and connector to download the data into a computer, and it comes with automatic sleep-scoring software (Action 4 and Action W Software Programs, Ambulatory Monitoring Inc., Ardsley, NY) for prompt analysis. The software programs offer various algorithms useful in scoring sleep/wake behaviors. Actigraphic data has been supported with electroencephalogram and polysomnographic measures of sleep with adequate validity ($r = 0.93-0.99$), sensitivity (80%), specificity (90%), and reliability in various groups of research subjects (Ancoli-Israel, Clopton, Klauber, Fell, & Mason, 1997; Hauri & Wisbey, 1992; Jean-Louis, Kripke, Mason, Elliott, & Youngstedt, 2001; Walsh et al., 1991).

According to recommendations put forth by The American Academy of Sleep Medicine as a result of a comprehensive review of the literature, wrist actigraphy has been useful and reliable in the assessment of many sleep, daytime sleepiness, and circadian rhythm disorders (Littner et al., 2003). Data obtained from the actigraph was used to estimate specific objective sleep/wake behaviors including sleep/wake minutes, sleep/wake episodes, minutes before sleep onset, sleep percentage, sleep efficiency, sleep fragmentation index, activity mean, activity index, and acceleration index. An operational definition for each of the sleep/wake indices is provided in the appendices.

Sleep Quality

Sleep quality in this study is the subjective perception of the restorative and undisturbed nature of the person's sleep pattern. The Pittsburgh Sleep Quality Index (PSQI) was used to measure the general perception of sleep quality and the Subjective Sleep Quality Questionnaire (SSQ) was used to measure a nightly pattern of sleep quality.

Pittsburgh Sleep Quality Index (PSQI). The Pittsburgh Sleep Quality Index (PSQI) is a 19-item self-report scale used to measure general sleep quality. The PSQI measures seven components of sleep experienced within the past month, including a subjective account of sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleep medications, and daytime functioning (Buysse et al., 1989). The respondent is first asked specific questions related to their usual sleep habits, like "During the past month, what time have you usually gone to bed at night?" Then, they are asked to rate various situations on a four-point Likert-type scale. For example, "During the past month, how often have you had trouble sleeping because you cannot breathe comfortably?" In each case, a score of "0" indicates no difficulty, while a score of "3" indicates severe difficulty. The 19 items together combined to yield one

“global” sleep quality score, ranging from 0 to 21. Higher scores indicate a decline in sleep quality or poor sleepers. Although a global score of 5 or greater has been the standard cutoff, some investigators, in testing HIV subjects, felt that 7 was a more conservative and reliable cutoff point to be able to differentiate good sleepers from poor sleepers (Buysse et al., 1991; Phillips, Sowell, et al., 2005). This index is one of the most widely used sleep quality instruments in sleep research, and it has been supported by sleep log and polysomnography data. The PSQI demonstrates 89.6% sensitivity, 86.5% specificity, a reliability coefficient of 0.83 (Cronbach), and a test-retest reliability of 0.85-0.87 (Backhaus, Junghanns, Broocks, Riemann & Hohagen, 2002; Buysse et al., 1989).

Subjective Sleep Quality Questionnaire (SSQ). The Subjective Sleep Quality Questionnaire (SSQ) is a 14-item self-report measurement used to examine the daily rhythmicity of the subjective feeling of sleep quality. The SSQ asks for the respondent’s impression of the quality and effectiveness of their last night’s sleep. An example of one of the items is “I had enough sleep last night”. The responses are based on a six-point Likert scale, ranging from 1 (strongly agree) to 6 (strongly disagree). Psychometric properties of the SSQ include an internal consistency well above acceptable range ($\alpha = 0.86-0.92$), a high correlation with a visual analogue sleep quality scale ($r = 0.93$), as well as being reflective of select objective sleep data obtained from wrist actigraphy (Nunnally, 1978; Smith & Davis, 2002).

Daytime Sleepiness

Daytime sleepiness in this study is the subjective perception of how alert or sleepy a person feels during waking hours. The Epworth Sleepiness Scale (ESS) was used to measure the general perception of daytime sleepiness and the Stanford Sleepiness Scale (SSS) was used to measure a daily pattern of daytime sleepiness.

Epworth Sleepiness Scale (ESS). The Epworth Sleepiness Scale (ESS) is an eight-item self-report questionnaire used to measure general daytime sleepiness. The ESS retrospectively assesses sleep propensity, or a subjective estimate of the behavioral likelihood of falling asleep based on the current lifestyle (Johns, 1991; Pilcher, Pury, & Muth, 2003). The respondent is asked to indicate how likely they are to doze off or fall asleep while engaged in eight different activities of varying levels of stimulation. Examples of the activities include watching TV, talking to someone, and riding as a passenger in a car. Responses are based on a Likert-type scale ranging from 0 (would never doze) to 3 (high chance of dozing). The total score may range from 0 to a maximum of 24; and while 0-10 qualifies as normal range, 10-12 is borderline abnormal and 12-24 is abnormal. The ESS is often used in sleep research, including HIV sleep research. ESS scores have a reported internal consistency of 0.88 and a test-retest reliability of 0.82 (Johns, 1992). The ESS has been significantly correlated to standard methods for measuring daytime sleepiness, the Multiple Sleep Latency Test (MSLT) and polysomnography (Johns, 1991; Fong, Ho, & Wing, 2005).

Stanford Sleepiness Scale (SSS). The Stanford Sleepiness Scale (SSS) is a one-item real-time self-report questionnaire used to determine the daily rhythmicity of the subjective feeling of daytime sleepiness (Hoddes, Dement, & Zarcone, 1971). The respondent is asked to “circle the statement which best describes your state of sleepiness right now.” The statements are based on a seven-point Likert-type scale, ranging from 1 (alert) to 7 (almost asleep), and describe the level of sleepiness at the specific time the scale is administered. The instructions include a reference point of ≥ 3 , indicative of a sleep debt or the need for more sleep. Also included is a note that times of high alertness are commonly 9am and 9pm, with 3pm being a time of low alertness. Quite sensitive to discrete changes in sleepiness (Hoddes, Zarcone, Smyth, Phillips, & Dement,

1973), the SSS has been used mostly in sleep deprivation, sleep fragmentation, and circadian phase studies. Pilcher, Pury, & Muth (2003), asserted that the SSS looked more at the subjective feeling or internal state of sleepiness (verses a physiological state or behavioral propensity), especially when it intercorrelated so strongly with other measures of internal states, like the Profile of Mood States (POMS) and a Sleepiness Visual Analogue Scale.

IL-6 Rhythm

The IL-6 rhythm in this study is a circadian pattern of plasma interleukin-6 levels within the body. The IL-6 rhythm is a construct of four time-specific plasma IL-6 levels, as measured by human IL-6 immunoassay, plotted on a graph. The times for the blood collections in this study were 0500, 0800, 1900, and 2100 hours \pm 10 minutes. These times were based on the biphasic nadirs and zeniths of healthy participants reported in the literature.

Human IL-6 Immunoassay. The Quantikine HSTM Human IL-6 Immunoassay (R&D Systems, Inc., Minneapolis, MN, USA) is a highly sensitivity enzyme-linked immunosorbent assay (ELISA) specifically engineered for the measurement of human IL-6 protein levels. IL-6 levels are expressed in pg/mL, and the highly sensitive assay has a mean minimum detectable dose of 0.039 pg/mL. The specificity of the assay recognizes recombinant and natural human interleukin-6. Both the inter-assay and intra-assay precision coefficients of variation are < 10%, and the recovery, linearity, and calibration evaluations of this assay are all favorable.

Quality of Life

Quality of life in this study is the subjective measure of the sense of wellbeing that stems from the level of satisfaction with the areas in life that are important to the person (Ferrans, 1990). The Quality of Life Index (QLI) was used to measure the general perception of quality of

life, and the Quality of Life Visual Analogue Scale (VAS-Q) was used to measure a daily pattern of quality of life.

Quality of Life Index (QLI). The Quality of Life Index (QLI) is a 66-item questionnaire used to measure the general sense of wellbeing that stems from the satisfaction or dissatisfaction with various areas in life that are considered important. Five aspects of life are assessed including overall quality of life, health/functioning, psychological/spiritual, social/economical, and family (Ferrans & Powers, 1985). Each is said to be interrelated with the other, yet may exert differing levels of influence on one's life as a whole (Ferrans, 1990; Mellors, Riley, & Erlen, 1997). Respondents are first asked to describe their satisfaction level with various circumstances, such as, "Your chances for a happy future" or "The amount of worries in your life". Respondents are then asked to rate those same circumstances in level of importance to them. Responses for both satisfaction and importance are based on a six-point Likert-scale ranging from 1 (very unsatisfied/unimportant) to 6 (very satisfied/important). By using the importance ratings to weight the satisfaction responses, items of greater importance have a greater impact on the scores, reflecting the satisfaction levels of the aspects in life that the respondent values most. Scores range from 0 to 30, with higher scores representing higher satisfaction and importance. Internal consistency reliability (0.73-0.99), test-retest reliability (0.78-0.87), sensitivity, and validity are supported by numerous studies, including those with HIV samples (Dougherty, Dewhurst, Nichol, & Spertus, 1998; Ferrans & Powers, 1992; Yang et al., 2003).

Quality of Life Visual Analogue Scale (VAS-Q). The Quality of Life Visual Analogue Scale (VAS-Q) is a quick one-item self-mark scale used to measure the daily rhythmicity of the perception of quality of life. Unlike scales with discrete jumps or forced categorizations (mild, moderate, and severe), visual analogue scales (VAS) measure a subjective phenomenon on a

continuous spectrum, across a continuum of values with minimum constraints (Crichton, 2001). A visual analogue scale consists of a 10cm horizontal line, anchored on each end by words describing the boundaries of the continuum (none and most extreme). The respondent is asked to place a mark that corresponds to the level of the variable they are experiencing. For example, on the VAS-Q, the perceived level of quality of life felt by a person can range anywhere from “the worst possible quality of life” to “the best possible quality of life”. VAS data is scored by measuring the distance of the mark, in centimeters, from the edge of the line on the left anchor (0cm). The simple VAS, which is sensitive to subjective changes (Hauser & Walsh, 2008), has proven to be an adequate, reliable, and valid measure of quality of life (de Boer et al., 2004; Haywood, Garratt, Dziedzic, & Dawes, 2002; Mrus et al., 2002; Nahm, Resnick, Shaughnessy, Michael, & Kopunek, 2006; Sherman, Eisen, Burwinkle, & Varni, 2006).

Data Collection Procedures

All aspects of the study were completed in accordance with HIPPA and Wayne State University guidelines. An overview of the research activities for each study period is presented as a flowchart in the appendices. Study related activities involved three phases: phase 1 included screening and baseline procedures, phase 2 included monitoring procedures, and phase 3 included specimen collection and end of study procedures.

Phase 1

Screening. Screening occurred at the initial study visit. The study was explained in detail, an informed consent signed, and a personal identification number assigned as previously described. Eligibility to participate in the study was determined per the inclusion/exclusion criteria of this protocol. Once eligibility was confirmed, the participant completed a medical

history and physical examination including height, weight, and vital signs. The physical exam was a safety measure conducted to verify safe participation in the study.

Baseline. Baseline data collection also occurred at the initial study visit just prior to the dispensing of the monitoring phase study packet. At baseline, the participant completed all general measures for a total of four questionnaires, including the Demographic and Lifestyle Questionnaire, Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), and Quality of Life Index (QLI). Their ID medical chart was reviewed to obtain the most recent CD4⁺ cell count and HIV RNA viral load as well as the historically lowest CD4⁺ cell count and highest HIV RNA viral load. Next, the participant received the monitoring study packet, which included a wrist actigraph, the daily questionnaires, and a written copy of the instructions and investigator's contact information. Detailed instructions on the monitoring phase procedures of the study included a review of the daily questionnaires and the maintenance, care, and proper fit of the monitoring device. The investigator conducted a fit test to check the safety of the wrist actigraph, and allowed extra time for any further questions and clarifications of instructions that arose. For each participant, a new battery was inserted before the actigraph was placed on the interface unit for initialization to record motion. Based on the manufacturer's recommendations for human motion studies, the actigraph was configured to Low Proportional Integrating Measure (LoPIM) as the mode of operation for this study. Once successful initialization was confirmed, the actigraph was placed on the non-dominant arm, and the participant instructed to avoid removal of the actigraph, even when showering, without first consulting with the investigator to troubleshoot any unforeseen difficulties.

Phase 2

Monitoring. The monitoring period occurred for four consecutive days (a 96-hour period) with the participant wearing a wrist actigraph on their non-dominant arm. Within 30 minutes from waking up each day, the participant completed two daily questionnaires related to sleep quality and quality of life, the Subjective Sleep Quality Questionnaire (SSQ) and Quality of Life Visual Analogue Scale (VAS-Q). Then, at four specific times throughout each of the four days (1000, 1300, 1600, and 1900 hours), the participant completed a daily questionnaire on daytime sleepiness, the Stanford Sleepiness Scale (SSS).

Phase 3

Specimen Collections. On Day 4, or the last day of the monitoring period, the participant had four plasma IL-6 samples collected at 0500, 0800, 1900, and 2100 hours. During business hours, participants had the option of the plasma specimens being collected either at the 3750 Woodward Ave UPG ID Clinic Laboratory or a home visit (i.e. participant's place of residence). These options were discussed in detail and agreed upon at the initial visit in order to minimize the risk of feelings of invasion of privacy. Using proper phlebotomy techniques, the investigator obtained the specimens via venipuncture with an EDTA venous blood vacuum collection tube \pm 10 minutes of the target draw times. The specimens were then processed locally according to manufacturer recommendations. The specimens underwent 15 minutes of centrifugation at 1000x g within 30 minutes of collection. The plasma was removed, transferred into aliquots, and then stored in a freezer at ≤ -20 C° until they were ready for shipment to the Cytokine Core Laboratory in Baltimore, Maryland for analysis.

End of Study. The end of study occurred after the 2100 hour plasma IL-6 specimen collection to close out the study protocol. The participant returned the study materials (monitoring device and the 24 monitoring questionnaires) to the investigator, was thanked for

their participation in the study, and received \$100 compensation for their time and inconvenience.

Data Management and Analysis

Participant research files were kept and accessed in accordance with HIPPA and Wayne State University guidelines. Data gathered was entered into a computer file for analysis using SPSS Version 17.0. In order to verify accuracy of data entry, the items entered were manually checked by the investigator and then rechecked by a member of the ID research staff. Important to note, there was no missing data for this study. Statistical analysis was divided into three sections. The first section used descriptive statistics to provide a sample profile of the participants in the study. The second section used descriptive statistics to depict the immunological integrity of the participants in the study. The third section of the analysis employed a combination of descriptive statistics, graphical representation, correlation, partial correlation, and agreement analysis to address the research questions posed for the specific aims of this study.

Sample Profile

A profile of the sample population, gathered from the ID medical chart and the Demographic and Lifestyle Questionnaire, included general demographic, medical, lifestyle, and sleep environment characteristics. Data from continuous profile characteristics are presented in terms of mean, standard deviation, and range. Data from categorical profile characteristics are described as frequency and percentage distributions.

Immunological Integrity

Current CD4⁺ cell count and HIV RNA viral load were obtained from the ID medical chart. Continuous data are presented in terms of mean, standard deviation, median, and range.

Categorical data are described as frequency and percentage distributions. In accordance with the model, Pearson's correlation coefficient analysis was used to test for potentially significant relationships between the variables of immunological integrity and the sleep/wake rhythm, sleep quality, daytime sleepiness, and IL-6. Each of the relationships tested for significance are presented in the appendices. The level of significance for analyses was set at $p < 0.05$ (two-tailed).

Specific Aims

Specific aim #1 end-point was to provide a clinical picture of the HIV-related sleep disruption experienced in asymptomatic HIV-seropositive African American women, as manifested by the variables of sleep homeodynamics (sleep/wake rhythm, sleep quality, daytime sleepiness, interleukin-6 rhythm).

Sleep/Wake Rhythm. The sleep/wake rhythm was the objective experience of the circadian pattern of rest and activity of the body, as measured by the MicroMini-Motionlogger® wrist actigraph. Each participant was able to wear the actigraph for the entire length of the four-day study without difficulty. The raw actigraphic data was downloaded via the interface unit, and visually inspected before analysis to screen for artifacts and malfunctioning. Due to the potential interference of the blood draws on Day 4, the data was trimmed to include only the first three consecutive 24-hour periods (72 hours) of the protocol, just meeting the minimum recommendation put forth by the American Academy of Sleep Medicine (Littner et al., 2003). The sleep segment or down time was custom marked as 2100 to 0859 hours and the wake segment or up was marked as 0900 to 2059 hours. To address research question 1(A), actigraphic data from the down time and up time segments, as well as the total 24-hour interval (from 2100 to 2059 hours) for each day of the protocol, was analyzed and scored using the University of

California, San Diego (UCSD) sleep estimation algorithm available within Action W 2.6 scoring software by Ambulatory Monitoring Inc. (Ardley, New York). Each participant's scored data was then entered into SPSS Version 17.0 for group analysis. Sleep/Wake indices are presented in terms of mean, standard deviation, and range. The strength and direction of the significant correlations with current CD4⁺ cell count and HIV RNA viral load are presented in the results section. The level of significance for analyses was set at $p < 0.05$ (two-tailed).

Sleep Quality. The Pittsburgh Sleep Quality Index (PSQI) and the Subjective Sleep Quality Questionnaire (SSQ) were scored according to supplier instructions. Descriptive and graphical statistics were used to summarize the general and rhythmic measures of sleep quality. Circadian rhythm data were plotted graphically for visual inspection and are included in the results section. Pearson's correlation coefficient analysis was used to calculate the reliability of the Sleep Quality Questionnaire (SSQ) of the protocol. The strength and direction of the correlations for reliability, as well as the significant correlations with current CD4⁺ cell count and HIV RNA viral load are presented in the results section. The level of significance for analyses was set at $p < 0.05$ (two-tailed).

Daytime Sleepiness. The Epworth Sleepiness Scale (ESS) and the Stanford Sleepiness Scale (SSS) were scored according to supplier instructions. Descriptive and graphical statistics were used to summarize the general and rhythmic measures of daytime sleepiness. Circadian rhythm data were plotted graphically for visual inspection and are included in the results section. Pearson's correlation coefficient analysis was used to calculate the reliability of the Stanford Sleepiness Scale (SSS) of the protocol. The strength and direction of the correlations for reliability, as well as the significant correlations with current CD4⁺ cell count and HIV RNA

viral load are presented in the results section. The level of significance for analyses was set at $p < 0.05$ (two-tailed).

Interleukin-6 Rhythm. Each plasma IL-6 level was assayed in duplicate at the Cytokine Core Laboratory in Baltimore, Maryland and the result expressed as a mean of the two values. The average IL-6 level was calculated by averaging the four time-specific plasma IL-6 results. Descriptive and graphical statistics were used to summarize the general and rhythmic measures of the IL-6 rhythm. Circadian rhythm data were plotted graphically for visual inspection and are included in the results section. The strength and direction of the significant correlations with current CD4⁺ cell count and HIV RNA viral load are presented in the results section. The level of significance for analyses was set at $p < 0.05$ (two-tailed).

Specific aim #2 end-point was to provide a depiction of the sense of wellbeing in asymptomatic HIV-seropositive African American women experiencing HIV-related sleep disruption, as manifested by quality of life. The Quality of Life Index (QLI) was scored according to supplier instructions, and the Quality of Life Visual Analogue Scale (VAS-Q) was scored by measuring the distance of the “mark” from the left anchor in millimeters. Descriptive and graphical statistics were used to summarize the general and rhythmic measures of the quality of life. Circadian rhythm data were plotted graphically for visual inspection and are included in the results section. Pearson’s correlation coefficient analysis was used to calculate the reliability of the Quality of Life Visual Analogue Scale (VAS-Q) of the protocol. The strength and direction of the correlations for reliability are presented in the results section. The level of significance for analyses was set at $p < 0.05$ (two-tailed).

Specific aim #3 end-point was to explore potential links between specified rhythmic variables of sleep homeodynamics and wellbeing in asymptomatic HIV-seropositive African

American women experiencing HIV-related sleep disruption. Partial correlation analysis was used to calculate the degree of association between actigraphic sleep efficiency and Quality of Life Visual Analogue Scale (VAS-Q), Subjective Sleep Quality Questionnaire (SSQ) and Quality of Life Visual Analogue Scale (VAS-Q), Stanford Sleepiness Scale (SSS) and Quality of Life Visual Analogue Scale (VAS-Q), and average IL-6 level and Quality of Life Visual Analogue Scale (VAS-Q), while accounting or adjusting for the effects of immunological integrity. The strength and direction of the partial correlation are presented in the results section. The level of significance was set at 0.05 (two-tailed).

Specific aim #4 end-point was to explore if the Quality of Life Visual Analogue Scale (VAS-Q) provided an adequate representation of the sense of wellbeing in asymptomatic HIV-seropositive African American women experiencing HIV-related sleep disruption as the Quality of Life Index (QLI). Bland-Altman agreement analysis was used to estimate the agreement or repeatability between the Quality of Life Index (QLI) and the Quality of Life Visual Analogue Scale (VAS-Q). Agreement results are presented in the results section.

CHAPTER 5

RESULTS

The purpose of this descriptive study was to examine the dynamics of HIV-related sleep disruption and wellbeing as experienced in asymptomatic HIV-seropositive AA women. The results of this inquiry are presented in this chapter.

Sample Profile

A database search, as described in Chapter 4, was performed to help identify potential participants fitting the criteria of an asymptomatic AA female, between the ages of 18 and 40, with a recent CD4⁺ cell count over 300. The query generated an initial list of 100 names, of which many were further excluded after additional inquiry into BMI (35%), ethnicity (5%), current pregnancy status (2%), and gender at birth (1%). After obtaining provider approval to approach the remaining potential participants, many were found to be unreachable due to outdated contact information (24%), while some were simply not interested (5%). The final 28 potential participants were enrolled in the study on a first come first serve basis for a final sample total of 20 (n = 20). Each participant who signed an informed consent form completed the four-day protocol, and thus data for a total of 20 AA women of childbearing age were gathered for this exploratory study.

General Demographic Profile

Table 5.1 presents the general demographic characteristics of the sample. The mean age of the sample was 32.20 (SD = 5.03) years. Actual ages ranged from 20 to 39 years old, with two (10%) subjects between the ages of 18-25 years old, eight (40%) were between 26-33 years old, and 10 (50%) were between 34-40 years old. In terms of marital status, 14 (70%) of the subjects were single, never married, while three (15%) were married, one (5%) was separated, and two

(10%) were divorced. Nineteen, or 95% of the subjects, reported a Christian religious affiliation. In terms of educational level, while five (25%) reported completing less than high school, 13, or 65% of the sample, attended some college, one (5%) earned a 2-year college degree, and one (5%) had a graduate level degree. Employment status was classified into four categories: unemployed, student, part-time employment, and full-time employment. Seven (35%) of the participants were unemployed, four (20%) were students, five (25%) were employed part-time, and four (20%) were employed full-time. To further describe those classified as unemployed, three (15%) had been without a job for more than one year while the other four (20%) were on disability and unable to work. About 15 (75%) of the participants reported a yearly income of less than \$10,000. Lastly, the reported household size for the sample ranged from 1 to 7 members with a mean of 3.60 (SD = 1.39) persons per household.

Table 5.1. General Demographic Profile (N=20)

Characteristics	Mean	SD	SE	N	%
Age (years)	32.20	5.03	1.12	--	--
Age 18-25 Yrs	--	--	--	2	10
Age 26-33 Yrs	--	--	--	8	40
Age 34-40 Yrs	--	--	--	10	50
Marital Status					
Single	--	--	--	14	70
Married	--	--	--	3	15
Separated	--	--	--	1	5
Divorced	--	--	--	2	10
Religious Affiliation					
Christian	--	--	--	19	95
Other/None	--	--	--	1	5
Educational Level					
Less than High School	--	--	--	5	25
Some College	--	--	--	13	65
2Yr College Degree	--	--	--	1	5
Graduate Level Degree	--	--	--	1	5
Employment Status					
Unemployed	--	--	--	7	35
Student	--	--	--	4	20
Part-Time	--	--	--	5	25
Full-Time	--	--	--	4	20
Unemployed					
More than 1Yr	--	--	--	3	15
Unable to Work	--	--	--	4	20
Income Range					
Less than \$10,000	--	--	--	15	75
\$10-19,000	--	--	--	2	10
\$20-39,000	--	--	--	2	10
\$40-59,000	--	--	--	1	5
Household Size	3.60	1.39	0.31	--	--

Medical Profile

Table 5.2 presents the medical variables for the sample. Participants had a mean body mass index (BMI) of 25.93 (SD = 3.22, Mdn = 26.40) with an inclusive range of 19.60 to 29.80. The mean pain level on a scale of 0 to 10 was 1.83 (SD = 1.90, Mdn = 1.00); inclusive range 0 to 5. In terms of the menstrual cycle phase of the participants while in the study, nine (45%) were in the follicular phase, five (25%) were in the luteal phase, four (20%) experienced a mix of both follicular and luteal phases during the four-day protocol, and two (10%) were unable to be determined due to a hysterectomy and complications from an IUD placement. Four (20%) participants reported having medication allergies to various pain medications, antibiotics, and other OTC and prescription drugs.

Table 5.2. Medical Profile (N=20)

Characteristics	Mean	SD	SE	Median	Minimum	Maximum	N	%
BMI	25.93	3.22	0.72	26.40	19.60	29.80	--	--
Pain Level	1.83	1.90	0.42	1.00	0.00	5.00	--	--
Menstrual Cycle Phase								
Follicular Phase	--	--	--	--	--	--	9	45
Luteal Phase	--	--	--	--	--	--	5	25
Both Follicular/Luteal	--	--	--	--	--	--	4	20
Unable to Determine	--	--	--	--	--	--	2	10
Medication Allergies	--	--	--	--	--	--	4	20

In reference to HIV disease, data collection included length of time since diagnosis, mode of transmission, history of the lowest CD4⁺ cell count, history of the highest HIV RNA viral load, total length of time on antiretroviral therapy (ART), current ART use, current ART regimen, and CNS penetration effectiveness (CPE) of the current ART regimen. Table 5.3

presents the HIV medical variables for the sample. The length of time since HIV diagnosis ranged from 8 to 309 months with a group mean of 92.12 (SD = 82.77) months. To express time since diagnosis in terms of years, 5% (n = 1) had been living with HIV less than 1 year, while 35% (n = 7) reported 1 to 5 years, 40% (n = 8) 5 to 10 years, and 20% (n = 4) more than 10 years. Eighteen, or 90% of participants contracted HIV from heterosexual contact; the remaining two (10%) experienced a mother-to-infant transmission at birth (MTIT). In terms of immune status history, 3 (15%) participants had a CD4 lower than 250 cells/mm³ at some point in the history of their disease progression. The group's lowest CD4 mean was 356.40 (SD = 155.35) cells/mm³. With regard to viral status, 16 (80%) participants had a HIV viral load higher than 1000 copies/mL at some point in the progression of their disease with a mean of 43,678.85 (SD = 70,278.39) copies/mL for the group's highest viral load.

Table 5.3. HIV Profile (N=20)

Characteristics	Mean	SD	SE	Median	Minimum	Maximum	N	%
Time since HIV Diagnosis (months)	92.12	82.77	18.51	64.40	8.00	309.00	--	--
HIV Diagnosis Range								
Less than 1 Yr	--	--	--	--	--	--	1	5
1 – 5 Yrs	--	--	--	--	--	--	7	35
5 – 10 Yrs	--	--	--	--	--	--	8	40
More than 10 Yrs	--	--	--	--	--	--	4	20
Transmission Mode								
Birth (MTIT)	--	--	--	--	--	--	2	10
Heterosexual Contact	--	--	--	--	--	--	18	90
Lowest CD4 (cells/mm ³)								
Lowest CD4 under 250	--	--	--	--	--	--	3	15
Highest VL (copies/mL)								
Highest VL over 1000	43678.85	70278.39	15714.73	11270.00	80	299000	--	--
Highest VL over 1000	--	--	--	--	--	--	16	80

In terms of treatment, ART characteristics for the sample are presented in Table 5.4. The mean time on ART was 67.25 months (SD = 92.07) with an inclusive range of 0 to 312 months. Expressed in years, 20% (n = 4) were ART-naïve, 35% (n = 7) had taken HIV medications less than 1 year, 15% (n = 3) 1 to 5 years, 20% (n = 4) 5 to 10 years, and 10% (n = 2) more than 10 years. Of the ART-experienced participants, 12 (60%) were on a current ART regimen at the time of study. The most common regimens were Norvir-boosted Reyataz with Truvada (ATV/R + TRU, n = 4, 20%), followed by Norvir-boosted Reyataz with Epzicom (ATV/R + EPZ, n = 2, 10%) and Norvir-boosted Prezista with Truvada (DRV/R + TRU, n = 2, 10%). Other regimens included Kaletra with Epzicom (LPV + EPZ, n = 1, 5%), Viramune with Epzicom (NVP + EPZ, n = 1, 5%), Raltegravir plus Reyataz with Truvada (RAL + ATV + TRU, n = 1, 5%), and Atripla (n = 1, 5%). In order of increasing effectiveness, the cumulative CNS penetration effectiveness scores (CPE) of the current ART regimens were six (n = 4, 20%), seven (n = 5, 25%), eight (n = 1, 5%), and nine (n = 2, 10%). Those who were not currently on an ART regimen were given a CPE score of zero (n = 8, 40%).

Table 5.4. ART Profile (N=20)

Characteristics	Mean	SD	SE	Minimum	Maximum	N	%
Time on ART (months)	67.25	92.07	20.59	0.00	312.00	--	--
ART Range (years)							
ART Naïve	--	--	--	--	--	4	20
Less than 1 Yr	--	--	--	--	--	7	35
1 – 5 Yrs	--	--	--	--	--	3	15
5 – 10 Yrs	--	--	--	--	--	4	20
More than 10 Yrs	--	--	--	--	--	2	10
Current ART Use	--	--	--	--	--	12	60
Current ART Regimen							
ART Naïve (CPE0)	--	--	--	--	--	4	20
ART Hx Only (CPE0)	--	--	--	--	--	4	20
ATV/R + TRU (CPE6)	--	--	--	--	--	4	20
ATV/R + EPZ (CPE7)	--	--	--	--	--	2	10
DRV/R + TRU (CPE7)	--	--	--	--	--	2	10
LPV + EPZ (CPE8)	--	--	--	--	--	1	5
NVP + EPZ (CPE9)	--	--	--	--	--	1	5
RAL + ATV + TRU (CPE9)	--	--	--	--	--	1	5
ATRIPLA (CPE7)	--	--	--	--	--	1	5
CNS Penetration Effectiveness (CPE)							
0	--	--	--	--	--	8	40
6	--	--	--	--	--	4	20
7	--	--	--	--	--	5	25
8	--	--	--	--	--	1	5
9	--	--	--	--	--	2	10

Lifestyle Profile

Lifestyle tendencies of the participants are presented in Table 5.5. Nine (45%) participants had used tobacco in the last four weeks prior to study participation. Those who smoked, smoked anywhere from 2 to 20 cigarettes per day (M = 7.89, SD = 5.75), for 3 to 22

years ($M = 13.89$, $SD = 6.39$). Seven (35%) of the 20 participants were frequently exposed to second-hand smoke in the household, five (25%) of who did not smoke themselves. In terms of alcohol use, 13 (65%) participants had consumed alcohol in the last four weeks. Two (10%) participants reported daily alcohol use, ranging from one to five drinks per day ($M = 3.00$, $SD = 2.83$), while five (25%) reported weekly use ranging from two to three drinks per week ($M = 2.20$, $SD = 0.45$), and the remaining six (30%) participants, reported 2 to 12 drinks per month ($M = 3.83$, $SD = 4.02$). In terms of caffeine intake, 90% ($n = 18$) of respondents had consumed one to six multi-serving size cups per day of various caffeinated beverages, such as coffee, tea, or soda in the last four weeks ($M = 3.17$, $SD = 1.86$). In reference to illicit substances, six (30%) participants disclosed marijuana use within the last four weeks. Fourteen (70%) of the participants reported eating their last meal of the day by mid-evening (6-8pm), five (25%) reported eating by late-evening (9-11pm), and one (5%) ate after midnight. Sixty percent ($n = 12$) of participants reported consuming their last liquids for the day right at bedtime. Finally, three (15%) of the participants reported regular exercise in the last four weeks. One (5%) of the three exercised at least once a week, while the other two (10%) reported exercising several times a week.

Table 5.5. Lifestyle Profile (N=20)

Characteristics	N	%	Mean	SD	SE
Tobacco Use	9	45	--	--	--
Cigarettes/Day	--	--	7.89	5.75	1.29
Years Smoked (years)	--	--	13.89	6.39	1.43
Second-Hand Smoke	7	35	--	--	--
Alcohol Use	13	65	--	--	--
Drinks/Day	--	--	3.00	2.83	0.63
Drinks/Week	--	--	2.20	0.45	0.10
Drinks/Month	--	--	3.83	4.02	0.90
Caffeine Intake	18	90	--	--	--
Large Cups/Day	--	--	3.17	1.86	0.42
Marijuana Use	6	30	--	--	--
Last Meal					
Mid Evening	14	70	--	--	--
Late Evening	5	25	--	--	--
Midnight or Later	1	5	--	--	--
Bedtime Liquids	12	60	--	--	--
Exercise	3	15	--	--	--
Once a Week	1	5	--	--	--
Several Times a Week	2	10	--	--	--

Sleep Environment Profile

The sleep environment conditions of the sample are presented in Table 5.6. As observed, 18 (90%) of the participants expressed that they actually enjoyed sleeping. None of the participants reported the use of sleeping aids or sleep medications in the last 4 weeks. Common idiosyncrasies noted to disrupt sleep were snoring (15%), teeth grinding (15%), sleep-talking (15%), bad dreams (15%), and sinus trouble during the night (25%). One hundred percent (n = 20) of the participants conveyed the need to sleep in a dark room. And while 16 (80%) of

participants stated that they preferred to sleep in a quiet environment, 65% (n = 13) admitted that they normally slept with the television on, and 15% (n = 3) slept with music. One (5%) participant expressed the need to read before going to sleep. As far as mattress comfort level, 14 (70%) of the respondents thought that their mattress was just right, whereas 4 (20%) found their mattress too hard and 2 (10%) reported their mattress too soft. Fifty-five percent (n = 11) of participants slept alone, while 30% (n = 6) reported an adult bed partner, and 15% (n = 3) had a child sleeping in the same bed and/or bedroom with them on a regular basis. Four (20%) participants described their bedroom as a multipurpose room used for more than just sleeping.

Table 5.6. Sleep Environment Profile (N=20)

Characteristics	N	%
Likes to Sleep	18	90
Sleep Aids/Medication Use	0	0
Snores	3	15
Teeth Grinding	3	15
Sleep-Talking	3	15
Bad Dreams	3	15
Sinus Trouble: Nighttime	5	25
Bedroom Lighting: Dark	20	100
Bedroom Noise: Quiet	16	80
Sleeps with TV	13	65
Sleeps with Music	3	15
Reads to Sleep	1	5
Mattress Comfort level		
Just Right (Comfortable)	14	70
Too Hard (Uncomfortable)	4	20
Too Soft (Uncomfortable)	2	10
Sleeps Alone	11	55
Bed/Bedroom Partner		
Adult Bed/Bedroom Partner	6	30
Child Bed/Bedroom Partner	3	15
Multipurpose Bedroom	4	20

Immunological Integrity

Immunological integrity was represented in this study by current CD4⁺ cell count and HIV RNA viral load, which were abstracted from the participant's ID medical chart. Results were obtained from blood collections within 12.36 months prior to enrollment into the study (M = 3.28 months, SD = 2.84) and are presented in Table 5.7. Current CD4⁺ cell counts ranged anywhere from 252 to 1080 cells/mm³ with 45% (n = 9) over 500 cells/mm³. The group mean

was 605.80 (SD = 264.58, Mdn = 483.00) cells/mm³ while the median was 483 cells/mm³. Current viral loads ranged from 40 to 75,900 copies/mL with 65% (n = 13) under 1000 copies/mL and 45% (n = 9) undetectable or less than 48 viral copies/mL. The group mean was 6,660.35 (SD = 18441.40, Mdn = 118.00) copies/mL while the median was 118 copies/mL.

Table 5.7. Immunological Integrity Profile (N=20)

Characteristics	Mean	SD	SE	Median	Minimum	Maximum	N	%
Time Since Labs (months)	3.28	2.84	0.64	2.55	0.33	12.36	--	--
Current CD4 (cells/mm ³)	605.80	264.58	59.16	483.00	252	1080	--	--
Current CD4 over 500	--	--	--	--	--	--	9	45
Current VL (copies/mL)	6660.35	18441.40	4123.62	118.00	40	75900	--	--
Current VL under 1000	--	--	--	--	--	--	13	65
Current VL under 48	--	--	--	--	--	--	9	45

Specific Study Aims

Data were gathered over a period of four days for each subject in an effort to answer the research questions of the specific aims posed in the present study. However, due to the potential interference imposed by the time-specified blood draws on Day 4 of the protocol, the following analyses only include the first three days of data collection.

Specific Aim 1

Specific aim one was to describe the sleep homeodynamics of HIV-related sleep disruption in asymptomatic HIV-seropositive African American women, as evidenced by sleep/wake rhythm, sleep quality, daytime sleepiness, and interleukin-6 rhythm.

Research Question 1(A): What are the characteristics of the sleep/wake rhythm?

Sleep Segment. Descriptive statistics of the sleep segment (down time) are presented in Table 5.8 and the 3-day rhythm graphs of specific variables in the sleep segment are presented in

Figure 5.1, 5.2, 5.3, and 5.4. The sleep segment spanned a total period of 720 minutes (12 hours), from 2100 hours to 0900 hours each of the three days included in the analysis. The mean total minutes scored as sleep, during down time, was 384.10 (SD = 99.62) minutes or 6.4 hours (SD = 1.67). Participants slept anywhere from 2.45 hours to 9.70 hours across the 3 nights, with 45% of the sample averaging less than 6 hours of sleep per night, 35% averaging 6 to 8 hours, and 25% over 8 hours. The mean number of minutes from 2100 hours to the start of the first continuous block of at least 20 minutes of scored sleep (down minutes before sleep onset) was 219.03 (SD = 114.80) minutes or 3.7 hours. And although most participants fell asleep sometime after midnight each night, four (6.7%) of the nights a participant initiated sleep onset prior to 2100 hours. Participants experienced an average of 18.25 (SD = 6.55) down wake episodes (awakenings) per night, and the mean total minutes, scored as wake, during down time, was 336.88 (SD = 99.63) minutes or 5.6 hours. Accordingly, the calculated mean down sleep percentage was 53.28 (SD = 13.28) percent, the mean down sleep efficiency was 81.27 (SD = 8.90) percent, and the mean down sleep fragmentation index was 5.08 (SD = 1.94). Current CD4⁺ cell count and HIV RNA viral load did not correlate significantly with any of the down segment indices in this protocol.

Wake Segment. Descriptive statistics of the wake segment (up time) are presented in Table 5.8 and the 3-day rhythm graphs of specific variables in the wake segment are presented in Figure 5.5, 5.6, 5.7, and 5.8. The wake segment spanned a total period of 720 minutes (12 hours), from 0900 hours to 2100 hours following each of the three sleep segments included in the analysis. Inspection of the raw actigraphic data revealed that three participants remained awake and active all three of the days in this study. In fact, 15 out of the 60 nights (25%) analyzed, participant's nocturnal sleep period ran past the 0900 hours marker into the wake segment.

Nonetheless, the mean total minutes scored as wake, during up time, for the sample was 645.55 (SD = 55.54) minutes or 10.76 hours (SD = 0.93). The percentage of time awake during this period ranged from 77.69% to 99.77%, with an average of $89.66\% \pm 7.71\%$. The mean activity score for the wake segment was 11402.77 (SD = 4350.05), while the mean total minutes scored as sleep, during this time was 75.32 (SD = 55.41) minutes or 1.25 hours. On average, the participants experienced 9.20 (SD = 6.50) up sleep episodes (naps) per day, and such naps lasting longer than 30 minutes were observed in 11 (55%) of the 20 women. Accordingly, the calculated mean up sleep percentage was 10.45% (SD = 7.69), mean up activity index was 99.17 (SD = 1.04), and mean up acceleration index was 0.07 (SD = 0.09). Current CD4⁺ cell count was significantly correlated with up wake minutes ($r = 0.61, p = 0.005$), up sleep minutes ($r = -0.61, p = 0.005$), and up sleep percentage ($r = -0.61, p = 0.005$); however, HIV RNA viral load did not correlate significantly with any of the up segment indices in this protocol.

Twenty-four Hour Rhythm. The 24-hour rhythm measures of total sleep/wake minutes are also presented in Table 5.8.

Table 5.8. Descriptive Statistics for Sleep/Wake Rhythm (N = 20)

Variables	Mean	SD	SE	Minimum	Maximum	N	%
Sleep prior to Down Time (Nights)	--	--	--	--	--	4/60	6.7
Down Sleep Minutes	384.10	99.62	22.28	192.67	536.67	--	--
Slept < 6 Hours per night	--	--	--	--	--	9	45
Slept 6-8 Hours per night	--	--	--	--	--	7	35
Slept > 8 Hours per night	--	--	--	--	--	4	20
Down Minutes before Sleep Onset	219.03	114.80	25.67	35.00	439.67	--	--
Down Wake Episodes (Awakenings)	18.25	6.55	1.46	10.00	30.33	--	--
Down Wake Minutes	336.88	99.63	22.28	184.33	528.33	--	--
Down Sleep Percentage	53.28	13.82	3.09	26.72	74.43	--	--
Down Sleep Efficiency	81.27	8.90	1.99	59.69	96.40	--	--
Down Sleep Fragmentation Index	5.08	1.94	0.43	2.12	8.64	--	--
Sleep thru Up Time (Nights)	--	--	--	--	--	15/60	25
Up Wake Minutes	645.55	55.54	12.42	559.33	718.33	--	--
Up Activity Mean	11402.77	4350.05	972.70	5913.16	21031.22	--	--
Up Sleep Episodes (Naps)	9.20	6.50	1.45	1.00	25.00	--	--
Up Sleep Minutes	75.32	55.41	12.39	2.67	161.67	--	--
Naps > 30 minutes	--	--	--	--	--	11	55
Up Sleep Percentage	10.45	7.69	1.72	0.37	22.42	--	--
Up Activity Index	99.17	1.04	0.23	97.09	100.00	--	--
Up Acceleration Index	0.07	0.09	0.02	-0.11	0.28	--	--
24-Hour Total Sleep Time	459.02	97.85	21.88	303.67	643.33	--	--
24-Hour Total Wake Time	980.98	97.85	21.88	796.67	1136.33	--	--

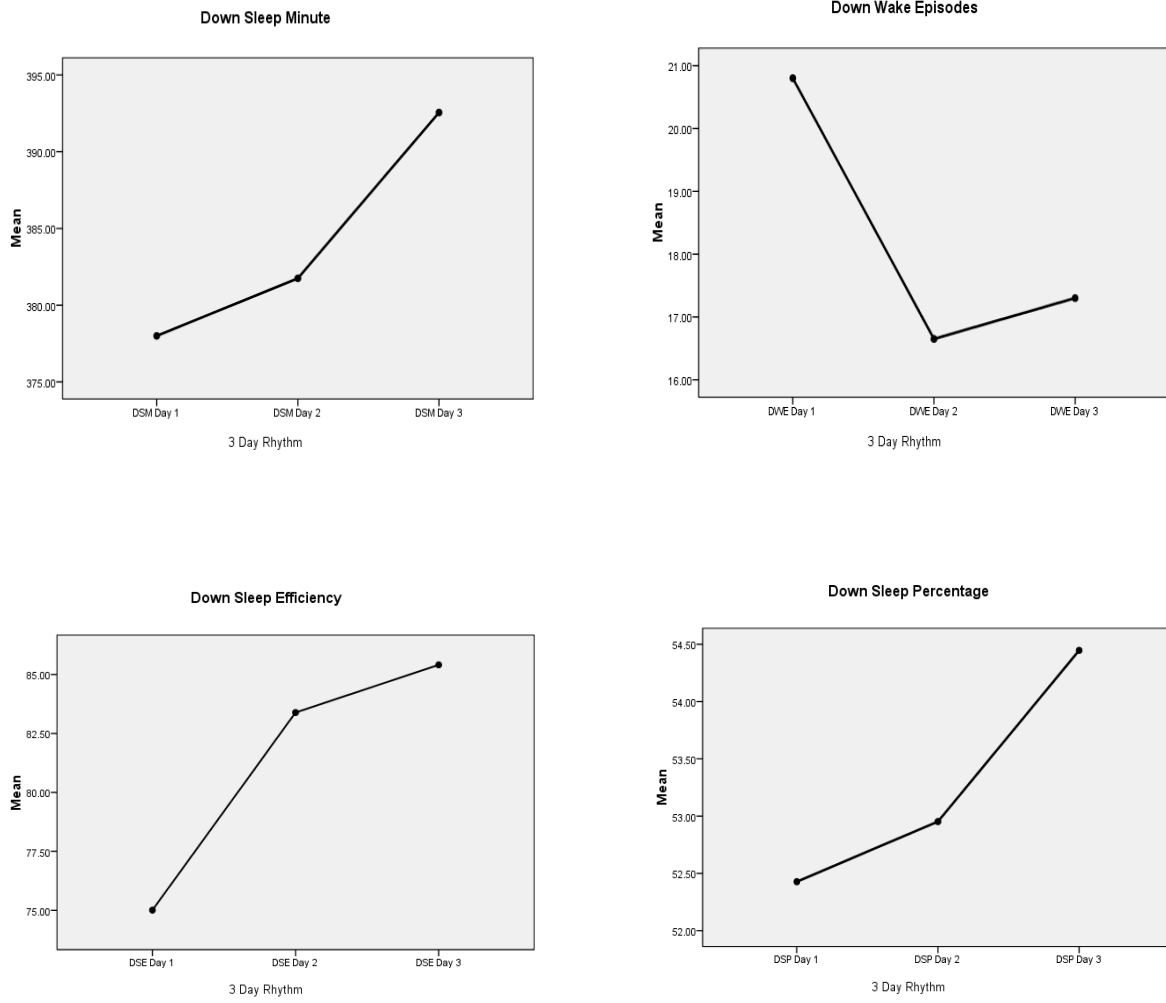


Figure 5.1-4. 3-Day Rhythm of the Sleep Segment as measured by Down Sleep Minutes, Down Wake Episodes, Down Sleep Efficiency, and Down Sleep Percentage

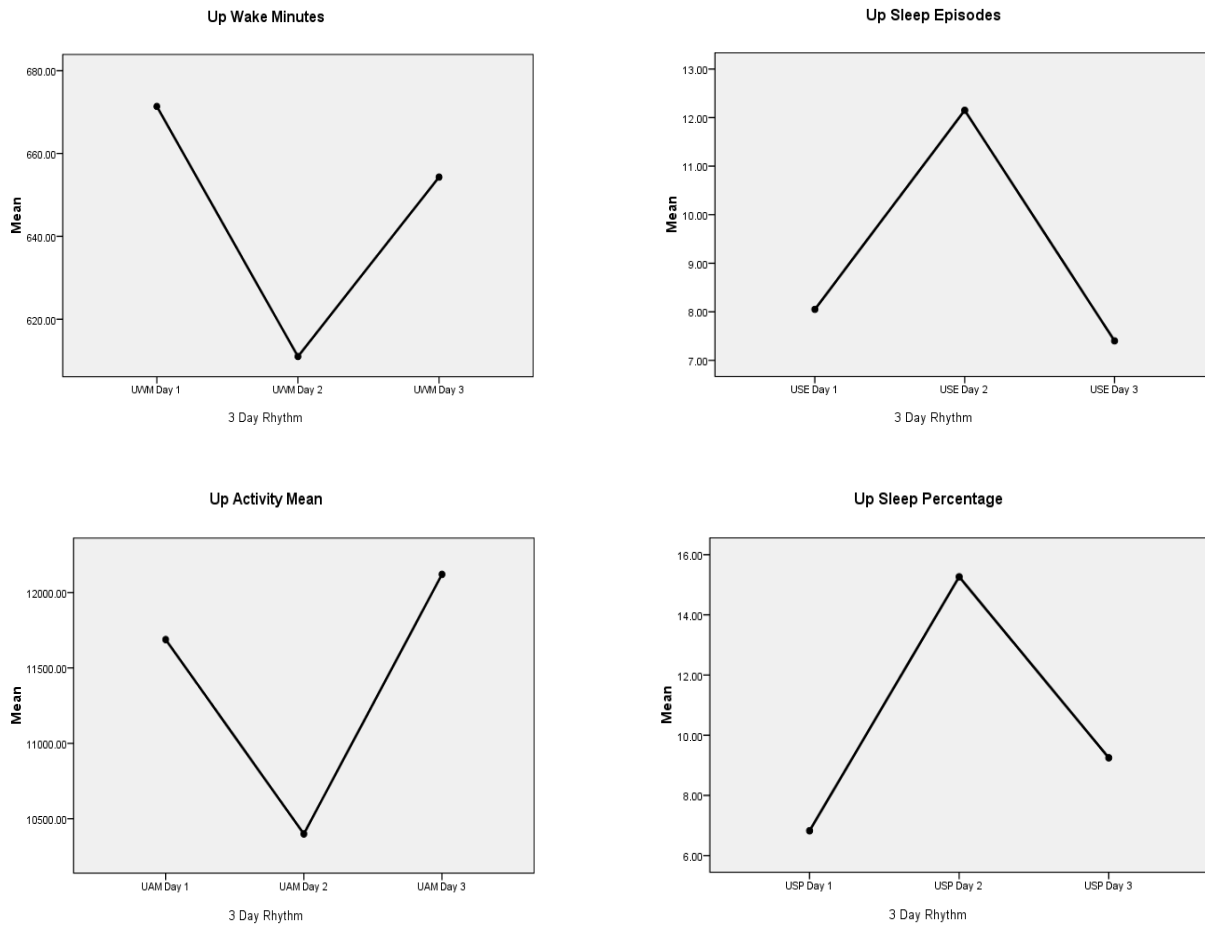


Figure 5.5-8. 3-Day Rhythm of the Wake Segment as measured by Up Wake Minutes, Up Sleep Episodes, Up Activity Mean, and Up Sleep Percentage

Research Question 1(B): What is the perception of sleep quality?

Table 5.9 and Figures 5.9 and 5.10 present the sample's overall perception of sleep quality, as measured by the well-known Pittsburgh Sleep Quality Index (PSQI), and the daily rhythm of perceived sleep quality, as measured by the Subjective Sleep Quality Questionnaire (SSQ).

Pittsburgh Sleep Quality Index (PSQI). The PSQI was completed at baseline to obtain a global sleep quality score in order to distinguish the good sleepers from the poor sleepers. Using a conservative cutoff score of seven modified for HIV samples (Phillips, Sowell, et al., 2005),

100% (n = 20) were either at or above the cutoff. The study yielded PSQI scores that ranged from 7 to 15, and the sample mean was 9.80 (SD = 2.44; Cronbach's alpha 0.547). Current CD4⁺ cell count and HIV RNA viral load did not correlate significantly with the Pittsburgh Sleep Quality Index in this protocol.

Subjective Sleep Quality Questionnaire (SSQ). The SSQ is a 14-item Likert-based scale that was completed within 30 minutes of awakening in order to give a subjective account of the previous night's quality of sleep. With higher scores reflective of a good night's rest, the sample showed a progressive decline throughout the protocol. The Day 1 mean was 3.87 (SD = 1.19; Cronbach's alpha 0.911), the Day 2 mean was 3.82 (SD = 1.25; Cronbach's alpha 0.929), and the Day 3 mean was 3.76 (SD = 0.94; Cronbach's alpha 0.835). Overall 3-day scores ranged from 2.02 to 5.36, and while the group mean was 3.82 (SD = 0.97), four (20%) participants scored below the tools mean of 3. The reliability correlations presented in Table 5.10 were significant between Day 1 and Day 2 SSQ measures ($r = 0.567$, $p = 0.009$) and Day 2 and Day 3 measures ($r = 0.823$, $p = 0.000$), but not Day 1 and Day 3 measures ($r = 0.427$, $p = 0.061$). Current CD4⁺ cell count and HIV RNA viral load did not correlate significantly with the Subjective Sleep Quality Questionnaire in this protocol.

Table 5.9. Descriptive Statistics for Sleep Quality Variables (N = 20)

Variables	Mean	SD	SE	Minimum	Maximum	N	%
PSQI	9.80	2.44	0.55	7	15	--	--
PSQI ≥ 7	--	--	--	--	--	20	100
SSQ Day 1	3.87	1.19	0.27	1.57	5.71	--	--
SSQ Day 2	3.82	1.25	0.28	2.00	5.86	--	--
SSQ Day 3	3.76	0.94	0.21	1.71	5.43	--	--
SSQ for 3 Days	3.82	0.97	0.22	2.02	5.36	--	--
SSQ < 3	--	--	--	--	--	4	20

Table 5.10. Reliability of Subjective Sleep Quality Questionnaire

		SSQ Day 1	SSQ Day2	SSQ Day3
SSQ Day1	Pearson Correlation	1	0.567**	0.427
	Sig. (2-tailed)		0.009	0.061
	N	20	20	20
SSQ Day2	Pearson Correlation	0.567**	1	0.823**
	Sig. (2-tailed)	0.009		0.000
	N	20	20	20
SSQ Day3	Pearson Correlation	0.427	0.823**	1
	Sig. (2-tailed)	0.061	0.000	
	N	20	20	20

*. Correlation is significant at the 0.05 level (2-tailed).

** . Correlation is significant at the 0.01 level (2-tailed).

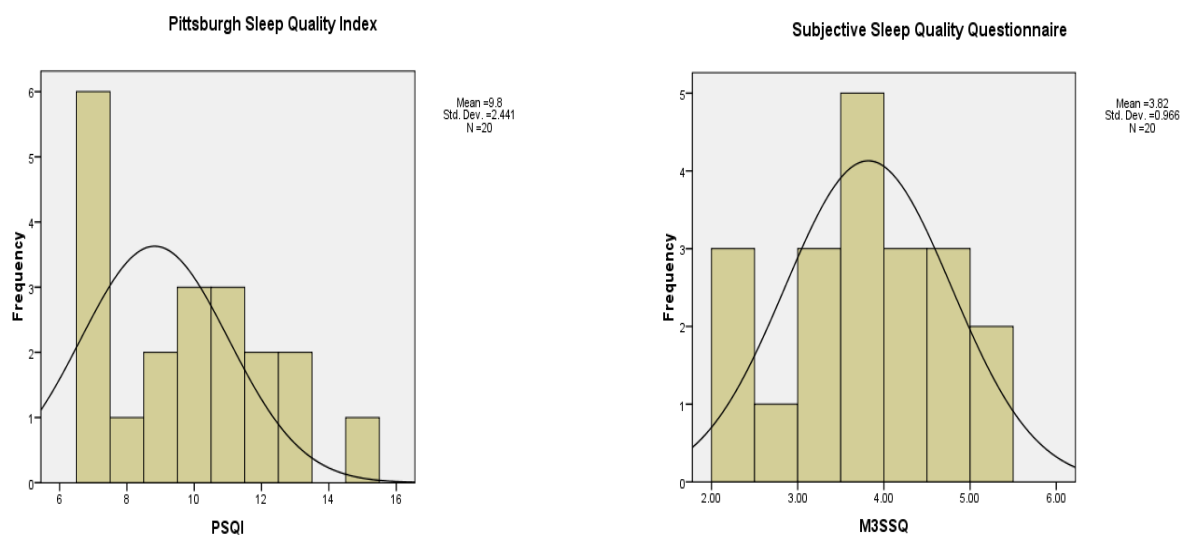


Figure 5.9. Histograms of Sleep Quality Variables as measured by PSQI and Mean SSQ

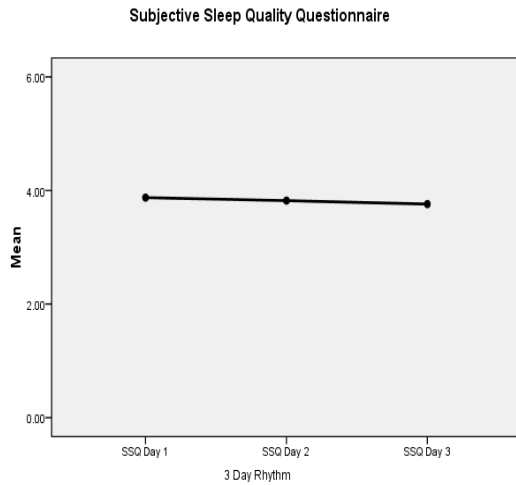


Figure 5.10. 3-Day Rhythm of Sleep Quality as measured by SSQ

Research Question 1(C): What is the perception of daytime sleepiness?

Table 5.11 and Figures 5.11 and 5.12 present the overall perception of daytime sleepiness, as measured by the Epworth Sleepiness Scale (ESS), and a daily rhythm of perceived daytime sleepiness, as measured by the Stanford Sleepiness Scale (SSS).

Epworth Sleepiness Scale (ESS). The ESS was completed at baseline to obtain a general sense of daytime sleepiness through estimates of how likely the subject could fall asleep in various settings (Johns, 1991; Pilcher, Pury, & Muth, 2003). ESS scores ranged from 1 to 17 with a sample mean of 8.90 (SD = 4.38; Cronbach's alpha 0.755). As observed in Figure 10, eight (40%) participants scored in the abnormal range with a 10 or above. Current CD4⁺ cell count and HIV RNA viral load did not correlate significantly with the Epworth Sleepiness Scale in this protocol.

Stanford Sleepiness Scale (SSS). Data from the SSS were gathered four times throughout each of the three days to determine the rhythmicity of the daytime sleepiness experienced throughout the protocol (Hoddes et al., 1971). Figure 11 depicts a daily rhythm by time and then

by day. Observed by time, the 1000-hour group mean was 2.50 (SD = 1.57), the 1300-hour mean was 1.97 (SD = 1.01), the 1600-hour mean was 2.75 (SD = 1.28), and the 2100h-hour mean was 3.30 (SD = 1.80). When observed by day, the group SSS score for Day 1 yielded a mean of 2.68 (SD = 1.12), Day 2 was 2.76 (SD = 1.29), and Day 3 was 2.45 (SD = 1.02). The 3-day cumulative scores ranged from 1.42 to 4.67, and although the group mean was 2.63 (SD = 0.94), five (25%) participants score above the tools cut-off indicating the need for more sleep. The reliability correlations presented in Table 5.12 were significant between Day 1 and Day 2 SSS measures ($r = 0.544$, $p = 0.013$) and Day 2 and Day 3 measures ($r = 0.580$, $p = 0.007$), but not Day 1 and Day 3 measures ($r = 0.403$, $p = 0.078$). Current CD4⁺ cell count and HIV RNA viral load did not correlate significantly with the Stanford Sleepiness Scale in this protocol.

Table 5.11. Descriptive Statistics for Daytime Sleepiness Variables (N = 20)

Variables	Mean	SD	SE	Minimum	Maximum	N	%
ESS	8.90	4.38	0.98	1.00	17.00	--	--
ESS > 10	--	--	--	--	--	8	40
SSS 1000	2.50	1.57	0.35	1.00	6.67	--	--
SSS 1300	1.97	1.01	0.23	1.00	4.67	--	--
SSS 1600	2.75	1.28	0.29	1.00	6.00	--	--
SSS 1900	3.30	1.80	0.40	1.00	6.33	--	--
SSS Day 1	2.68	1.12	0.25	1.00	4.50	--	--
SSS Day2	2.76	1.29	0.29	1.00	5.00	--	--
SSS Day 3	2.45	1.02	0.23	1.25	4.50	--	--
SSS for 3 Days	2.63	0.94	0.21	1.42	4.67	--	--
SSS > 3	--	--	--	--	--	5	25

Table 5.12. Reliability of Stanford Sleepiness Scale

		SSS Day 1	SSS Day2	SSS Day3
SSS Day1	Pearson Correlation	1	0.544 [*]	0.403
	Sig. (2-tailed)		0.013	0.078
	N	20	20	20
SSS Day2	Pearson Correlation	0.544 [*]	1	0.580 ^{**}
	Sig. (2-tailed)	0.013		0.007
	N	20	20	20
SSS Day3	Pearson Correlation	0.403	0.580 ^{**}	1
	Sig. (2-tailed)	0.078	0.007	
	N	20	20	20

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

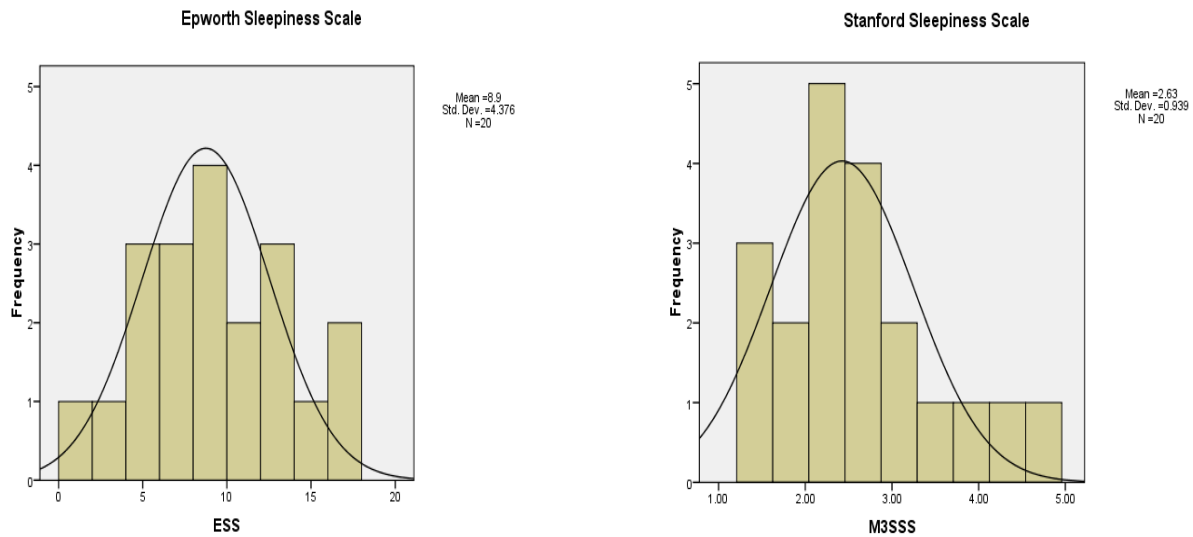


Figure 5.11. Histogram of Daytime Sleepiness Variables

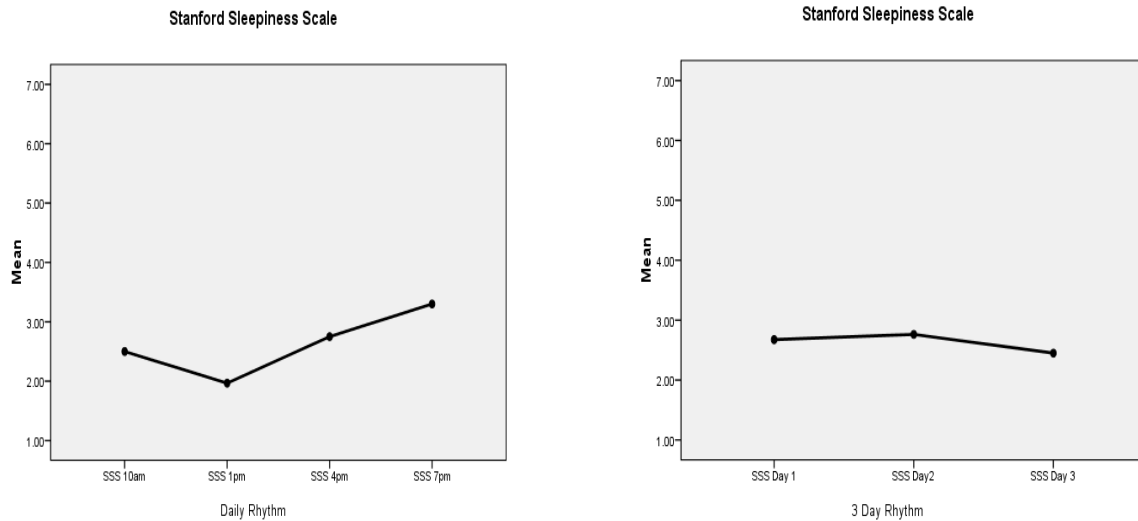


Figure 5.12. Daily Rhythm and 3-Day Rhythm of Daytime Sleepiness as measured by SSS.

Research Question 1(D): What are the characteristics of the interleukin-6 rhythm?

The IL-6 rhythm was comprised of four time-specific plasma IL-6 levels over a 24-hour period based on the published peak (0500 and 1900 hours) and trough (0800 and 2100 hours) times. Data for the four IL-6 levels and the resulting circadian pattern are presented in Table 5.13 and Figure 5.13. The sample's 0500-hour results ranged from 0.50 to 8.46 pg/mL, and the mean was 2.46 (SD = 1.93). The 0800-hour results ranged from 0.27 to 9.23 pg/mL, the mean was 2.15 (SD = 1.91). The 1900-hour results ranged from 0.37 to 8.79 pg/mL, the mean was 1.67 (SD = 1.81). The 2100-hour results ranged from 0.34 to 8.89 pg/mL, the mean was 1.85 (SD = 1.85). After plotting the four IL-6 levels for each participant, four (20%) were found to follow a similar biphasic circadian pattern noted in the literature with the 0500 and 1900 hour levels higher than the 0800 and 2100 hour levels. Meanwhile, four (20%) participants followed an exact opposite biphasic pattern with 0500 and 1900 hour levels lower than the 0800 and 2100-hour levels. Three of the 20 (15%) started off with a high 0500-hour level with each subsequent value lower than

the previous level. The remaining nine (45%) participants had a mixture of other various patterns of peaks and troughs.

Finally, an average of the four plasma IL-6 levels was calculated for each of the participants; the results are also presented in Table 13 and Figure 12. Average IL-6 levels ranged from 0.45 to 8.84 pg/mL, and the mean for the group was 2.03 (SD = 1.81). Current CD4⁺ cell count and HIV RNA viral load did not correlate significantly with average IL-6 level in this protocol.

Table 5.13. Descriptive Statistics for IL-6 Rhythm (N = 20)

Variables	Mean	SD	SE	Minimum	Maximum
Plasma IL-6 0500	2.46	1.93	0.43	0.50	8.46
Plasma IL-6 0800	2.15	1.91	0.43	0.27	9.23
Plasma IL-6 1900	1.67	1.81	0.40	0.37	8.79
Plasma IL-6 2100	1.85	1.85	0.41	0.34	8.89
Average IL6 Level	2.03	1.81	0.40	0.45	8.84

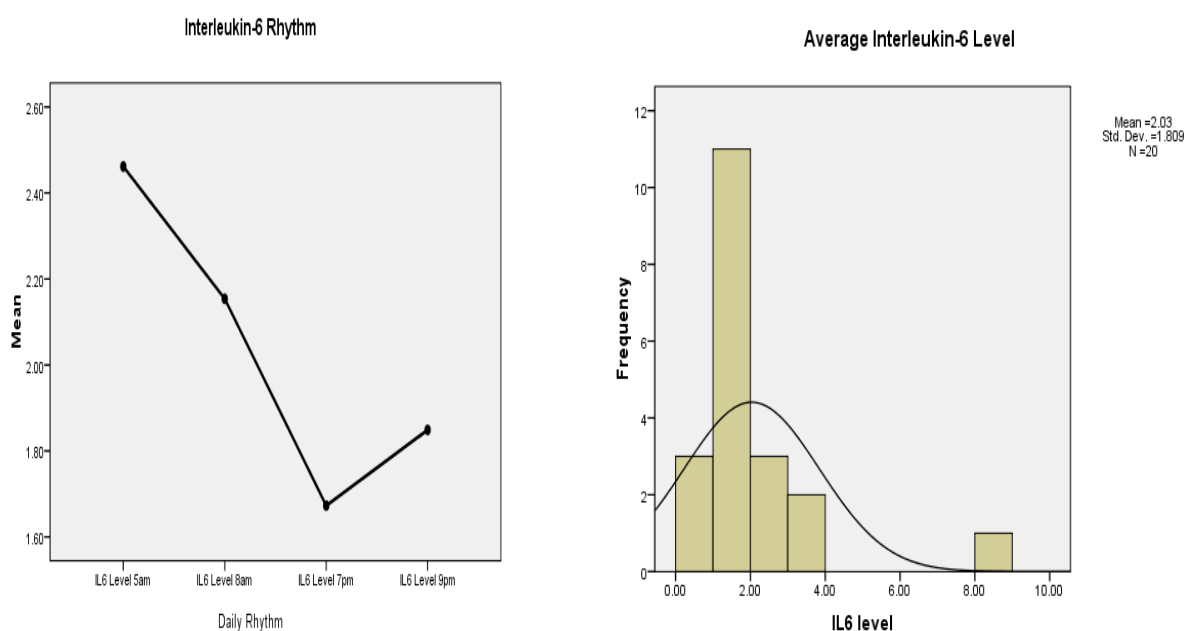


Figure 5.13. Circadian IL-6 Rhythm and Frequency Histogram of the Average IL-6 Level.

Specific Aim 2

Specific aim two was to describe wellbeing in asymptomatic HIV-seropositive African American women experiencing HIV-related sleep disruption, as evidenced by quality of life.

Research Question 2: What is the perception of quality of life?

To address research question 2, the Quality of Life Index (QLI) was used to gain an overall general perception of quality of life, while the Quality of Life Visual Analogue Scale (VAS-Q) was used to obtain a daily rhythm of quality of life. Results are presented in Table 5.14 and Figures 5.14 and 5.15.

Quality of Life Index (QLI). The QLI is a 66-item scale, which was administered at baseline to measure the sense of wellbeing stemming from the satisfaction or dissatisfaction with various areas in life that are considered important. Out of a possible 30 points, scores ranged from 7.16 to 28.31, and the sample's mean was 21.28 (SD = 5.14; Cronbach's alpha 0.890). Twelve (60%) participants scored above 20 on the index, expressing satisfaction with their quality of life, while only two (10%) scored below 15.

Quality of Life Visual Analogue Scale (VAS-Q). The VAS-Q, on the other hand, is a 1-item scale administered within 30 minutes of awakening each morning to measure the rhythmicity of the daily perception of quality of life on a scale from 0 (worst possible quality of life) to 10 (best possible quality of life). As observed in Figure 14, the mean score on Day 1 was 6.36 (SD = 2.12) with a range from 2.25 to 9.80, the Day 2 mean score was 6.28 (SD = 2.33), range 0.20 to 10, and the Day 3 mean score was 6.31 (SD = 2.17), range 2.35 to 10. Collectively, the 3-day mean VAS-Q score was 6.32 (SD = 1.89), range 2.82 to 9.18, with 25% (n=5) of the participants scoring below the tool's mean of 5. The reliability correlations presented in Table 5.15 were significant between Day 2 and Day 3 VAS-Q measures ($r = 0.774$, $p = 0.000$) and Day

1 and Day 3 measures ($r = 0.654$, $p = 0.002$), but not Day 1 and Day 2 measures ($r = 0.373$, $p = 0.105$).

Table 5.14. Descriptive Statistics for Quality for Life Variables (N = 20)

Variables	Mean	SD	SE	Minimum	Maximum	N	%
QLI	21.28	5.14	1.15	7.16	28.31	--	--
QLI < 15	--	--	--	--	--	2	10
VAS-Q Day 1	6.36	2.12	0.47	2.25	9.80	--	--
VAS-Q Day 2	6.28	2.33	0.52	0.20	10.00	--	--
VAS-Q Day 3	6.31	2.17	0.49	2.35	10.00	--	--
VAS-Q for 3 Days	6.32	1.89	0.42	2.82	9.18	--	--
VAS-Q < 5	--	--	--	--	--	5	25

Table 5.15. Reliability of Quality of Life Visual Analogue Scale

		VAS-Q Day 1	VAS-Q Day2	VAS-Q Day3
VAS-Q Day1	Pearson Correlation	1	0.373	0.654**
	Sig. (2-tailed)		0.105	0.002
	N	20	20	20
VAS-Q Day2	Pearson Correlation	0.373	1	0.774**
	Sig. (2-tailed)	0.105		0.000
	N	20	20	20
VAS-Q Day3	Pearson Correlation	0.645**	0.774**	1
	Sig. (2-tailed)	0.002	0.000	
	N	20	20	20

*. Correlation is significant at the 0.05 level (2-tailed).

** . Correlation is significant at the 0.01 level (2-tailed).

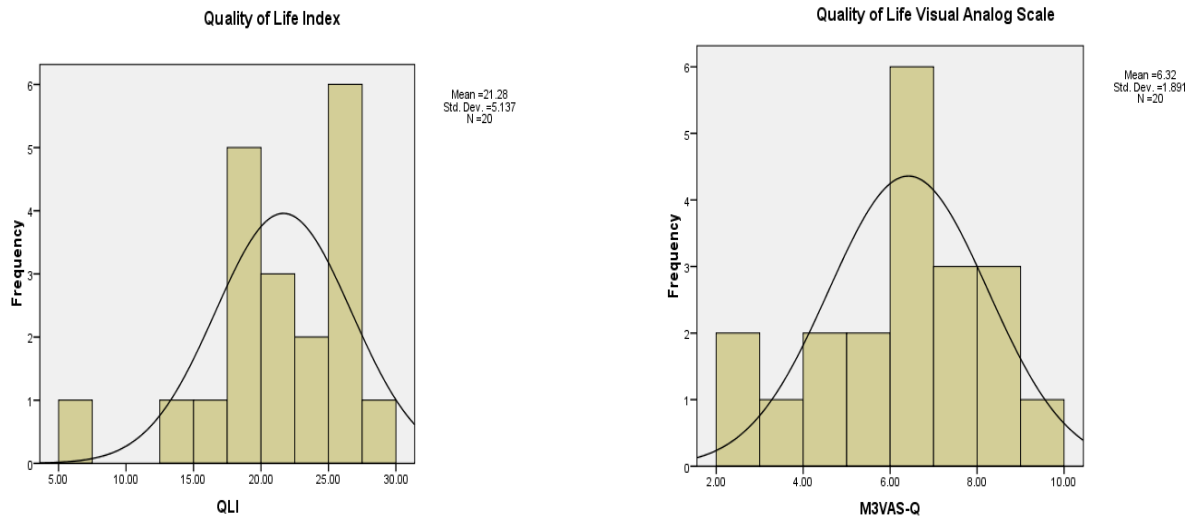


Figure 5.14. Histogram of Quality of Life Variables

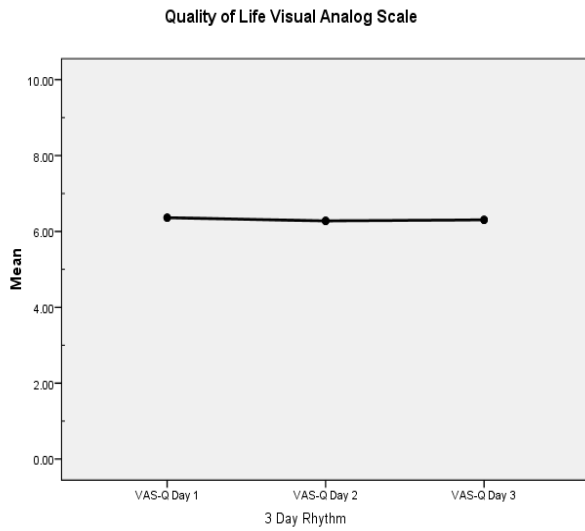


Figure 5.15. 3-Day Rhythm of Quality of Life as measured by VAS-Q

Specific Aim 3

Specific aim three was to determine the relationship between selected variables of sleep homeodynamics and wellbeing in asymptomatic HIV-seropositive African American women experiencing HIV-related sleep disruption.

In order to address specific aim 3, partial correlation analysis was used to assess the degree of association between down sleep efficiency of the sleep/wake rhythm, subjective sleep quality, subjective daytime sleepiness, and the average IL-6 level of the IL-6 rhythm and wellbeing, while accounting for or adjusting for the effects of the immunological integrity study variables, current CD4⁺ cell count and current HIV RNA viral load. The results of the partial correlation analysis are presented with a level of significance set at 0.05 (two-tailed) in Table 5.16. Summary graphs of the study variable rhythms monitored across days and the rhythms monitored across 24 hours are presented in the appendix, respectively.

Research Question 3(A): What is the strength and direction of the correlation between the sleep/wake rhythm and wellbeing, as measured by mean actigraphic down sleep efficiency and the Quality of Life Visual Analogue Scale?

The correlation between mean actigraphic down sleep efficiency and mean Quality of Life Visual Analogue Scale was $r = -0.050$, $p = 0.842$. This is a weak negative relationship with no statistical significance between objective sleep efficiency of the sleep/wake rhythm and wellbeing when adjusting for the effects of immunological integrity.

Research Question 3(B): What is the strength and direction of the correlation between sleep quality and wellbeing, as measured by the Subjective Sleep Quality Questionnaire and the Quality of Life Visual Analogue Scale?

The correlation between mean Subjective Sleep Quality Questionnaire and mean Quality of Life Visual Analogue Scale was $r = 0.415$, $p = 0.087$. This is a weak positive relationship with no statistical significance between subjective sleep quality and wellbeing when adjusting for the effects of immunological integrity.

Research Question 3(C): What is the strength and direction of the correlation between daytime sleepiness and wellbeing, as measured by the Stanford Sleepiness Scale and the Quality of Life Visual Analogue Scale?

The correlation between mean Stanford Sleepiness Scale and mean Quality of Life Visual Analogue Scale was $r = 0.023$, $p = 0.927$. This is a weak positive relationship with no statistical significance between subjective daytime sleepiness and wellbeing when adjusting for the effects of immunological integrity.

Research Question 3(D): What is the strength and direction of the correlation between the interleukin-6 rhythm and wellbeing, as measured by the average interleukin-6 level and the Quality of Life Visual Analogue Scale?

The correlation between average IL-6 and mean Quality of Life Visual Analogue Scale was $r = -0.296$, $p = 0.233$. This is a weak negative relationship with no statistical significance between IL-6 and wellbeing when adjusting for the effects of immunological integrity.

Table 5.16. Partial Correlation Analysis

Variable Scores		Quality of Life Visual Analogue Scale (VAS-Q)
Down Sleep Efficiency (DSE)	Correlation	- 0.50
	Significance (2-tailed)	0.842
	Df	16
Subjective Sleep Quality Questionnaire Score (SSQ)	Correlation	0.415
	Significance (2-tailed)	0.087
	Df	16
Stanford Sleepiness Scale Score (SSS)	Correlation	0.023
	Significance (2-tailed)	0.927
	Df	16
Average Interleukin-6 Level (IL-6)	Correlation	- 0.296
	Significance (2-tailed)	0.233
	Df	16

Control Variables: CD4 (cells/mm³) and VL (copies/mL)

Specific Aim 4

Specific aim four was to determine the agreement or repeatability between the quality of life measurements in asymptomatic HIV-seropositive African American women experiencing HIV-related sleep disruption.

Research Question 4: What is the agreement between the Quality of Life Index and the Quality of Life Visual Analogue Scale?

In order to address specific aim 4, Bland-Altman agreement analysis was used to determine the agreement between the Quality of Life Index (QLI) and each of the days of Quality of Life Visual Analogue Scale (VAS-Q).

Agreement Analysis: Quality of Life Index and Quality of Life Visual Analogue Scale Day 1

A 95% confidence interval calculated a lower limit of agreement -2.358 to -1.002 and an upper limit of agreement 1.002 to 2.358 in QLI and QOL Day 1 scores. Thus, the 95% confidence interval for either the lower and upper limit of agreement was as wide as 1.36 standard deviations under a standard normal curve. This width is less than 2 standard deviations, and thus, the intervals were small enough to imply good agreement between the two methods. Descriptive statistics of the differences in QLI and QOL Day 1 scores is presented in Table 5.17 and a scatter plot in Figure 5.16.

Table 5.17. Agreement Analysis: QLI vs. QOL Day1

Descriptive Statistics				
	N	Mean	Std. Deviation	
	Statistic	Statistic	Std. Error	Statistic
DIFFQLIQOL1	20	14.9180	0.91503	4.09216
ZDIFFQLIQOL1	20	0.0000	0.18740	0.83808
Valid N (listwise)	20			

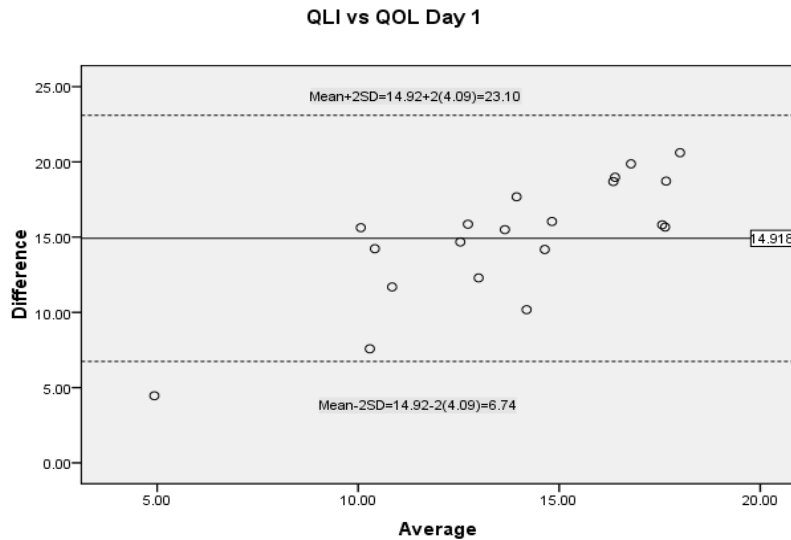


Figure 5.16. Agreement Scatter plot QLI vs. VAS-Q Day 1

Agreement Analysis: Quality of Life Index and Quality of Life Visual Analogue Scale Day 2

A 95% confidence interval calculated a lower limit of agreement -3.300 to -1.400 and an upper limit of agreement 1.400 to 3.300 in QLI and QOL Day 2 scores. Thus, the 95% confidence interval for either the lower and upper limit of agreement was as wide as 1.90 standard deviations under a standard normal curve. This width is less than 2 standard deviations, and thus, the intervals were small enough to imply good agreement between the two methods. Descriptive statistics of the differences in QLI and QOL Day 2 scores is presented in Table 5.18 and a scatter plot in Figure 5.17.

Table 5.18. Agreement Analysis: QLI vs. QOL Day2

Descriptive Statistics				
	N	Mean	Std. Deviation	
	Statistic	Statistic	Std. Error	Statistic
DIFFQLIQOL2	20	15.0030	1.10385	4.93659
ZDIFFQLIQOL2	20	0.0000	0.26242	1.17356
Valid N (listwise)	20			

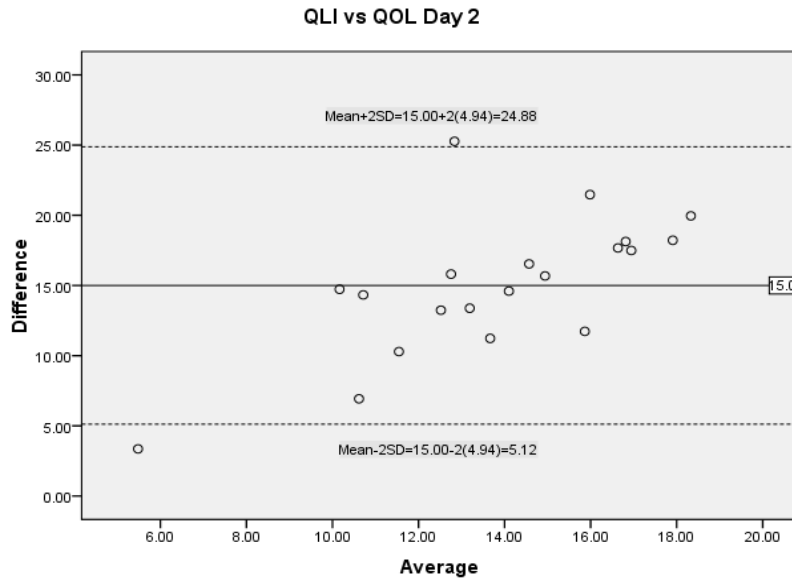


Figure 5.17. Agreement Scatter plot QLI vs. VAS-Q Day 2

Agreement Analysis: Quality of Life Index and Quality of Life Visual Analogue Scale Day 3

A 95% confidence interval calculated a lower limit of agreement -2.514 to -1.066 and an upper limit of agreement 1.066 to 2.514 in QLI and QOL Day 3 scores. Thus, the 95% confidence interval for either the lower and upper limit of agreement was as wide as 1.45 standard deviations under a standard normal curve. This width is less than 2 standard deviations, and thus, the intervals were small enough to imply good agreement between the two methods. Descriptive statistics of the differences in QLI and QOL Day 3 scores is presented in Table 5.19 and a scatter plot in Figure 5.18.

Table 5.19 Agreement Analysis: QLI vs. QOL Day3

Descriptive Statistics				
	N	Mean	Std. Deviation	
	Statistic	Statistic	Std. Error	Statistic
DIFFQLIQOL3	20	14.9755	0.94119	4.20912
ZDIFFQLIQOL3	20	0.0000	0.19987	0.89383
Valid N (listwise)	20			

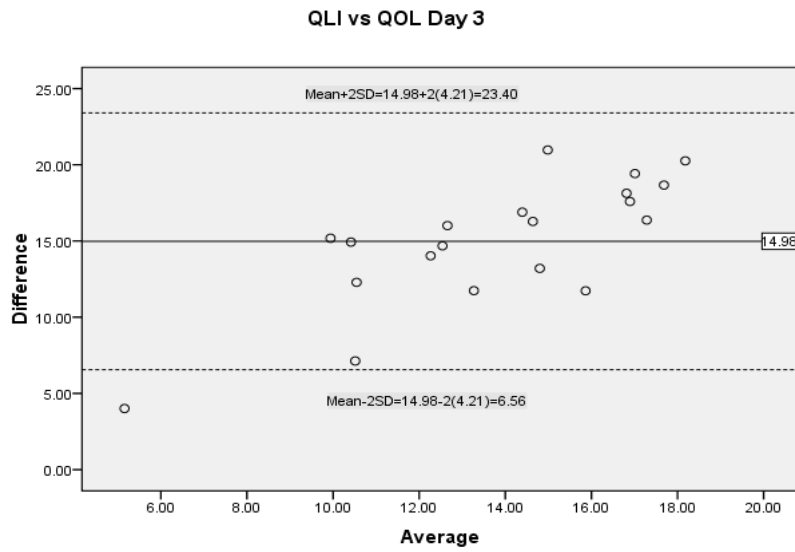


Figure 5.18. Agreement Scatter plot QLI vs. VAS-Q Day 3

CHAPTER 6

DISCUSSION

A preliminary investigation of HIV-related sleep disruption and quality of life among asymptomatic HIV-seropositive African American women of childbearing age was understudied. The specific aims of this study were to describe the homeodynamics of sleep and wellbeing in one of the fastest growing HIV populations today, as well as identify any significant relationships that may exist between them. This chapter presents a discussion of the research findings of this clinically significant sample. Study limitations, conclusions, and implication for practice, theory, and future research are also addressed.

Sample Profile

Twenty asymptomatic HIV-seropositive African American women receiving care from an infectious diseases clinic in the Detroit Metropolitan Area were recruited to participate in this study. The majority of participants in this purposeful sample were single, between the ages of 34 and 39 years, with a Christian religious affiliation, and an average household size of three to four people. Most had an income of less than \$10,000 per year and little exposure to higher education. These findings are consistent with regional HIV demographic results, as poverty in single female-headed households is a major contributor of the HIV/AIDS disparities seen among African American women (CDC, 2010).

The sample measured slightly overweight with both the mean and median BMI over 25, which is the standard cut-off put forth by the WHO (http://apps.who.int/bmi/index.jsp?introPage=intro_3.html). Pain levels were minimal with the sample mean and median greater than one and two deviations lower than the tool's mean, respectively. Almost half (45%) of the sample was in

the follicular phase of their menstrual cycle during the 4-day protocol, and medication allergies to one or more OTC and/or prescription medications were reported in 20% of the participants.

Regarding their disease-specific medical history, the majority of the women reported contracting HIV through heterosexual transmission more than five years ago. Characteristic of asymptomatic disease, past immunologic stability was verified with only a few participants having had a CD4⁺ cell count lower than 250 cells/mm³ in the history of their disease progression. Most participants had had a prior viral load greater than 1000 copies/mL; and while some had never been on HIV medications before, the majority of the women had less than a one-year history of ART experience. Over half (60%) of the sample was on a current ART regimen, with Norvir-boosted Reyataz plus Truvada being the most common regimen.

Less than half of the women disclosed current marijuana (30%) and tobacco (45%) use within the last four weeks prior to study participation. The average tobacco user smoked up to eight cigarettes a day for almost 14 years; while a little more than a third (35%) of the women were exposed to second-hand smoke in their households. More than half reported consuming high caffeine (90%) and alcoholic (65%) beverages regularly within the last four weeks. The average caffeine intake, consistent with the high caffeine consumption reported in previous HIV-studies (Dreher, 2003), was just over three large (multi-serving size) cups per day. Most participants reported eating their last meal of the day between 6pm and 8pm, and their last liquids for the day right at bedtime. Very few reported any exercise on a regular basis.

The majority of the sample conveyed that they truly liked to sleep; they also expressed a preference of sleeping in a dark, quiet environment. Over half reported sleeping alone (55%), on a comfortable mattress (70%), with the television on (65%), and in a room dedicated solely as a bedroom (80%). And while some reported sleep-related problems such as snoring, teeth

grinding, sleep-talking, bad dreams, and sinus trouble at night; each participant denied the use of any sleeping aids or sleep medications.

Immunological Integrity

Controlled by design, the women demonstrated current signs of stable immune system functioning with a relatively low risk for related symptomologies and opportunistic infections. This was evidenced by almost half (45%) of the sample having a current CD4⁺ cell count above 500 cells/mm³ (within normal range) and no vulnerable cell counts below 250 cells/mm³. The sample also presented with a relatively low viral burden to enforce the acerbic effects of HIV on the immune system. This was evidenced by a median current viral load of 118 copies/mL. The sample mean was not used due to two outliers that were well over 10,000 copies/mL, nevertheless, almost half of the sample had an undetectable current viral load under 48 copies/mL. In this study, CD4⁺ cell count had a significant association with the wake segment, which will be discussed further in the wake segment section below.

Specific Aim 1

The end-point for specific aim 1 was to provide a clinical picture of the HIV-related sleep disruption experienced in asymptomatic HIV-seropositive African American women, as manifested by the variables of sleep homeodynamics (sleep/wake rhythm, sleep quality, daytime sleepiness, and IL-6 rhythm). They are as follows:

Sleep/Wake Rhythm

Sleep Segment. Analysis of 72 continuous hours of actigraphic data showed that, as a group, participants slept an average of 6.4 ± 1.7 hours during the night, with 45% averaging less than 6 hours a night. The women usually did not fall asleep until sometime after midnight, and the number of nighttime arousals recorded by the actigraph averaged 18.25 ± 6.55 times per

night. The group's sleep fragmentation index was calculated at 5.08 ± 1.94 ; whilst the average sleep efficiency (81.27%) was less than the ideal 85%.

The current study corroborated prior findings from Lee, Portillo, and Miramontes' (2001) sample of 100 HIV-positive women, 59% of which were African American. They reported an average of 6.5 hours of sleep per night, 75% sleep efficiency, and an average number of awakenings of 18.7 times upon actigraphic investigation. Thirty of these original women (60% African American) reconfirmed the results in a subsequent intervention study, with a pre-intervention total sleep time of 6.4 hours, 72.7% sleep efficiency, and an average of 20.6 number of awakenings a night (Hudson et al., 2008).

Wake Segment. During the 12-hour daytime segments, participants were awake and active an average of 10.8 ± 0.9 hours, however, they were likely to doze off or nap approximately 9 times throughout the day for a mean total of 1.3 ± 0.9 hours. As a result, the daytime sleep percentage was $10.8\% \pm 7.5\%$ and the mean activity score was 11402.77. The activity index and acceleration index were calculated at 99.17% and 0.07%, respectively. The length of daytime wakefulness was positively associated with current CD4⁺ count in that those with a weak immune system were found to be awake less during the day.

Hudson, Portillo, and Lee (2008) noted similar pre-intervention daytime sleep percentage findings ($10.0 \pm 11.5\%$) in the sample of the 30 women mentioned above. They described those over 4% as being "nappers". Perhaps the most significant finding of this current study is that immune status was linked to the subject's objective daytime experience (wake segment variables). Which is in contrast to Lee and researchers (2001, 2012), who found CD4⁺ cell counts related to objective nocturnal variables. They reported CD4⁺ counts inversely associated with the

number of nighttime awakenings (2001), and significantly lower CD4⁺ counts in short sleepers who slept < 6 hours per night (2012).

Sleep Quality

Given the fact that 100% of the current sample scored between 7 and 15 on the PSQI (M = 9.80, SD = 2.44), the general subjective experience of sleep quality in this sample was very poor. Using a conservative cutoff point of 7 to identify poor sleepers, this study strongly supports the indication that asymptomatic HIV-seropositive African American women often suffer from substantial sleep disruption. Although daily mean SSQ scores somewhat declined throughout the course of the study, this sample demonstrated a relatively stable rhythm of subjective sleep quality slightly above the tool's mean.

Prevalence rates of poor sleep quality up to 100% have been corroborated by several studies (Hand et al., 2003; Phillips et al., 2006; Robbins et al., 2004); and although more recent PSQI scores have been a bit lower than the present group, results are consistent with that found in HIV-sleep studies (Lee et al., 2001; Nokes & Kendrew, 2001; Salahuddin et al., 2009).

Daytime Sleepiness

The study yielded a general daytime sleepiness score of 8.90 (SD = 4.38) on the ESS, which is indicative of normal to mild sleepiness for the tool. However, 8 (40%) women in this pilot study scored a 10 or above on the scale, indicating a pathological propensity to fall asleep at inappropriate times during the day. Observed by time, mean SSS scores yielded a rhythm with its lowest level of drowsiness noted at 1pm followed by a progressive increase in drowsiness throughout the day. Making the sample's optimal level of alertness in the afternoon, right before most individuals are getting ready to experience their drowsiest time of the day (3pm). The 7pm score was the only score to reach above the tool's cutoff point of 3, indicating that the group was

more likely to demonstrate symptoms of sleep debt in the evening. Interestingly, discrepancies were noted between actigraphy data and SSS scores, and will be further discussed in the studies limitation section. Observed by day, mean SSS scores had a narrow range and were all less than the cutoff, indicating that the overall daily average of drowsiness was stable and within normal limits over each of the three days analyzed in this protocol.

The fact that the women experienced and perceived such disrupted sleep patterns during the night, yet did not perceive an excessively abnormal amount of daytime sleepiness is a particularly interesting finding. It might easily be explained by looking at the sample's 24-hour total sleep time, which calculates to about 7.66 hours of sleep per 24-hour day. This data suggests that the participants were able to make up, in the daytime, whatever sleep they lacked during the night, getting a little more than seven and a half hours of sleep total per day.

IL-6 Rhythm

Human IL-6 Immunoassay. Although four time-specific plasma IL-6 levels cannot provide an accurate depiction of a comprehensive IL-6 circadian rhythm, the goal was to get a sense of whether the sample's rhythm matched the peaks and troughs described as "normal" in the literature. Observed by time, mean plasma IL-6 levels demonstrated a slight progressive decline until the last time point, which showed a minor increase. These findings were atypical, yet expected due to HIV-related dysregulation described in the literature. Further examination revealed that only 4 (20%) of the 20 participants had a diurnal-like plotting as described by Alesci (2005) and Vgontzas (1999, 2005). Perhaps the most unexpected finding in this study, however, was that the average IL-6 level for the group was 2.03 pg/mL.

Current IL-6 levels were quite a bit lower than that found in Honda's study (1990) of 18 asymptomatic HIV-seropositive individuals (M = 55.5 pg/mL). Then again, more recent studies

have noted levels similar to that of the current sample (Bastard et al., 2012; Fumaz et al., 2012). It is also possible that the racial/ethnic variations found by Míguez and researchers (2012) may explain the low levels in this current African American sample.

Specific Aim 2

The end-point for specific aim 2 was to provide a depiction of the sense of wellbeing in asymptomatic HIV-seropositive African American women experiencing HIV-related sleep disruption, as manifested by quality of life.

Quality of Life

Consistent with other asymptomatic samples like Mellors and associates (1997), the general perception of quality of life in this preliminary work was well above the tool's mean for satisfaction and importance (sample mean = 21.28, SD = 5.14). In fact, only 2 (10%) participants scored below the tool's mean of 15, while 12 (60%) participants scored higher than one standard deviation above the tool's mean. Comparatively, the group mean was also higher than Yang's (2003) sample mean of 18.50 (SD = 4.30). The sample also demonstrated a consistent and stable daily rhythm of subjective quality of life above the tool's mean.

Specific Aim 3

The end-point for specific aim 3 was to explore potential links between specific variables of sleep homeodynamics and wellbeing while accounting for the effects of immunological integrity in asymptomatic HIV-seropositive African American women experiencing HIV-related sleep disruption. Due to lack of significance, no partial correlation was found between actigraphic down sleep efficiency (DSE) and the Quality of Life Visual Analogue Scale (VAS-Q). Thus, objective sleep was not associated with the daily perception of quality of life in this sample. Due to lack of significance, no partial correlation was found between the Subjective

Sleep Quality Questionnaire (SSQ) and the Quality of Life Visual Analogue Scale (VAS-Q). Thus, daily subjective sleep quality was not associated with the daily perception of quality of life in this sample. Due to lack of significance, no partial correlation was found between the Stanford Sleepiness Scale (SSS) and the Quality of Life Visual Analogue Scale (VAS-Q). Thus, daily subjective daytime sleepiness was not associated with the daily perception of quality of life in this sample. Due to lack of significance, no partial correlation was found between the average IL-6 level (IL-6) and the Quality of Life Visual Analogue Scale (VAS-Q). Thus, cytokine level was not associated with the daily perception of quality of life in this sample.

So, no significant associations were found between any of the specified study variables and the daily perception of quality of life using partial correlation analysis accounting for the effects of immunological integrity. Additionally, no significant associations were found between any of the specified study variables and the daily perception of quality of life using simple linear correlation analyses either. Yet, the women perceived a positive sense of quality of life. One could speculate that the sample was not large enough to be able to demonstrate significant correlations between the variables. It may also be that the variables chosen to represent the constructs need to be reevaluated, or at least tested.

Specific Aim 4

The end-point for specific aim 4 was to explore whether a 1-item quality of life instrument provided a comparable representation of the sense of wellbeing as a 66-item quality of life instrument in asymptomatic HIV-seropositive African American women experiencing HIV-related sleep disruption. Due to adequate interval widths, an agreement was found between the Quality of Life Index (QLI) and the Quality of Life Visual Analogue Scale (VAS-Q). Thus, in hopes of decreasing assessment burdens in this population, the short questionnaire may be

used with confidence in place of the long questionnaire. It is very important to be mindful of the assessment burden of research studies involving this particular population, especially when seeking thoughtful and accurate data.

Study Limitations

This preliminary study implemented a cross-sectional, descriptive correlation design to gather baseline data regarding HIV-related sleep disruption experienced by an underrepresented subpopulation of those living with HIV. Although appropriate, utilization of such a low-level study design is not without restrictions. Cross-sectional studies are limited in that they do not permit one to draw conclusions regarding causal relationships between variables of interest or confirm the direction for causality of the relationships observed. They are also limited when considering the notion of change over time. Cross-sectional studies provide only a snapshot, and thus sacrifice issues related to chronicity, recurrence, progression of disease, or even long-term clinical significance. Therefore, data from the current study should be interpreted cautiously.

The exploratory nature of this study design involves significance testing of multiple correlations, which introduces the potential for a false discovery rate as described by John D. Storey (2003). A false discovery rate is the proportion of relationships that falsely appear statistically significant due to random error or some artifact of random variation. This study did not control or adjust for this multiple comparisons hazard, and must then acknowledge that when enough relationships are tested, a certain portion of them will falsely appear as statistically significant. Therefore, statistically significant relationships in this study should also be interpreted cautiously.

The sample for the present study was limited in size by design to 20 participants, thus it lacked statistical power and generalizability of the findings is limited. Nonetheless, the number

of participants is consistent with other pilot studies in the literature seeking to describe phenomena, while looking for trends that may warrant further investigation. The number of participants is also consistent with that of published sleep studies, HIV-sleep research, dissertation projects, and other exploratory endeavors of a biophysical nature, seeking new knowledge and potential significance to science. Obviously, a larger sample would be more advantageous; however, for a number of reasons, including time and resources, most studies of this nature are conducted using small samples.

The sample was also limited by design to asymptomatic HIV-seropositive AA women, between the ages of 18 and 40 years, being seen at the ID clinic in Detroit, MI. Consequently, the results of such a convenience sample may be biased and not generalizable to any other HIV-seropositive AA women, specifically those with symptomatic disease, those seeking treatment from private-practice clinics, or those vulnerable to not seeking treatment at all. The fact that the entire sample was recruited from one healthcare clinic indicates that these women may somehow be distinct in their circumstances and not truly representative of the overall subpopulation. A randomly selected sample may have strengthened the design of the study; however, this is not usually possible, especially when looking to explore a specific phenomenon. A relevant comparison group of comparable HIV-seronegative African American women might have also been used to strengthen the design of the study; however, the goal of this preliminary effort was to gain as much baseline data as possible related to the phenomenon of interest.

Despite the intricate theoretical underpinnings used in the development of this study, the variables chosen to represent the constructs of sleep homeodynamics, immunological integrity, and wellbeing may not be comprehensive. This is a potential threat to the construct validity of this study. However, the flexibility of the conceptual framework allowed room for scholarly

interpretation and a selection of variables that held significance in the literature. The variables chosen in this study were found to have consequence in both the sleep and the HIV literature.

Due to funding constraints, CD4⁺ cell count and HIV RNA viral load values were obtained via chart abstraction from the most recent blood collection documented in the participant's medical chart. These values were from a single time-point prior to recruitment and data collection, and thus, may not be reflective of the values at the time of the study. The average timing of blood collection for the sample was approximately 3 months prior to enrollment into the study, which is congruent with the standard of care for monitoring immune function every 3-4 months. Additionally, with the chronic nature of the asymptomatic phase, it is common practice in HIV studies with a limited budget to assume that the CD4⁺ cell count and the HIV RNA viral load will not vary significantly within that short period of time.

Although the use of wrist actigraphy is becoming an increasingly popular method for estimating sleep and sleep patterns, it is limited in that it is only able to measure movement and not actual sleep or wake itself. From the movement, sleep-wake inferences are made with an understanding of the inability to discern true sleep from quiet rest. Actigraphy is also limited in that it requires correlation with a sleep log in order to obtain a true calculation of some sleep measures, such as sleep latency. Without a sleep log, it is impossible to calculate sleep latency since the time that the participant actually laid down or went to bed is unknown. As a result, sleep latency in this study was substituted with minutes before sleep onset (total minutes after 2100 hours until the first continuous block of at least 20 minutes of scored sleep). Another possible limitation this study faced is that it did not by design restrict the 72 hours of continuous monitoring to weekdays only, which might have caused some variability within the study.

However, no significant statistical difference was found between those whose protocol monitoring period included weekend days and those whose did not.

Lastly, cognitive bias was a potential threat to the integrity of this study. This happens if participants fail to provide accurate answers to self-report questionnaires. Accuracy often depends on, but is not limited to the interpretation of the instrument, the speed with which it is completed (back filling verses real-time answers), and the participant's estimation or recall abilities, especially after a substantial amount of time has passed. Misinformation of true experiences may also be provided if the respondents are in denial, feel embarrassed of the truth, or if they complete the instruments based on how they perceive the researcher wants them to respond (Kerlinger & Lee, 2000). In effort to strengthen the results of the study, each questionnaire was reviewed with the subject, as well as written instructions and contact information for the investigator provided in the event that the participant had any questions. The goal of creating a true clinical picture, a reflection uniquely theirs (an underrepresented subpopulation) was used to reinforce the importance of timely and accurate self-reporting. Yet, some inconsistencies between the objective actigraphic assessments and the daily subjective Stanford Sleepiness Scale (SSS) were found. For example, a participant might have self-reported feeling wide-awake and active on the 1pm SSS, yet the corresponding actigraphic data from that day's wake segment clearly demonstrates minutes scored as sleep around that same particular time point.

Despite serious constraints, the current research was exploratory in nature, and the significance of the contributions it has provided is principal.

Conclusion

In general, this sample consisted of poor, uneducated, slightly overweight, single African American women in their 30's; that had contracted HIV from heterosexual contact more than five years ago. Most of the women slept alone, usually with the television on, and reported a moderately high caffeine intake to keep them going throughout the day. Furthermore, they were immunologically stable; with CD4⁺ counts associated with wake variables.

The women's objective sleep experience demonstrated severe sleep disruption and disorganized sleep patterns with almost half of the night spent awake. Their self-reported experience of sleep quality, both general and daily pattern, was consistent with that of substantial sleep disruption. The daily sleep quality pattern, however, did seem to be a bit less obtrusive. The women's objective measurement of daytime function correspondingly showed to be disrupted as well; with frequent dozing throughout the day verifying the inadequacy of their nocturnal sleep. Interestingly enough, their self-reported experience of daytime sleepiness, both general and daily pattern, was within normal limits. While IL-6 levels confirmed a rhythm-like nature, such levels were not consistent with the normal peaks and troughs of the diurnal pattern described in the literature. In fact, average IL-6 levels were much lower than that found in normal controls and other asymptomatic HIV-seropositive samples.

General quality of life, in agreement with the daily pattern of quality of life, indicated a positive sense of general wellbeing in this sample. However, the daily pattern of quality of life measure was not associated with the daily pattern of sleep efficiency, subjective sleep quality, daytime sleepiness, or IL-6 levels when controlling for CD4⁺ cell count and HIV RNA viral load. So, despite the severe disruption in sleep homeodynamics, the young women's sense of wellbeing remained intact. This finding supports Levine's Conservation Theory, which postulates that other factors (ie. personal and social) may be at play, helping to maintain

successful adaptation and conserve (or keep together) wholeness even in the face of disruption. The data also suggests that it is plausible that the total sleep time that the women were able to obtain during a full 24-hour period was adequate enough to sustain their sense of wellbeing.

Implications for Practice

Implications for practice reflect the study findings related to sleep disruption in asymptomatic HIV-seropositive African American women of childbearing age. There were several clinically meaningful findings in this study that hold significant implications for HIV healthcare practitioners. A major finding in this study was the overwhelming presence of disrupted sleep/wake patterns in this sample. This supports the fact that HIV-related sleep disruption is a frequently encountered problem, even in asymptomatic HIV disease, yet none of these women were being treated for such disruptions to ensure that quality of life remains intact. The lack of diagnosis and treatment of short sleepers and nappers suggests inadequate screening practices, undeveloped treatment modalities, and/or insufficient communication with HIV care providers. Therefore, it is imperative to implement routine assessments focused on sleep disruption as part of every patient's holistic nursing assessment in HIV care, and document as such. Initial emphasis should be placed on environmental and sleep hygiene factors, given their potential impact on sleep duration and sleep fragmentation. Instruments, similar to the ones used in this study, may be incorporated at different phases in the comprehensive health maintenance plan with protocols designed to include appropriate referrals and treatment modalities.

The study also assessed a host of demographic, psychosocial, and behavioral characteristics that have been associated with sleep/wake patterns in the literature. Clinicians must be able to appreciate the complexity of the multidimensional nature of the disparities that African American women living with HIV face. Findings also reinforce the importance of

routine comprehensive assessments for potential vulnerabilities. Such factors may or may not be assessed at a regular clinical appointment, however, such inquiry should be as routine as obtaining laboratory evaluations. That way, patient education regarding risk-taking behaviors and lifestyle modification strategies can be tailored to fit the patient's needs as they arise.

The completion of study instruments led many patients to truly reflect upon their life circumstances and sleep/wake experiences since their HIV diagnosis, thereby opening communication with the clinical researcher. This type of introspection needs to be facilitated in clinical practice. Thus, study findings support the importance of early patient education regarding potential changes in sleep/wake patterns, how to communicate concerns with their provider, along with practice interventions aimed to support healthy sleep hygiene specific to this population.

Contributions to Nursing Science

Published sleep literature fails to depict much advancement in nursing science through the examination of explicit exemplars guided by conceptual nursing frameworks. This small-scale research effort was the first to systematically explore the objective and subjective, as well as the general and daily experience of HIV-related sleep disruption from within the ontological grounding of a specific philosophical nursing perspective. The conceptual framework of Levine's Conservation Model was the foundation used to substruct a middle-range theory, the Sleep Conservation Model, from which the empirical structure and defining limits of this study were delineated. Utilization of such a substantive model not only provides the scientific rationale for the dynamics of the human health experience being studied and the essential dimensions for scholarly research rooted in the nursing discipline; but it also facilitates the synthesis of relationships between theory, measurement, and data interpretation phases of the research

process (Grant, Kinney, & Davis, 1993; Moody, 1990). Findings from this investigation supports the integration of Levine's Conservation Model as a useful disciplinary research perspective, which has great potential to generate nursing knowledge needed to continue to promote societal priorities of health and wellbeing. Therefore, this study was able to fill a gap in nursing science by establishing an underlying validity in the application of Levine's Conservation Model in the area of sleep research.

Published literature also fails to depict much advancement in nursing science through the use of Levine's Conservation Model within the context of specific underrepresented populations. This pilot study serves as a preliminary investigation for the utilization of the Conservation Model as an organizing framework to explore the complexities of asymptomatic HIV-seropositive African American women as they relate to HIV-related sleep disruption. Mapping the diverse pathways of key biological and psychosociobehavioral measures specific to a population provides the very foundation needed for the formulation of innovative health-promoting interventions specific to that population. Findings from this inquiry support the need for the systematic assessment of unique inherited and acquired vulnerabilities that may contribute to HIV-related sleep disruption in asymptomatic HIV-seropositive African American women of childbearing age. Therefore, this study was able to fill a gap in nursing science by establishing an underlying validity in the utilization of Levine's Conservation Model with an underrepresented population in the midst of great disparity.

Recommendations for Future Research

Given the complexity of the phenomenon, uniqueness of the population, and vastness of the theory, prospects for continued research are numerous. Recommendations for future research to extend the preliminary work reported here are discussed in this section.

Much more work lies ahead before scientists can truly understand all the dynamics of HIV-related sleep disruption. Larger cross-sectional and longitudinal studies are needed to expound upon and refine the variables of sleep homeodynamics and wellbeing in asymptomatic HIV-seropositive African American women. Researchers need to continue to search for significant trends and relationships among the sleep/wake rhythm, sleep quality, daytime sleepiness, the IL-6 rhythm, and quality of life in this population. Future studies into the potential roles and predictive nature of various confounding variables may prove beneficial, in helping to identify those at high-risk for this sleeping disorder. Comparison protocols with matched-control groups may help with drawing conclusions in such observational studies where the researcher has little or no control. Sleep logs will need to be incorporated into the protocol for publication goals. Further investigation into the suboptimal IL-6 levels is warranted, and efficacies of culturally suitable interventions to treat this disorder and strategies that foster better sleep hygiene have not yet been tested.

The exploration of cultural differences is imperative, especially given the multiple disparities that influence African American women. For example, on the QLI, this group of African American women seemed to place very low importance on satisfaction with their immediate family and/or significant other, yet quality of life scores were generally high. It would be prudent to explore whether this truly is a culturally-driven difference or just unique to this group of women. Greater understanding will help when trying to tailor interventions specific to this population. Sleep homeodynamics should also be explored within a family context. Findings from this present study suggest that it is likely that social and family dynamics are essential in understanding the various cultural elements affecting sleep in this population.

The development of the Sleep Conservation Model is still in its early phases, so future studies, which utilize path analysis or structural equation modeling (SEM), will not only allow for the testing of the model, but its refinement as well. SEM is beneficial in that it is a statistical technique, which allows for the analysis of complex models with multiple relationships to be tested simultaneously. It also allows for numerous indicators of the theoretical constructs and incorporates measurement error in the variables. So, all the relationships between the variables of sleep homeodynamics and wellbeing, as well as those of immunological integrity, psychological integrity, and relational integrity will be good-fit tested simultaneously. Further attention will be given to the refinement of the model. This is possible through the model generating techniques of SEM that permits new relationships to emerge from the data. The goal is to end up with a testable and parsimonious middle-range theory substructured from Levine's Conservation Model framework.

APPENDIX A

DEMOGRAPHIC & LIFESTYLE QUESTIONNAIRE

Study ID: _____

Date: _____

Demographic & Lifestyle Questionnaire**Part 1 General Demographics**

1. What is your Date of Birth? _____ Age? _____ (study age is 18-40)
2. What is your highest level of education you have completed?

<input type="checkbox"/> Less than High School	<input type="checkbox"/> 2-year College Degree
<input type="checkbox"/> High School/GED	<input type="checkbox"/> 4-year College Degree
<input type="checkbox"/> Some College	<input type="checkbox"/> Graduate School
3. What is your current marital status?

<input type="checkbox"/> Single, Never Married	<input type="checkbox"/> Divorced
<input type="checkbox"/> Married	<input type="checkbox"/> Widowed
<input type="checkbox"/> Separated	
4. What is your religious affiliation?

<input type="checkbox"/> Christian (Protestant or Evangelical)	<input type="checkbox"/> Muslim
<input type="checkbox"/> Roman Catholic	<input type="checkbox"/> Buddhist
<input type="checkbox"/> Jewish	<input type="checkbox"/> Other _____
5. What is your own yearly income?

<input type="checkbox"/> Less than \$10,000	<input type="checkbox"/> \$40,000-\$59,999
<input type="checkbox"/> \$10,000-\$19,999	<input type="checkbox"/> \$60,000-\$79,999
<input type="checkbox"/> \$20,000-\$39,999	<input type="checkbox"/> More than \$80,000
6. What is your employment status?

<input type="checkbox"/> Student	<input type="checkbox"/> Part-time
<input type="checkbox"/> Self-employed	<input type="checkbox"/> Full-time
<input type="checkbox"/> Unemployed → <input type="checkbox"/> Out less than 1 year <input type="checkbox"/> Out more than 1 year <input type="checkbox"/> Unable to work	
7. How many people live in your household? _____
8. What year were you first Diagnosed with HIV? _____
9. Mode of Transmission (Please check all that apply)

<input type="checkbox"/> Intervenus Needles	<input type="checkbox"/> Birth or Breastfeeding
<input type="checkbox"/> Heterosexual Contact	<input type="checkbox"/> Homosexual Contact
<input type="checkbox"/> Blood Products	<input type="checkbox"/> Other _____

Study ID: _____

Date: _____

Part 2 SLEEP History (In the last 4 weeks)10. Do you like to sleep? Yes No 11. Please check any of the following that apply: Loud snoring Sleep talking Breathing stops for brief periods in my sleep Sleep walking Awaken gasping for breath Nightmares Fall out of bed Bed wetting Teeth grinding Sinus trouble at night

12. My bedroom is (loud/quiet). (circle one)

13. My bedroom is (light/dark). (circle one)

14. My mattress is (soft/hard/just right)? (circle one)

15. Do you normally go to sleep with the television on? Yes No 16. Do you normally go to sleep with music on? Yes No 17. Do you normally read before you go to sleep? Yes No 18. Do you use your bedroom for other daily activities other than sleeping? Yes No

If yes, what other activities do you do in your bedroom? _____

19. How many people sleep in the same room with you?

___Adults ___Children ___Pets

20. How many people sleep in the same bed with you?

___Adults ___Children ___Pets

21. Do you take anything to help you sleep? Yes No

If yes, what? _____

How often? _____

Last use? _____

22. Other information regarding your sleep that you would like to describe? Yes No

If yes, please describe _____

Study ID: _____

Date: _____

PART 3 Personal Habits/Medication History (In the last 4 weeks)**23. Do you use tobacco (cigarettes, cigars, pipe)?** Yes No

If yes, how many per day? _____ For how many years? _____

What time of day is your last use, normally? _____

24. Does anyone else in the household use tobacco? Yes No **25. Do you drink alcohol (beer, wine, liquor)?** Yes No

If yes, how many drinks? _____ per day / per week / per month (circle one)

What time of day is your last drink, normally? _____

26. Do you drink caffeinated beverages? Yes No

If yes, how many caffeinated beverages do you drink per day? _____

What time of day is your last drink, normally? _____

27. When do you usually eat your last meal of the day? Early evening Mid- evening Late evening Mid-night or later**28. Do you exercise regularly?** Yes No

If yes, how often do you exercise?

 Rarely Once a week Several times a week Daily

What time of day do you usually exercise? _____

29. Do you have any allergies to drugs, food, or the environment? Yes No

If yes, please list them _____

30. Medication List (In the last 4 weeks)**HIV Medications**

Other Prescriptions/ OTC

Supplements/Herbs


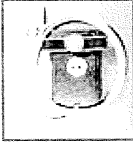
APPENDIX B

MICROMINI-MOTIONLOGGER® WRIST ACTIGRAPH BY AMI

2

Motionlogger® Actigraph Systems

AMI offers an Actigraph to fit all budget and protocol requirements. Various model Motionloggers offer applications that include basic sleep estimation, high resolution analog data collection, simultaneous environmental data collection, subjective wearer input features, and comprehensive sleep scoring and sleep distribution data on the wrist. A range of recording capabilities exist including four validated sleep algorithms, PLM analysis, and a suite of circadian rhythm analyses. Software for device operation and data analysis is available for Windows 2000/XP, and comparable systems – and our ActMe Operational Software allows for quick, easy download of actigraph data into the Fatigue Avoidance Scheduling Tool (“FAST”) program. All models are Lithium battery powered for long use and come with a full one-year warranty.

Description	Catalog Number
 <p data-bbox="375 898 490 919"><i>Faux Watch Face</i></p>	<p data-bbox="597 730 1089 772">MicroMini-Motionlogger® Actigraph with User Battery Exchange Feature</p> <p data-bbox="597 772 1117 961">1-3/8" diameter waterproof MicroMini-Motionlogger weighing 0.9 oz. encased in a plastic enclosure. This model enables the user to exchange the instrument's battery after the approximate 4,000-hour battery run time. Contains 32K non-volatile memory; 16 Hz sample rate; 2-3 Hz bandwidth; modes of operation: Zero Crossing (ZC) or Proportional Integrating Measure (PIM, selectable high or low sensitivity); one-minute fixed epoch length (yielding up to 22 days of recording time per initialization in ZC and 11 days in PIM). Requires Micro Interface/Connector (Cat. #24.000RC) to download data. Ask about custom graphics for the unit's face. Can also be used with 1,000 hour rechargeable battery (see page 3, item #21.195)</p> <p data-bbox="1174 730 1260 747">24.000BEF</p>
	<p data-bbox="597 995 1117 1037">MicroMini-Motionlogger® Actigraph Interface/Connector with ACT Operational Software</p> <p data-bbox="597 1037 1084 1087">Required for initializing and downloading data from MicroMini-Motionloggers. Comes with Serial Port Tester. (Analysis Software sold separately.)</p> <p data-bbox="1174 978 1243 995">24.000C</p>

Family of MicroMini's

Consists of single sensors similar to the MicroMini-Motionlogger activity monitor, which (together or separately) allow for multi-parameter data collection by means of a common Interface (Cat. #24.000C) and multi-channel integrated graphic display in ACTION4 analysis software.

**MicroMini Light Sensor**

Ambient light sensor with a 1 part in 256 resolution. Possible ranges include 0 to 1,000 LUX in 4 LUX increments or 0 to 4,000 LUX in 16 LUX increments (specify when ordering). 32K memory allows for 22 days of recording. 5 second samples averaged and stored each minute.

24.000LS

**MicroMini Temperature Sensor**

Single sensor to collect skin or ambient temperature. 32K memory allows for 22 days of recording. 5 second samples averaged and stored each minute. With a range of 19 to 43.6°C; 0.1°C resolution; and ±2°C precision.

24.000TS

**MicroMini Sound Sensor**

Environmental sound sensor. 32K memory for 22 days of recording. 5 second samples averaged and stored each minute. With a range of 40 to 85 dB SPL “C” weighting 400 hz Sine, 0.1-5 dB resolution; precision ±5 dB SPL.

24.000SS

Ask about CPT reimbursement codes!

FDA# K854030B

APPENDIX C

MSDS MOTIONLOGGER ACTIGRAPH BY PRECISION CONTROL DESIGN, INC

FROM :PRECISION CONTROL DESIGN

FAX NO. :8502441172

Jul. 17 2007 12:31PM P2

**PRECISION CONTROL DESIGN, INC.**

135 EGLIN PARKWAY S.E., FORT WALTON BEACH, FLORIDA 32548
(850) 244-1923 • FAX (850) 244-1172

Material Safety Data Sheet

July 16, 2007

Manufacturer's Name and Address:

Precision Control Design, Inc.
135 Eglin Parkway SE
Fort Walton Beach, FL 32548
(850) 244-1923

Supplier's Name and Address:

Ambulatory Monitoring, Inc.
731 Saw Mill River Road
Ardsley, NY 10502
(800) 341-0066

RE: Motionlogger Actigraph

This product is not considered to be or to contain hazardous chemicals based on evaluations made by our company.

Precision Control Design, Inc.

APPENDIX D

OPERATIONAL DEFINITIONS FOR THE SLEEP/WAKE INDICES

Operational Definitions for the Sleep/Wake Indices	
Down Segment	Nocturnal hours between 2100 and 0859
Sleep Minutes	Total minutes of inactivity epochs scored as sleep between 2100 and 0859 hours
Minutes Before Sleep Onset	Total minutes after 2100 hours until the first continuous block of at least 20 minutes of scored sleep
Wake Episodes (awakenings)	Number of blocks of contiguous activity epochs scored as wake between 2100 and 0859 hours
Wake Minutes	Total minutes of activity epochs scored as wake between 2100 and 0859 hours
Sleep Percentage	Percent minutes of inactivity epochs scored as sleep between 2100 and 0859 hours ($100 * \text{Sleep} / \text{Duration}$)
Sleep Efficiency	$[100 * \text{Sleep Minutes} / (\text{Onset} - \text{Offset Duration})]$ between 2100 and 0859 hours
Sleep Fragmentation Index	Number of awakenings / Total sleep time in minutes between 2100 and 0859 hours
Wake Segment	Daytime hours between 0900 and 2059
Wake Minutes	Total minutes of activity epochs scored as wake between 0900 and 2059 hours
Activity Mean	Mean activity score (counts/epoch) between 0900 and 2059 hours
Sleep Episodes (naps)	Number of blocks of contiguous inactivity epochs scored as sleep between 0900 and 2059 hours
Sleep Minutes	Total minutes of inactivity epochs scored as sleep between 0900 and 2059 hours
Sleep Percentage	Percent minutes of inactivity epochs scored as sleep between 0900 and 2059 hours ($100 * \text{Sleep} / \text{Duration}$)
Activity Index	Percentage of epochs with >0 activity score between 0900 and 2059 hours
Acceleration Index	Change in activity rate between 0900 and 2059 hours

24-Hour Rhythm	24-hour day with one sleep segment and one wake segment between 2100 and 2059 hours
24-Hour Total Sleep Time	Total minutes of inactivity epochs scored as sleep between 2100 and 2059 hours
24-Hour Total Wake Time	Total minutes of activity epochs scored as sleep between 2100 and 2059 hours

APPENDIX E

PITTSBURGH SLEEP QUALITY INDEX

ID Number _____

Date _____

Pittsburgh Sleep Quality Index (PSQI)

Name _____ ID # _____ Date _____ Age _____

Instructions:

The following questions relate to your usual sleep habits during the past month *only*. Your answers should indicate the most accurate reply for the *majority* of days and nights in the past month. Please answer all the questions.

1. During the past month, when have you usually gone to bed at night?
USUAL BED TIME _____
2. During the past month, how long (in minutes) has it usually taken you to fall asleep each night?
NUMBER OF MINUTES _____
3. During the past month, when have you usually gotten up in the morning?
USUAL GETTING UP TIME _____
4. During the past month, how many hours of *actual sleep* did you get at night?
(This may be different than the number of hours you spend in bed.)
HOURS OF SLEEP PER NIGHT _____

For each of the remaining questions, check the one best response. Please answer *all* questions.

5. During the past month, how often have you had trouble sleeping because you...

- (a) Cannot get to sleep within 30 minutes

Not during the past month	_____	Less than once a week	_____	Once or twice a week	_____	Three or more times a week	_____
---------------------------------	-------	--------------------------	-------	----------------------------	-------	----------------------------------	-------

- (b) Wake up in the middle of the night or early morning

Not during the past month	_____	Less than once a week	_____	Once or twice a week	_____	Three or more times a week	_____
---------------------------------	-------	--------------------------	-------	----------------------------	-------	----------------------------------	-------

- (c) Have to get up to use the bathroom

Not during the past month	_____	Less than once a week	_____	Once or twice a week	_____	Three or more times a week	_____
---------------------------------	-------	--------------------------	-------	----------------------------	-------	----------------------------------	-------

- (d) Cannot breathe comfortably

Not during the past month	_____	Less than once a week	_____	Once or twice a week	_____	Three or more times a week	_____
---------------------------------	-------	--------------------------	-------	----------------------------	-------	----------------------------------	-------

- (e) Cough or snore loudly

Not during the past month	_____	Less than once a week	_____	Once or twice a week	_____	Three or more times a week	_____
---------------------------------	-------	--------------------------	-------	----------------------------	-------	----------------------------------	-------

- (f) Feel too cold

Not during the past month	_____	Less than once a week	_____	Once or twice a week	_____	Three or more times a week	_____
---------------------------------	-------	--------------------------	-------	----------------------------	-------	----------------------------------	-------

ID Number _____

Date _____

- (g) Feel too hot
 Not during the past month _____ Less than once a week _____ Once or twice a week _____ Three or more times a week _____
- (h) Had bad dreams
 Not during the past month _____ Less than once a week _____ Once or twice a week _____ Three or more times a week _____
- (i) Have pain
 Not during the past month _____ Less than once a week _____ Once or twice a week _____ Three or more times a week _____
- (j) Other reason(s), please describe _____

How often during the past month have you had trouble sleeping because of this?

Not during the past month _____ Less than once a week _____ Once or twice a week _____ Three or more times a week _____

6. During the past month, how would you rate your sleep quality overall?
 Very good _____
 Fairly good _____
 Fairly bad _____
 Very bad _____
7. During the past month, how often have you taken medicine (prescribed or "over the counter") to help you sleep?
 Not during the past month _____ Less than once a week _____ Once or twice a week _____ Three or more times a week _____
8. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?
 Not during the past month _____ Less than once a week _____ Once or twice a week _____ Three or more times a week _____
9. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?
 No problem at all _____
 Only a very slight problem _____
 Somewhat of a problem _____
 A very big problem _____
10. Do you have a bed partner or roommate?
 No bed partner or roommate _____
 Partner/roommate in other room _____
 Partner in same room, but not same bed _____
 Partner in same bed _____

APPENDIX F

SUBJECTIVE SLEEP QUALITY QUESTIONNAIRE

Subjective Sleep Quality Questionnaire

ID Number _____

Date _____

DIRECTIONS: Your impressions of how you slept last night are important. The following 14 items pertain just to your sleep last night. The responses range from "Strongly Agree" to "Strongly Disagree." Please read each item and circle the appropriate response.

1. I SLEPT VERY WELL LAST NIGHT.

Strongly Agree	Moderately Agree	Slightly Agree	Slightly Disagree	Moderately Disagree	Strongly Disagree
-------------------	---------------------	-------------------	----------------------	------------------------	----------------------

2. I HAD A HARD TIME WAKING UP THIS MORNING.

Strongly Agree	Moderately Agree	Slightly Agree	Slightly Disagree	Moderately Disagree	Strongly Disagree
-------------------	---------------------	-------------------	----------------------	------------------------	----------------------

3. I FELT RESTED WHEN I WOKE UP.

Strongly Agree	Moderately Agree	Slightly Agree	Slightly Disagree	Moderately Disagree	Strongly Disagree
-------------------	---------------------	-------------------	----------------------	------------------------	----------------------

4. I HAD ENOUGH SLEEP LAST NIGHT.

Strongly Agree	Moderately Agree	Slightly Agree	Slightly Disagree	Moderately Disagree	Strongly Disagree
-------------------	---------------------	-------------------	----------------------	------------------------	----------------------

5. I WOKE UP TOO EARLY AND COULDN'T GET BACK TO SLEEP.

Strongly Agree	Moderately Agree	Slightly Agree	Slightly Disagree	Moderately Disagree	Strongly Disagree
-------------------	---------------------	-------------------	----------------------	------------------------	----------------------

6. I HAD LONG PERIODS OF WAKEFULNESS DURING THE NIGHT.

Strongly Agree	Moderately Agree	Slightly Agree	Slightly Disagree	Moderately Disagree	Strongly Disagree
-------------------	---------------------	-------------------	----------------------	------------------------	----------------------

7. I DIDN'T WAKE UP ALL NIGHT.

Strongly Agree	Moderately Agree	Slightly Agree	Slightly Disagree	Moderately Disagree	Strongly Disagree
-------------------	---------------------	-------------------	----------------------	------------------------	----------------------

8. I KEPT TOSSING AND TURNING IN BED ALL NIGHT.

Strongly Agree	Moderately Agree	Slightly Agree	Slightly Disagree	Moderately Disagree	Strongly Disagree
-------------------	---------------------	-------------------	----------------------	------------------------	----------------------

APPENDIX G

EPWORTH SLEEPINESS SCALE

The Epworth Sleepiness Scale

ID # _____
Date _____

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times. Even if you have not done some of these things recently try to work out how they would have affected you. Use the following scale to choose the *most appropriate number* for each situation:

- 0 = would *never* doze
1 = *slight* chance of dozing
2 = *moderate* chance of dozing
3 = *high* chance of dozing

Situation	Chance of dozing
Sitting and reading	_____
Watching TV	_____
Sitting, inactive in a public place (e.g. a theater or a meeting)	_____
As a passenger in a car for an hour without a break	_____
Lying down to rest in the afternoon when circumstances permit	_____
Sitting and talking to someone	_____
Sitting quietly after a lunch without alcohol	_____
In a car, while stopped for a few minutes in the traffic	_____

APPENDIX H

STANFORD SLEEPINESS SCALE

ID # _____
Date _____
Time _____

STANFORD SLEEPINESS SCALE

Directions: Circle the scale value of the statement which best describes your state of sleepiness right now.

1. Feeling active and vital; alert; wide awake.
2. Functioning at a high level, but not at peak; able to concentrate.
3. Relaxed; awake; not at full alertness; responsive.
4. A little foggy; not at peak; let down.
5. Fogginess; beginning to lose interest in remaining awake; slowed down.
6. Sleepiness; prefer to be lying down; fighting sleep; woozy.
7. Almost in reverie, sleep onset soon; lost struggle to remain awake.

APPENDIX I

QUALITY OF LIFE INDEX

**Ferrans and Powers
QUALITY OF LIFE INDEX®
GENERIC VERSION - III**

PART 1. For each of the following, please choose the answer that best describes how *satisfied* you are with that area of your life. Please mark your answer by circling the number. There are no right or wrong answers.

HOW SATISFIED ARE YOU WITH:	Very Dissatisfied	Moderately Dissatisfied	Slightly Dissatisfied	Slightly Satisfied	Moderately Satisfied	Very Satisfied
1. Your health?	1	2	3	4	5	6
2. Your health care?	1	2	3	4	5	6
3. The amount of pain that you have?	1	2	3	4	5	6
4. The amount of energy you have for everyday activities?	1	2	3	4	5	6
5. Your ability to take care of yourself without help?	1	2	3	4	5	6
6. The amount of control you have over your life?	1	2	3	4	5	6
7. Your chances of living as long as you would like?	1	2	3	4	5	6
8. Your family's health?	1	2	3	4	5	6
9. Your children?	1	2	3	4	5	6
10. Your family's happiness?	1	2	3	4	5	6
11. Your sex life?	1	2	3	4	5	6
12. Your spouse, lover, or partner?	1	2	3	4	5	6
13. Your friends?	1	2	3	4	5	6
14. The emotional support you get from your family?	1	2	3	4	5	6
15. The emotional support you get from people other than your family?	1	2	3	4	5	6

(Please Go To Next Page)

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HOW SATISFIED ARE YOU WITH:	Very Dissatisfied	Moderately Dissatisfied	Slightly Dissatisfied	Slightly Satisfied	Moderately Satisfied	Very Satisfied
16. Your ability to take care of family responsibilities?	1	2	3	4	5	6
17. How useful you are to others?	1	2	3	4	5	6
18. The amount of worries in your life?	1	2	3	4	5	6
19. Your neighborhood?	1	2	3	4	5	6
20. Your home, apartment, or place where you live?	1	2	3	4	5	6
21. Your job (if employed)?	1	2	3	4	5	6
22. Not having a job (if unemployed, retired, or disabled)?	1	2	3	4	5	6
23. Your education?	1	2	3	4	5	6
24. How well you can take care of your financial needs?	1	2	3	4	5	6
25. The things you do for fun?	1	2	3	4	5	6
26. Your chances for a happy future?	1	2	3	4	5	6
27. Your peace of mind?	1	2	3	4	5	6
28. Your faith in God?	1	2	3	4	5	6
29. Your achievement of personal goals?	1	2	3	4	5	6
30. Your happiness in general?	1	2	3	4	5	6
31. Your life in general?	1	2	3	4	5	6
32. Your personal appearance?	1	2	3	4	5	6
33. Yourself in general?	1	2	3	4	5	6

(Please Go To Next Page)

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PART 2. For each of the following, please choose the answer that best describes how *important* that area of your life is to you. Please mark your answer by circling the number. There are no right or wrong answers.

HOW IMPORTANT TO YOU IS:	Very Unimportant	Moderately Unimportant	Slightly Unimportant	Slightly Important	Moderately Important	Very Important
1. Your health?	1	2	3	4	5	6
2. Your health care?	1	2	3	4	5	6
3. Having no pain?	1	2	3	4	5	6
4. Having enough energy for everyday activities?	1	2	3	4	5	6
5. Taking care of yourself without help?	1	2	3	4	5	6
6. Having control over your life?	1	2	3	4	5	6
7. Living as long as you would like?	1	2	3	4	5	6
8. Your family's health?	1	2	3	4	5	6
9. Your children?	1	2	3	4	5	6
10. Your family's happiness?	1	2	3	4	5	6
11. Your sex life?	1	2	3	4	5	6
12. Your spouse, lover, or partner?	1	2	3	4	5	6
13. Your friends?	1	2	3	4	5	6
14. The emotional support you get from your family?	1	2	3	4	5	6
15. The emotional support you get from people other than your family?	1	2	3	4	5	6

(Please Go To Next Page)

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HOW IMPORTANT TO YOU IS:	Very Unimportant	Moderately Unimportant	Slightly Unimportant	Slightly Important	Moderately Important	Very Important
16. Taking care of family responsibilities?	1	2	3	4	5	6
17. Being useful to others?	1	2	3	4	5	6
18. Having no worries?	1	2	3	4	5	6
19. Your neighborhood?	1	2	3	4	5	6
20. Your home, apartment, or place where you live?	1	2	3	4	5	6
21. Your job (if employed)?	1	2	3	4	5	6
22. Having a job (if unemployed, retired, or disabled)?	1	2	3	4	5	6
23. Your education?	1	2	3	4	5	6
24. Being able to take care of your financial needs?	1	2	3	4	5	6
25. Doing things for fun?	1	2	3	4	5	6
26. Having a happy future?	1	2	3	4	5	6
27. Peace of mind?	1	2	3	4	5	6
28. Your faith in God?	1	2	3	4	5	6
29. Achieving your personal goals?	1	2	3	4	5	6
30. Your happiness in general?	1	2	3	4	5	6
31. Being satisfied with life?	1	2	3	4	5	6
32. Your personal appearance?	1	2	3	4	5	6
33. Are you to yourself?	1	2	3	4	5	6

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APPENDIX J

QUALITY OF LIFE VISUAL ANALOGUE SCALE

ID Number _____

Date _____

QUALITY OF LIFE
VISUAL ANALOG SCALERIGHT NOW, I would rate my level of QUALITY OF LIFE as:WORST possible
QUALITY OF LIFEBEST possible
QUALITY OF LIFE

APPENDIX K

SCHEDULE OF EVENTS

Schedule of Events							
Sleep Homeodynamics and Wellbeing in Asymptomatic HIV-Seropositive African American Women							
Research Activities	Screening	Baseline	Monitoring				End of Study
	Initial Visit		Day 1	Day 2	Day 3	Day 4	
Provider Permission	X						
Informed Consent	X						
Inclusion/Exclusion Criteria	X						
Medical History Assessment	X						
Physical Exam with Vital Signs	X						
Calculate BMI = Weight (kg)/ Height (m ²)	X						
Demographic & Lifestyle Variables Questionnaire		X					
CD4+ Cell Count		X					
HIV RNA Viral Load		X					
Pittsburgh Sleep Quality Index (PSQI)		X					
Epworth Sleepiness Scale (ESS)		X					
Quality of Life Index (QLI)		X					
Instruction / Dispense Supplies		X					
Fit Test		X					
Wrist Actigraph			X	X	X	X	
Subjective Sleep Quality Questionnaire (SSQ)			X	X	X	X	
Quality of Life Visual Analog Scale (VAS-Q)			X	X	X	X	
Stanford Sleepiness Scale (SSS)			XXXX	XXXX	XXXX	XXXX	
Plasma IL-6 levels						XXXX	
Return supplies							X
Compensation							X

Screening and Baseline activities can be completed on the same day at the initial visit.
 Monitoring period is 4 consecutive days or 96 consecutive hours, which begins at 9pm the day of the baseline visit.
 Subjective Sleep Quality Questionnaire and Quality of Life VAS should be completed within 30 minutes of waking up.
 Stanford Sleepiness Scale should be completed 4 times per day at 10am, 1pm, 4pm, and 7pm.
 IL-6 plasma blood draws should be completed 4 times on Day 4 at 5am, 8am, 7pm, and 9pm, \pm 30 minutes.
 End of Study activities should occur within 24 hours of the conclusion of the monitoring period.

APPENDIX L

CORRELATIONS FOR THE VARIABLES OF IMMUNOLOGICAL INTEGRITY

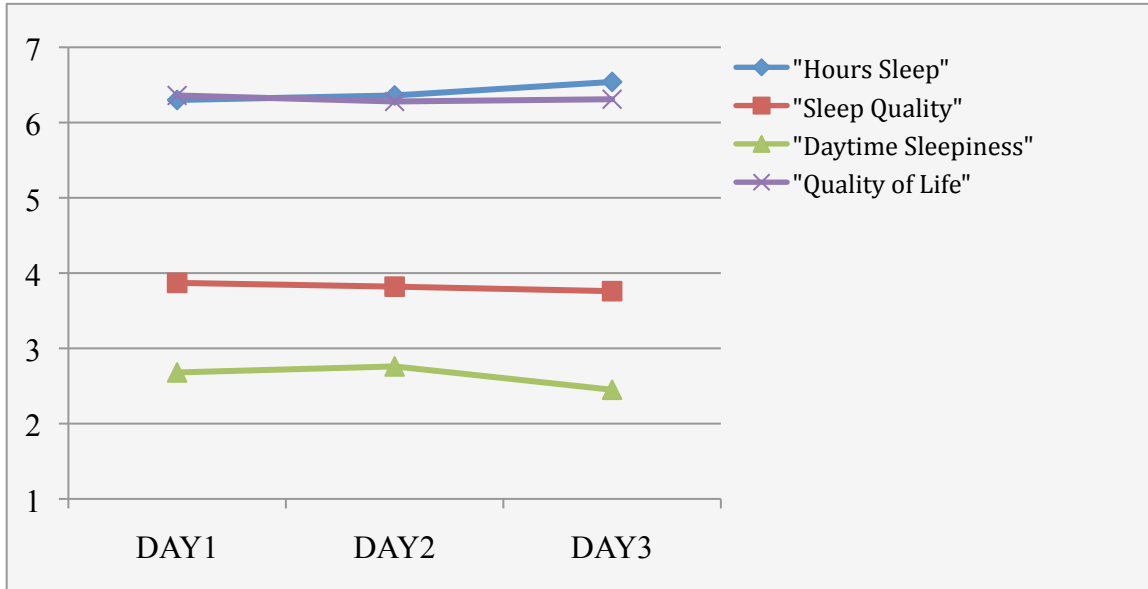
<i>Correlations for Immunological Integrity (N = 20)</i>			
Variables		CD4 (cells/mm ³)	VL (RNA copies)
Down Sleep Minutes	Pearson Correlation	.180	.278
	Sig. (2-tailed)	.448	.236
Down Minutes Before Sleep Onset	Pearson Correlation	-.213	-.077
	Sig. (2-tailed)	.368	.747
Down Wake Episodes	Pearson Correlation	-.111	.311
	Sig. (2-tailed)	.643	.183
Down Wake Minutes	Pearson Correlation	-.179	-.278
	Sig. (2-tailed)	.449	.236
Down Sleep Percentage	Pearson Correlation	.180	.278
	Sig. (2-tailed)	.449	.236
Down Sleep Efficiency	Pearson Correlation	.138	.276
	Sig. (2-tailed)	.562	.238
Down Sleep Fragmentation Index	Pearson Correlation	-.203	.011
	Sig. (2-tailed)	.391	.963
Up Wake Minutes	Pearson Correlation	.607**	-.156
	Sig. (2-tailed)	.005	.510
Up Activity Mean	Pearson Correlation	.045	-.241
	Sig. (2-tailed)	.852	.306
Up Sleep Episodes	Pearson Correlation	-.385	.388
	Sig. (2-tailed)	.094	.091
Up Sleep Minutes	Pearson Correlation	-.605**	.157
	Sig. (2-tailed)	.005	.509
Up Sleep Percentage	Pearson Correlation	-.605**	.157
	Sig. (2-tailed)	.005	.509
Up Activity Index	Pearson Correlation	.218	-.036
	Sig. (2-tailed)	.355	.879
Up Acceleration Index	Pearson Correlation	-.383	.108
	Sig. (2-tailed)	.096	.652
Pittsburgh Sleep Quality Index	Pearson Correlation	.22	-.376
	Sig. (2-tailed)	.334	.102
Subjective Sleep Quality Questionnaire	Pearson Correlation	-.074	.242
	Sig. (2-tailed)	.756	.303
Epworth Sleepiness Scale	Pearson Correlation	-.214	-.025
	Sig. (2-tailed)	.366	.916
Stanford Sleepiness Scale	Pearson Correlation	.000	-.224
	Sig. (2-tailed)	.998	.341
IL-6 Level	Pearson Correlation	.303	-.141
	Sig. (2-tailed)	.195	.553

*. Correlation is significant at the 0.05 level (2-tailed).

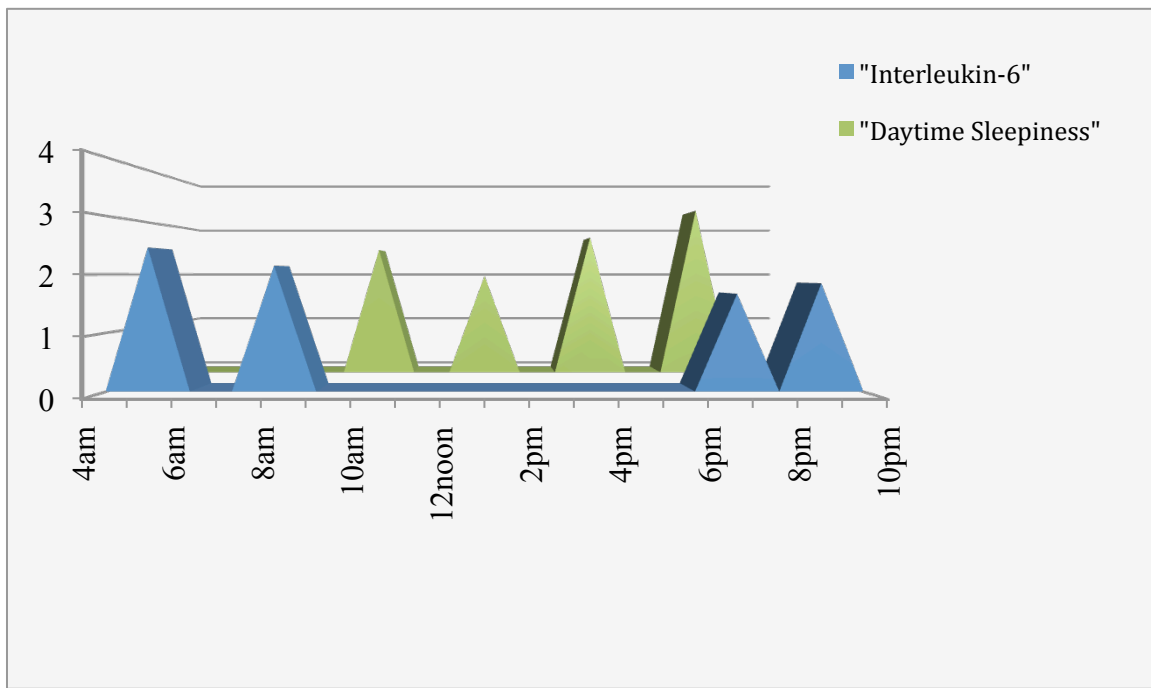
** .Correlation is significant at the 0.01 level (2-tailed).

APPENDIX M

SUMMARY GRAPHS FOR STUDY VARIABLE RHYTHMS



Summary for the Daily Rhythms



Summary for the 24-Hour Rhythms

APPENDIX N

IRB APPROVAL

**WAYNE STATE
UNIVERSITY**

HUMAN INVESTIGATION COMMITTEE
87 East Canfield, Second Floor
Detroit, Michigan 48201
Phone: (313) 577-1628
FAX: (313) 993-7122
<http://hic.wayne.edu>



NOTICE OF FULL BOARD AMENDMENT APPROVAL

To: Tabettha Gayton
Internal Medicine
7C-15 UHC ID Research

From: Lawrence R. Crane, M.D. *L. Crane* *(Ekan)*
Chairman, Medical Institutional Review Board (M1)

Date: October 22, 2010

RE: HIC #: 080907M1F
Protocol Title: Pilot Study: Sleep Homeodynamics and Well-Being in Asymptomatic HIV-Seropositive African American Women

Sponsor:
Protocol #: 0707005075

Expiration Date: March 31, 2011

Risk Level / Category: Research not involving greater than minimal risk

The above-referenced protocol amendment, as itemized below, was reviewed by the Wayne State University Institutional Review Board (M1) and is **APPROVED** effective immediately.

- Protocol (Version: 2.0; dated: 9/10/10) - Modified to reflect administrative/editorial, enrollment criteria, data collection method, and protocol title changes clearly detailed on the submitted amendment form. The revisions do not affect the risk to participants.
- Advertising Materials - Flyer to be posted in UPG ID clinics.
- Consent Form (revision date: 9/10/10) - Modified to reflect the protocol changes. These changes do not affect the risk to participants. Currently enrolled participants will not be re-consented.
- Other - Receipt of a booklet which includes all instructions and questionnaires for the monitoring phase and end of study research activities that will be provided to participants for convenience.

APPENDIX O

SITE PERMISSION LETTER



WAYNE STATE
UNIVERSITY
PHYSICIAN GROUP

Lawrence R. Crane, M.D., FACP
Professor of Medicine
Director, Division of Infectious
Diseases
University Health Center – 7D
4201 St. Antoine
Detroit, MI 48201
Phone 313-993-0330
Fax 313-745-3638

July 16, 2007

To Whom It May Concern:

Tabetha L. Gayton has received my permission to conduct a pilot study for her dissertation work through the 7B Infectious Diseases Clinic. This will include access to the clinic population for recruitment, client medical records, and the HIV/AIDS program database.

Sincerely,

Lawrence Crane, MD
Medical Director

WORLD-CLASS doctors. WORLD CLASS care.

APPENDIX P

SLEEP HOMEODYNAMICS AND WELLBEING FLYER

SLEEP HOMEODYNAMICS AND WELLBEING IN ASYMPTOMATIC HIV-SEROPOSITIVE AFRICAN AMERICAN WOMEN

WANT TO BE APART OF A SLEEP STUDY?



REQUIREMENTS:

African American

Female

Ages 18-40

Will Be Monitoring:

- Sleep/Wake Rhythm
- Sleep quality
- Daytime Sleepiness
- IL-6 Rhythm
- Quality of Life
- Other things that may affect sleep

Cannot Be:

- Pregnant
- Diagnosed with a major Inflammotry disease
- Diagnosed with a major Psychiatric disorder
- Working the Night-Shift
- Suffering from severe pain
- Suffering from HIV -progression of disease
- Suffering from AIDS-related events

For More Information Contact: APPROVAL PERIOD

Tabetha L. Gayton, RN
313-966-7025

OCT 22 '10 MAR 31 '11

HUMAN INVESTIGATION COMMITTEE

REFERENCES

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ABSTRACT**SLEEP HOMEODYNAMICS AND WELLBEING IN ASYMPTOMATIC HIV-SEROPOSITIVE AFRICAN AMERICAN WOMEN**

by

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BACKGROUND: HIV-related sleep disruption is a common complaint of persons with HIV infection. With the demographical shifts, African American women have now emerged as one of the fastest growing HIV populations today, yet they remain a vulnerable and underrepresented population in the sleep literature.

OBJECTIVE: The purpose of this pilot study was to explore the dynamics of HIV-related sleep disruption and wellbeing in asymptomatic HIV-seropositive AA women of childbearing age within the context of a holistic, theoretical substruction from Myra Levine's Conservation Model (1967). The rationale for the proposed study was to provide a foundation of both the objective and subjective experience of HIV-related sleep disruption, which as a stressor can affect wellbeing.

METHODS: A descriptive correlational design was used to examine the immunological integrity, sleep/wake rhythm, sleep quality, daytime sleepiness, IL-6 rhythm, and quality of life in 20 asymptomatic HIV-seropositive African American women receiving care at Wayne State University Physicians Group Infectious Diseases Clinic in Detroit, MI. In this 4-day protocol, measures included CD4⁺ cell count, HIV RNA viral load, wrist actigraphy, Pittsburgh Sleep

Quality Index, Subjective Sleep Quality Questionnaire, Epworth Sleepiness Scale, Stanford Sleepiness Scale, plasma IL-6, Quality of Life Index, and Quality of Life Visual Analogue Scale.

RESULTS: Both the objective and subjective experience of sleep demonstrated severe sleep disruption and disorganized sleep patterns. Nearly half (45%) of the sample slept < 6 hours per night, usually not falling asleep until sometime after 12 midnight. Objective daytime functioning was also disrupted with frequent dozing (> 9 sleep episodes) noted throughout the day. Self-reported daytime sleepiness was inconsistent with the objective assessment and was within normal limits. The sample's mean IL-6 level was 2.03 pg/mL, which is much lower than that reported in other asymptomatic samples or normal controls. Quality of life measures indicated a positive sense of wellbeing, but the daily pattern of quality of life was not associated with the daily pattern of sleep efficiency, subjective sleep quality, daytime sleepiness, or IL6 levels when controlling for CD4⁺ cell count and HIV RNA viral load. And lastly, the 1-item quality of life scale showed agreement with the 66-item quality of life index using Bland-Altman agreement analysis, which may help in decreasing participant burden in clinical trials enrolling this population.

CONCLUSION: This sample suffered from severe HIV-related sleep disruption, as evidenced by an average sleep time of 6.4 hours per night and frequent dozing throughout the day. Despite this disruption, the sample perceived a positive sense of quality of life. These results provide further evidence that future studies exploring efforts to improve sleep and daytime functioning in asymptomatic HIV-seropositive African American women are essential in order to maintain quality of life and wellbeing in this population.

AUTOBIOGRAPHICAL STATEMENT

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