The Effects Of Exercise On Sleep Parameters Among Older Women

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THE EFFECTS OF EXERCISE ON SLEEP PARAMETERS AMONG OLDER WOMEN

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ABSTRACT

Sleep is a modifiable behavior that commonly fluctuates from night to night within the same individual and varies across the lifespan. Over the years, sleep research has identified physical activity (PA)/exercise as a non-pharmacological approach to improving sleep. The overall goal of this dissertation was to investigate the acute effect of exercise on sleep outcomes as well as examine the relationship between night-to-night fluctuations in sleep parameters with exercise training among healthy older women.

Two studies, both utilizing a longitudinal study design, were conducted to 1) understand how acute exercise affects both behavioral and physiological sleep outcomes during the corresponding night among trained older women and 2) to determine whether 4 months of moderate-intensity exercise impacts night-to-night variability in sleep among older women. Data collected from the WEWALK study, a clinical exercise trial involving older women, were used in both studies. Multiple assessments of sleep parameters were objectively measured via actigraphy at baseline, mid-intervention, and post-intervention and cardiorespiratory fitness levels using a graded treadmill test at baseline and post-intervention.

The first study found that behavioral sleep parameters were significantly impacted by structured exercise in which bedtimes were significantly earlier on nights following a day of structured exercise versus bedtimes on days with no structured exercise. No significant differences were observed between structured exercise versus non-structured
exercise days in any of the physiological (i.e. total sleep time [TST], sleep onset latency [SOL], wake time after sleep onset [WASO], number of awakenings, and activity counts) sleep parameters.

In the second study, there was a borderline to significant time effect observed for WASO and number of awakenings for both measures of variability at post-intervention, which may indicate more consistent sleep over several nights with a possible improvement to sleep quality. Additionally, higher VO$_2$peak levels at baseline were associated with a shorter amount of time in bed and lower night-to-night variability in TST throughout the exercise intervention.

Overall, this dissertation found that acute exercise bouts significantly influenced behavioral sleep parameters in healthy, trained older women, and that nightly variability in WASO and number of awakenings was observed to decrease with exercise training over time. These changes in nightly variability suggest possibly greater consistency with improved sleep quality. Collectively, exercise affects sleep acutely and chronically. However, the health implications of the demonstrated changes need further investigation.
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<th>Full Form</th>
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<tr>
<td>BMI</td>
<td>Body Mass Index</td>
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<td>CES-D</td>
<td>Center for Epidemiologic Studies Depression</td>
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<td>CRF</td>
<td>Cardiorespiratory Fitness</td>
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<td>DXA</td>
<td>Dual-Energy X-Ray Absorptiometry</td>
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<tr>
<td>ECG</td>
<td>Electrocardiogram</td>
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<td>HRR</td>
<td>Heart Rate Reserve</td>
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<tr>
<td>ICC</td>
<td>Intra-Class Correlation</td>
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<tr>
<td>LTPA</td>
<td>Leisure-Time Physical Activity</td>
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<td>MVPA</td>
<td>Moderate-to-Vigorous Physical Activity</td>
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<td>Non-REM</td>
<td>Non-Rapid Eye Movement</td>
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<td>PA</td>
<td>Physical Activity</td>
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<td>PSG</td>
<td>Polysomnography</td>
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<tr>
<td>PSQI</td>
<td>Pittsburgh Sleep Quality Index</td>
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<tr>
<td>REM</td>
<td>Rapid Eye Movement</td>
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<tr>
<td>SE</td>
<td>Sleep Efficiency</td>
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<td>SOL</td>
<td>Sleep Onset Latency</td>
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<td>SQ</td>
<td>Sleep Quality</td>
<td></td>
</tr>
<tr>
<td>SWS</td>
<td>Slow Wave Sleep</td>
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</tr>
<tr>
<td>TIB</td>
<td>Time in Bed</td>
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<tr>
<td>TST</td>
<td>Total Sleep Time</td>
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USDHHS......................................................... U.S. Department of Health and Human Services

VO₂ ................................................................. Volume of Oxygen Consumption

VO₂peak .......................................................... Peak Oxygen Consumption

WASO............................................................... Wake time After Sleep Onset

WEWALK ......................................................... Women’s Energy Expenditure in Walking Programs
CHAPTER 1

INTRODUCTION

Sleep is a necessary biologic process that sustains life and poor sleep can adversely impact overall health and quality of life (Mukherjee et al., 2015; Okun, 2011; Shepard et al., 2005). Normal human sleep can be divided into two distinct states: rapid eye movement (REM) and non-REM sleep (Carskadon & Dement, 2011). Normal adult humans enter sleep through the non-REM state which is further subdivided into three stages in which sleep progressively becomes deeper with each subsequent stage (Carskadon & Dement, 2011). The first REM sleep episode occurs about 80 to 100 minutes after sleep onset and then thereafter, non-REM and REM sleep alternate throughout the sleep period in a cyclical pattern at approximately 90 to 110-minute intervals (Carskadon & Dement, 2011).

Despite the biological necessity of sleep, sleep disorders and impairments are common in the United States (Ford, Cunningham, Giles, & Croft, 2015; Ram, Seirawan, Kumar, & Clark, 2010). Poor or insufficient sleep has been consistently demonstrated in sleep research to have adverse effects on performance of routine daily tasks, carbohydrate metabolism, endocrine and immune function, appetite regulation, and mental health (Ford & Cooper-Patrick, 2001; Spiegel, Leproult, & Cauter, 1999; Spiegel, Tasali, Penev, & Van Cauter, 2004; Terre, 2014; Van Cauter et al., 1994; Van Cauter, Spiegel, Tasali, & Leproult, 2008) which may subsequently lead to an increased risk of morbidity (e.g.
obesity, cancer, cardiovascular and metabolic diseases, and psychological disorders) and all-cause mortality (Jean-Louis et al., 2014; Koyanagi et al., 2014; Liu, Wheaton, Chapman, & Croft, 2013; Luyster, Strollo, Zee, & Walsh, 2012; Zawisza, Tobiasz-Adamczyk, Galas, & Brzyska, 2014).

Sleep is a modifiable behavior that commonly fluctuates from night to night within the same individual and varies across the lifespan (Dillon et al., 2014). These nightly variations are present in both behavioral (i.e. bedtime, arising time, and time-in-bed [TIB]) and physiological (i.e. total sleep time [TST], sleep onset latency [SOL], wake time after sleep onset [WASO], number of awakenings, and activity counts) sleep parameters (Dillon et al., 2014; Knutson, Rathouz, Yan, Liu, & Lauderdale, 2007; van Hilten et al., 1993). Most of the existing sleep research has examined the mean levels of sleep parameters even though multiple nights of data are collected (Bei, Wiley, Trinder, & Manber, 2015). On the other hand, night-to-night variations in sleep have been less studied; however, elevated night-to-night variability in sleep/wake schedule is a common characteristic of insomnia and has been observed to impact sleep architecture, subjective mood states, psychomotor performance, and physiological arousal (Buysse et al., 2010; Taub, 1978; Vallieres, Ivers, Bastien, Beaulieu-Bonneau, & Morin, 2005). Also, high night-to-night variability in sleep duration was demonstrated to be associated with several health outcomes including obesity, diabetes, depression, and heart failure as well as poorer self-reported health status (Bei et al., 2015; Patel et al., 2014).

Identifying non-pharmacological approaches to improving sleep is necessary and physical activity (PA) is one alternative that has received considerable attention. In epidemiological studies, a significant positive association between PA levels and self-
reported sleep quality (SQ) has been demonstrated in multiple populations varying in age and demographics (Brassington & Hicks, 1995; Wennman et al., 2014; Youngstedt & Kline, 2006). Recently, there is evidence demonstrating a bidirectional relationship between sleep and PA (Lambiase, Gabriel, Kuller, & Matthews, 2013). The individual and seasonal variations in sleep and PA patterns add complexity to examining this reciprocal relationship, which is one reason why the relationship between sleep and exercise, a component of PA, is not fully understood. Furthermore, the bidirectional relationship between sleep and exercise may be moderated by multiple factors including sex, age, cardiorespiratory fitness (CRF) levels, and body composition (Kredlow, Capozzoli, Hearon, Calkins, & Otto, 2015; Kubitz, Landers, Petruzzello, & Han, 1996).

Similar to the general trend in sleep research, the traditional approach in the literature has investigated how PA/exercise produces changes in sleep at the mean level even though both of these behaviors vary within an individual from day to day and are measured over several days/ nights. Additionally, there is night-to-night variability in the physiological sleep parameters, and one of such parameters is activity counts after sleep onset (van Hilten et al., 1993).

Further, examination of the relationship between night-to-night fluctuations in sleep parameters, behavioral and physiological, with PA/exercise is of particular interest given the modifiability of both behaviors which could greatly influence the health and well-being of an individual. Recently, researchers have begun to examine this relationship at the intra-individual level (Buman, Hekler, Bliwise, & King, 2010; Lambiase et al., 2013; McGlinchey, Gershon, Eidelman, Kaplan, & Harvey, 2014; Tang & Sanborn, 2014). However, older women are understudied.
SCOPE OF THE STUDY

The overall goal of this dissertation was 1) to understand how acute exercise affects both behavioral and physiological sleep outcomes among older women during a training intervention and 2) to determine the impact of a four-month moderate-intensity exercise intervention on night-to-night variability in sleep among older women. The specific aims and research questions of this dissertation are outlined below.

Specific Aim 1

To investigate the acute effect of exercise on sleep outcomes among healthy, physically inactive older women by comparing structured exercise versus non-structured exercise control days during 4 months of exercise training.

Research Question 1.1: What acute effect does structured exercise have on sleep outcomes?

Research Question 1.2: Does exercise training impact the acute effect of exercise on sleep outcomes?

Specific Aim 2

To examine the impact of a four-month moderate-intensity exercise intervention on night-to-night variability in sleep among healthy, physically inactive older women.

Research Question 2.1: What effect does an exercise intervention have on night-to-night variability in sleep?

Research Question 2.2: Does exercise dose impact the effect of an exercise intervention on night-to-night variability in sleep?

Research Question 2.3: What effect does baseline CRF and changes in CRF have on night-to-night variability in sleep?
SOCIETAL TRENDS IN SLEEP PATTERNS

The timing of sleep in humans is influenced by several factors including the circadian pacemaker as well as external and internal influences (Beersma & Gordijn, 2006). Several models have been conceptualized to describe the influence of the circadian pacemaker on the alteration between states of wakefulness and sleep. One example is the two-process model of sleep regulation which suggests an interaction between homeostatic (i.e. need for sleep) and circadian processes (Daan, Beersma, & Borbely, 1984). The existence of within- and between-person differences in sleep timing indicates that in the context of everyday life, the sleep-wake cycle is influenced heavily by conscious decisions made within the framework of internal and external cues (Daan et al., 1984). These cues include personal habits, work schedules, cultural norms, and other social factors which may impact both the need for sleep and the circadian pacemaker (Beersma & Gordijn, 2006; Daan et al., 1984).

There are noticeable differences in sleep patterns and sleep-related difficulties by age, gender, and ethnicity (Adenekan et al., 2013; Dillon et al., 2014). However, discrepancies are evident in the literature regarding secular trends in sleep duration, which a recent review by Youngstedt et al. (2015) noted may be due to differences between cohorts and assessment tools as well as the limitations associated with self-
reported measures of sleep duration. This review observed no significant decrements in objectively measured sleep duration over the past 50 years among healthy sleepers, which contradicts the notion that our society is currently experiencing an epidemic of insufficient sleep (Youngstedt et al., 2015). On the other hand, poor SQ is very prevalent in the U.S. with one study demonstrating that about 62% of a large representative sample of Americans self-reported this sleep problem (Leger, Poursain, Neubauer, & Uchiyama, 2008). The prevalence of sleep disorders, such as insomnia and sleep-disordered breathing, has also increased over the years in the U.S. (Ford et al., 2015; Peppard et al., 2013).

Furthermore, sleep patterns tend to change over the course of one’s life which is evident by the existence of age-related trends in sleep duration and other sleep parameters (Basner et al., 2007; Ohayon, Carskadon, Guilleminault, & Vitiello, 2004). Basner and colleagues (2007) described the relationship between self-reported sleep duration and age as U-shaped with the shortest sleep duration occurring at ages 45 to 54 years. There are also age-related differences in sleep behaviors including bedtime, arising time, and TIB (Thomas, Lichstein, Taylor, Riedel, & Bush, 2014). Older adults are more likely to spend the greatest amount of TIB because their sleep patterns consist of earlier bedtimes and later arising times compared to other age groups (Thomas et al., 2014). In terms of objectively measured sleep variables among adults, sleep latency, percentages of stage 1 and 2 sleep, and WASO increase significantly with age, while TST, sleep efficiency (SE), and percentage of slow wave sleep (SWS) and REM sleep decrease significantly with age (Ohayon et al., 2004). These noted changes in sleep architecture indicate that sleep becomes lighter and more fragmented as one ages. Also, the prevalence of sleep
disturbances increases with age and may be secondary to comorbid conditions and other complications associated with aging (Dillon et al., 2014).

Additionally, the amount of night-to-night variability in self-reported TST and number of nighttime awakenings is inversely related with age (Dillon et al., 2014). Possible reasons for this declining trend in variability among older adults may be due to a reduction in the daily demands that once influenced the amount of sleep obtained in their younger years, including parenting responsibilities and work schedules (Dillon et al., 2014). Also, the sex of an individual impacts nightly variability in some sleep parameters as evident by how females are more likely to demonstrate greater night-to-night variability in self-reported number of nighttime awakenings and SOL compared to males (Dillon et al., 2014). This possibly indicates that sleep among females may be more vulnerable to disruptions caused by environmental and/or hormonal changes (Dillon et al., 2014; Moline, Broch, Zak, & Gross, 2003). Specifically, longer menstrual cycle has been associated with poorer SE, greater total wake time, and elevated WASO measured via actigraphy in females between the ages of 20 and 40 years (Tworoger, Davis, Vitiello, Lentz, & McTiernan, 2005). Additional life cycle events that disrupt sleep among women include pregnancy, the postpartum period, and menopause (Moline et al., 2003).

Also, the transitioning period through menopause is associated with sleep-related difficulties, which become more prevalent after menopause as evident by how approximately 35%-60% of postmenopausal women self-report sleep disturbances as compared to 16%-42% of premenopausal women (National Institutes of Health, 2005). Specifically, insomnia is one sleep disorder prevalent among postmenopausal women and is commonly accompanied by elevated night-to-night variability in sleep patterns (Buysse
et al., 2010; Krystal, Edinger, Wohlgemuth, & Marsh, 1998; Moline et al., 2003; Vallieres et al., 2005).

Taken together, older adults tend to experience a higher prevalence of sleep disturbances in addition to changes in sleep architecture that results in lighter and more fragmented sleep in comparison to younger adults. Additionally, older women are particularly vulnerable to sleep disturbances and disorders that may affect the night-to-night variability in their sleep. Typically in sleep research, older women are understudied; thus, studying sleep outcomes, particularly night-to-night variability, among this population will advance the literature substantially.

**Effects of Sleep on Health Outcomes**

The growing evidence supporting the association between sleep and health identifies poor or insufficient sleep as a potential risk factor for several health outcomes including obesity, cancer, cardiovascular and metabolic diseases, psychological disorders, and premature mortality (Jean-Louis et al., 2014; Koyanagi et al., 2014; Liu et al., 2013; Luyster et al., 2012; Zawisza et al., 2014). The underlying mechanisms for this relationship between sleep and increased morbidity may be explained by how sleep is physiologically involved in glucose metabolism, endocrine and immune function, and appetite regulation (Ford & Cooper-Patrick, 2001; Spiegel et al., 1999, 2004; Terre, 2014; Van Cauter et al., 1994, 2008). Further, night-to-night fluctuations in sleep are common in which both behavioral and physiological sleep parameters may vary from night to night within the same individual (Knutson et al., 2007; van Hilten et al., 1993). Also, there is evidence demonstrating an association between several health outcomes, including obesity, diabetes, depression, heart failure, and poorer self-reported health
status, with greater night-to-night variability in sleep duration and timing (Bei et al., 2015; Patel et al., 2014).

**Epidemiological Studies – Evidence of a Reciprocal Relationship between Sleep and Exercise in Females**

As mentioned previously, older women are particularly vulnerable to sleep disturbances and disorders. Epidemiological evidence, from both cross-sectional and longitudinal study designs, has accumulated in support of a relationship between sleep and PA in older females. For example, cross-sectional studies with predominantly female samples (>55%) demonstrate that older adults who are physically active are more likely to self-report better SQ as measured by the Pittsburgh Sleep Quality Index (PSQI) scores as well as be more satisfied with the amount of sleep obtained, while those who are less active are more likely to report frequent insomnia symptoms and poor SQ (Brassington & Hicks, 1995; Chasens, Sereika, Weaver, & Umlauf, 2007; Wennman et al., 2014). These findings concur with one cross-sectional study among middle-aged women which concluded that high levels of self-reported leisure time PA (LTPA) were associated with higher values of subjective SQ and SE (sleep diaries and PSQI) and objective sleep depth (polysomnography – PSG), all indicative of better sleep (Kline et al., 2013). Furthermore, older women that are physically active were more likely to self-report significantly longer TST, lower WASO, and greater SQ in comparison to their age, weight, and height matched inactive counterparts (de Guimaraes, de Carvalho, Yanaguibashi, & do Prado, 2008). While in another sample of older women, greater PA counts and more time spent in moderate-to-vigorous PA (MVPA) was significantly associated with less TST measured via actigraphy (Lambiase et al., 2013). Taken together, these data suggest that
high levels of PA are cross-sectionally associated with better subjective sleep and some objective measures.

Although findings from cross-sectional studies establish a relationship between sleep and PA in older women, the number of studies examining this relationship longitudinally is few. A recent two-year longitudinal study with a predominantly female sample (>55%) observed significant positive reciprocal correlations between baseline self-reported PA levels with follow-up measures of self-reported SQ as well as between baseline SQ with follow-up measures of PA among community-dwelling older adults (Holfeld & Ruthig, 2014). When performing additional statistical analyses using hierarchical regression models, higher self-reported SQ at baseline was demonstrated to be a significant predictor of higher levels of self-reported PA two years later, whereas baseline PA levels failed to predict subsequent SQ (Holfeld & Ruthig, 2014). Recent reviews summarizing the existing literature also concluded that poor sleep is predictive of lower PA in the general adult population (Chennaoui, Arnal, Sauvet, & Leger, 2015; Kline, 2014).

Overall, the above observational studies focused primarily on the relationship between mean-level sleep parameters and PA even though sleep is measured over the course of several nights. Recent observational studies have begun to examine the relationship at the intra-individual level using multilevel analyses (Lambiase et al., 2013; Tang & Sanborn, 2014). These studies show that night-to-night fluctuations in some of the sleep parameters are predictive of PA levels the following day in older women. However, the number of observational studies are limited for this population and the evidence from experimental studies is less convincing. The following sections examined
critically how experimental manipulation (i.e. acute and chronic) of exercise impacts sleep in order to provide additional evidence to support the proposed research for investigating night-to-night variability in sleep.

**EFFECTS OF EXERCISE ON SLEEP**

**Effects of Acute Exercise on Sleep**

An epidemiological survey demonstrated that middle-aged individuals generally perceive exercise as one of the most important behaviors for promoting good quality sleep the subsequent night (Urponen, Vuori, Hasan, & Partinen, 1988). Findings from meta-analyses consistently demonstrate that acute exercise has small to modest effects on TST, SWS, and REM sleep, indicating longer and deeper sleep following a single bout of exercise (Kredlow et al., 2015; Kubitz et al., 1996; Youngstedt, O'Connor, & Dishman, 1997). There were mixed findings or no associations observed for the remaining sleep parameters (Kredlow et al., 2015; Kubitz et al., 1996; Youngstedt et al. 1997). The findings of these meta-analyses pertained to the general adult population and the results may be slightly different for older women since both age and sex have been identified as significant moderators of the association between sleep and an acute bout of exercise (Kredlow et al., 2015; Kubitz et al., 1996).

However, there is a lack of studies examining the acute effects of exercise among older women. A recent study by Wang and Youngstedt (2014) demonstrated among inactive non-obese older women that an acute bout of moderate-intensity aerobic exercise resulted in significant improvements in SQ by reducing objective measures of WASO, number of nighttime awakenings, and movement while asleep as compared to baseline measures. King and colleagues (2008) also examined the acute effects of a single bout of
moderate-intensity endurance exercise on sleep during a 12-month training intervention among older adults (> 65% female) with sleep complaints. In the trained state, they did not observe any significant differences in any of the PSG sleep parameters (e.g. SOL, TST, SE, etc.) between exercise versus non-exercise days. Additionally, Baron et al. (2013) used multilevel modelling to analyze whether exercise duration was a predictor of sleep during the subsequent night among older women with insomnia who participated in a 16-week training intervention. They also did not observe a significant association between exercise duration and actigraphy measures of SOL, TST, WASO, and SE during the corresponding night. The timing of exercise during the day differed between these studies as did the health and training status of the participants, which may explain some of the inconsistencies. Additionally, prominent limitations include small sample sizes (≤ 15 participants) and limited assessments (i.e., two measured sleep objectively for only two consecutive nights, with one following a day of exercise and the other following a non-exercise day) (King et al., 2008; Wang & Youngstedt, 2014).

Another recent study performed a secondary analysis of a lifestyle intervention trial in 79 community-dwelling older adults (female > 80%) and observed that a greater amount of self-reported MVPA the day before was significantly associated with a higher self-reported SQ the subsequent night (Dzierzewski et al., 2014). This relationship was reciprocal in that participants reported being more physically active following nights in which they self-reported higher SQ. However, these findings may be biased due to the participants recording the previous day’s exercise along with SQ from the night before in the morning upon awakening. Although the sample size was larger than the other studies, the use of only subjective measures for sleep and exercise was a limitation. Additional
research is needed among older women since the literature is quite limited due to the number of studies, sample size, and methods for quantifying sleep, thus making it difficult to determine the effect of an acute bout of exercise on sleep parameters among older women.

**Effects of Chronic Exercise on Sleep**

Regularly exercising over time leads to physiological adaptations that may impact sleep differently than an acute bout of exercise. There is evidence suggesting that chronic exercise improves sleep (Buman & King, 2010; Driver & Taylor, 2000). However, there are noted differences depending on population characteristics, training protocols, subjective versus objective measures of sleep, and statistical control for moderating factors. Overall, exercise training appears to have small to moderate effects on subjective and objective metrics of sleep in older adults. Yang and colleagues (2012) demonstrated in a pooled analysis of five trials among middle-aged to older adults that participation in exercise training resulted in significant improvements in global PSQI scores and two of its subdomains: SOL and use of sleep medication. In regards to the effects of chronic exercise on objectively measured sleep parameters, two meta-analyses demonstrated significant but small effect sizes for SOL and TST in the general adult population (Kredlow et al., 2015; Kubitz et al., 1996). Mixed findings were observed for the other sleep parameters (Kredlow et al., 2015; Kubitz et al., 1996).

Experimental training studies with a sample size greater than 50 participants typically measure sleep subjectively via questionnaires, sleep diaries, PSQI, and/or Likert-scale indices. Several studies with predominantly female samples (>55%) have shown aerobic exercise of moderate-intensity to have a positive effect on self-reported
SQ among older adults (Benloucif et al., 2004; Fragoso et al., 2015; King et al., 2008; King, Oman, Brassington, Bliwise, & Haskell, 1997; Reid et al., 2010). In contrast, Stevenson & Topp (1990) did not observe self-reported SQ to improve significantly in either the low- (30-40% of heart rate reserve [HRR]) or moderate-intensity (60-70% HRR) exercise groups post-intervention among older community-dwelling adults nor was there a difference in self-reported SQ between exercise interventions. However, the amount of sleep did improve significantly in both groups, but there were no between group differences (Stevenson & Topp, 1990). Exercise training programs employing alternative modes of exercise, including progressive resistance training and Tai chi, also demonstrated significant improvements in the global PSQI score and some of its subscales post-intervention among older adults (Irwin, Olmstead, & Motivala, 2008; Nguyen & Kruse, 2012; Singh, Clements, & Fiatarone, 1997; Singh et al., 2005).

In regards to studies with all-female participants, the majority report similar findings as previously established in that self-reported SQ improved significantly over time in the exercise group (Baron et al., 2013; Cai, Chen, & Wen, 2014; Kline et al., 2012; Mansikkamaki et al., 2012; Payne, Held, Thorpe, & Shaw, 2008); while others found no significant associations (Elavsky & McAuley, 2007; Tworoger et al., 2003; Wilbur, Miller, McDevitt, Wang, & Miller, 2005). Among those studies that reported no significant intervention effect on subjective measures of sleep, adherence rates, physical activity levels outside of the structured intervention as well as the amount and timing of exercise impacted the effect of the exercise intervention on SQ (Tworoger et al., 2003; Wilbur et al., 2005). One study noted that, as adherence to the exercise prescription increased, sleep symptoms among middle-aged women improved significantly (Wilbur et
Tworoger and colleagues (2003) also observed an effect of timing of exercise: those who averaged at least 225 minutes/week of moderate intensity exercise in the morning were less likely to self-report poor SQ in comparison to those who exercised less than 180 minutes/week, while among evening exercisers, poor SQ was more likely to be reported by those averaging at least 180 minutes/week as compared to those who exercised less than 180 minutes/week. Furthermore, a significant linear dose-response relationship between exercise dose varying in energy expenditure and subjective SQ was demonstrated among postmenopausal (Kline et al., 2012). All of the exercise groups demonstrated significantly lower odds of self-reporting sleep disturbances post-intervention in comparison to the control group. However, only women in the exercise group expending 12 kcals per kg of body weight experienced a significantly greater improvement in subjective SQ compared to the control group post-intervention (Kline et al., 2012). This observation possibly indicates that the amount of exercise may impact its effect on self-reported SQ in comparison to a no-exercise control group. Taken together, these intervention studies demonstrate that exercise training has beneficial effects on subjective measures of sleep in older women.

These findings are expanded upon in other studies composed of a predominantly female sample (>65%) in which objective measures of sleep were used. Among some of these studies, chronic exercise resulted in beneficial effects on actigraphic SE and PSG measures of the number of nighttime awakenings during the first third of the sleep period and time spent in Stages 1 and 2 (King et al., 2008; Tanaka et al., 2002). On the other hand, mixed findings are noted for exercise interventions that incorporated a social activity as part of the intervention; some demonstrated significant increases in objectively
measured TST, SE, percentage of time in SWS, and duration of REM sleep among older adults (Naylor et al., 2000; Richards et al., 2011), while others reported no change (Benloucif et al., 2004). Among the few studies that measured sleep objectively via wrist actigraphy in all-female samples, TST and SE increased significantly among older women with insomnia who were randomized to the exercise group (Baron et al., 2013); whereas among older women with breast cancer, the only sleep parameters to significantly improve post-intervention were WASO and activity counts (Payne et al., 2008). Thus, the health status of the participant and the type of intervention may impact the effect of chronic exercise on objectively measured sleep in older women.

Research examining the effect of exercise training on night-to-night fluctuations in sleep among older adults is quite limited. The health implications for high night-to-night variability in sleep duration and timing are suggestive of several health outcomes including obesity, diabetes, depression, heart failure, and poorer self-reported health status (Bei et al., 2015; Patel et al., 2014). Thus, there is a strong need for further research to refine our understanding of the health impact(s) of night-to-night variability in sleep, particularly in response to an exercise intervention. One study, composed of a predominantly female sample (n > 65%) of sedentary older adults (mean age = 61 years) with sleep complaints, investigated the impact of a 12-month moderate-intensity aerobic exercise intervention on night-to-night fluctuations in self-reported sleep (Buman et al., 2010). At 12-months, the exercise group demonstrated a significant lower amount of night-to-night fluctuations in self-reported SOL in comparison to the control group (Buman et al., 2010). There was an average reduction in night-to-night variability in SOL by about 10 minutes in the exercise group as compared to an increase of 6 minutes in the
control group post-intervention (Buman et al., 2010). This decrease occurred independent of changes in nightly variations in TIB and mean-level changes in SOL. However, the use of self-reported measures of sleep is a noted limitation. But the improvements observed in night-to-night variation are promising and support continued investigation of this important sleep parameter.

The lack of studies using objective measures of sleep in older women as well as the noted inconsistencies in the findings demonstrate that additional research with a better design is needed in this population in order to clarify the effect of chronic exercise on sleep. Specifically, there is little evidence investigating the effect that exercise may have on night-to-night variability in sleep outcomes among older women using objective measures of sleep.

**MODERATING/MEDIATING FACTORS**

Since individuals have some control over the amount of TIB they spend each night, variability is common within an individual and between individuals and it is difficult to determine what constitutes normal variability. Furthermore, both sleep and exercise are modifiable behaviors that change over time, which explains why the relationship between sleep and exercise could be modulated/mediated by several factors including individual (e.g. sex, age, baseline PA levels, body composition, and CRF level) and exercise characteristics (e.g. intensity, time of day, and duration). Moderators precede the outcome and include characteristics of the participant at baseline (Kraemer, Wilson, Fairburn, & Agras, 2002). In contrast, mediators occur in between the factor it mediates and the outcome and include changes occurring during the intervention period (Kraemer et al., 2002).
Participant Characteristics

Sex and Age

Sex differences in TIB have been noted in the literature in which females tend to spend significantly more TIB in comparison to males (Thomas et al., 2014). Also, females report significantly longer SOL and a greater number of nighttime awakenings as well as a higher intra-individual variability in these sleep parameters compared to males (Dillon et al., 2014; Middelkoop, Smilde-van den Doel, Neven, Kamphuisen, & Springer, 1996). Furthermore, two meta-analyses identified participant sex as a significant moderator of the relationship between acute exercise and sleep in the general adult population (Kredlow et al., 2015; Kubitz et al., 1996). Specifically, Kredlow and colleagues (2015) observed that acute exercise reduced Stage 1 sleep and WASO in males more than in females; furthermore, Kubitz et al. (1996) found that the beneficial effect of acute exercise on REM sleep was greater in females. Mixed findings were also reported for the effect of sex on the relationship between chronic exercise and REM sleep in the general adult population (Kredlow et al., 2015; Kubitz et al., 1996), in which only Kubitz and colleagues (1996) noted that chronic exercise benefited REM sleep more in females than in males. The inconsistency in the moderating analyses of the effect of sex on the relationship between sleep and exercise may be impacted by the underrepresentation of females in the studies included in the meta-analyses. Also, when females were included, a noted limitation among studies was the failure to control for life events that disrupt sleep among women including menopausal status (Driver & Taylor, 2000).
Age is consistently identified in the literature as being a strong modifying factor of sleep patterns and quality (Carskadon & Dement, 2011; Thomas et al., 2014). In general, bedtimes tend to move earlier with increasing age, whereas a quadratic relation is observed between arising time and total TIB with age (Thomas et al., 2014). Given these age-related differences in sleep behaviors, two meta-analyses did not find the acute effects of exercise on sleep to be significantly moderated by age in the general adult population (Kredlow et al., 2015; Kubitz et al., 1996). Additionally, CRF level plays a role in the association among exercise, age, and sleep, in which the greatest effect of an acute bout of exercise on sleep was more likely to be observed among older non-fit individuals (Kubitz et al., 1996).

As for chronic exercise, the findings are inconsistent in that there is evidence to support that older adults experience greater beneficial effects of exercise on sleep than younger adults (Driver & Taylor, 2000; Kubitz et al., 1996) while others show the reverse and show reduced benefits among older adults (Kredlow et al., 2015; Oudegeest-Sander et al., 2012). Kredlow and colleagues (2015) established in a recent meta-analysis that age significantly moderated the relationship between chronic exercise and SOL in the general adult population, indicating that older adults had smaller reductions in SOL from chronic exercise than younger adults. On the other hand, Kubitz et al. (1996) observed chronic exercise to have a greater beneficial effect on REM sleep among older adults in comparison to younger adults. Additionally, a recent study observed a significant positive correlation between energy expenditure and SE among young adults (mean age: 27 years), but not among the older participants (mean age: 65 years) (Oudegeest-Sander et al., 2012). In contrast, age did not significantly moderate the effect of chronic exercise on
any of the PSG sleep parameters among older adults between the ages of 55 and 79 years with sleep complaints (Buman, Heckler, Bliwise, & King, 2011). However, the restriction of age to older adults may have mitigated the moderating effect of age by limiting the range of ages included within the sample. Based on these variable study findings, it remains unclear whether the effect of exercise on certain sleep parameters may be impacted by age and sex of the participant.

**Stress/Perceived Stress and Depressive Symptoms**

Epidemiological evidence demonstrates that high levels of stress are significantly associated with increased depressive symptoms and sleep complaints (Leblanc, Desjardins, & Desgagne, 2015; Sawatzky et al., 2012). Furthermore, individuals who are physically active are more likely to report lower levels of perceived stress and depressive symptoms as well as fewer sleep complaints (Dunn, Trivedi, & O’Neal, 2001; Feng, Zhang, Du, Ye, & He, 2014; Gerber et al., 2014), demonstrating an interrelationship between these variables. Perceived exposure to stress has been noted in the literature to be significantly associated with low self-reported SQ, but not with actigraphic measures of sleep (Friedman, Brooks, Bliwise, Yesavage, & Wicks, 1995; Tworoger et al., 2005). Similarly, there were no significant differences in the majority of PSG sleep parameters between midlife women with varying levels of chronic stress with the exception of WASO, which was observed to be significantly higher among midlife women with high chronic stress in comparison to those characterized as having low or moderate chronic stress (Hall et al., 2015).

Older adults self-reporting regular participation in an exercise program are more likely to report lower levels of anxiety, depression, and stress in comparison to those who
were more sedentary (Brassington & Hicks, 1995). Additionally, another study demonstrated that a 10-week progressive resistance training program elicited improvements in both depressive symptoms and self-reported SOL and sleep disturbances among depressed older adults (Singh et al., 1997). Similarly, Buman and colleagues (2011) demonstrated in a mediation analysis that decreased depressive symptoms significantly mediated change in percentage of time in Stage 1 sleep and number of awakenings after sleep onset at 12 months among older adults randomized to the exercise group.

Baseline PA Levels

Individuals who are less active at baseline may experience greater benefits in sleep as a result of exercise, as was seen in a study of older adults with sleep complaints who participated in a 12-month moderate-intensity exercise program (Buman et al., 2011). Specifically, individuals with low self-reported baseline MVPA levels were more likely to see greater increases in the percentage of time spent in Stage 2 sleep and reductions in the number of awakenings in the first third of their sleep period, indicative of greater improvement in sleep, relative to those self-reporting more MVPA at baseline (Buman et al., 2011). This concurs with findings from cross-sectional studies which have consistently demonstrated that individuals who are less active are more likely to self-report poor SQ (Chasens et al., 2007). Therefore, an exercise intervention may have a greater impact on sleep among those who are physically inactive and have poor quality of sleep.
Body Composition

Epidemiological evidence demonstrates a significant relationship between body composition and sleep patterns as well as a significant relationship between PA and body weight (Bailey et al., 2014; U.S. Department of Health and Human Services [USDHHS], 2008; van den Berg et al., 2008). Specifically, sleep duration measured objectively and subjectively portrays a U-shaped association with body mass index (BMI) and body fat percentage depending on the study design and sample characteristics (Bailey et al., 2014; Knutson et al., 2007; van den Berg et al., 2008). A change in BMI was identified as a significant mediator of the relationship between chronic exercise and number of awakenings in the first third of sleep among older adults with sleep complaints (Buman et al., 2011), indicating that individuals who experienced a greater reduction in their BMI as a result of the exercise intervention were more likely to experience a larger decline in the number of awakenings. This reduction in the number of awakenings may be reflective of changes in sleep-disordered breathing; however, the exclusion criteria for the main study excluded participants with sleep apnea (Buman et al., 2011). In contrast, Tworoger et al. (2003) did not observe a change in BMI as a potential mechanism mediating the effect of exercise on subjective SQ among overweight/obese postmenopausal women.

CRF Levels

The effect of CRF on the relationship between sleep and exercise remains unclear; however, CRF has been identified in several reviews and meta-analyses as a potential moderating/mediating factor of sleep (Buman & King, 2010; Chennaoui et al., 2015; Horne, 1981; Uchida et al., 2012; Youngstedt et al., 1997). Furthermore, there is evidence of interrelationships between exercise, sleep, and CRF (USDHHS, 2008), which may
explain the difficulty associated with quantifying the mediating effect of CRF on the relationship between sleep and exercise due to mixed findings. Several studies have been conducted to evaluate this association by comparing sleep parameters between physically fit and unfit individuals as well as by examining the effect of improved CRF on sleep following a training intervention; however, the majority of these studies have been conducted in males and/or younger individuals.

Among cross-sectional studies (>55% female), significant differences in several sleep parameters/symptoms measured subjectively and objectively have been noted between fit versus unfit individuals (Lee & Lin, 2007; Porter & Horne, 1981; Strand et al., 2013). Specifically, young and middle-aged adults classified with high fitness were observed to have significantly greater SWS time, lower global PSQI scores, fewer insomnia symptoms, later self-reported bed times, shorter self-reported SOL, and shorter sleep duration in comparison to unfit individuals (Lee & Lin, 2007; Porter & Horne, 1981; Strand et al., 2013). Additionally, a recent prospective analysis of the relationship between CRF and sleep demonstrated that each one-minute decline in treadmill performance during a maximal treadmill test between the ages of 51 and 56 years was associated with a 1.3% increase in the odds of incident sleep complaints among a subsample of women from the Aerobics Center Longitudinal Study (Dishman et al., 2015). In contrast, among young and older adults, CRF was not significantly correlated with accelerometry measured SE, SOL, TST, and number of awakenings (Oudegeest-Sander et al., 2012).

Furthermore, improvements in physical fitness following a training program among young women did not elicit significant changes to any of the objectively measured
sleep parameters (Driver, Meintjes, Rogers, & Shapiro, 1988; Meintjes, Driver, & Shapiro, 1989). Specifically, no changes occurred in SOL, SWS onset latency, REM onset latency, TST, SE, nor number of awakenings, regardless of significant improvements in CRF (Meintjes et al., 1989). King et al. (1997) also found in their randomized controlled trial among older adults (> 60% female) that changes in CRF following a 16-week moderate-intensity exercise program did not predict significant improvements in any of the subjectively measured sleep parameters. In contrast, Tworoger et al. (2003) compared the percentage of change in CRF across participants randomized to either a moderate-intensity exercise or stretching program and observed that postmenopausal women who had at least a 10% increase in their CRF were significantly less likely to self-report poor SQ or short sleep duration in comparison to those with decreased or stable CRF levels. Thus, the magnitude of change in CRF may be an important indicator of whether an exercise intervention elicits favorable changes in sleep post-intervention.

**Exercise Characteristics**

The effect of exercise on sleep may be impacted by the characteristics of the exercise session including duration, volume, time of day, intensity, light exposure, and type of exercise. These potential moderators may have contradictory effects on this relationship similar to the individual characteristics. However, a recent meta-analysis by Kredlow and colleagues (2015) noted that several of the 66 studies included were vague in their description of the exercise performed by participants which limited the ability to perform a more comprehensive moderator analysis.
Regardless, duration of exercise has been identified as a consistent moderator of the relationship between sleep and exercise (Kredlow et al., 2015; Kubitz et al., 1996; Youngstedt et al., 1997). Specifically, longer durations of acute exercise bouts were significantly associated greater increases in TST, SWS, and Stage 4 sleep as well as larger decreases in SOL and REM sleep as compared to non-exercise days; whereas longer bouts of chronic exercise was only significantly related to shorter SOL. Total number of weeks as well as the total duration of an exercise program were also noted to significantly moderate the effects of chronic exercise on TST in which the effect sizes were smaller for exercise programs of longer duration (Kredlow et al., 2015). Furthermore, the effect of chronic exercise on SQ, SOL, or SE was not significantly moderated by the duration of an exercise program (Kredlow et al., 2015).

Time of day that exercise is performed may be another significant moderator impacting the relationship between sleep and exercise; however the findings are mixed (Kredlow et al., 2015; Kubitz et al., 1996; Youngstedt et al., 1997). Some reviews report a positive effect of an acute bout of exercise on sleep in which a significant decrease in SOL, WASO, and REM sleep was observed when the exercise session was performed three to eight hours before sleep (Chennaoui et al., 2015; Youngstedt et al., 1997). While another meta-analysis reported the opposite in that an acute bout of exercise performed three to eight hours before sleep had a negative effect (Kredlow et al., 2015). The effects of acute exercise on TST, SE, SWS, Stage 2 sleep, or REM sleep onset were not moderated by time of day (Kredlow et al., 2015). The number of studies that measured or controlled for the moderating effects of exercise time in chronic exercise interventions are few among older adults. One pilot study assessed whether daily exercise performed in
the morning or evening for 14 continuous days was sufficient enough to elicit favorable changes to sleep and did not observe any significant differences between morning and evening exercisers in self-reported SQ among older adults (Benloucif et al., 2004). Fourteen days may not be considered a chronic exercise program, but these finding are in accordance with other research using a longer intervention period among adults between the ages of 30 to 55 years (Passos et al., 2011). In contrast, another study lasting 12 months among postmenopausal women demonstrated that morning exercisers who accumulated at least 225 minutes per week were less likely to self-report difficulty falling asleep in comparison to those who accumulated less than 180 minutes per week (Tworoger et al., 2003). Evening exercisers who exercised 180 or more minutes per week had an increased risk of self-reporting difficulty with falling asleep as compared to those who exercised less (Tworoger et al., 2003). The moderating effect of exercise characteristics may be a combination of multiple factors in which both the total volume of exercise as well as the time of day may impact the effect of chronic exercise on sleep.

**SUMMARY**

The relationship between sleep and exercise is quite complex with several moderating/mediating factors that add to the difficulty of disassociating the role of either component. Furthermore, the majority of the studies among older adults with women (>50%) have used self-reported measures of sleep, especially among larger experimental studies with a sample size greater than 50 participants. Additionally, most studies often examine the relationship between sleep and exercise at the mean-level even though sleep is measured over the course of several nights and night-to-night fluctuations in sleep are common. In the few studies that have investigated night-to-night variability in sleep
among older adults, there was insufficient data collection for comparing sleep parameters following exercise versus non-exercise days. Furthermore, older women are an understudied population. Therefore, the proposed studies of this dissertation advanced the literature by using objective measures of sleep via actigraphy to estimate sleep patterns across multiple nights in the home environment in addition to using more sophisticated statistical analyses to investigate night-to-night fluctuations in sleep among physically inactive older women. Specifically, these studies examined how an acute bout of exercise impacts sleep during the corresponding night as well as how participating in 4 months of moderate-intensity exercise impacts night-to-night variability in objectively-measured sleep outcomes.
CHAPTER 3

GENERAL METHODOLOGY

The two studies that comprise this dissertation used data collected in the Women’s Energy Expenditure in Walking Programs (WEWALK) study. The WEWALK study was a clinical exercise trial examining the effects of two walking programs with different energy expenditures on non-exercise activity thermogenesis in physically inactive older women (ClinicalTrials.gov identifier: NCT01722136).

PARTICIPANTS AND ENROLLMENT PROCESS

Participants were recruited from the Columbia, South Carolina metropolitan area between October, 2012 and December, 2014. Potential participants were required to be female, non-smoker, weight stable (+/- 3%) for the previous three months, physically inactive (did not exercise more than 20 minutes three times per week), had a BMI \( \geq 18 \) and \( \leq 30 \) kg/m\(^2\), aged 60 – 75 years, and were free from cardiovascular disease, diabetes, or any other condition that may prevent them from adhering to the study protocol. Also, individuals reporting excessive use of caffeine (> 500 mg) or contraindications to exercise according to American College of Sports Medicine were not allowed to participate. The use of medications that affected metabolism was an additional criterion for exclusion from the study.

All participants answered questionnaires and underwent a series of medical tests to identify any medical conditions that could potentially interfere with participation in the
exercise intervention. These included medical history and exam, depression (Center for Epidemiologic Studies Depression Scale [CES-D]), resting blood pressure, resting electrocardiogram (ECG), graded exercise test, dual-energy X-ray absorptiometry (DXA), and standard blood tests that included a comprehensive metabolic profile, a complete blood count with differential, and a thyroid profile. Individuals with abnormal results were excluded.

**STUDY INTERVENTION**

Participants were randomized to one of two moderate-intensity walking programs with different doses of energy expenditure: low dose (8 kilocalories (kcal) per kilogram (kg) of body weight per week) or high dose (14 kcal/kg of body weight per week). The exercise training period for both groups was 4 months and each training session occurred in a research facility under supervision. Participants in both groups walked three to four times a week on treadmills. The two different doses were achieved by varying the duration of exercise in order for the participants to reach their energy expenditure goals according to body size and exercise dosage (8 kcal/kg versus 14 kcal/kg). Weekly energy expenditure was determined by multiplying the participant’s weight by their assigned dosage and this was closely monitored throughout the duration of the 4-month intervention.

Due to the physically inactive state of the participants, the exercise intensity and weekly caloric expenditure increased incrementally to reduce the risk of injury. Training intensity increased by 5% every two weeks from 40% to a target level of 50-55% of the participant’s heart rate reserve (HRR), which was obtained during the baseline fitness test. Both exercise groups began at a weekly caloric expenditure of 4 kcal/kg body weight
during the first week of the intervention and then progressed until their assigned exercise dosage (low-dose: 8 kcal/kg body weight; high-dose: 14 kcal/kg body weight) was reached by week five in the low-dose group and week eight in the high-dose group. Each exercise session began and ended with a 3-minute warm-up and cool-down. HR monitors (FT1; Polar, Lake Success, NY, USA) were worn to monitor training intensity continuously throughout each exercise session and HR was recorded every five minutes. Blood pressure was measured before, at the mid-point, and after each exercise session.

Compliance to the exercise protocol (frequency, intensity, and duration) for each participant was reviewed weekly and any participant missing an exercise session without notifying study personnel was contacted via phone to encourage further attendance. Also, each time a participant completed an exercise session, their ID was entered into a monthly raffle with a $20 incentive to promote adherence.

Measurements

Cardiorespiratory Fitness (CRF)

CRF was measured in all participants at baseline and post-intervention (month 4) using a graded treadmill test. The test involved an incremental protocol where participants walked at a self-selected, comfortable but challenging speed that remained constant throughout the test with the incline increasing by 2% every 2 minutes. Volume of oxygen consumption (VO₂) via a metabolic cart (True Max 2400; ParvoMedics, Sandy, UT, USA) and HR via a standard 12-lead ECG (Q-Stress ®; Cardiac Science, Bothell, WA, USA) were monitored continuously during the progression of the test. Blood pressure was measured 30 seconds into each stage of the test. Two of four criteria needed to be achieved in order for the test to be considered satisfactory: a respiratory
exchange ratio greater than or equal to 1.10; a rating of perceived exertion greater than or equal to 17 on a scale ranging from 6 to 20; achieving a maximum heart rate greater than 90% of age-predicted maximum HR (= 220 – age); and/or a plateau in HR or VO₂. Peak oxygen consumption (VO₂peak) was determined by the highest 30-second averaged VO₂ value during the test.

**Sleep Parameters**

Sleep parameters were assessed objectively by an actigraphic accelerometer (GT3X+; Actigraph, Pensacola, FL, USA). Participants wore the monitors on the wrist of the non-dominant arm for up to 14 days of continual wear at baseline, mid-, and post-intervention. The participants were required to keep daily logs in which participants recorded the time they lay down and the time they moved to a sitting position or got out of bed. No other subjective information on how well one slept the night before was assessed.

Software provided by the manufacturer (ActiLife version 6.11.2) was used to analyze the actigraphy data. The data were assessed in 60-second epochs and the times recorded on the sleep logs were manually entered into the program to quantify TIB. The GT3X+ provides objective measures of activity counts and body position as well as information on the environment via an ambient light sensor. A standardized approach developed by Patel and colleagues (2015) was used to define TIB. Missing entries on logs and inaccurate recordings of bed/awake times were estimated or adjusted, respectively, based on the hierarchical ranking of inputs (i.e., sleep diary, light intensity, and activity counts) in order to improve the reproducibility of the values. The Cole-Kripke sleep scoring algorithm was used to determine when each participant was asleep or awake.
Application of this algorithm provides information on SOL (duration from specified bedtime to when the algorithm scored sleeping), TST (total length of time specified by the algorithm as being “asleep”), WASO (number of minutes the algorithm scored as being “awake” after sleep onset), frequency of awakenings (number of awakenings occurring during the sleep period), and activity counts during TIB.

Wrist actigraphy is a more cost-effective and less intensive alternative to PSG in sleep research as demonstrated by its utility in estimating sleep patterns across multiple nights in a home environment. A limitation of wrist actigraphy is that sleep is indirectly assessed through the application of an algorithm to distinguish between sleep and wakefulness. However, epoch-by-epoch analysis demonstrates the feasibility of wrist actigraphy in gathering objective measures of sleep data that are valid and in accordance with PSG recordings (de Souza et al., 2003; Taibi, Landis, & Vitiello, 2013). Furthermore, the use of the Cole-Kripke algorithm with the GT3X+ Actigraph worn on the non-dominant wrist has been observed to correctly identify 84.1% of all PSG epochs, including both sleep and wakefulness, demonstrating an overall satisfactory accuracy (Slater et al., 2015). Specifically, the GT3X+ produced similar estimates of TST and SE, an underestimation of SOL, and an overestimation of WASO in comparison to PSG recordings (Slater et al., 2015). Also, moderate relationships were indicated by intra-class correlations (ICCs) between PSG and GT3X+ measures of TST, SE, and WASO while a poor relationship was noted for SOL (Slater et al., 2015). When performing an epoch-by-epoch comparison with PSG measures of sleep, the GT3X+ correctly identified 89.7% of PSG sleep epochs as sleep and 45.6% of PSG wake epochs as awake indicating a
moderately high sensitivity and low specificity (Slater et al., 2015). The low specificity indicates another limitation in regards to the use of actigraphy for identification of wakefulness during sleep.

**Body Composition**

The DXA (Model 8743; GE Healthcare, Little Chalfont, United Kingdom) full body scan was used to measure body fat percentage, lean mass (kg), fat mass (kg), and fat free mass (kg) at baseline and post-intervention. Height was measured to the nearest 0.1 cm and weight was measured to the nearest 0.1 kg. Two measurements were taken for both height and weight and averages of each were used to calculate BMI (kg/m²). The effect of exercise on individual variability in sleep outcomes was assessed in both aims of this dissertation by controlling for BMI.

**STUDY 1 METHODOLOGY**

**Purpose**

This study addressed Specific Aim #1 which was to investigate the acute effect of exercise on sleep outcomes among healthy older women by comparing structured exercise versus non-structured exercise control days during 4 months of exercise training.

*Research Question 1.1:* What acute effect does structured exercise have on sleep outcomes?

*Research Question 1.2:* Does exercise training impact the acute effect of exercise on sleep outcomes?

**Hypothesis**

Objective sleep outcomes via actigraphy identified in the literature to change significantly following an acute bout of aerobic exercise in postmenopausal women
include WASO, number of awakenings, and activity counts (Wang & Youngstedt, 2014); and therefore, these sleep outcomes were hypothesized to be the most likely impacted by an acute bout of exercise.

**Study Design**

This study utilized a longitudinal study design.

**Study Population**

This study included a subsample (n = 51) who had sleep data available following at least three days of structured exercise and at least three days of without structured exercise at mid- and post-intervention. The justification for specifying three days of structured exercise and three days of non-structured exercise is based on one study which demonstrated that there was no difference between actigraphic measures of central tendency for sleep variables obtained over a three-day aggregate in comparison to seven- or fourteen-day aggregates among older adults (Rowe et al., 2008). The number of observations available per participant at each time point ranged from 6 to 14 nights (total number across both time points: 12 to 28 nights). The use of a multilevel regression model allowed for this wide range of data to be analyzed because this modelling technique is less sensitive to missing data as it does not assume each participant has the same number of observations or equal time intervals between observations (Hox, 2002). A term denoting time point was added to the analyses so that differences in training status between mid- and post-intervention could be accounted for. Also, since exercise sessions were scheduled during the week and occurred frequently on Fridays, weekend nights (Friday and Saturday) were included in order to increase the number of participants meeting the inclusion criteria. To control for the variability associated with including
weekend nights in the analysis, a dichotomous variable was included to compare weekdays (Sunday through Thursday) to weekends (Friday and Saturday) (Hashizaki, Nakajima, & Kume, 2015).

At mid-intervention, participants in both exercise groups would have reached their target energy expenditure dose. Also, by this time point, both groups were walking three to four times per week at an intensity of 50-55% of the participant’s HRR. The only difference between the groups in their exercise prescription was the duration of each session which varied from 35 to 40 minutes in the low-dose group to 55 to 60 minutes in the high-dose group. Given the incremental increase in the intensity and dose by mid-intervention, the acute effects of structured exercise were evaluated at this time point and at post-intervention.

**Statistical Analyses**

Baseline descriptive statistics were calculated and reported as means and standard deviations. Independent sample t-tests and chi-square tests were used to identify baseline differences between randomized conditions (low-dose versus high-dose) and those with complete versus incomplete actigraphy data. A multilevel statistical analysis was performed since the data were organized hierarchically where multiple nights of actigraphic sleep recordings were nested within 51 participants. This modeling approach allowed for the opportunity to determine whether structured exercise impacted sleep outcomes during the corresponding night both within (level 1: across days) and between (level 2: across persons) persons. Both behavioral (i.e. bedtime, arising time, and TIB) and physiological (i.e. TST, SOL, activity counts, WASO, and number of awakenings) sleep parameters were investigated in this study. Separate multilevel models with random
intercepts were run with each sleep outcome as the dependent variable. The independent variable of interest was structured exercise versus non-structured exercise days which was included in the models as a dichotomous variable. Each analysis was adjusted for time point (mid versus post-intervention), exercise dose (low versus high), and mean baseline value of the respective sleep parameter in Model 1 followed by additionally controlling for day of the week (weekday versus weekend), baseline BMI, and changes in BMI in Model 2. Due to the collinearity between BMI and VO2peak levels, Model 3 was also an extension of Model 1, but controlled for baseline VO2peak levels and changes in VO2peak levels instead of BMI. An interaction term for the ‘time point’ and ‘exercise/non-exercise day’ was added to the models to assess whether the acute effect of exercise on sleep varied as a function of training status. This interaction term was non-significant for all sleep parameters and therefore, was not included in the final models. Additionally, SOL, activity counts after sleep onset, and WASO were not normally distributed and therefore, the values were transformed to achieve normality of distribution. No other data transformations were needed for the remaining sleep parameters. Data were analyzed using PROC MIXED procedure in SAS software, Version 9.4 (SAS Institute, Cary, NC) and statistical significance was set at an alpha level of 0.05.

**Statistical Power**

The literature examining the effect of an acute bout of exercise on sleep parameters among older women is limited and therefore, the power estimations were based on a study in women of similar age (Wang & Youngstedt, 2014). Complete data were available on 15 physically inactive, postmenopausal women who wore an accelerometer at baseline (non-exercise condition) and then again after an exercise bout
at 60% of their peak oxygen consumption (VO₂peak). A multilevel model was run for each sleep parameter as the dependent variable with exercise condition (non-exercise versus exercise) as the independent variable in order to calculate the ICC. The standard error for the slope of exercise condition was calculated using the ICC and the available sample sizes at level 1 (n=6 days) and level 2 (n=51 participants) for this study (Raudenbush, Spybrook, Liu, & Congdon, 2005). The power estimates were calculated using the previously calculated standard errors, a small to medium sized effect (i.e. a Cohen’s d of 0.3), and an alpha of 0.05 (Snijders & Bosker, 1993). Given these criteria and the hypothesis, this study has an estimated power of 65.9%, 75.2%, and 65.9% for the three sleep parameters that are hypothesized to be impacted by exercise: WASO, number of awakenings, and activity counts, respectively. The magnitude of the change in these parameters may be affected by the lack of training and therefore, the estimated effect size may be an elevated estimate.

**Strengths and Limitations of Study 1**

The strengths of this study included the use of objective measures of sleep via actigraphy to estimate sleep patterns across multiple nights in the home environment, and using statistical analyses that account for night-to-night fluctuations in sleep among physically inactive older women. In addition, each exercise session was performed under supervision in a laboratory setting which allowed for adherence to exercise protocol to be monitored. There are limitations for this proposed study including how the results can only be generalized to healthy older women between the ages of 60 to 75 years. Additionally, the participants were not assessed for sleep complaints or disorders at baseline since sleep was neither a primary outcome of interest nor an exclusionary
criterion in the WEWALK study. This may potentially impact the results of this study in that the effect of exercise on sleep among participants with sleep complaints or disorders may be different in comparison to those without these problems. This study was also unable to account for every possible covariate of the sleep-exercise relationship including light exposure, naps, and stress/perceived stress levels. Also, the use of actigraphy does not allow for sleep stages to be examined; nevertheless, this objective measure is a more cost-effective and less intensive alternative to PSG because it provides the opportunity to measure multiple nights so that a comparison can be made between nights following exercise versus non-exercise days. Lastly, this study may not have enough power to detect an effect size of 0.3 for WASO, number of awakenings, and activity counts; however, the actual effect size may be different from that used in the power estimates, which were based on the limited data available in the literature from a physically inactive sample of postmenopausal women.

STUDY 2 METHODOLOGY

Purpose

This study addressed Specific Aim #2 which was to examine whether four months of moderate-intensity exercise impacted night-to-night variability in sleep among healthy, physically inactive older women.

Research Question 2.1: What effect does an exercise intervention have on night-to-night variability in sleep?

Research Question 2.2: Does exercise dose impact the effect of an exercise intervention on night-to-night variability in sleep?
Research Question 2.3: What effect does baseline CRF and changes in CRF have on night-to-night variability in sleep?

Hypotheses

It was hypothesized that chronic exercise training would significantly reduce night-to-night variability in sleep with the greatest reduction occurring among those participants randomized to the high-dose group in comparison to the low-dose group. Also, those participants with low baseline CRF or those with the greatest improvement in CRF would experience a greater reduction in night-to-night variability post-intervention.

Study Design

This study utilized a longitudinal study design.

Study Population

This study included a subsample of females enrolled in the WEWALK study (n = 53) who had at least 7 days of actigraphy sleep recordings for baseline, mid-intervention (2-month), and post-intervention (4-month) measurements. The first seven consecutive days of actigraphy data were used in this study in order to standardize the number of days among participants with complete baseline, mid-, and post-intervention data. This inclusion criterion was based on the findings of a previous study that concluded that at least seven nights of data collection is necessary for obtaining consistent measures of sleep via actigraphy among older adults when night-to-night variability is of primary interest (Rowe et al., 2008). This was done in order to reduce the amount of additional variability that may occur due to reasons other than normal night-to-night variability (e.g. variability due to longer data collection time [7+ days], variability due to varying number of weekend days across individuals, etc.).
Statistical Analyses

Baseline descriptive statistics, including individual means and standard deviations (SD) were calculated. Of the 72 women who completed the WEWALK study, only those with complete baseline, mid-, and post-intervention actigraphy data were included in the analysis (n=53). Additional analyses were performed to make comparisons between those with complete actigraphy data at baseline, mid-, and post-intervention with those missing any of the time points (n=19). Group differences in baseline characteristics between those participants with complete versus incomplete data in addition to those randomized to the low-dose versus high-dose exercise prescriptions were tested using t-tests and chi-square tests.

Means for each of the sleep parameters were calculated at each time point by averaging the 7 days of sleep data together for each individual. Nightly variability in each of the sleep parameters was calculated using the 7-day SD. Additionally, a coefficient of variation (CV) was computed for each sleep outcome by dividing the 7-day SD by the mean (SD/mean x 100%) for each individual in order to provide another measure of intra-individual variability (Buman, Hekler, Bliwise, & King, 2010; Knutson et al., 2007; Rowe et al., 2008). High values in either of these measures of nightly variability indicate irregularity. The literature considers CV as a more conservative measure of intra-individual variability over the 7-day SD because it references the mean (Buman et al., 2010). Since SD is a measure of how much the data points deviate from the mean, it is possible that higher individual-level means will occur with higher variability when using the raw score of variability (SD). The likelihood of this occurring would be adjusted for when using the CV. Therefore, both measures of variability were examined and any
differences were noted. Additionally, both measures of variability were found to not be normally distributed and therefore, the values were transformed using the (natural) logarithm function to achieve normality of distribution. No data transformations were needed for the mean-level measures of each sleep parameter.

The amount of nightly variability via 7-day SD and CV were calculated at each time point (baseline, mid-, and post-intervention) in the study in order to assess whether changes occurred across time in response to 4 months of moderate-intensity exercise and to assess whether those changes differed between the two doses of energy expenditure. Separate models were run for each sleep parameter with the individual 7-day SD or the CV as the dependent variable. Similar but separate models were run using the individual mean for each sleep outcome as the dependent variable to determine if similar changes occurred along with both measure of nightly variability. A repeated measures analysis was conducted using a mixed effects model to test the main effects of time and group. Due to the collinearity between the covariates, separate models were run. Model 1 adjusted for baseline VO$_{2peak}$ levels and changes in VO$_{2peak}$ as covariates and Model 2 adjusted for BMI (treated as a time-dependent covariate). Significant time effects were followed by post hoc tests to determine which specific time points differed significantly. P-values were adjusted for multiple comparisons using the Tukey-Kramer procedure. A group x time effect was tested and found to be non-significant for all of the sleep parameters and therefore, this interaction term was not included in the final models. Estimates of unstandardized effect sizes were calculated for each sleep parameter and represent the difference between mid- and post-intervention with baseline. The magnitude of the effect size was based on Cohen’s d (Cohen, 1988). Statistical
significance was set at $P < 0.05$ and all analyses were performed in SAS 9.4 (SAS Institute Inc., Cary, NC).

**Statistical Power**

The literature examining the intra-individual variability of objectively measured sleep outcomes is limited and therefore, the effect sizes were obtained from one investigation examining the impact of a moderate-intensity aerobic exercise intervention on night-to-night fluctuations in self-reported sleep (Buman et al., 2010). The study found an effect size (Cohen’s d) of 0.41, 0.29, 0.35, 0.15, and 0.04 for 6-month measures of self-reported SOL, TIB, and number of awakenings, bedtimes, and arising times, respectively. To estimate power, alpha was set at 0.05 and the correlation among repeated measures was set at moderate level of 0.5 due to this parameter not being available in the literature. Based on a sample size of 54 participants and a repeated measures analysis, this study has > 80% power to detect an effect size greater than 0.18 which indicates that this study may not have enough power to detect the effect sizes found in the literature for bedtime or arising time.

**Strengths and Limitations of Study 2**

The strengths of this study included the use of objective measures of sleep via actigraphy to estimate sleep patterns across multiple nights in the home environment. The study population is ideal for studying night-to-night variability given females are more likely to demonstrate greater night-to-night variability in self-reported number of nighttime awakenings and SOL compared to males (Dillon et al., 2014). Additionally, exercise sessions were performed in a laboratory setting under constant supervision which allowed for adherence to exercise protocol to be monitored. Also, the length of
observation includes weekend nights which is another strength since sleeping patterns tend to change on the weekends.

There are several limitations for this proposed study including how the results can only be generalized to healthy older women between the ages of 60 to 75 years. Additionally, the participants were not assessed for sleep complaints or disorders at baseline since sleep was neither a primary outcome of interest nor an exclusionary criterion in the WEWALK study. This may impact the results of this study because of the common occurrence of night-to-night variability in sleep/wake schedule among individuals with insomnia. This study was unable to account for every possible covariate of the sleep-exercise relationship including light exposure, naps, and stress/perceived stress levels. Also, the use of actigraphy does not allow for sleep stages to be examined; however, this objective measure is a more cost-effective and less intensive alternative to PSG. Lastly, this study may have low statistical power to detect a relationship for bedtimes and arising times; however, the estimated power was based on subjective measures while this proposed study used objective measures which may result in a different statistical power.
CHAPTER 4

MANUSCRIPT 1 – THE EFFECT OF STRUCTURED EXERCISE ON SLEEP DURING THE CORRESPONDING NIGHT AMONG TRAINED OLDER WOMEN

1 Breneman, CB, Kline, CE, West, D, Sui, X, & Wang, X. To be submitted to Behavioral Sleep Medicine.
Abstract

Objective

This study investigated the acute effect of exercise on sleep outcomes among healthy older women by comparing days with structured exercise versus non-structured exercise control days during 4 months of exercise training.

Methods

This study included a subsample (n = 51) who had sleep data available following at least three days of exercise and at least three days of non-exercise at mid- (2 months) and post-intervention (4 months). The number of observations available per participant at each time point ranged from 6 to 14 nights (total number across both time points: 12 to 28 nights). The exercise intervention was treadmill walking and weekly energy expenditure was based on the participant’s body weight and assigned exercise dosage (low-dose: 8 kcal/kg versus high-dose: 14 kcal/kg). Sleep was assessed objectively via wrist-worn actigraphy at baseline, mid- (2-month), and post-intervention (4-month). Behavioral sleep parameters that were considered included bedtime, arising time, and time-in-bed. Physiological sleep parameters assessed included total sleep time, sleep onset latency, wake time after sleep onset, number of awakenings, and activity counts. Multilevel models were used to examine whether structured exercise impacted sleep outcomes during the corresponding night.

Results

Behavioral sleep parameters were observed to be significantly impacted by structured exercise; specifically, bedtimes were significantly earlier on nights following a day with structured exercise versus a day without structured exercise (p = 0.04). Arising
times were also significantly earlier the next morning following a day with structured exercise; however, this association was attenuated after adjusting for day of the week, baseline body mass index (BMI), and changes in BMI, or day of the week, baseline VO$_{2\text{peak}}$ levels, and changes in VO$_{2\text{peak}}$ (p > 0.05). No other sleep parameters differed significantly on days with structured exercise and days without structured exercise.

**Conclusion**

Bedtimes were the only sleep parameter to differ following days with an acute bout of structured exercise versus days without structured exercise among healthy, trained older women. This behavioral change did not correspond with any improvements to the physiological sleep parameters.

**INTRODUCTION**

There are noticeable age-related trends in sleep duration and quality in which older adults spend a greater amount of time in bed as compared to younger individuals (Thomas et al., 2014), but have declines in several metrics of sleep quality (SQ) that indicate lighter and more fragmented sleep as one ages (Ohayon, Carskadon, Guilleminault, & Vitiello, 2004). Despite these changes in sleep architecture with age, the literature demonstrates that the timing and quality of sleep are influenced by health behaviors during waking time (Irish et al., 2014). Regular exercise, a component of physical activity (PA), is one waking health behavior that is perceived in the general population to promote better sleep during the corresponding night (Urponen, Vuori, Hasan, & Partinen, 1988) and is commonly identified as a sleep hygiene recommendation (Irish, Kline, Gunn, Buysse, & Hall, 2015).
However, recent evidence examining the day-to-day relationship between sleep and PA has produced mixed findings in which some studies support the perception that PA/exercise promotes better sleep (Dzierzewski et al., 2014; Kishida & Elavsky, 2016) while others report no significant associations or negative effects of PA on sleep among middle-aged to older adults (Irish et al., 2014; Lambiase, Gabriel, Kuller, & Matthews, 2013; Mitchell et al., 2016). Specifically, the studies reporting significant positive findings reported that greater PA counts and more time spent in moderate-to-vigorous PA during the day were significantly associated with more total sleep time (TST) measured via actigraphy and higher self-reported SQ during the corresponding night (Dzierzewski et al., 2014; Kishida & Elavsky, 2016).

Although observational studies have strengths for investigating the daily relationship between exercise and sleep, there are some limitations to be considered. Several of the abovementioned studies reported low PA levels in their free-living samples of middle-aged to older adults and therefore, slight variations in either of these behaviors may not have been sufficient enough for detecting the daily (acute) effect of PA/exercise on sleep (Dzierzewski et al., 2014; Irish et al., 2014; Lambiase et al., 2013; Mitchell et al., 2016). One of those studies noted that about 55.5% of the middle-aged women in their sample self-reported their daily exercise as light with another 6.9% self-reporting no participation in exercise during the observational period (Irish et al., 2014). Thus, the differences in PA levels between days may be minimal, resulting in little impact on sleep parameters. A clearer picture of the acute impact of PA on sleep may be found in individuals who participate in a structured exercise training regimen that creates a greater
variation between days with and without structured exercise, and therefore allows for the examination of the acute effect of exercise on sleep.

However, to date, there are only a few studies that have examined the acute effects of exercise on sleep during an exercise training intervention among adults (Baron, Reid, & Zee, 2013; King et al., 2008; Melancon, Lorrain, & Dionne, 2015). Further, among these few studies, there are some prominent limitations which preclude clear conclusions about the acute effect of sleep among older women. The available studies have small sample size (n < 25 participants), and limited assessments (i.e., two of the three published studies measured sleep objectively for only two consecutive nights). Since there is night-to-night variability in sleep (Dillon et al., 2014; Knutson, Rathouz, Yan, Liu, & Lauderdale, 2007; van Hilten et al., 1993), assessing only two nights, one following a day of exercise and the other a day of non-exercise, may insufficient to capture the acute effect of exercise on sleep. Multiple assessments of sleep following days with structured exercise and no structured exercise are needed to examine the acute effect of exercise on sleep beyond the nightly variations.

Further, there is evidence suggesting that training status influences sleep’s response to exercise in which self-reported SQ, and several objective sleep measures obtained from actigraphy and polysomnography have been noted to improve among older adults following moderate-intensity exercise training (Baron et al., 2013; Cai, Chen, & Wen, 2014; Mansikkamaki et al., 2012; Payne, Held, Thorpe, & Shaw, 2008; Tanaka et al., 2002). Given these chronic responses to exercise training and the evidence suggesting the existence of day-to-day relationship between sleep and exercise, there is the possibility that training status may impact the effect of an acute bout of exercise on sleep.
among older women. The measurement of sleep over the course of an exercise training intervention would allow for the examination of training status on the acute effect of exercise on sleep, which has rarely been done previously among older adults (Baron et al., 2013; King et al., 2008; Melancon et al., 2015). Therefore, the purpose of this study was to investigate the acute effect of exercise on sleep outcomes among healthy older women by comparing structured exercise versus non-structured exercise control days, and to investigate whether training status affects any acute effect of exercise by comparing mid-intervention versus post-intervention sleep during 4 months of exercise training.

METHODS

Study Population

The Women’s Energy Expenditure in Walking Programs (WEWALK) study was a randomized clinical trial examining the effect of two walking programs of moderate-intensity on total daily energy expenditure and its components (resting metabolic rate, thermic effect of food, and non-exercise activity thermogenesis) (ClinicalTrials.gov identifier: NCT01722136). The inclusion criteria for the WEWALK study included female gender, a BMI between 18 and 30 kg/m², physically inactive (less than 20 minutes of structured exercise three times per week), weight stable for the previous three months (+/- 3%), non-smoking, older age (60 – 75 years), and no physical limitations interfering with walking on a treadmill. The research protocol for the WEWALK study was approved by the University of South Carolina Institutional Review Board, and informed consent was obtained from all participants. A total of 72 women completed the WEWALK study.
This study included a subsample (n = 51) who had sleep data available following at least three days with structured exercise at our research facility and at least three days without such structured exercise at both mid- and post-intervention. The justification for specifying three days of structured exercise and three days without structured exercise is based on research that demonstrated that there was no difference between actigraphic measures of central tendency for sleep variables obtained over a three-day aggregate in comparison to seven- or fourteen-day aggregates among older adults (Rowe et al., 2008). The number of observations available per participant at each time point ranged from 6 to 14 nights (total number across both time points: 12 to 28 nights). The use of a multilevel regression model allowed for this wide range of data to be analyzed because this modelling technique does not assume each participant has the same number of observations or equal time intervals between observations and is, therefore, less sensitive to missing data (Hox, 2002). A term denoting time point was added to the analyses to account for differences in training status between mid- and post-intervention. Also, since exercise sessions were scheduled during the week and occurred frequently on Fridays, weekend nights (Friday and Saturday) were included in order to increase the number of participants meeting the inclusion criteria. To control for the variability associated with including weekend nights in the analysis, a dichotomous variable was included to compare weekdays (Sunday through Thursday) to weekends (Friday and Saturday) (Hashizaki, Nakajima, & Kume, 2015).

**Study Intervention**

In the WEWALK study, participants were randomly assigned to either the low-dose walking group (8 kilocalories (kcal) per kilogram (kg) of body weight per week) or
the high-dose walking group (14 kcal/kg of body weight per week). Both exercise groups walked three to four times a week on a treadmill for 4 months under supervision in a research facility at the University of South Carolina. Weekly energy expenditure was individualized and based on the participant’s body weight and assigned exercise dosage (8 kcal/kg versus 14 kcal/kg). Training intensity for both groups was set at 50-55% of each participant’s heart rate reserve (HRR), which was calculated using their maximum heart rate obtained during their baseline fitness test.

In order to reduce the risk of injury in this physically inactive sample, both groups began training at an intensity of 40% of the participant’s HRR, which was then increased every two weeks by 5% until the target training intensity was reached in week five. Weekly caloric expenditure began at 4 kcal/kg body weight during the first week of the intervention for both groups and then increased in weekly increments (low-dose: 1 kcal/kg body weight per week; high-dose: 2 kcal/kg body weight per week for the first month and then 1 kcal/kg body weight per week for the second month) until the assigned exercise dosage was reached by week five in the low-dose group and week eight in the high-dose group. Training intensity was monitored continuously throughout each session via heart rate monitors (FT1; Polar, Lake Success, NY, USA) in which heart rate was recorded every 5 minutes.

At mid-intervention, participants in both exercise groups would have reached their target energy expenditure dose. Also, by this time point, both groups were walking three to four times per week at an intensity of 50-55% of the participant’s HRR. The only difference between the groups in their exercise prescription was the duration of each session which varied from 35 to 40 minutes in the low-dose group to 55 to 60 minutes in
the high-dose group. Given the incremental increase in the intensity and dose by mid-intervention, the acute effects of exercise were evaluated at this time point and at post-intervention to see if there were any differences.

Measurements

Sleep Parameters

Sleep was measured objectively via actigraphy (GT3X+; Actigraph, Pensacola, FL, USA). All participants were instructed to wear an actigraphic accelerometer on their non-dominant wrist continuously for up to 14 days at baseline, mid-intervention, and post-intervention. Daily sleep logs were kept by all participants in which bedtimes and arising times were recorded. The manufacturer’s software (ActiLife version 6.11.2) was used to analyze the actigraphy data in 60-second epochs. Sleep log data were entered manually into the program in order to determine the amount of time in bed (TIB). A standardized approach was used to increase the reproducibility of values for TIB by estimating missing or adjusting inaccurate bed/awake times using a hierarchical ranking of inputs (i.e. sleep diary, light intensity, and activity counts) (Patel et al., 2015). Light intensity and activity counts were objectively measured by the GT3X+ and were used in the standardization of TIB. Each minute that a participant spent in bed was analyzed using the Cole-Kripke sleep scoring algorithm in order to quantify several sleep parameters: SOL, TST, wake after sleep onset (WASO – total time in minutes that the algorithm scored as “awake” during the sleep period), number of awakenings after sleep onset, and activity counts occurring within TIB (Cole, Kripke, Gruen, Mullaney, & Gillin, 1992).
Body Mass Index (BMI)

Height was measured to the nearest 0.1 cm and weight was measured to the nearest 0.1 kg. Two measurements were taken for both height and weight and averages of each were used to calculate BMI (kg/m$^2$) at baseline, mid-, and post-intervention. Change in BMI was calculated by subtracting baseline values from post-intervention values. Epidemiological evidence demonstrates a significant relationship between body composition and sleep patterns as well as a significant relationship between PA and body weight (Bailey et al., 2014; U.S. Department of Health and Human Services, 2008; van den Berg et al., 2008). Therefore, both BMI and changes in BMI were included as covariates in the analyses.

Cardiorespiratory Fitness (CRF)

A graded treadmill test was used to measure CRF in all participants at baseline and post-intervention (month 4). Participants began walking at a self-selected but challenging speed that did not change during the test protocol. Incline incrementally increased by 2% every two minutes. Volume of oxygen consumption (VO$_2$) was monitored continuously via a metabolic cart (True Max 2400; ParvoMedics, Sandy, UT, USA) and heart rate (HR) via a standard 12-lead ECG (Q-Stress ®; Cardiac Science, Bothell, WA, USA) during the test. The highest 30-second averaged VO$_2$ value during the test was considered peak oxygen consumption (VO$_{2peak}$). Change in VO$_{2peak}$ was calculated by subtracting the baseline from post-intervention values. Several reviews and meta-analyses have identified CRF as a potential moderating/mediating factor of sleep (Buman & King, 2010; Chennaoui et al., 2015; Horne, 1981; Uchida et al., 2012;
Youngstedt et al., 1997). Therefore, both baseline VO\textsubscript{2peak} and changes in VO\textsubscript{2peak} were used as covariates.

**PA Levels**

The GT3X+ monitor worn to assess sleep parameters was also used to measure PA levels during the same time period at baseline, mid-, and post-intervention. The manufacturer’s software (ActiLife version 6.11.2) was used to calculate mean daily activity counts per minute (CPM) for each participant.

**Statistical Analyses**

Baseline descriptive statistics were calculated and reported as means and standard deviations. Independent sample t-tests and chi-square tests were used to identify baseline differences between randomized conditions (low-dose versus high-dose) and those with complete versus incomplete actigraphy data. A multilevel statistical analysis was performed since the data were organized hierarchically where multiple nights of actigraphic sleep recordings were nested within 51 participants. This modeling approach allowed for the opportunity to determine whether structured exercise impacted sleep outcomes during the corresponding night both within (level 1: across days) and between (level 2: across persons) persons. Both behavioral (i.e. bedtime, arising time, and TIB) and physiological (i.e. TST, SOL, activity counts, WASO, and number of awakenings) sleep parameters were investigated in this study. Separate multilevel models with random intercepts were run with each sleep outcome as the dependent variable. The independent variable of interest was exercise versus non-exercise days which was included in the models as a dichotomous variable. Each analysis was adjusted for time point (mid- versus post-intervention), exercise dose (low versus high), and mean baseline
value of the respective sleep parameter in Model 1 followed by additionally controlling for day of the week (weekday versus weekend), baseline BMI, and changes in BMI in Model 2. Due to the collinearity between BMI and VO2peak levels, Model 3 was also an extension of Model 1, but controlled for baseline VO2peak levels and changes in VO2peak levels instead of BMI. An interaction term for the ‘time point’ and ‘exercise/non-exercise day’ was added to the models to assess whether the acute effect of exercise on sleep varied as a function of training status. This interaction term was non-significant for all sleep parameters and therefore, was not included in the final models. Additionally, SOL, activity counts after sleep onset, and WASO were not normally distributed and therefore, the values were transformed (natural logarithm [x + 1], natural logarithm[x], and square root, respectively) to achieve normality of distribution. No other data transformations were needed for the remaining sleep parameters. Data were analyzed using PROC MIXED procedure in SAS software, Version 9.4 (SAS Institute, Cary, NC) and statistical significance was set at an alpha level of 0.05.

RESULTS

Participant Characteristics

The final sample with complete actigraphy data included 51 participants and their characteristics are included in Table 4.1 and categorized according to exercise dose. The majority of the women were non-Hispanic white with at least some college education. On average, the participants were 64.5 years of age and had a BMI of 25.3 kg/m². The low-dose group had significantly later arising times compared to the high-dose group. No other baseline between-group differences were found in the remaining sleep parameters or in participant characteristics. Adherence to the prescribed exercise dose was
approximately 98.7% in both groups. When a comparison was made between those included in this analysis (n=51) versus those excluded due to incomplete actigraphy data (n=21), no differences were observed between any of the baseline characteristics.

**Acute Effects of Exercise on Sleep during the Corresponding Night**

Table 4.2 provides the results from the multilevel models for all sleep parameters. There were no significant differences between the two exercise groups of differing doses of energy expenditure; therefore, they were combined to examine the acute effects of exercise and exercise training effects. In the combined sample, there was a significant difference between days with structured exercise and days without structured exercise for bedtimes, in that participants went to bed about 9.5 minutes earlier on structured exercise days as compared to days without structured exercise across both time points in the intervention. This difference decreased slightly but remained significant even after controlling for time point (mid- versus post-intervention), exercise dose (low versus high), average bedtime at baseline, day of the week (weekday versus weekend), baseline BMI, and changes in BMI, or day of the week, baseline VO$_{2peak}$ levels, and changes in VO$_{2peak}$. Additionally, arising times were significantly earlier (about 8.4 minutes) after exercising the day before as compared to a day following no exercise in the combined sample. However, this finding became non-significant in Model 2 after further adjusting for the day of the week, baseline BMI, and changes in BMI as well as in Model 3 which adjusted for day of the week, baseline VO$_{2peak}$ levels, and changes in VO$_{2peak}$. There were no other significant differences found between structured exercise versus non-structured exercise days in any of the remaining behavioral or physiological sleep parameters.
Effects of Training Status and Day of the Week on Sleep

The acute effect of exercise on sleep did not vary as a function of duration in the training program (mid- versus post-intervention) for any of the sleep parameters. Comparison of weekdays versus weekends revealed significant differences in each of the sleep parameters with the exception of SOL (p-value > 0.05). Specifically, TIB and TST were significantly longer and bedtimes and arising times were significantly later on the weekends in comparison to weekdays (504.6 versus 573.3 minutes, 454.5 versus 426.3 minutes, 11:06 PM versus 10:52 PM, 7:30 AM versus 6:45 AM, for TIB, TST, bedtimes, and arising times, respectively). Additionally, activity counts (30,505 counts versus 28,416 counts), WASO (44.4 minutes versus 41.1 minutes), and the number of awakenings (15.1 versus 13.3) were observed to be significantly greater on the weekends as compared to the weekdays.

Subgroup Analysis

Overall, there was a significant difference in total PA between structured exercise versus non-structured exercise days (p = 0.02). However, when examined separately by exercise group, the high-dose group demonstrated that the participants were more physically active on structured exercise days as compared to non-structured exercise days (1,737 ± 510.8 CPM versus 1,638 ± 578.1 CPM; p = 0.02). Among those in the low-dose group, there was no significant difference between structured exercise versus non-structured exercise days (1,657 ± 448.5 CPM versus 1,620 ± 533.3 CPM; p = 0.40).

Since there was a significant difference in the amount of PA between structured exercise versus non-structured exercise days among the high-dose group, a subgroup analysis was performed using this group only. The observed significant difference in
bedtimes between structured exercise and non-structured exercise days in the overall sample was no longer significant \((p = 0.14)\) in the full models for the subgroup analysis. Additionally, the significant difference observed between mid- and post-intervention for bedtimes in the overall sample was attenuated to non-significance \((p = 0.07)\) in the subgroup analysis.

**DISCUSSION**

This study examined the acute effects of exercise on sleep during an exercise training intervention among older women. Overall, behavioral sleep parameters were observed to be significantly impacted by structured exercise in which bedtimes were significantly earlier on nights following a day with structured exercise versus a day with no structured exercise. Arising times were also significantly earlier the next morning following a day of structured exercise; however, this association was partly dependent upon the day of the week (weekdays versus weekends), baseline BMI, changes in BMI, or day of the week, baseline VO\(_{2\text{peak}}\) levels, and changes in VO\(_{2\text{peak}}\) levels given the attenuated and non-significant regression coefficients in both of the adjusted models.

The acute effect of exercise on sleep was demonstrated in this study to impact only behavioral sleep parameters. The significant difference in bedtimes on nights in which the participants exercised during the day versus bedtimes on days with no structured exercise supports that within the context of everyday life, the sleep-wake cycle is influenced by conscious decisions made within the framework of internal and external cues (Daan, Beersma, & Borbely, 1984). These cues include personal habits, such as exercise, that may impact both the need for sleep and the circadian pacemaker (Beersma & Gordijn, 2006; Daan et al., 1984). These changes in bedtimes are independent of the
duration in the training program (mid- versus post-intervention), and have not been previously demonstrated in other studies investigating the acute relationship between sleep and exercise during an exercise intervention (Baron et al., 2013; King et al., 2008; Melancon et al., 2015).

We did not find an acute bout of exercise to significantly impact any of the physiological sleep parameters during the corresponding night. However, there is evidence suggesting that an acute bout of exercise affects the physiological parameters of sleep in untrained individuals. A study by Wang and Youngstedt (2014) demonstrated among inactive non-obese older women that an acute bout of moderate-intensity aerobic exercise resulted in significant improvements in SQ by improving actigraphic measures of WASO, number of nighttime awakenings, and movement while asleep as compared to baseline measures. In another study, a bout of moderate-intensity aerobic exercise was observed to improve PSG measures of TST, SOL, total wake time, and SE as well as self-reported TST and SOL in a sample of physically inactive middle-aged adults with insomnia (Passos et al., 2010). Similarly, at baseline in the untrained state, the proportion of time spent in non-REM sleep via PSG was significantly higher following an acute bout of exercise as compared to the non-exercise control day in older community-dwelling males (Melancon et al., 2015). The inconsistent finding between ours and these studies may be related to how our study only evaluated the effect of an acute exercise bout on sleep at mid- versus post-intervention, rather than at baseline in an untrained state.

This is further supported by another study, where King and colleagues (2008) examined the acute effects of a single bout of moderate-intensity exercise on sleep during a 12-month training intervention among a subsample of older adults with sleep
complaints. In the trained state, they did not observe any significant differences in any of the PSG sleep parameters (e.g. SOL, TST, SE, etc.) following one day of structured exercise compared to one day without structured exercise at mid- and post-intervention. Additionally, Baron et al. (2013) used multilevel modelling to analyze whether exercise duration was a predictor of sleep during the corresponding night among older women with insomnia who participated in a 16-week training intervention. They also did not observe a significant association between exercise duration and actigraphy measures of SOL, TST, WASO, and SE during the corresponding night.

There is additional evidence suggesting the acute effect of exercise depends on training status. Melancon and colleagues (2015) assessed the acute effect of a bout of exercise before and after 4 months of exercise training among community-dwelling older males. The authors found that the percentage of slow wave sleep was significantly greater after an acute bout of exercise in the trained state as compared to pre-training values obtained after a day of no exercise. This significant difference may indicate a possible training effect. We did not find a significant interaction between time point in the exercise intervention (mid- versus post-intervention) and exercise/non-exercise condition. This may be due to the participants reaching their exercise dose by mid-intervention which was then maintained for the remaining 2 months of the exercise intervention; therefore, no changes occurred in the exercise dose between mid- and post-intervention. Coupled with the study findings among untrained individuals, it may be that the chronic effect of training versus no training, rather than the duration of being in an exercise intervention, has a greater impact on the acute effect of exercise on sleep.
The strengths of this study include the use of actigraphy to objectively measure sleep over multiple nights in the home environment which allowed for comparison between several nights following days with exercise versus days of no exercise. Additionally, the structure of the data were organized hierarchically where multiple nights of actigraphic sleep recordings were nested within participants which allowed for the acute effect of exercise on sleep to be examined longitudinally. Also, structured exercise in a supervised facility was the main exposure in our study and the overall adherence to the exercise dose in the main study was high for both groups. In addition to the study strengths, there are limitations that should be considered. One limitation includes the restricted generalizability of the results to healthy, trained older women. Also, the effect of exercise on sleep may be different among individuals with sleep complaints or disorders; however, due to the main study not assessing this at baseline, this study was not able to answer this question. A crude evaluation of actigraphic data at baseline indicates that the majority of this sample consisted of good sleepers; therefore, our sample may have had little room for improved sleep. Another limitation of this study is the inability to investigate or compare the effects of an acute bout of exercise in the untrained state versus mid- or post-intervention. Additionally, the lack of a control group is another limitation of this study because we were unable to determine whether the observed results were due to the structured exercise interventions or some other factors. Another limitation is that we could not account for time of day in which the acute bout of exercise occurred; it is possible that the acute effect of exercise may depend upon the time of day in which the exercise occurred. An additional limitation is that we could only categorize days based on whether the structured exercise occurred in our facility; we have
no information on whether individuals engaged in additional exercise congruent with their exercise prescription outside of the center-based structured sessions. Underscoring this concern, only the high-dose group demonstrated a significant difference in activity levels between exercise and non-exercise days which indicates that there was not a sufficient difference in activity levels among the low-dose group. The subgroup analysis using only the high-dose group did not reveal any significant findings possibly due to decreased sample size.

In summary, we only observed a significant difference in bedtimes following days with structured exercise versus no structured exercise in healthy, trained older women. This behavioral change did not correspond with any improvements to the physiological sleep parameters; which suggests training status may impact the acute effects of exercise on sleep. Future exercise training studies should longitudinally measure sleep subjectively and objectively at multiple time points in the training period with one of those time points occurring within the first week of training, in order to better understand how training status impacts the acute effects of exercise on sleep.
Table 4.1 Baseline Participant Characteristics by Exercise Dose

<table>
<thead>
<tr>
<th></th>
<th>Total (n=51)</th>
<th>Low-Dose (n=24)</th>
<th>High-Dose (n=27)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>64.47 (3.74)</td>
<td>64.50 (4.21)</td>
<td>64.44 (3.34)</td>
<td>0.96</td>
</tr>
<tr>
<td>Race, % (#)</td>
<td></td>
<td></td>
<td></td>
<td>0.34</td>
</tr>
<tr>
<td>White</td>
<td>84.31 (43)</td>
<td>91.67 (22)</td>
<td>77.78 (21)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>13.73 (7)</td>
<td>8.33 (2)</td>
<td>18.52 (5)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1.96 (1)</td>
<td>0.00 (0)</td>
<td>3.70 (1)</td>
<td></td>
</tr>
<tr>
<td>Education, % (#)*</td>
<td></td>
<td></td>
<td></td>
<td>0.82</td>
</tr>
<tr>
<td>High School Graduate</td>
<td>15.69 (8)</td>
<td>12.50 (3)</td>
<td>18.52 (5)</td>
<td></td>
</tr>
<tr>
<td>College 1 to 3 years</td>
<td>29.41 (15)</td>
<td>29.17 (7)</td>
<td>29.63 (8)</td>
<td></td>
</tr>
<tr>
<td>College 4 years or more</td>
<td>54.90 (28)</td>
<td>58.33 (14)</td>
<td>51.85 (14)</td>
<td></td>
</tr>
<tr>
<td>Household Income, % (#)*</td>
<td></td>
<td></td>
<td></td>
<td>0.91</td>
</tr>
<tr>
<td>&lt;$30,000</td>
<td>9.80 (5)</td>
<td>12.50 (3)</td>
<td>7.41 (2)</td>
<td></td>
</tr>
<tr>
<td>$30,000 – 49,999</td>
<td>15.69 (8)</td>
<td>16.67 (4)</td>
<td>14.81 (4)</td>
<td></td>
</tr>
<tr>
<td>$50,000 – 69,999</td>
<td>19.61 (10)</td>
<td>16.67 (4)</td>
<td>22.22 (6)</td>
<td></td>
</tr>
<tr>
<td>$70,000+</td>
<td>49.02 (25)</td>
<td>50.00 (12)</td>
<td>48.15 (13)</td>
<td></td>
</tr>
<tr>
<td>CES-D</td>
<td>4.86 (5.20)</td>
<td>4.91 (5.81)</td>
<td>4.81 (4.72)</td>
<td>0.95</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.38 (3.44)</td>
<td>25.91 (3.74)</td>
<td>24.91 (3.15)</td>
<td>0.30</td>
</tr>
<tr>
<td>VO₂peak (ml/kg/min)</td>
<td>20.28 (3.93)</td>
<td>20.33 (3.78)</td>
<td>20.25 (4.12)</td>
<td>0.95</td>
</tr>
<tr>
<td>Average Sleep Parameters</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bedtime (h:min)</td>
<td>11:02 PM</td>
<td>10:45 PM</td>
<td>11:11 PM</td>
<td>0.11</td>
</tr>
<tr>
<td>Arising Time (h:min)</td>
<td>6:58 AM</td>
<td>6:40 AM</td>
<td>7:13 AM</td>
<td>0.02</td>
</tr>
<tr>
<td>TIB (min)</td>
<td>479.70 (45.46)</td>
<td>476.50 (42.96)</td>
<td>482.50 (48.21)</td>
<td>0.65</td>
</tr>
<tr>
<td>TST (min)</td>
<td>432.40 (43.05)</td>
<td>433.00 (43.86)</td>
<td>431.80 (43.14)</td>
<td>0.92</td>
</tr>
<tr>
<td>SOL (min)</td>
<td>5.35 (0.81)</td>
<td>5.28 (0.80)</td>
<td>5.41 (0.83)</td>
<td>0.57</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------------</td>
<td>-------</td>
<td>-------</td>
<td>-------</td>
<td></td>
</tr>
<tr>
<td>Activity Counts (#)</td>
<td>30,157.50</td>
<td>27,763.90</td>
<td>32,285.20</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(12,985.50)</td>
<td>(10,259.90)</td>
<td>(14,871.70)</td>
<td></td>
</tr>
<tr>
<td>WASO (min)</td>
<td>41.98 (17.93)</td>
<td>38.23 (14.37)</td>
<td>45.31 (20.28)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.22</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of Awakenings (#)</td>
<td>13.97 (4.34)</td>
<td>13.04 (3.77)</td>
<td>14.80 (4.71)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.15</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: CES-D, Center for Epidemiologic Studies Depression score; SOL, sleep onset latency; TIB, total time in bed; TST, total sleep time; WASO, wake after sleep onset. Values presented as mean (standard deviation) or as otherwise stated. P-values were obtained from chi-square and t-tests, with statistical significance defined at the alpha < 0.05 level.

*Indicates missing values which results in some percentages not totaling up to 100%.
Table 4.2: Objectively Measured Sleep Variables Estimated from Multilevel Models (n = 51)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Behavioral Sleep Parameters</th>
<th>Physiological Sleep Parameters</th>
<th>Number of Awakenings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TIB</td>
<td>Bedtime</td>
<td>Arising Time</td>
</tr>
<tr>
<td></td>
<td>Model 1</td>
<td>Model 2</td>
<td>Model 1</td>
</tr>
<tr>
<td>Exercise</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>Non-exercise</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>Exercise</td>
<td>1.31 (4.43)</td>
<td>-0.16 (0.06)†</td>
<td>-0.12 (0.06)‡</td>
</tr>
<tr>
<td>Time</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>Mid</td>
<td>4.82 (4.27)</td>
<td>-0.18 (0.06)†</td>
<td>-0.18 (0.06)†</td>
</tr>
<tr>
<td>Post</td>
<td>5.61 (4.20)</td>
<td>(0.05)†</td>
<td>(0.06)†</td>
</tr>
<tr>
<td>Day of Week</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weekday</td>
<td>-</td>
<td>Ref</td>
<td>-</td>
</tr>
<tr>
<td>Weekend</td>
<td>31.29 (4.70)†</td>
<td>(0.06)†</td>
<td>(0.06)†</td>
</tr>
</tbody>
</table>

Note: BMI, body mass index; SOL, sleep onset latency; TIB, total time in bed; TST, total sleep time; WASO, wake after sleep onset. Unstandardized regression coefficients are presented along with standard errors. Model 1 controlled for time point, exercise group, mean baseline value of the respective sleep parameter. The regression coefficients for the main effects of exercise condition and time were similar between Model 2 (adjusted for day of the week, baseline BMI, and changes in BMI from baseline to post-
intervention) and Model 3 (adjusted for day of the week, baseline VO_{2peak}, and changes in VO_{2peak} from baseline to post-intervention); and therefore, only Model 2 is displayed.

a Log(x+1) transformation used for statistical analysis and variable reported on transformed scale.
b Log(x) transformation used for statistical analysis and variable reported on transformed scale.
c Square root transformation used for statistical analysis and variable reported on transformed scale.

† p < 0.01
‡ p < 0.05
REFERENCES


CHAPTER 5

MANUSCRIPT 2 – THE EFFECT OF MODERATE-INTENSITY EXERCISE ON NIGHTLY VARIABILITY IN OBJECTIVELY MEASURED SLEEP PARAMETERS AMONG OLDER WOMEN²

² Breneman, CB, Kline, CE, West, D, Sui, X, & Wang, X. To be submitted to Journal of Clinical Sleep Medicine.
ABSTRACT

Objective

This study examined whether 4 months of moderate-intensity exercise impacted night-to-night variability in sleep among healthy, physically inactive older women.

Methods

This study included a subsample of females enrolled in the WEWALK study (n=49). Participants in the main study were randomized to one of two moderate-intensity walking programs with different doses of energy expenditure: low-dose (n = 23: 8 kilocalories (kcal) per kilogram (kg) of body weight per week) or high-dose (n = 26: 14 kcal/kg of body weight per week). The training period for both groups was 4 months and participants walked on treadmills in a research facility under supervision at an intensity of 50-55% of participants’ heart rate reserve. Sleep parameters were assessed objectively by a wrist-worn actigraph which was worn at baseline, mid- (2-month), and post-intervention (4-month). The first seven consecutive days of actigraphy data during each measurement point were analyzed. Nightly variability in each of the sleep parameters was calculated using the 7-day standard deviations (SD) and a coefficient of variation (SD/mean x 100%). Cardiorespiratory fitness (VO_{2peak}) was measured in all participants at baseline and post-intervention (4-month) using a graded treadmill test. Body mass index was assessed at each time point (baseline, mid-, and post-intervention).

Results

Because there was no significant group x time interaction found for any of the sleep parameters, the two exercise groups were combined to examine exercise training effects. Both measures of nightly variability demonstrated a borderline to significant
lower amount of night-to-night variability in wake time after sleep onset (WASO) and number of awakenings at post-intervention (4 months) in comparison to baseline ($p \leq 0.05$). Higher $VO_{2\text{peak}}$ levels at baseline were associated with a shorter amount of time in bed and lower night-to-night variability in total sleep time throughout the exercise intervention.

**Conclusion**

Participation in moderate-intensity exercise was observed to reduce the amount of nightly variability for WASO and number of awakenings over time in older women. Additionally, greater fitness levels at baseline were associated with more consistent sleep durations and less time in bed throughout the exercise intervention.

**INTRODUCTION**

Sleep is a modifiable behavior that commonly fluctuates from night to night within the same individual and varies across the lifespan (Dillon et al., 2014). These nightly variations are present in both behavioral (i.e. bedtime, arising time, and time in bed [TIB]) and physiological (i.e. total sleep time [TST], sleep onset latency [SOL], wake time after sleep onset [WASO], number of awakenings, and activity counts) sleep parameters (Dillon et al., 2014; Knutson, Rathouz, Yan, Liu, & Lauderdale, 2007; van Hilten et al., 1993).

Furthermore, nightly variability in sleep varies by sex with females being more likely to demonstrate greater night-to-night variability in self-reported number of nighttime awakenings and SOL as compared to males (Dillon et al., 2014). This possibly indicates that sleep among females may be more susceptible to disruptions caused by environmental or hormonal changes (Dillon et al., 2014; Moline, Broch, Zak, & Gross,
2003) including the menstrual cycle and life events like pregnancy, the postpartum period, and menopause (Moline et al., 2003). Also, sleep-related difficulties become more prevalent after menopause as evident by approximately 35-60% of postmenopausal women self-reporting sleep disturbances as compared to 16-42% of premenopausal women (National Institutes of Health, 2005). Specifically, insomnia is a prevalent sleep disorder among postmenopausal women and is commonly accompanied by elevated night-to-night variability in sleep patterns (Buysse et al., 2010; Krystal, Edinger, Wohlgemuth, & Marsh, 1998; Moline et al., 2003; Vallieres et al., 2005). Taken together, older women are particularly vulnerable to sleep disturbances and disorders that may result in significant night-to-night variability in their sleep.

Recently, researchers have taken interest in examining how night-to-night fluctuations in sleep parameters may influence health; however, the literature has yet to define what is considered an optimal amount of nightly variability. The emerging evidence demonstrates the clinical significance for studying this dimension of sleep given that highly variable sleeping patterns are associated with several negative health outcomes, including higher concentrations of circulating pro-inflammatory markers, obesity, increased morbidity (e.g. diabetes, depression, heart failure), and poorer self-reported health status (Bei et al., 2015; Knutson et al., 2007; Okun, 2011; Patel et al., 2014). Additionally, there is evidence suggesting that the associations between night-to-night variability and poorer perceived health are independent of mean-level sleep measures. This was demonstrated in one study which found that greater nightly variability in objectively measured TST via wrist actigraphy was significantly associated with poorer subjective well-being and greater symptoms of distress, while mean-level
measures of TST were not (Lemola, Ledermann, & Friedman, 2013). These findings suggest that studying nightly variability in sleep parameters may provide new insight to the relationship between sleep and health in addition to what has already been demonstrated at the mean-level.

Sleep has been found to respond positively to non-pharmacological treatments, such as cognitive-behavioral therapy (Edinger & Means, 2005; Espie, Inglis, & Harvey, 2001), which was found to significantly reduce night-to-night variability in self-reported TST, TIB, WASO, and sleep efficiency post-treatment (Edinger, Hoelscher, Marsh, Lipper, & Ionescu-Pioggia, 1992). Additionally, a more recent study demonstrated significant reductions in sleep variability for actigraphic measures of WASO and sleep efficiency following an intervention that included both exercise and sleep hygiene education (Baron, Reid, Malkani, Kang, & Zee, 2016). This suggests that exercise is worthy of additional study as a strategy to reduce nightly variability in sleep parameters. However, the traditional approach in the literature has investigated how exercise or physical activity produces mean-level changes in sleep. Specifically, among studies that measured sleep objectively via wrist actigraphy, TST and SE increased significantly among older women with insomnia who were randomized to the exercise group (Baron et al., 2013); whereas in another study among older women with breast cancer, the only sleep parameters to significantly improve post-intervention were WASO and activity counts (Payne et al., 2008). Taken together, these interventional studies demonstrate that exercise training has beneficial effects on mean-level measures of sleep; however, these studies ignored how the intervention influenced night-to-night variability in sleep.
Additionally, older women, the population that is particularly vulnerable to sleep disturbances and disorders, are understudied and little is known about the influence of exercise on nightly sleep variability. Also, the collection of data longitudinally on individuals provides the opportunity to examine variability across several nights as well as changes in variability over time. Therefore, the main purpose of this study was to examine whether 4 months of moderate-intensity exercise impacted night-to-night variability in objectively measured sleep among healthy, physically inactive older women.

METHODS

Study Population

This study included a subsample of females enrolled in the WEWALK study who had at least 7 days of actigraphy sleep recordings for baseline, mid-intervention (2-month), and post-intervention (4-month) measurements (n = 53). If the change to/from Daylight Saving Time (one Sunday in March or November) was included in the 7 days of actigraphy at any of the time points, the participant was excluded from this analysis due to the potential impact time change may have on sleep variability (n=4). This resulted in a total of 49 participants from the WEWALK study being included in this analysis. The WEWALK study was a clinical exercise trial examining the effects of two walking programs with different energy expenditures on non-exercise activity thermogenesis in physically inactive older women (n=72) (ClinicalTrials.gov identifier: NCT01722136). Participants of the WEWALK study were female, aged 60 – 75 years, non-smokers, weight stable (+/- 3%) for the previous three months, physically inactive (did not participate in structured exercise more than 20 minutes three times per week), had a BMI
≥ 18 and ≤ 30 kg/m\(^2\), and were free from cardiovascular disease, diabetes, or any other condition that might prevent them from adhering to the study protocol. The WEWALK study protocol was approved by the University of South Carolina Institutional Review Board and all participants signed an informed consent form.

**Study Intervention**

Participants in the WEWALK study were randomized to one of two moderate-intensity walking programs with different doses of energy expenditure: low-dose (8 kilocalories (kcal) per kilogram (kg) of body weight per week) or high-dose (14 kcal/kg of body weight per week). The exercise training period for both groups was 4 months and each training session occurred in a research facility under supervision. Participants in both groups walked three to four times a week on treadmills. The two different doses were achieved by varying the weekly duration of exercise in order for the participants to reach their energy expenditure goals according to body size and exercise dosage (8 kcal/kg versus 14 kcal/kg). Weekly energy expenditure was determined by multiplying the participant’s weight by their assigned dosage and was closely monitored throughout the duration of the 4-month intervention.

Due to the physically inactive state of the participants at baseline, the exercise intensity and weekly caloric expenditure increased incrementally to reduce the risk of injury. Training intensity increased in both groups by 5% every two weeks from 40% to a target level of 50-55% of the participant’s heart rate reserve (HRR), which was obtained during the baseline fitness test. Both exercise groups began at a weekly caloric expenditure of 4 kcal/kg body weight during the first week of the intervention and then progressed until the assigned exercise dosage (low-dose: 8 kcal/kg body weight; high-
dose: 14 kcal/kg body weight) was reached by week five in the low-dose group and week eight in the high-dose group.

**Measurements**

*Sleep Parameters*

Sleep parameters were assessed objectively by an actigraphic accelerometer (GT3X+; Actigraph, Pensacola, FL, USA). Participants wore the monitors on the wrist of the non-dominant arm for up to 14 days of continual wear at baseline, mid-intervention (2 months), and post-intervention (4 months). The first seven consecutive days of actigraphy data were used in this study in order to standardize the number of days among participants with complete baseline, mid-, and post-intervention data. This inclusion criterion was based on the findings of a previous study that concluded that at least seven nights of data collection is necessary for obtaining consistent measures of sleep via actigraphy among older adults when night-to-night variability is of primary interest (Rowe et al., 2008). This was done in order to reduce the amount of additional variability that may occur due to reasons other than normal night-to-night variability (e.g. variability due to longer data collection time [7+ days], variability due to varying number of weekend days across individuals, etc.). Additionally, the participants were required to keep daily logs in which bedtimes and arising times were recorded.

Software provided by the manufacturer (ActiLife version 6.11.2) was used to analyze the actigraphy data. The data were assessed in 60-second epochs and the times recorded on the sleep logs were manually entered into the program to quantify TIB. The GT3X+ provides objective measures of activity counts and body position as well as information on the environment via an ambient light sensor. A standardized approach
developed by Patel and colleagues (2015) was used to define TIB. Missing entries on logs and inaccurate recordings of bed/awake times were estimated or adjusted, respectively, based on the hierarchical ranking of inputs (i.e., sleep diary, light intensity, and activity counts) in order to improve the reproducibility of the values. The Cole-Kripke sleep scoring algorithm was used to determine when each participant was asleep or awake (Cole, Kripke, Gruen, Mullaney, & Gillin, 1992). Application of this algorithm provides information on SOL (duration from specified bedtime to when the algorithm scored sleeping), TST (total length of time specified by the algorithm as being “asleep”), WASO (number of minutes the algorithm scored as being “awake” after sleep onset), frequency of awakenings (number of awakenings occurring during the sleep period), and activity counts during TIB.

**Cardiorespiratory Fitness (CRF)**

CRF was measured in all participants at baseline and post-intervention (month 4) using a graded treadmill test. The test involved an incremental protocol where participants walked at a self-selected, comfortable but challenging speed that remained constant throughout the test with the incline increasing by 2% every two minutes. Volume of oxygen consumption (VO₂) via a metabolic cart (True Max 2400; ParvoMedics, Sandy, UT, USA) and heart rate (HR) via a standard 12-lead ECG (Q-Stress ®; Cardiac Science, Bothell, WA, USA) were monitored continuously during the progression of the test. Two of four criteria needed to be achieved in order for the test to be considered satisfactory: a respiratory exchange ratio greater than or equal to 1.10; a rating of perceived exertion greater than or equal to 17 on a scale ranging from 6 to 20; achieving a maximum heart rate greater than 90% of age-predicted maximum HR (≈ 220
age); and/or a plateau in HR or VO₂. Peak oxygen consumption (VO₂peak) was determined by the highest 30-second averaged VO₂ value during the test. Change in VO₂peak was calculated by subtracting the baseline value from post-intervention measure. The effect of CRF on the relationship between sleep and exercise remains unclear; however, CRF has been identified in several reviews and meta-analyses as a potential moderating/mediating factor of sleep (Buman & King, 2010; Chennaoui et al., 2015; Horne, 1981; Uchida et al., 2012; Youngstedt et al., 1997). Therefore, both baseline VO₂peak and changes in VO₂peak were used as covariates.

**Body Mass Index (BMI)**

Height (to the nearest 0.1 cm) and weight (to the nearest 0.1 kg) were measured at each time point (baseline, mid-, and post-intervention) and were used to calculate BMI (kg/m²). The literature demonstrates a significant relationship between body composition and sleep patterns (Bailey et al., 2014; U.S. Department of Health and Human Services, 2008; van den Berg et al., 2008). Since this measure of body composition was measured at the same time points as sleep, BMI was treated as a time-dependent covariate in order to more accurately capture how fluctuations in both sleep and BMI are related over time. Additionally, the examination of BMI over time revealed different patterns of weight change occurring within the sample. Therefore, using BMI as a time-dependent covariate would account for various changes of participants across all three time points.

**Statistical Analyses**

Baseline descriptive statistics, including individual means and standard deviations (SD) were calculated. Additional analyses were performed to make comparisons between those with complete actigraphy data at baseline, mid-, and post-intervention (n = 49) with
those missing any of the time points (n=19). Group differences in baseline characteristics between those participants with complete versus incomplete data in addition to those randomized to the low-dose versus high-dose exercise prescriptions were tested using t-tests and chi-square tests, as appropriate.

Means for each of the sleep parameters were calculated at each time point by averaging the 7 days of sleep data together for each individual. Nightly variability in each of the sleep parameters was calculated using the 7-day SD. Additionally, a coefficient of variation (CV) was computed for each sleep outcome by dividing the 7-day SD by the mean (SD/mean x 100%) for each individual in order to provide another measure of intra-individual variability (Buman, Hekler, Bliwise, & King, 2010; Knutson et al., 2007; Rowe et al., 2008). High values in either of these measures of nightly variability indicate irregularity. The literature considers CV as a more conservative measure of intra-individual variability over the 7-day SD because it references the mean (Buman et al., 2010). Since SD is a measure of how much the data points deviate from the mean, it is possible that higher individual-level means will occur with higher variability when using the raw score of variability (SD). The likelihood of this occurring would be adjusted for when using the CV. Therefore, both measures of variability were examined and any differences were noted. Additionally, both measures of variability were found to not be normally distributed; therefore, the values were transformed using the natural logarithm function to achieve normality of distribution. No data transformations were needed for the mean-level measures of each sleep parameter.

The amount of nightly variability via 7-day SD and CV were calculated at each time point (baseline, mid-, and post-intervention) in the study in order to assess whether
changes occurred across time in response to 4 months of moderate-intensity exercise and to assess whether those changes differed between the two doses of energy expenditure. Separate models were run for each sleep parameter with the individual 7-day SD or the CV as the dependent variable. Similar but separate models were run using the individual mean for each sleep outcome as the dependent variable to determine if similar changes occurred along with both measure of nightly variability. A repeated measures analysis was conducted using a mixed effects model to test the main effects of time and group. Due to the collinearity between the covariates, separate models were run. Since VO$_2$peak levels were only measured at baseline and post-intervention, Model 1 adjusted for baseline VO$_2$peak levels and changes in VO$_2$peak as covariates. Model 2 adjusted for BMI as a time-dependent covariate because of the available data at all three time points and the presence of different patterns of weight change over time within the sample. Significant time effects were followed by post hoc tests to determine which specific time points differed significantly. P-values were adjusted for multiple comparisons using the Tukey-Kramer procedure. A group x time effect was tested and found to be non-significant for all of the sleep parameters and, therefore, this interaction term was not included in the final models. Estimates of unstandardized effect sizes were calculated for any sleep parameter demonstrating significant changes over time in order to convey the difference between mid- and post-intervention values with baseline values. Effect size magnitude was based upon standards set forth by Cohen (1988), with d = 0.2, 0.5, or 0.8 representing a small, medium, or large effect, respectively. Statistical significance was set at P < 0.05 and all analyses were performed in SAS 9.4 (SAS Institute Inc., Cary, NC).
RESULTS

Participant Characteristics

The sample consisted of 49 women with complete baseline, mid-, and post-intervention data for sleep, which included 23 within the low-dose group and 26 in the high-dose group. Table 5.1 presents the means and standard deviations of the baseline characteristics of the sample. Overall, the women were predominantly non-Hispanic white with a college education. On average, they were 64.5 years of age with a VO\(_2\)peak of 19.8 ml/kg/min and a body mass index of 25.5 kg/m\(^2\). They spent, on average, 489.6 minutes in bed with 441.4 of those minutes asleep. Comparison between the low- and high-dose groups demonstrated that the low-dose group had significantly higher variability in WASO at baseline as quantified by the CV. No other baseline differences were noted. The training intervention significantly increased VO\(_2\)peak levels in both groups with an average increase of 7.4% (1.43 ml/kg/min) in the low-dose group (p = 0.01) and 14.3% (2.86 ml/kg/min) in the high-dose group (p < 0.001). Additionally, BMI did not change significantly in the low-dose group post-intervention (p = 0.11), but did decrease significantly by 1.7% (0.43 kg/m\(^2\)) in the high-dose group (p = 0.01).

When comparing those included in the present analyses (n=49) against those excluded because of incomplete data (n=19), those with incomplete data had significantly lower nightly variability in the WASO (quantified by CV) in comparison to those with complete data (Table 5.2). There were no other differences noted in the remaining measures of night-to-night variability or participant characteristics between these two groups.
Night-to-Night Variability in Sleep Parameters

Because there was no significant group x time interaction found for any of the sleep parameters, the two exercise training groups were collapsed for all subsequent analyses. Table 5.3 provides the results from the mixed effects models examining the changes in nightly variability (7-day SDs and CVs) over time in each sleep parameter using the two exercise groups combined.

There was no significant difference between the two exercise doses when using 7-day SDs as a measure of nightly variability. A significant time effect was observed for the 7-day SD variability in WASO (p = 0.02) after controlling for each of the covariates separately in Models 1 and 2. Specifically, the amount of night-to-night variability in WASO was significantly lower at mid- and post-intervention in comparison to baseline. Effect size estimates indicated a small to medium effect size for WASO at mid- and post-intervention (Cohen’s d = 0.31 and 0.38, respectively). Additionally, the amount of night-to-night variability in the number of awakenings was significantly lower at post-intervention in comparison to baseline (p = 0.048) after adjusting for baseline VO₂peak levels and changes in VO₂peak. The estimated effect size for the number of awakenings also indicated a small to medium effect size (Cohen’s d = 0.34). However, this reduction became non-significant in Model 2 after adjusting for BMI as a time-dependent covariate (p = 0.06). No other significant time differences were noted.

When using CV as a measure of nightly variability, there was a significant group effect for activity counts after sleep onset and WASO in which the low-dose group demonstrated significantly greater variability in comparison to the high-dose group (41.0 versus 33.1 [p = 0.02]; 44.5 versus 35.8 [p < 0.01], respectively). Additionally, there was
a borderline significant time difference between baseline and post-intervention for the amount of night-to-night variability in WASO and the number of awakenings (p = 0.05) after adjusting for baseline VO\textsubscript{2peak} and changes in VO\textsubscript{2peak}. Specifically, the amount of night-to-night variability in WASO and the number of awakenings was lower at post-intervention in comparison to baseline (effect sizes = 0.33 and 0.30, respectively). However, after adjusting for BMI in Model 2, this association was no longer significant (p = 0.06). No other significant time differences were noted.

When using the 7-day SD, the amount of night-to-night variability for TST (regression coefficient on log scale = -0.03, p = 0.03) and WASO (regression coefficient on log scale = -0.03, p = 0.048) were significantly and negatively associated with baseline VO\textsubscript{2peak}. This indicates that higher values of VO\textsubscript{2peak} at baseline were associated with lower night-to-night variability in TST and WASO throughout the exercise intervention. Furthermore, a significant and positive association was observed between night-to-night variability in activity counts after sleep onset (regression coefficient on log scale = 0.04, p = 0.02) and WASO (regression coefficient on log scale = 0.04, p = 0.02) with BMI. This indicates that higher BMIs were associated with greater night-to-night variability in movement and WASO throughout the exercise intervention. When examining the relationship between CV and each of the covariates, the amount of night-to-night variability for TST (regression coefficient on log scale = -0.03, p = 0.04) was significantly and negatively associated with baseline VO\textsubscript{2peak}, indicating that higher values of VO\textsubscript{2peak} at baseline were also associated with lower night-to-night variability in TST throughout the exercise intervention. The inclusion of BMI in Model 2 revealed no significant associations between BMI with any of the sleep parameters for CV.
Mean-Level Sleep Parameters

Table 5.3 also provides the results from the mixed effects models examining the changes in the means for each of the sleep parameters over time. There were no significant group x time effects or group effects for any of the mean-level sleep parameters. However, there was a significant time effect observed for mean-level bedtimes (p-value = 0.04) in both models. Post-hoc comparisons revealed that bedtimes were significantly later at mid-intervention in comparison to post-intervention (adjusted p-value = 0.04). No other significant time differences were noted in the other mean-level sleep parameters. Furthermore, the inclusion of baseline VO$_{2\text{peak}}$ and changes in VO$_{2\text{peak}}$ in the models revealed a significant negative association between baseline VO$_{2\text{peak}}$ and TIB (regression coefficient = -3.97, p-value = 0.03). This indicates that higher values of baseline VO$_{2\text{peak}}$ were associated with a shorter amount of TIB throughout the exercise intervention. No other significant associations were noted between these measures of fitness with the remaining mean-level sleep parameters. Additionally, the inclusion of BMI in Model 2 revealed no significant associations between BMI with any of the mean-level sleep parameters.

DISCUSSION

The purpose of this study was to examine whether 4 months of moderate-intensity exercise impacted night-to-night variability in sleep among healthy, physically inactive older women using objective measures of sleep. Overall, there was a borderline to significant time effect of small to medium size observed for WASO and number of awakenings depending on the measure of night-to-night variability and the covariates, indicating that variability in these parameters decreased over time as women participated
in moderate-intensity exercise. Additionally, greater fitness levels at baseline were associated with more consistent sleep durations and less TIB, as demonstrated by the significant inverse association between baseline VO_{2peak} levels with both measures of nightly variability in TST and mean-level TIB.

The observed reduction in both indices of variability for WASO and number of awakenings post-intervention in our study may be an indication of a possible improvement in sleep quality. Previous studies have found greater variability in WASO, sleep efficiency, and sleep fragmentation to be significantly associated with poorer self-reported sleep quality (Baron, Reid, Malkani, Kang, & Zee, 2016; Sánchez-Ortuño & Edinger, 2012). Additionally, a previous study observed a significant correlation between reductions in the amount of variability of SOL, WASO, and sleep efficiency with improvements in self-reported sleep quality among individuals with comorbid insomnia following cognitive-behavioral therapy (Sánchez-Ortuño & Edinger, 2012). Also, our results are consistent with the existing literature in which moderate-intensity aerobic exercise has been demonstrated to significantly reduce nightly variability in self-reported SOL (Buman et al., 2010) and actigraphic sleep efficiency and WASO (Baron et al., 2016) post-intervention in older adults. Thus, these findings provide further evidence supporting exercise as a non-pharmacological approach to improving sleep quality via reductions in night-to-night variability for several physiological sleep parameters.

The reduction in nightly variability found in our study for WASO and number of awakenings were seen despite a lack of change in mean-level sleep parameters. This is consistent with another study that reported that the significant reductions in SOL were independent of mean-level changes in SOL (Buman et al., 2010). This indicates that
nightly variability is an independent dimension of sleep that should be investigated in conjunction with individual means in order to fully understand the relationship between exercise and sleep.

Additionally, the inverse association demonstrated in our study between baseline VO_{2peak} levels and nightly variability in TST has not been previously examined in the literature. Several studies have evaluated the association between sleep and fitness levels at the mean-level by comparing sleep parameters between physically fit and unfit individuals. Specifically, young and middle-aged adults classified with high fitness were observed to have significantly greater slow wave sleep time, lower global Pittsburgh Sleep Quality Index scores, fewer insomnia symptoms, later self-reported bed times, shorter self-reported SOL, and shorter sleep duration in comparison to unfit individuals (Lee & Lin, 2007; Porter & Horne, 1981; Strand et al., 2013). Our study also demonstrated that high baseline VO_{2peak} levels were associated with less TIB throughout the exercise intervention. These findings in combination with the literature on mean-level associations demonstrate that higher fitness levels are associated with better quality of sleep and more consistent sleep durations. However, changes in VO_{2peak} were not found in our study to be associated with more consistent sleep patterns or improvements to mean-level sleep parameters. The lack of an association may be due to there not being enough change in fitness levels post-intervention (average change in VO_{2peak} = 11.1% [2.2 ml/kg/min]).

Although there were similarities between both measures of variability, there were some associations observed when using the 7-day SDs that were not replicated for CV. Specifically, high night-to-night variability (quantified via 7-day SDs) in the amount of
movement after sleep onset and WASO throughout the intervention was associated with a greater BMI. These associations were not observed when using CV. Other studies quantifying night-to-night variability via SDs have also observed that greater nightly variability in TST, bedtimes, and arising times were significantly associated with higher BMI and body fat percentage (Bailey et al., 2014; Moore et al., 2011; Patel et al., 2014). These differences are likely due to the CV being a more conservative measure of intra-individual variability since it takes into account the individual-level mean over the same time period as the SD. The majority of the literature predominantly quantifies night-variability via SDs more than CV or any other analytic method (Bei et al., 2015) which may be due to the ease of calculation and interpretability.

This study has several strengths. We studied older women, who are more likely to demonstrate greater night-to-night variability in self-reported sleep parameters as compared to males (Dillon et al., 2014), which makes this population ideal for studying night-to-night variability. The use of objective measures of sleep via actigraphy is another strength that allows for sleep patterns and night-to-night variability to be estimated across multiple nights in the home environment. In addition, the length of observation includes weekend nights in the calculation of nightly variability which is notable since sleep patterns tend to change on the weekends (Hashizaki, Nakajima, & Kume, 2015).

There are several limitations for this study. One limitation involves its generalizability, as the results can only be generalized to healthy older, inactive women. Individuals with insomnia or other sleep disorders may have different responses to exercise than those who do not; however, this study was unable to address this question.
because sleep complaints and disorders were not assessed. Additionally, other variables, which were not assessed, might impact the sleep-exercise relationship, including light exposure, naps, and stress/perceived stress levels (Dunn et al., 2001; Feng et al., 2014; Gerber et al., 2014; Tanaka et al., 2002; Youngstedt et al., 1997). The lack of a control group is another limitation of this study because we were unable to determine whether the observed changes in nightly variability and mean-level sleep parameters were the result of the exercise intervention or some other factor. Therefore, the lack of comparison between those in a control group with those receiving the treatment limits our ability to derive causal inferences on a sequence of events. Also, VO_{2peak} levels were only measured at baseline and post-intervention which prevented us from evaluating this covariate as a time-dependent variable in relation to sleep. Lastly, we did not assess self-reported sleep parameters and therefore, were unable to determine whether the subjective indices of sleep improved in conjugation with the observed reductions in objectively measured nightly-variability.

In summary, participation in moderate-intensity exercise training was observed to reduce the amount of nightly variability for WASO and number of awakenings over time in older women. The reductions in nightly variability of these sleep parameters suggest improved sleep quality; however, it is unknown whether these are key sleep parameters to reduce or the health implications of the observed magnitude of reductions. This study also demonstrated that higher VO_{2peak} levels at baseline were associated with more consistent sleep durations and shorter time in bed throughout the exercise intervention, but further research is warranted in order to confirm this finding in other populations and to better understand the relationship between fitness levels and nightly sleep variability.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n=49)</th>
<th>Low-Dose (n=23)</th>
<th>High-Dose (n=26)</th>
<th>p-value</th>
</tr>
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<tr>
<td><strong>Age (years)</strong></td>
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<td>64.52 (4.37)</td>
<td>64.54 (3.37)</td>
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</tr>
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<td><strong>Race, % (#)</strong></td>
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<td></td>
<td></td>
<td>0.34</td>
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<td>White</td>
<td>83.67 (41)</td>
<td>91.30 (21)</td>
<td>76.92 (20)</td>
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<td>Black</td>
<td>14.29 (7)</td>
<td>8.70 (2)</td>
<td>19.23 (5)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>2.04 (1)</td>
<td>0.00 (0)</td>
<td>3.85 (1)</td>
<td></td>
</tr>
<tr>
<td><strong>Education, % (#)</strong></td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>High School Graduate</td>
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<td>13.04 (3)</td>
<td>19.23 (5)</td>
<td></td>
</tr>
<tr>
<td>College 1 to 3 years</td>
<td>28.57 (14)</td>
<td>26.09 (6)</td>
<td>30.77 (8)</td>
<td></td>
</tr>
<tr>
<td>College 4 years or more</td>
<td>53.06 (26)</td>
<td>56.52 (13)</td>
<td>50.00 (13)</td>
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</tr>
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<td><strong>Household Income, % (#)</strong></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>&lt;$30,000</td>
<td>8.16 (4)</td>
<td>8.70 (2)</td>
<td>7.69 (2)</td>
<td></td>
</tr>
<tr>
<td>$30,000 – 49,999</td>
<td>16.33 (8)</td>
<td>17.39 (4)</td>
<td>15.38 (4)</td>
<td></td>
</tr>
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<td>$50,000 – 69,999</td>
<td>20.41 (10)</td>
<td>17.39 (4)</td>
<td>23.08 (6)</td>
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</tr>
<tr>
<td>$70,000+</td>
<td>46.94 (23)</td>
<td>47.83 (11)</td>
<td>46.15 (12)</td>
<td></td>
</tr>
<tr>
<td><strong>BMI (kg/m^2)</strong></td>
<td>25.48 (3.57)</td>
<td>26.34 (3.93)</td>
<td>24.72 (3.11)</td>
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<tr>
<td><strong>VO_{2peak} (ml/kg/min)</strong></td>
<td>19.76 (3.74)</td>
<td>19.43 (3.25)</td>
<td>20.05 (4.18)</td>
<td>0.57</td>
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<tr>
<td><strong>CES-D</strong></td>
<td>5.00 (5.01)</td>
<td>5.17 (5.46)</td>
<td>4.85 (4.68)</td>
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<td><strong>Average Sleep Parameters</strong></td>
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<tr>
<td>Bedtime (h:min)</td>
<td>10:54 PM</td>
<td>10:50 PM</td>
<td>10:57 PM</td>
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</tr>
<tr>
<td>Arising Time (h:min)</td>
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<td>6:55 AM</td>
<td>7:10 AM</td>
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</tr>
<tr>
<td>TIB (min)</td>
<td>489.62 (47.43)</td>
<td>485.30 (44.37)</td>
<td>493.50 (50.54)</td>
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</tr>
<tr>
<td>TST (min)</td>
<td>441.36 (42.52)</td>
<td>440.0 (41.30)</td>
<td>442.60 (44.35)</td>
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</tr>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>CV</td>
<td>Note</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>--------</td>
<td>--------</td>
<td>--------</td>
<td>------</td>
</tr>
<tr>
<td>SOL (min)</td>
<td>5.27 (0.95)</td>
<td>5.08 (0.90)</td>
<td>5.44 (0.98)</td>
<td></td>
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<tr>
<td></td>
<td>0.19</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Activity Counts (#)</td>
<td>30,989.65</td>
<td>29,001.80</td>
<td>32,748.10</td>
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<tr>
<td></td>
<td>(15,210.13)</td>
<td>(13,256.60)</td>
<td>(16,813.30)</td>
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<tr>
<td>WASO (min)</td>
<td>42.99 (20.92)</td>
<td>40.18 (19.12)</td>
<td>45.48 (22.47)</td>
<td>0.38</td>
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<tr>
<td>Number of Awakenings (#)</td>
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<td>13.51 (4.14)</td>
<td>14.80 (4.84)</td>
<td>0.32</td>
</tr>
<tr>
<td><strong>Night-to-Night Variability (SD)</strong></td>
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<tr>
<td>Bedtime (min)</td>
<td>57.20 (36.85)</td>
<td>63.37 (41.42)</td>
<td>51.73 (32.10)</td>
<td>0.27</td>
</tr>
<tr>
<td>Arising Time (min)</td>
<td>50.89 (27.11)</td>
<td>54.88 (32.41)</td>
<td>47.35 (21.42)</td>
<td>0.34</td>
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<tr>
<td>TIB (min)</td>
<td>69.07 (45.26)</td>
<td>77.35 (51.49)</td>
<td>61.74 (38.48)</td>
<td>0.23</td>
</tr>
<tr>
<td>TST (min)</td>
<td>63.31 (37.34)</td>
<td>68.78 (44.06)</td>
<td>58.48 (30.29)</td>
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</tr>
<tr>
<td>SOL (min)</td>
<td>1.36 (1.09)</td>
<td>1.19 (0.93)</td>
<td>1.50 (1.21)</td>
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<tr>
<td>Activity Counts (#)</td>
<td>13,423.87</td>
<td>14,350.40</td>
<td>12,604.20</td>
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<tr>
<td></td>
<td>(10321.29)</td>
<td>(11,817.70)</td>
<td>(8,952.60)</td>
<td></td>
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<tr>
<td>WASO (min)</td>
<td>18.57 (9.96)</td>
<td>19.35 (9.70)</td>
<td>17.87 (10.32)</td>
<td>0.61</td>
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<td>Number of Awakenings (#)</td>
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<td>4.58 (1.65)</td>
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<tr>
<td><strong>Night-to-Night Variability (CV)</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Bedtime</td>
<td>4.16 (2.69)</td>
<td>4.64 (3.12)</td>
<td>3.73 (2.21)</td>
<td>0.24</td>
</tr>
<tr>
<td>Arising Time</td>
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<td>12.79 (6.25)</td>
<td>10.90 (4.42)</td>
<td>0.22</td>
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<td>TIB</td>
<td>14.12 (9.03)</td>
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<td>12.62 (8.20)</td>
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<tr>
<td>TST</td>
<td>14.47 (8.59)</td>
<td>15.63 (9.58)</td>
<td>13.44 (7.66)</td>
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</tr>
<tr>
<td>SOL</td>
<td>25.47 (18.90)</td>
<td>24.73 (21.64)</td>
<td>26.12 (16.51)</td>
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<tr>
<td>Activity Counts</td>
<td>42.45 (18.23)</td>
<td>47.80 (19.85)</td>
<td>37.72 (15.54)</td>
<td>0.05</td>
</tr>
<tr>
<td>WASO</td>
<td>45.95 (16.85)</td>
<td>51.49 (17.22)</td>
<td>41.04 (15.20)</td>
<td><strong>0.03</strong></td>
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<tr>
<td>Number of Awakenings</td>
<td>34.10 (13.90)</td>
<td>34.48 (13.32)</td>
<td>33.77 (14.64)</td>
<td>0.86</td>
</tr>
</tbody>
</table>

Note: CES-D, Center for Epidemiologic Studies Depression score; CV, coefficient of variation; SD, standard deviation; SOL, sleep onset latency; TIB, total time in bed; TST,
total sleep time; WASO, wake after sleep onset; VO\textsubscript{peak}: peak oxygen consumption. Values presented are means (standard deviations) unless otherwise stated. P-values were obtained from chi-square and t-tests, with statistical significance defined at the alpha < 0.05 level.

*Indicates missing values which results in some percentages not totaling up to 100%.
Table 5.2 Differences between Participants with Complete vs. Incomplete Data

<table>
<thead>
<tr>
<th></th>
<th>Complete (n=49)</th>
<th>Incomplete (n=19)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>64.53 (3.83)</td>
<td>66.26 (4.92)</td>
<td>0.23</td>
</tr>
<tr>
<td>Race, % (#)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>83.67 (41)</td>
<td>94.74 (18)</td>
<td>0.47</td>
</tr>
<tr>
<td>Black</td>
<td>14.29 (7)</td>
<td>5.53 (1)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1.39 (1)</td>
<td>0.00 (0)</td>
<td></td>
</tr>
<tr>
<td>Education, % (#)*</td>
<td></td>
<td></td>
<td>0.05</td>
</tr>
<tr>
<td>High School Graduate</td>
<td>16.33 (8)</td>
<td>0.00 (0)</td>
<td></td>
</tr>
<tr>
<td>College 1 to 3 years</td>
<td>28.57 (14)</td>
<td>15.79 (3)</td>
<td></td>
</tr>
<tr>
<td>College 4 years or more</td>
<td>53.06 (26)</td>
<td>84.21 (16)</td>
<td></td>
</tr>
<tr>
<td>Household Income, % (#)*</td>
<td></td>
<td></td>
<td>0.54</td>
</tr>
<tr>
<td>&lt;$30,000</td>
<td>8.16 (4)</td>
<td>10.53 (2)</td>
<td></td>
</tr>
<tr>
<td>$30,000 – 49,999</td>
<td>16.33 (8)</td>
<td>10.53 (2)</td>
<td></td>
</tr>
<tr>
<td>$50,000 – 69,999</td>
<td>20.41 (10)</td>
<td>10.53 (2)</td>
<td></td>
</tr>
<tr>
<td>$70,000+</td>
<td>46.94 (23)</td>
<td>68.42 (13)</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.48 (3.57)</td>
<td>24.88 (3.33)</td>
<td>0.54</td>
</tr>
<tr>
<td>VO_{2peak} (ml/kg/min)</td>
<td>19.76 (3.74)</td>
<td>21.29 (3.01)</td>
<td>0.18</td>
</tr>
<tr>
<td>CES-D</td>
<td>5.00 (5.01)</td>
<td>4.42 (5.58)</td>
<td>0.65</td>
</tr>
<tr>
<td>Average Sleep Parameters</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bedtime (h:min)</td>
<td>10:54 PM</td>
<td>11:18 PM</td>
<td>0.17</td>
</tr>
<tr>
<td>Arising Time (h:min)</td>
<td>7:03 AM</td>
<td>7:21 AM</td>
<td>0.27</td>
</tr>
<tr>
<td>TIB (min)</td>
<td>489.62 (47.43)</td>
<td>482.70 (65.38)</td>
<td>0.63</td>
</tr>
<tr>
<td>TST (min)</td>
<td>441.36 (42.52)</td>
<td>439.50 (63.03)</td>
<td>0.90</td>
</tr>
<tr>
<td>SOL (min)</td>
<td>5.27 (0.95)</td>
<td>5.45 (0.74)</td>
<td>0.48</td>
</tr>
<tr>
<td>Activity Counts (#)</td>
<td>30,989.65 (15,210.13)</td>
<td>28,184.30 (10,581.20)</td>
<td>0.47</td>
</tr>
<tr>
<td>------------------------</td>
<td>------------------------</td>
<td>------------------------</td>
<td>------</td>
</tr>
<tr>
<td>WASO (min)</td>
<td>42.99 (20.92)</td>
<td>37.79 (14.82)</td>
<td>0.34</td>
</tr>
<tr>
<td>Number of Awakenings (#)</td>
<td>14.20 (4.53)</td>
<td>13.55 (4.14)</td>
<td>0.60</td>
</tr>
</tbody>
</table>

**Night-to-Night Variability (SD)**

<table>
<thead>
<tr>
<th>Activity Counts (#)</th>
<th>13,423.87 (10,321.29)</th>
<th>11,102.00 (8,943.50)</th>
<th>0.40</th>
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</thead>
<tbody>
<tr>
<td>WASO (min)</td>
<td>18.57 (9.96)</td>
<td>13.63 (9.00)</td>
<td>0.07</td>
</tr>
<tr>
<td>Number of Awakenings (#)</td>
<td>4.52 (1.70)</td>
<td>3.64 (1.63)</td>
<td>0.06</td>
</tr>
</tbody>
</table>

**Night-to-Night Variability (CV)**

<table>
<thead>
<tr>
<th>Activity Counts (#)</th>
<th>42.45 (18.23)</th>
<th>36.86 (21.92)</th>
<th>0.30</th>
</tr>
</thead>
<tbody>
<tr>
<td>WASO</td>
<td>45.95 (16.85)</td>
<td>35.24 (12.49)</td>
<td><strong>0.02</strong></td>
</tr>
<tr>
<td>Number of Awakenings</td>
<td>34.10 (13.90)</td>
<td>29.56 (16.71)</td>
<td>0.27</td>
</tr>
</tbody>
</table>

Note: CES-D, Center for Epidemiologic Studies Depression score; CV, coefficient of variation; SD, standard deviation; SOL, sleep onset latency; TIB, total time in bed; TST, total sleep time; WASO, wake after sleep onset; VO\textsubscript{2peak}, peak oxygen consumption. Values presented as mean (standard deviation) or as otherwise stated. P-values were obtained from chi-square and t-tests, with statistical significance defined at the alpha < 0.05 level.
*Indicates missing values which results in some percentages not totaling up to 100% in the complete group.
<table>
<thead>
<tr>
<th>Behavioral Sleep Parameters</th>
<th>7-Day SD</th>
<th>CV</th>
<th>Mean-level</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIB</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>Baseline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mid</td>
<td>0.05 (0.08)</td>
<td>0.57</td>
<td>0.07 (0.09)</td>
</tr>
<tr>
<td>Post</td>
<td>0.09 (0.07)</td>
<td>0.26</td>
<td>0.10 (0.07)</td>
</tr>
<tr>
<td>Bedtime</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>Baseline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mid</td>
<td>-0.11 (0.08)</td>
<td>0.15</td>
<td>-0.11 (0.08)</td>
</tr>
<tr>
<td>Post</td>
<td>0.08 (0.08)</td>
<td>0.32</td>
<td>0.08 (0.08)</td>
</tr>
<tr>
<td>Arising Time</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>Baseline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mid</td>
<td>0.01 (0.08)</td>
<td>0.86</td>
<td>0.03 (0.08)</td>
</tr>
<tr>
<td>Post</td>
<td>-0.01 (0.08)</td>
<td>0.90</td>
<td>0.02 (0.08)</td>
</tr>
<tr>
<td>Physiological Sleep Parameters</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TST</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>Baseline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mid</td>
<td>0.002 (0.07)</td>
<td>0.98</td>
<td>0.03 (0.07)</td>
</tr>
<tr>
<td>Post</td>
<td>0.04 (0.07)</td>
<td>0.58</td>
<td>0.05 (0.07)</td>
</tr>
<tr>
<td>SOL</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>Baseline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mid</td>
<td>0.21 (0.15)</td>
<td>0.16</td>
<td>0.15 (0.14)</td>
</tr>
<tr>
<td>Post</td>
<td>0.12 (0.15)</td>
<td>0.41</td>
<td>0.06 (0.14)</td>
</tr>
<tr>
<td>Activity</td>
<td>Baseline</td>
<td>Ref</td>
<td>Mid</td>
</tr>
<tr>
<td>----------------</td>
<td>----------</td>
<td>-----</td>
<td>---------</td>
</tr>
<tr>
<td>Activity Counts</td>
<td></td>
<td></td>
<td>-0.17 (0.09)</td>
</tr>
<tr>
<td>WASO</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of Awakenings</td>
<td></td>
<td></td>
<td>-0.02 (0.07)</td>
</tr>
</tbody>
</table>

Note: BMI, body mass index; CV, coefficient of variation; SD, standard deviation; SE, standard error; TIB, total time in bed; TST, total sleep time; WASO, wake after sleep onset.

*Unstandardized regression coefficients are presented on the log scale along with their SE. The regression coefficients for the main effect of time were similar between Model 1 (adjusted for baseline VO\textsubscript{2peak}, and changes in VO\textsubscript{2peak} from baseline to post-intervention) and Model 2 (adjusted for BMI); and therefore, Model 1 is displayed. Any major difference in p-values between Model 1 and Model 2 are noted with superscripts.

^a The p-value for the comparison between post-intervention versus baseline was 0.058 in Model 2.

^b The p-value for the comparison between post-intervention versus baseline was 0.057 in Model 2.

^c The p-value for the comparison between mid-intervention versus baseline was 0.05 in Model 2.

† Represents a significant time effect (p = 0.04, Mid vs. Post).
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CHAPTER 6
OVERALL DISCUSSION

Sleep is a modifiable behavior that commonly fluctuates from night-to-night within the same individual and varies across the lifespan (Dillon et al., 2014). There are noticeable age-related trends in sleep duration and quality in which older adults spend the greatest amount of time in bed as compared to younger individuals (Thomas et al., 2014), but have declines in several metrics of sleep quality that indicate lighter and more fragmented sleep as one ages (Ohayon et al., 2004). Despite these changes in sleep architecture with age, the literature demonstrates that the timing and quality of sleep are influenced by patterns of waking health behaviors (Irish, Kline, Gunn, Buysse, & Hall, 2015). Regular exercise, a component of physical activity (PA), is one waking health behavior that is commonly identified as a sleep hygiene recommendation as well as a non-pharmacological approach to improve sleep (Irish, Kline, Gunn, Buysse, & Hall, 2015).

Recent evidence examining the day-to-day relationship between sleep and PA has produced mixed findings, possibly due to low PA/exercise levels within free-living middle-aged to older adults (Dzierzewski et al., 2014; Irish et al., 2014; Kishida & Elavsky, 2016; Lambiase, Gabriel, Kuller, & Matthews, 2013; Mitchell et al., 2016). The mixed findings from these observational studies may be due to how slight variations in either of these behaviors may not be sufficient enough to produce a daily (acute) effect of
PA/exercise on sleep (Kishida & Elavsky, 2016). A clearer picture of the acute impact of PA on sleep may emerge by examining individuals who participate in exercise training that induces greater daily variation in PA between days with and without structured exercise. The interventional studies examining the acute effects of exercise on sleep during an exercise training intervention among older adults are few and could be expanded upon (Baron et al., 2013; King et al., 2008; Melancon, Lorrain, & Dionne, 2015).

Furthermore, the traditional approach in the literature has focused on how PA/exercise produces mean-level changes in sleep. This approach largely ignores the night-to-night variations in sleep, which is another important dimension of sleeping patterns that should be investigated in conjunction with individual means (Bei 2015; Tworoger 2005). Although the literature has yet to define what is considered an optimal amount of nightly variability, there is clinical significance for studying this dimension of sleep given the emerging evidence demonstrating that highly variable sleep patterns are associated with several negative health outcomes, including obesity, increased morbidity (e.g. diabetes, depression, heart failure), and poorer self-reported health status (Bei, Wiley, Trinder, & Manber, 2015; Patel et al., 2014).

Data collected longitudinally via actigraphy on individuals would allow for multiple assessments of sleep following days of exercise and no exercise to be examined over the course of an exercise training intervention. Additionally, this data collection method provides the opportunity to examine variability across several nights, the occurrence of changes in variability over time, and potential factors, such as exercise, that may contribute to the presence of night-to-night variability. Therefore, this dissertation sought to investigate the acute effect of exercise on sleep outcomes during an exercise
training intervention as well as examine the changes in night-to-night fluctuations in sleep parameters, behavioral and physiological, after exercise training among healthy older women. This is of particular interest given the limited number of studies within this population and the modifiability of both behaviors which could greatly influence the health and well-being of an individual.

The overall goal of this dissertation was to 1) understand how acute exercise affects both behavioral and physiological sleep outcomes during the corresponding night among trained older women and 2) to determine the impact of a four-month moderate-intensity exercise intervention on night-to-night variability in sleep among older women.

The two studies that comprise this dissertation used data collected in the WEWALK study, a clinical exercise trial that examined the effects of a walking program with two different energy expenditures on non-exercise activity thermogenesis in physically inactive older women. Multiple assessments of sleep parameters were objectively measured at baseline, mid-intervention (2 months), and post-intervention (4 months) via actigraphy.

Both of the studies contained in this dissertation utilized a longitudinal study design to identify different aspects of the relationship between exercise and sleep. Specifically, the first study included a subsample of females enrolled in the WEWALK study (n = 51) who had sleep data available following at least three days with structured exercise at our research facility and at least three days without such structured exercise at mid- and post-intervention. The number of observations available per participant at each time point ranged from 6 to 14 nights with a total number across both time points ranging from 12 to 28 nights. In the second study, a subsample of females enrolled in the
WEWALK study (n = 49) were included in the analysis if they had at least seven days of complete actigraphy sleep recordings for baseline, mid-, and post-intervention measurements and did not wear the actigraph during Daylight Saving Time transitions. Nightly variability in each of the sleep parameters was calculated using two different approaches: 1) the 7-day SD and 2) a coefficient of variation (CV), which was computed by dividing the 7-day SD by the mean (SD/mean x 100%).

The studies that comprise this dissertation investigated different aspects of the relationship between exercise and sleep; however, both studies provide evidence of within-person variability for most of the sleep parameters. Overall, the first study demonstrated in the overall sample that behavioral sleep parameters were significantly impacted by structured exercise in which bedtimes were significantly earlier on nights following a day with an acute bout of structured exercise versus a day without structured exercise. Arising times were also significantly earlier the next morning following a day that an acute bout of exercise occurred as compared to a day following no structured exercise; however, this association was no longer significant after adjusting for day of the week (weekdays versus weekends), baseline BMI, and changes in BMI, or day of the week, baseline VO_{2peak} levels, and changes in VO_{2peak}. In the second study, there was a borderline to significant time effect observed for WASO and number of awakenings depending on the measure of variability examined and the covariates controlled for in which nightly variability decreased post-intervention but not at 2 months. This may indicate a possible effect of the duration of being in a training program in that changes in nightly variability for some sleep parameters may need a longer training period to occur. However, some changes in other sleep parameters occurred sooner, as evident by mean-
level changes in bedtimes at mid-intervention. These findings of reductions in night-to-night variability in WASO and number of awakenings indicate more consistent sleep over several nights with a possible improvement to SQ (Sánchez-Ortuño & Edinger, 2012). Additionally, higher VO$_2$peak levels at baseline were associated with a shorter amount of time in bed and lower night-to-night variability in TST throughout the exercise intervention. Although there were similarities between both measures of variability, there were some associations observed when using the 7-day SDs that were not replicated for CV. Specifically, high night-to-night variability (quantified via 7-day SDs) in the amount of movement after sleep onset and WASO throughout the intervention was associated with a greater BMI at baseline. These associations were not observed when using CV as a measure of night-to-variability.

When considering the results from the two studies collectively, there are several interesting findings. Specifically, bedtimes were observed in both studies to significantly change over time as demonstrated by bedtimes being significantly later at mid-intervention compared to post-intervention, and there were also significant differences in bedtimes on nights following a day with an acute bout of exercise versus bedtimes following a day with no exercise. These findings indicate that personal habits, such as exercise, may impact both the need for sleep and the circadian pacemaker (Beersma & Gordijn, 2006; Daan et al., 1984). However, a 9.5 minute difference in bedtimes between days with an acute bout of exercise versus days with no exercise may not have been sufficient enough to change the amount of variability during the intervention as evident by the non-significant changes in the amount of variability in bedtimes over time.
In terms of physiological sleep parameters, the behavioral changes observed during the intervention did not correspond with significant mean-level improvements in any of the physiological sleep parameters following an acute bout of exercise or post-intervention. The lack of improvement over time for the physiological sleep parameters is not consistent with the literature and may possibly be explained by differences in baseline characteristics. A crude comparison between our sample with other cohorts reveals that the women in our studies appear to be better sleepers with low sleep fragmentation and greater TST (Baron et al., 2013; King et al., 2008). This may limit the amount of improvement possible at post-intervention given that they were already good sleepers at baseline. Additionally, the intervention may not have been potent enough to produce significant changes in objectively measured sleep parameters among older women. The training intensity of the WEWALK study was between 50-55% of the participants’ HRR while the intensity of other studies that demonstrated significant improvements in objective measures of sleep was between 55-85% of peak HR within similar populations. Subjective ratings of sleep have been demonstrated to improve in several other exercise intervention studies with similar training intensity levels, which may indicate that SQ improved over time in our study with the significant reductions in nightly variability for WASO and number of awakenings. Previous studies have found greater variability in WASO, sleep efficiency, and sleep fragmentation index to be significantly associated with poorer self-reported SQ (Baron, Reid, Malkani, Kang, & Zee, 2016; Sánchez-Ortuño & Edinger, 2012) suggesting that the observed reduction in variability for WASO and number of awakenings post-intervention may be an indication of a possible improvement in subjective ratings of SQ. However, sleep was only measured objectively via actigraphy
and therefore, any improvements in subjective indices of sleep were unable to be assessed.

Additionally, there were no significant differences in any of the physiological sleep parameters between nights following a day with an acute bout of exercise versus a day of no exercise in trained older women. However, there is evidence suggesting the acute effect of exercise depends on training status. Among untrained middle-aged to older adults, a bout of moderate-intensity aerobic exercise has been observed to increase SQ by improving actigraphic measures of WASO, number of nighttime awakenings, and movement as well as PSG measures of SOL, total wake time, and SE while asleep as compared to baseline measures (Passos et al., 2011; Wang & Youngstedt, 2014). Additionally, Melancon and colleagues (2015) assessed the acute effect of a bout of exercise before and after 4 months of exercise training among community-dwelling older males and found the percentage of SWS to be significantly greater after an acute bout of exercise in the trained state as compared to pre-training values obtained after a day of no exercise. We were unable to find a significant interaction between time point in the exercise intervention (mid- versus post-intervention) and exercise/non-exercise condition which may be due to no changes occurring in the exercise protocol between mid- and post-intervention. This finding in conjugation with the findings among individuals with no exercise training may suggest that the chronic effect of training versus no training has a greater impact on the acute effect of exercise on sleep, rather than the duration of being in an exercise intervention. However, an additional analysis revealed that activity levels were significantly greater on structured exercise days versus non-structured exercise days in the high-dose group only, which indicates that the shorter walking duration in the low-
dose group was not sufficient enough to produce a significant difference in activity levels on days participants exercised in our facility versus days they did not. This limits the ability to examine the effect of an acute bout of structured exercise on sleep in the overall sample when only the high-dose group was observed to have a greater variation in activity levels between days with and without the prescribed structured exercise.

There are several questions that have arisen from these studies that require further investigation. The perception that exercise may positively impact sleep during the corresponding night was not reflected in the first study which did not find a significant difference in physiological sleep parameters between nights following an acute bout of structured exercise versus nights following no structured exercise. Since sleep was not measured subjectively in the WEWALK study, there was no opportunity to determine whether the participants subjectively felt that their sleep improved or not following an acute bout of structured exercise. Future research should use a larger sample size with a control group and measure sleep subjectively and objectively at multiple time points in the training period with one of those time points taking place within the first week of training. The inclusion of an interaction term between training status (baseline versus post-intervention) and exercise/non-exercise condition in the analysis would provide a way to test whether training status impacts the effect of an acute bout of exercise on sleep during the corresponding night. Additionally, days with structured exercise should be sufficient enough to increase PA levels so that there is a significant difference between structured exercise and non-structured exercise days.

Although a reduction in the variability of WASO has been demonstrated in the literature to be associated with improvements to self-reported SQ (Sánchez-Ortuño &
Edinger, 2012), it is unknown whether the selected sleep parameters found to change post-intervention in the second study are key to reduce or the health implications of the observed magnitude of reductions. Also, the finding of a significant reduction in the amount of variability for WASO and number of awakenings was not displayed at the mean-level, thus demonstrating the need to evaluate both individual-level means and measures of variability together in order to fully understand how exercise impacts sleep. Multiple measurements of nightly variability in combination with assessing other factors that impact sleep (e.g. napping habits, stress, etc) may help to answer this question so that changes in trends can be examined over time within an exercise intervention. The significant finding that higher VO\textsubscript{2peak} levels at baseline were associated with more consistent sleep patterns and less TIB needs to be confirmed in other populations and additional research is needed to understand the role of fitness levels in reducing nightly sleep variability.

In conclusion, this dissertation found that acute exercise bouts significantly influenced behavioral sleep parameters in which bedtimes were significantly earlier on nights following a day with structured exercise versus a day with no structured exercise in healthy, trained older women. Additionally, nightly variability in WASO and number of awakenings was observed to decrease with exercise training over time. These changes in nightly variability suggest possibly greater consistency in sleep with improved SQ. Lastly, higher VO\textsubscript{2peak} levels at baseline were associated with a shorter amount of TIB and lower night-to-night variability in TST which further supports the importance of maintaining fitness levels with age. Additional studies are warranted to continue investigating the relationship between night-to-night fluctuations in sleep parameters with
PA/exercise at the intra-individual level among older women who are particularly vulnerable to sleep disturbances.


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