

# ASSOCIATION OF NIGHTTIME SLEEP AND DAYTIME FUNCTION IN OLDER ADULTS

by

**Suzanne E. Goldman**

BS, University of Michigan, 1974

BSN, Pace University, 1993

MBA, University of Southern Mississippi, 1983

MSN, Pace University, 1994

Submitted to the Graduate Faculty of  
The Graduate School of Public Health in partial fulfillment  
of the requirements for the degree of  
Doctor of Philosophy

University of Pittsburgh

2006

UNIVERSITY OF PITTSBURGH  
GRADUATE SCHOOL OF PUBLIC HEALTH

This dissertation was presented

by

**Suzanne E. Goldman**

It was defended on

**June 6, 2006**

and approved by

***Robert Boudreau, PhD***

Assistant Professor, Department of Epidemiology, Graduate School of Public Health  
University of Pittsburgh

***Jane A. Cauley, DrPH***

Vice Chair for Research and Professor, Department of Epidemiology, Graduate School of Public Health  
Associate Professor, School of Nursing  
University of Pittsburgh

***Martica Hall, PhD***

Assistant Professor of Psychiatry and Psychology  
Department of Psychiatry, School of Medicine  
University of Pittsburgh

***Karen A. Matthews, PhD***

Professor of Epidemiology and Psychiatry  
Department of Epidemiology, Graduate School of Public Health  
Department of Psychiatry, School of Medicine  
University of Pittsburgh

***Dissertation Advisor***

***Anne B. Newman, MD, MPH***

Professor of Epidemiology and Medicine  
Department of Epidemiology, Graduate School of Public Health  
Department of Gerontology, School of Medicine  
University of Pittsburgh

**ASSOCIATION OF NIGHTTIME SLEEP AND DAYTIME FUNCTION IN OLDER  
ADULTS**

Suzanne E. Goldman, PhD

University of Pittsburgh, 2006

Changes in nighttime sleep, daytime napping, and fatigue are common complaints in older adults. This study investigated the association between nighttime and daytime sleep, fatigue, and daytime physical function in two cohorts of older adults (75-85 years); The Study of Osteoporotic Fractures (SOF) and the Health Aging and Body Composition Study (Health ABC).

In SOF, measured short sleep duration ( $\leq 6$  hours) was associated with slower gait speed and long sleep duration ( $\geq 7.5$  hours) was associated with longer time to complete 5 chair stands. More wake after sleep onset was associated with slower gait speed, longer time to complete 5 chair stands, lower grip strength and higher odds of Instrumental Activities of Daily Living (IADL) impairment. Women with higher daytime sleep took longer to complete 5 chair stands and had higher odds of IADL impairment. These findings supported the hypothesis that older women with disturbed sleep would have poorer function.

In Health ABC, there was a wide range of fatigue symptoms. Compared to self-reported sleep durations of 7 hrs/night,  $>8$  hrs/night was associated with 7% higher fatigue. Awakening during the night or wakening too early in the morning were each associated with 6% higher fatigue. These results remained after multivariate adjustment independent of comorbidity. The association between disturbed nighttime sleep and reported fatigue symptoms suggests that better and more effective behavioral management of sleep may help reduce fatigue in older adults.

In the Health ABC ancillary sleep study, 75.7% of the participant's recorded at least one nap/week in their sleep-wake diary. Individuals with more fragmented nighttime sleep, self-reported diabetes, pain, or respiratory symptoms had higher odds of recording a nap. In the group that napped neither sleep duration nor fragmentation the night before the nap was associated with nap duration the next day. Identification of causes and methods to reduce fragmented sleep may help lessen daytime napping in older adults.

The public health importance of these findings is that sleep duration and quality are important factors in the daytime function of older adults, and may be important targets for intervention to improve quality of life.

## TABLE OF CONTENTS

<b>ACKNOWLEDGEMENTS .....</b>	<b>X</b>
<b>DEDICATION.....</b>	<b>XI</b>
<b>1.0 INTRODUCTION.....</b>	<b>1</b>
<b>1.1 DISSERTATION OVERVIEW AND OBJECTIVE.....</b>	<b>1</b>
<b>1.2 BACKGROUND AND SIGNIFICANCE.....</b>	<b>2</b>
<b>1.2.1 Sleep changes in older adults .....</b>	<b>2</b>
<b>1.2.2 Prevalence and burden of disturbed sleep, napping, and fatigue in community-dwelling older adults .....</b>	<b>3</b>
<b>1.2.3 Assessment of sleep, napping, and fatigue in the community .....</b>	<b>4</b>
<b>1.2.4 Association of disturbed nighttime sleep and daytime performance in older adults .....</b>	<b>6</b>
<b>1.2.5 Association of disturbed nighttime sleep and fatigue in community- dwelling older adults.....</b>	<b>7</b>
<b>1.2.6 Association of disturbed nighttime sleep and napping in community- dwelling older adults.....</b>	<b>8</b>
<b>1.2.7 Limitations of the existing literature.....</b>	<b>9</b>
<b>1.3 REFERENCES .....</b>	<b>10</b>
<b>2.0 ARTICLE ONE: ACTIGRAPHIC MEASURES OF SLEEP ARE ASSOCIATED WITH POORER DAYTIME FUNCTIONING IN OLDER WOMEN.....</b>	<b>18</b>
<b>2.1 ABSTRACT.....</b>	<b>19</b>
<b>2.2 INTRODUCTION .....</b>	<b>20</b>
<b>2.3 METHODS.....</b>	<b>20</b>
<b>2.3.1 Participants.....</b>	<b>20</b>
<b>2.3.2 Sleep evaluation.....</b>	<b>21</b>

2.3.3	Physical function .....	22
2.3.4	Potential confounders .....	22
2.3.5	Statistical Analysis .....	23
2.4	RESULTS .....	24
2.5	DISCUSSION.....	25
2.6	ACKNOWLEDGEMENTS .....	28
2.7	REFERENCES .....	29
3.0	<b>ARTICLE TWO: SLEEP PROBLEMS AND ASSOCIATED DAYTIME FATIGUE IN COMMUNITY DWELLING OLDER INDIVIDUALS.....</b>	<b>40</b>
3.1	ABSTRACT.....	41
3.2	INTRODUCTION .....	42
3.3	METHODS.....	42
3.3.1	Study Population.....	42
3.3.2	Procedure.....	43
3.3.3	Data Analysis.....	44
3.4	RESULTS .....	45
3.5	DISCUSSION.....	46
3.6	ACKNOWLEDGEMENTS .....	48
3.7	REFERENCES .....	49
4.0	<b>ARTICLE THREE: ASSOCIATION BETWEEN NIGHTTIME SLEEP AND NAPPING IN OLDER.....</b>	<b>58</b>
4.1	ABSTRACT.....	59
4.2	INTRODUCTION .....	60
4.3	METHODS.....	60
4.3.1	Study Population.....	60
4.3.2	Sleep .....	61
4.3.3	Demographics and General Health .....	63
4.3.4	Outcome.....	63
4.3.5	Comorbid health conditions.....	63
4.3.6	Other potential confounders .....	64
4.3.7	Statistical analyses .....	64

4.4	<b>RESULTS .....</b>	<b>65</b>
4.5	<b>DISCUSSION.....</b>	<b>67</b>
4.6	<b>ACKNOWLEDGMENT .....</b>	<b>70</b>
4.7	<b>REFERENCES .....</b>	<b>71</b>
<b>5.0</b>	<b>GENERAL DISCUSSION .....</b>	<b>81</b>
5.1	<b>SUMMARY OF FINDINGS.....</b>	<b>81</b>
5.2	<b>PUBLIC HEALTH SIGNIFICANCE.....</b>	<b>87</b>
5.3	<b>FUTURE RESEARCH.....</b>	<b>87</b>
5.4	<b>CONCLUSION .....</b>	<b>89</b>
5.5	<b>REFERENCES .....</b>	<b>91</b>
	<b>APPENDIX A SUMMARY OF STUDIES ON SLEEP, NAPPING, AND ACTIGRAPHY</b>	<b>99</b>
	<b>APPENDIX B ANCILLARY STUDY .....</b>	<b>113</b>
	<b>BIBLIOGRAPHY .....</b>	<b>126</b>

## LIST OF TABLES

<b>Table 2-1</b> Comparison of Demographic, Health and Performance Variables in the SOF Cohort at the 8 <sup>th</sup> clinic visit (2002 – 2004). .....	34
<b>Table 2-2</b> Comparison of demographic, health, actigraphic sleep and performance measurements by race in the analysis group of the SOF cohort at the eighth clinic visit (2002-2004). .....	35
<b>Table 2-3</b> Daytime performance measures by quartile of Total Nighttime Sleep, Wake After Sleep Onset and Daytime Sleep in the Study of Osteoporotic Fracture participants at the eighth clinic visit <sup>2</sup> . .....	37
<b>Table 2-4</b> Odds of having an IADL impairment by quartile of Total Nighttime Sleep, Wake After Sleep Onset and Daytime Sleep in the Study of Osteoporotic Fracture participants at the eighth clinic visit.....	39
<b>Table 3-1</b> Participant characteristics at the Health ABC year 5 (2001-2002) clinic visit.....	53
<b>Table 3-2</b> Correlation of the fatigue scale components to the total fatigue score and symptoms of disturbed nighttime sleep (Spearman’s rho $r_s$ ) in Health ABC year 5 (n=2264).....	55
<b>Table 3-3</b> Factors associated with fatigue in multivariable models adjusted for age, race and gender and fully adjusted.....	56
<b>Table 4-1</b> Characteristics of Health Aging and Body Composition sleep study participants by napping status (N=236).....	74
<b>Table 4-2</b> Odds of taking a daytime nap in the Health Aging and Body Composition Sleep Study (n = 235) <sup>1</sup> .....	76
<b>Table 4-3</b> Regression models showing the temporal association of measured nighttime sleep duration and fragmentation.....	77
<b>Table 4-4</b> Multivariable associates of nap duration in the Health ABC sleep study participants who reported naps (n = 159). .....	78



<b>Table 4-5</b> Multivariable associates of previous night sleep and nap duration on nap night sleep duration using mixed model analysis in Health ABC sleep study participants who reported daytime nap (n = 159).....	79
<b>Table 4-6</b> Predictors of average nap duration (hour) in Health ABC sleep study participants who reported a daytime nap (n = 178) .....	80
<b>Table A.5-1</b> Summary of epidemiologic studies evaluating sleep in older adults.....	100
<b>Table A.5-2</b> Summary of epidemiological studies evaluating sleep duration and mortality .....	105
<b>Table A.5-3</b> Summary of studies on napping in the community .....	107
<b>Table A.5-4</b> Summary of studies of on napping and actigraphy in older adults.....	109

## ACKNOWLEDGEMENTS

I would like to thank everyone who made this accomplishment possible:

Dr. Anne B. Newman, my advisor and doctoral committee chair, for her unwavering patience, guidance, and support. The depth of knowledge she instilled was invaluable to my professional growth. Thank you for pushing me past limits I never thought possible.

The remainder of my doctoral committee: Dr. Robert Boudreau, not only for taking the time to help with the analyses, but for filling in the gaps in my biostatistical education. Dr. Jane A. Cauley, my original advisor and a major source of my GSR funding, for her invaluable feedback throughout my graduate program and research studies. Dr. Martica Hall, for her guidance into the realm of sleep research, and Dr. Karen A. Matthews, for her in-depth review and critique of my dissertation research.

I would also like to acknowledge the staff at the Department of Epidemiology, Health Studies Research Center, for their help in my independent research project, support and friendship throughout my time as a GSR at the facility. In particular, The Health ABC study research staff, for their help and assistance in assuring my research was included in their already busy clinic visit.

Special appreciation goes to my family for their continual support, especially my husband Tracy Ott without whom this endeavor would not have been possible.

Last, but not least, the participants in Health ABC and SOF studies for their participation in these research projects.

## **DEDICATION**

This dissertation is dedicated to the people who mean the most to me in the world.

To Tracy, my best friend and partner for life, for whom this endeavor would not have been undertaken or completed. To Amy, my sister and other best friend, for always being there especially through those darkest days. To Gayle, my mom, for her support and always believing in me. To my grandparents, Helen and Mac Resnick, who are always with me in thought and who would have been so happy to see this day.

Finally, to my two sources of unconditional love, Honey Bear and Teddy Bear.

## **1.0 INTRODUCTION**

### **1.1 DISSERTATION OVERVIEW AND OBJECTIVE**

Changes in nighttime sleep, daytime napping, and fatigue are common complaints in older adults, and are associated with reduced daytime performance and function, medical comorbidity and cognitive decline<sup>1</sup>. These changes may have negative consequences on functioning and quality of life<sup>2,3</sup>. Over half of all adults 65 years of age, or older, suffer with disturbed sleep at some point in time. About two-thirds of older individuals experience some type of sleep problem at least a few nights per week<sup>4,5</sup>. Existing information on the association of nighttime sleep problems with daytime napping, fatigue, and daytime function is primarily based on self-report data rather than with objectively measured sleep and/or function. Sleep duration and quality are important factors in the daytime function of older adults. Research is needed to determine how nighttime sleep patterns are associated with subsequent daytime napping, fatigue, and function in individuals as they reach the eighth decade of life. These associations may be important target areas for intervention to improve quality of life.

The objective of this dissertation was to examine the relationship between nighttime and daytime sleep behaviors, daytime fatigue, and daytime function in older adults. Nighttime and daytime sleep was evaluated subjectively by self-report and objectively quantified with wrist actigraphy. The three dissertation papers addressed the following:

1. Are total night time sleep duration and sleep fragmentation, measured with actigraphy, associated with daytime function in community dwelling older women?
2. Is daytime fatigue, measured with a standardized fatigue questionnaire, related to self-reported hours of sleep, disturbed nighttime sleep, or napping in community dwelling older adults?

3. Are nighttime sleep duration or fragmentation, measured with actigraphy, associated with measured daytime sleep (napping) and nap duration in community dwelling older adults?

## **1.2 BACKGROUND AND SIGNIFICANCE**

### **1.2.1 Sleep changes in older adults**

Sleep changes with aging<sup>1, 6, 7</sup>. Changes occur in sleep quality, duration, continuity, architecture, and circadian cycles<sup>8</sup>. Older individuals spend more time in stage 1 sleep, stage 2 sleep is either longer or shows no change, and there is less stage 3, stage 4 sleep (deep sleep), and REM sleep<sup>6, 9, 10</sup>. As stage 1 sleep is considered to indicate the degree of sleep disruption the increase in time denotes a greater percentage of sleep fragmentation.

In general, older individuals spend more time in bed, obtain over an hour less sleep nightly, have more night time awakenings, reduced sleep efficiency, and take more naps<sup>11, 12</sup>. Sleep disturbances commonly associated with older individuals include difficulty initiating or maintaining sleep, nocturnal wakening, waking up too early in the morning, waking not rested, as well as irregular sleep times, short total sleep duration, and daytime napping<sup>1, 7, 13-15</sup>.

Compared with younger individuals older individuals sleep more (average of 7.1 (weekdays) to 7.2 (weekends) hours and 6.9 to 7.1 hours, respectively), and their sleep problems are often associated with existing comorbid medical and psychiatric diseases, physical, and psycho-social factors<sup>1, 4, 16, 17</sup>. Further, older people are sleepy during the day, suggesting that the ability to sleep at night is shortened with age<sup>7, 18, 19</sup>. Upwards of 15% of older people have sleepiness so severe during the day that it interferes with their daily activities, while an additional 11-12% experience it a few days a month<sup>4</sup>.

## **1.2.2 Prevalence and burden of disturbed sleep, napping, and fatigue in community-dwelling older adults**

Sleep disturbances in older adults are associated with significant morbidity and mortality<sup>3, 20-24</sup>, can result in daytime impairment<sup>1, 25</sup>, and are increasingly recognized as part of a geriatric syndrome<sup>23</sup>. Sleep disturbances can have a strong, negative effect on the quality of life<sup>2</sup>. The association of short ( $\leq 6$  hours) and long sleep duration ( $> 8$  hours) with up to 15% higher mortality has been reported in multiple studies<sup>11, 23, 26-29</sup> (Table A.1.1).

Prevalence rates of poor sleep in older adults range from 13–57% dependent on the specific sleep complaint being evaluated<sup>1, 3, 21, 24, 30</sup>. Based on the types of direct and indirect costs included in the estimate, costs of insomnia across the life-span have been estimated to range from approximately \$13.9 billion to over \$30 billion dollars (1995 dollars)<sup>31-34</sup> and tens of billions annually in 2005<sup>35</sup>. Additional associated costs range from \$50 billion<sup>36</sup> to as high as \$100 billion annually when lost productivity, medical expenses, sick leave, property, and environmental damages are included<sup>5, 34</sup>. A summary of epidemiological studies evaluating sleep in older adults is presented in Table A.1.2.

Napping is common in older individuals<sup>37, 38</sup>. Estimates of the proportion of older individuals who nap range from 24 – 64%<sup>1, 4, 13, 39-41</sup>. The economic burden directly associated with napping in older adults has not been established. However, daytime napping can result in impaired cognition, impaired performance, more accidents, and psycho-social problems that can compromise the individuals quality of life<sup>1, 33, 42, 43</sup>.

The prevalence and economic burden associated with fatigue in community-dwelling older adults is not known; however the prevalence of fatigue in older adults living in assisted living facilities was found to be as high as 98% with over 50% of the residents expressing mild to severe fatigue levels<sup>44</sup>. The prevalence of fatigue in other populations, ranges from 6–45 % in primary care patients<sup>45-47</sup>, to as high as 67% in older women a year after a myocardial infarction<sup>48</sup>, to over 75% in individuals receiving chemotherapy.

### 1.2.3 Assessment of sleep, napping, and fatigue in the community

Assessment of sleep can be performed in the laboratory or home. Methods include polysomnography (PSG), wrist actigraphy, sleep logs and diaries, and questionnaires. PSG is considered the gold standard for measuring sleep<sup>49</sup>. PSG allows for measurement of at least 3 types of data (EEG, EOG, and EMG) which jointly determine sleep architecture and if a person is asleep or awake. It also allows for simultaneous recording of multiple physiologic parameters during sleep<sup>7, 50, 51</sup>. However, PSG has several drawbacks. PSG needs to be manually scored and interpreted by trained specialists, it is costly to obtain and score, and even with home monitoring it is difficult to administer in large population studies. Additionally, PSG is cumbersome, semi-invasive, and can disturb an individuals' sleep which often leads to a "first night" effect as the individual adjusts to the equipment. Finally, PSG provides data for only the time of recording<sup>7, 49, 51</sup>.

Wrist actigraphy has been used to evaluate sleep/wake patterns for over 20 years. It is based on the premise that during sleep there is little movement, while during wake there is more movement. Actigraphy has been demonstrated to be an effective means of measuring sleep in older adults<sup>49, 50</sup>. Wrist actigraphs can record data continuously over 24 hour periods, can be used as an adjunct to routine evaluation of sleep disorders, and is useful in special populations like demented older adults. Further, it is suitable for population studies due to its ease of administration and use and lower cost than PSG. Actigraphy data are analyzed with computer algorithms designed to determine levels of activity/inactivity, rhythm parameters, and sleep/wake variables<sup>50</sup>. Results from reliability studies, comparing actigraphy and EEG to distinguish wake from sleep, have ranged from 0.89–0.98 in healthy normal sleepers to 0.78 to 0.88 in individuals presenting to sleep disorder clinics<sup>49</sup>. Studies generally agree that although actigraphy is not as accurate as PSG for specific sleep measurements only obtainable by PSG, it is more reliable than sleep logs, and can record continuously for 24-hrs a day for long periods of time<sup>49, 50, 52-54</sup>. Actigraphy can also provide information obtained in no other way, such as in demented individuals, or in situations where PSG or sleep diaries are not suitable<sup>50</sup>. A summary of studies using actigraphy to measure sleep are presented in table A.1.3.

Sleep diaries provide subjective estimates of sleep parameters<sup>55</sup>. Sleep diaries vary in complexity, from a simple chart to a complex diary, dependent on the particular research project.

Sleep diaries have a high percentage of agreement with polysomnography ( $\kappa=0.87$ ), with a sensitivity and specificity of 92.3% and 95.6%, respectively <sup>56</sup>. When compared to actigraphy, the reliability for measurement of night time sleep duration was  $r=0.69$  ( $p<0.001$ ) <sup>57</sup>. While sleep diaries and wrist actigraphy provide comparable estimates of total sleep duration and sleep efficiency, the wrist actigraph records more nocturnal awakenings than recalled on sleep diaries <sup>57</sup>. Sleep diaries can provide fairly reliable information, however they require considerable commitment on the part of the individual to complete <sup>58</sup>.

In population studies interview-administered questionnaires are frequently used to assess disorders of initiating and maintaining sleep <sup>59</sup>. Sleep questions may include: “How many hours of sleep do you usually get at night?”; “During a usual week, how many times do you nap?”; “At what time do you usually go to bed?”; “At what time do you usually awake?”; “How often do you experience difficulty falling asleep?”; “How often do you wake up during the night and have difficulty getting back to sleep (frequent awakenings)?”; “How often do you wake up too early in the morning and are unable to get back to sleep (early morning awakenings)?”; “How often do you take sleeping pills or other medication to help you sleep?”; and “Do you ever have sleepiness during the day that is so severe it required a nap or interferes with your activities?”

Test-retest reliability of sleep questionnaires has been shown to be fairly high. In a 6 and 12 month follow-up of cardiac surgery patients the reliability was found to be 0.58, with internal consistency coefficients of 0.63 for a 3 item scale and 0.79 for a 4 item scale <sup>59</sup>. Test-retest correlations in a younger cohort (mean age 29.3 years) for total sleep time in 2 interviews 1 month apart was 0.87 and 0.93 respectively ( $p<0.01$ ) <sup>60</sup>. In that same study, self-reported point estimates of bedtime and wake time were strongly correlated with the median time reported in the sleep diaries ( $r=0.93$ ,  $p<0.001$ ) <sup>60</sup>.

In summary, PSG is the “gold standard” for sleep measurement. Sleep diaries and actigraphy however have been shown, in multiple studies, to provide reliable data in situations where PSG would be unavailable, not feasible or impractical. Situations where the evaluations of sleep-wake patterns over multiple nights are of interest, such as large population studies, are particularly suited to the use of sleep diaries and/or actigraphy. Actigraphy is more reliable than sleep diaries that rely on an individual's recall <sup>50, 53</sup>, it is a cost-effective method to evaluate sleep patterns <sup>61</sup>, and less cumbersome to the individual.



Assessment of daytime naps usually has been done by interview-administered questionnaires, or with self-reported sleep logs<sup>37, 62</sup>. However, sleep diaries may underestimate actual napping frequency as naps are often not recorded by the individual<sup>12, 37</sup>. Wrist actigraphy has been used in conjunction with sleep logs<sup>12, 38, 62, 63</sup>, however this can be biased towards higher numbers of naps if periods of wakefulness without movement such as watching TV are scored as napping<sup>12, 62, 64</sup>.

Fatigue is more difficult to measure than nighttime sleep or napping. Fatigue is multi-dimensional<sup>46, 65-67</sup> and there are over 30 measurement scales reported in the literature<sup>68</sup>. These scales have been developed, and tested, in various populations in order to quantify the multidimensionality of this syndrome<sup>44, 66, 69-74</sup>. The more complex fatigue scales typically include questions to assess areas of behavior, affect, cognition and mood, and global distress. The majority of scales were developed and tested in cancer patients, or other populations with chronic illness. A study has been performed in older adults living in assisted living facilities using the modified Piper fatigue scale<sup>44</sup>.

As discussed later, the term fatigue is often used interchangeably with daytime sleepiness, although these are distinct concepts. Most fatigue scales do not evaluate or exclude sleepiness. Daytime sleepiness however, can be measured in the clinic setting with scales such as the Epworth Sleepiness Scale, or the Stanford Sleepiness Scale that are designed to estimate the likelihood of falling asleep in different situations<sup>75</sup>. In the laboratory sleepiness is measured with the Multiple Sleep Latency Test which is a test of the physiological measure of sleepiness<sup>76</sup>.

#### **1.2.4 Association of disturbed nighttime sleep and daytime performance in older adults**

Correlations between disturbed sleep and morbidity have been consistently observed, however a causal relationship between sleep disturbances and decreased physical performance has not been established<sup>33</sup>. In middle aged adults, chronic insomnia is associated with work days missed, impaired work performance, and automobile accidents<sup>35</sup>. In older adults, sleep complaints are associated with a higher prevalence of physical disabilities<sup>13</sup>. In one large study of older adults those with self-reported symptoms of insomnia had 17% higher odds of an ADL limitation,

while those who woke feeling not rested were 23% more likely to have a limitation with ambulation<sup>13</sup>.

### **1.2.5 Association of disturbed nighttime sleep and fatigue in community-dwelling older adults**

The association between disturbed nighttime sleep (short and long sleep durations, difficulty initiating and maintaining sleep and waking up during the night) and fatigue has not been established. Fatigue is a multi-dimensional, non-specific, syndrome<sup>47, 65, 71, 77-79</sup> described as weariness, weakness, and depleted energy. Fatigue is a common complaint in older adults that can affect quality of life<sup>44, 80</sup>. The association of fatigue and chronic disease has been well established. Fatigue is related to depression<sup>78</sup>, myocardial infarction<sup>48</sup> and to changes in the sleep/wake cycles and quality and quantity of sleep in cancer<sup>65, 66, 71, 73, 81</sup> and rheumatoid arthritis patients<sup>65, 82</sup>.

Fatigue is often confused with daytime sleepiness. Although separate constructs<sup>83</sup>, fatigue and daytime sleepiness may overlap due to the multidimensionality of fatigue and the measurement tool used to define fatigue or sleepiness. Both include an aspect of tiredness, and are often used interchangeably, even though they are distinct phenomenon<sup>45, 47, 65, 68, 84</sup>. Tiredness and fatigue have been shown to predict development of disability with basic activities of daily living<sup>85</sup>. The impact of fatigue on daily living, in older adults, is about twice that of the impact of daytime sleepiness in younger adults<sup>80</sup>. Due to its confusion with sleepiness, or other complaints, fatigue may be under-recognized and under-treated<sup>47, 68, 86, 87</sup>.

It has been suggested that fatigue is an important health indicator in the elderly<sup>88</sup>. It is known that older adults who complain of tiredness are at a higher risk of becoming disabled<sup>89, 90</sup>. Since tiredness is a component of fatigue, and fatigue is thought to be distinct from daytime sleepiness, the potential that fatigue is associated with changes in sleep in older adults which may subsequently affect physical activity and performance exist.

## **1.2.6 Association of disturbed nighttime sleep and napping in community-dwelling older adults**

Daytime napping increases in frequency and duration with aging<sup>8, 30, 37, 39, 91, 92</sup> and does not appear to differ significantly by age or gender<sup>39, 40</sup>. The association between nighttime sleep and napping, and napping and daytime function, in older adults is not clearly defined. A cycle of fragmented nighttime sleep, reduced sleep efficiency, fatigue and napping has been reported<sup>93</sup>, with nap duration a major factor in the association<sup>8</sup>. Studies evaluating napping in older adults have been performed in the nursing home<sup>94, 95</sup>; as small laboratory controlled studies where napping is measured with PSG; evaluated by one or two questions in a larger study; or assessed with actigraphy as part of larger study (Table A.1.2 and Table A.1.3.).

A variety of studies that have used PSG, actigraphy, or self-report data have found nighttime sleep variables (total sleep time, sleep efficiency, wakening up during the night, waking up too early) did not differ between days when the individual napped and days when there were no naps. These studies also found no differences between the individuals who took more frequent or less frequent naps<sup>37, 55, 64, 96-98</sup>. Other studies have found higher frequencies of daytime naps to be associated with: shorter total sleep time<sup>99</sup>, awakening not feeling rested in the morning<sup>92, 100</sup>, early morning wakening (6:04 am  $\pm$ 1:06 hr versus 7:02 am  $\pm$ 1:12 hr,  $p=0.001$ )<sup>62, 101</sup>, and more sleep complaints. One small laboratory study (n=9) found when total sleep time was added to nap time, in the nap group although there was a non-significant difference between total day plus night sleep time between the nap participants and the non-nap participants (nap group 6.3 (1.0) hrs, non nap group 6.6 (1.1) hrs  $p>0.25$ )<sup>41</sup>.

The association of napping on the overall well being, and performance, of older adults is not clear<sup>8</sup>. Laboratory studies measuring the effects of daytime naps with performance, generally have evaluated cognitive and psychomotor performance tasks using tests such as the visual detection tasks, logical reasoning task, two-letter visual search task, Stroop congruency task, Wilkinson four-choice reaction time test, and the mini-mental status exam. Significant improvement in these performances has been shown in some studies<sup>96, 98, 102</sup>. However, other studies have shown reduced performance<sup>103</sup>, reduced physical activity<sup>104</sup>, or no improvement<sup>41, 92</sup>. Based on existing studies it is difficult to make a conclusion to whether or not night time sleep

is directly associated with daytime napping, as well as if napping benefits daytime functioning in the community dwelling older.

### **1.2.7 Limitations of the existing literature**

Although sleep disturbances, daytime napping, and fatigue are known to be common in older adults they are not to be considered consequences of aging<sup>17, 105</sup>. There are few studies of the associations between disturbed sleep and daytime function, disturbed sleep and fatigue, and disturbed sleep and daytime napping focused specifically on these associations in community-dwelling older adults. Especially lacking are studies in this population using objective measures of sleep and nap behaviors. Although studies have evaluated the effects of sleep disturbances<sup>20</sup>, daytime sleepiness<sup>23</sup>, napping, and fatigue<sup>44</sup> on populations that include older individuals, these epidemiologic studies in general did not have sleep or nap parameters as either the primary exposure or primary outcome. Other studies on napping and function have been performed in small groups of individuals in controlled laboratory settings. Research specifically designed to evaluate the complex relationship between sleep, napping, and fatigue is needed to further understand the association between them and daytime function in community dwelling older adults.

### 1.3 REFERENCES

1. Ancoli-Israel S. Sleep and aging: prevalence of disturbed sleep and treatment considerations in older adults. *J Clin Psychiatry* 2005;66(suppl 9):24-30.
2. National Institutes of Health Consensus Development Conference Statement. The treatment of sleep disorders of older people. *Sleep* 1991;14:169.
3. Maggi S, Langlois JA, Minicuci N, et al. Sleep complaints in community-dwelling older persons: prevalence, associated factors, and reported causes. *J Amer Geriatrics Soc* 1998;46(2):161-8.
4. National Sleep Foundation. 2003 Sleep in America Poll; 2003.
5. Wakening America to the Importance of Sleep. 2004. (Accessed at <http://www.sleepfoundation.org/>)
6. Bliwise DL. Normal Aging. In: Kryger MH, Roth T, Dement WC, eds. *Principles and Practice of Sleep Medicine*. 3rd edition ed: W. B. Saunders Company; 2005.
7. Feinsilver SH. Sleep in the elderly: What is normal? *Clinics in Geriatric Medicine* 2003;19(1):10.
8. Ancoli-Israel S MJ. Insomnia and daytime napping in older adults. *J Clin Sleep Med* 2006;accepted 4/17/06.
9. Quan SF, Bamford CR, Beutler LA. Sleep disturbances in the elderly. *Geriatrics* 1984;39(9):42 - 7.
10. Pressman MR, Fry JM. What is normal sleep in the elderly? *Clinics in Geriatric Medicine* 1988;4(1):71 - 82.
11. Youngstedt SD, Kripke DF. Long sleep and mortality: rationale for sleep restriction. *Sleep Medicine Reviews* 2004;8:159-74.
12. Evans BD, Rogers AE. 24 -Hour sleep/wake patterns in healthy elderly persons. *Applied Nursing Research* 1994;7(2):75 - 83.
13. Foley DJ, Monjan AA, Brown SL. Sleep complaints among elderly persons: an epidemiologic study of three communities. *Sleep* 1995;18:425 - 32.
14. Neubauer DN. Sleep problems in the elderly. *Am Fam Physician* 1999;59(9):11 pp.

15. Jacobs JM, Cohen A, Hammerman-Rozenberg R, Stessman J. Global sleep satisfaction of older people: The Jerusalem Cohort Study. *Journal of the American Geriatrics Society* 2006;54(2):325-9.
16. Foley DJ, Ancoli-Israel S, Britz P, Walsh JK. Sleep disturbances and chronic disease in older adults: Results of the 2003 National Sleep Foundation Sleep in America Survey. *Journal of Psychosomatic Research* 2004;56(5):497-502.
17. Ohayon MM, Zulley J, Guilleminault C, Smirne S, Priest RG. How age and daytime activities are related to insomnia in the general population: consequences for older people. *JAGS* 2001;49:360-6.
18. Miles LE, Dement WC. Sleep and aging. *Sleep* 1980;3:119-220.
19. Ancoli-Israel S. Sleep problems in older adults: putting myths to bed. *Geriatrics* 1997;52:20 - 30.
20. McCall WV. Sleep in the elderly: Burden, diagnosis, and treatment. *Prim Care Companion J Clin Psych* 2004;6(1):9-19.
21. Foley DJ, Monjan AA, Brown SL, Simonsick EM ea. Incidence and remission of insomnia among elderly adults: an epidemiologic study of 6,800 persons over three years. *Sleep* 1999;22((suppl 2)):5366-72.
22. Jean-Louis G, Kripke DF, Ancoli-Israel S. Sleep and quality of well-being. *Sleep* 2000;23(8):1-7.
23. Newman AB, Spiekerman CF, Enright P, et al. Daytime sleepiness predicts mortality and cardiovascular disease in older adults. *JAGS* 2000;48:115-23.
24. Quan SF, Katz R, Olson J, et al. Factors associated with incidence and persistence of symptoms of disturbed sleep in an elderly cohort: The Cardiovascular Health Study. *Am J Med Sci* 2005;329(4):163-72.
25. Ancoli-Israel S, Cooke JR. Prevalence and comorbidity of insomnia and effect on functioning in elderly populations. *Journal of the American Geriatrics Society* 2005;53(s7):S264-S71.
26. Kripke DF, Simons RN, Garfunkel L, Hammond C. Short and long sleep and sleeping pills. *Arch Gen Psych* 1979;36:103-16.
27. Kripke DF, Garfinkel L, Wingard DL, Klauber MR, Marler MR. Mortality associated with sleep duration and insomnia. *Archives Of General Psychiatry* 2002;59(2):131-6.
28. Grandner MA, Kripke DF. Self-reported sleep complaints with long and short sleep: A nationally representative sample. *Psychosomatic Medicine* 2004;66:239-41.

29. Patel SR, Ayas NT, Malhotra MR, et al. A prospective study of sleep duration and mortality risk in women. *Sleep* 2004;27(3):440-4.
30. Gislason T RH, Kristbjarnarson H, Benediktsdottir B. Sleep habits and sleep disturbances among the elderly - an epidemiological survey. *Journal of Internal Medicine* 1993;234:31 - 9.
31. Walsh JK, Englehardt CL. The direct economic costs of insomnia in the United States for 1995. *Sleep* 1999;suppl 2:S386-S93.
32. Edinger JD, Means MK. Overview of insomnia: definitions, epidemiology, differential diagnosis, and assessment. In: Kryger M RT, Dement WC, ed. *Principles and Practices of Sleep Medicine*. Philadelphia AP: Elsevier Saunders; 2005.
33. Walsh JK. Clinical and socioeconomic correlates of insomnia. *J Clin Psychiatry* 2004;65(suppl8):13-9.
34. Chilcott LA, Shapiro CM. The socioeconomic impact of insomnia: An overview. *Pharmacoeconomics* 1996;10(suppl 1):1-14.
35. National Institutes of Health State-of-the-Science Conference Statement. Manifestations and management of chronic insomnia in adults. June 13-15, 2005.
36. Quan SF. Frontiers of knowledge in sleep and sleep disorders: opportunities for improving health and quality of life. *J Clin Sleep Med* 2005;1(1):83 - 9.
37. Buysse DJ, Browman BA, Monk TH, Reynolds CF, Fascizka AL, Kupfer DJ. Napping and 24-hr sleep/wake patterns in healthy elderly and younger adults. *J Am Geriatric Society* 1992;40:779-86.
38. Usui A IY, Hachuda M, Noda T, Kanba S. Elderly people often have naps that are not subjectively recognized as naps. *Sleep and biological rhythms* 2003;1(2):141-2.
39. Metz ME, Bunnell DE. Napping and sleep disturbances in the elderly. *Fam Pract Res Journ* 1990;10(1):47-56.
40. Lai H-L. Self-reported napping and nocturnal sleep in Taiwanese elderly insomniacs. *Public Health Nurs* 2005;22(3):240 - 7.
41. Monk TH, Buysse DJ, Carrier J, Billy BD, Rose LR. Effects of afternoon "siesta" naps on sleep, alertness, performance, and circadian rhythms in the elderly. *Sleep* 2001;24(6):680-7.
42. Avidan AY. Insomnia in the geriatric patient. *Clinical Cornerstone* 2003;5(3):12.
43. Leger D GC, Bader G, Levy E, Paillard M. Medical and socio-professional impact of insomnia. *Sleep* 2002;25(6):621-5.

44. Liao S, Ferrell B. Fatigue in an older population. *JAGS* 2000;48(8):426-30.
45. Hossain JL, Ahmad P, Reinish LW, Kayumov L, Hossain NK, Shapiro CM. Subjective fatigue and subjective sleepiness: two independent consequences of sleep disorders? *Journal of Sleep Research* 2005;14(3):245-53.
46. Cullen W, Kearney Y, Bury G. Prevalence of fatigue in general practice. *Ir J Med Sci* 2002;171(1):10-2.
47. Pigeon WR, Sateia MJ, Ferguson RJ. Distinguishing between excessive daytime sleepiness and fatigue. Toward improved detection and treatment. *J Psychosomatic Res* 2003;54:61-9.
48. Crane PB. Fatigue and physical activity in older women after myocardial infarction. *Heart & Lung: The Journal of Acute and Critical Care* 2005;34(1):30-8.
49. Ancoli-Israel S. Actigraphy. In: Kryger M RT, Dement WC, ed. *Principles and Practices of Sleep Medicine*. Fifth ed. Philadelphia: Elsevier-W.B. Saunders & Co.; 2005.
50. Ancoli-Israel S, Cole R, Alessi C, Chambers M, Moorcroft, Pollack CP. The role of actigraphy in the study of sleep and circadian rhythms. *Sleep* 2003;26(3):342-71.
51. Carskadon AM R. Monitoring and staging human sleep. In: Kryger M RT, Dement WC, ed. *Principles and practice of sleep medicine*. fifth ed. Philadelphia: Elsevier; 2005.
52. Kushida CA, Chang A, Gadkary C, Guilleminault C, Carrillo O, Dement WC. Comparison of actigraphic, polysomnographic, and subjective assessment of sleep parameters in sleep-disordered patients. *Sleep Medicine* 2001;2(5):389-96.
53. Lockley SW, Skene DJ, Arendt J. Comparison between subjective and actigraphic measurement of sleep and sleep rhythms. *J Sleep Res* 1999;8(3):175-83.
54. Blood ML, Sack RL, Percy DC, Pen JC. A comparison of sleep detection by wrist actigraphy, behavioral response, and polysomnography. *Sleep* 1997;20(6):388-95.
55. Morin CM, Gramling SE. Sleep patterns and aging: comparison of older adults with and without insomnia complaints. *Psych Aging* 1989;4(3):290-4.
56. Rogers AE, Caruso CC, Aldrich MS. Reliability of sleep diaries for assessment of sleep/wake patterns. *Nurs Res* 1993;42(6):368-72.
57. Wilson KG, Watson ST, Currie SR. Daily diary and ambulatory activity monitoring of sleep in patients with insomnia associated with chronic musculoskeletal pain. *Pain* 1998;75(1):75-84.
58. Monk TH, Buysse DJ, Kennedy KS, Potts JM, DeGrazia JM, Miewald JM. Measuring sleep habits without using a diary: the sleep timing questionnaire. *Sleep* 2003;26(2):208-12.



59. Jenkins CD, Stanton B-A, Niemcryk SJ, Rose RM. A scale for the estimation of sleep problems in clinical research. *Journal of Clinical Epidemiology* 1988;41(4):313-21.
60. Gehrman P, Matt G, Turingan M, Dinh Q, Ancoli-Israel S. Towards and understanding of self-reports of sleep. *J Sleep Res* 2002;11(229 - 236).
61. Sadeh A, Hauri PJ, Kripke DF, Lavie P. The role of actigraphy in the evaluation of sleep disorders. *Sleep* 1995;18(3):288-302.
62. Yoon IY, Kripke DF, Youngstedt SD, Elliot JA. Actigraphy suggests age-related differences in napping and nocturnal sleep. *J Sleep Res* 2003;12:87 - 93.
63. Jean-Louis G, Kripke DF, Mason WJ, Elliott JA, Youngstedt SD. Sleep estimation from wrist movement quantified by different actigraphic modalities. *Journal of Neuroscience Methods* 2001;105(2):185-91.
64. Yoon IY, Kripke DF, Elliot JA, Langer RD. Naps and circadian rhythms in postmenopausal women. *Journal of Gerontology* 2004;59A(8):844 - 8.
65. Ancoli-Israel S, Moore PJ, Jones V. The relationship between fatigue and sleep in cancer patients: a review. *European Journal of Cancer Care* 2001;10(4):245-55.
66. Piper BF, Dibble SL, Dodd MJ, Weiss MC, Slaughter RE, Paul SM. The revised Piper Fatigue Scale: Psychometric evaluation in women with breast cancer. *ONF* 1998;25(4):677 - 84.
67. Lichstein KL, Means MK, Noe SL, Aguillard RN. Fatigue and sleep disorders. *Behaviour Research and Therapy* 1997;35(8):733-40.
68. Shen J, Barbera J, Shapiro CM. Distinguishing sleepiness and fatigue: focus on definition and measurement. *Sleep Med Rev* 2006;10:63-76.
69. Multidimensional assessment of fatigue (MAF) user's guide., 2005. (Accessed at <http://www.son.washington.edu/research/maf>.)
70. Chalder T, Berelowitz G, Pawlikowska T, et al. Development of a fatigue scale. *Journal of Psychosomatic Research* 1993;37(2):147-53.
71. Stein KD, Martin SC, Hann DM, Jacobsen PB. A multidimensional measure of fatigue for use with cancer patients. *Cancer Practice* 1998;6(3):143-52.
72. Smets EMA, Garssen B, Bonke B, De Haes JC. The multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. *Journal of Psychosomatic Research* 1995;39(3):315-25.
73. Lee KA, Hicks G, Nino-Murcia G. Validity and reliability of a scale to assess fatigue. *Psychiatry Research* 1991;36(3):291-8.

74. Schwartz JE, Jandorf L, Krupp LB. The measurement of fatigue: A new instrument. *Journal of Psychosomatic Research* 1993;37(7):753-62.
75. Moldofsky H, MacFarlane JG. Fibromyalgia and chronic fatigue syndromes. In: Kryger M RT, Dement WC, ed. *Principles and Practice of Sleep Medicine*, fourth edition. Philadelphia, PA: Elsevier Saunders; 2005.
76. Roehrs T CM, Dement WC, Roth T,. Daytime sleepiness and alertness. In: Kryger M RT, Dement WC, ed. *Principles and Practice of Sleep Medicine*, fourth edition. Philadelphia, PA: Elsevier Saunders; 2005.
77. Trendall J. Concept analysis: chronic fatigue. *J Advanced Nursing* 2000;32(5):1126-31.
78. Addington AM, Gallo JJ, Ford DE, Eaton WW. Epidemiology of unexplained fatigue and major depression in the community: The Baltimore ECA follow-up, 1981-1994. *Psych Med* 2001;31:1037-44.
79. Dimsdale JE, Ancoli-Israel S, Elmsore TF, Gruen W. Taking fatigue seriously: I. Variations in fatigue sampled repeatedly in healthy controls. *J Med Engineering & Technol* 2003;27(5):218-22.
80. Young T. Epidemiology of daytime sleepiness: definitions, symptomatology, and prevalence. *J Clin Psychiatry* 2004;65(suppl 16):12-6.
81. Berger AM, Higginbotham P. Correlates of fatigue during and following adjuvant breast cancer chemotherapy: a pilot study. *Oncol Nurs Forum* 2000;27(9):1443-8.
82. Hewlett S, Cockshott Z, Byron M, et al. Patients' perceptions of fatigue in rheumatoid arthritis: Overwhelming, uncontrollable, ignored. *Arthritis Care & Research* 2005;53(5):697-702.
83. Bardwell WA, Moore P, Ancoli-Israel S, Dimsdale JE. Fatigue in obstructive sleep apnea: driven by depressive symptoms instead of apnea severity? *Am J Psychiatry* 2003;160(2):350-5.
84. Alapin I, Fichten CS, Libman E, Creti L, Bailes S, Wright J. How is good and poor sleep in older adults and college students related to daytime sleepiness, fatigue, and ability to concentrate? *Journal of Psychosomatic Research* 2000;49(5):381-90.
85. Avlund K DM, Sakari-Rantala R, Laukkanen P, Schroll M. Tiredness in daily activities among nondisabled old people as determinant of onset of disability. *J Clin Epidem* 2002;55:965-73.
86. De Rijk AE, Schreurs KMG, Bensing JM. General practitioners' attributions of fatigue. *Social Science & Medicine* 1998;47(4):487-96.
87. Chervin RD. Sleepiness, fatigue, tiredness, and lack of energy in obstructive sleep apnea. *Chest* 2000;118(2):372-9.

88. Warner G, Borawski E, Kahana E, Stange K. Fatigue as an important health indicator for the elderly. In: 129th Annual Meeting of APHA; 2001.
89. Avlund K VM, Hendriksen C. Onset of mobility disability among community-dwelling old men and women. The role of tiredness in daily activities. *Age and ageing* 2003;32:579 - 84.
90. Whooley MA, Kip KE, Cauley JA, et al. Depression, falls, and risk of fracture in older women. *Arch Intern Med* 1999;159(5):484-90.
91. Bliwise DL, Ansari FP, Straight L-B, Parker KP. Age changes in timing and 24 hour distribution of self-reported sleep. *Am J Geriatr Psych* 2005;12(12):1077 - 82.
92. Frisoni GB, DeLeo D, Rozzini R, Trabucchi M. Aspects of the elderly. Napping in the elderly and its association with night sleep and psychological status. *Internat Psychogeriatrics* 1996;8(3):477-87.
93. Carskadon MA, Brown ED, Dement WC. Sleep fragmentation in the elderly: Relationship to daytime sleep tendency. *Neurobiology of Aging* 1982;3(4):321-7.
94. Shochat T, Loredo J, Ancoli-Israel S. Sleep disorders in the elderly. *Current Treatment Options in Neurology* 2001;3(1):19 - 36.
95. Shochat T, Martin J, Marler M, Ancoli-Israel S. Illumination levels in nursing home patients: Effects on sleep and activity rhythms. *J Sleep Res* 2000;9(4):373-80.
96. Campbell SS, Murphy PJ, Stauble TN. Effects of a nap on nighttime sleep and waking function in older subjects. *J Am Geriatr Soc* 2005;53(1):48-53.
97. Takahashi M. The role of prescribed napping in sleep medicine. *Sleep Medicine* 2003;7(3):227 - 35.
98. Tamaki M, Shirota A, Tanaka H, Hayashi M, Hori T. Restorative effects of a short afternoon nap (<30 min) in the elderly on subjective mood, performance and EEG activity. *Sleep Research Online* 2000 2000;3:131-9.
99. Dautovich ND, McCrae CS, Rowe MS. High and low frequency napping behavior in relation to total sleep time in older adults. *Sleep* 2005;28(S):A119.
100. Yaggi HK, Araujo AB, McKlinlay JB. Sleep duration as a risk factor for the development of type 2 diabetes. *Diabetes Care* 2006;29(3):657 - 61.
101. Yoon IY, Kripke DF, Elliott JA, Youngstedt SD, Rex KM, Hauger RL. Age-related changes of circadian rhythms and sleep-wake cycles. *J Am Geriatr Soc* 2003;51(8):1085-91.
102. Tamaki M, Shirota A, Tanaka H, Hayashi M, Hori T. Aging and sleep. Effects of a daytime nap in the aged. *Psychiatry and Clinical Neurosciences* 1999;53:273 - 5.

103. Bliwise DL, Swan GE. Habitual napping and performance on the trail making test. *J Sleep Res* 2005;14:209-10.
104. Hays JC, Blazer DG, Foley DJ. Risk of napping: Excessive daytime sleepiness and mortality in an older community population. *J Am Geriatr Soc* 1996;44:693 - 8.
105. Ancoli-Israel S, Ayalon L. Diagnosis and treatment of sleep disorders in older adults. *Am J Geriatr Psych* 2006;14:85-103.

**2.0 ARTICLE ONE: ACTIGRAPHIC MEASURES OF SLEEP ARE ASSOCIATED  
WITH POORER DAYTIME FUNCTIONING IN OLDER WOMEN**

Suzanne E. Goldman, CRNP, MSN<sup>1</sup>, Katie L. Stone, PhD<sup>2</sup>, Sonia Ancoli-Israel, PhD<sup>3</sup>,  
Terri Blackwell<sup>2</sup>, Susan K. Ewing<sup>4</sup>, Robert Boudreau, PhD<sup>1</sup>, Martica Hall PhD<sup>5</sup>, Jane A. Cauley,  
DrPH<sup>1</sup>, Karen A. Matthews, PhD<sup>5</sup>, Anne B. Newman, MD, MPH<sup>1</sup>

<sup>1</sup> Department of Epidemiology, University of Pittsburgh, Pittsburgh, PA

<sup>2</sup> San Francisco Coordinating Center and California Pacific Medical Center Research Institute,  
San Francisco, CA

<sup>3</sup> Department of Psychiatry, University of California, San Diego, Ca

<sup>4</sup> Department of Epidemiology and Biostatistics, University of California, San Francisco, CA

<sup>5</sup> Department of Psychiatry, University of Pittsburgh, Pittsburgh, PA

Manuscript in preparation

## 2.1 ABSTRACT

**Introduction:** Poor sleep is associated with impaired daytime performance. Few studies have quantified sleep patterns and daytime function with objective measures. We hypothesized that older women with disturbed sleep would have poorer daytime function.

**Methods:** Nighttime sleep activity was assessed in 2962 women (mean age (SD) = 83.3(3.6) years; 10.7% were black) who wore wrist actigraphs (average (SD)=4.1(0.8) nights) during the 2002-2004 examination of the Study of Osteoporotic Fractures. Total nighttime sleep, hours awake after sleep onset, and total daytime sleep were assessed along with gait speed, time to complete five chair stands, grip strength, and self-reported difficulty with one or more of six instrumental activities of daily living (IADL). Associations between quartiles of total nighttime sleep, wake after sleep onset, and daytime sleep and daytime function were evaluated using linear regression models adjusted for factors associated with sleep and/or function. Relationships between sleep and nap patterns and IADL impairments were analyzed using logistic regression.

**Results:** Women who slept <6 hours walked 3.5% slower than those who slept 6-6.8 hours/night; while those who slept  $\geq 7.5$  hours took 4.7% longer to complete 5 chair stands than those who slept 6.8-7.5 hours/night. As wake after sleep onset rose from <0.7 to  $\geq 1.6$  hours gait speed was 11.4% slower, it took 7.4% longer to complete 5 chair stands, and odds of IADL impairment rose to 1.5(95%CI 1.2, 2.0). Women with 1-1.8 hrs of daytime sleep had higher odds of IADL impairment (1.3(95%CI 1.0, 1.6) than women with <0.5 hours of daytime sleep.

**Conclusion:** Older women with short and long sleep durations, more wake after sleep onset, and longer daytime sleep functioned poorer and were more likely to report IADL impairments. Results were not completely explained by poor health status among those with disturbed sleep. Treatment of sleep disturbance in older women may prevent some of the functional decline attributed to aging.

## 2.2 INTRODUCTION

Sleep problems are common in older adults with over half of community dwelling adults reporting some chronic sleep complaint<sup>106, 107</sup>. Sleep durations of <7 or >8 hours per night, as well as complaints of daytime sleepiness, are associated with higher morbidity and mortality<sup>23, 27, 104, 108, 109</sup>. Subjective measures of poor sleep have been associated with poorer health<sup>110-112</sup> and reduced physical function in older adults<sup>13, 16, 109, 113</sup>. In addition, subjective evidence suggests that over 15% of older adults reporting ambulatory limitations also report abnormal sleep patterns<sup>4</sup>. Prior studies have been limited by the lack of objective measures of sleep and physical function.

Maintenance of function is important for maintaining quality of life in older adults. Functional evaluation provides critical information on the health status of older adults<sup>114</sup>. Measures of lower-extremity function<sup>115</sup> and hand grip strength<sup>116</sup> have been shown to be related to disability, morbidity and mortality.

The present analysis uses data from the multi-center Study of Osteoporotic Fractures, to examine the relationship of objective measures of sleep and nap patterns and daytime function in a large cohort of community-dwelling older women. We hypothesized that older women with short or long nighttime sleep duration, more disrupted sleep, and more daytime sleep would have poorer daytime function.

## 2.3 METHODS

### 2.3.1 Participants

Women were enrolled in The Study of Osteoporotic Fractures (SOF), a longitudinal study of risk factors for fracture. To be eligible to participate, women had to be community-dwelling, at least 65 years of age, and ambulatory at the initial visit 1986-88. Women who reported a bilateral hip replacement were excluded. Women were recruited from population-based listings at four

clinical centers in the United States: Baltimore, Maryland; Minneapolis, Minnesota; Portland, Oregon; and the Monongahela Valley near Pittsburgh, PA. The initial study cohort consisted of 9704 Caucasian women recruited between 1986–1988<sup>117</sup> and an additional 662 African American women added in 1996-1998<sup>117, 118</sup>. After enrollment, follow-up clinic visits were conducted approximately every two years. A total of 4,727 women participated in an eighth clinic visit (year 16) between January 2002 and April 2004. At this visit 3,127 performed wrist actigraphy, of which 165 were excluded from this analysis because they resided in either a personal care facility or nursing home. The SOF study was approved by the institutional review board at each participating institution, and all participants provided written informed consent.

### **2.3.2 Sleep evaluation**

Sleep and nap patterns were assessed objectively using wrist actigraphy (Sleep-Watch-O<sup>®</sup>, Ambulatory Monitoring, Inc., Ardsley, NY). Actigraphs were worn on the non-dominant wrist for a minimum of three 24-hour periods (mean  $4.1 \pm 0.83$  nights, range 1-9 nights)<sup>50</sup>. Details of the actigraphy collection and scoring have previously been reported<sup>119</sup>. Briefly, actigraphy data used in this analysis were collected in the proportional integration mode (PIM), also referred to as the digital integration mode. Sleep and wake cycles were differentiated using the UCSD sleep-scoring algorithm<sup>120</sup>. The algorithm calculates a moving average taking into account the activity levels immediately before and after the current minute to determine if the time point should be coded as sleep or wake. Participants also completed a sleep diary for the duration of time they wore the actigraph, which was used in the editing of the actigraphy data to determine bed time and final up time, and to record naps and periods of watch removal (e.g. for bathing).

Actigraphy variables computed included total nighttime sleep time calculated as the hours scored as sleep between bedtime and final up time. Wake after sleep onset was calculated as the average number of hours awake after sleep onset, where sleep onset was scored as the completion of 20 continuous minutes of sleep after getting into bed. Total sleep during the day (or number of hours of napping) was calculated as the average minutes of inactivity (minimal movement detected by the actigraphy) between the final get up time that morning and the



subsequent bedtime. Actigraphy data for each participant was averaged over all 24-hour periods to reduce night-to-night variability.

Self reported sleep problems, including physician diagnosis of a sleep disorder, awakening during the night to urinate, trouble sleeping due to leg jerks or cramps, breathing difficulties while sleeping, or snoring were also collected.

### **2.3.3 Physical function**

Physical function was assessed by trained examiners at the eighth clinic visit and included: gait speed measured with the 6 meter usual pace test (meters/sec); time to complete 5 chair stands (seconds); and the average of right and left grip strength (kg) <sup>121</sup>. Physical function was also assessed by self-report of difficulty performing any of six instrumental activities of daily living (IADL) that included walking 2-3 blocks, climbing or walking down 10 steps, preparing meals, heavy housework, and shopping <sup>122, 123</sup>.

### **2.3.4 Potential confounders**

Information about potential confounders previously identified as associated with sleep in the SOF cohort <sup>124</sup> was collected at the eighth clinic visit along with the sleep variables and actigraphy data. Information included medical history, anthropomorphic measurements of weight (kg) and height (m), and self reported walking for exercise. Depressive symptoms were measured with the Geriatric Depression Scale <sup>125</sup>. Anxiety was measured using the Goldberg Anxiety Scale Score <sup>126</sup>. Mental status was measured with the Mini-Mental Status Exam (range 0-30), with higher scores representing better cognitive function <sup>127, 128</sup>. A comorbidity index (number of comorbid conditions coded as 0, 1, 2, 3+) was created that consisted of self reported history of stroke, diabetes, Parkinson's disease, Alzheimer's disease, heart disease, congestive heart failure, COPD, and hypertension at the eighth clinic visit. Hand tremors were evaluated by the clinic staff during the trails B test.

### 2.3.5 Statistical Analysis

In descriptive univariate analysis physical performance measures and variables previously reported as associated with disturbed sleep in the SOF cohort<sup>124</sup> were compared in participants attending the eighth clinic visit who were and were not included in this analysis. Sleep parameters, performance outcomes, and potential confounders were also compared between the black and white participants who were included in this analysis sample. Characteristics were summarized as means and standard deviations for continuous variables and counts and percentages for categorical variables. Comparisons were performed using t-tests for normally distributed continuous data, Wilcoxon rank sum tests for skewed continuous data, and Pearson's chi-squared test for categorical data.

Sleep parameters were categorized into quartiles to examine potential non-linear, or U-shaped, relationships with performance measurements. The U-shaped distribution between total nighttime sleep and the physical performance measurements was further evaluated by entering a quadratic term for total nighttime sleep in regression models. Individual sleep variables were examined as the independent variable with gait speed, chair stand time, grip strength, and IADL impairment as the dependent variables. IADL impairment (yes/no) was defined as having any difficulty with at least one of the six IADL's. Linear regression models were used to examine the relationship between sleep variables and continuous performance outcomes. Logistic regression models were used to examine the relationship between sleep variables and the dichotomous IADL outcome. All models were adjusted for potential confounders known to affect both physical function and sleep<sup>124</sup>. These included age, race, BMI (body mass index ( $\text{kg}/\text{m}^2$ )), depression, anxiety, cognitive function, comorbidities, and walking for exercise. Results for time to complete 5 chair stands were additionally adjusted for whether the participant used their arms during the chair stand test, and results for grip strength were adjusted for presence of hand tremors. Statistically significant differences between each pair of quartiles were assessed using the least square means procedure. Data were analyzed using STATA V8.1 (Stata Corporation, College Station, TX) and SAS V8 (SAS Institute, Cary, NC ) software. Two-sided p-values < 0.05 were considered statistically significant.

## 2.4 RESULTS

Characteristics of the 2962 participants in the analysis sample compared with the remaining 1765 participants at the eighth clinic visit (2002 – 2004) are shown in Table 2.1. The mean age of the participants with actigraphy was significantly lower than the rest of the participants. Those with actigraphy had a higher BMI, better self-reported health status, fewer comorbid health conditions, less depression and more self reported sleep problems. More individuals with actigraphy walked for exercise and had a faster walk speed. Fewer of these individuals had any IADL impairments. They were also able to get up and down from a chair faster and had stronger average grip strength.

Confounding characteristics, sleep measurements, as recorded by actigraphy, and performance measurements for the white and black participants are presented in Table 2.2. Significant racial differences were found in all sleep categories except self-reported sleep problems and daytime sleep duration. Black women had less total nighttime sleep and more fragmented sleep as represented by the time spent awake during the sleep period. Black women functioned more poorly on the 6 meter walk test (m/sec) and the time to complete 5 chair stands, however their grip strength was stronger. In addition, the black women were younger, had a higher BMI, poorer self-reported health, and more comorbidities. All subsequent analyses were adjusted for race.

The multivariate distribution of performance measures across quartiles of total nighttime sleep, wake after sleep onset, and daytime sleep are presented in Table 2.3, and the odds for IADL impairment are presented in Table 2.4. Women in the lowest and highest quartiles of total nighttime sleep performed more poorly on the gait test and took longer to complete 5 chair stands. In the fully adjusted model women who averaged <6 hours sleep per night still had 3.5% slower gait speed than the women who averaged 6-6.8 hours of sleep, and women who averaged  $\geq 7.5$  hours of sleep per night took 4.7% longer to complete 5 chair stands than those who slept 6.8-7.5 hours/night. The quadratic term was significant ( $p < 0.001$ ) between total nighttime sleep and gait speed, but not between total nighttime sleep and time to complete 5 chair stands.

Women who spent more time awake during the night (more wake after sleep onset) had slower gait speed, took longer to complete 5 chair stands, and had weaker grip strength. These findings were slightly attenuated in the fully adjusted model. Women with more wake after sleep

onset also had more IADL impairment. After adjustment women in the highest quartile ( $\geq 1.6$  hrs) still had 1.54(95%CI 1.20, 2.00) higher odds for an IADL impairment compared to women with less than 0.7 hours of wake after sleep onset. Women who slept more during the day walked slower, took longer to complete 5 chair stands, and had weaker grip strength. These findings however were attenuated by adjustment. Compared to women with daytime sleep  $< 0.5$  hrs a day those women who slept 1-1.8 hrs or  $\geq 1.8$  hrs during the day had higher odds of IADL impairment after adjustment (1.28(95%CI 1.01, 1.63) and 1.23(95%CI 0.96, 1.57), respectively).

## 2.5 DISCUSSION

This analysis is one of the first large scale analyses to examine the effect of sleep patterns in community dwelling older women on daytime function using objective measurements of sleep and physical function. This study showed that actigraphically measured short or long nightly sleep duration and more wake after sleep onset (fragmentation) were associated with slower gait speed and increased time to complete 5 chair stands. Higher levels of fragmentation, as well as more daytime sleep, were also associated with higher odds of IADL impairment. These findings persisted even after adjustment for risk factors associated with both sleep and function.

Detrimental effects of sleep deprivation on alertness and performance have been shown in controlled studies<sup>129, 130</sup>, however it has not been demonstrated in a population based setting. The use of actigraphy to measure nighttime activity and sleep fragmentation has been documented in several studies<sup>131-133</sup>. Further, the use of performance assessment has been shown to be an important tool as a measurement of functioning in older adults<sup>134</sup>. With the use of both techniques we have been able to show that the women in SOF with poorer sleep performed more poorly on standardized tests.

We found that black women had shorter total nighttime sleep and more wake after sleep onset than white women. Ethnic differences have been reported on how individuals experience normal sleep. Studies have found that blacks are less likely to complain of sleep disturbances than are whites<sup>135-137</sup>. However, in general blacks have been shown to take longer to fall asleep, to have more disruptive sleep, and to sleep more during the day<sup>137</sup>. The black women in the SOF

cohort were recruited an average of 10 years after the white women and therefore tended to be significantly younger than the white women. However, similar to previous reports<sup>137</sup> the SOF black women had more risk factors for poor sleep such as higher BMI, poorer self-reported health status, and more medical comorbidity.

In this study a U shaped distribution was found for total nighttime sleep and gait speed with women at both extremes functioning more poorly when compared to the women who averaged 6-7.5 hours of sleep. Adjustment for multiple confounders explained only a portion of the relationship between total nighttime sleep and the performance measures. The association of both long and short nightly sleep time with poorer function is in concordance with the patterns associated with sleep time and self reports of health problems<sup>4, 138</sup>, or mortality<sup>23, 27, 139, 140</sup> previously reported in the literature. Individuals sleeping 6 to 7 hours per night have been reported to have the lowest risk of mortality<sup>11, 27-29, 141, 142</sup>. The women with a total nighttime sleep between 6 – 7.5 hrs appeared to function better. Potentially, regulating total nighttime sleep may play an important role in minimizing functional decline.

Fragmented sleep occurs chronically in older populations<sup>130</sup> and has been correlated with daytime sleepiness<sup>93</sup>. Indeed frequent nighttime awakening is a cardinal symptom of sleep complaints in the older adult. A major finding of this study was the more fragmented the participants' nighttime sleep, the worse the daytime performance was even after adjustment for multiple potential confounders. This was true for all performance measures. Brief disruptions of sleep have been shown to be less restorative than consolidated sleep, to result in significantly altered sleep stage distribution, the appearance of daytime sleepiness, and decreased performance on reaction time and digit symbol substitution tests<sup>93, 143-147</sup>. Although frequent awakenings have not been shown to be associated with mortality<sup>23</sup>, the significant reduction in daytime function associated with it warrants attention to the complaint in a clinical setting.

In this study we found that periods of daytime sleep  $\geq 1$  hour when compared to those with  $< 0.5$  hours, as measured by actigraphy, were also related to poorer daytime performance. Studies have shown an association between napping and self reports of daytime sleepiness, self reported poorer health, impaired physical function or mood, being overweight, mortality, cardiovascular disease, myocardial infarction, and congestive heart failure<sup>23, 104, 138, 148</sup>. Reports of daytime sleepiness have also been shown to be an independent predictor of mortality and cardiovascular disease in older adults<sup>23, 104, 148</sup>. We adjusted for the aforementioned variables and

the relationship between daytime sleep and performance was only partially explained. In small, controlled studies the effects of napping on cognitive and psychomotor performance have been contradictory. Some studies have shown significant improvement<sup>96, 102</sup> while another showed negligible effects<sup>41</sup>.

The relationship between sleep behavior and physical performance is complex with this study suggesting that poor sleep may impact daily function. We found slower gait speed associated with both short and long sleep durations, as well as with more wake after sleep onset. Walking speed has been shown to be an independent determinant of self-rated health with slower walk speed associated with poor self-rated health<sup>149</sup>. Physical performance measures of lower extremity function, and particularly gait speed, have been shown to predict the onset of progressive ADL impairment, mobility, and upper extremity disability in older women<sup>115, 150</sup>. In the SOF cohort direct measurement of neuromuscular performance including gait speed has been strongly related to disability<sup>151</sup>.

Handgrip strength has also been shown to be a strong predictor of cause-specific and total mortality in older disabled women<sup>116</sup> and to be associated with reports of more difficulties in the physical activities of daily living<sup>152</sup>. We found a decrease in handgrip strength as the amount of wake after sleep onset increased. Our women had an average grip strength already considered to be low<sup>116, 152</sup>. Since they are still functional, improvement in their sleep behavior may minimize subsequent decline.

Strengths of this study include the data are from a large sample of community dwelling women, both black and white, in a well established and followed cohort. State of the art wrist actigraphs were used for sleep measurements. Performance measurements were made by well-trained clinicians. However, this study also has some limitations. The analysis subset is healthier than the overall SOF cohort, and may not be representative of the general cohort of older women. This would be expected to bias relationships towards the null. Further, our findings may not be generalizable to other populations including non-ambulatory women, younger women, men, or institutionalized individuals. Finally, results are cross-sectional and one cannot determine if sleep disturbance precedes impairments in performance, or vice versa.

In summary, disrupted sleep was associated with poorer daytime function in these older women. As total nighttime sleep deviated from an approximate average of 7 hours, gait speed was slower and it took longer to complete 5 chair stands. As quartile of wake after sleep onset

increased gait speed was slower and it took longer to complete 5 chair stands. Finally, as the amount of fragmentation or daytime sleep increased odds for IADL impairment were higher. These findings were not fully explained by adjustment for demographic or health conditions. Longitudinal studies are needed to determine if poor sleep patterns are causally associated with functional decline. Potentially, treatment of sleep disorders can prevent part of the functional decline attributed to aging.

## **2.6 ACKNOWLEDGEMENTS**

Supported by NIH Grants AG05407, AR35582, AG05394, AR35584, AR35583 and AG08415

## 2.7 REFERENCES

1. Ancoli-Israel S. Insomnia in the elderly: A review for the primary care practitioner. *Sleep* 2000;23(Suppl 1):S23-S30.
2. Martin J, Stepnowsky C, Ancoli-Israel S. Sleep apnea in the elderly. *Breathing Disorders During Sleep* 1999.
3. Hays JC, Blazer DG, Foley DJ. Risk of napping: Excessive daytime sleepiness and mortality in an older community population. *J Am Geriatr Soc* 1996;44:693 - 8.
4. Kripke DF, Garfinkel L, Wingard DL, Klauber MR, Marler MR. Mortality associated with sleep duration and insomnia. *Archives Of General Psychiatry* 2002;59(2):131-6.
5. Newman AB, Spiekerman CF, Enright P, et al. Daytime sleepiness predicts mortality and cardiovascular disease in older adults. *JAGS* 2000;48:115-23.
6. Newman AB EP, Manolio T, et al. Sleep disturbance, psychosocial correlates, and cardiovascular disease in 5201 older adults. *J Am Geriatr Soc* 1997;45:1-7.
7. Whitney CW, Enright PL, Newman AB, Bonekat W, Foley D, Quan SF. Correlates of daytime sleepiness in 4578 elderly persons: the cardiovascular health study. *Sleep* 1998;21(q):27 - 36.
8. McCrae CS, Rowe MA, Tierney CG, Dautovich ND, DeFinis AL, McNamara JPH. Sleep complaints, subjective and objective sleep patterns, health, psychological adjustment, and daytime functioning in community-dwelling older adults. *J of Gerontology Psychological Sciences* 2005;60B(4):182-9.
9. Ohayon MM. Epidemiology of insomnia: what we know and what we still need to learn. *Sleep Medicine Reviews* 2002;6(2):97-111.
10. Vitiello MV, Moe KE, Prinz PN. Sleep complaints cosegregate illness in older adults: clinical research informed by and informing epidemiological studies of sleep. *J of Psychosomatic Res* 2002;53:555-9.
11. Foley DJ, Monjan AA, Brown SL. Sleep complaints among elderly persons: an epidemiologic study of three communities. *Sleep* 1995;18:425 - 32.
12. Kutner NG SK, Ory MG, Baker DI, FICSIT Group. Older adults perceptions of their health and functioning in relation to sleep disturbance, falling, and urinary incontinence. *JAGS* 1994;42:757-62.



13. Foley DJ, Ancoli-Israel S, Britz P, Walsh JK. Sleep disturbances and chronic disease in older adults: Results of the 2003 National Sleep Foundation Sleep in America Survey. *Journal of Psychosomatic Research* 2004;56(5):497-502.
14. National Sleep Foundation. 2003 Sleep in America Poll; 2003.
15. Applegate WB, Blass JP, Williams TF. Instruments for the functional assessment of older patients. *N Engl J Med* 1990;322:1207-14.
16. Guralnik JM, Ferrucci L, Pieper, Carl F., Leveille, Suzanne G., Markides, Kyriakos S., Ostir, Glenn V., Studenski, Stephanie, Berkman, Lisa F., Wallace, Robert B. Lower extremity function and subsequent disability: Consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. *J Gerontol A Biol Sci Med Sci* 2000;55:M221-31.
17. Rantanen T, Volpato S, Ferrucci L, Heikkinen E, Fried LP, Guralnik JM. Handgrip strength and cause-specific and total mortality in older disabled women: exploring the mechanism. *JAGS* 2003;51:636-41.
18. Cummings SR, Nevitt MC, et al. Appendicular bone density and age predict hip fracture in women: the Study of Osteoporotic Fractures Research Group. *JAMA* 1990;263:665-8.
19. Vogt MT, Palermo L, et al.,. Lumbar spine listhesis in older African American women. *Spine J* 2003;3(4):255-61.
20. Ancoli-Israel S, Cole R, Alessi C, Chambers M, Moorcroft, Pollack CP. The role of actigraphy in the study of sleep and circadian rhythms. *Sleep* 2003;26(3):342-71.
21. Blackwell T, Ancoli-Israel SA, Gehrman PR, Schneider JL, Pdeula KL, Stone KL. Actigraphy scoring reliability in the Study of Osteoporotic Fractures. *Sleep* 2005;28(12):1599-603.
22. Girardin JL, Kripke DF, Mason WJ, Elliott JA, Youngstedt SD. Sleep estimation from wrist movement quantified by different modalities. *J of Neuroscience Methods* 2001;105:185-91.
23. Cummings SR, Nevitt MC, Browner WS, et al. Risk factors for hip fracture in white women. *N Engl J Med* 1995;332(12):767-74.
24. Pincus T, Summey JA, Soraci SA, Wallston KA, Hummon NP. Assessment of patient satisfaction in activities of daily living using a modified Stanford Health Assessment Questionnaire. *Arthritis Rheum* 1983;26(11):1346-53.
25. Fitti JE, Kovar MG. The supplement on aging to the 1984 national health interview survey.; 1987.

26. Schneider J, Blackwell T, Hillier TA, Stone KL. Characteristics of objective and subjective sleep in older women. *The Study of Osteoporotic Fractures (SOF)*. *Sleep* 2004;27(Abtract Supplement):A123.
27. Sheikh JI, Yesavage JA. Geriatric depression scale (GDS): recent evidence and development of a shorter version. *Clin Gerontol* 1986;5:165-73.
28. Goldberg D, Bridges K. Detecting anxiety and depression in general medical settings. *BMJ* 1988;297(6653):897-9.
29. Blackwell T, Yaffe K, Ancoli-Israel S, et al. Poor sleep is associated with impaired cognitive function in older women: The Study of Osteoporotic Fractures. *J Gerontol: Medical Sciences* 2006;61A(4):405-10.
30. Folstein MF, Robins LN, Helzer JE. The Mini-Mental State Examination. *Arch Gen Psychiatry* 1983;40 1983.
31. Pilcher JJ, Huffcutt AL. Effects of sleep deprivation on performance: A meta-analysis. *Sleep* 1996;19(4):318-26.
32. Wesensten NJ, Balkin TJ, Belenky G. Does sleep fragmentation impact recuperation? A review and reanalysis. *J Sleep Res* 1999;8:237-45.
33. Landis CA, Frey CA, Lentz MJ, Rothermel J, Buchwald D, Shaver JLF. Self-reported sleep quality and fatigue correlates with actigraphy in midlife women with fibromyalgia. *Nursing Research* 2003;52(3):140 -7.
34. Korszun A, Young EA, Engleberg NC, Brucksch CB, Greden JF, Crofford LA. Use of actigraphy for monitoring sleep and activity levels in patients with fibromyalgia and depression. *J of Psychosomatic Res* 2002;52:439-43.
35. Rotem AY SA, Krugliak P, Freidman B, Tal A, Tarasiuk A. Polysomnographic and actigraphic evidence of sleep fragmentation in patients with irritable bowel syndrome. *Sleep* 2003;26(6):747-52.
36. Guralnik JM BL, Cummings SR, Curb JD. Physical performance measures in aging research. *J of Gerontology Medical Sciences*;44(5):M141-8.
37. Blazer DG, Hays JC, Foley DJ. Sleep complaints in older adults: a racial comparison. *J Gerontol A Biol Sci Med Sci* 1995;50(5):M280-4.
38. Jean-Louis G, Magai CM, Cohen CI, et al. Ethnic differences in self-reported sleep problems in older adults. *Sleep* 2001;24(8):926-33.
39. Durrence HH, Lichstein KL. The sleep of African Americans: a comparative review. *Behav Sleep Med* 2006;4(1):29-44.

40. Ohayon MM VM. Normative sleep data, cognitive function and daily living activities in older adults in the community. *Sleep* 2005;28(8):981-9.
41. Burazeri G, Gofin J, Kark JD. Over 8 hours of sleep--marker of increased mortality in Mediterranean population: follow-up population study. *Croatian Medical Journal* 2003;44(2):193-8.
42. Bursztyrn M, Ginsberg G, Stessman J. The siesta and mortality in the elderly: effect of rest without sleep and daytime sleep duration. *Sleep* 2002;25:187-91.
43. Patel SR, Ayas NT, Malhotra MR, et al. A prospective study of sleep duration and mortality risk in women. *Sleep* 2004;27(3):440-4.
44. Ayas NT, White DP, Manson JE, et al. A prospective study of sleep duration and coronary heart disease in women. *Archives Internal Medicine* 2003;163:205-9.
45. Tamakoshi A, Ohno Y. Self-reported sleep duration as a predictor of all-cause mortality: results from the JACC study, Japan. *Sleep* 2004;27(1):51-4.
46. Youngstedt SD, Kripke DF. Long sleep and mortality: rationale for sleep restriction. *Sleep Medicine Reviews* 2004;8:159-74.
47. Grandner MA, Kripke DF. Self-reported sleep complaints with long and short sleep: A nationally representative sample. *Psychosomatic Medicine* 2004;66:239-41.
48. Carskadon MA, Brown ED, Dement WC. Sleep fragmentation in the elderly: Relationship to daytime sleep tendency. *Neurobiology of Aging* 1982;3(4):321-7.
49. Sforza E H-RJ, De Bilbao F, Rochat T, Ibanez V. Performance, vigilance task and sleepiness in patients with sleep-disordered breathing. *Eur Respir J* 2004;24:279-85.
50. Martin SE, Engleman HM, Deary IJ, Douglas NJ. The effect of sleep fragmentation on daytime function. *Am J Respir Crit Care Med* 1996;153(4):1328-32.
51. Bonnet MH, Arand DL. Clinical effects of sleep fragmentation versus sleep deprivation. *Sleep Medicine Reviews* 2003;7(4):297-310.
52. Stepanski EJ. The effect of sleep fragmentation on daytime function. *Sleep* 2002;25(3):268-75.
53. Stepanski E, Lamphere J, Badia P, Zorick F, Roth T. Sleep fragmentation and daytime sleepiness. *Sleep* 1984;7(1):18-25.
54. Asplund R. Daytime sleepiness and napping amongst the elderly in relation to somatic health and medical treatment. *J Internal Medicine* 1996;239:261-7.
55. Campbell SS, Murphy PJ, Stauble TN. Effects of a nap on nighttime sleep and waking function in older subjects. *J Am Geriatr Soc* 2005;53(1):48-53.

56. Tamaki M, Shirota A, Tanaka H, Hayashi M, Hori T. Aging and sleep. Effects of a daytime nap in the aged. *Psychiatry and Clinical Neurosciences* 1999;53:273 - 5.
57. Monk TH, Buysse DJ, Carrier J, Billy BD, Rose LR. Effects of afternoon "siesta" naps on sleep, alertness, performance, and circadian rhythms in the elderly. *Sleep* 2001;24(6):680-7.
58. Jylha M, Guralnik JM, Balfour J, Fried LP. Walking difficulty, walking speed, and age as predictors of self-rated health: The Women's Health and Aging Study. *J Gerontol A Biol Sci Med Sci* 2001;56(10):M609-17.
59. OnderG, Ferrucci L, Fried LP, Guralnik JM, Pahor M. Measures of physical performance and risk for progressive and catastrophic disability: Results from the Women's Health and Aging Study. *J Gerontol A Biol Sci Med Sci* 2005;60(1):74-9.
60. Ensrud KE NM, Yunis C, Cauley JA, Seeley DG, Fox KM, Cummings SR. Correlates of impaired function in older women. *JAGS* 1994;42:481-9.
61. Rantanen T GJ, Sakari-Rantala R. Disability, physical activity, and muscle strength in older disabled women. The Women's Health and Aging Study. *Arch Phys Med Rehabil* 1999;80:130 - 5.

**Table 2-1 Comparison of Demographic, Health and Performance Variables in the SOF Cohort at the 8<sup>th</sup> clinic visit (2002 – 2004).**

	<b>Analysis Sample n=2962</b>	<b>Remaining Sample n=1765</b>	<b>p-value</b>
<b>Age (years) (mean ± SD)</b>	83.3 ± 3.6	84.9 ± 4.3	< 0.001
<b>Race:</b>			0.01
<b>Black (n (%))</b>	317 (10.7)	149 (8.4)	
<b>White (n (%))</b>	2645 (89.3)	1616 (91.6)	
<b>BMI (kg/m<sup>2</sup>) (mean ± SD)</b>	26.9 ± 4.9	26.0 ± 5.2	0.009
<b>Self reported health status (n (%))</b>			<0.001
<b>Excellent</b>	567 (19.2)	277 (15.9)	
<b>Good</b>	1673 (56.5)	839 (48.2)	
<b>Fair</b>	659 (22.3)	490 (28.1)	
<b>Poor</b>	59 ( 2.0)	137 (7.9)	
<b>Comorbidity<sup>1</sup> (n (%))</b>			<0.001
<b>None</b>	809 (27.3)	352 (21.7)	
<b>One</b>	1221 (41.3)	646 (39.9)	
<b>Two</b>	618 (20.9)	382 (23.5)	
<b>≥ Three</b>	310 (10.5)	242 (14.9)	
<b>Sleep Problems<sup>2</sup> (mean ± SD)</b>	3.9 ± 1.9	3.5 ± 1.9	<0.001
<b>Depression (GDS15) (mean ± SD)</b>	3.5 (3.4)	2.4 (2.6)	<0.001
<b>Anxiety (Goldberg Anxiety Score) (mean ± SD)</b>	1.4 ± 2.3	1.3 ± 2.2	0.57
<b>Mini Mental Status Exam (mean ± SD)</b>	27.0 (2.7)	27.8 (2.0)	<0.001
<b>Walks for exercise (n (%))</b>	1092 (37.3)	504 (31.6)	<0.001
<b>Gait Speed (m/sec) (mean ± SD)</b>	0.8 ± 0.2	0.7 ± 0.3	<0.001
<b>IADL<sup>3</sup> (n (%)) with no impairment)</b>	1415 (47.8)	235 (13.3)	<0.001
<b>Chair Stands<sup>4</sup> (seconds) (mean± SD)</b>	13.5 ± 4.7	14.1 ± 4.8	<0.001
<b>Grip Strength<sup>5</sup> (kg) (mean ± SD)</b>	16.5 ± 4.0	14.7 ± 4.4	<0.001

<sup>1</sup> Comorbid conditions at the eighth clinic visit (stroke, diabetes, Parkinson’s disease, Alzheimer’s disease, COPD, heart disease, congestive heart failure, and hypertension).

<sup>2</sup> Number of self reported sleep problems (self report of sleep disorder, getting up to go to the bathroom, leg jerks while sleeping, breathing difficulty while sleeping, snoring, or sleep apnea).

<sup>3</sup> Instrumental Activities of Daily Living: walking 2-3 blocks, climbing or walking down 10 steps, preparing meals, heavy housework, and shopping.

<sup>4</sup> Seconds to complete 5 chair stands.

<sup>5</sup> Average of right and left grip strength.

**Table 2-2 Comparison of demographic, health, actigraphic sleep and performance measurements by race in the analysis group of the SOF cohort at the eighth clinic visit (2002-2004).**

		<b>White (N=2645)</b>		<b>Black (N=317)</b>	
<b>DEMOGRAPHICS:</b>	<b>(n)</b>		<b>(n)</b>		<b>p</b>
<b>Age (years) (mean±SD)</b>	2645	83.7±3.2	317	79.6±4.5	<.01
<b>BMI (kg/m<sup>2</sup>) (mean±SD)</b>	2609	26.5±4.6	313	29.3±5.6	<.01
<b>HEALTH STATUS:</b>					
<b>Self-reported health status (n (%))</b>	2642		317		.03
<b>Excellent</b>		521 (19.7)		46 (14.5)	
<b>Good</b>		1496 (56.6)		177 (55.8)	
<b>Fair</b>		576 (21.8)		84 (26.5)	
<b>Poor</b>		49 (1.9)		10 (3.2)	
<b>Comorbidity<sup>1</sup> (n (%))</b>	2642		317		<.01
<b>None</b>		764 (28.9)		45 (14.2)	
<b>One</b>		1087 (41.1)		134 (42.3)	
<b>Two</b>		535 (20.3)		84 (26.5)	
<b>≥ Three</b>		256 (9.7)		54 (17.0)	
<b>Depression (GDS15) (mean ± SD)</b>	2639	2.4 (2.6)	317	2.2 (2.3)	0.09
<b>Anxiety (Goldberg Anxiety Score) (mean ± SD)</b>	2638	1.3 (2.2)	317	1.5 (2.4)	0.34
<b>Mini Mental Status Exam (mean ± SD)</b>	2517	27.9 (1.9)	295	27.3 (2.4)	<0.001

<b>Table 2.2 cont.</b>		<b>White (N=2645)</b>		<b>Black (N=317)</b>	
<b>SLEEP (mean ± SD):</b>					
<b>Sleep Problems<sup>2</sup></b>	1672	3.9±1.9	208	3.6±1.8	.5
<b>Total Nocturnal Sleep Time (hrs)<sup>3</sup></b>	2576	6.8±1.3	314	6.3±1.3	<0.01
<b>Wake After Sleep Onset (hrs)<sup>3</sup></b>	2575	1.2±0.7	314	1.5±0.8	<0.01
<b>Total Daytime Sleep Time (hrs)<sup>3</sup></b>	2542	1.2±1.0	303	1.1±1.2	0.7
<b>FUNCTION:</b>					
<b>Walks for exercise (n (%))</b>	2610	972 (37.2)	316	120 (38.0)	.8
<b>Gait Speed (m/sec)<sup>4</sup> (mean ± SD)</b>	2466	0.83±0.2	292	0.77±.2	<0.01
<b>IADL (n (%) with none)<sup>6</sup></b>	2645	1263 (47.7)	317	152 (48.0)	0.9
<b>Average Grip Strength (kg)<sup>7</sup> (mean ± SD)</b>	2453	16.2±3.8	294	18.3±4.4	<0.01
<b>Chair Stands (seconds)<sup>8</sup> (mean ± SD)</b>	1955	13.4±4.7	226	13.7±4.1	0.02

<sup>1</sup> Comorbid conditions at the eighth clinic visit (Self report of stroke, diabetes, Parkinson's disease, Alzheimer's disease, COPD, heart disease, congestive heart failure, and hypertension).

<sup>2</sup> Number of self reported sleep problems (self report of sleep disorder, getting up to go to the bathroom, leg jerks while sleeping, breathing difficulty while sleeping, snoring, and sleep apnea).

<sup>3</sup> Measured by actigraphy.

<sup>4</sup> 6 meter usual pace

<sup>6</sup> Instrumental Activities of Daily Living: walking 2-3 blocks, climbing or walking down 10 steps, preparing meals, heavy housework, and shopping.

<sup>7</sup> Average of right and left grip strength.

<sup>8</sup> Seconds to complete 5 chair stands.

**Table 2-3 Daytime performance measures by quartile of Total Nighttime Sleep<sup>1</sup>, Wake After Sleep Onset <sup>1</sup>and Daytime Sleep<sup>1</sup> in the Study of Osteoporotic Fracture participants at the eighth clinic visit<sup>2</sup>.**

	<b>Total Nighttime Sleep (Hours)</b>			
<b>Means(standard error)</b>	<b>&lt; 6.0</b>	<b>6.0 - 6.8</b>	<b>6.8 -7.5</b>	<b>≥7.5</b>
<b>Gait Speed (m/sec) Unadjusted</b>	0.81(0.01) <sup>a</sup>	0.85(0.01) <sup>a,b</sup>	0.86(0.01) <sup>a,c</sup>	0.83(0.01) <sup>b,c</sup>
<b>Adjusted<sup>2</sup></b>	0.83(0.01) <sup>a</sup>	0.86(0.01) <sup>a</sup>	0.85(.01)	0.84(0.01)
<b>Chair Stands (sec) Unadjusted</b>	14.05(0.22) <sup>a</sup>	13.56(0.21)	13.23(0.21) <sup>a,c</sup>	13.89(0.21) <sup>c</sup>
<b>Adjusted<sup>2,3</sup></b>	13.77(0.21)	13.51(0.19)	13.31(0.20) <sup>c</sup>	13.93(0.20) <sup>c</sup>
<b>Grip Strength (kg) Unadjusted</b>	16.78(0.16)	16.71(0.10)	16.58(0.16)	16.72(0.16)
<b>Adjusted<sup>2,4</sup></b>	16.66(0.16)	16.76(0.15)	16.72(0.15)	16.72(0.16)
	<b>Wake After Sleep Onset (Hours)</b>			
	<b>&lt;0.7</b>	<b>0.7 – 1.1</b>	<b>1.1 – 1.6</b>	<b>≥1.6</b>
<b>Gait Speed (m/sec) Unadjusted</b>	0.90(0.01) <sup>a</sup>	0.85(0.01) <sup>a,b</sup>	0.84(0.01) <sup>a,c</sup>	0.76(0.01) <sup>a,b,c</sup>
<b>Adjusted<sup>2</sup></b>	0.88(0.01) <sup>a</sup>	0.84(0.01) <sup>a,b</sup>	0.85(0.01) <sup>a,c</sup>	0.78(0.01) <sup>a,b,c</sup>
<b>Chair Stands (sec) Unadjusted</b>	13.05(0.20) <sup>a</sup>	13.43(0.20) <sup>b</sup>	13.77(0.21) <sup>a,c</sup>	14.70(0.23) <sup>a,b,c</sup>
<b>Adjusted<sup>2,3</sup></b>	13.24(0.19) <sup>a</sup>	13.58(0.19) <sup>b</sup>	13.61(0.20) <sup>c</sup>	14.22(0.23) <sup>a,b,c</sup>
<b>Grip Strength (kg) Unadjusted</b>	16.93(0.16) <sup>a</sup>	16.63(0.16)	16.69(0.16)	16.25(0.16) <sup>a</sup>
<b>Adjusted<sup>2,4</sup></b>	16.91(0.15) <sup>a</sup>	16.74(0.15)	16.80(0.15)	16.37(0.17) <sup>a</sup>



Table 2.3 cont.	Daytime Sleep (Hours)			
	< 0.5	0.5 -1.0	1.0 -1.8	≥1.8
<b>Gait Speed (m/sec) Unadjusted</b>	0.88(0.01) <sup>a</sup>	0.85(0.01) <sup>a,b</sup>	0.83(0.01) <sup>a,b,c</sup>	0.80(0.01) <sup>a,b,c</sup>
<b>Adjusted<sup>2</sup></b>	0.85(0.01)	0.85(0.01)	0.84(0.01)	0.84(0.01)
<b>Chair Stands (sec) Unadjusted</b>	13.33(0.02) <sup>a</sup>	13.20(0.21) <sup>b</sup>	13.51(0.21) <sup>c</sup>	14.68(0.22) <sup>a,b,c</sup>
<b>Adjusted<sup>2,3</sup></b>	13.57(0.19)	13.27(0.20) <sup>b</sup>	13.53(0.20)	14.04(0.28) <sup>b</sup>
<b>Grip Strength (kg) Unadjusted</b>	16.87(0.16) <sup>a</sup>	16.68(0.16)	16.75(0.16) <sup>c</sup>	16.29(0.16) <sup>a,c</sup>
<b>Adjusted<sup>2,4</sup></b>	16.71(0.16)	16.75(0.16)	16.80(0.16)	16.63(0.16)

<sup>1</sup> Measured with wrist actigraphy (Actillum®). Total nighttime sleep=average hours sleep in bed at night; Wake after sleep onset=average hours of wake after sleep onset; Daytime sleep = average hours of sleep, out of bed.

<sup>2</sup> Adjusted for age, race, BMI, depression (GDS15), anxiety (Goldberg Anxiety Score 0-9), cognitive function (MMSE), number of comorbidities (Doctor ever told you: stroke, diabetes, Parkinson's disease, Alzheimer's disease, chronic obstructive pulmonary disease, heart disease (heart attack or coronary event), congestive heart failure, and hypertension), and walking for exercise.

<sup>3</sup> Also adjusted for use of arms.

<sup>4</sup> Also adjusted for hand tremors.

<sup>a,b,c</sup> Differences between quartile with same letter are statistically significant p<0.05.

**Table 2-4 Odds of having an IADL impairment<sup>1</sup> by quartile of Total Nighttime Sleep<sup>2</sup>, Wake After Sleep Onset<sup>2</sup> and Daytime Sleep<sup>2</sup> in the Study of Osteoporotic Fracture participants at the eighth clinic visit.**

		<b>Total Nighttime Sleep (Hours)</b>			
		<b>&lt; 6.0</b>	<b>6.0- 6.8</b>	<b>6.8 -7.5</b>	<b>≥7.5</b>
<b>Odds ratio (CI)</b>	<b>Unadjusted</b>	1.14(0.92, 1.40)	Referent	0.75(0.61, 0.92)	1.14(0.93, 1.40)
	<b>Adjusted<sup>3</sup></b>	0.95(0.75, 1.21)	Referent	0.77(0.61, 0.97)	1.13(0.89, 1.44)
		<b>Wake After Sleep Onset (Hours)</b>			
		<b>&lt;0.7</b>	<b>0.7 – 1.1</b>	<b>1.1 – 1.6</b>	<b>≥1.6</b>
<b>Odds ratio (CI)</b>	<b>Unadjusted</b>	Referent	1.20(0.98, 1.50)	1.50(1.21, 1.83)	2.41(1.90, 2.98)
	<b>Adjusted<sup>3</sup></b>	Referent	1.10(0.87, 1.40)	1.26(0.99, 1.60)	1.54(1.20, 2.00)
		<b>Daytime Sleep (Hours)</b>			
		<b>&lt; 0.5</b>	<b>0.5 -1</b>	<b>1 -1.8</b>	<b>≥1.8</b>
<b>Odds ratio (CI)</b>	<b>Unadjusted</b>	Referent	1.14(0.91,1.41)	1.74(1.41, 2.15)	2.18(1.76, 2.70)
	<b>Adjusted<sup>3</sup></b>	Referent	0.95(0.75,1.32)	1.28(1.01, 1.63)	1.23(0.96, 1.57)

<sup>1</sup> Difficulty with at least 1 of the following 6 Instrumental Activities of Daily Living: walking 2-3 blocks, climbing or walking down 10 steps, preparing meals, heavy housework, and shopping.

<sup>2</sup> Total nighttime sleep = Average hours sleep in bed at night; Wake after sleep onset=Average hours Wake After Sleep Onset; Daytime sleep=average hours sleep, out of bed.

<sup>3</sup> Adjusted for age, race, BMI, depression (Geriatric Depression Score), anxiety (Goldberg Anxiety Score), cognitive function (MMSE), number of comorbidities (Doctor ever told you: stroke, diabetes, Parkinson’s disease, Alzheimer’s disease, chronic obstructive pulmonary disease, heart disease (heart attack or coronary event), congestive heart failure, and hypertension), and walking for exercise.

**3.0 ARTICLE TWO: SLEEP PROBLEMS AND ASSOCIATED DAYTIME FATIGUE  
IN COMMUNITY DWELLING OLDER INDIVIDUALS**

Goldman SE<sup>1</sup>, Ancoli-Israel S<sup>2</sup>, Boudreau R<sup>1</sup>, Hall M<sup>3</sup>, Cauley JA<sup>1</sup>, Stone K<sup>4</sup>, Harris T<sup>5</sup>,  
Satterfield S<sup>6</sup>, Simonsick EM<sup>7</sup>, Rubin S<sup>8</sup>, Newman AB<sup>1</sup>

Department of Epidemiology, University of Pittsburgh, Pittsburgh, PA<sup>1</sup>

Department of Psychiatry, University of California, San Diego, Ca<sup>2</sup>

Department of Psychiatry, University of Pittsburgh, Pittsburgh, PA<sup>3</sup>

San Francisco Coordinating Center and California Pacific Medical Center Research  
Institute, San Francisco, CA<sup>4</sup>

Laboratory of Epidemiology, Demography, and Biometry, National Institute on Aging,  
Bethesda, MD<sup>5</sup>

Department of Preventive Medicine, University of Tennessee, Memphis, TN<sup>6</sup>

Clinical Research Branch, National Institute on Aging, Baltimore, MD<sup>7</sup>

University of California, San Francisco, CA<sup>8</sup>

Manuscript in preparation

### 3.1 ABSTRACT

**Introduction:** Fatigue contributes to disability and restricted activity in older adults, yet specific determinants of fatigue are not well defined. Sleep duration and insomnia complaints may represent modifiable risk factors to reduce fatigue.

**Methods:** Fatigue was examined with a subscale of the Modified Piper Fatigue Scale (0-50; higher score indicating higher fatigue) in 2264 (52% women, 37% black) older adults aged 75-84 years (mean(SD) 77.5(2.9)) participating in the 2001-2002 visit of the Health Aging and Body Composition (Health ABC) study. Associations of fatigue with self-reported hours of sleep/night and insomnia complaints of difficulty initiating or maintaining sleep, and use of sleep medications were evaluated separately, and then in multivariable models adjusted for age, sex, race, body mass index, self-reported health, depression, cardio-pulmonary disease, dyspnea, and physical activity.

**Results:** The average fatigue score was 17.7(8.4) (scale 0-50). Compared to sleeping 7 hrs/night, >8 hrs/night was associated with a 7% higher fatigue score and awakening during the night or wakening too early in the morning were each associated with a 6% higher fatigue score. These associations remained after multivariate adjustment independent of comorbidity.

**Conclusion:** There was a wide range of fatigue symptoms in these community dwelling older adults. The association between disturbed nighttime sleep and reported fatigue symptoms suggests that better and more effective behavioral management of sleep may help reduce fatigue in older adults.

## 3.2 INTRODUCTION

Fatigue is a multi-dimensional, non-specific, syndrome<sup>1-8</sup> that has been described as weariness, weakness, tiredness and depleted energy<sup>5, 9</sup>. Fatigue is common in older adults, can affect quality of life<sup>10</sup>, and is often confused with daytime sleepiness. Although separate constructs<sup>11</sup>, fatigue and daytime sleepiness may overlap due to the multidimensionality of fatigue and the measurement tool used to define fatigue or sleepiness. Questionnaires to determine fatigue may<sup>12, 13</sup>, or may not<sup>14</sup>, evaluate sleepiness as a component of fatigue. The estimated prevalence of fatigue ranges from 6 to 45% depending on the population surveyed and measurement scale used<sup>5, 15, 16</sup>. In older adults tiredness and fatigue predict development of disability in basic activities of daily living<sup>17</sup>. The impact of fatigue on daily living in older adults is about twice as high as the impact of daytime sleepiness on daily living in younger adults<sup>18</sup>.

Insomnia and other sleep disturbances are also common in older adults with prevalence rates estimated as high as 50%<sup>19, 20</sup>. These also can result in decreased quality of life<sup>19</sup>. Although sleep complaints and fatigue are thought to be related, this association has not been evaluated with consideration of the contribution of comorbidity in community dwelling older adults. This study assessed the prevalence of fatigue in community-dwelling older adults and hypothesized that fewer hours of sleep and/or difficulty with initiating or maintaining sleep would be associated with higher fatigue scores.

## 3.3 METHODS

### 3.3.1 Study Population

The Health Aging and Body Composition (Health ABC) study, a prospective cohort study of 3,075 well functioning black (42%) and white (58%) men (48.4%) and women (51.6%), was

designed to investigate changes in body composition, health conditions, social and behavioral factors on physical and functional decline. Participants were recruited from a random sample of white Medicare beneficiaries, and all community-dwelling black residents, in designated zip-code areas around Pittsburgh PA and Memphis TN. Eligibility criteria included: age 70–79 years during the recruitment period from March 1997-1998, self-report of no difficulty walking one-quarter of a mile, or walking up 10 steps without resting, having no difficulties performing basic activities of daily living, no use of assistive devices or equipment to get around, being free of life-threatening illness, no history of active treatment for cancer in the past 3 years, no current enrollment in a lifestyle intervention treatment, and no plans for moving out of the area within 3 years. Participants were re-examined annually. This report concerns 2264 participants examined in 2001-2002. All participants gave informed written consent and the consent forms and protocol were approved by the Institutional Review Boards at each center.

### **3.3.2 Procedure**

At the year 5 clinic visit (2001-2002) interviewer-administered questionnaires included detailed questions about sleep, fatigue, medical history, and physical activity. Sleep and napping behavior were assessed by the following questions: “How many hours of sleep do you usually get at night during a usual week?” and “How many times a week do you nap for 5 minutes or more?” Insomnia symptoms were evaluated with a series of questions in which participants were asked how often they experienced: 1) trouble falling asleep, 2) waking up during the night and having difficulty getting back to sleep, 3) waking up too early in the morning and being unable to get back to sleep, 4) taking sleeping pills or other medication to help sleep. Responses were categorized as: never, rarely ( $\leq$ once/month), sometimes (2–4 times/month), often (5–15 times/month), or almost always (16–30 times/month).

Fatigue was measured with a subscale identified from factor analysis of the original 25-item Piper Fatigue Scale originally developed for use in breast cancer patients<sup>12</sup>. This scale has also been used in a group of older individuals residing in a long-term care facility<sup>10</sup>. Participants were asked the following questions in reference to the past month: 1) how weak did you feel; 2) how sleepy did you feel during the day; 3) how lively did you feel; 4) how tired did you feel; and

5) what was your usual energy level. Responses could range from 0-10 with 10 indicating the most severe level. A total fatigue score ranging from 0 (no fatigue) to 50 (highest fatigue) was obtained by summing the scores for each item after reversing the scoring for the questions on liveliness and energy level as in the Revised Piper Fatigue Scale <sup>12</sup>.

Self-reported health status was assessed with the question “In general how would you say your health is?” with response options excellent, very good, fair, poor, or don’t know. Cardio-pulmonary disease was assessed as self-report of congestive heart failure, coronary heart disease, or stroke. Self-reported dyspnea on exertion was classified separately. Physical activity was assessed by self report and calculated as the total kilocalories/week engaged in walking and climbing stairs <sup>21</sup>. Depression was assessed with the 10-item Center for Epidemiologic Studies Depression Scale (CESD 10) <sup>22</sup>. Anthropometric measurements, including height measured with a stadiometer and weight measured with a balance beam scale were also obtained. Body mass index (BMI) ( $\text{kg}/\text{m}^2$ ) was computed and categorized into 3 groups:  $<25 \text{ kg}/\text{m}^2$  as normal, 25-29  $\text{kg}/\text{m}^2$  as overweight, and  $\geq 30 \text{ kg}/\text{m}^2$  as obese <sup>23</sup>. Demographic characteristics (age, sex, and race) were defined by self report.

### **3.3.3 Data Analysis**

Descriptive statistics were performed on all variables to evaluate range, frequencies, normality, and inconsistencies in the data. Differences between race and gender were tested using chi-square tests and student’s t-tests. Age, race, BMI, depression, self-reported health status, cardio-pulmonary disease, physical activity, and performance factors were all considered as possible confounders of the association between sleep and fatigue and were treated as covariates <sup>1, 10, 11, 24-29</sup>.

For analyses purposes, based on initial examination of the data, hours of sleep were categorized as 6 or fewer hours, 7, 8, and more than 8 hours. Insomnia symptoms of trouble falling asleep, waking up during the night, waking up too early in the morning, and taking sleeping medicines were collapsed into 2 categories: “infrequent” comprising never or rarely experiencing any symptom; and “frequent” comprising experiencing at least one symptom

sometimes, often, or almost always. Approximately 60% of the participants fell into the infrequent category for each sleep symptom.

Potential associations between the individual fatigue scale components and nighttime sleep behaviors were examined using Spearman rank order correlation coefficients. The association between the total fatigue score and each sleep variable was examined using separate linear regression models. Additional factors found significant in univariate analysis were then included using progressively more complex multivariable models. Model 1 adjusted for age, race, and gender. Model 2 added all sleep variables plus age, race and gender. Model 3 added BMI, depressive symptom score, self-reported health status, and cardio-pulmonary factors. Model 4 added kilocalories/kg/week expended walking and climbing stairs. To express the strength of the associations, percent differences were calculated from the regression coefficients with the formula  $(\text{beta} \times \text{unit} / \text{mean fatigue score})^{30}$ . Factors found significantly associated with fatigue are reported at  $p \leq 0.05$ . Analyses were performed using SAS version 8.2 (SAS Institute, Cary, NC) and STATA version 8 (STATA Corporation, College Station, TX).

### 3.4 RESULTS

Fatigue scores ranged from 0 to 50 with a mean(SD) fatigue score of 17.7(8.4). Men reported lower fatigue than women. There was no difference in average fatigue levels between blacks and whites. Black women did not differ from white women and black men did not differ significantly from white men, in their average fatigue score. Mean hours of self-reported nightly sleep did not differ by gender, although a higher percentage of men napped at least 7 times a week compared to women. Over 39% of participants reported at least 1 insomnia symptom, with higher percentages of women reporting each insomnia symptom relative to men (Table 5).

Total fatigue, as well as each question on the fatigue scale, was slightly correlated with the individual symptoms of disturbed sleep. Removal of the question “over the past month how sleepy did you feel during the day” from the fatigue scale did not change the associations between fatigue and the individual sleep behaviors (Table 6). In separate linear regression models for each nighttime sleep variable, adjusted for age, race, and gender, both short ( $\leq 6$



hours) and long sleep duration (>8 hours) were associated with higher levels of fatigue when compared to self-reported sleep duration of 7 hours. Higher levels of fatigue were also associated with trouble falling asleep, waking up during the night, waking up too early, and use of sleep medications (Table 7). Results were similar when all sleep variables were considered together in the same model.

In the fully adjusted multivariable regression model, self-reported long sleep duration (>8 hours), waking up during the night, and waking up too early remained associated with higher fatigue scores. In general, these associations were slightly attenuated after adjustment. Trouble falling asleep at night, while associated with higher fatigue in the unadjusted models, was not associated with fatigue in the fully adjusted model. Also associated with higher average fatigue scores were: poorer self-reported health status, high depressive symptoms, prevalent cardio-pulmonary disease and dyspnea. These associations were also attenuated in the fully adjusted model. Individuals who engaged in walking or climbing stairs equivalent to >5.3 kcal/kg/week had lower fatigue scores than individuals with  $\leq 0.03$  kcal/kg/week of activity. The final multivariable model explained 36% of the overall variance in the fatigue score. Finally, factors associated with high levels of fatigue (fatigue score >30) were examined to determine if any factors were specifically related to these higher levels. Results were consistent with the results of the linear model.

### 3.5 DISCUSSION

This study is one of the first to examine the independent contribution of sleep with fatigue in a large cohort of predominately high functioning community dwelling older adults. In this cohort there was a wide range of fatigue symptoms. Individuals who reported sleeping >8 hours a night had higher total fatigue scores than those sleeping  $\leq 8$  hours. Persons who reported waking up during the night or waking up too early in the morning, also had higher total fatigue scores. These associations remained even after adjustment for multiple confounders. In those individuals who reported sleeping  $\leq 6$  hours per night, or who had trouble falling asleep, the fatigue appeared to be attenuated by other health reasons. The association of symptoms of poor sleep and fatigue

may be important in explaining aspects of fatigue beyond those due to comorbidity and supports the role of poor sleep as a risk factor for fatigue.

Fatigue is usually considered in the context of cancer<sup>4, 6, 12, 24, 31</sup>, or chronic disease<sup>32-38</sup>, although it impacts other populations as well. While a common complaint in older adults, it has rarely been addressed as a specific outcome in studies of this population. Studies performed in younger cohorts have reported fatigue symptoms in 12-25% of the population<sup>16, 39, 40</sup>. In one group of older adults, living in an assisted living facility, over 50% these individuals exhibited at least mild fatigue<sup>10</sup>. In addition to the dissimilar population groups assessed in these studies, the use of multiple, non-standardized fatigue scales makes it difficult to compare the fatigue rates found in the Health ABC cohort with these other studies. However, over 37% of the Health ABC cohort had a fatigue score  $\geq 20$  that would indicate a mild-moderate fatigue level.

To fully differentiate fatigue from sleepiness is difficult since sleepiness is often used to define fatigue<sup>8</sup>. Removal of the question “How sleepy are you during the day” from the total fatigue score, in this study, did not change the associations found between disturbed sleep and total fatigue. Fatigue has been associated with a wide range of sleep disorders and behaviors however, the causes of fatigue in sleep disordered populations is relatively unknown<sup>1, 24, 28</sup>. In individuals referred to sleep clinics, subjective fatigue has been shown to be independent of sleep disorder severity and daytime sleepiness in<sup>1, 15, 27, 41</sup>. Results of this study suggest an independent association of self-reported disturbed sleep and fatigue.

The direct association of chronic health conditions with fatigue in this population cannot be disregarded. Unlike tiredness, fatigue in chronic illness is pervasive and multi-dimensional, with different perceived causes and implications<sup>2, 29</sup>. In this study self-reported health status, cardiopulmonary disease, dyspnea, and depression were also strong associates of fatigue, even after adjustment for other variables. These associations were consistent with known associations of fatigue and medical comorbidities reported in other populations<sup>3, 7, 10, 26, 28, 40, 42</sup>. To what extent chronic disease might cause fatigue; or chronic disease might cause disturbed sleep which in turn causes fatigue, is not well defined even in cancer in sleep apnea patients. Results from this study suggest poor sleep has an independent contribution.

This study had several limitations. The study was cross-sectional representing one point in time; therefore a temporal relationship between sleep and fatigue cannot be determined. Fatigue is a subjective syndrome and there is no gold standard to assess it. Various other fatigue

scales, or components of scales, currently in use may provide different correlates of fatigue <sup>6</sup>. Usual sleep time and sleep behaviors were obtained by self-report. Although the validity of self-report sleep data has been demonstrated with actigraphy <sup>43</sup> some variability between actual and self-report exists. This study was of community dwelling older adults and may not be similar in other populations.

In summary, the results of this study of well-functioning community dwelling older adults suggest that fatigue was associated with several aspects of sleep including long sleep duration, frequent napping, and disrupted sleep independent of other health-related conditions commonly associated with fatigue. Part of this association may be explained by poorer self-reported health status. Improvement in nighttime sleep patterns and self-perceived health status may improve fatigue symptoms in community dwelling older adults.

### **3.6 ACKNOWLEDGEMENTS**

Supported By: NIH Contracts N01-AG-6-2101, 2103, 2106. NIA AG08415, NCI CA85264, NCI CA112035. Aging Training Grant Number: 2, T32, AG000181-16.

### 3.7 REFERENCES

1. Lichstein KL, Means MK, Noe SL, Aguillard RN. Fatigue and sleep disorders. *Behaviour Research and Therapy* 1997;35(8):733-40.
2. Trendall J. Concept analysis: chronic fatigue. *J Advanced Nursing* 2000;32(5):1126-31.
3. Addington AM, Gallo JJ, Ford DE, Eaton WW. Epidemiology of unexplained fatigue and major depression in the community: The Baltimore ECA follow-up, 1981-1994. *Psyc Med* 2001;31:1037-44.
4. Ancoli-Israel S, Moore PJ, Jones V. The relationship between fatigue and sleep in cancer patients: a review. *European Journal of Cancer Care* 2001;10(4):245-55.
5. Pigeon WR, Sateia MJ, Ferguson RJ. Distinguishing between excessive daytime sleepiness and fatigue. Toward improved detection and treatment. *J Psychosomatic Res* 2003;54:61-9.
6. Stein KD, Martin SC, Hann DM, Jacobsen PB. A multidimensional measure of fatigue for use with cancer patients. *Cancer Practice* 1998;6(3):143-52.
7. Dimsdale JE, Ancoli-Israel S, Elsmore TF, Gruen W. Taking fatigue seriously: I. Variations in fatigue sampled repeatedly in healthy controls. *J Med Engineering & Technol* 2003;27(5):218-22.
8. Shen J, Barbera J, Shapiro CM. Distinguishing sleepiness and fatigue: focus on definition and measurement. *Sleep Med Rev* 2006;10:63-76.
9. Ancoli-Israel S, Kripke DF, Klauber MR. Morbidity, mortality and sleep disordered breathing in community dwelling elderly. . *Sleep* 1996;19:277 - 82.
10. Liao S, Ferrell BA. Fatigue in an older population. *J Am Geriatr Soc* 2000;48(8):426-30.
11. Bardwell WA, Moore P, Ancoli-Israel S, Dimsdale JE. Fatigue in obstructive sleep apnea: driven by depressive symptoms instead of apnea severity? *Am J Psychiatry* 2003;160(2):350-5.
12. Piper BF, Dibble SL, Dodd MJ, Weiss MC, Slaughter RE, Paul SM. The revised Piper Fatigue Scale: psychometric evaluation in women with breast cancer. *ONF* 1998;25(4):677 - 84.
13. Morriss RK, Wearden AJ, Mullis R. Exploring the validity of the Chalder fatigue scale in chronic fatigue syndrome. *J Psychosomatic Res* 1998;45(5):411-7.

14. Moldofsky H, MacFarlane JG. Fibromyalgia and chronic fatigue syndromes. In: Kryger M RT, Dement WC, ed. Principles and Practice of Sleep Medicine, fourth edition. Philadelphia, PA: Elsevier Saunders; 2005.
15. Hossain JL, Ahmad P, Reinish LW, Kayumov L, Hossain NK, Shapiro CM. Subjective fatigue and subjective sleepiness: two independent consequences of sleep disorders? Journal of Sleep Research 2005;14(3):245-53.
16. Cullen W, Kearney Y, Bury G. Prevalence of fatigue in general practice. Ir J Med Sci 2002;171(1):10-2.
17. Avlund K DM, Sakari-Rantala R, Laukkanen P, Schroll M. Tiredness in daily activities among nondisabled old people as determinant of onset of disability. J Clin Epidem 2002;55:965-73.
18. Young T. Epidemiology of daytime sleepiness: definitions, symptomatology, and prevalence. J Clin Psychiatry 2004;65(suppl 16):12-6.
19. Foley DJ, Monjan AA, Brown SL. Sleep complaints among elderly persons: an epidemiologic study of three communities. Sleep 1995;18:425 - 32.
20. Jensen E, Dehlin O, Hagberg B, Samulsson G, Svensson T. Insomnia in an 80-year-old population: Relationship to medical, psychological and social factors. J Sleep Res 1998;7(183-189).
21. Brach JS, Simonsick EM, Kritchevsky S, Yaffe K, Newman AB. The association between physical function and lifestyle activity and exercise in the Health, Aging and Body Composition Study. Journal of the American Geriatrics Society 2004;52(4):502-9.
22. Irwin M, Haydan Artin K, Oxman MN. Screening for depression in the older adult: criterion validity of the 10-Item center for epidemiological studies depression scale (CES-D). Arch Intern Med 1999;159(15):1701-4.
23. National Institutes of Health. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults. The evidence report. In; 1998:228.
24. Berger AM, Higginbotham P. Correlates of fatigue during and following adjuvant breast cancer chemotherapy: a pilot study. Oncol Nurs Forum 2000;27(9):1443-8.
25. Vgontzas AN, Papanicolaou DA, Bixler EO, et al. Sleep apnea and daytime sleepiness and fatigue: Relation to visceral obesity, insulin resistance, and hypercytokinemia. J Clin Endocrinol Metab 2000;85(3):1151-8.
26. Warner G, Borawski E, Kahana E, Stange K. Fatigue as an important health indicator for the elderly. In: 129th Annual Meeting of APHA; 2001.
27. Chervin RD. Sleepiness, fatigue, tiredness, and lack of energy in obstructive sleep apnea. Chest 2000;118(2):372-9.

28. Crane PB. Fatigue and physical activity in older women after myocardial infarction. *Heart & Lung: The Journal of Acute and Critical Care* 2005;34(1):30-8.
29. Hewlett S, Cockshott Z, Byron M, et al. Patients' perceptions of fatigue in rheumatoid arthritis: Overwhelming, uncontrollable, ignored. *Arthritis Care & Research* 2005;53(5):697-702.
30. Cauley JA, Fullman RL, Stone KL, et al. Factors associated with the lumbar spine and proximal femur bone mineral density in older men. *Osteoporosis Int* 2005;16:1525-37.
31. Richardson A. Measuring fatigue in patients with cancer. *Support Care Cancer* 1998;6(94-100).
32. Sharpe M, Hawton K, Simkin S, et al. Cognitive behaviour therapy for the chronic fatigue syndrome: a randomised controlled trial. *BMJ* 1996;312(7022):22-6.
33. De Rijk AE, Schreurs KMG, Bensing JM. General practitioners' attributions of fatigue. *Social Science & Medicine* 1998;47(4):487-96.
34. Robbins JL, Phillips KD, Dudgeon WD, Hand GA. Physiological and Psychological Correlates of Sleep in HIV Infection. *Clin Nurs Res* 2004;13(1):33-52.
35. Mahowald ML, Mahowald MW. Nighttime sleep and daytime functioning (sleepiness and fatigue) in well-defined chronic rheumatic diseases. *Sleep Medicine* 2000;1(3):179-93.
36. Bowman SJ, Booth DA, Platts RG. Measurement of fatigue and discomfort in primary Sjogren's syndrome using a new questionnaire tool. *Rheumatology* 2004;43(6):758-64.
37. Heesen C, Nawrath L, Reich C, Bauer N, Schulz KH GS. Fatigue in multiple sclerosis: an example of cytokine mediated sickness behaviour? *J Neurol Neurosurg Psychiatry* 2006;77(1):34-9.
38. Mullington JM, Hinze-Selch D, Pollmacher T. Mediators of inflammation and their interaction with sleep. Relevance for Chronic Fatigue Syndrome and related conditions. *Annals of the New York Academy of Sciences* 2001;933(1):201-10.
39. Song S, Jason LA, Taylor RR, Torres-Harding SR, Helgeson J, Witter E. Fatigue severity among African Americans: gender and age interactions. *Journal of Black Psychology* 2002;28(1):53-65.
40. Van Der Linden, Chalder T, Hickie I, Koschera A, Sham P, Wessely S. Fatigue and psychiatric disorder: different or the same? *Psych Med* 1999;29(863-868).
41. Aguillard RN, Riedel BW, Lichstein KL, Grieve FG, Johnson CT, Noe SL. Daytime functioning in obstructive sleep apnea patients: exercise tolerance, subjective fatigue, and sleepiness. *Applied Psychophysiology and Biofeedback* 1998;23(4):207-17.
42. Tralongo P RD, Ferrau F. Fatigue and aging. *Critical Reviews in Oncology/Hematology* 2003;48(Supplement 1):S57-S64.

43. Lockley SW, Skene DJ, Arendt J. Comparison between subjective and actigraphic measurement of sleep and sleep rhythms. *J Sleep Res* 1999;8(3):175-83

**Table 3-1 Participant characteristics at the Health ABC year 5 (2001-2002) clinic visit**

	<b>Men n = 1078 (47.6%)</b>	<b>Women n = 1186 (52.4%)</b>	<b>Total N=2264</b>
<b>Demographics:</b>			
Age (years) mean(sd)	77.7 (2.8)	77.3 (2.9)	77.5(2.9)
<b>Race</b>			
Black %	32.1	41.9	37.2
White %	67.9	58.1	62.8
Average Fatigue Score	16.8 (8.3)	18.5(8.5) ***	17.7 (8.4)
<b>Self-reported sleep variables:</b>			
	<b>n(%)</b>	<b>n(%)</b>	<b>n(%)</b>
<b>Sleep Duration:</b>			
≤ 6hrs (n=857)	35.4	40.0	37.9
7 hrs (n=628)	27.9	27.6	27.7
8 hrs (n=619)	28.9	25.9	27.3
> 8 hrs (n=160)	7.7	6.5	7.1
Naps ≥7/wk %	37.5	28.9 ***	33
Trouble falling asleep (> 1night/mo)%	33.9	46.2 ***	40.3
Wake up during night(> 1night/mo)%	48.1	54.0 **	51.2
Wake up too early (> 1night/mo)%	37.0	41.4 *	39.3
Sleep medications (> 1night/mo)%	10.6	14.6 **	12.7
<b>Health variables:</b>			
<b>BMI (kg/m<sup>2</sup>):</b>			
BMI < 25 (kg/m <sup>2</sup> ) %	31.4	35.2	33.4
BMI 25 - 30 (kg/m <sup>2</sup> ) %	47.5	35.2	41.1
BMI >30 (kg/m <sup>2</sup> ) %	21.2	29.5	25.5
<b>Self reported health status:</b>			
Excellent (n=240)	11.7	9.6	10.6
Very good (n=733)	33.3	31.6	32.4
Good (n=865)	36	40.3	38.2
Fair – Poor (n=424)	19.1	18.5	18.7
Stroke (n=81)	4.0	3.2	3.6
Coronary heart disease (n=316)	17.5	10.7 ***	14
Congestive heart failure (n=166)	7.8	6.9	7.3
Dyspnea (n=798)	29.1	41.1 ***	35.4
Depression (mean(SD))	4.4 (4.0)	5.5(4.6) ***	5.0 (4.3)



<b>Table 3-1cont.</b>	<b>Men n = 1078 (47.6%)</b>	<b>Women n = 1186 (52.4%)</b>	<b>Total N=2264</b>
<b>kcal/kg/wk walking + climbing stairs:</b>			
<b>&lt;0.03 (n=381)</b>	16.8	26.2 ***	21.8
<b>0.03 - ≤1.23 (n=648)</b>	23.3	28.8	26.2
<b>&gt;1.23 - ≤5.53 (n=617)</b>	27.3	24.7	25.9
<b>&gt;5.53 (n=618)</b>	32.6	20.4	26.1

\*  $p \leq 0.05$

\*\*  $p \leq 0.01$

\*\*  $p \leq 0.001$

**Table 3-2 Correlation of the fatigue scale components to the total fatigue score and symptoms of disturbed nighttime sleep (Spearman's rho  $r_s$ ) in Health ABC year 5 (n=2264)**

Fatigue Scale Components	Nighttime Sleep Behaviors			
	TFS <sup>1</sup>	WUDN <sup>1</sup>	WUTE <sup>1</sup>	MEDS <sup>1</sup>
<b>During the past month how:</b>				
Weak did you feel ? <sup>2</sup>	0.13***	0.19***	0.16***	0.12***
Sleepy did you feel during day ? <sup>2</sup>	0.07**	0.17***	0.14***	0.05**
Lively did you feel ? <sup>2,3</sup>	-0.13***	-0.14***	-0.17***	-0.13***
Tired did you feel ? <sup>2</sup>	0.15***	0.18***	0.17***	0.10***
Describe your usual energy level. <sup>2,3</sup>	-0.11***	-0.18***	-0.18***	-0.10***
<b>Total fatigue score (5 item scale)<sup>4</sup></b>	<b>0.15***</b>	<b>0.23***</b>	<b>0.22***</b>	<b>0.14***</b>
<b>Total fatigue score (4 item scale)<sup>5</sup></b>	<b>0.16***</b>	<b>0.23***</b>	<b>0.22***</b>	<b>0.15***</b>

<sup>1</sup> TFS = trouble falling asleep at night; WUDN = wake up during the night; WUTE = wake up too early; MEDS = use of medication to help sleep. Questions were asked on an ordinal Scale 0= never, 1 = ≤ once/month; 2 = 2-4 times/month; 3= 5-15 times/month 4 = 16 – 30 times/month.

<sup>2</sup> Scale of 0 – 10 (worst) over the past month

<sup>3</sup> Correlations reported for direction the question was asked. When part of the fatigue scale they were reversed.

<sup>4</sup> Total fatigue score (see methods section).

<sup>5</sup> Total fatigue score made up of the following questions: How weak did you feel, how lively did you feel, how tired did you feel, and describe your usual energy level.

\*\* <0.001

\*\*\* <0.0001

**Table 3-3 Factors associated with fatigue in multivariable models adjusted for age, race and gender and fully adjusted**

Variable	Mean (SD) or prevalence (%)	Unit/Referent <sup>1</sup>	Percentage difference in fatigue per unit (95% CI)	
			Adjusted model (age, race, and gender)	Fully adjusted model <sup>1</sup>
<b>Age (years)</b>	77.5 (2.9)	1	0.6 (-0.1, 1.3)	0.3 (-0.3, 0.9)
<b>Gender: Female</b>	52.4 %	Male	10.0 (6.1, 13.9)	3.2 (-0.2, 6.6)
<b>Race: Black</b>	37.2 %	White	0.4 (-3.6, 4.5)	-11.9 (-15.4,-8.2)
<b>Sleep Duration:</b>				
≤ 6hrs	37.9 %	Referent	15.4 (10.5, 20.2)	4.2 (-0.01, 8.3)
7 hrs	27.7 %			
8 hrs	27.3 %		3.6 (-1.6, 8.8)	3.2 (-1.2, 7.6)
> 8 hrs	7.1 %		8.5 (0.4, 16.7)	7.2 (0.2, 14.3)
<b>Trouble falling asleep &gt;1night/mo</b>	40.3 %		11.5 (7.5, 15.5)	-3.9 (-7.7, 0.2)
<b>Wake up during night &gt;1night/mo</b>	51.2 %		19.6 (15.8, 23.5)	5.8 (2.0, 9.6)
<b>Wake up too early &gt; 1night/mo</b>	39.3 %		20.4 (16.5, 24.3)	6.3 (2.4, 10.1)
<b>Sleep medications &gt; 1night/mo</b>	12.6 %		16.9 (11.0, 22.8)	1.3 (-3.8, 6.3)
<b>Self-reported health status:</b>				
Excellent	10.6 %	referent		
Very Good	32.4 %		17.0 (10.7, 23.2)	10.8 (5.1, 16.6)
Fair	38.2 %		37.8 (31.6, 44.0)	23.7 (17.9, 29.5)
Poor	18.7 %		66.5 (59.6, 73.5)	38.4 (31.3, 45.2)
<b>Cardio-pulmonary disease<sup>2</sup>:</b>				
1 disease	13.7%		12.5 (6.8,18.2)	4.2 (-0.8, 9.2)
2 + diseases	5.4%		23.7 (15.1, 32.3)	13.1(5.4, 20.7)

<b>Table 3-3 cont.</b>		<b>Percentage difference in fatigue per unit (95% CI)</b>		
<b>Variable</b>	<b>Mean (SD) or prevalence (%)</b>	<b>Unit/Referent<sup>1</sup></b>	<b>Adjusted model (age, race, and gender)</b>	<b>Fully adjusted model<sup>1</sup></b>
<b>Dyspnea (any symptoms)</b>	35.4%		31.2 (27.3, 35.1)	14.0 (10.3,17.8)
<b>Depression</b>	5.0 (4.3)	1 SD	101.0 (93.6, 108.5)	69.6 (61.5, 77.6)
<b>kcal/kg/wk walking + climbing</b>				
<b>stairs:</b>				
<b>0.03 - ≤1.23 (n=648)</b>	26.2%	<0.03	-6.1 (-11.9, -0.4)	3.3 (-1.5, 8.0)
<b>&gt;1.23 - ≤5.53 (n=617)</b>	25.9%		-13.6 (-19.4, -7.8)	-0.7 (-5.6, 4.2)
<b>&gt;5.53 (n=618)</b>	26.1%		-24.3 (-30.2, -18.5)	-7.2 (-12.2,4.2)
				<b>model r<sup>2</sup> 0.36</b>

<sup>1</sup> Referent group is group with none of the characteristic.

<sup>2</sup> Cardiopulmonary disease includes congestive heart failure, coronary heart disease, and/or stroke.

**4.0 ARTICLE THREE: ASSOCIATION BETWEEN NIGHTTIME SLEEP AND  
NAPPING IN OLDER**

Goldman SE<sup>1</sup>, Hall M<sup>2</sup>, Boudreau R<sup>1</sup>, Matthews KA<sup>2</sup>, Cauley JA<sup>1</sup>, Ancoli-Israel S<sup>3</sup>, Rubin S<sup>4</sup>,  
Satterfield S<sup>5</sup>, Simonsick E<sup>6</sup>, Stone KL<sup>7</sup>, Newman AB<sup>1</sup>

Department of Epidemiology, University of Pittsburgh, Pittsburgh, PA<sup>1</sup>

Department of Psychiatry, University of Pittsburgh, Pittsburgh, PA<sup>2</sup>

Department of Psychiatry, University of California, San Diego, Ca<sup>3</sup>

University of California, San Francisco, CA<sup>4</sup>

Department of Preventive Medicine, University of Tennessee, Memphis, TN<sup>5</sup>

Laboratory of Epidemiology, Demography, and Biometry, National Institute on Aging,  
Bethesda, MD<sup>5</sup>

Clinical Research Branch, National Institute on Aging, Baltimore, MD<sup>6</sup>

San Francisco Coordinating Center and California Pacific Medical Center Research Institute, San  
Francisco, CA<sup>7</sup>

Manuscript in preparation

## 4.1 ABSTRACT

**Study objectives:** Daytime sleep (napping) might indicate deficiencies in nighttime sleep, but the relationship is not well defined. This study assessed the association of nighttime sleep duration and fragmentation with daytime sleep in community dwelling older adults.

**Design:** Cross-sectional study.

**Participants:** 235 individuals (47.5% men, 29.7% black), age 80.1(2.9) years.

**Measurements and Results:** Nighttime and daytime sleep were measured with wrist actigraphy (Actiwatch AW-16<sup>®</sup>, Mini Mitter, Inc.) and sleep diaries for an average of 6.8(0.7) nights. Sleep parameters measured included total nighttime sleep (hrs), movement and fragmentation index (fragmentation), and total daytime sleep (nap) (hrs). The relationship of total nighttime sleep and fragmentation to napping (yes/no) was assessed using logistic regression. In only the individuals who napped, mixed random effect models were used to determine the association between the previous night sleep duration and fragmentation and nap duration, and nap duration and subsequent night sleep duration. All models were adjusted for age, gender, race, BMI, cognitive status, depression, number of times waken during the night, cardiovascular disease, respiratory symptoms, pain, and fatigue. Naps were recorded by 178(75.7%) participants. The odds of napping were higher for individuals with high levels of nighttime fragmentation, diabetes, and pain (2.8 (95% CI, 1.1, 7.1), 5.9 (1.2, 28.9), and 2.3 (1.1, 4.8) respectively). In the group that napped neither sleep duration nor fragmentation the night before the nap was associated with nap duration the next day.

**Conclusion:** Higher nighttime sleep fragmentation was associated with higher odds of whether or not an older adult naps, however it was not associated with nap duration within nappers. The identification of causes and methods to reduce fragmented sleep may help lessen daytime napping in older adults.

## 4.2 INTRODUCTION

Daytime sleep (napping) and frequent nocturnal awakenings are sleep changes associated with aging<sup>6, 10, 12, 17, 37, 62, 91, 174, 175</sup>. The relationship between nighttime sleep and napping in older adults has been determined primarily by self-report, or from laboratory studies in small groups of individuals. The association of measured nighttime sleep patterns with measured daytime napping, and measured daytime napping on measured nighttime sleep, is unclear<sup>41, 96, 140</sup>. Some studies have shown napping to have little impact on subsequent night sleep quality or duration<sup>62, 96, 98</sup> while another reported a negative impact on sleep quality and duration in the subsequent nights<sup>41</sup>.

In active community-dwelling older adults the association between disturbed nighttime sleep and whether an individual takes a nap during the day is not well defined. Further, the temporal relation between disturbed nighttime sleep and daytime napping is unclear. The study's objectives were to determine sleep behaviors and other factors associated with taking a nap in older adults; and to evaluate the association with daytime nap duration. This study hypothesis was shorter nighttime sleep duration, and higher amounts of fragmentation would be associated with higher odds for taking a nap, as well as with longer nap duration. It also hypothesized a longer daytime nap would be associated with a shorter nighttime sleep on the nap night.

## 4.3 METHODS

### 4.3.1 Study Population

Participants were a subgroup from the Pittsburgh site of the Health Aging and Body Composition (Health ABC) study at the eighth year (2004–2005) clinic visit who agreed to participate in a sleep study where they would wear a wrist actigraph continuously for one week and complete a 24 hour sleep-wake diary at bedtime and wake time. The Health

ABC study was designed to evaluate the relationship between weight, body composition, and various health conditions in community dwelling older adults. The study enrolled 3075 adults aged 70–79 years, 42% black, and 52% women between 1996–1997 in Pittsburgh PA, and Memphis TN. Individuals were excluded if they reported difficulty walking a quarter of a mile, climbing 10 steps without resting, or with activities of daily living. They were also excluded if they had cancer under active treatment within the past 3 years, or planed to move within 3 years.

Participation in the sleep study was voluntary and offered to participants based on availability of a wrist actigraph during their study visit. Participants were excluded if they would not be able to wear the watch and/or complete the diary, used CPAP or oxygen at night, were cognitively impaired, were undergoing treatment for cancer, or if they had any end-stage disease. Two hundred and thirty six individuals wore wrist actigraphs and successfully completed the daily sleep-wake diary. The nap duration on two days for one participant exceeded seven hours. It was subsequently determined she was ill and was hospitalized on the sixth day of the study. She was removed from the analyses. The institutional review board at The University of Pittsburgh approved the study and written informed consent was obtained from all participants.

#### **4.3.2 Sleep**

Nighttime and daytime sleep was measured by actigraphy with the Mini-Mitter Actiwatch<sup>®</sup> (AW-16). The actiwatch was worn on the non-dominant wrist over 7 consecutive 24 hour periods starting at the clinic visit. The wrist actiwatch monitors gross motor activity and was set to record in one minute epochs at a medium sensitivity level for scoring sleep and wake times (40 activity counts/minute)<sup>176, 177</sup>. Participants were given a sleep-wake diary to complete concurrent with wearing the watch. Daily they recorded the time they: went to bed, tried to go to sleep, woke up in the morning, got out of bed in the morning, number of times they awoke during the night; and the start time and end time for each daytime nap  $\geq 5$  minutes. To differentiate nap time from periods of inactivity there was a separate entry on the daily form for periods of sitting still for over



an hour such as watching television, reading, and riding in a car. All participants were instructed in the use of the wrist actigraph and how to complete the sleep-diary during their clinic visit. Phone support was available to the participants throughout the study.

Data from the wrist actigraphs were downloaded to a personal computer and analyzed with Mini-Mitter<sup>®</sup> version 5 software using a validated algorithm, set at medium sensitivity, to identify sleep and wake<sup>176</sup>. The threshold for medium sensitivity is 40 activity counts. Nighttime sleep and morning wake times were set based on review of the downloaded actogram and verified against the time recorded in the participants' diary. If >5 minute discrepancy occurred between the actogram and the diary the actogram time was used. To determine if a participant took a nap, as well as the duration of the nap, nap intervals were only set on the actogram if the participant had entered a start and stop time for the nap in their sleep-wake diary. One individual read all of the actograms with an intra-reader reliability >0.95 based on a random sample of 10 participant actograms.

Sleep and nap measurements were calculated with Mini-Mitter<sup>®</sup> V5 software. The total nighttime sleep duration was the sum of all sleep epochs within the interval between set sleep and set wake time. Wake after sleep onset was measured as the sum of all wake epochs during the sleep period. The movement and fragmentation index consisted of the sum of the percent of mobile minutes and the percent of immobile bouts less than 1 minute duration to the number of immobile bouts, for a given interval, hereafter referred to as fragmentation. Daytime sleep was scored the same as the total duration of nighttime sleep<sup>176</sup>.

Self reported sleep duration and nap behavior in a typical week were determined by participant response to the questions: "How many hours of sleep do you usually get at night?", and "During a usual week, how many times do you nap for 5 minutes or more?" To determine problems with nighttime sleep participants were asked the following questions on a 5-point Likert scale: During a typical month how often do you have: Trouble falling asleep?"; "Wake up during the night and have difficulty getting back to sleep?"; "Wake up too early in the morning and are unable to get back to sleep?"; and "Take sleeping pills or other medication to help you sleep?". Response options to these questions were: never, ≤once a month, two to four times a month, five to 15 times a month, and >15 times a month. For analysis, these variables were collapsed into:

“infrequent” consisting of never and  $\leq$ once per month and “frequent”  $\geq 2$  times per month.

### **4.3.3 Demographics and General Health**

At the eighth annual clinic visit a detailed interview and exam was conducted to obtain and update demographic and health history. Data obtained included age, sex, race, height, weight, socio-economic variables, history of diseases, and medications.

### **4.3.4 Outcome**

At the eighth annual clinic visit a detailed interview and exam was conducted to obtain and update demographic and health history. Data obtained included age, sex, race, height, weight, socio-economic variables, history of diseases, and medications.

### **4.3.5 Comorbid health conditions**

Cardiovascular disease was defined as history of myocardial infarction, angina, stroke, transient ischemic attack, or congestive heart failure at the sixth year Health ABC visit, an average of two years prior to the current one. Unfortunately, this data was not available for the same time period as the sleep study. Due to the low incidence of each individual disease in the sleep study cohort, a summary cardiovascular disease variable was developed to represent the presence or absence of any one of the diseases. Diabetes was defined by self-report of the disease at the eighth year visit. Respiratory disease was defined as self-report of any of the following: dyspnea on exertion, need to stop for breath when walking, history of asthma, chronic obstructive pulmonary disease, emphysema, or bronchitis. Similar to cardiovascular disease a summary variable was created that represented presence or absence of any of the symptoms. Depression was

measured with the 10 item Center for Epidemiologic Studies Depression scale <sup>159</sup> was used to measure depression.

#### **4.3.6 Other potential confounders**

Factors associated with napping considered as potential confounders, or mediators, previously identified associated with sleep or nap <sup>1, 13-15, 175</sup> and included: body mass index (BMI) (kg/m<sup>2</sup>); self-reported health status (excellent-good, fair, poor); mental status (Teng Mini-Mental Status Exam); smoking (yes or no); or use of alcohol. Pain was defined as a response of yes to the question, “have you experienced any bodily pain in the past 30 days”. Fatigue was evaluated with a subscale from the Piper Modified Fatigue Scale (scale 0-50 highest) <sup>44, 66</sup>. Due to the low prevalence of smoking (n (%) 4(2)) it was not included in the analyses.

#### **4.3.7 Statistical analyses**

Participants were classified into those who napped, or did not nap, based on whether a nap interval was recorded on any day in the sleep-wake diary. Student t-tests were used to test differences in means between dichotomous variables, and chi-square analysis was used for categorical variables between individuals who did or did not nap. A series of logistic regression models were performed to obtain the odds ratios for taking or not taking a nap. Models were adjusted for variables associated with either sleep or nap in univariate analysis, or that have been reported in the literature <sup>1, 13-15, 175</sup>. The final model included age, race, BMI (kg/m<sup>2</sup>), measured night time sleep (hrs), measured movement and fragmentation, depression, mental status, pain in the past 30 days, cardio-pulmonary disease, respiratory disease, diabetes, and fatigue. Measured movement and fragmentation was evaluated as a continuous variable, as well as divided into tertiles.

In those participants who recorded naps mixed models were fit to determine the association of the previous night measured sleep duration and fragmentation with the next day measured nap duration. Also evaluated in this group was the association of the

previous night measured sleep duration, fragmentation, and the next day measured nap duration on the measured sleep duration for the night of the nap. Participant was the random effect in the models and the same variables considered in the logistic regression models above were considered as fixed effects in the mixed models.

Linear regression models were also performed, in those who reported naps, to determine the association between the average nighttime sleep duration and average fragmentation with the duration of the average daytime nap over the time period the participant wore the wrist actigraph. Variables considered in the logistic and mixed-model analyses described above were evaluated here as well. To express the strength of the associations, units of percent differences were calculated from the regression coefficients with the formula  $(\text{beta} \cdot \text{unit} / \text{mean nap duration (hrs)})^{163}$ . All analyses were run in STATA version 8 (Stata College Station, TX), or SAS version 8 (Cary, NC). Analyses were considered significant at  $p \leq 0.05$  unless otherwise noted.

#### 4.4 RESULTS

Wrist actigraphs were worn for an average 6.8(0.7) (mean (SD)) nights, with a nap of  $\geq 5$  minutes recorded by 178(75.7%) participants. The average age of those who recorded naps was 80.1(2.9) years, 92(51.7%) were women, 86(48.3%) were men, 124(69.7%) were white and 111(30.3%) were black. Basic demographic characteristics were similar between those who did or did not record a nap. Those who napped recorded an average of 3.9(2.6) naps over the period they wore the watch, with an average nap duration of 1.1(0.6) hours/nap. Average nighttime sleep duration, measured by actigraphy, was similar between the individuals who napped or did not nap. Individuals who napped had higher nighttime fragmentation, as measured by both the movement and fragmentation index and wake after sleep onset (Table 4.1).

Self-reported hours of sleep per night, trouble falling asleep, waking up during the night, waking up too early in the morning, using medications to help sleep, or daytime sleepiness did not differ between those who did or did not record naps. The self-reported

number of naps per week and fatigue score was higher in those who recorded naps. Higher percentages of individuals who recorded naps also reported pain over the past 30 days, respiratory symptoms, or diabetes (Table 4.1).

In unadjusted logistic regression models, to identify potential determinants for having recorded a nap, odds of recording a nap were higher for individuals with higher levels of fragmentation, symptoms of pain in the past 30 days, respiratory symptoms, diabetes, or higher fatigue levels. In the fully adjusted model individuals with pain over the past 30 days, respiratory symptoms, diabetes and higher fatigue score had higher odds for napping that were not attenuated by adjustment. Individuals with fragmentation in the second tertile (28–40) had slightly higher odds of having recorded a nap after full adjustment, while the odds for napping in those individuals in the third tertile ( $\geq 40$ ) were slightly attenuated (Table 4.2).

In individuals who recorded a nap, the temporal relationship between the previous night measured sleep duration and fragmentation with the next day measured nap duration was evaluated first with separate linear regression models using specific sequential night-day intervals. In two separate sequential intervals, although not significant, there was a pattern where shorter nighttime sleep, and more nighttime fragmentation, was associated with longer daytime nap duration (Table 4.3).

The association between the measured previous nighttime sleep duration and fragmentation with the next day nap duration was examined further with mixed model analysis. Neither of these sleep variables were associated with nap duration the next day (Table 11). In the fully adjusted mixed model variables associated with nap duration were self-report of pain in the past 30 days (22.4% shorter nap duration), black race (25.9% longer nap duration), and self-reported diabetes (34.9% longer nap duration) (Table 4.4).

The association between the measured previous night sleep duration, fragmentation, and next day nap duration with the next night measured sleep duration was examined with mixed model analysis in the individuals who napped (Table 4.5). Neither previous night sleep duration, nor fragmentation, were significantly associated with sleep duration the next night. Every hour of daytime sleep (nap) however, was associated with 7.5% less sleep duration on the night of the nap. The previous night sleep duration X daytime sleep duration interaction was significant. However, the 0.8% higher

nighttime sleep duration associated with the interaction would have minimal effect on overall sleep duration.

Linear regression models were performed to determine the association of measured sleep duration, fragmentation with nap duration averaged over the time period the wrist actigraph was worn. In the fully adjusted model self report of body pain was associated with shorter nap duration and diabetes with longer nap duration (Table 4.6). Fragmentation while strongly associated with the odds for napping was not associated with nap duration either as a continuous variable or by tertile.

#### 4.5 DISCUSSION

Higher nighttime fragmentation, measured by wrist actigraphy, was associated with up to 3.2(95%CI 1.1, 7.1) times higher odds of recording a nap in this cohort of 80 year old adults. This association remained after adjustment for age, race, gender, and measured nighttime sleep duration (hours). Further adjustment for self-reported use of sleep medication, BMI, depression, cognitive status, pain, respiratory symptoms, cardiopulmonary disease, diabetes and fatigue did not attenuate this finding. In the individuals who recorded naps, longer nap durations were associated with self-report of diabetes and shorter nap durations were associated with self report of pain. Longer nap durations were not, however, explained by either the average measured sleep duration or nighttime fragmentation over the time period the participants wore the wrist actigraph.

Fragmentation was the nighttime sleep measurement that differentiated individuals who reported naps from those who did not. Frequent nighttime awakenings in older adults have been reported in multiple studies<sup>6, 10, 91, 93, 147, 174, 175, 178</sup>. These arousals have been associated with reduced daytime well-being, daytime sleepiness, and napping<sup>93, 147, 178, 179</sup>. This study supports prior research and corroborates the association between fragmented nighttime sleep and daytime napping. In addition, we were able to demonstrate that higher levels of fragmentation were associated with higher odds of having taken a nap. Neither measured nighttime sleep duration, nor fragmentation was

associated with recorded nap duration. While this may be attributable to lack of power, this lack of association still requires further investigation.

A major factor associated with nighttime fragmentation, not measured in this study is sleep disordered breathing, or obstructive sleep apnea. Use of the movement and fragmentation index, does however, provide an estimate of sleep apnea syndrome, or sleep disordered breathing. This index has been shown to be highly correlated ( $r=0.98$ )<sup>180</sup>, and to have high sensitivity and specificity, 89% and 95% respectively<sup>181</sup> with polysomnography (PSG) to measure sleep apnea syndrome (or sleep disordered breathing).

Sleep disordered breathing, defined as an apnea-hypopnea index (AHI)  $\geq 10-15$ , has been estimated to range from 45-62% in adults  $\geq 60$  years<sup>180, 181</sup>. Fifty nine percent of participants in this study had a movement and fragmentation index  $\geq 30$ , a value associated with severe sleep apnea syndrome in a patient population with a mean age of  $52 \pm 15$  years<sup>180</sup>. This suggests a large portion of these individuals might have some form of undiagnosed sleep disordered breathing that might be amenable to treatment.

Self-reported diabetes and pain were the conditions most highly associated with nap duration. A higher risk for diabetes has been associated with short (<6 hours) or long (>9 hours) sleep duration<sup>100, 148, 182, 183</sup>. Diabetes has also been associated with excessive daytime sleepiness<sup>148, 184</sup>, however whether or not diabetics actually take a nap has not been demonstrated. This study extends the relationship and suggests an association between diabetes and napping as well.

To make an overall association between napping and general health in this population is unequivocal based on our data. We found no association with cardio-pulmonary diseases, however a strong association was found with self reported diabetes. The lack of association with cardiovascular disease differs from reports in other populations of older adults where not only was a siesta more common in individuals with a past history of myocardial infarction, but the siesta was predictive of cardiovascular disease<sup>185, 186</sup>. However, it must be noted that the measure of cardiovascular disease, in this study, represents disease status two years earlier and might not reflect current disease status.

A recent review of the role of napping in sleep medicine concluded that there was not enough evidence accounting for the association between napping and health risks<sup>97</sup>. Napping in old age has been suggested to help older adults maintain their daytime functioning at an adequate level<sup>97, 102</sup>. However, napping has also been associated with an increase in mortality<sup>104, 140, 185</sup>.

Whether or not older adults should nap or avoid napping is debatable. A daytime nap has been associated with activity-related health deficits and poor sleep hygiene<sup>104</sup> and avoiding it to improve nighttime sleep has been advised<sup>55</sup>. However, napping as a way to increase 24 hour sleep quality, duration, or to offset insomnia has also been suggested<sup>41, 55, 96</sup>. Our study demonstrated that total sleep time was significantly higher on the days that the study participants recorded a nap. A short nap can improve alertness after restricted sleep<sup>97, 102, 187</sup>. Napping, as well as the ability to fall asleep, has been shown to be more common in older adults with a good night's sleep compared to those with a poor night sleep<sup>96, 148</sup> and it was not restricted to those complaining of insomnia.

Several limitations in interpreting these data warrant discussing. The participants represent a survival cohort of the original Health ABC study of community dwelling older adults. The individuals in this ancillary study were primarily individuals still active and participating in daily events. As such, poorer functioning or institutionalized older adults are not represented in this sample. Measurements of nighttime and daytime sleep were obtained by actigraphy in conjunction with self report and might differ from polysomnography measured sleep. Further, as naps were only measured if recorded this might result in underestimation of napping in the population. Finally, cardiovascular status was determined based on disease status 2 years earlier and diabetes and respiratory symptoms were measured by self-report. This might underestimate the incidence of these diseases in our cohort and bias the results towards shorter nap duration.

These findings have important clinical implications and point to the need for health care providers to discuss nighttime and daytime sleep characteristics with their older patients. This study showed that nighttime fragmentation was associated with higher odds of whether or not an older adult took a nap during the day. Research to reduce causes of fragmented nighttime sleep in older adults might help reduce the number of naps taken in community dwelling older individuals.



## **4.6 ACKNOWLEDGMENT**

Supported By: NIH Contracts N01-AG-6-2101, 2103, 2106. NIA AG08415, NCI CA85264, NCI CA112035. Aging Training Grant Number: 2, T32, AG000181-16.

#### 4.7 REFERENCES

1. Pressman MR, Fry JM. What is normal sleep in the elderly? *Clinics in Geriatric Medicine* 1988;4(1):71 - 82.
2. Bliwise DL. Normal Aging. In: Kryger MH, Roth T, Dement WC, eds. *Principles and Practice of Sleep Medicine*. 3rd edition: W. B. Saunders Company; 2005.
3. Bliwise DL, Ansari FP, Straight L-B, Parker KP. Age changes in timing and 24 hour distribution of self-reported sleep. *Am J Geriatr Psych* 2005;12(12):1077 - 82.
4. Buysse DJ, Browman BA, Monk TH, Reynolds CF, Fascizka AL, Kupfer DJ. Napping and 24-hr sleep/wake patterns in healthy elderly and younger adults. *J Am Geriatric Society* 1992;40:779-86.
5. Yoon IY, Kripke DF, Youngstedt SD, Elliot JA. Actigraphy suggests age-related differences in napping and nocturnal sleep. *J Sleep Res* 2003;12:87 - 93.
6. Dement WC, Miles LE, Carskadon MA. "White paper" on sleep and aging. *JAGS* 1982;30:25-50.
7. Bliwise DL. Sleep in normal aging and dementia. *Sleep* 1993;16(1):40-81.
8. Ohayon MM, Zulley J, Guilleminault C, Smirne S, Priest RG. How age and daytime activities are related to insomnia in the general population: consequences for older people. *JAGS* 2001;49:360-6.
9. Evans BD, Rogers AE. 24 -Hour sleep/wake patterns in healthy elderly persons. *Applied Nursing Research* 1994;7(2):75 - 83.
10. Monk TH, Buysse DJ, Carrier J, Billy BD, Rose LR. Effects of afternoon "siesta" naps on sleep, alertness, performance, and circadian rhythms in the elderly. *Sleep* 2001;24(6):680-7.
11. Campbell SS, Murphy PJ, Stauble TN. Effects of a nap on nighttime sleep and waking function in older subjects. *J Am Geriatr Soc* 2005;53(1):48-53.
12. Bursztyn M, Ginsberg G, Stessman J. The siesta and mortality in the elderly: effect of rest without sleep and daytime sleep duration. *Sleep* 2002;25:187-91.
13. Tamaki M, Shirota A, Tanaka H, Hayashi M, Hori T. Restorative effects of a short afternoon nap (<30 min) in the elderly on subjective mood, performance and EEG activity. *Sleep Research Online* 2000 2000;3:131-9.

14. Oakley NR. Validation with polysomnography of the Sleepwatch sleep/wake scoring algorithm used by the Actiwatch activity monitoring system. Bend, OR: Mini Mitter Co., Inc.; 1997.
15. Mini-Mitter Co. Inc. The role of actiwatch in the study of sleep and circadian rhythms. 2004.
16. Irwin M, Haydan Artin K, Oxman MN. Screening for depression in the older adult: Criterion validity of the 10-Item Center for Epidemiological Studies Depression Scale (CES-D). *Arch Intern Med* 1999;159(15):1701-4.
17. Ancoli-Israel S. Sleep and aging: prevalence of disturbed sleep and treatment considerations in older adults. *J Clin Psychiatry* 2005;66(suppl 9):24-30.
18. Neubauer DN. Sleep problems in the elderly. *Am Fam Physician* 1999;59(9):11
19. Foley DJ, Monjan AA, Brown SL. Sleep complaints among elderly persons: an epidemiologic study of three communities. *Sleep* 1995;18:425 - 32.
20. Jacobs JM, Cohen A, Hammerman-Rozenberg R, Stessman J. Global sleep satisfaction of older people: The Jerusalem Cohort Study. *Journal of the American Geriatrics Society* 2006;54(2):325-9.
21. Piper BF, Dibble SL, Dodd MJ, Weiss MC, Slaughter RE, Paul SM. The revised Piper Fatigue Scale: Psychometric evaluation in women with breast cancer. *ONF* 1998;25(4):677 - 84.
22. Liao S, Ferrell B. Fatigue in an older population. *JAGS* 2000;48(8):426-30.
23. Cauley JA, Fullman RL, Stone KL, et al. Factors associated with the lumbar spine and proximal femur bone mineral density in older men. *Osteoporosis Int* 2005;16:1525-37.
24. Carskadon MA, Brown ED, Dement WC. Sleep fragmentation in the elderly: Relationship to daytime sleep tendency. *Neurobiology of Aging* 1982;3(4):321-7.
25. Stepanski E, Lamphere J, Badia P, Zorick F, Roth T. Sleep fragmentation and daytime sleepiness. *Sleep* 1984;7(1):18-25.
26. Rosenthal L, Roehrs T, Sicklesteel J, Zorick F, Wittig R, Roth T. Periodic movements during sleep, sleep fragmentation, and sleep-wake complaints. *Sleep* 1984;7(4):326-30.
27. Asplund R. Sleep disorders in the elderly. *Drugs and Aging* 1999;14(2):91-103.
28. Elbaz M, Roue GM, Lofaso F, Quera Salva MA. Utility of actigraphy in the diagnosis of obstructive sleep apnea. *Sleep* 2002;25(5):525-9.

29. Aubert-Tulkens G, Culee C, Harmant-Van Rijckevorsel K, Rodenstein DO. Ambulatory evaluation of sleep disturbance and therapeutic effects in sleep apnea syndrome by wrist activity monitoring. *Am Rev Respir Dis* 1987;136:851 - 6.
30. Asplund R. Daytime sleepiness and napping amongst the elderly in relation to somatic health and medical treatment. *J Internal Medicine* 1996;239:261-7.
31. Ayas NT, White DP, Al-Delaimy WK, et al. A prospective study of self-reported sleep duration and incident diabetes in women. *Diabetes Care* February 2003;26(2):380-4.
32. Yaggi HK, Araujo AB, McKlinlay JB. Sleep duration as a risk factor for the development of type 2 diabetes. *Diabetes Care* 2006;29(3):657 - 61.
33. Gottlieb DJ, Punjabi NM, Newman AB, et al. Association of sleep time with diabetes mellitus and impaired glucose tolerance. *Arch Intern Med* 2005;In - press (accepted 2004).
34. Bixler EO, Vgontzas AN, Lin H-M, Calhoun SL V-BA, Kales A. Excessive daytime sleepiness in a general population sample: the role of sleep apnea, age, obesity, diabetes and depression. *J Clin Endocrinol Metab* 2005;jc.2005-0035.
35. Bursztyn M, Ginsberg G, Hammerman-Rozenberg R. The siesta in the elderly: risk factor for mortality? *Arch Intern Med* 1999;159(1582-1586).
36. Campos H, Siles X. Siesta and the risk of coronary heart disease: results from a population-based, case-control study in Costa Rica. *Int J Epidemiol* 2000;29(3):429-37.
37. Takahashi M. The role of prescribed napping in sleep medicine. *Sleep Medicine* 2003;7(3):227 - 35.
38. Tamaki M, Shirota A, Tanaka H, Hayashi M, Hori T. Aging and sleep. Effects of a daytime nap in the aged. *Psychiatry and Clinical Neurosciences* 1999;53:273 - 5.
39. Hays JC, Blazer DG, Foley DJ. Risk of napping: Excessive daytime sleepiness and mortality in an older community population. *J Am Geriatric Soc* 1996;44:693 - 8.
40. Morin CM, Gramling SE. Sleep patterns and aging: comparison of older adults with and without insomnia complaints. *Psych Aging* 1989;4(3):290-4.
41. Gilberg M KG, Axelsson J, and Akerstedt T. The effects of a short daytime nap after restricted night sleep. *Sleep* 1996;19(7):570 - 5.

**Table 4-1 Characteristics of Health Aging and Body Composition sleep study participants by napping status (N=236).**

	No Recorded Naps (n=57)	Recorded Naps (n=178)
	mean (SD)	mean (SD)
Age (yr)	80.2 (2.8)	80.1 (2.9)
BMI (kg/m <sup>2</sup> )	28.0 (5.2)	28.1 (4.2)
Self report number of naps/week	1.6 (2.2)	5.3 (4.7)***
Self report hours of sleep/night	6.9 (1.4)	6.7 (1.4)
Nap duration (hrs) <sup>1</sup>	0	0.6 (0.5)
Nighttime sleep (hrs) <sup>1</sup>	7.6 (1.0)	7.5 (1.1)
Movement & Fragmentation Index <sup>1</sup>	31.0 (11.4)	37.7 (15.2)**
Wake after sleep onset (hrs) <sup>1</sup>	0.9 (1.0)	1.0 (0.5)*
Number of times up at night (sleep diary)	1.7 (1.2)	1.8 (0.9)
Mental Status (Teng 3 MS)	93.7 (5.2)	92.8 (5.9)
Depression (CES D10)	4.5 (4.0)	4.6 (3.7)
Fatigue (scale 0-50) <sup>2</sup>	15.0 (7.9)	18.2 (7.6)**
	<b>n (%) yes</b>	<b>n (%) yes</b>
Gender – Male (n=112)	26 (45.6)	86 (48.3)
- Female (n=124)	31 (54.4)	92 (51.7)
Race – White (n=166)	42 (73.7)	124 (69.7)
- Black (n=70)	15 (26.3)	54 (30.3)
Trouble falling asleep <sup>3</sup>	23 (40.4)	74 (41.6)
Wake up during the night <sup>3</sup>	23 (40.4)	96 (54.2)
Wake up too early <sup>3</sup>	24 (42.1)	77 (43.5)
Use medicine to help sleep <sup>3</sup>	8 (14.0)	17 (9.6)
Daytime sleepiness <sup>3</sup>	25 (43.9)	87 (48.8)
Movement & Fragmentation Index (Tertiles)		
< 28	27 (47.4)	51 (28.7)
≥ 28 - <40	19 (33.3)	60 (33.7)
≥ 40	11 (19.3)	67 (37.6)*
Alcoholic beverages (any)	33 (57.9)	84 (47.5)
History of falling in past year	17 (29.8)	53 (29.8)
Pain past 30 days	31 (54.4)	127 (71.4)***
Respiratory symptoms <sup>4</sup>	16 (28.1)	81 (46.0)**
Cardiovascular disease <sup>5</sup>	5 (8.8)	28 (15.7)
Diabetes (self report)	2 (3.9)	30 (18.8)**

**Table 4.1 cont.**

<sup>1</sup> Measured with actigraphy. All values represent average duration for the period the participant wore the watch.

<sup>2</sup> Actual range was 0 – 38. Population median = 18.

<sup>3</sup> Self report: less than one time per month, or more than one time per month.

<sup>4</sup> Self-report of any of the following: dyspnea on exertion, need to stop for breath when walking, history of asthma, chronic obstructive pulmonary disease, emphysema, or bronchitis.

<sup>5</sup> History of myocardial infarction, angina, stroke, transient ischemic attack, or congestive heart failure at the Health ABC year six visit (average of two years earlier).

\*p =0.05

\*\*p ≤ 0.01

\*\*\*p≤0.001

**Table 4-2 Odds of taking a daytime nap in the Health Aging and Body Composition Sleep Study (n = 235)<sup>1</sup>**

	Unit/Referent	Unadjusted		Adjusted – Sleep <sup>2</sup>		Fully Adjusted Model <sup>3</sup>	
		OR	(CI)	OR	CI	OR	CI
Race	White	1.2	(0.6, 2.4)	1.1	(0.6, 2.2)	1.1	(0.4, 2.7)
Gender	Male	0.9	(0.5, 1.6)	1.0	(0.6, 2.0)	1.1	(0.5, 2.4)
Night time sleep duration <sup>4</sup>	Hour	0.9	(0.7, 1.2)	0.9	(0.7, 1.2)	0.8	(0.5, 1.1)
Movement and fragmentation (tertile) <sup>4</sup>	< 28						
	28 – 40	1.7	(0.8, 3.4)	1.8	(0.9, 3.5)	1.9	(0.8, 4.5)
	≥ 40	3.2	(1.5, 7.1)	3.3	(1.5,7.3)	2.8	(1.1, 7.1)
Depression score	3.8	1.0	(0.8, 1.4)	1.0	(0.7, 1.2)	0.7	(0.5, 1.1)
Pain past 30 days (n=128)	None	2.1	(1.1, 3.9)	2.1	(1.1, 4.0)	2.3	(1.1, 4.8)
Respiratory symptoms (n = 98)	None	2.2	(1.1, 4.2)	2.3	(1.1, 4.8)	2.4	(1.1, 5.3)
Diabetes (n=32)	None	5.8	(1.3, 25.0)	5.1	(1.1, 22.7)	5.9	(1.2, 28.8)
Fatigue score	7.7	1.5	(1.1, 2.1)	1.5	(1.1, 2.1)	1.6	(1.0, 2.5)

<sup>1</sup> Only variables with a significance level of  $p \leq 0.10$  in univariate, logistic or regression models are shown here.

<sup>2</sup> Adjusted for age, race, gender, total night time sleep (hrs), and tertile of movement and fragmentation index, self reported use of sleep medications, self-report of pain in the last 30 days, cardiovascular disease at the Health ABC year six visit, self-reported respiratory symptoms, self-reported diabetes, depression score, mental status, and fatigue. Units for continuous variables approximate 1 standard deviation; for dichotomous variables, the referent group does not have the characteristic.

<sup>4</sup> Measured with Mini Mitter® AW-16 and Actiware ® v5 software

**Table 4-3 Regression models showing the temporal association of measured nighttime sleep duration and fragmentation with daytime sleep (nap) duration in Health ABC sleep study participants who recorded naps (n=178)**

<b>Independent Variable</b>	<b>Percentage difference in nap duration per unit (95% CI) (First randomly selected night-day interval)</b>	<b>Percentage difference in nap duration per unit (95% CI) (Second randomly selected night-day interval)</b>
Previous night sleep duration (hr)	-3.7 (-10.62, 3.48)	-2.3 (-9.5, 4.9)
Previous night movement and fragmentation <sup>1</sup>	-49.6 (-173.8, 74.6)	-38.8 (-153.4, 75.9)

<sup>1</sup> Standardized per unit of 1 standard deviation =14.6.



**Table 4-4 Multivariable associates of nap duration in the Health ABC sleep study participants who reported naps (n = 159).**

Variable	Unit/ referent	Percentage difference in nap duration per unit (95% CI) (unadjusted)		Percentage difference in nap duration per unit (95% CI) fully adjusted model <sup>1</sup>	
Gender	Male	-3.3	(-19.5, 27.3)	-2.7	(-22.7, 36.8)
Race	White	18.3	(0.4, 76.7)	25.9	(4.3, 100.5)
Previous night sleep duration (hrs)	Hour	-3.7	(-7.5, 0.2)	-2.4	(-6.5, 3.8)
Previous night - Movement and fragmentation	14.63	-28.5	(-97.2, 40.2)	-8.5	(-86.0, 69.1)
Depression score	3.76	20.9	(-11.0, 52.8)	37.3	(-1.9, 76.4)
Mental State	5.8	-23.8	(-70.0, 22.3)	-1.7	(-53.7, 50.4)
Bodily pain last 30 days	None	-14.2	(-31.9, 7.4)	-22.4	(-42.8, -4.3)
Respiratory symptoms	None	-9.1	(-25.6, 15.5)	-6.3	(-24.9, 30.0)
Self reported diabetes	None	34.1	(11.9, 119)	34.9	(11.0, 124.5)
Fatigue	7.7	24.9	(-39.8, 89.6)	24.0	(-53.2, 103.2)

<sup>1</sup> Fully adjusted mixed model included nighttime sleep duration (hours from actigraphy), movement and fragmentation index (nightly actigraphy), age (years), race, gender, BMI (kg/m<sup>2</sup>), depression, mental status, bodily pain in the last 30 days (yes/no), cardiovascular disease at the year 6 visit (yes/no), self-reported respiratory symptoms (yes/no), self-reported diabetes (yes/no), self reported number of times up each night, fatigue score. Units for continuous variables approximate 1 standard deviation; for dichotomous variables, the referent group does not have the characteristic.

**Table 4-5 Multivariable associates of previous night sleep and nap duration on nap night sleep duration using mixed model analysis in Health ABC sleep study participants who reported daytime nap (n = 159) <sup>1</sup>**

<b>Variable</b>	<b>Unit/ Referent</b>	<b>Percentage difference in nighttime sleep duration<sup>1</sup> per unit (95% CI) (unadjusted)</b>		<b>Percentage difference in nighttime sleep duration<sup>1</sup> per unit (95% CI) adjusted for multiple variables<sup>2</sup></b>	
Race	White	-4.4	(-9.3, 0.5)	-7.4	(-13.4, -1.4)
Gender	Male	-1.9	(-6.4, 2.7)	-1.3	(-6.8, 4.3)
Previous night sleep duration	Hour	-0.03	(-0.7, 0.7)	0.5	(-1.1, 2.0)
Previous night - Movement and fragmentation	14.6	-4.5	(-17.4, 8.4)	-8.4	(-28.4, 11.6)
Same day sleep (nap) duration	Hour	-2.5	(-4.1, -1.0)	-7.5	(-13.0, -2.0)
Previous night sleep duration X Nap duration	Hour	0.8	(0.1, 1.5)	0.8	(0.1, 1.5)
Depression score	3.8	0.9	(-7.9, 9.6)	-1.2	(-12.0, 9.6)
Mental State	5.8	-9.2	(-21.9, 3.4)	-10.0	(-24.5, 4.4)
Bodily pain last 30 days	none	-2.0	(-7.0, 3.0)	-1.3	(-7.0, 4.4)
Respiratory symptoms	none	5.4	(0.9, 9.9)	5.5	(0.4, 10.6)
Self reported diabetes	none	-1.8	(-8.0, 4.3)	-1.1	(-7.7, 5.6)
Fatigue	7.7	1.0	(-17.0, 19.0)	-0.3	(-21.4, 21.9)

<sup>1</sup> Nighttime sleep duration on the night of the nap.

<sup>2</sup> Fully adjusted mixed model included nighttime sleep (hours from actigraphy), movement and fragmentation index (from nightly actigraphy), age (years), race, gender, BMI (kg/m<sup>2</sup>), depression, mental status, bodily pain in the last 30 days (yes/no), cardiovascular disease at the year 6 visit (yes/no), self-reported respiratory symptoms (yes/no), self-reported diabetes (yes/no), times up each night, fatigue score.

Units for continuous variables approximate 1 standard deviation; for dichotomous variables, the referent group does not have the characteristic.

**Table 4-6 Predictors of average nap duration (hour) in Health ABC sleep study participants who reported a daytime nap (n = 178) <sup>1</sup>**

Variable	Unit/Referent	Percentage difference in average nap duration per unit (95% CI) (unadjusted)		Percentage difference in average nap duration per unit (95% CI) adjusted for multiple variables <sup>1</sup>	
Race	White	-0.7	(-28.3, 30.0)	10.9	(-22.7, 44.5)
Gender	Male	-20.8	(-4.0, 4.4)	-14.4	(-46.1, 17.4)
Average nighttime sleep duration	Hour	-1.6	(-12.8, 9.5)	-4.1	(-16.6, 8.4)
Movement and fragmentation	14.6	57.1	(-121.7, 235.8)	57.3	(-152.0, 266.5)
Depression score	3.8	8.3	(-40.8, 57.3)	-12.3	(-72.4, 47.8)
Mental State	5.8	-20.4	(-91.8, 51.1)	-22.5	(-106.8, 61.8)
Bodily pain last 30 days	none	-30.4	(-58.1, -2.6)	-40.5	(-73.1, -8.0)
Respiratory symptoms	none	-15.7	(-41.3, 10.0)	-8.5	(-37.7, 20.6)
Self reported diabetes	none	40.7	(6.3, 75.1)	39.7	(2.4, 77.1)
Fatigue	7.7	95.1	(-5.0, 195.4)	140.9	(17.3, 262.2)

<sup>1</sup> Full linear regression model included nighttime sleep duration (hours from actigraphy), movement and fragmentation index (from actigraphy), age (years), race, gender, BMI (kg/m<sup>2</sup>), depression, mental status, bodily pain in the last 30 days (yes/no), cardiovascular disease at the year 6 visit (yes/no), self-reported respiratory symptoms (yes/no), self-reported diabetes (yes/no), times up each night, fatigue score. Units for continuous variables approximate 1 standard deviation; for dichotomous variables, the referent group does not have the characteristics.

## **5.0 GENERAL DISCUSSION**

### **5.1 SUMMARY OF FINDINGS**

Older adults experience multiple changes throughout all dimensions of sleep. Changes occur in sleep quality, duration, continuity, architecture, rhythm, and homeostasis<sup>1-4</sup>. These changes occur independently and concurrent with medical and/or psycho-social comorbidities<sup>5-8</sup>. Through the use of self-report data, interviewer administered questionnaires, and wrist actigraphy we were able to examine associations between sleep dimensions, daytime function, fatigue, and daytime sleep in older adults.

Specifically, this dissertation investigated the association of disturbed nighttime sleep with daytime function, daytime fatigue, and daytime sleep (nap) in two large ongoing population studies of community dwelling black and white men and women with an average age  $\geq 80$  years. Study participants were from the Study of Fractures (SOF) and the Health Aging and Body Composition Study (Health ABC).

In the SOF cohort, actigraphy measured nighttime and daytime sleep in older women was associated with poorer daytime function. In the Health ABC cohort, self-reported disturbed nighttime sleep was associated with higher fatigue in older men and women. In the Health ABC ancillary sleep study, actigraphy measured fragmented sleep was associated with higher odds for daytime napping. In addition, both Health ABC studies showed strong associations between comorbid health conditions and fatigue and napping.

The above studies contribute valuable information on sleep duration, sleep continuity, daytime sleep, and fatigue in older adults and support an association between nighttime sleep and knowledge. The association between poorer nighttime sleep and poorer daytime function was consistent with previous research showing poorer nighttime sleep to be associated with poorer performance, in these cases primarily based on standardized laboratory tasks<sup>9-14</sup>. The association

between disturbed nighttime sleep and daytime fatigue supported the study hypothesis, and the study proposed a global concept of fatigue to include a component of daytime sleepiness. The association between fragmented sleep and daytime napping is consistent with the theory of homeostatic sleep Process S<sup>15, 16</sup>. Finally, the association of comorbid health conditions as important confounders and/or mediators in the relationship between sleep and function, sleep and fatigue, and between nighttime and daytime sleep was substantiated and found to be consistent with previously reported associations.

A U shaped distribution was found, in the SOF cohort, for total nighttime sleep and measures of physical function with women at both extremes functioning more poorly than women who averaged 6-7.5 hours of sleep. In the Health ABC cohort men and women with <7 or >7 hours of self-reported sleep had higher average fatigue scores. Adjustment for multiple confounders explained only a portion of the relationship between total nighttime sleep, physical function, and fatigue. These U shaped distributions are similar to patterns reported for the association of sleep time and self reports of health problems<sup>4, 17</sup>. U shaped sleep distributions have also been associated with higher risk of morbidity and mortality<sup>18-22</sup> with individuals sleeping 6 to 7 hours per night having the lowest mortality risk<sup>18, 20, 23-26</sup>. Short sleep duration has been associated with an increased risk of chronic health conditions including diabetes and impaired glucose tolerance<sup>19, 27-30</sup>, heart disease<sup>24, 31</sup>, and hypertension<sup>32</sup>. Studies of imposed sleep restriction have shown predication toward higher mortality, as well as contributing to risk factors for several diseases such as diabetes, impaired glucose tolerance, and hypertension<sup>25, 27, 33</sup>. Long sleep (>9 hours) has been associated with higher risk of diabetes<sup>24, 29, 30</sup> and coronary heart disease in women<sup>24</sup>. The SOF women with total nighttime sleep between 6–7.5 hours appeared to function better and the Health ABC men and women who reported 7 hours of sleep had lower fatigue scores. These suggest that regulating total nighttime sleep may play an important role in minimizing functional decline.

Maintenance of sleep, a major complaint of older adults<sup>8</sup>, was the sleep parameter most strongly associated with poorer daytime function, fatigue, and daytime sleep (nap) in this study. This research found poorer daytime function, fatigue, and napping associated with higher levels of wake after sleep onset in the SOF women; with self reported waking up during the night in the Health ABC cohort; and with movement and fragmentation in the Health ABC sleep cohort. These findings were consistent with previous literature. Higher levels of nighttime fragmentation

occur with aging<sup>1, 3, 34-36</sup> and are associated with: poorer mood and performance on cognition and vigilance tests<sup>12, 37, 38</sup>, chronic illness<sup>3, 35, 39-42</sup>, higher blood pressure, higher cortisol levels, higher lipid levels<sup>33, 41</sup>, inflammatory cytokines<sup>43</sup>, and can result in daytime sleepiness<sup>44, 45</sup>. This research extended this knowledge to include physical function, fatigue, and napping.

To determine fragmentation this research used wrist-actigraph measures of wake after sleep onset (SOF) and movement and fragmentation (Health ABC sleep study), and self-reported waking up during the night (Health ABC). Factors known to cause nighttime fragmentation, not measured by this research, include measures of sleep disordered breathing (or obstructive sleep apnea) and periodic leg movements (or restless leg syndrome)<sup>3, 37, 38, 46</sup>.

Sleep disordered breathing, defined by the number of apnea (complete cessation of respiration) and hypopnea (partial respirations) episodes per hour of sleep is prevalent in older adults<sup>3, 47-50</sup>. Based on an apnea-hypopnea index (AHI)  $\geq 10-15$  (referent ranges: AHI 5-15 = mild; AHI 15-30 = moderate<sup>51</sup>), sleep disordered breathing has been estimated to range from 45-62% in adults 60 years or older<sup>48, 52</sup>. Large population studies, using an AHI $\geq 15$ , in adults 60 years or older, showed the prevalence of sleep disordered breathing was approximately 20% the Sleep Heart Health Study (SHHS)<sup>53</sup>; and 32% (women) and 42% (men) in the Cleveland Family Study<sup>54</sup>. For adults 71-100 years, in the Vitoria-Gasteiz, Spain Cohort, the prevalence was 49% was women and 57% for men<sup>55</sup>. In San Diego County, CA 56% of the women and 70% of the men in adults aged 65-95 years with an AHI $\geq 10$  were found to have sleep disordered breathing<sup>48</sup>. The high prevalence of sleep disordered breathing in older adults found in these studies suggests that sleep disordered breathing is one potential contributing factor to the sleep fragmentation exhibited in the Health ABC sleep study participants. Future studies measuring disrupted sleep should also include measurements of sleep disordered breathing.

Another major cause of fragmented sleep in older adults is periodic limb movement and restless leg syndrome which have an average prevalence of 45% and estimated range of 25-58%<sup>52, 56</sup>. Although not measured in this study, the possibility these conditions contributed to sleep fragmentation in the Health ABC sleep study participants can not be discounted. Similar to sleep disordered breathing, future studies measuring disrupted sleep should also include measurements of periodic limb movements and restless leg syndrome.

This study's finding that sleep fragmentation was strongly associated with taking a daytime nap was not surprising, as sleep fragmentation has been shown to be associated with

daytime sleepiness<sup>37, 44, 45, 57</sup>. The association between nighttime sleep duration, amount of fragmentation, and duration of the next days nap was not significant when examined temporally. However, when the data was averaged over the week period, the direction of association between the nighttime sleep parameters and daytime nap were in the direction expected (shorter duration of nighttime sleep, or higher levels of fragmentation were associated with longer nap duration).

Potential reasons for the lack of association between nighttime sleep behaviors and duration of the next days nap may be associated with the study design. The mixed model analysis may have lacked sufficient power; not all naps may have been captured; or the study duration may have been too short. Future studies should be performed to address these insufficiencies either by increasing sample size, or extending the time the wrist actigraph is worn. Additionally, the study did not evaluate periods of daytime immobility, or quiet rest periods, which conceptually might play an important role in the overall sleep-wake process. The role of these immobile periods in the temporal sleep wake cycle could be evaluated by additional analyses of the existing Health ABC sleep study actograms, or as a basis for a future research study.

The lack of a temporal association may represent a more complex relationship between sleep homeostasis and the circadian clock over a longer period of time than accounted for in this study. In this case not only would the timing of sleep and wake be an issue, but the course of daytime alertness would be accounted for by the interaction of the homeostatic and circadian process<sup>58</sup>. Future delineation of this association would best be determined in a sleep laboratory environment.

The association of a daytime nap, and/or nap duration, with nap night sleep is still uncertain. One laboratory study has reported no effect<sup>9</sup>, while another found reductions in nap night sleep<sup>59</sup>. This study's data, showing a slight reduction in nap night sleep, is consistent with the latter. Future research using longer time intervals and/or more participants would elucidate this association.

The association of self-reported disturbed nighttime sleep with fatigue was confirmed in the Health ABC cohort. This dissertation focused on fatigue as a daytime symptom, and potential consequence, of poor sleep and poor health after noting the high correlation of daytime sleepiness (participant self report of napping or participant response to the question how often do you feel excessively sleepy during the day) with fatigue. Fatigue, a multi-dimensional, non-specific syndrome<sup>60-65</sup> is common in older adults, while daytime sleepiness, which is also

common, is the specific behavior denoting the propensity to fall asleep during the day,<sup>66, 67</sup>. A review of the literature shows the incongruent terminology associated with these concepts. The final study results suggested the concept of fatigue should include an aspect of sleepiness and supported a picture of global fatigue with fatigue as one conceptualization of multiple daytime symptoms.

In general fatigue has been examined in relationship with specific biological (i.e. cancer, rheumatoid arthritis, chronic fatigue syndrome) or psychiatric diseases<sup>60, 63, 64, 68-77</sup> and studies have not been able to show causality between fatigue and disease, or disease and fatigue, even after controlling for multiple confounders. A biological association between fatigue and nighttime sleep behaviors is plausible. In the Health ABC cohort, high levels of fatigue were associated with self-reported waking up during the night. Multiple nighttime awakening is associated with sleep apnea syndrome. Further, fatigue has been associated with sleep apnea<sup>62, 78-82</sup>. Although biologically plausible that the disturbed nighttime sleep associated with fatigue, in the Health ABC cohort, is the result of sleep apnea, this most likely is only one portion of the syndromes' multi-dimensional aspect. Potentially treatment of sleep apnea syndrome would reduce fatigue in these older adults.

The association between nighttime sleep parameters, daytime sleep, and function with medical comorbidities is complex, and was noted in this research. This association involves multiple biologic pathways, as well as interaction with genetics and environment. Further, the associations not only overlap<sup>83</sup>, but most likely are bidirectional where comorbidity can potentiate disturbed sleep or sleep complaints, and disturbed sleep can potentiate higher risks for comorbidity. For example, chronic health conditions can initiate an immune system response that may increase inflammatory cytokines subsequently making people sleepy. Conversely, sleep loss as a stressor can trigger activation of the early immune response, such as cytokines, that are also involved in host-disease response<sup>27, 84</sup>.

This study found self-report of diabetes associated with higher odds of taking a nap, as well as with longer nap duration. The hypothesized pathway between diabetes and disturbed sleep is complex, and most likely bidirectional. Untreated diabetes has been postulated as a cause of daytime somnolence<sup>85</sup> and has been associated with higher odds for daytime sleepiness<sup>6, 86</sup>. Evidence also suggests disturbed breathing during sleep, as well as chronic sleep loss, is associated with the pathogenesis of altered glucose metabolism<sup>27, 29, 87, 88</sup>. Future studies



incorporating measurements of sleep and nap with measurements of biomarkers and insulin resistance may provide evidence to further explain the specific relationship between sleep, nap, and diabetes.

Self-reported respiratory symptoms were associated with higher fatigue and higher odds of taking a nap in the Health ABC cohort, consistent with reports in the literature<sup>8, 52, 89-92</sup>. Respiratory symptoms such as coughing and wheezing also display a bidirectional association with sleep apnea syndrome being associated with both the cause<sup>93, 94</sup> and the effect<sup>93</sup>. It has been postulated that sleep apnea is a heterogeneous disorder with multiple pathogenic causes contributing to upper airway collapse during sleep<sup>95</sup>. Future refinement of the relationship between fatigue and daytime respiratory events, napping and daytime respiratory events, as well as the role of sleep apnea syndrome in this relationship specifically targeted towards older adults is needed.

In general, older adults have more chronic health conditions. Recent studies have shown associations of inflammatory cytokines with both disturbed sleep and many disease processes, and may prove to be a common link. In addition to the associations discussed in the proceeding sections, inflammatory cytokines have been associated with short or long sleep duration, sleep apnea<sup>79, 96, 97</sup>, fatigue<sup>79, 84, 98, 99</sup>, daytime sleepiness<sup>79</sup>, and acute and chronic diseases<sup>97, 100</sup><sup>74</sup>. Future research where specific markers of inflammation are collected, simultaneous with measurements of sleep and function, would help elucidate this relationship.

This dissertation research was limited by the cross-sectional design that precluded determination of causality. It needs to be recognized that while the cross-sectional investigation of the association of sleep and poorer function might tend to infer that poorer function and daytime fatigue and sleepiness are results of poor nighttime sleep, the other direction of association must be considered and future research supported bi-directionally.

This research was performed in older adults still residing independently in the community; therefore care must be taken to extrapolate these findings to other populations. Sleep was measured with self-report, diary, and actigraphy. Therefore, measurements only obtainable through PSG, such as EEG, EMG, ECG, and respiratory monitors, as well as measurements of periodic leg movement, or restless leg syndrome, were unobtainable.

## 5.2 PUBLIC HEALTH SIGNIFICANCE

Disturbed sleep and daytime sleepiness are common complaints resulting in daytime napping, reduced performance, accidents, medical comorbidities, and poorer quality of life <sup>101, 102</sup>. Prevalence rates of poor sleep in older adults range from 13–57% <sup>7, 91, 92, 103, 104</sup>. Disturbed sleep and its associated sequelae represent major public health problems and have a significant impact on older adults.

The financial burden related to poor sleep is considerable with estimated direct and indirect costs ranging from approximately \$13.9 billion to over \$30 billion dollars (1995 dollars) <sup>105-108</sup> to tens of billions annually in 2005 <sup>109</sup>. Additional associated costs range from \$50 billion <sup>110</sup> to as high as \$100 billion annually when lost productivity, medical expenses, sick leave, property, and environmental damages are included <sup>101, 108</sup>.

This dissertation research has substantiated the relationship of poorer daytime function and fatigue with inefficient sleep duration and nighttime sleep fragmentation. This research has highlighted the association of disturbed sleep with medical comorbidity; especially diabetes, respiratory symptoms, and pain with daytime napping. This additional knowledge may help with future identification of the causal pathway between disturbed sleep and daytime function. This in turn may promote additional research in the area and open the field towards potential therapeutic or targeted interventions.

As the population ages, recognizing the association between sleep and subsequent daytime sequelae may help to reduce subsequent comorbidities and improve the quality of life in community-dwelling older individuals. Overall, these findings provide epidemiological evidence for an association between poor nighttime sleep and daytime napping, fatigue, and poorer daytime function in older adults.

## 5.3 FUTURE RESEARCH

At this time there is minimal empirical data to guide older adults, their caregivers, and physicians on how to optimize nighttime sleep, minimize daytime fatigue, and to suggest whether or not napping should be avoided or recommended. While the association of comorbid medical

conditions with disturbed sleep has been shown, there is minimal evidence validating the role of disease management in improving nighttime sleep, daytime fatigue, daytime napping, and subsequent morbidity and mortality. Future research is needed to confirm these associations and clarify associated risk factors.

Additional longitudinal cohort studies are needed to confirm this study's findings that disturbed nighttime sleep was associated with poorer daytime function, fatigue, and napping in other cohorts of older adults; and to confirm the associated risk factors. As the associations found in this study are based on cross-sectional data, further longitudinal analyses may elucidate these associations. Further, clarification of associated risk factors might identify potential treatment options.

Sleep fragmentation was found to be associated with poorer daytime function in all three dissertation papers. Interventions to reduce nighttime fragmentation and subsequently improve nighttime sleep, and improve daytime function are needed specifically targeted at older adults. Potential interventions could include positive airway pressure for treatment of sleep apnea, or sleep disordered breathing; medications for periodic limb movements; improvement of sleep hygiene; or treatment of the underlying disease processes.

The associations found between self-reported comorbid diseases, particularly self-reported diabetes and self-reported respiratory disease and daytime sleep indicates the need for future research to confirm the disease status in this population, as well as in other populations, to validate the disease-nap association.

A cross-sectional study could be performed in the Health ABC sleep study cohort to elucidate the association of poor nighttime sleep, daytime sleep and fatigue with self-reported respiratory conditions. Examination of existing pulmonary function test data can be assessed to determine if the self-reported respiratory conditions are associated with obstructive or restrictive pulmonary disease. Additional analyses could subsequently address the association between obstructive, or restrictive, respiratory disease with fragmented nighttime, daytime sleep and fatigue. If associations are found future research could evaluate interventions targeted at the cause of the reduced function as a potential avenue to improve nighttime sleep.

Another cross-sectional study could be performed to corroborate the association between actually reporting a nap during the day, nap duration, and diabetes. Research where serum

samples are collected and medication use is verified to confirm disease status, simultaneous with objective measures of sleep would help confirm and refine this association.

Future research on the association of comorbid health conditions with nighttime sleep behaviors, fatigue, and daytime napping is warranted. The role of disease management in improving nighttime sleep, fatigue, and daytime sleep is not clear. A case-control study could be performed to test the hypothesis that tight disease control will improve night-time sleep, minimize daytime fatigue and/or napping is needed. This study would provide information on whether or not tight disease control would facilitate better nighttime sleep and daytime function. Comorbidities, amenable to control that have been associated with sleep, napping, and fatigue such as diabetes, cardio-pulmonary diseases, hypertension, and pain could be addressed. The research would establish guidelines as to what level of disease management is optimal.

Methods exist to perform studies pertaining to nighttime sleep over an extended period of time in community based settings using wrist actigraphy and/or PSG. However, improvement in methods to measure both fatigue and daytime sleep in community based settings is needed before the impact of these parameters, in older adults, can be fully determined. Fatigue scales validated in other populations exist and would be suitable to measure fatigue in older adults. However, these should be formally tested and validated in the older adult population. Research to refinement and validate wrist actigraphy algorithms to quantify daytime sleep, versus periods of inactivity, would provide more accurate estimates of the impact of daytime sleep independent of inactivity in older adults.

## **5.4 CONCLUSION**

Sleep behavior and daytime function change with aging. Poor nighttime sleep has been associated with poorer daytime performance, fatigue, and increased daytime napping in older adults. A cross-sectional association of poor nighttime sleep, measured with wrist actigraphy, and poorer gait speed, time to complete five chair stands, grip strength and IADL impairment was found. Fragmented nighttime sleep, measured by self report and actigraphy, was found to be associated with higher odds for napping, poorer daytime function, and a higher fatigue score.

The role of comorbid health conditions, in particular self-reported diabetes and respiratory symptoms, with daytime fatigue and napping was observed.

Factors associated with nighttime fragmentation in older adults have been identified in other studies, and methods to reduce this fragmentation need to be tested specifically in older adults. Future studies are needed to confirm the longitudinal association between poor sleep behaviors, fatigue and daytime function (or disability); to determine the association of poor sleep behaviors and morbidity and mortality over time; to refine the association of comorbid disease with nighttime and daytime sleep; and to better validate methods to assess daytime napping and fatigue specifically in older adults. Mechanisms to improve sleep behaviors specifically targeted to older adults need to be identified, evaluated by clinical trial, and integrated into practice. Once these associations have been established the true public health impact can be determined. Intuitively, improvement in sleep behaviors may help improve performance, reduce daytime napping and reduce daytime fatigue.

## 5.5 REFERENCES

1. Ohayon MM CM, Guilleminault C, Vitiello MV. Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: developing normative sleep values across the human lifespan. *Sleep* 2004;27(7):1255-73.
2. Ancoli-Israel S, Alessi C. Sleep and Aging. *Am J Geriatr Psychiatry* 2005;13(5):341-3.
3. Bliwise DL. Normal aging. In: Kryger MH, Roth T, Dement WC, eds. *Principles and Practice of Sleep Medicine*. Third Edition, ed: Saunders; 2005.
4. Ohayon MM VM. Normative sleep data, cognitive function and daily living activities in older adults in the community. *Sleep* 2005;28(8):981-9.
5. Ancoli-Israel S, Martin JL. Insomnia and daytime napping in older adults. *J Clin Sleep Med* 2006;accepted 4/17/06.
6. Foley DJ, Ancoli-Israel S, Britz P, Walsh JK. Sleep disturbances and chronic disease in older adults: Results of the 2003 National Sleep Foundation Sleep in America Survey. *Journal of Psychosomatic Research* 2004;56(5):497-502.
7. Foley DJ, Monjan AA, Brown SL, Simonsick EM, et al. Incidence and remission of insomnia among elderly adults: an epidemiologic study of 6,800 persons over three years. *Sleep* 1999;22((suppl 2)):5366-72.
8. Foley DJ, Monjan AA, Brown SL. Sleep complaints among elderly persons: an epidemiologic study of three communities. *Sleep* 1995;18:425 - 32.
9. Campbell SS, Murphy PJ, Stauble TN. Effects of a nap on nighttime sleep and waking function in older subjects. *J Am Geriatr Soc* 2005;53(1):48-53.
10. Hofer-Tinguely G, Achermann P, Landolt H-P, et al. Sleep inertia: performance changes after sleep, rest and active waking. *Cognitive Brain Research* 2005;22(3):323-31.
11. Pilcher JJ, Huffcutt AL. Effects of sleep deprivation on performance: A meta-analysis. *Sleep* 1996;19(4):318-26.
12. Bonnet MH. Effect of sleep disruption on sleep, performance, and mood. *Sleep* 1985;8(11-19).
13. Dinges DF, Pack F, Williams K, et al. Cumulative sleepiness, mood disturbance, and psychomotor vigilance performance decrements during a week of sleep restricted to 4-5 hours per night. *Sleep* 1997;20(4):267-77.

14. Schneider C, Fulda S SH. Daytime variation in performance and tiredness/sleepiness ratings in patients with insomnia, narcolepsy, sleep apnea and normal controls. *Journal of Sleep Research* 2004;13(4):373-83.
15. Borbely AA, Achermann P. Sleep homeostasis and models of sleep regulation. In: Kryger M, Roth T, Dement WC, eds. *Principles and Practices of Sleep Medicine*. Fourth ed. Philadelphia: Elsevier; 2005.
16. Knowles JB, Coulter M, Wahnou S, Reitz W, MacLean AW. Variation in process S: effects on sleep continuity and architecture. *Sleep* 1990;13(2):97-107.
17. National Sleep Foundation. 2003 Sleep in America Poll; 2003.
18. Tamakoshi A, Ohno Y. Self-reported sleep duration as a predictor of all-cause mortality: results from the JACC study, Japan. *Sleep* 2004;27(1):51-4.
19. Yaggi HK, Araujo AB, McKlinlay JB. Sleep duration as a risk factor for the development of type 2 diabetes. *Diabetes Care* 2006;29(3):657 - 61.
20. Kripke DF, Garfinkel L, Wingard DL, Klauber MR, Marler MR. Mortality associated with sleep duration and insomnia. *Archives Of General Psychiatry* 2002;59(2):131-6.
21. Newman AB, Spiekerman CF, Enright P, et al. Daytime sleepiness predicts mortality and cardiovascular disease in older adults. *JAGS* 2000;48:115-23.
22. Kripke DF, Simons RN, Garfunkel L, Hammond C. Short and long sleep and sleeping pills. *Arch Gen Psych* 1979;36:103-16.
23. Patel SR, Ayas NT, Malhotra MR, et al. A prospective study of sleep duration and mortality risk in women. *Sleep* 2004;27(3):440-4.
24. Ayas NT, White DP, Manson JE, et al. A prospective study of sleep duration and coronary heart disease in women. *Archive Internal Medicine* 2003;163:205-9.
25. Youngstedt SD, Kripke DF. Long sleep and mortality: rationale for sleep restriction. *Sleep Medicine Reviews* 2004;8:159-74.
26. Grandner MA, Kripke DF. Self-reported sleep complaints with long and short sleep: A nationally representative sample. *Psychosomatic Medicine* 2004;66:239-41.
27. Spiegel K, Knutson K, Leproult R, Tasali E, Cauter EV. Sleep loss: a novel risk factor for insulin resistance and Type 2 diabetes. *J Appl Physiol* 2005;99(5):2008-19.
28. Klar Yaggi H, Araujo AB, McKinlay JB. Sleep Duration as a Risk Factor for the Development of Type 2 Diabetes. . *Diabetes Care* 2006;29(3):657-61.
29. Gottlieb DJ, Punjabi NM, Newman AB, et al. Association of sleep time with diabetes mellitus and impaired glucose tolerance. *Arch Intern Med* 2005.

30. Ayas NT, White DP, Al-Delaimy WK, et al. A prospective study of self-reported sleep duration and incident diabetes in women. *Diabetes Care* February 2003;26(2):380-4.
31. Heslop P SG, Metcalfe C, Macleod J, Hart C,. Sleep duration and mortality: the effect of short or long sleep duration on cardiovascular and all-cause mortality in working men and women. *Sleep Medicine* 2002;3:305-14.
32. Gangwisch JE HS, Boden-Albala BB, Bujsis RM, Kreier F, Pickering TG, Rundle AG, Zammit GK, Malaspina D,. Short sleep duration as a risk factor for hypertension. Analyses of the first National Health and Nutrition Examination Survey. *Hypertension* 2006;47:833-9.
33. Ekstedt M, Akerstedt T, Soderstrom M. Microarousals during sleep are associated with increased levels of lipids, cortisol, and blood pressure. *Psychosomatic Medicine* 2004;66(6):925-31.
34. Bliwise DL. Sleep in normal aging and dementia. *Sleep* 1993;16(1):40-81.
35. Ancoli-Israel S, DF K. Now I lay me down to sleep: the problem of sleep fragmentation in elderly and demented residents of nursing homes. . *Bull Clin Neurosci* 1989;54:127 - 32.
36. Bliwise DL, Ansari FP, Straight L-B, Parker KP. Age changes in timing and 24 hour distribution of self-reported sleep. *Am J Geriatr Psych* 2005;12(12):1077 - 82.
37. Bonnet MH, Arand DL. Clinical effects of sleep fragmentation versus sleep deprivation. *Sleep Medicine Reviews* 2003;7(4):297-310.
38. Thomas RE. Sleep fragmentation and arousals from sleep-time scales, associations, and implications. *Clinical Neurophysiology* 2006;117:707-11.
39. Rotem AY SA, Krugliak P, Freidman B, Tal A, Tarasiuk A. Polysomnographic and actigraphic evidence of sleep fragmentation in patients with irritable bowel syndrome. *Sleep* 2003;26(6):747-52.
40. Brostrom A, Stromberg A, Dahlstrom U, Fridlund B. Sleep difficulties, daytime sleepiness, and health-related quality of life in patients with chronic heart failure. . *Journal of Cardiovascular Nursing* July/August 2004;19(4):234-242 2004.
41. Morrell MJ, Finn L, Kin H, Peppard PE, Badr MS, Young T. Sleep fragmentation, awake blood pressure, and sleep-disordered breathing in a population-based study. *Am J Respir Crit Care Med* 2000;162:2091-6.
42. Mahowald ML, Mahowald MW. Nighttime sleep and daytime functioning (sleepiness and fatigue) in well-defined chronic rheumatic diseases. *Sleep Medicine* 2000;1(3):179-93.



43. von Kanel R DJ, Ancoli-Israel S, Mills PJ, Patterson TL, McKibbin CL, Archuleta C, Grant I. Poor sleep is associated with higher plasma proinflammatory cytokine interleukin-6 and procoagulant marker fibrin d-dimer in older caregivers of people with Alzheimer's disease. *J Am Geriatr Soc* 2006;54:431-7.
44. Stepanski E, Lamphere J, Badia P, Zorick F, Roth T. Sleep fragmentation and daytime sleepiness. *Sleep* 1984;7(1):18-25.
45. Stepanski EJ. The effect of sleep fragmentation on daytime function. *Sleep* 2002;25(3):268-75.
46. Young T, Palta M, J D. The occurrence of sleep disordered breathing among middle-aged adults. *N Engl J Med* 1993;328:1230 - 5.
47. Bailes S, Baltzan M, Alapin I, Fichten CS, Libman E. Diagnostic indicators of sleep apnea in older women and men: A prospective study. *Journal of Psychosomatic Research* 2005;59(6):365-73.
48. Ancoli-Israel S, Kripke DF, MR K. Sleep disordered breathing in community-dwelling elderly. *Sleep* 1991;14:486 - 95.
49. Young T, Peppard PE, Gottlieb DJ. Epidemiology of Obstructive Sleep Apnea: A Population Health Perspective. *Am J Respir Crit Care Med* 2002;165(9):1217-39.
50. Avidan AY. Sleep disorders in the older patient. *Prim Care Clin Office Pract* 2005;32:563-86.
51. Kryger M. Management of obstructive sleep apnea-hypopnea syndrome: overview. In: Kryger M, Roth T, Dement WC, eds. *Principles and Practice of Sleep Medicine*. Third edition ed: W.B. Saunders, Company; 2004.
52. Ancoli-Israel S, Ayalon L. Diagnosis and treatment of sleep disorders in older adults. *Am J Geriatr Psych* 2006;14:\*5-103.
53. Young T, Shahar E, Nieto FJ, et al. Predictors of sleep-disordered breathing in community dwelling adults. *Arch Intern Med* 2002;162:893-900.
54. Redline S. Epidemiology of sleep-disordered breathing. *Semin Respir Crit Care Med* 1998;19:113-22.
55. Duran J, Esnaola S, Rubio R, Iztueta A. Obstructive sleep apnea-hypopnea and related clinical features in a population-based sample of subjects aged 30-70 yr. *Am J Respir Crit Care Med* 2001;163(685-689).
56. Ancoli-Israel S, Kripke DF, MR K. Periodic limb movements in sleep in community-dwelling elderly. *Sleep* 1991;14:496 - 500.

57. Carskadon MA, Brown ED, Dement WC. Sleep fragmentation in the elderly: Relationship to daytime sleep tendency. *Neurobiology of Aging* 1982;3(4):321-7.
58. Borbely AA, Achermann P. Sleep homeostasis and models of sleep regulation. *J Biol Rhythms* 1999;14(6):559-68.
59. Monk TH, Buysse DJ, Carrier J, Billy BD, Rose LR. Effects of afternoon "siesta" naps on sleep, alertness, performance, and circadian rhythms in the elderly. *Sleep* 2001;24(6):680-7.
60. Trendall J. Concept analysis: chronic fatigue. *J Advanced Nursing* 2000;32(5):1126-31.
61. Stein KD, Martin SC, Hann DM, Jacobsen PB. A multidimensional measure of fatigue for use with cancer patients. *Cancer Practice* 1998;6(3):143-52.
62. Lichstein KL, Means MK, Noe SL, Aguillard RN. Fatigue and sleep disorders. *Behaviour Research and Therapy* 1997;35(8):733-40.
63. Addington AM, Gallo JJ, Ford DE, Eaton WW. Epidemiology of unexplained fatigue and major depression in the community: The Baltimore ECA follow-up, 1981-1994. *Psyc Med* 2001;31:1037-44.
64. Ancoli-Israel S, Moore PJ, Jones V. The relationship between fatigue and sleep in cancer patients: a review. *European Journal of Cancer Care* 2001;10(4):245-55.
65. Pigeon WR, Sateia MJ, Ferguson RJ. Distinguishing between excessive daytime sleepiness and fatigue. Toward improved detection and treatment. *J Psychosomatic Res* 2003;54:61-9.
66. Johns MW. Reliability and factor analysis of the Epworth Sleepiness Scale. *Sleep* 1992;15(4):376-81.
67. Johns MW. A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale. *Sleep* 1991;14(6):540-454.
68. Morriss RK, Wearden AJ, Mullis R. Exploring the validity of the chalde fatigue scale in chronic fatigue syndrome. *J Psychosomatic Res* 1998;45(5):411-7.
69. Smets EMA, Garssen B, Bonke B, De Haes JC. The multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. *Journal of Psychosomatic Research* 1995;39(3):315-25.
70. Piper BF, Dibble SL, Dodd MJ, Weiss MC, Slaughter RE, Paul SM. The revised Piper Fatigue Scale: psychometric evaluation in women with breast cancer. *ONF* 1998;25(4):677 - 84.
71. Berger AM, Higginbotham P. Correlates of fatigue during and following adjuvant breast cancer chemotherapy: a pilot study. *Oncol Nurs Forum* 2000;27(9):1443-8.

72. Laberge L, Gagnon C, Jean S, Mathieu J. Fatigue and daytime sleepiness rating scales in myotonic dystrophy: a study of reliability. *J Neurol Neurosurg Psychiatry* 2005;76(10):1403-5.
73. Moldofsky H, MacFarlane JG. Fibromyalgia and chronic fatigue syndromes. In: Kryger M RT, Dement WC, ed. *Principles and Practice of Sleep Medicine*, fourth edition. Philadelphia, PA: Elsevier Saunders; 2005.
74. Hewlett S, Cockshott Z, Byron M, et al. Patients' perceptions of fatigue in rheumatoid arthritis: Overwhelming, uncontrollable, ignored. *Arthritis Care & Research* 2005;53(5):697-702.
75. Crane PB. Fatigue and physical activity in older women after myocardial infarction. *Heart & Lung: The Journal of Acute and Critical Care* 2005;34(1):30-8.
76. Van Der Linden, Chalder T, Hickie I, Koschera A, Sham P, Wessely S. Fatigue and psychiatric disorder: different or the same? *Psych Med* 1999;29(863-868).
77. Ekman I, Ehrenberg A. Fatigue in chronic heart failure-does gender make a difference? *E Journ Cardio Nurs* 2002;1:77-82.
78. Bardwell WA, Moore P, Ancoli-Israel S, Dimsdale JE. Fatigue in obstructive sleep apnea: driven by depressive symptoms instead of apnea severity? *Am J Psychiatry* 2003;160(2):350-5.
79. Vgontzas AN, Papanicolaou DA, Bixler EO, et al. Sleep apnea and daytime sleepiness and fatigue: Relation to visceral obesity, insulin resistance, and hypercytokinemia. *J Clin Endocrinol Metab* 2000;85(3):1151-8.
80. Chervin RD. Sleepiness, fatigue, tiredness, and lack of energy in obstructive sleep apnea. *Chest* 2000;118(2):372-9.
81. Aguillard RN, Riedel BW, Lichstein KL, Grieve FG, Johnson CT, Noe SL. Daytime functioning in obstructive sleep apnea patients: exercise tolerance, subjective fatigue, and sleepiness. *Applied Psychophysiology and Biofeedback* 1998;23(4):207-17.
82. Bailes S, Baltzan M, Alapin I, Fichten CS, Libman E. Diagnostic indicators of sleep apnea in older women and men: A prospective study. *Journal of Psychosomatic Research* 2005;59(6):365-73.
83. Chokoverly S. Diagnosis and treatment of sleep disorders caused by co-morbid disease. *Neurology* 2000;54(5. Supplement 1):S8-S15.
84. Mullington JM, Hinze-Selch D, Pollmacher T. Mediators of inflammation and their interaction with sleep. Relevance for Chronic Fatigue Syndrome and related conditions. *Annals of the New York Academy of Sciences* 2001;933(1):201-10.

85. Feinberg I. Untreated type 2 diabetes as a cause of daytime somnolence. *Sleep* 1993;16(1):82.
86. Bixler EO, Vgontzas AN, Lin H-M, Calhoun SL V-BA, Kales A. Excessive Daytime Sleepiness in a General Population Sample: The Role of Sleep Apnea, Age, Obesity, Diabetes and Depression. *J Clin Endocrinol Metab* 2005;99(5):0035.
87. Punjabi NM, Polotsky VY. Disorders of glucose metabolism in sleep apnea. *J Appl Physiol* 2005;99(5):1998-2007.
88. Sanders MH, Givelber R. Sleep disordered breathing may not be an independent risk factor for diabetes, but diabetes may contribute to the occurrence of periodic breathing in sleep. *Sleep Medicine* 2003;4(4):349-50.
89. Klink M QS. Prevalence of reported sleep disturbances in a general adult population and their relationship to obstructive airways diseases. *Chest* 1987;91:540-6.
90. Dodge R, Cline MG, Quan SF. The natural history of insomnia and its relationship to respiratory symptoms. *Arch Intern Med* 1995;155:1797-800.
91. Gislason T RH, Kristbjarnarson H, Benediksdottir B. Sleep habits and sleep disturbances among the elderly - an epidemiological survey. *Journal of Internal Medicine* 1993;234:31 - 9.
92. Quan SF, Katz R, Olson J, et al. Factors associated with incidence and persistence of symptoms of disturbed sleep in an elderly cohort: The Cardiovascular Health Study. *Am J Med Sci* 2005;329(4):163-72.
93. Larsson LG, Lundback B JE, Lindberg A, Sandstrom T. Are symptoms of obstructive sleep apnoea syndrome related to bronchitic symptoms or lung function impairment? Report from the obstructive lung disease in Northern Sweden study. *Respiratory Medicine* 1998;92(2):283-8.
94. Larsson LG, Lundback B JA, Lindstrom M, Jonsson E. Symptoms related to snoring and sleep apnoea in subjects with chronic bronchitis: report from the Obstructive Lung Disease in Northern Sweden Study. *Respiratory Medicine* 1997;91(1):5-12.
95. Ryan CM, Bradley TD. Pathogenesis of obstructive sleep apnea. *J Appl Physiol* 2005;99(6):2440-50.
96. Mills PJ, Dimsdale JE. Sleep apnea: a model for studying cytokines, sleep, and sleep disruption. *Brain, Behavior, and Immunity* 2004;18(4):298-303.
97. Vgontzas AN, Bixler EO, Chrousos GP. Sleep apnea is a manifestation of the metabolic syndrome. *Sleep Medicine Reviews* 2005;9(3):211-24.

98. Heesen C, Nawrath L, Reich C, Bauer N, Schulz KH GS. Fatigue in multiple sclerosis: an example of cytokine mediated sickness behaviour? *J Neurol Neurosurg Psychiatry* 2006;77(1):34-9.
99. Lim W, Hong S, Nelesen R, Dimsdale JE. The Association of obesity, cytokine Levels, and depressive symptoms with diverse measures of fatigue in healthy subjects. *Arch Intern Med* 2005;165(8):910-5.
100. Cohen S, Doyle WJ, Skoner DP. Psychological stress, cytokine production, and severity of upper respiratory illness. *Psychosomatic Medicine* 1999;61:176-80.
101. Wakening America to the Importance of Sleep. 2004. (Accessed at <http://www.sleepfoundation.org/>)
102. The National Sleep Foundation: Mission and Programs. 2004. (Accessed at <http://www.sleepfoundation.org/>)
103. Ancoli-Israel S. Sleep and aging: prevalence of disturbed sleep and treatment considerations in older adults. *J Clin Psychiatry* 2005;66(suppl 9):24-30.
104. Maggi S, Langlois JA, Minicuci N, et al. Sleep complaints in community-dwelling older persons: prevalence, associated factors, and reported causes. *J Am Geriatr Soc* 1998;46(2):161-8.
105. Walsh JK, Englehardt CL. The direct economic costs of insomnia in the United States for 1995. *Sleep* 1999;suppl 2:S386-S93.
106. Edinger JD, Means MK. Overview of insomnia: definitions, epidemiology, differential diagnosis, and assessment. In: Kryger M, Roth T, Dement WC, eds. *Principles and Practices of Sleep Medicine*. Philadelphia PA: Elsevier Saunders; 2005.
107. Walsh JK. Clinical and socioeconomic correlates of insomnia. *J Clin Psychiatry* 2004;65(suppl8):13-9.
108. Chilcott LA, Shapiro CM. The socioeconomic impact of insomnia: An overview. *Pharmacoeconomics* 1996;10(suppl 1):1-14.
109. National Institutes of Health State-of-the-Science Conference Statement. Manifestations and management of chronic insomnia in adults. June 13-15, 2005. In: National Institute of Mental Health and Office of Medical Applications of Research, ed.; 2005.
110. Quan SF. Frontiers of knowledge in sleep and sleep disorders: opportunities for improving health and quality of life. *J Clin Sleep Med* 2005;1(1):83 - 9.

## **Appendix A**

### **SUMMARY OF STUDIES ON SLEEP, NAPPING, AND ACTIGRAPHY**

**Table A5-1 Summary of epidemiologic studies evaluating sleep in older adults**

Author – Study	Population	Methods	Risk	Results	Comments
Ohayon MM 2005 <sup>190</sup>	n = 25,580  Location: France, United Kingdom, Germany, Italy, Portugal, Spain, Finland.	Telephone Interview-Sleep EVAL system (computerized questionnaire).  Non-restorative sleep (NRS) analyzed in relationship to socio-demographic, environmental factors, life habits, health, sleep-wake schedule, psychological factors.	Prevalence of non restorative sleep was higher in women than in men (12.5% vs. 9.0%; P=0.001), and decreased with age.	Prevalence of NRS was 10.8% (95% confidence interval, 10.4%-11.2%) in the sample. The United Kingdom (16.1%) and Germany (15.5%) had the highest prevalence of NRS and Spain (2.4%), the lowest.	
Foley D et al 1995  EPESE <sup>13</sup>	n = 9,282  Locations: East Boston, MA New Haven, CT, and Iowa  Average age: 73.3 – 74.5. Age range did not differ significantly by site.  Females 61%  Blacks only included at New Haven, (% of population not given).	Interview (in person): Sleep questions- how often experience (no reference period of time): -falling asleep -wakening up in the night, -wakening up to early, - if they got so sleepy during the day or evening that they have to take a nap, - if they felt rested when they wake up in the morning. A sleep complaint score representing the sum for the frequency of the responses was used.  Three measures to reflect the dichotomies for sleep deprived syndromes: - difficulty initiating and	Age: - average sleep complaint score generally higher with age -insomnia increased with age in Iowa only.  Female sex: -Average sleep complaint score significantly higher in women. -Insomnia significantly higher OR 1.36(1.23-1.50) - Less likely to nap more during the day.  African Americans; New Haven only. Significantly lower complaint scores on average (18%) Percent for whites only was not given.  BMI no association	Difficulty initiating & maintaining sleep was the most prevalent sleep deprived syndrome (35 – 40% of cohort).  Insomnia 2 <sup>nd</sup> most prevalent complaint (23-34%).  Awakening not rested reported by 15% in East Boston & New Haven, but only 7% in Iowa.  Prevalence of: DIS 19% DMS 29% EMA 18% INS 28% Not feeling rested after am awakening 13% No complaints 12% - Poorer self-rated	57% reported at least 1 chronic complaint occurring most of the time;  Longitudinal analyses of sleep complaints associated with 3 yr mortality found napping was associated with a marginal increase in risk OR 1.17(1.03-1.33) and nighttime awakening. A marginal decrease in risk OR 0.80(0.7000-0.91). (no information was given on nap behavior)  No association between insomnia and mortality or nursing home admission after adjustment for age, sex

<b>Table A5-1 cont.</b>		maintaining sleep (DIMS), -insomnia -awakening not rested.	Poorer self-rated health OR 1.20(1.08-1.34), elevated depressive symptomatology OR 2.53(2.25-2.85), and increasing number of physical disabilities OR 1.16(1.05-1.29) (note reported for 2 or more conditions), respiratory symptoms, medication use were associated with higher frequency of overall complaints represented by sleep summary score. OR also increased but not significant with any ADL limitation 1.17 (1.00 – 1.38) and ambulatory limitation 1.12(0.99-1.27) Note OR's here are for those with reported insomnia (29% of population).  Use of anxiolytics and barbiturates were associated with sleep complaints. OR 1.80(1.51-2.15)	health, elevated depressive symptomatology, increasing number of physical disabilities, respiratory symptoms and non-prescription medications associated with a higher frequency of overall complaints (summary sleep score range 57-60).	& disability.  Data suggested that considerable proportion of sleep complaints may be associated with chronic disease and other health problems that are more prevalent among older persons.
Jean-Louis G, 2000 <sup>22</sup>	San Diego n = 273 144 W 129 M 203 Non-Hispanic whites 70 Minorities  mean age 51 ± 7	Interview: -subjective sleep duration -difficulty falling asleep @ night -sleep satisfaction (1-5 scale) -health status (1-5 scale) -caffeine, alcohol & smoking -Quality of Well Being Scale -CES-D	18% of the variance in QWB explained by: -greater sleep satisfaction -younger age, -less obesity, -non Hispanic White -greater illumination	80% satisfied with their sleep  Reported sleep satisfaction was correlated with reported habitual sleep time (r=-0.28, p<0.001).  Neither subjective or actigraphic sleep duration were associated with QWB	QWB did not have a U-shaped relationship with sleep duration.  No evidence that greater sleep duration was associated with greater health related QOL.



<b>Table A5-1 cont.</b>		Actigraphy (Actillum) for 3 days at home to measure: -nocturnal sleep duration, sleep onset latency, -sleep efficiency		Self-reported & actigraphic sleep durations moderately correlated ( $r=0.35$ , $p<0.001$ ).	
Whitney CW et al 1998	5201 recruited from 1989-1990, with 687 additional non-white from 1993-1994.	Daytime sleepiness by ESS;	African American men: - less likely to report DMS (22% vs. 27% white men, 31% black female, 35% white female)	20% usually sleepy in the daytime	Mean levels of EDS in this study were similar to those in younger persons.
CHS study 1993- 1994 exam	Forsyth County, NC Sacramento Co, CA, Washington Co, MD Allegheny Co, PA	Other sleep questions included: -Do you often wake up at night? -if so what are the reasons -Do you often feely groggy and unrefreshed for more than an hr after waking up in the AM? -Are you usually sleepy in the daytime/	- significantly higher mean ESS scores (7.13 vs. 6.59, 4.50, 3.59)	Average ESS score was 5.85±4 (range 0-24).	ESS higher in men & non-whites.
109	age range 65 – 99, mean age 76 yrs.  White 4578 African American 3808  59% Female	General health question. Brain MRI; Cognitive function tests; Questionnaires of cardiopulmonary; Depressive symptoms (CES-D); social support; ADL's; Physical activity; Medications	Self reported general health status strongly associated with ESS scores. Older women with poor health 7.48 compared with 4.06 for excellent health.  Men and non-white participants had higher ESS scores than women. -men in excellent health had a mean ESS score of 6.29 ± 4.06 compared to 4.06 ± 3.21 in women. Men in poor health men had a score of 7.61 ± 4.92 vs. 7.48 ± 5.63 in women.  Higher depression ( scores > 14) in men & women had higher mean ESS scores  Obesity indicators –BMI, waist circumference & waist to hip ratio positively	In gender specific models independently assoc with higher ESS: non-white, depression, loud snoring, awakening with dyspnea, DIMS, CHS meds, non-use of sleeping pills, sedentary life-style, limitation of ADL's.  No association with EDS in models; age, education, beer or wine to aid sleep, tricyclic, benzodiazepines, asthma, angina, MI, CHF, FVC, social support, cognitive function, MRI atrophy or white matter abnormality.	Higher rate of EDS with OSA, nocturnal sleep disruption, depression, diminished physical activity, heart disease, and age in both bivariate & multiple regression.  Nocturnal awakenings to use the bathroom and from leg cramps were predictive of EDS.  ESS only slightly associated with cognitive impairment.  Inverse relationship with activity (Kcals)

**Table A5-1 cont.**

			associated in univariate analysis, only hip circumference was an independent factor in multiple regression.		
			No finding with pulmonary function (however significant associated with digitalis & diuretics).		
Redline S et al 2004	n=2,685 of 6,443 (total SHHS)	In home overnight PSG: percentage time each sleep stage, arousal index and sleep efficiency.	Men lighter sleep than women (Stages 1 & 2) (p<.001)	Females tended to spend on average 23% less percentage stage1, about 12% less percentage stage 2, about 5% more percentage REM and 106% more percentage stage 3-4. Women also spent a longer period asleep than men (6.05±1.00 vs. 5.75±1.00 hrs, p<.001)	RDI > 45% found in 45%
SHHS (PSG sub study) <sup>191</sup>	age 61.9 ± 10.9 (37-92) 49.6% Female 77.8% White  excluded individuals with exposures or conditions likely to effect sleep architecture other than SDB	Sleep habits questionnaire for perceived sleep disturbances & quality.  Independent variables age, sex, ethnicity,, comorbidity status, RDI	AA & American Indians lighter sleep compared to other ethnic groups.  Age: increasing age associated with impaired sleep in men, less consistent with women % stage 1 & %stage2 significantly higher in 61+ yrs compared with 54 yr or younger. % REM significantly lower in those ≥ 61 Sleep efficiency decreased significantly with age  Women: on average, 106% more slow wave sleep Obesity – little effect on sleep Current smokers- lighter sleep	Age was negatively and linearly associated with all measures of sleep architecture other than percentage stage 1.	10% CVD & lung disease 34% HTN  Finding of objective measures of better sleep quality in women contrast with previous studies that have shown greater perceived sleep difficulties in women. Association of sleep architecture with chronic disease after adjustment for age, SDB, & sex was only significant with a history of HTN (relative to SLE) & prior history of stroke (relative to stage1). These analyses however were in relatively healthy individuals without frequent nocturnal awakenings.
Quan, SF et al, 2005	n=4,467	Sleep questionnaire at baseline then 1-4 yrs later:			Most important factors related to development

---

**TableA5-1 cont.**

- EDS, snoring, trouble  
falling asleep

of sleep disturbance is  
poorer mental health,  
although somatic  
disease contributes

CHS  
24

**Table A.5-2 Summary of epidemiological studies evaluating sleep duration and mortality**

Author - Study	Number	Age	Method	Results	Comments
Hall et al. 2005 Health ABC	3075 (52% F) 42% AA	68 - 80	Self report at 5 <sup>th</sup> annual study visit. Crude mortality at yr 5 confirmed by death certificates & medical history.	Women more likely to report < 6 hrs sleep. Blacks more likely to report both <6 and > 8 hrs Mortality was related to sleep duration, highest rates in those with < 6 hrs and > 8hrs. HR adjusted for demographics, health & smoking: <6hr 1.56 (1.11-2.18) and >8 hr 1.93 (1.28 – 2.79)	Unpublished data. Mortality was higher in both lower & higher duration. Associations partly explained by poorer health status and elevated inflammatory markers.
Youngstedt SD 2004 Long sleep and mortality 11	various	various	Review article of 17 epidemiological studies.	Sleep above 8 hr is associated with higher mortality. U shaped association of sleep duration with mortality was found in all studies comparing several sleep durations. In large studies comparisons of men & women showed similar sleep-associated risks. Control of covariate risk factors had only modest effects in some studies.	Unknown the extent that reported sleep durations represent physiologic sleep duration of just TIB.
Grandner MA et al 2004 Self reported sleep complaints with long & short sleep 28	1004 (49.8% M) 82% White	44.28±16.46 (range 18-86)	Self-reported sleep complaints (latency, nighttime awakenings, morning awakenings, non restorative sleep, and DS compared with reported hrs of sleep. From NSF 2001 Sleep in America Poll.	Overall TNST was 6.99 ± 1.48 hrs. TNST was significantly related to all sleep complaints. U shaped distribution for TNST and sleep duration and note how it parallels the U shaped distribution associated with TNST and mortality TNST showed 8 hr sleepers reported less frequent symptoms than long sleepers or 7 hr sleepers. Those who slept >8 hrs reported significantly more sleep complaints.	Did not present analysis for sleepers < 7 hrs. Data collected by telephone interview therefore reliability and validity is limited.
Kripke DF et al. 1979 1959-1960 American Cancer Society volunteers 26	366,493 M & 456,572 F	range 30 - >90	Questionnaire. Sleep questions: how many hrs of sleep do you usually get a night? Check yes or no for insomnia. How often do you use sleeping pills.	Most common usual sleep duration was 8 – 8.9 hrs in men & women. Insomnia often reported usually sleeping about 1 hr less than those with none. Women reported insomnia about 2X more than men. Both more likely to have died in the 6 yr follow-up if they reported usually sleeping either more or less than 7 – 7.9 hrs. U shaped	Questionnaire reported extremes of usual sleep duration, < 5 or ≥ 10 hrs were almost as strong predictors of 6 yr mortality as reports of having ever had diabetes, heart

Author - Study	Number	Age	Method	Results	Comments
<b>Table A5-2 cont.</b>			Mortalities traced for 6 yrs. Referent group 7 – 7.9 yrs	relationship of sleep duration to mortality highly significant (p <.005) Men reporting < 4 hrs were 2.80 times as likely to die & Women 1.48 times.	disease, stroke or HTN in both sexes and all age groups. No referent sleep time.
Kripke DF et al. 2002  Mortality associated with sleep duration and insomnia. 1982 CPSII  27	1.1 million	W: 57 ± 11 yrs; M: 58 ± 10 yrs	Questionnaire: On average, how many hours do you sleep each night, and how many times a month do you have insomnia. Survival or death rate (from death certificate) 6 yrs later.	Modal sleep duration 8 hrs. Almost 50% reported ≥ 7.5 hrs. After adjustment for 32 covariates best survival was in those reporting usual sleep duration of 7 hrs. In W HR > 7 ranged from 1.07 – 1.33(3 hrs) and in men 1.08 to 1.19. For > 7 hrs the HR in W ranged 1.13 – 1.41 (≥10hrs) and in men from 1.12 – 1.34. Insomnia was not well defined. Was not assisted with any excess mortality. Comparison of the 32 covariate models with simplified models & CPSI tabulations showed most mortality risk associated with short sleep could be explained by comorbidities.	Population surveyed was limited to ACS volunteers and associated. Only one sleep question was asked.
Patel SR et al 2004  Sleep duration and mortality risk. (Nurses Health Study)  29	82,969 W answered sleep question.	average 53±7 (approximated from data given)	Questionnaire at baseline in 1986Indicate total hours of actual sleep in a 24 hr period. . Mortality ascertained over 14 yrs (1986-2000), Referent group 7 hrs.	Women reporting long and short sleep durations tended to be older & heavier and to have more illnesses (for 7 hrs age 52.8±7.2 vs. 53.8±7.4 for ≥9 hrs). History of night shifts more common in those sleeping ≤ 5hrs. Significant increase in mortality risk for both short and long sleepers. For ≤ 5hrs RR 1.41(1.25-1.28), in 9hrs 1.72 (1.55-1.91). Adjustment for HTN and diabetes, and shift-work history in short sleepers resulted in reduction in excess mortality risk to a level not significantly different than 7 hrs. Adjustment had little effect on over 7 hrs.	Lowest sleep category was ≤ 5. Physical activity, depression and alcohol were the largest confounders of short sleep, and physical activity was the primary confounder of long. These variables were not defined further.

**Table A.5-3 Summary of studies on napping in the community**

Author - Study	Number	Age	Intervention	Results	Comments
Tamaki et al. 1999 Effects of daytime naps (Japanese) <sup>12</sup>	6 (Sex not given)	72.2 (range 66 – 78)	Nap and rest condition with 1 wk between. Nap – went to bed 13:00 and awakened 30 min from onset of stage 1 sleep. Rest condition – watched videotape for 30 min.	Reaction time shorter in the nap after 14:00h & percentage correct on visual detection task was higher, & subjective sleepiness was lower (however no data provided)  EEG $\alpha$ band activity higher after rest more than nap showing arousal level improved with nap (relative amplitude 2uV vs. .5uV) DBP decreased from 80-70 after nap vs. 78 – 80 after rest ( $p < 0.05$ ).	Small study. Minimal data presented. Participants were habitual nappers.
Tamaki et al. 2000 Effects of <30 min afternoon nap on mood, performance, & EEG (Japanese) <sup>13</sup>	10 (5M & 5F)	73.0 $\pm$ 3.62	Nap and rest condition with 1 wk between. Nap – went to bed 13:00 and awakened 30 min from onset of stage 1 sleep. Rest condition – watched videotape for 45 min.	Mood after waking from nap (average 5.2/7) and at 3 min after rising (6.3/7) Percentage correct on the visual detection test showed the percentage correct significantly decreased at 14:40h in the no-nap (99.4%) vs. the nap(99.8%) in the nap ( $p < 0.05$ ). Amplitudes of theta, alpha 1, alpha2 & alpha 3 band activities on EEG were lower or maintained after the nap, and higher without the nap.	Nap time was set at 13:00h during intervention. Authors also looked at one-week actigraph activity in normal life. Frequency of daytime naps in 1 week averaged 4.6 $\pm$ 0.33. Duration of nap episode was 37.8 $\pm$ 5.21 min. No. of daytime nap episodes/day was 1.4 $\pm$ 0.09. Of 115 daytime naps recorded, 24% occurred from 13:00 – 13:30 h and 84% between 12:00 & 15:00 h
Campbell et al. 2005 Effects of nap on nighttime sleep and waking function. (New York) <sup>14</sup>	32 (16M & 16F)	68.5 $\pm$ 8.1 range:55 - 85	Two lab sessions, each 3 nights & following days, separated by 1 wk. Nap or sedentary between 2 & 4 pm.	Average sleep time during the 2-h nap 81 $\pm$ 25.9 min (range 11.5 – 108.5 min). Sleep onset latency after the nap took average of 6.3 min longer than under sedentary conditions. Performance measured by the Wilkinson four-choice reaction and the Stroop task showed significant improvement. Napping also associated with significant improvement on next-day performance for accuracy on the logical reasoning task, and throughput on the 2 letter reasoning test ( $p < .03$ )	In 24 hr period containing the nap compared to 24 hr sedentary, subject's average more than an hr more total sleep (7.4 vs. 6.2 hr). Primarily in the form of REM & Stage 2 sleep. Results presented in bar graph showing percentage difference in performance from the sedentary to the nap condition,

<b>Table A5-3 cont.</b>	n = 442 (Gender not given)	70 yrs	Questionnaire: - Do you nap every day? - Duration of your nap?	No difference in sex.	(no tables). Performance changes were only correlated with nap variables not nighttime sleep variables.
Hays JC et al 1996  Risk of napping: Excessive DS & mortality  (EPESE – NC) 15	3962(1381M & 2581F)	65 – 101	Four year prospective cohort study. Questionnaire – sleep related variables self-report.	Point prevalence of EDS = 25.2%. Frequent daytime nappers were more likely to report nighttime sleep complaints, to be male, to report more depressive symptoms, more limited physical activity, more functional impairment, & to be overweight.  23.9% of frequent nappers died compared with 15.4% of infrequent, The 4-yr mortality rate was accelerated 1.73 times in those who napped most of the time and made 2 or more errors on cognitive status examination,	First large scale population based controlled study to look at mortality risk associated with napping.  Excessive napping appeared to be associated primarily with impaired sleep hygiene which the authors note as the polyphasic patterns of fragmented nighttime sleep.
Frisoni GB et al 1996  Napping - association with night sleep and psychological status  (Italy) 16	n = 223 W(67.7%)	M 80.3(4.2) W 81.5(4.6)	Questionnaire: - How often in the past week did you take nap because you felt sleepy? - Sleep measures: TFS, WUDN, EMW, NFRAM	Napping had bimodal distribution: no nap 76.2%, ≥ 1day/week 23.8%. Unadjusted: - EMA OR 1.2 (0.03 – 0.37, p=0.18) - NFRAM OR 1.2 (0.00 – 0.33, p=0.05) Adjusted: - EMA OR 1.1 (-1.63-1.85, p=0.215) - NFRAM OR 1.2 (0.00 – 0.353, p=0.05)	Obsessive-compulsive behavior's psychological symptom most closely associated with napping OR 1.95 (0.08 – 1.26, p=0.03)
Asplund R, 1996  DS and napping in relation to somatic health. (Sweden) 17	n = 6143 M(39.5%)	M 73(6) W(72.6(6.7)	Questionnaire: - I'm often sleepy in the daytime - I usually sleep for a while in the daytime - I'm often unable to fall asleep despite sleepiness in the day	- Cardiovascular diseases, snoring, pain, diabetes was associated with higher DS - WUDN were more sleepy during the day M 2.7(2.2-3.4), W 2.7(2.3-3.2); TFS M 2.4(1.8-3.1), W 2.3(1.9 – 2.8) - Age-related increase in nap seen in M & W with a good night's sleep	Nap information was extrapolated from DS information. - 32%M and 23.2%W sleepy during day - Odds of DS increased in relation to number of nocturnal voiding episodes. - Odd of DS increased with impaired sensory or neurological function.

**Table A.5-4 Summary of studies of on napping and actigraphy in older adults**

Author - Study	Number	Age	Method	Results	Comments
Usui A et al. 2003 <sup>38</sup>  Naps that are not recognized as naps.	14 (no gender given)	mean 73.8 yrs	Wrist actigraph (Motionlogger Actigraph) for 4 – 7 days. Sleep-log.	Fell asleep 21:04 and woke 05:51. The 1hr agreement ratios for actigraph & sleep log dropped in the periods 04:00-07:00, 13:00-16:00 and 19:00-22:00. False sleep ratios were high during 04:00-07:00 and false wake ratios were high during 13:00-16:00 and 19:00-22:00.	False wake ratios imply that older often have naps not subjectively recognized as naps. Study also had 25 controls (27.6) however actigraph-log comparisons not given.
Yoon IY et al 2004 <sup>64</sup>  Naps & circadian rhythms in WHI	436	67.8 ± 7.9 (range 50 - 81_	Wrist actigraph (Actillum) for 1 week. Daily sleep logs.	All day nap duration significantly increased in 70-81 yr olds compared to 50-59 yrs or 60-69 yrs old (p<.01). Evening nap duration tended to increase with age being higher in the 70-81 yr group compared with the other 2 age groups (p=.064). Averaged all-day and evening nap durations were 31.3 & 7.75 min. A significant inverse correlation occurred between evening nap duration and wake-up time, but not with all day nap or non-evening. Nap duration was correlated with wake-up time.	Study designed to look at depressed (n=30) vs. non-depressed women (n=222). Study also looked at aMT6s acropahse.
Yoon IY et al 2003 <sup>62</sup>  Age-related differences in napping & nocturnal sleep	60 older (38W & 22M); 73 young (47W & 26M)	66.2 ± 4.9 23.5 ± 3.8 -generally healthy	Wrist actigraph (Actillum) for 1 week. Daily sleep logs. Naps were counted as ‘any short sleep episode’ out of bed without criteria on the duration Used 10h after wake-up & 10 h before bedtime Afternoon naps defined as naps from 4 h after wake-up to 6 h before sleep. Evening naps defined as out of bed sleep from 2 hr to just before bedtime	Bed & wake-up times, sleep onset & offset times significantly earlier in older age group (p<0.001) 76% of older and 61.6% of younger had at least 1 nap (p=0.064). Nap time 23.3 and 17.3 min/day respectively. Younger group exhibited more napping during the 10 h after wake-up (p<0.01) (Greater in the afternoon) Older had significant increase 2 h before bedtime.	While no difference in duration of naps, older adults napped more in the evening. Older adults with evening naps had earlier nocturnal wake-up times and decreased nocturnal sleep duration compared with those without.
Evans et al 1994 <sup>12</sup>  24 hr sleep wake patterns	14 (13F & 1M)	81.2 ± 5.9 (range 71 – 91)	Wrist actigraph (Actillum) for 48 hrs. Activity diaries every 15 min.	Naps were longest in the afternoon, 42.9% occurred between 12 & 6 pm. 37.6% occurred between 6pm and midnight, and 19.5% from 6am to 12 noon. Subjects reported taking an average of 1.79	Data based on 48 hrs



Author - Study	Number	Age	Method	Results	Comments
<b>Table A5-4 cont.</b>				naps/day compared with an average of 5.2 naps recorded by actigraphy. No relationship was found between ages and napping.	
Buysse DJ et al 1992 <sup>237</sup>  Napping & 24 h sleep/wake patterns	45 older (21M & 24 F); 33 young	83.1 ± 2.1  24.9 ± 3.0	2 – week sleep/wake diary 2 nights PSG	Older reported > mean number of naps over 2 weeks (3.4 ± 1.3 vs. 1.1 ± 1.4 p=0.004). 35.5% of older and 54.4% of the young reported no naps. Average time of naps was not significantly different between groups. Trend for women to be more frequent nappers than men X <sup>2</sup> =2.81, p=0.09. More frequent nappers had lower mean scores than infrequent nappers on the Hamilton Rating Scale for Depression and the Folstein Mini mental State, however not clinically significant.	PSG reports older had shorter sleep time, more awakenings, more time awake during the night, less REM and slow wave sleep. Sleep latency did not differ. These were consistent with self report.
Ceolim NF et al. 2000 <sup>192</sup>  Sleep/wake cycle & activity	23	70.17 ± 3.55 (range 65 – 76)	Wrist actigraph for 2 weeks. Sleep logs and activity diaries.	Long exercisers reported slightly higher number of naps than SE group (0.49±0.51/day and 0.39±0.50/day), with the mean duration of naps in LE group being slightly higher (46±42 median 30min, and 44±42, median 30).	Authors note that the association between a longer duration of physical exercise and the semi circadian sleep wake cycle imply a possible beneficial role for naps as part of a healthy lifestyle.
Monk TH et al 2001 <sup>41</sup>  90 min afternoon nap on nocturnal sleep, circadian rhythms, evening alertness & performance levels	9 (4M & 5F)	mean 78.6 range 74 - 87	PSG, wrist actigraphy, sleep diary. Two studies with nap & no nap conditions for 14 home days and 3 lab days. Nap condition: 90 min nap between 13:30 & 15:00 every day. No nap condition: no napping & activity was encouraged.	Estimated TNST (naps) for the week 40 – 83 min (58 ± 14 min). Nocturnal sleep in the nap condition (377 min) vs. no nap (397) p>0.15, No significant differences or trends in nocturnal sleep between nap & no – nap condition in the lab (375(57) & 366(31) p>0.25). Alertness based on the global vigor scale there appeared to be no significant difference between the nap and no nap conditions (66 vs. 65, p>0.25). Performance data indicated no evidence that the nap had any significant effect (p>0.25)	Total 24 hr sleep duration > with nap sleep: Nap sleep + nocturnal sleep TNST: nap: 435 min, no nap: 397 min, p<0.025).

## A.1 REFERENCES

1. Ohayon MM. Prevalence and correlates of nonrestorative sleep complaints. *Arch Intern Med* 2005;165:35-41.
2. Foley DJ, Monjan AA, Brown SL. Sleep complaints among elderly persons: an epidemiologic study of three communities. *Sleep* 1995;18:425 - 32.
3. Jean-Louis G, Kripke DF, Ancoli-Israel S. Sleep and quality of well-being. *Sleep* 2000;23(8):1-7.
4. Whitney CW, Enright PL, Newman AB, Bonekat W, Foley D, Quan SF. Correlates of daytime sleepiness in 4578 elderly persons: the cardiovascular health study. *Sleep* 1998;21(q):27 - 36.
5. Redline S, Kirchner L, Quan SF, Gottlieb DJ, Kapur V, Newman A. The effects of age, sex, ethnicity, and sleep disordered breathing on sleep architecture. *Arch Intern Med* 2004;164:406 -18.
6. Quan SF, Katz R, Olson J, et al. Factors associated with incidence and persistence of symptoms of disturbed sleep in an elderly cohort: The Cardiovascular Health Study. *Am J Med Sci* 2005;329(4):163-72.
7. Youngstedt SD, Kripke DF. Long sleep and mortality: rationale for sleep restriction. *Sleep Medicine Reviews* 2004;8:159-74.
8. Grandner MA, Kripke DF. Self-reported sleep complaints with long and short sleep: A nationally representative sample. *Psychosomatic Medicine* 2004;66:239-41.
9. Kripke DF, Simons RN, Garfunkel L, Hammond C. Short and long sleep and sleeping pills. *Arch Gen Psych* 1979;36:103-16.
10. Kripke DF, Garfinkel L, Wingard DL, Klauber MR, Marler MR. Mortality associated with sleep duration and insomnia. *Archives Of General Psychiatry* 2002;59(2):131-6.
11. Patel SR, Ayas NT, Malhotra MR, et al. A prospective study of sleep duration and mortality risk in women. *Sleep* 2004;27(3):440-4.
12. Tamaki M, Shirota A, Tanaka H, Hayashi M, Hori T. Aging and sleep. Effects of a daytime nap in the aged. *Psychiatry and Clinical Neurosciences* 1999;53:273 - 5.
13. Tamaki M, Shirota A, Tanaka H, Hayashi M, Hori T. Restorative effects of a short afternoon nap (<30 min) in the elderly on subjective mood, performance and EEG activity. *Sleep Research Online* 2000 2000;3:131-9.

14. Campbell SS, Murphy PJ, Stauble TN. Effects of a nap on nighttime sleep and waking function in older subjects. *J Am Geriatr Soc* 2005;53(1):48-53.
15. Hays JC, Blazer DG, Foley DJ. Risk of napping: Excessive daytime sleepiness and mortality in an older community population. *J Am Geriatr Soc* 1996;44:693 - 8.
16. Frisoni GB, DeLeo D, Rozzini R, Trabucchi M. Aspects of the elderly. Napping in the elderly and its association with night sleep and psychological status. *Internat Psychogeriatrics* 1996;8(3):477-87.
17. Asplund R. Daytime sleepiness and napping amongst the elderly in relation to somatic health and medical treatment. *J Internal Medicine* 1996;239:261-7.
18. Bursztyn M, Ginsberg G, Stessman J. The siesta and mortality in the elderly: effect of rest without sleep and daytime sleep duration. *Sleep* 2002;25:187-91.
19. Usui A IY, Hachuda M, Noda T, Kanba S. Elderly people often have naps that are not subjectively recognized as naps. *Sleep and biological rhythms* 2003;1(2):141-2.
20. Yoon IY, Kripke DF, Elliot JA, Langer RD. Naps and circadian rhythms in postmenopausal women. *Journal of Gerontology* 2004;59A(8):844 - 8.
21. Yoon IY, Kripke DF, Youngstedt SD, Elliot JA. Actigraphy suggests age-related differences in napping and nocturnal sleep. *J Sleep Res* 2003;12:87 - 93.
22. Evans BD, Rogers AE. 24 -Hour sleep/wake patterns in healthy elderly persons. *Applied Nursing Research* 1994;7(2):75 - 83.
23. Buysse DJ, Browman BA, Monk TH, Reynolds CF, Fascizka AL, Kupfer DJ. Napping and 24-hr sleep/wake patterns in healthy elderly and younger adults. *J Am Geriatric Society* 1992;40:779-86.
24. Ceolim MF, Menna-Barreto L. Sleep/wake cycle and physical activity in healthy elderly people. *Sleep Research Online* 2000;3(3):87-95.
25. Monk TH, Buysse DJ, Carrier J, Billy BD, Rose LR. Effects of afternoon "siesta" naps on sleep, alertness, performance, and circadian rhythms in the elderly. *Sleep* 2001;24(6):680-7.

## **Appendix B**

### **ANCILLARY STUDY**

## **B.1 THE HEALTH AGING AND BODY COMPOSITION – ANCILLARY STUDY: THE EFFECTS OF SLEEP ON DAYTIME FUNCTION**

This study was an ancillary study performed in conjunction with the Health Aging and Body Composition (Health ABC) eighth year clinic visit (2005). This study was designed, implemented, conducted, and analyzed as part of Ms. Goldman's PhD thesis.

## **B.2 RESEARCH AIMS AND HYPOTHESES**

Night time sleep problems and daytime sleepiness are common complaints in society, and especially in the older population. Both have been directly and indirectly correlated with reduced daytime performance and functioning, medical comorbidity and cognitive decline. We planned to use a combination sleep diary and wrist actigraphy to measure and quantify sleep duration, sleep fragmentation, and sleep quality in older adults. Our goal was to collect these data to address the following aims and hypotheses:

**Aim I: Determine if sleep duration, fragmentation, or quality as measured by sleep diaries and wrist actigraphy is related to fatigue as measured by:**

- a) subjective daily report of fatigue and napping behavior, and**
- b) objective measurement of performance as measured by the 400m walk test, grip strength, chair stands and standing balance test.**

Hypothesis I: Older adults who sleep <6 hours or >8 hours per night will report more fatigue and perform more poorly, than those who sleep between 6 to 8 hours.

Hypothesis II: Older adults with more sleep fragmentation (nighttime movement) measured by wrist actigraphy will report more daytime fatigue and have lower daytime functioning compared to those with less sleep fragmentation (nighttime movement).

Hypothesis III: Older adults who report a better quality of sleep will report less fatigue, fewer naps, and perform better than those who report poorer quality sleep.

**Aim II: Determine if sleep duration, fragmentation, or quality are related to the prevalence of one or more falls in the past year by self report**

Hypothesis I: Older adults who sleep <6 hours or >8 hours per night will report fewer falls over the past year than older adults who sleep 7 to 8 hours.

Hypothesis II: Older adults with more sleep fragmentation (nighttime movement) measured by wrist actigraphy will report a history of fewer falls in the past year than those older adults with lower sleep fragmentation (nighttime movement).

Hypothesis III: Older adults who report a better quality of sleep will report fewer falls over the past year than older adults who report poorer sleep quality.

**Aim III: Determine if sleep duration, fragmentation, or quality are related to cognitive functions as measured by the Teng Mini Mental Status Exam**

Hypothesis I: Older adults who sleep <6 hours or >8 hours per night will have lower cognitive function than older adults who sleep 7 to 8 hours.

Hypothesis II: Older adults with a more sleep fragmentation (nighttime movement) measured by wrist actigraphy will have lower cognitive function than older adults with lower sleep fragmentation (nighttime movement).

Hypothesis III: Older adults who report better a better quality of sleep will perform better on cognitive function tests than older adults who report a poorer sleep quality.

## B.2.1 Background and rationale

Sleepiness, is generally felt to reflect a physiological need for sleep, impairing the ability of an individual to function effectively, subsequently reducing the quality of life<sup>83, 109</sup>. Changes in sleep and sleep architecture that occur with aging can lead to sleep complaints in older adults<sup>193</sup>. Fatigue, is often used interchangeably with sleepiness, and reflects a sensation of exhaustion during or after usual activities, or inadequate energy to begin activities<sup>194</sup>. Both, daytime sleepiness and fatigue, are important factors in the health and quality of life in older individuals<sup>148, 195</sup>. While sleep needs remain similar throughout the lifespan, daytime sleepiness is more prevalent in the older and many factors make it difficult to obtain the requisite sleep<sup>196, 197</sup>.

Older individuals experience a wide range of sleep problems related to changes in medical, physical and behavioral factors. These include daytime sleepiness and fatigue, an inadequate amount of sleep (<6 hours), naps, obstructive sleep apnea, insomnia, restless legs syndrome, circadian rhythm disorders, and delayed sleep phase syndrome<sup>16, 148, 196-199</sup>. Excessive daytime sleepiness has been reported to range from 10% to over 30% in the older<sup>109, 200</sup>. Daytime sleepiness has been associated with multiple outcomes such as cardiovascular mortality<sup>23, 201</sup>, diabetes mellitus and impaired glucose tolerance<sup>191</sup>, falls<sup>202</sup>, cognitive and psychiatric disorders and impaired functional outcomes<sup>200</sup>. While it has been suggested that daytime sleepiness is probably due to nocturnal disturbances such as frequent awakenings<sup>109</sup> the relationship between night time sleep patterns, daytime sleepiness, and health related outcomes are not fully understood.

Individuals are thought to require between seven to nine hours of sleep nightly for optimum health and performance<sup>196</sup>. Older adults (55-84 year olds) average 7.0 hours of sleep on weeknights and 7.1 hours of sleep on weekends, however 13% sleep less than six hours and 8% sleep more than nine hours and approximately 50% or higher, complain of some sleep difficulty<sup>3, 4, 198</sup>. Evidence of adverse health effects associated with short or long sleep times, and daytime sleepiness is increasing. Individuals with four or more major medical conditions tend to sleep less than six hours, report poorer sleep quality and some type of sleep disorder compared to individuals who have three or less health problems<sup>4</sup>.

The Health ABC study population has well documented measurements of the study participants' health and overall physical and mental function. The 8<sup>th</sup> year visit while measuring

medical, physical and behavioral components does not include any sleep related measures. As part of this ancillary study, we propose to add a sleep questionnaire, a self-administered sleep diary, and an actigraphy measurement of sleep performance to a subset of the Pittsburgh cohort to test the above hypotheses and evaluate the association of nighttime sleep, daytime napping, and fatigue on daytime function.

### **B.3 METHODS AND PROCEDURES**

We asked 372 Health ABC participants from the Pittsburgh site at their 8<sup>th</sup> clinic visit (start date for the sleep study was 1/2005) to participate in this study. Participation in this study was entirely voluntary. Individuals were excluded if they had: end stage disease, lung disease or heart disease requiring oxygen, cancer under active treatment, cognitive impairment, or were unable to follow directions or complete a sleep diary. Participants were initially recruited based on the availability of a wrist actigraph (Mini-Mitter<sup>®</sup> AW-16) at the time of their visit. If a wrist actigraph was available, a staff member approached the participant and offered them the opportunity to participate in the ancillary study. In late-February 2005 enough watches had been obtained to offer a watch to all qualified participants.

Participants who consented to participate in the sleep actigraphy study were asked a few additional questions about their daytime energy level, napping behavior, and sleep patterns. They were then asked to wear a small wrist actigraph on the non dominant arm designed to measure sleep duration and movement continuously for one week. They were also asked to record sleep related behaviors at bed time and during their wake time (e.g. sleep and wake times, naps, exercise) in a diary. The day after the week sleep study ended a driver for the study picked up the wrist actigraphy and diary from the participants' home. In the middle of February the decision was made to ask the additional questionnaire to all Health ABC participants whether or not they chose to participate in the home portion of the study. The additional questions and instructions extended the clinic visit approximately 10 minutes.



### **B.3.1 Data analysis and statistical power**

### **B.3.2 Assumptions for statistical power calculations.**

We initially anticipated sampling to start the first week of Jan 2005 and to finish with the conclusion of the 8<sup>th</sup> year of the Health ABC study at the end of May 2005. Initial sample size was based on the availability of 15 wrist actiwatches worn by a participant for seven days plus a three to four day return and maintenance period. Assuming an average of nine wrist actigraphs in circulation at a time, four weeks in a month, and a 5 month sampling period, we projected being able to sample a minimum of 180 participants. In late February we obtained additional watches that enabled us to offer watches to all eligible participants. Based on our response to that time we projected a final sample size of 252.

Initial sample size calculations were based on dividing the 180 participants into five groups based on data from the Health ABC baseline self report of hours slept each night (personal communication Dr. A. Newman): those who slept less than six hours; slept six hours; slept seven hours; slept 8 hours; and greater than eight hours, by percent (13.6%, 25.6%, 26.1%, 28.8% and 6.1% respectively) based. We performed t-tests on the equality of self reported energy (0 – 10 scale), Health ABC short performance battery (SPPB), and the Teng mini-mental exam (MMSE) using the calculated actual means and standard deviations from the Health ABC study at the 5<sup>th</sup> clinic visit (MMSE) and the 6<sup>th</sup> visit (Energy Scale, SPPB). We used the actual SD rate of change of 1.6477 for the energy scale, 1.8538 for the SPPB, and 0.1233 for the MME. Alpha was set at 0.05 and power = 0.80. To achieve adequate power, based on the previous data collected at the Health ABC baseline visit on hours slept per night, we double sampled the end populations (< 6 hours and > 8 hours) and assumed the remaining 3 categories to be equal. Mean detectable differences are presented below (Table 1). By using the actual mean (SD) from Health ABC we would be able to detect from 0.6084 SD when comparing 48 to 38 participants to 0.72 SD between 48 - 22 participants. Table 2 presents revised calculations based on the revised sample size of 252 watches.

**Table 1 Mean detectable difference based on 15 watches, estimated sample size (n= 180)**

Distribution based on Health ABC baseline self reported sleep data with sample size doubled at both ends:

	<u>&lt; 6 hrs</u>	<u>6hrs</u>	<u>7 hrs</u>	<u>8 hrs</u>	<u>&gt;8 hrs</u>
<b>Baseline</b>	<b>13.6%</b>	<b>25.6%</b>	<b>26.1%</b>	<b>28.8%</b>	<b>6.1%</b>
<b>n = <sup>1</sup></b>	<b>48</b>	<b>36</b>	<b>36</b>	<b>38</b>	<b>22</b>
<b>Sample Sizes Compared</b>	<b>48 – 22</b>	<b>48 – 36</b>	<b>48 – 38</b>	<b>36 - 22</b>	
<b>Energy Scale (0-10)</b> 6.4739 (1.6477) <sup>2</sup>	1.1885 (0.7213)	1.0177 (0.6176)	1.0025 (0.6084)	1.2490 (0.7580)	
<b>SPPB (12 point scale)</b> 9.5633 (1.8538) <sup>3</sup>	1.3372 (0.7213)	1.1450 (0.6177)	1.1278 (0.6084)	1.4053 (0.7581)	
<b>MMSE</b> 1.007 (0.1233) <sup>4</sup>	0.0889 (0.7210)	0.0762 (0.6180)	0.0750 (0.6083)	0.0935 (0.7583)	

<sup>1</sup> Sample size reflects double sampling of the <6 hrs and >8 hrs groups

<sup>2</sup> mean (SD)

<sup>3</sup> mean detectable difference between the 2 sample sizes.

<sup>4</sup> SD difference detectable.

**Table 2 Mean detectable difference based on actual sample size (n=252)**

Distribution based on Health ABC self report data:

n =	<u>&lt; 6 hrs</u> 51	<u>6hrs</u> 60	<u>7 hrs</u> 67	<u>8 hrs</u> 53	<u>&gt;8 hrs</u> 21
<b>Sample Sizes Compared</b>		<b>51 - 21</b>	<b>60 - 21</b>		<b>60 - 67</b>
<b>Energy Scale (0-10)</b> 6.1633(1.9435)(actual)		1.4116 <sup>2</sup>	1.3805		.9677
<b>SPPB (12 point scale)</b> 9.5633 (1.8538) <sup>1</sup>		1.346	1.3168		.9231
<b>MMSE</b> 1.007 (0.1233) <sup>1</sup>		.0896	.0876		.0614

<sup>1</sup> mean (SD)

<sup>2</sup> mean detectable difference between the 2 sample sizes.

### **B.3.3 Outcomes and covariates**

This ancillary study provided data for several analyses and analysis plans. The outcomes and potential confounders varied slightly for each analysis plan proposed. The following is a generalized list.

#### **Outcomes:**

- Wrist actigraphy:
  - Total nighttime sleep
  - Movement and fragmentation index
  - Wake after sleep onset
  - Total daytime sleep (naps)
- Fatigue
- Performance measures (400 meter walk speed, average grip strength, time to complete 5 chair stands).

#### **Covariates:**

Available from the Health ABC year 8 visit or through the ancillary study:

- Age
- Race
- Sex
- Body weight
- BMI (kg/m<sup>2</sup>)
- Self reported health status
- Cardiopulmonary disease
- Use of sleep medication
- Cognitive Decline (3MS)
- Depression (CES-D10)
- Stress (Perceived stress scale)
- Smoking
- Alcohol use
- Physical activity – minutes walking per week.

### **B.3.4 Statistical methods**

- Actigraphy data was collected using the Mini-Mitter Actiwatch that contains an electronic device that counts the number of arm movements per one-minute epoch, recording each minute's total movement on a memory chip. Data collected was downloaded and analyzed with the Mini-Mitter Actiware sleep software v5<sup>®</sup>.

- Descriptive statistics were performed on all major variables.

- Sleep duration was calculated and participants categorized into quartiles, as well as into the 5 sleep classes defined above.

- Movement & fragmentation percent was calculated using the Mini-Mitter software and evaluated and categorized into groups as appropriate.

- Comparisons will be made between sleep groups with respect to potential covariates.

- Correlations will be run between the main outcomes and major covariates with parametric and non-parametric methods as appropriate

- Linear regression analyses will be performed to evaluate the relationships between the major outcomes and the independent variables. Based on univariate significance multiple linear regressions will be performed as appropriate.

### **B.3.5 Impact on the main study**

Our proposal had minimal impact on the main study and clinic site. Minimal burden was placed on the participant. The actual time of the clinic visit did not increase over 15 – 20 minutes for the participant. The participants were expected to wear the wrist-actigraph continuously for one week and to complete a sleep diary daily at bedtime and upon arising daily for a week (anticipated time about 10 minutes per day). The watches and diaries were picked up by the clinic drivers upon completion.

### **B.3.6 Costs.**

The ancillary study was funded through a Department of Epidemiology Small Grants Award to Ms. Goldman and supplemented with research and development funds from the study site. Ms. Goldman received a complimentary copy of the Actiware software from Mini-Mitter<sup>®</sup> for participating in testing the software upgrade. As a graduate student research assistant Ms. Goldman was funded by Dr. A. Newman. No additional costs were incurred by the main study or the coordinating center. Data was entered locally and will be merged with clean files upon completion of the ancillary study.

## B.4 REFERENCES

1. Bardwell WA, Moore P, Ancoli-Israel S, Dimsdale JE. Fatigue in obstructive sleep apnea: driven by depressive symptoms instead of apnea severity? *Am J Psychiatry* 2003;160(2):350-5.
2. Whitney CW, Enright PL, Newman AB, Bonekat W, Foley D, Quan SF. Correlates of daytime sleepiness in 4578 elderly persons: the cardiovascular health study. *Sleep* 1998;21(q):27 - 36.
3. Ancoli-Israel S, Alessi C. Sleep and Aging. *Am J Geriatr Psychiatry* 2005;13(5):341-3.
4. Approach to the patient with fatigue. UpToDate, 2004. (Accessed April 2004, at <http://www.uptodate.com>.)
5. Asplund R. Daytime sleepiness and napping amongst the elderly in relation to somatic health and medical treatment. *J Internal Medicine* 1996;239:261-7.
6. Bliwise DL, King AC. Sleepiness in clinical and nonclinical populations. *Neuroepidemiology* 1996(15):161-5.
7. National Sleep Foundation. Myths--and facts--about sleep; 2004.
8. Moldofsky H. Evaluation of daytime sleepiness. *Clinics in Chest Medicine* 1992;13(3):417 - 25.
9. Foley DJ, Ancoli-Israel S, Britz P, Walsh JK. Sleep disturbances and chronic disease in older adults: Results of the 2003 National Sleep Foundation Sleep in America Survey. *Journal of Psychosomatic Research* 2004;56(5):497-502.
10. Ayalon L LL, Ancoli-Israel A. Diagnosing and treating sleep disorders in the older adult. *Medical Clinics of North America* 2004;88(3):12.
11. Campbell SS, Murphy P. Relationships between sleep and body temperature in middle-aged and older subjects. *Journal of the American Geriatrics Society* 1998;46(4):458 - 62.
12. Gooneratne NS, Weaver TE, Cater JR, et al. Functional outcomes of excessive daytime sleepiness in older adults. *JAGS* 2003;51:642 - 9.
13. Newman AB, Spiekerman CF, Enright P, et al. Daytime sleepiness predicts mortality and cardiovascular disease in older adults. *JAGS* 2000;48:115-23.

14. Asplund R. Sleep and cardiac diseases amongst elderly people. *J Internal Medicine* 1994;236:65 - 71.
15. Redline S, Kirchner L, Quan SF, Gottlieb DJ, Kapur V, Newman A. The effects of age, sex, ethnicity, and sleep disordered breathing on sleep architecture. *Arch Intern Med* 2004;164:406 -18.
16. Brassington GS, King AC, Bliwise DL. Sleep problems as a risk factor for falls in a sample of community-dwelling adults aged 64-99 years. *J Am Geriatric Society* 2000;48:1234 -40.
17. National Sleep Foundation. 2003 Sleep in America Poll; 2003.
18. Maggi S, Langlois JA, Minicuci N, et al. Sleep complaints in community-dwelling older persons: prevalence, associated factors, and reported causes. *J Amer Geriatrics Soc* 1998;46(2):161-8.



## BIBLIOGRAPHY

1. Ancoli-Israel S. Sleep and aging: prevalence of disturbed sleep and treatment considerations in older adults. *J Clin Psychiatry* 2005;66(suppl 9):24-30.
2. National Institutes of Health Consensus Development Conference Statement. The treatment of sleep disorders of older people. *Sleep* 1991;14:169.
3. Maggi S, Langlois JA, Minicuci N, et al. Sleep complaints in community-dwelling older persons: prevalence, associated factors, and reported causes. *J Amer Geriatrics Soc* 1998;46(2):161-8.
4. National Sleep Foundation. 2003 Sleep in America Poll; 2003.
5. Wakening America to the Importance of Sleep. 2004. (Accessed at <http://www.sleepfoundation.org/>)
6. Bliwise DL. Normal Aging. In: Kryger MH, Roth T, Dement WC, eds. *Principles and Practice of Sleep Medicine*. 3rd edition ed: W. B. Saunders Company; 2005.
7. Feinsilver SH. Sleep in the elderly: What is normal? *Clinics in Geriatric Medicine* 2003;19(1):10.
8. Ancoli-Israel S MJ. Insomnia and daytime napping in older adults. *J Clin Sleep Med* 2006;accepted 4/17/06.
9. Quan SF, Bamford CR, Beutler LA. Sleep disturbances in the elderly. *Geriatrics* 1984;39(9):42 - 7.
10. Pressman MR, Fry JM. What is normal sleep in the elderly? *Clinics in Geriatric Medicine* 1988;4(1):71 - 82.
11. Youngstedt SD, Kripke DF. Long sleep and mortality: rationale for sleep restriction. *Sleep Medicine Reviews* 2004;8:159-74.
12. Evans BD, Rogers AE. 24 -Hour sleep/wake patterns in healthy elderly persons. *Applied Nursing Research* 1994;7(2):75 - 83.
13. Foley DJ, Monjan AA, Brown SL. Sleep complaints among elderly persons: an epidemiologic study of three communities. *Sleep* 1995;18:425 - 32.

14. Neubauer DN. Sleep problems in the elderly. *Am Fam Physician* 1999;59(9):11 pp.
15. Jacobs JM, Cohen A, Hammerman-Rozenberg R, Stessman J. Global sleep satisfaction of older people: The Jerusalem Cohort Study. *Journal of the American Geriatrics Society* 2006;54(2):325-9.
16. Foley DJ, Ancoli-Israel S, Britz P, Walsh JK. Sleep disturbances and chronic disease in older adults: Results of the 2003 National Sleep Foundation Sleep in America Survey. *Journal of Psychosomatic Research* 2004;56(5):497-502.
17. Ohayon MM, Zulley J, Guilleminault C, Smirne S, Priest RG. How age and daytime activities are related to insomnia in the general population: consequences for older people. *JAGS* 2001;49:360-6.
18. Miles LE, Dement WC. Sleep and aging. *Sleep* 1980;3:119-220.
19. Ancoli-Israel S. Sleep problems in older adults: putting myths to bed. *Geriatrics* 1997;52:20 - 30.
20. McCall WV. Sleep in the elderly: Burden, diagnosis, and treatment. *Prim Care Companion J Clin Psych* 2004;6(1):9-19.
21. Foley DJ, Monjan AA, Brown SL, Simonsick EM ea. Incidence and remission of insomnia among elderly adults: an epidemiologic study of 6,800 persons over three years. *Sleep* 1999;22((suppl 2)):5366-72.
22. Jean-Louis G, Kripke DF, Ancoli-Israel S. Sleep and quality of well-being. *Sleep* 2000;23(8):1-7.
23. Newman AB, Spiekerman CF, Enright P, et al. Daytime sleepiness predicts mortality and cardiovascular disease in older adults. *JAGS* 2000;48:115-23.
24. Quan SF, Katz R, Olson J, et al. Factors associated with incidence and persistence of symptoms of disturbed sleep in an elderly cohort: The Cardiovascular Health Study. *Am J Med Sci* 2005;329(4):163-72.
25. Ancoli-Israel S, Cooke JR. Prevalence and comorbidity of insomnia and effect on functioning in elderly populations. *Journal of the American Geriatrics Society* 2005;53(s7):S264-S71.
26. Kripke DF, Simons RN, Garfunkel L, Hammond C. Short and long sleep and sleeping pills. *Arch Gen Psych* 1979;36:103-16.
27. Kripke DF, Garfinkel L, Wingard DL, Klauber MR, Marler MR. Mortality associated with sleep duration and insomnia. *Archives Of General Psychiatry* 2002;59(2):131-6.
28. Grandner MA, Kripke DF. Self-reported sleep complaints with long and short sleep: A nationally representative sample. *Psychosomatic Medicine* 2004;66:239-41.

29. Patel SR, Ayas NT, Malhotra MR, et al. A prospective study of sleep duration and mortality risk in women. *Sleep* 2004;27(3):440-4.
30. Gislason T RH, Kristbjarnarson H, Benediktsdottir B. Sleep habits and sleep disturbances among the elderly - an epidemiological survey. *Journal of Internal Medicine* 1993;234:31 - 9.
31. Walsh JK, Englehardt CL. The direct economic costs of insomnia in the United States for 1995. *Sleep* 1999;suppl 2:S386-S93.
32. Edinger JD, Means MK. Overview of insomnia: definitions, epidemiology, differential diagnosis, and assessment. In: Kryger M RT, Dement WC, ed. *Principles and Practices of Sleep Medicine*. Philadelphia AP: Elsevier Saunders; 2005.
33. Walsh JK. Clinical and socioeconomic correlates of insomnia. *J Clin Psychiatry* 2004;65(suppl8):13-9.
34. Chilcott LA, Shapiro CM. The socioeconomic impact of insomnia: An overview. *Pharmacoeconomics* 1996;10(suppl 1):1-14.
35. National Institutes of Health State-of-the-Science Conference Statement. Manifestations and management of chronic insomnia in adults. June 13-15, 2005. In: *Research NIOMHaOoMAo*, ed.; 2005.
36. Quan SF. Frontiers of knowledge in sleep and sleep disorders: opportunities for improving health and quality of life. *J Clin Sleep Med* 2005;1(1):83 - 9.
37. Buysse DJ, Browman BA, Monk TH, Reynolds CF, Fascizka AL, Kupfer DJ. Napping and 24-hr sleep/wake patterns in healthy elderly and younger adults. *J Am Geriatric Society* 1992;40:779-86.
38. Usui A IY, Hachuda M, Noda T, Kanba S. Elderly people often have naps that are not subjectively recognized as naps. *Sleep and biological rhythms* 2003;1(2):141-2.
39. Metz ME, Bunnell DE. Napping and sleep disturbances in the elderly. *Fam Pract Res Journ* 1990;10(1):47-56.
40. Lai H-L. Self-reported napping and nocturnal sleep in Taiwanese elderly insomniacs. *Public Health Nurs* 2005;22(3):240 - 7.
41. Monk TH, Buysse DJ, Carrier J, Billy BD, Rose LR. Effects of afternoon "siesta" naps on sleep, alertness, performance, and circadian rhythms in the elderly. *Sleep* 2001;24(6):680-7.
42. Avidan AY. Insomnia in the geriatric patient. *Clinical Cornerstone* 2003;5(3):12.
43. Leger D GC, Bader G, Levy E, Paillard M,. Medical and socio-professional impact of insomnia. *Sleep* 2002;25(6):621-5.

44. Liao S, Ferrell B. Fatigue in an older population. *JAGS* 2000;48(8):426-30.
45. Hossain JL, Ahmad P, Reinish LW, Kayumov L, Hossain NK, Shapiro CM. Subjective fatigue and subjective sleepiness: two independent consequences of sleep disorders? *Journal of Sleep Research* 2005;14(3):245-53.
46. Cullen W, Kearney Y, Bury G. Prevalence of fatigue in general practice. *Ir J Med Sci* 2002;171(1):10-2.
47. Pigeon WR, Sateia MJ, Ferguson RJ. Distinguishing between excessive daytime sleepiness and fatigue. Toward improved detection and treatment. *J Psychosomatic Res* 2003;54:61-9.
48. Crane PB. Fatigue and physical activity in older women after myocardial infarction. *Heart & Lung: The Journal of Acute and Critical Care* 2005;34(1):30-8.
49. Ancoli-Israel S. Actigraphy. In: Kryger M RT, Dement WC, ed. *Principles and Practices of Sleep Medicine*. Fifth ed. Philadelphia: Elsevier-W.B. Saunders & Co.; 2005.
50. Ancoli-Israel S, Cole R, Alessi C, Chambers M, Moorcroft, Pollack CP. The role of actigraphy in the study of sleep and circadian rhythms. *Sleep* 2003;26(3):342-71.
51. Carskadon AM R. Monitoring and staging human sleep. In: Kryger M RT, Dement WC, ed. *Principles and practice of sleep medicine*. fifth ed. Philadelphia: Elsevier; 2005.
52. Kushida CA, Chang A, Gadkary C, Guilleminault C, Carrillo O, Dement WC. Comparison of actigraphic, polysomnographic, and subjective assessment of sleep parameters in sleep-disordered patients. *Sleep Medicine* 2001;2(5):389-96.
53. Lockley SW, Skene DJ, Arendt J. Comparison between subjective and actigraphic measurement of sleep and sleep rhythms. *J Sleep Res* 1999;8(3):175-83.
54. Blood ML, Sack RL, Percy DC, Pen JC. A comparison of sleep detection by wrist actigraphy, behavioral response, and polysomnography. *Sleep* 1997;20(6):388-95.
55. Morin CM, Gramling SE. Sleep patterns and aging: comparison of older adults with and without insomnia complaints. *Psych Aging* 1989;4(3):290-4.
56. Rogers AE, Caruso CC, Aldrich MS. Reliability of sleep diaries for assessment of sleep/wake patterns. *Nurs Res* 1993;42(6):368-72.
57. Wilson KG, Watson ST, Currie SR. Daily diary and ambulatory activity monitoring of sleep in patients with insomnia associated with chronic musculoskeletal pain. *Pain* 1998;75(1):75-84.
58. Monk TH, Buysse DJ, Kennedy KS, Potts JM, DeGrazia JM, Miewald JM. Measuring sleep habits without using a diary: the sleep timing questionnaire. *Sleep* 2003;26(2):208-12.

59. Jenkins CD, Stanton B-A, Niemcryk SJ, Rose RM. A scale for the estimation of sleep problems in clinical research. *Journal of Clinical Epidemiology* 1988;41(4):313-21.
60. Gehrman P, Matt G, Turingan M, Dinh Q, Ancoli-Israel S. Towards and understanding of self-reports of sleep. *J Sleep Res* 2002;11(229 - 236).
61. Sadeh A, Hauri PJ, Kripke DF, Lavie P. The role of actigraphy in the evaluation of sleep disorders. *Sleep* 1995;18(3):288-302.
62. Yoon IY, Kripke DF, Youngstedt SD, Elliot JA. Actigraphy suggests age-related differences in napping and nocturnal sleep. *J Sleep Res* 2003;12:87 - 93.
63. Jean-Louis G, Kripke DF, Mason WJ, Elliott JA, Youngstedt SD. Sleep estimation from wrist movement quantified by different actigraphic modalities. *Journal of Neuroscience Methods* 2001;105(2):185-91.
64. Yoon IY, Kripke DF, Elliot JA, Langer RD. Naps and circadian rhythms in postmenopausal women. *Journal of Gerontology* 2004;59A(8):844 - 8.
65. Ancoli-Israel S, Moore PJ, Jones V. The relationship between fatigue and sleep in cancer patients: a review. *European Journal of Cancer Care* 2001;10(4):245-55.
66. Piper BF, Dibble SL, Dodd MJ, Weiss MC, Slaughter RE, Paul SM. The revised Piper Fatigue Scale: psychometric evaluation in women with breast cancer. *ONF* 1998;25(4):677 - 84.
67. Lichstein KL, Means MK, Noe SL, Aguillard RN. Fatigue and sleep disorders. *Behaviour Research and Therapy* 1997;35(8):733-40.
68. Shen J, Barbera J, Shapiro CM. Distinguishing sleepiness and fatigue: focus on definition and measurement. *Sleep Med Rev* 2006;10:63-76.
69. Multidimensional assessment of fatigue (MAF) user's guide., 2005. (Accessed at <http://www.son.washington.edu/research/maf>.)
70. Chalder T, Berelowitz G, Pawlikowska T, et al. Development of a fatigue scale. *Journal of Psychosomatic Research* 1993;37(2):147-53.
71. Stein KD, Martin SC, Hann DM, Jacobsen PB. A Multidimensional Measure of Fatigue for Use with Cancer Patients. *Cancer Practice* 1998;6(3):143-52.
72. Smets EMA, Garssen B, Bonke B, De Haes JC. The multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. *Journal of Psychosomatic Research* 1995;39(3):315-25.
73. Lee KA, Hicks G, Nino-Murcia G. Validity and reliability of a scale to assess fatigue. *Psychiatry Research* 1991;36(3):291-8.

74. Schwartz JE, Jandorf L, Krupp LB. The measurement of fatigue: A new instrument. *Journal of Psychosomatic Research* 1993;37(7):753-62.
75. Moldofsky H, MacFarlane JG. Fibromyalgia and chronic fatigue syndromes. In: Kryger M RT, Dement WC, ed. *Principles and Practice of Sleep Medicine*, fourth edition. Philadelphia, PA: Elsevier Saunders; 2005.
76. Roehrs T CM, Dement WC, Roth T,. Daytime sleepiness and alertness. In: Kryger M RT, Dement WC, ed. *Principles and Practice of Sleep Medicine*, fourth edition. Philadelphia, PA: Elsevier Saunders; 2005.
77. Trendall J. Concept analysis: chronic fatigue. *J Advanced Nursing* 2000;32(5):1126-31.
78. Addington AM, Gallo JJ, Ford DE, Eaton WW. Epidemiology of unexplained fatigue and major depression in the community: The Baltimore ECA follow-up, 1981-1994. *Psych Med* 2001;31:1037-44.
79. Dimsdale JE, Ancoli-Israel S, Elmsore TF, Gruen W. Taking fatigue seriously: I. Variations in fatigue sampled repeatedly in healthy controls. *J Med Engineering & Technol* 2003;27(5):218-22.
80. Young T. Epidemiology of daytime sleepiness: definitions, symptomatology, and prevalence. *J Clin Psychiatry* 2004;65(suppl 16):12-6.
81. Berger AM, Higginbotham P. Correlates of fatigue during and following adjuvant breast cancer chemotherapy: a pilot study. *Oncol Nurs Forum* 2000;27(9):1443-8.
82. Hewlett S, Cockshott Z, Byron M, et al. Patients' perceptions of fatigue in rheumatoid arthritis: Overwhelming, uncontrollable, ignored. *Arthritis Care & Research* 2005;53(5):697-702.
83. Bardwell WA, Moore P, Ancoli-Israel S, Dimsdale JE. Fatigue in obstructive sleep apnea: driven by depressive symptoms instead of apnea severity? *Am J Psychiatry* 2003;160(2):350-5.
84. Alapin I, Fichten CS, Libman E, Creti L, Bailes S, Wright J. How is good and poor sleep in older adults and college students related to daytime sleepiness, fatigue, and ability to concentrate? *Journal of Psychosomatic Research* 2000;49(5):381-90.
85. Avlund K DM, Sakari-Rantala R, Laukkanen P, Schroll M. Tiredness in daily activities among nondisabled old people as determinant of onset of disability. *J Clin Epidem* 2002;55:965-73.
86. De Rijk AE, Schreurs KMG, Bensing JM. General practitioners' attributions of fatigue. *Social Science & Medicine* 1998;47(4):487-96.
87. Chervin RD. Sleepiness, fatigue, tiredness, and lack of energy in Obstructive Sleep Apnea. *Chest* 2000;118(2):372-9.

88. Warner G, Borawski E, Kahana E, Stange K. Fatigue as an important health indicator for the elderly. In: 129th Annual Meeting of APHA; 2001.
89. Avlund K VM, Hendriksen C. Onset of mobility disability among community-dwelling old men and women. The role of tiredness in daily activities. *Age and ageing* 2003;32:579 - 84.
90. Whooley MA, Kip KE, Cauley JA, et al. Depression, falls, and risk of fracture in older women. *Arch Intern Med* 1999;159(5):484-90.
91. Bliwise DL, Ansari FP, Straight L-B, Parker KP. Age changes in timing and 24 hour distribution of self-reported sleep. *Am J Geriatr Psych* 2005;12(12):1077 - 82.
92. Frisoni GB, DeLeo D, Rozzini R, Trabucchi M. Aspects of the elderly. Napping in the elderly and its association with night sleep and psychological status. *Internat Psychogeriatrics* 1996;8(3):477-87.
93. Carskadon MA, Brown ED, Dement WC. Sleep fragmentation in the elderly: Relationship to daytime sleep tendency. *Neurobiology of Aging* 1982;3(4):321-7.
94. Shochat T, Loreda J, Ancoli-Israel S. Sleep Disorders in the Elderly. Current Treatment Options in Neurology 2001;3(1):19 - 36.
95. Shochat T, Martin J, Marler M, Ancoli-Israel S. Illumination levels in nursing home patients: Effects on sleep and activity rhythms. *J Sleep Res* 2000;9(4):373-80.
96. Campbell SS, Murphy PJ, Stauble TN. Effects of a nap on nighttime sleep and waking function in older subjects. *J Am Geriatr Soc* 2005;53(1):48-53.
97. Takahashi M. The role of prescribed napping in sleep medicine. *Sleep Medicine* 2003;7(3):227 - 35.
98. Tamaki M, Shirota A, Tanaka H, Hayashi M, Hori T. Restorative effects of a short afternoon nap (<30 min) in the elderly on subjective mood, performance and EEG activity. *Sleep Research Online* 2000 2000;3:131-9.
99. Dautovich ND, McCrae CS, Rowe MS. High and low frequency napping behavior in relation to total sleep time in older adults. *Sleep* 2005;28(S):A119.
100. Yaggi HK, Araujo AB, McKlinlay JB. Sleep duration as a risk factor for the development of type 2 diabetes. *Diabetes Care* 2006;29(3):657 - 61.
101. Yoon IY, Kripke DF, Elliott JA, Youngstedt SD, Rex KM, Hauger RL. Age-related changes of circadian rhythms and sleep-wake cycles. *J Am Geriatr Soc* 2003;51(8):1085-91.
102. Tamaki M, Shirota A, Tanaka H, Hayashi M, Hori T. Aging and sleep. Effects of a daytime nap in the aged. *Psychiatry and Clinical Neurosciences* 1999;53:273 - 5.

103. Bliwise DL, Swan GE. Habitual napping and performance on the trail making test. *J Sleep Res* 2005;14:209-10.
104. Hays JC, Blazer DG, Foley DJ. Risk of napping: Excessive daytime sleepiness and mortality in an older community population. *J Am Geriatr Soc* 1996;44:693 - 8.
105. Ancoli-Israel S, Ayalon L. Diagnosis and treatment of sleep disorders in older adults. *Am J Geriatr Psych* 2006;14:85-103.
106. Ancoli-Israel S. Insomnia in the elderly: A review for the primary care practitioner. *Sleep* 2000;23(Suppl 1):S23-S30.
107. Martin J, Stepnowsky C, Ancoli-Israel S. Sleep apnea in the elderly. *Breathing Disorders During Sleep* 1999.
108. Newman AB EP, Manolio T, et al. Sleep disturbance, psychosocial correlates, and cardiovascular disease in 5201 older adults. *J Am Geriatr Soc* 1997;45:1-7.
109. Whitney CW, Enright PL, Newman AB, Bonekat W, Foley D, Quan SF. Correlates of daytime sleepiness in 4578 elderly persons: the cardiovascular health study. *Sleep* 1998;21(q):27 - 36.
110. McCrae CS, Rowe MA, Tierney CG, Dautovich ND, DeFinis AL, McNamara JPH. Sleep complaints, subjective and objective sleep patterns, health, psychological adjustment, and daytime functioning in community-dwelling older adults. *J of Gerontology Psychological Sciences* 2005;60B(4):182-9.
111. Ohayon MM. Epidemiology of insomnia: what we know and what we still need to learn. *Sleep Medicine Reviews* 2002;6(2):97-111.
112. Vitiello MV, Moe KE, Prinz PN. Sleep complaints cosegregate illness in older adults: clinical research informed by and informing epidemiological studies of sleep. *J of Psychosomatic Res* 2002;53:555-9.
113. Kutner NG SK, Ory MG, Baker DI, FICSIT Group. Older adults perceptions of their health and functioning in relation to sleep disturbance, falling, and urinary incontinence. *JAGS* 1994;42:757-62.
114. Applegate WB, Blass JP, Williams TF. Instruments for the functional assessment of older patients. *N Engl J Med* 1990;322:1207-14.
115. Guralnik JM, Ferrucci L, Pieper, Carl F., Leveille, Suzanne G., Markides, Kyriakos S., Ostir, Glenn V., Studenski, Stephanie, Berkman, Lisa F., Wallace, Robert B. Lower Extremity Function and Subsequent Disability: Consistency Across Studies, Predictive Models, and Value of Gait Speed Alone Compared With the Short Physical Performance Battery. *J Gerontol A Biol Sci Med Sci* 2000;55:M221-31.



116. Rantanen T, Volpato S, Ferrucci L, Heikkinen E, Fried LP, Guralnik JM. Handgrip strength and cause-specific and total mortality in older disabled women: exploring the mechanism. *JAGS* 2003;51:636-41.
117. Cummings SR, Nevitt MC, Browner WS, et al. Appendicular bone density and age predict hip fracture in women: the Study of Osteoporotic Fractures Research Group. *JAMA* 1990;263:665-8.
118. Vogt MT, Palermo L, et al.,. Lumbar spine listhesis in older African American women. *Spine J* 2003;3(4):255-61.
119. Blackwell T, Ancoli-Israel SA, Gehrman PR, Schneider JL, Pdeula KL, Stone KL. Actigraphy scoring reliability in the Study of Osteoporotic Fractures. *Sleep* 2005;28(12):1599-603.
120. Girardin JL, Kripke DF, Mason WJ, Elliott JA, Youngstedt SD. Sleep estimation from wrist movement quantified by different modalities. *J of Neuroscience Methods* 2001;105:185-91.
121. Cummings SR, Nevitt MC, Browner WS, et al. Risk factors for hip fracture in white women. *N Engl J Med* 1995;332(12):767-74.
122. Pincus T, Summey JA, Soraci SA, Wallston KA, Hummon NP. Assessment of patient satisfaction in activities of daily living using a modified Stanford Health Assessment Questionnaire. *Arthritis Rheum* 1983;26(11):1346-53.
123. Fitti JE, Kovar MG. The supplement on aging to the 1984 national health interview survey.; 1987.
124. Schneider J, Blackwell T, Hillier TA, Stone KL. Characteristics of objective and subjective sleep in older women. The Study of Osteoporotic Fractures (SOF). *Sleep* 2004;27(Abtract Supplement):A123.
125. Sheikh JI, Yesavage JA. Geriatric depression scale (GDS): recent evidence and development of a shorter version. *Clin Gerontol* 1986;5:165-73.
126. Goldberg D, Bridges K. Detecting anxiety and depression in general medical settings. *BMJ* 1988;297(6653):897-9.
127. Blackwell T, Yaffe K, Ancoli-Israel S, et al. Poor sleep is associated with impaired cognitive function in older women: The Study of Osteoporotic Fractures. *J Gerontol: Medical Sciences* 2006;61A(4):405-10.
128. Folstein MF, Robins LN, Helzer JE. The Mini-Mental State Examination. *Arch Gen Psychiatry* 1983;40 1983.

129. Pilcher JJ, Huffcutt AL. Effects of sleep deprivation on performance: A meta-analysis. *Sleep* 1996;19(4):318-26.
130. Wesensten NJ, Balkin TJ, Belenky G. Does sleep fragmentation impact recuperation? A review and reanalysis. *J Sleep Res* 1999;8:237-45.
131. Landis CA, Frey CA, Lentz MJ, Rothermel J, Buchwald D, Shaver JLF. Self-reported sleep quality and fatigue correlates with actigraphy in midlife women with fibromyalgia. *Nursing Research* 2003;52(3):140 -7.
132. Korszun A, Young EA, Engleberg NC, Brucksch CB, Greden JF, Crofford LA. Use of actigraphy for monitoring sleep and activity levels in patients with fibromyalgia and depression. *J of Psychosomatic Res* 2002;52:439-43.
133. Rotem AY SA, Krugliak P, Freidman B, Tal A, Tarasiuk A. Polysomnographic and actigraphic evidence of sleep fragmentation in patients with irritable bowel syndrome. *Sleep* 2003;26(6):747-52.
134. Guralnik JM BL, Cummings SR, Curb JD. Physical performance measures in aging research. *J of Gerontology Medical Sciences*;44(5):M141-8.
135. Blazer DG, Hays JC, Foley DJ. Sleep complaints in older adults: a racial comparison. *J Gerontol A Biol Sci Med Sci* 1995;50(5):M280-4.
136. Jean-Louis G, Magai CM, Cohen CI, et al. Ethnic differences in self-reported sleep problems in older adults. *Sleep* 2001;24(8):926-33.
137. Durrence HH, Lichstein KL. The sleep of African Americans: a comparative review. *Behav Sleep Med* 2006;4(1):29-44.
138. Ohayon MM VM. Normative sleep data, cognitive function and daily living activities in older adults in the community. *Sleep* 2005;28(8):981-9.
139. Burazeri G, Gofin J, Kark JD. Over 8 hours of sleep--marker of increased mortality in Mediterranean population: follow-up population study. *Croatian Medical Journal* 2003;44(2):193-8.
140. Bursztyn M, Ginsberg G, Stessman J. The siesta and mortality in the elderly: effect of rest without sleep and daytime sleep duration. *Sleep* 2002;25:187-91.
141. Ayas NT, White DP, Manson JE, et al. A prospective study of sleep duration and coronary heart disease in women. *Archive Internal Medicine* 2003;163:205-9.
142. Tamakoshi A, Ohno Y. Self-reported sleep duration as a predictor of all-cause mortality: results from the JACC study, Japan. *Sleep* 2004;27(1):51-4.
143. Sforza E H-RJ, De Bilbao F, Rochat T, Ibanez V,. Performance vigilance task and sleepiness in patients with sleep-disordered breathing. *Eur Respir J* 2004;24:279-85.

144. Martin SE, Engleman HM, Deary IJ, Douglas NJ. The effect of sleep fragmentation on daytime function. *Am J Respir Crit Care Med* 1996;153(4):1328-32.
145. Bonnet MH, Arand DL. Clinical effects of sleep fragmentation versus sleep deprivation. *Sleep Medicine Reviews* 2003;7(4):297-310.
146. Stepanski EJ. The effect of sleep fragmentation on daytime function. *Sleep* 2002;25(3):268-75.
147. Stepanski E, Lamphere J, Badia P, Zorick F, Roth T. Sleep fragmentation and daytime sleepiness. *Sleep* 1984;7(1):18-25.
148. Asplund R. Daytime sleepiness and napping amongst the elderly in relation to somatic health and medical treatment. *J Internal Medicine* 1996;239:261-7.
149. Jylha M, Guralnik JM, Balfour J, Fried LP. Walking difficulty, walking speed, and age as predictors of self-rated health: The Women's Health and Aging Study. *J Gerontol A Biol Sci Med Sci* 2001;56(10):M609-17.
150. OnderG, Ferrucci L, Fried LP, Guralnik JM, Pahor M. Measures of Physical Performance and Risk for Progressive and Catastrophic Disability: Results From the Women's Health and Aging Study. *J Gerontol A Biol Sci Med Sci* 2005;60(1):74-9.
151. Ensrud KE, NM, Yunis C, Cauley JA, Seeley DG, Fox KM, Cummings SR. Correlates of impaired function in older women. *JAGS* 1994;42:481-9.
152. Rantanen T, GJ, Sakari-Rantala R. Disability, physical activity, and muscle strength in older disabled women. The Women's Health and Aging Study. *Arch Phys Med Rehabil* 1999;80:130 - 5.
153. Ancoli-Israel S, Kripke DF, Klauber MR. Morbidity, mortality and sleep disordered breathing in community dwelling elderly. *Sleep* 1996;19:277 - 82.
154. Liao S, Ferrell BA. Fatigue in an older population. *J Am Geriatr Soc* 2000;48(8):426-30.
155. Morriss RK, Wearden AJ, Mullis R. Exploring the validity of the Chalder fatigue scale in chronic fatigue syndrome. *J Psychosomatic Res* 1998;45(5):411-7.
156. Avlund K, DM, Sakari-Rantala R, Laukkanen P, Schroll M. Tiredness in daily activities among nondisabled old people as determinant of onset of disability. *J Clin Epidemiol* 2002;55:965-73.
157. Jensen E, Dehlin O, Hagberg B, Samulsson G, Svensson T. Insomnia in an 80-year-old population: Relationship to medical, psychological and social factors. *J Sleep Res* 1998;7(183-189).

158. Brach JS, Simonsick EM, Kritchevsky S, Yaffe K, Newman AB. The association between physical function and lifestyle activity and exercise in the Health, Aging and Body Composition Study. *Journal of the American Geriatrics Society* 2004;52(4):502-9.
159. Irwin M, Haydan Artin K, Oxman MN. Screening for Depression in the Older Adult: Criterion Validity of the 10-Item Center for Epidemiological Studies Depression Scale (CES-D). *Arch Intern Med* 1999;159(15):1701-4.
160. National Institutes of Health. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults. The evidence report. In; 1998:228.
161. Berger AM, Higginbotham P. Correlates of fatigue during and following adjuvant breast cancer chemotherapy: a pilot study. *Oncol Nurs Forum* 2000;27(9):1443-8.
162. Vgontzas AN, Papanicolaou DA, Bixler EO, et al. Sleep apnea and daytime sleepiness and fatigue: Relation to visceral obesity, insulin resistance, and hypercytokinemia. *J Clin Endocrinol Metab* 2000;85(3):1151-8.
163. Cauley JA, Fullman RL, Stone KL, et al. Factors associated with the lumbar spine and proximal femur bone mineral density in older men. *Osteoporosis Int* 2005;16:1525-37.
164. Richardson A. Measuring fatigue in patients with cancer. *Support Care Cancer* 1998;6(94-100).
165. Sharpe M, Hawton K, Simkin S, et al. Cognitive behaviour therapy for the chronic fatigue syndrome: a randomised controlled trial. *BMJ* 1996;312(7022):22-6.
166. Robbins JL, Phillips KD, Dudgeon WD, Hand GA. Physiological and Psychological Correlates of Sleep in HIV Infection. *Clin Nurs Res* 2004;13(1):33-52.
167. Mahowald ML, Mahowald MW. Nighttime sleep and daytime functioning (sleepiness and fatigue) in well-defined chronic rheumatic diseases. *Sleep Medicine* 2000;1(3):179-93.
168. Bowman SJ, Booth DA, Platts RG. Measurement of fatigue and discomfort in primary Sjogren's syndrome using a new questionnaire tool. *Rheumatology* 2004;43(6):758-64.
169. Heesen C, Nawrath L, Reich C, Bauer N, Schulz KH GS. Fatigue in multiple sclerosis: an example of cytokine mediated sickness behaviour? *J Neurol Neurosurg Psychiatry* 2006;77(1):34-9.
170. Mullington JM, Hinze-Selch D, Pollmacher T. Mediators of inflammation and their interaction with sleep. Relevance for Chronic Fatigue Syndrome and related conditions. *Annals of the New York Academy of Sciences* 2001;933(1):201-10.
171. Aguillard RN, Riedel BW, Lichstein KL, Grieve FG, Johnson CT, Noe SL. Daytime functioning in obstructive sleep apnea patients: exercise tolerance, subjective fatigue, and sleepiness. *Applied Psychophysiology and Biofeedback* 1998;23(4):207-17.

172. Tralongo P RD, Ferrau F. Fatigue and aging. *Critical Reviews in Oncology/Hematology* 2003;48(Supplement 1):S57-S64.
173. Van Der Linden, Chalder T, Hickie I, Koschera A, Sham P, Wessely S. Fatigue and psychiatric disorder: different or the same? *Psyc Med* 1999;29(863-868).
174. Dement WC, Miles LE, Carskadon MA. "White paper" on sleep and aging. *JAGS* 1982;30:25-50.
175. Bliwise DL. Sleep in normal aging and dementia. *Sleep* 1993;16(1):40-81.
176. Oakley NR. Validation with polysomnography of the Sleepwatch sleep/wake scoring algorithm used by the Actiwatch activity monitoring system. Bend, OR: Mini Mitter Co., Inc.; 1997.
177. Mini-Mitter Co. Inc. The role of actiwatch in the study of sleep and circadian rhythms. 2004.
178. Rosenthal L, Roehrs T, Sicklesteel J, Zorick F, Wittig R, Roth T. Periodic movements during sleep, sleep fragmentation, and sleep-wake complaints. *Sleep* 1984;7(4):326-30.
179. Asplund R. Sleep disorders in the elderly. *Drugs and Aging* 1999;14(2):91-103.
180. Elbaz M, Roue GM, Lofaso F, Quera Salva MA. Utility of actigraphy in the diagnosis of obstructive sleep apnea. *Sleep* 2002;25(5):525-9.
181. Aubert-Tulkens G, Culee C, Harmant-Van Rijckevorsel K, Rodenstein DO. Ambulatory evaluation of sleep disturbance and therapeutic effects in sleep apnea syndrome by wrist activity monitoring. *Am Rev Respir Dis* 1987;136:851 - 6.
182. Ayas NT, White DP, Al-Delaimy WK, et al. A prospective study of self-reported sleep duration and incident diabetes in women. *Diabetes Care* February 2003;26(2):380-4.
183. Gottlieb DJ, Punjabi NM, Newman AB, et al. Association of sleep time with diabetes mellitus and impaired glucose tolerance. *Arch Intern Med* 2005;In - press (accepted 2004).
184. Bixler EO, Vgontzas AN, Lin H-M, Calhoun SL V-BA, Kales A. Excessive daytime sleepiness in a general population sample: the role of sleep apnea, age, obesity, diabetes and depression. *J Clin Endocrinol Metab* 2005;jc.2005-0035.
185. Bursztyjn M, Ginsberg G, Hammerman-Rozenberg R. The siesta in the elderly: risk factor for mortality? *Arch Intern Med* 1999;159(1582-1586).
186. Campos H, Siles X. Siesta and the risk of coronary heart disease: results from a population-based, case-control study in Costa Rica. *Int J Epidemiol* 2000;29(3):429-37.

187. Gilberg M KG, Axelsson J, and Akerstedt T. The effects of a short daytime nap after restricted night sleep. *Sleep* 1996;19(7):570 - 5.
188. Olejniczak PW, Fisch BJ. Sleep disorders. *The Medical Clinics of North America* 2003;87:803 - 33.
189. U. S. Department of Health & Human Services NIH. 2003 National Sleep Disorders Research Plan: NIH Publication No. 03-5209; 2003.
190. Ohayon MM. Prevalence and correlates of nonrestorative sleep complaints. *Arch Intern Med* 2005;165:35-41.
191. Redline S, Kirchner L, Quan SF, Gottlieb DJ, Kapur V, Newman A. The effects of age, sex, ethnicity, and sleep disordered breathing on sleep architecture. *Arch Intern Med* 2004;164:406 -18.
192. Ceolim MF, Menna-Barreto L. Sleep/wake cycle and physical activity in healthy elderly people. *Sleep Research Online* 2000;3(3):87-95.
193. Ancoli-Israel S, Alessi C. Sleep and Aging. *Am J Geriatr Psychiatry* 2005;13(5):341-3.
194. Approach to the patient with fatigue. UpToDate, 2004. (Accessed April 2004, at <http://www.uptodate.com>.)
195. Bliwise DL, King AC. Sleepiness in clinical and nonclinical populations. *Neuroepidemiology* 1996(15):161-5.
196. National Sleep Foundation. Myths--and facts--about sleep; 2004.
197. Moldofsky H. Evaluation of daytime sleepiness. *Clinics in Chest Medicine* 1992;13(3):417 - 25.
198. Ayalon L LL, Ancoli-Israel A. Diagnosing and treating sleep disorders in the older adult. *Medical Clinics of North America* 2004;88(3):12.
199. Campbell SS, Murphy P. Relationships between sleep and body temperature in middle-aged and older subjects. *Journal of the American Geriatrics Society* 1998;46(4):458 - 62.
200. Gooneratne NS, Weaver TE, Cater JR, et al. Functional outcomes of excessive daytime sleepiness in older adults. *JAGS* 2003;51:642 - 9.
201. Asplund R. Sleep and cardiac diseases amongst elderly people. *J Internal Medicine* 1994;236:65 - 71.
202. Brassington GS, King AC, Bliwise DL. Sleep problems as a risk factor for falls in a sample of community-dwelling adults aged 64-99 years. *J Am Geriatric Society* 2000;48:1234 -40.