SLEEP AND MYOCARDIAL INFARCTION REOCCURENCE

by

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Abstract

Roughly every 42 seconds an American experiences a myocardial infarction (MI). More importantly, over a third will have another MI within 6 years. Approximately 34% of deaths from heart disease could have been delayed or prevented through changes in health habits such as sleep. Examining sleep in those post MI is important to understanding the associations between sleep and cardiovascular health. The purpose of this senior honors project was to examine the associations between sleep duration and sleep quality and the reoccurrence of MI in adults. A secondary analysis of data from a comparative research study (N=156) that examined MI reoccurrence in Blacks and Whites was used to investigate the relationships between sleep duration, sleep quality, and MI reoccurrence via Pearson's correlation, chi-square, and *t*-test. Short and long sleep durations were not significantly associated with MI reoccurrence (χ^2 = 3.603 (3), p = 0.31). However, there was a significant difference in sleep efficiency (χ^2 = 11.16 [3], p = 0.01) and overall sleep quality and MI reoccurrence ($\chi 2$ = 14.88 [1], $p < 0.001$). Together, these findings suggest that sleep quality and efficiency may have a stronger influence on cardiovascular health than sleep duration alone.

Sleep and Myocardial Infarction Reoccurrence

The rapid rise in the prevalence of heart disease in America has become one of the major challenges facing the global healthcare delivery system. Cardiovascular disease (CVD) accounts for 1 out of every 4 deaths in the United States, killing over 800,000 people in in 2016. More importantly, 34% of the deaths attributed to CVD could have potentially been prevented or delayed through changes in health habits such as sleep (Centers for Disease Control and Prevention [CDC], 2016). Following a healthy lifestyle can help individuals prevent and reduce CVD risk. One of the most common types of CVD and a novel indicator of health risk is coronary heart disease (CHD). Every 42 seconds, a person suffers a heart attack in the United States (CDC, 2016). Survivors of first time myocardial infarctions (MI) face a considerable risk of future cardiovascular events, including ischemic strokes, recurrent MIs, heart failure, and death (Wilson, Douglas, Alpert, Simons & Breall, 2017). The World Health Organization (2016) reports that compared to those without an MI, those who have experienced an MI have a higher death rate. In fact, when comparing these two groups by age, those who have had an MI are 6 times more likely to die than those in the same age group who have not experienced an MI. Thus, focusing on individuals post MI is essential to reducing mortality risk.

Sleep duration has been identified as a risk factor for cardio-metabolic disease and mortality as adverse outcomes and comorbidities have been associated with both short and long sleep duration (Léger, Beck, Richard, Sauvet & Faraut, 2014; Torre-Bouscoulet et al., 2013). Existing literature examining sleep duration as a risk factor for CHD has shown inconsistent associations. Collective comparisons on sleep duration studies are difficult because of the varying categories of sleep durations and research methodologies. Research concerning the modifiable and non-modifiable factors, including sleep, and CHD are necessary to understand

the relationship between sleep and MIs. Examining the influence and relationship that sleep has on the body may help clinicians reduce acute MI reoccurrences and deaths in the future. Studies of sleep duration and secondary MI risk are extremely limited. Large scale studies have demonstrated varying relationships and findings concerning sleep and MI (Cappuccio et. al, 2010; Kronholm, Laatikainen, Peltonen, Sippola & Partonen, 2011). A prompting the need for additional research.

This project aims to address the cardiovascular focus of the Healthy People 2020 guideline by "improving cardiovascular health and quality of life through prevention, detection, and treatment of risk factors for heart attack; prevention of repeat cardiovascular events; and reduction in deaths from CVD" (Office of Disease Prevention and Health Promotion [ODPHP], 2017, para. 1). Currently, sleep is not widely considered to be a modifiable risk factor for developing heart disease. However, examining the associations of sleep on MI reoccurrence may yield information on relationships or perhaps confirm previous findings on the influences of sleep on cardiovascular risk. Such research may impact health policies in the future.

Preventing CHD can also decrease its associated health care costs. The central and eastern North Carolina regions have the highest death rates attributed to MIs in the state, costing the state healthcare system an estimated $2 billion annually. Further research and analysis are necessary to better understand the variables associated with MI reoccurrence to develop guidelines that include various factors of healthy living and emphasize the importance of healthy sleeping habits and mental health. The priority health need for NC residents is to prevent the progression and prevalence of CHD.

Literature Review

An electronic-based search was conducted using Ovid, PubMed, MEDLINE, Cumulative Index to Nursing and Allied Health (CINAHL), and the Cochrane Library databases for original research articles published in English from 2005-2016. Medical subject headings (MeSH) terms were used when available and appropriate. Various terms such as “sleep duration,” “myocardial infarction,” “cardiovascular disease,” “PSQI,” “coronary heart disease,” “recurrent myocardial infarction,” and “subjective sleep” were searched using a boolean technique to limit relevant study designs and subjects for inclusion in the review. The article titles and abstracts were reviewed for significance, and pertinent full-text studies were extracted for review and synthesis.

Subjective Measurement of Sleep

One of the most widely used subjective measures of sleep includes the Pittsburgh Sleep Quality Index (PSQI) measurement tool. Researchers at the University of Pittsburgh Medical Center developed the PSQI in 1989 as an instrument specifically designed to measure subjective sleep quality in clinical populations for application in future psychiatric practices and research. The PSQI is a self-rated questionnaire that assesses sleep quality and disturbances over a 1-month period. Nineteen individual items measured on a scale of 0-3 generate seven “component” scores: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. The sum of the scores for these seven components yield one global score which has a range of 0 to 21 with higher scores indicating worse sleep quality.

Two studies measuring the application of the PSQI found strong positive evidence for reliability and validity in a variety of non-clinical and clinical adult samples. A global PSQI score >5 yielded a diagnostic sensitivity of 89.6% and specificity of 86.5% (kappa = 0.75, *p*

<0.001) in distinguishing good and poor sleepers (Buysse et al., 1989). A meta-analysis of 37 studies examined the PSQI as a screening tool for sleep dysfunction in clinical and non-clinical adult samples. These studies analyzed the construct/group validity, internal consistency, and test-retest reliability of the PSQI measurement. The PSQI showed measures of strong reliability and validity, and moderate structural validity in a variety of samples, suggesting that the PSQI tool fulfills its intended utility in sleep quality measurement (Mollayeva et al., 2015). Despite the number of studies reporting subjective measurements as a limitation to research, (Cappuccio, Cooper, D'Elia, Strazzullo & Miller, 2011; Léger et al., 2014; Torre-Bouscoulet et al., 2013) studies concerning the use of subjective sleep measurements found that although sleep duration is often over-reported, subjective sleep quality is strongly correlated with polysomnographic and other objective sleep measurements (Lauderdale, Knutson, Yan, Liu, & Rathouz 2008; Mollayeva et al., 2015).

Demographics

There is a clear trend of reduced sleep duration emerging in the general population of western countries like the United States. The proportion of adults who sleep less than six hours per night in the United States is now greater than at any other time period (Jones, 2013). A cross-sectional population based study investigating sleep patterns for a nationally representative sample of 110,441 American adults, noted that 1 in 3 Americans were either sleeping too much (> 9 hours) or not getting enough sleep (< 6 hours). The findings of this study (Krueger & Friedman, 2009) suggest that numerous demographic, familial, socioeconomic, and health behavior factors may shape sleep duration; emphasizing the need for further research that adjusts for such factors when analyzing the relationship between sleep and other health or mortality outcomes

There are difference in sleep duration by race. Krueger and Friedman found that older individuals were more likely to report either short or long sleep when compared with younger individuals (2009). Compared with Caucasians, Hispanics are more likely to report short sleep (Hale & Do, 2007), and African American's are more likely to report both short and long sleep (Hale & Do, 2007; Krueger & Friedman, 2009). Reporting short or long sleep is also associated with low socioeconomic status (Cappuccio et al., 2011; Krueger & Friedman, 2009; Patel et al., 2009), and those working long hours (Krueger & Friedman, 2009).

Studies have found varying associations of sleep duration and CHD after factoring for covariates such as socioeconomic status, health, gender, and age (Lauderdale et al., 2008; Marie-Pierre, 2016; Torre-Bouscoulet et al., 2013). One large international systematic review of 15 studies and 24 cohorts totaling nearly half a million people yielded evidence of the relationships between duration of sleep and morbidity/mortality from CHD, stroke, and total CVD (Cappuccio et al., 2011). In contrast to individual studies (Meisinger, Heier, Löwel, Schneider, & Döring 2007; Léger at al., 2014; Kronholm et. al, 2011), this meta-analysis found no gender differences associated with short or long duration of sleep and cardiovascular outcomes. In summary, differences in age, race, social economic status, and work hours, but not sex, have consistently been associated with sleep duration and negative cardiovascular outcomes. Therefore, it is important to examine these variables when studying sleep and MIs.

Sleep Duration and Myocardial Infarction

Short sleep duration imposed on healthy individuals increases sympathetic activity in the nervous system and elevates blood pressure. Thus, altered sleep duration could potentially lead to adverse cardiovascular sympathetic consequences and death. Recent reviews find that sleep duration is associated with mortality in a U-shaped fashion (Grandner, Hale, Moore & Patel

2010; Cappuccio et al., 2011; Gallicchio, 2009). However, a review conducted by Kurina and colleagues (2013) suggested that the consensus on these associations is unclear. The conclusions of this study stress that careful attention should be paid to measurement bias, reverse causation, and confounding factors when interpreting associations between sleep duration and mortality.

Gallicchio & Kalesan conducted a meta-analysis of 23 international studies including men and women from 1979 to 2007 exploring the association between sleep duration and mortality. Using a random effects meta-analysis, the authors reported the pooled relative risk (RR) of all-cause mortality for short sleep (< 7 hours) as 1.10 (95% confidence interval [CI] 1.06-1.15) and a cardiovascular-related RR of 1.06 (95% CI 0.94-1.30). While short sleep carries an increased risk for mortality, this association is not totally explained by CVD. Long duration of sleep (> 8 hours) significantly increased the risk for all-cause, cancer and cardiovascular mortality (2009).

A meta-analysis of 16 published studies from 1993 to 2009, including 1,382,999 male and female participants, and 112,566 confirmed deaths, found a relationship between all-cause mortality and sleep duration. The relative risk for sleep duration and mortality produced similar results of previous studies: RR of 1.12 (95% CI 1.06-1.18) for short sleep and RR of 1.30 (95% CI 1.22-1.38) for long sleep. A secondary meta-analysis by Cappuccio et al., (2011) reviewed an additional 15 studies from 1966 to 2009 including 474,684 male and female participants. Investigators found that short sleep durations (≤ 5-6 hours) were associated with a RR of 1.48 (95% CI 1.22-1.80) while long sleep durations (> 8-9 hours) were associated with a RR of 1.38 (95% CI 1.15-1.66) of developing CHD or dying.

The relationship between sleep duration and CVD mortality risk is also supported by a Finnish study of 25,000 participants that found the highest risk of CVD mortality exists for those

on the extreme ends of sleep duration distribution (Kronholm et al., 2011). A review paper from Grandner and colleagues (2010) confirmed that "there is strong evidence for sleep duration, both short and long, as a risk factor for CVD, even though the mechanisms are not understood" (p. 95). More recently, a cross-sectional study examining sleep duration in 30,000 American adults showed that the shortest (< 5 hours) and longest (> 10 hours) durations of sleep were associated with the highest odds for MI occurrence. Short sleep in particular, indicated significant predictor for the occurrence of MI (B= 2.513; $p < 0.01$) (Altman et.al, 2012). There were no relevant studies that examined sleep and cardiovascular risk for MI recurrence.

Collectively, these studies clearly suggest that sleep duration is associated with mortality and cardiovascular outcomes. Specifically, both short and long sleep duration are associated with elevated risk. While much of the recent literature has focused on the relationship of sleep duration, mortality, and first occurrence cardiovascular morbidities, less is known about the relationships of sleep duration and secondary CVD events such as MI and stroke; highlighting the continuous need for improved risk prediction and correlation for secondary prevention.

Sleep Quality and Myocardial Infarction

Impairments in sleep quality, changes in sleep duration, and sleep disorders are one of the major complaints following an acute MI and evidence indicates that components of sleep, other than sleep duration, are important to investigate in post MI patients (Cappuccio et. al, 2010; Grandner et. al, 2010; Altman et. al, 2012). A 2015 study investigating sleep quality and adverse outcomes (death, recurrent MIs, and stroke) in 113 patients with acute MIs, found that poor sleep quality was frequent in hospitalized patients with MIs and negatively affected the recovery process. The final PSQI score was the only variable independently associated with worsening of clinical outcomes. The PSQI scores were significantly higher in those whose clinical progression

had worsened after an MI compared to those who improved ($p < 0.005$), indicating that worse sleep quality is associated with negative cardiovascular outcomes. Sleep efficiency, as assessed through the PSQI was significantly different between those with worsening clinical conditions and improved or stable clinical conditions, 62.5% and 81.2% respectively ($p < 0.005$) (Andrechuk & Ceolim, 2015). Similarly, a Japanese study using a population based survey of 3,403 participants discovered a significant positive association between the PSQI global score and MI occurrence ($p < 0.05$) as well as the number of existing comorbidities ($p < 0.0001$). As the number of comorbidities rise, the PSQI scores also increased in a linear fashion (Hayashino et. al, 2010). These studies highlight and support the complex relationship between sleep quality and cardiovascular health.

Purpose

The purpose of this senior honors project was to examine the relationship between sleep, and the reoccurrence of MI in adults who have experienced one or more MIs in the last 3-7 years. The application of this study is intended to address the increasing health concern of CVD, and more specifically, CHD by studying the relationships between sleep duration, sleep quality, and recurrent MIs. The ultimate goal of this study was to understand how sleep is associated with MI reoccurrence.

Research Question

Is there a difference in sleep duration and sleep quality in adults who have had one MI compared to those who have had more than one MI?

Methodology

Design

This investigation consisted of a cross-sectional secondary analysis utilizing data from a comparative research study that analyzed differences between Blacks and Whites in MI reoccurrences. The relationships between sleep and MI reoccurrence were investigated via Pearson's correlation, chi-square, and *t*-test. The data were described using descriptive statistics (means, standard deviations, percentiles) to better understand the sample population. Sleep durations were categorized into short (≤ 7 hours), adequate (7-9 hours), and long (≥ 9 hours). Total PSQI scores were dichotomized into 2 groups: scores ≤ 4 indicating good sleep quality and scores > 4 indicating poor sleep quality. All data were analyzed using the statistical package for social science (SPSS v.22). Statistical significance was accepted as $p \leq 0.05$.

Sample

The sample was comprised of English speaking male and female adults aged 25 and older who experienced an MI within last 3-7 years. White and Black subjects were recruited as a convenience sample from two medical centers in North Carolina. Blacks were over sampled to reflect the racial prevalence of MIs in the region. Exclusion criteria included the presence of memory deficit as identified by the Abbreviated Mental Test, taking antidepressants for less than 3 months, and major surgery within the last 6 months.

Data Collection

For this secondary analysis, the data included descriptive data, the PSQI seven individual components of sleep, total PSQI score, and number of MIs, one or more than one. Participants in the study completed a self-reported Demographic Health Form, while sleep duration and quality were assessed with the PSQI tool − a subjective sleep questionnaire.

Results

Demographics

The convenience sample (N=156) consisted of 89 men and 67 women who experienced a MI. The mean age of participants was 65.4 years old (*SD* = 12.1). Most of the sample were men (57%), married (62%), and White (68%). Half (51%) had a high school education or less, and 65% had a history of only one MI. Baseline characteristics are summarized in Table 1. Self-reports of sleep duration per night ranged from 2 to 10 hours (See Figure 1). Participants averaged about 6 hours and 35 minutes (*SD* = 1.68) of sleep per night, with 75% of individuals reporting ≥ 8 hours of sleep per night, while 50% reported sleeping at least 7 hours. The mean PSQI total score was 6.97 (*SD* = 3.87; Range 2-7), and 63% reported poor sleep quality (PSQI total score > 4).

Sleep Quality

There was a significant difference in sleep efficiency (χ^2 = 11.16 [3], p = 0.01) and overall sleep quality and MI reoccurrence (χ^2 = 14.88 [1], $p < 0.001$). There was a significant difference ($p < 0.01$) in total PSQI scores with those having a recurrent MI having significantly higher mean scores (t = -2.775).

Sleep Duration

When sleep duration was compared directly with MI reoccurrence, there was no significant difference in sleep duration (>7, 6-7, 5-6, or <5 hours) and MI reoccurrence (> 1 MI) $\chi 2$ = 3.603 (3), p = 0.31.

Discussion

Contrary to the literature, this study did not support a predictive U-shaped relationship between self-reported sleep duration and MI reoccurrence. Sleep durations for short and long

sleep were not associated with recurrent MIs. Participants who had only one MI reported better sleep efficiency scores than those who experienced a recurrent MI. Overall, poorer sleep quality was associated with those who had a recurrent MI.

Findings of this study are consistent with previous studies investigating poor sleep quality and acute MIs. The evidence echoes a significant difference in total PSQI scores and sleep efficiency between patients who improved following an MI and those whose clinical conditions worsened (Andrechuk & Ceolim, 2015; Hayashino et. al, 2010). Alterations in sleep following an MI are prevalent. The results of this secondary analysis demonstrate the importance of examining the associations between sleep quality and MI occurrence to minimize cardiovascular risk through interventions designed to improve sleep quality and manage sleep disorders, particularly in those post MI. Results of this study suggest that sleep duration may play lesser of a role than the efficiency and quality of sleep. Individuals with poor sleep quality who sleep the recommended 7-8 hours of sleep per night may still be at an increased risk for further MIs. Thus, short and long sleepers may be protected from cardiovascular mortality with good quality sleep. Further study is warranted to understand sleep efficiency and CHD risk.

One of the best ways to reduce future cardiovascular mortality risk in those post-MI is to strengthen the myocardium through physical activity. Inadequate sleep and poor sleep quality often precedes fatigue, one of the prevailing causes of a lack of exercise in post-myocardial infarction populations (Alsén & Brink, 2013; Crane, Abel, & McCoy, 2014). Fatigue presents a significant barrier to cardiovascular rehabilitation by decreasing an individual's ability to engage in physical activity. Therefore, sleep is especially important in this population who have a heightened need for increased physical activity to strengthen the heart muscle and reduce future mortality risk. Because exercise is an important aspect in preventing or delaying recurrent MIs

and is often influenced by a person's level of fatigue, examining sleep and MI reoccurrence is important as a prerequisite to understanding the pathophysiology behind fatigue and CHD. Understanding these associations may help clinicians develop effective interventions for MI patients in the future.

Limitations of this study include the convenience sampling and cross sectional design of this study. Sleep duration and quality were assessed through a subjective questionnaire, may not reflect true sleep duration numbers. Various factors were not included in the analysis that may have influenced sleep, such as medications, sleep apnea, and age.

Inconsistent categorizations of sleep duration in the literature make it difficult to standardize sleep duration. There is limited research that exists on the influence of sleep on the incidence of MIs, particularly studies of sleep and MI reoccurrence. Future research studies should focus on the associations between sleep and both primary/secondary MI occurrences while accounting for various factors such as inflammatory marker levels, medications, physical activity levels, and fatigue.

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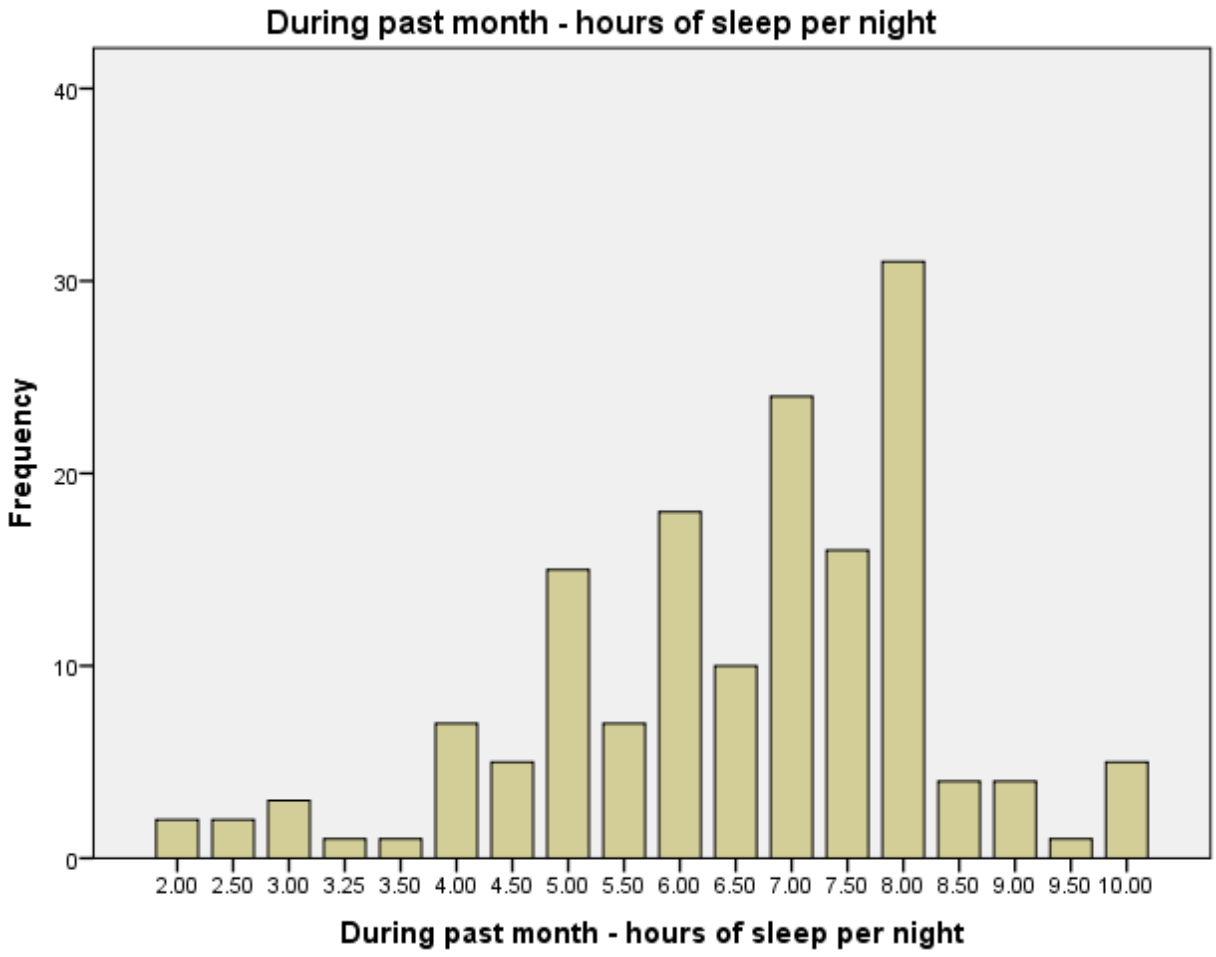
Table 1

Demographic Statistics by MI Occurrence

Variable	1 MI n (%)*	> 1 MI n (%)*
Age		
<60	30 (30)	17 (32)
60-70	37 (36)	17 (32)
70+	35 (34)	20 (36)
Gender		
Male	53 (52)	36 (67)
Female	49 (48)	18 (33)
Marital Status		
Single & Never Married	8 (8)	10 (19)
Married	67 (66)	29 (54)
Divorced/Separated	15 (15)	12 (22)
Widowed	12 (12)	3 (6)
Education		
< High School	19 (19)	13 (24)
High School Graduate/GED	28 (27)	19 (35)
Some College/Technical School	27 (27)	11 (20)
Graduate of College/Technical School	28 (28)	11 (20)
Body Mass Index		
Under < 19	1 (1)	2 (6)
Ideal 19-24.9	19 (20)	7 (20)
Over 25-29.9	30 (29)	16 (30)
Obese > 30	52 (51)	34 (44)
Ethnicity/Race		
African American / Black	31 (30)	15 (28)
Caucasian / White	69 (68)	37 (69)
Other	2 (2)	2 (4)
Combined Yearly Household Income		
< $30,000	43 (42)	30 (56)
$30,000-$80,000	40 (39)	17 (31)
> $80,000	9 (9)	4 (7)
Unknown	10 (10)	3 (6)

* rounded percentages

Figure 1


During past month - hours of sleep per night
Frequency
40
30
20
10
0
2.00 2.50 3.00 3.25 3.50 4.00 4.50 5.00 5.50 6.00 6.50 7.00 7.50 8.00 8.50 9.00 9.50 10.00
During past month - hours of sleep per night