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Association Of Objective Measures Of Sleep And Inflammation Markers On Police Officers: A Cross-Sectional Analysis

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ASSOCIATION OF OBJECTIVE MEASURES OF SLEEP AND INFLAMMATION MARKERS ON POLICE OFFICERS: A CROSS-SECTIONAL ANALYSIS

By

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ABSTRACT

Police officers are a unique occupational group due to the fact that they have more health problems than many other occupations. These health problems could be a result of elevated inflammation markers caused by poor sleep. Sleep influences circadian rhythms, which thereby influences the function of the immune system. The immune system is responsible for the body's inflammatory response using pro-inflammatory cytokines such as IL-6, CRP, Fibrinogen, and TNF-α. These cytokines can become elevated if disruption of the sleep cycle occurs. Elevated levels of inflammatory markers are associated with increased risk of cardiovascular disease. Police officers also work shifts and have a large amount of occupational stress that may contribute to increased levels of pro-inflammatory markers as well.

This analysis aimed to examine the influence that objective and subjective measures of sleep have on inflammatory markers among police officers within the Buffalo Cardio-Metabolic Occupational Police Stress (BCOPS) cohort cross-sectionally. Body mass index (BMI), shift work, and stress measures were examined as potential effect modifiers. Subjective measures of sleep were obtained by the Pittsburgh Sleep Quality Index (PSQI) and objective measures of sleep were obtained through actigraph data. Police officers wore an Actiwatch for 15 consecutive days, where data was made into different sleep parameters.

Sleep latency, quality, duration, efficiency and daytime dysfunction were used from the PSQI, and wake after sleep onset, sleep onset latency, sleep duration, and efficiency were used from the actigraph measures. The inflammation markers were collected from blood samples after a 12 hour fast. Each inflammatory marker was measured using different assays at the University of Vermont.

General linear models were used to compare adjusted means of categorical sleep measures and beta coefficients for continuous sleep measures for each inflammation marker. Analyses were stratified by normal (18.5-24.9 BMI), overweight (25-29.9 BMI), and obese (≥30 BMI), and then by day and evening/night shiftwork. Logistic regression was performed on a dichotomous version of CRP, using a clinial cut point, and odds ratios were obtained for high-risk CRP. Statistically significant associations were seen between various sleep measures and inflammation markers. It is seen that as sleep worsens, there is an elevation in pro-inflammatory markers.

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CHAPTER 1

Introduction

In the health conscious world we live in today, tracking sleep has become a new trend among the public (1). Although still largely unstudied, there has been increased interest in the role sleep plays in health. Underlying this are the circadian rhythms that control sleep and other bodily systems (2). When sleep is disrupted, circadian rhythms become misaligned, which in turn affects the other circadian or clock-controlled bodily functions. One large system controlled by circadian rhythms is the immune system (3).

The immune system controls the pro- and anti-inflammatory cytokines found in the blood. The proliferation of these cytokines occurs under a circadian rhythm; during the light phase anti-inflammatory cytokines are released and during the dark phase pro-inflammatory cytokines are released (4, 5). If circadian misalignment occurs, the balance of the cytokine release becomes uneven, and a higher rate of pro-inflammatory cytokine production happens (6). Pro-inflammatory cytokines also are released during an infection; this is referred to as acute inflammation. In acute inflammation, once the injury is healed, the pro-inflammatory cytokines are broken down. However, if interleukin-6 (IL-6) remains persistent after the injury is healed, it will trigger an immune response to release

more pro-inflammatory cytokines, creating chronic inflammation (7-10). A common form of chronic inflammation is obesity. Obesity is a low-grade chronic inflammatory state caused by the release of pro-inflammatory cytokines from adipose tissue due to overflow (11).

Occupational stress also can play a role in the quality and quantity of sleep a person receives. Of all occupational stressors, the ones that police officers experience are the most detrimental (12). They are subject to environmental stimuli that can cause stress like shootings and violence, as well as shift work (13, 14). Shiftwork can cause circadian misalignment because shift workers tend to work during the dark phase and sleep during the light phase (15). When coupling stress and shiftwork, police officers are at a higher risk of developing disease, and more specifically, chronic diseases (16, 17).

Although there has been research on the effect of sleep on inflammation markers, most previous studies have measured sleep subjectively or performed an experiment on non-habitual sleep (4, 18-25). Most of the observational studies that have measured sleep subjectively show no association between poor sleep and an increase in inflammation markers (19-22). Experimental studies, using objective measures of sleep, however, do find associations indicating a difference between subjective and objective measures of sleep (4, 22-25). This study attempts to bridge this gap by using an objective measure of sleep, actigraphy, proven to be similar to the polysomnography (PSG) measure of sleep used in experimental studies (26). This study is performed within the Buffalo Cardio-

Metabolic Occupational Police Stress (BCOPS) study, and involves collection of blood samples, objective and subjective measures of sleep, past records of shiftwork, a range of psychosocial metrics, and occupational stress measures. This will allow for a more objectively-measured investigation of the relationship between sleep and inflammation markers.

The specific aims of this study are to:

1. Determine if sleep affects levels of inflammatory markers c-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-α), and fibrinogen by addressing the following hypotheses:
    a. A poorer sleep profile (shorter sleep duration, lower sleep efficiency, longer sleep latency, and higher wake after sleep onset [WASO]) is associated with higher levels of inflammation markers
    b. Those with scores indicating poorer sleep on the Pittsburgh Sleep Quality Index will have higher levels of inflammation
2. There will be a difference in the relationship between sleep and inflammation by BMI levels after:
    a. Stratification by body mass index (BMI)
    b. Stratification by shiftwork
    c. Stratification by stress

CHAPTER 2

Background

2.1 Sleep

Sleep is an essential part of everyone's lives, but the concept of sleep and what is does for the body is sometimes not understood (27). Sleep deprivation or poor sleep is now becoming a larger issue because we are beginning to understand some of the mechanisms that sleep controls (28). Studies have shown that it is not only the amount of sleep we get, but the quality that puts people at higher risk for disease (27, 29, 30).

Sleep is separated into two stages: non-rapid-eye-movement-sleep (NREMS) and rapid-eye-movement sleep (REMS)(2, 31-33). The first stage of sleep is further separated into 4 sections, all having distinct functions. Stage 1 is believed to be the transition between wakefulness and sleep and is referred to as light sleep. Stage 2 shows an increase in higher-frequency brain waves and is where greater depth of sleep begins. Stages 3 and 4 are characterized by slow-wave sleep and then followed by REMS (31). In humans, sleep is typically a 90-minute cycle of NREMS to REMS, which can repeat 5-6 times a night (34). The length of each cycle, however, can vary drastically depending on the type of sleep a person is getting.

Good sleep can be defined as optimal length of each sleep stage with proper distribution of sleep stages and low arousal from sleep. Good sleep is comprised of approximately 80% NREMS (31). A person receiving good sleep should experience no fatigue upon full wakefulness. Sleep also plays a role in memory consolidation, the transition of newly learned tasks or materials into memories (35). Poor sleep is characterized as deviant sleep patterns in either quantity and/or quality. With deviant sleep patterns comes an increased risk of physical and psychological problems (19, 36-39). A few of these problems include risk of diabetes (36), hypertension (37), coronary heart disease (38), occupational functioning, mood disturbance (39), depression, and anxiety (19).

The regulation of sleep, however, is dependent upon a homeostatic need and circadian rhythms (2). The circadian rhythm is controlled by a natural clock within the suprachiasmatic nucleus (SCN) of the brain that runs on a 24-hour cycle that tends to follow the 24-hour light-dark cycle of the environment, but can be active even in the absence of light-cues. Circadian clock mechanisms are present in many cell types and organs. Cells related to the immune system are an example of these types of cells (40, 41). Within the central clock located in the SCN are three proteins that have a large impact on the immune function. These proteins are circadian locomotor output cycles kaput (CLOCK), brain and muscle aryl hydrocarbon receptor nuclear translocator-like 1 (BMAL1), three period regulators (PER1, PER2, PER3), and reverse-Erb alpha (REV-ERBα) (3, 42-45). It has been shown that BMAL1 acts as a link between the immune system and the central clock

in limiting inflammation(3). PER 3 can have varying lengths that have an effect on morning preference, cognitive performance, and circulating concentrations on IL-6 (44).

2.2 Inflammation

The immune system can be monitored by measuring the production of inflammation biomarkers through measurements of blood cytokines. Cytokines can be categorized as pro-inflammatory (type 1) and anti-inflammatory (type 2) (5, 46, 47). Maximum production of pro-inflammatory cytokines, including type-1, IL-2, IL-6, IL-12, TNF-α, and interferon (IFN)-gamma, occurs during the dark phase or nocturnal sleep. The production of IL-12 and TNF-α are completely dependent on sleep, whereas production of anti-inflammatory cytokines are dependent on wakefulness (48-51). However, a study on sleep deprivation showed a shift from type 1-type 2 cytokine balance to type 1 cytokine production, indicating an elevation of pro-inflammatory cytokines (4, 6).

Inflammation can be beneficial; in its acute phase, it aids in fighting infections. However, chronic inflammation leads to tissue damage and disease. Acute inflammation is defined by the recruitment of neutrophils and then monocytic cells to damaged tissue by the immune response. Chronic inflammation is associated with a large presence of macrophages and lymphocytes (7-10). The switch from acute to chronic inflammation can be linked through IL-6. IL-6 acts as a mediator during acute inflammation, but when IL-6 remains after the infection is controlled due to immune stressors, chronic infection occurs (52). If IL-6 persists

another immune response is activated, causing mononuclear cell accumulation and chronic inflammation proliferation (53). This then creates a cycle of chronic inflammation because of the increase in IL-6 re-triggering the immune response.

2.3 Inflammation and Sleep

The association between sleep and inflammation has been studied, but previous results are conflicting and founded on subjective measures of sleep, creating the potential for information bias. In an experimental study assessing sleep deprivation and activation of morning levels inflammation markers, 30 healthy adults spent 4 days in the National Institute of Health General Clinical Research Center. The first 3 days they were permitted to sleep between 11 pm and 7 am, for baseline information, and on the 4th day sleep was permitted from 3 am to 7 am, for the sleep deprivation information. Blood samples were taken on each day at 8am, 12pm, 4pm, 8pm, and 11pm. The study results showed that after partial sleep deprivation, IL-6 and TNF-α showed a significant increase (t_{107}= -2.3, P<.05) compared to the baseline sleep duration in the morning. The cytokine levels approached baseline ranges as the day progressed (22).

Vgontzas et al. and Meier-Ewert et al. showed the same inverse association with IL-6 and CRP, respectively, in an experimental study design (23, 24). In another experimental study by Vgontzas et al., the effect of modest sleep deprivation (a loss of 2 hours compared to the normal 8 hours) on levels of inflammatory markers was assessed. Once again, this study showed that on the days of sleep deprivation, the levels of IL-6 and TNF-α were significantly higher

than when individuals received all 8 hours of sleep (4). Another laboratory study assigned participants to 12 days of sleeping 8 hours a night or 4 hours a night to compare the effect of sleep restriction on inflammatory markers (54). Haack et. al. found elevated levels of IL-6 in people sleeping 4 hours a night compared to 8 hours a night ($p<0.05$) but no significant increase in CRP (54).

Patel et al. used individuals from the Cleveland Family Study to look at the association between sleep duration and biomarkers of inflammation. The sleep measure was based on self-reported habitual sleep time and a separate PSG study. For the observational and the experimental study, the inflammatory markers CRP, IL-6, TNF-α, IL-1, and IL-10 were collected between 7 am and 8 am after the PSG and an overnight fast. The experimental section of this study used an overnight PSG to measure sleep duration. The observational study found a positive linear relationship between sleep duration and CRP and IL-6. Conversely, the experimental study found an inverse association between sleep duration and TNF-α (25). The different findings suggest that the self-reported sleep data is modeling a different relationship than the PSG.

The findings from the NSDA study, however, contradict the laboratory performed studies showing the difference between experimental and real-world associations (19). A study on sleep duration, insomnia and markers of systemic inflammation was conducted within the Netherlands Study of Depression and Anxiety (NSDA). Sleep was measured through a questionnaire completed after an interview or at home. Inflammation markers CRP, IL-6, and TNF-α were collected

at baseline from fasting blood samples collected between 8am-9am (19). They found that longer sleep durations were associated with significantly higher levels of CRP (p-value=0.005) and IL-6 (p-value<0.001) compared to short sleep duration and when comparing normal sleep to short sleep duration levels of CRP (p-value=0.575) and IL-6 (p-value=0.916). This study failed to see a significant association between short sleep duration and inflammatory markers (19). These results also were found in a study of sleep duration and quality among a Taiwanese population and a cross-sectional study performed within the 2007-2008 cycle of NHANES (20, 21).

There also are observational studies that have examined at the association between poor sleep quality and inflammation markers. In the Heart and Soul Study, a prospective cohort of men and women with established coronary heart disease, a cross-sectional analysis was done on self-reported sleep quality and biomarkers of systematic inflammation (18). The self-reported sleep measure was from the Pittsburgh Sleep Quality Index (PSQI), and asked participants at baseline and 5 years later, "During the past month, how would you rate your sleep?" Secondary sleep variables also were included. Inflammation markers were collected at baseline and at the 5-year follow up after a 12-hour fast. The inflammation markers collected were CRP, IL-6, and fibrinogen. After analysis there was no evidence that self-reported sleep quality was associated with cross-sectional or 5-year difference in levels of IL-6, CRP, and fibrinogen. Prather et al. did find that women reporting poorer sleep quality showed a significant increase

in IL-6 (p=0.003) , CRP (p=0.02), and fibrinogen (p=0.02) after a 5-year increase (18). This study suggests that gender has an effect on the association between sleep and inflammation markers.

Another cross-sectional study performed within the 2005-2006 US National Health and Nutrition Examination Survey (NHANES) cycle looked at the association between self-reported sleep quality, using two questions from the Sleep Disorders Questionnaire, and mediators of cardio-metabolic health, one being CRP (28). The findings concluded that, although above clinical reference range, there is a J-shaped relationship between sleep quality and CRP levels. On this J-shaped curve, there is a steep increase in CRP from fair to very poor sleep quality, with the association between very poor sleep quality and CRP being statistically significant (28).

A study examining the link between sleep, exaggerated inflammatory response and adverse health outcomes focused on gender-specific responses. In women, poor sleep quality was associated with higher CRP levels but there were no relationships of note between PSQI scores and IL-6 or TNF-α (55). A cohort made of western Australian men also looked at the association between inflammation and poor sleep. They found a significant association between difficulty falling asleep and higher levels of CRP(56).

This relationship has been examined extensively in individuals with obstructive sleep apnea (OSA). After comparing 15 studies, it is seen that on average CRP levels are higher in individuals with OSA than in controls and that this

difference increased significantly when individuals were obese (57). These studies show that poor sleep can affect inflammation.

All of these previous cross-sectional studies have used self-reported sleep measures, and four of them demonstrated a positive linear association between sleep and inflammation markers. One study showed an inverse relationship when stratified by gender for all inflammation markers, and the other showed an inverse relationship for just CRP. However, all of the experimental studies showed an inverse relationship between sleep duration/quality and levels of inflammation markers. The next step in this field of research is to combine the experimental research findings using PSG with an observational study. This can be done by performing a cross-sectional analysis using objective measures of sleep.

2.4 Potential Effect Modifiers, Sleep, and Inflammation

Obesity is one of the most burdensome diseases in the world, and is a result of excessive energy intake (58). Obesity is characterized not only by high BMI, but is also an inflammatory state (58, 59). Obesity has an impact on immune function just like malnutrition, because it is a form of malnutrition caused by excess dietary intake (59). The link between immune function and obesity is the adipose tissue where fat is stored. When obesity persists, the pro-inflammatory cytokines localized within the adipose tissue are pushed into systemic circulation creating a state of low-grade chronic inflammation (11, 60).

As sleep duration and sleep quality have been decreasing over the past decades, obesity has been increasing (27, 61). When studying obesity, body mass index (BMI, kg/m^2) is the standard measurement used, because it incorporates height and weight into the relationship. Overweight is defined as 25 $kg/m^2 \geq$ BMI $\leq$ 30 kg/m^2, and obesity is defined as a BMI $\geq$ 30 kg/m^2 (62). The link between short sleep duration and obesity has been observed and shows positive associations for children and adults. The nature of the relationship, however, remains a mystery (63). Some indicate a linear inverse association, showing that as sleep duration decreases, BMI increases. Other studies indicate more of a U-shaped association, showing that short and long sleep duration are associated with high BMIs (64). The U-shaped associations signal that the relationship does differ by age category but it is still present (63).

Occupational stress is a major element of physical and mental health. Law enforcement and more specifically police officers experience some of the highest levels of stress related to work (13, 14). Stress is the strain placed on an individual by environmental stimuli (65). A normal day of work for a police officer can entail duties such as crime scene violence, involvement in shootings, seeing and handling dead bodies, injury on the job, and negative news coverage. Police officers are exposed to these environmental stimuli which can contribute to greater stress than other occupational stress stimuli. Therefore, police officers are at a higher risk for developing diseases that are associated with stress (17).

Hypothalamic-pituitary-adrenal axis (HPA) and the autonomic nervous system show the highest response to stress. These systems are therefore used to look at the impact stress has on the body (66). Events that occur on the job can cause a wide range of diseases. Acute Post-Traumatic Stress Disorder (PTSD) is caused by occupational stress. PTSD in police officers can become long-term because of the cycle of stimuli re-occurring. Long-term effects can lead to an increase in behavioral dysfunction (17, 67, 68). Psychological stress also can be shown to play a role in the development of heart disease, like atherosclerosis and coronary heart disease (69-71).

The development of a disease due to stress can in part be explained by cortisol secretion. Constant challenges to the HPA axis can create abnormal cortisol secretion patterns. These patterns could change so that cortisol is not being secreted upon awakening or is failing to return to normative values after several hours. Another way to explain the development of risk factors for cardiovascular disease, type II diabetes, and stroke can be low variability in pathological HPA axis (72-74).

In addition to occupational stress caused by events, police officers also are exposed to shift work, another occupational stressor. Shift work is when an individual's work schedule will change regularly in terms of number of shifts worked and time of day those shifts start (75). This type of work is common among police officers and plays a significant role in their health (76, 77). When timing of sleep and wakefulness are switched, circadian misalignment occurs (15).

Individuals working the night shift or switching between night and day shifts experience circadian stress resulting in sleep deprivation and stress reaction (78). Distribution of circadian timing of food intake shows weight gain among shift workers. Excess weight gain can lead to obesity and an increase in pro-inflammatory cytokines (15, 79). Circadian misalignment causes dysregulation of the immune system, meaning an increased risk of chronic disease is also associated with shiftwork (16, 80-83).

Shiftwork and other occupational stressors that police officers experience affect quality and quantity of sleep. Sleep disorders experienced by police officers include obstructive sleep apnea, insomnia, restless legs syndrome, and narcolepsy. Among shift workers, excessive wake-time sleepiness, insomnia, and wake-time drowsiness are found (84).

Previous studies have examined the association between sleep and inflammation but show a lack in information. Observational studies used only a subjective measure of sleep and were inconsistent with respect to poor sleep's effect on inflammation levels. There is not a lot of associations that hold true across the different types of studies. This could be due to the different cohorts used or differences in measures of sleep. Experimental studies show similar results across each study indicating that subjective measures of sleep may not be capturing actual sleep quality. Therefore, this study will employ both objective measures of sleep and inflammation and subjective measures.

CHAPTER 3

Methods

The study population consisted of officers within The Buffalo Cardio-Metabolic Occupational Police Stress (BCOPS) study (n=464). BCOPS is a retrospective cohort starting in 1998-1999, looking back to 1994, and a prospective cohort starting in 1998-1999. Data for this cross-sectional analysis was from visit 3, which occurred between 2004-2009 (most clinic visits occurred between 2004-2005) and derived from a single examination (17). Visit 1 and visit 2 were pilot studies with only selected officers.

The BCOPS study provided a cohort to examine biological processes associated with police work and its influence on health outcomes. The protocol includes characterization of basic demographics, anthropometric information, a blood draw, questionnaire data, stress biomarkers, psychosocial factors, shiftwork from electronic payroll records from 1994 to the date of the officer's examination, sleep, markers of adverse health outcomes (17, 77). All officers provided written informed consent prior to examination. The BCOPS study received Institutional Review Board approval from The State University of New York at Buffalo and the National Institute for Occupational Safety and Health (17, 77).

3.1 Sleep

The primary exposures for this cross-sectional analysis were sleep quality and quantity. For the objective measures of sleep quality and quantity, actigraphy was used. Actigraphy correlates with PSG, but allows for continuous recording of data, eliminating the need of overnight stays in the laboratory (26). However, actigraphy cannot be used to detect specific sleep disorders. The Actiwatch used was the Octagonal Motionlogger Sleep Watch #26.100 with an Octagonal Motionlogger Computer Interface with ACT #25.111PS and ACTION analysis software 21.123 (85).

Actigraph assessment spanned a 15-day cycle of: four days on shift, four days off-duty, four days back on shift, and three days off-duty. Officers were instructed to only remove watches when they were going to be exposed to water. Determination of sleep-wake cycle for each participant was processed through a variety of sleep scoring algorithms to show if a person was awake or asleep at any given moment. Sleep parameters were then developed based on this sleep score. We used four of the sleep parameters available: sleep duration, sleep efficiency, sleep onset latency (SOL), and wake after sleep onset (WASO). Napping information was not available for this analysis. Sleep duration is defined as the number of hours spent asleep. Sleep efficiency is described as the hours spent asleep divided by hours in bed; this gives the ratio of time actually sleeping versus time just lying in bed. SOL is the interval of time between the participant starting to try to fall asleep and the participant actually falling asleep. WASO is the total

time of periods of wakefulness that occur after the participant actually falls asleep (86).

Subjective measures of sleep were analyzed as a secondary exposure. The Pittsburgh Sleep Quality Index (PSQI) was used to assess self-reported sleep quality. It has been shown that the PSQI has high homogeneity, reliability, and validity (87-89). This self-administered questionnaire contains 11 questions that can measure sleep quality and disturbances over the past month. Among the 11 questions, there are multiple parts that address habitual bed time, time spent falling asleep, habitual waking time, habitual hours slept per night, various forms of sleep disturbances, sleep quality, use of sleep medication, day time sleepiness, lack of enthusiasm, sharing room or bed, and symptoms of sleep disordered breathing. Responses range from 0-3 with a different meaning per question and adjustment for reverse coding. The codes were created to give scores for the following components: sleep quality, sleep latency, hours of actual sleep, sleep efficiency, sleep problems, sleep medication, and daytime dysfunction. When added together, these create a global quality sleep score.

Sleep quality ranges from very good to very bad with 0 denoting very good. This measure refers to participants' opnions of how well they are sleeping. Sleep duration has the following response range: $\geq$7 hours is 0, 6-7 hours is 1, 5-6 hours is 2, and $\leq$ 5 hours is 3. Sleep efficiency in the PSQI is defined the same as it was for the actigraph measures (89). The responses are categorized as $\geq$ 85% as 0, 75-84% as 1, 65-74% as 2, and $\leq$ 65% as 3. Sleep latency is the time spent falling

asleep and was calculated by combining different questions. Time increases from level 0 to 3 for sleep latency. Daytime dysfunction is a composite of how often participants have trouble staying awake while performing activities and how much of a problem they have had with keeping up enough enthusiasm to get things done. Sleep problems and sleep medication were not used in the analysis because they had a distribution of responses that made it impossible to examine them as exposures, more than one group had less than 10% of the population within them. Sleep quality was distributed uniformly, but sleep latency, sleep duration, and day time dysfunction did not have more than 10% of the population in at least one of the four levels. For all components, we combined levels 2 and 3 together except for sleep quality which did not need to be recoded. Global sleep was given as a contious variable.

3.2 Outcomes

The primary outcomes were inflammation markers found in the blood. A staff phlebotomist obtained blood from an officer, in the morning, who had fasted for 12 hours. The blood was then centrifuged to separate and remove serum and was frozen. To allow for quality control checks and future measurements, an adequate amount of blood must be collected. Samples were stored at -80 C with only an identifying number at the UB biological specimen bank. The biological specimen bank was created as part of the baseline activates of the Western New York Health Study at the Center for Health Research in the Department of Social and Preventive Medicine. Samples were banked in 0.25 ml and directly used for

analytical determinates to avoid exposure to thawing and re-freezing cycles. Quality control for lab analytes included 5% blind replicate assay.

The inflammation markers analyzed were CRP (produced in the liver in response to inflammation); fibrinogen (protein used in blood clot formation); IL-6 (regulates the immune system which have pro- and anti- inflammatory components); and TNF- α (signaling protein involved in systemic inflammation) (23, 90, 91). The assays for the four inflammation markers were performed by laboratory personnel from the University of Vermont. High-sensitivity CRP was measured on serum, heparin-, or EDTA- anticoagulated plasma using BNII nephelometer from Dade Behring utilizing a particle-enhanced immunonephelometric assay. Fibrinogen was measured by using the BNII nephelometer (92). IL-6 was measured by an ultra-sensitive ELISA technique (93). TNF-α was measured using the Human Serum Adipokine Panel B LINCOplex Kit (94).

3.3 Covariates

Basic demographic information, including sex, age, race/ethnicity were viewed as potential covariates. Body mass index (BMI) was calculated from measurements taken by staff who were trained and certified specifically for anthropometric measurements. Height and weight were measured with shoes removed. Height was recorded to the nearest half of a centimeter. Weight was recorded by rounding up to the nearest quarter of a pound. Behavioral factors,

including physical activity, smoking status, and drinks per week were also reviewed as potential covariates.

Shift work was developed as an objective measure through payroll records. Day-to-day accounts of shift work and overtime were compiled for each officer over from beginning of their police career or 1994, whichever came last, to the date of the exam. Shifts were categorized as day shift, start time between 0400 and 1100 hours; afternoon shift, start time between 1200 and 1900 hours; and midnight shift, start time of 2000 and 0300 hours. Officers also were classified into one of those three shifts based on which shift had the largest percentage of hours worked.

The following stress measures were used in the analysis: Spielberger Police Stress Survey (SPSS), Perceived Stress Scale (PSS-14), and Impact of Events-Revised (IES-R). The SPSS consist of 60 items used to report self-reported stress rating and frequency of occurrence. Each item describes an event or condition and is given a stress rating of 0 to 100 and check boxes for the frequency that has occurred within the past month and year. Total stress score is calculated by multiplying the subjective stress rating by the frequency and then adding together all 60 items (95).

The PSS-14 is a measure of global stress levels. It is a 14-item self-reported inventory used to measure the degree to which situations, during the past month, are appraised as stressful on a 5-point scale. The summary score was calculated by reverse coding the scores for the seven positive items and then adding together

the resulting scores for the 14 items. The PSS-14 is internally consistent and recommended when assessing non-specific stress in relation to disease outcomes or behavioral disorders (96, 97).

The IES-R is widely used and noted for providing continuous measures of PTSD symptoms. It consists of 22 items describing the subjective impact of a traumatic event. These are related to three subscales: Intrusion, Avoidance, and Hyperarousal. Each item has a 5-point response measuring how much participants were bothered by these "difficulties" in the past 7 days. Subscales are obtained by calculating the mean of the appropriate items. The overall IES-R is obtained by summing all 22 items (98).

Depressive symptoms are measured using the Center for Epidemiological Studies Depression scale (CESD). This is a 20-item questionnaire with a 4-point scale for each response (99). The scale represents how often each symptom occurred over the past 7 days with the highest score being most of the time. The test is scored by reverse coding appropriate items and then adding together all scores. This scale has been shown to correlate with other measures of depression and shows similar psychometric properties across different populations (100).

3.4 Statistical Analysis

All analyses were performed using SAS® version 9.4 (Cary, North Carolina, USA). The exposure variables were: sleep duration (numeric), sleep efficiency (numeric), sleep latency (numeric), wake-after-sleep onset (numeric), and PSQI

scores (numeric and categorical). The outcome variables were: IL-6 (continuous), TNF-α (numeric), fibrinogen (numeric), and CRP (numeric and categorical). Effect Modifiers were: stress measures (numeric), BMI (categorical), and shift work (categorical). Gender, age, race, ethnicity, education, rank, years of service, work status, smoking status, drinks per week, physical activity score, metabolic syndrome, systolic and diastolic blood pressure, HDL, triglyceride, glucose, insulin, adipose, HBA1C, and leptin were analyzed as potential confounders.

All outcomes and exposures were assessed to verify no more than 10% of people in the sample were missing these values. Subjectively measured sleep-related analyses had a total 457 officers available for analysis and 149 individuals did not have actigraph data. Correlations were performed on the descriptive variables, outcomes, sleep parameters, and stress measures. BMI and waist circumference were highly correlated (0.87), so only BMI was examined as an effect modifier because of the well-known cut points. None of the stress measures showed strong correlations to each other. Hence, all were examined as potential effect modifiers. Correlations for the actigraph measures indicated that time in bed and sleep duration were highly correlated (0.85). We decided to use just sleep duration. Wake after sleep onset and sleep efficiency also were highly correlated (0.92). Both were used in the analysis because WASO measures time they woke up during the night and sleep efficiency is the ratio of time spent asleep and time spent in bed. Sleep duration and sleep efficiency were moderately correlated

(0.75) and the rest of the measures had low correlations. Neither the inflammation markers nor the PSQI measures were highly correlated with each other.

A descriptive table was created using means and standard deviations with test of significance based on *t*-tests for the continuous variables. For categorical variables, frequencies and percentages were determined and chi-square tests were used for significance. PSQI global has a cut point of 5 and was used to classify participants as either having good sleep (PSQI global <5) or bad sleep (PSQI global ≥5) (89). Characteristics were compared between individuals with good sleep and bad sleep. After creating the descriptive table, we compared the descriptive statistics of objective sleep measures to subjective sleep measures since the number of observations for objective measures was 149 less than for subjective measures of sleep. The same procedures were used for this comparison defined for the descriptive table. The difference in shiftwork among the actigraph individuals was also assessed by looking at the distribution between day and evening/night shift workers.

Variable selection was performed for various outcomes and exposures of interest. Possible covariates were added into separate models (e.g., CRP= sleep duration + gender) and any potential covariate with a p value of <0.20 were added to a full model. After the full model was produced, a backward confounder reduction process to remove covariates one at a time was applied. This was performed starting with variables that had p-values >0.05. Once removed, if the beta coefficient for the sleep measure changed more than 10%, the covariate was

retained in the model. Any statistically significant covariates remained in the model as well.

When the final model was made for each immune marker and sleep parameter, the assumptions of linear regression were assessed using the model's residuals. For CRP and IL-6, a cut point of 10 was assigned because CRP mg/L and IL-6 pg/mL levels above 10 are indicative of acute infections. IL-6 then had six more observations coded as missing with the following IL-6 levels: 7.32, 7.33, 8.45, 7.49, 6.55, and 7.04 because these values had high studentized residuals leading to non-normal model residuals. After applying these limitations to CRP and IL-6, the residual graphs showed no violation of the assumptions of linear regression. This held true for TNF-α and fibrinogen.

General linear models were used to conduct the main analysis. GLM allows for calculation of least squares means and 95% confidence intervals for each inflammation markers according to the sleep measure used. Linear regression was performed on all sleep measures (sleep duration, sleep efficiency, sleep latency, WASO, and the PSQI) by each inflammation marker (CRP, IL-6, TNF-α, and fibrinogen) using the final model created during variable selection. Table 3.1 shows the exposures and their data format (i.e., numeric vs. categorical). Sleep duration was categorized into three groups ($\geq$ 7 hours, 7-6 hours, and $\leq$ 6 hours) for the actigraph data because just as not enough sleep is bad so is too much sleep. The middle level of sleep duration for the PSQI components was also used as the referent as well.

It was decided *a priori* that the analysis would be stratified by shiftwork. Adjusted means and 95% confidence intervals for each outcome were obtained for the categorical measures of sleep and beta coefficients with standard errors for the continuous measures by shiftwork category. A similar approach was used for the BMI categories. Interactions between the sleep parameters and stress measures were then assessed to see if stress acts as an effect modifier in the relationship between sleep and inflammation markers. The interactions between the exposures and CESD and PSS were examined. Given the limited number of significant interactions, this information is not tabulated. However, the significant interactions are described in the results in greater detail.

Logistic regression was used for analysis of CRP when it was dichotomized at its standard of 3.0 mg/L (101). Logistic regression was performed for each sleep measure with greater than 3.0 mg/L being the outcome of interest for CRP. Using our logistic model, we obtained the odds ratios and 95% confidence interval for the high-risk levels of CRP.

Table 3.1 Types of Sleep Parameters Used

	Objective	Subjective	Categorical	Numeric
Sleep Efficiency	Yes			Yes
Sleep Duration	Yes			Yes
Sleep onset Latency	Yes			Yes
Wake After Sleep Onset	Yes			Yes
PSQI Sleep Quality		Yes	Yes	
PSQI Sleep Latency		Yes	Yes	
PSQI Daytime Dysfunction		Yes	Yes	
PSQI Sleep Duration		Yes	Yes	
PSQI Global		Yes	Yes	Yes

Abbreviations: PSQI=Pittsburgh Sleep Qualty Index

CHAPTER 4

Results

There was a total of 464 officers in BCOPS during the 2004-2005 data collection time point. However, 7 had missing data for either for all exposures or for all outcomes. The final sample size was 457 with 233 people in the good sleep category and 224 in the bad sleep category as defined by the PSQI. Table 4.1 shows the general characteristics of the participants by good and bad sleep according to the PSQI. Overall the population was primarily white, middle-aged men ranked as police officers. The population also was primarily overweight with a mean BMI of 29.28 ± 4.75 kg/m^2. There was a statistically significant difference between good and bad sleepers for systolic blood pressure (mean= 120.13 vs 122.61 mmHG, respectively, *p*-value=0.03) and drinks per week (mean= 4.68 vs 6.45, respectively *p*-value=<0.01), with bad sleep having higher mean values. No other statistically significant differences were seen.

The objective measures of sleep were missing 149 observations due to missing data. Table 4.2 compares the differences in the general characteristics between those with and without objective measures of sleep. Small statistically significant differences were observed for smoking status where without objective meaures there was a larger present of never smokers compares to those with

objective meaures (67% vs. 54%, respectively, *p*-value=0.04) and systolic blood pressure (mean= 120.40 vs 123.41 mmHG, respectively, *p*-value=0.02). Table 4.3 shows that the distribution of observations between good and bad sleep were almost identical with 233 individuals in the good sleep category and 224 in the bad sleep. Sleep duration distribution shows that more officers were sleeping $\geq$ 6 hours on average. This table also shows that more than 50% of officers were have a poor sleep quality. The population had an average 6.42 global PSQI score, categorized as bad sleep. A descriptive analysis on the objective measures of sleep, presented in Table 4.4, found the average sleep duration was 6.2 $\pm$ 1.4 hours with average sleep efficiency being 84.8 $\pm$ 10.1%. Wake after sleep onset had an average of 54.2 $\pm$ 46.6 minutes. The average minutes of sleep onset latency for all observations in objective sleep measures was 3.6 $\pm$ 3.3. After looking at the distribution of actigraph measures by their shift type there was no significant difference between day and evening/night workers (Table 4.5).

The models that were used for the rest of the analysis are as follows. For all inflammation markers and all PSQI components, models were adjusted for age, systolic blood pressure, and total drinks per week.For all actigraphy metrics, models were adjusted for metabolic syndrome and age. Additionally models with actigraph sleep duration as the exposure were adjusted for systolic blood pressure, total physical activity score, and rank. For models meauresing TNF-α, race and gender were adjusted for as well. For models measuring CRP, additional adjustments for rank were made.

The results from the linear regression of the inflammation markers with the subjective exposure are in Table 4.6. PSQI global, as a numeric exposure, was significantly associated with fibrinogen (beta=-2.15, *p*-value=0.04). The mean of CRP among those in the highest level of daytime dysfunction (worst category) was significantly higher compared to the best level (mean=1.94 vs. 2.63 mg/L, respectively, *p*-value=0.04). These were the only statistically significant associations found between inflammation markers and subjective measures of sleep.

The linear regression with the objective measures of sleep as the exposure are found in Table 4.7. Sleep efficiency was significantly associated with CRP (beta=-0.03, *p*-value=0.02). Sleep onset latency (beta=0.07, *p*-value=0.05) and wake after sleep onset (beta=0.01, *p*-value=<0.01) also were significantly associated with CRP. No other associations were statistically significant.

The interactions between the stress and depression measures (i.e., PSS and CESD) and sleep paramters were examined. It was found that the association between CRP and sleep onset latency was modified by CESD (p-value=0.01). The association between TNF-α and PSQI sleep duration also was modified by the PSS (p-value=0.03). When IL-6 was the outcome, interactions were found between the CESD and PSQI daytime dysfunction component (p-value=0.02). There was an interaction for wake after sleep onset and CESD when modeling fibrinogen (p-value=0.01). CESD and PSS were categorized with cut points (CESD$\geq$16, PSS$\geq$25) indicating high risk (99, 102) to create stratified tables. The relationship between

CRP and sleep onset latency was statistically significant for people with a high CESD score (beta=0.75, p-value=<0.01), but it was not among those with a low CESD score (beta=0.07, p-value=0.06). The relationship between fibrinogen and wake after sleep onset was statistically significant for people with a high CESD score (beta=1.01, p-value=0.01) but it was not among those with a low CESD score (beta=1.06, p-vlaue=0.44). TNF-α was statistical significantly associated with the middle sleep duration category (5-6 hour) for people with a high PSS score compared to the referent category, ($\geq$ 7 hours, means=5.95 vs. 4.71 pg/mL, respectively, p-value=0.02), but not among people with a low PSS score (means=5.01 vs. 5.43 pg/mL, respectively, p-vlaue=0.08). After categorization, there was no statistically significant association found between IL-6 and PSQI daytime dysfunction for CESD.

Among obese officers, the highest level of sleep latency (worst category) was found to be significantly associated with fibrinogen (mean=306.49 vs. 336.26 mg/dL, respectively, p-value=0.03) compared to the best category of sleep latency. Again, in those who are obese, the highest level of daytime dysfunction (worst category) was significantly associated with fibrinogen (means=339.11 vs. 305.23 mg/dL, respectively, p-value=0.05) compared to the best category of daytime dysfunction. There were numerous significant interactions which can be found in Table 4.8. Table 4.9 presents results for stratification by BMI for objective measures of sleep. It was found that sleep onset latency was statistically significantly associated with IL-6 for people with an obese BMI (beta=-0.05, p-

value=0.01). These relationships were not found for normal weight and overweight. No other statistically significant associations for the interaction with BMI for all other outcomes were found.

Lastly, analyses were stratified by shiftwork, with results present in Table 4.10. Daytime dysfunction for the middle category (level 2) was significantly associated with CRP among people working dayshifts (mean=1.98 vs. 3.23 mg/L, respectively, p-value=0.03) compared to the best category of daytime dysfunction. Sleep duration also was found to be significantly associated with IL-6 for day shift workers in the $\geq$ 7 hours category (means=2.43 vs. 1.81 pg/mL, respectively, p-value=0.03) compared to the middle sleep duration level (6-7 hours). For the worst sleep duration category ($\leq$ 5), there also was a significant association with IL-6 for day shift workers (means= 2.37 vs. 1.81 pg/mL, respectively, p-value=0.04) compared to the middle sleep duration level (6-7 hours).

The stratification by shiftwork for the objective measures showed statistically significant associations for CRP and fibrinogen, presented in Table 4.11. Sleep duration was found to be significantly associated with CRP for day shift workers in the $\geq$ 7 hours category (means=3.19 vs. 2.34 mg/L, respectively, p-value=0.02) compared to the middle sleep duration level (6-7 hours). Sleep onset latency (beta=0.20, p-value=0.04) was significantly associated with CRP for day shift workers while the evening/night shift showed no statically significant associations for CRp. Wake after sleep onset (beta=0.006, p-value=0.01) was significantly associated with CRP for evening/night shift workers. This association

was not observed among day shift workers. Sleep duration was found to be significantly associated with fibrinogen for eveing/night shift workers in the $\geq$ 7 hours category (means=377.89 vs. 351.27 pg/mL, respectively, p-value=0.04) compared to the middle sleep duration level (6-7 hours).

CRP has a recognized cut point of $\geq$ 3.0mg/L (101). The results of logistic regression with CRP as a categorical outcome with all of the exposures can be found in Table 4.12. It was found that the odds ratio for a one-unit increase in sleep efficiency was 0.97 (0.95, 0.99) for a CRP $\geq$ 3.0. Logistic regression was repeated for a 5 and a 10 unit increase for the continuous actigraph measures. The 5 unit increases results showed the odds for sleep efficiency was 0.86 (0.76, 0.97), sleep onset latency was 1.47 (1.00, 2.17), and wake after sleep onset was 1.06 (1.02, 1.10) for high-risk CRP. The 10 unit increased the odds for sleep efficiency was 0.74 (0.58, 0.95), sleep onset latency was 2.17 (1.00, 4.71), and wake after sleep onset was 1.12 (1.03, 1.21) for high-risk CRP.

Table 4.1 Characteristics of BCOPS Population by PSQI Global

Parameter	Total (n=457)	Good Sleep (n=233)	Bad Sleep (n=224)	p-value
Gender (n,%)				
Male	343 (75)	180 (39)	163 (36)	0.27
Female	114 (25)	53 (12)	61 (13)	
Race (n,%)				
White	354 (79)	178 (40)	176 (39)	0.56
Other	95 (21)	51 (11)	44 (10)	
Education (n,%)				
<College	60 (13)	36 (8)	24 (5)	
Some College	154 (33)	81 (17)	73 (16)	0.28
Associates Degree	95 (20)	42 (9)	53 (11)	
Bachelors or Grad	155 (33)	81 (17)	74 (16)	
Rank (n,%)				
Police Officer	302 (65)	155 (33)	147 (32)	
Sergeant. Lieutenant, or Captain	75 (16)	37 (8)	38 (8)	0.87
Detective	43 (9)	23 (5)	20 (4)	
Other	44 (9)	25 (5.39)	19 (4.09)	
Metabolic Syndrome (n,%)				
Yes	126 (28)	66 (15)	60 (13)	0.55
No	321 (72)	158 (35)	163 (36)	
Smoking Status (n, %)				
Current	73 (16)	35 (8)	38 (8)	
Former	116 (26)	58 (13)	58 (13)	0.87
Never	263 (58)	135 (30)	128 (28)	
Age (years, mean ± SD)	42.23 ± 8.60	42.32 ± 8.99	42.13 ± 8.18	0.81
Systolic Blood Pressure (mmHG, mean ± SD)	121.35 ± 12.48	120.13 ± 12.13	122.61 ± 12.74	0.03
Physical Activity Score (score, mean ± SD)	21.11 ± 17.97	19.62 ± 16.23	22.65 ± 19.53	0.08
Drinks Per Week (number, mean ± SD)	5.55 ± 9.53	4.68 ± 8.70	6.45 ± 10.25	<0.01
BMI (kg/m^2, mean ± SD)	29.28 ± 4.75	29.24 ± 4.39	29.32 ± 5.11	0.86

Column percentages may not equal 100% due to rounding. Stratum numbers may not equal column total due to missing data. All categorical variable p-values based on chi-squared test and all continues p-values are based on t-tests or Wilcoxon rank sums test. **Abbreviations**: BCOPS=The Buffalo Cardio-Metabolic Occupational Police Stress, PSQI=Pittsburgh Sleep Quality Index, BMI=Body Mass Index. **Cut points:** good sleep<5 PSQI Global, bad sleep>=5 PSQI Global.

Table 4.2 Comparison of BCOPS Population Characteristics by Subjective and Objective Sleep

Parameter	Subjective Measures of Sleep	Objective Measures of Sleep	p-value
	(n=149)	(n=308)	
Gender (n,%)			
Male	120 (81)	223 (72)	0.06
Female	29 (19)	85 (28)	
Race (n,%)			
White	108 (74)	246 (81)	0.08
Other	38 (26)	57 (19)	
Education (n,%)			
<College	15 (11)	38 (12)	
Some College	52 (36)	101 (33)	
Associates Degree	31 (22)	61 (20)	0.74
Bachelors or Grad	45 (32)	108 (35)	
Rank (n,%)			
Police Officer	87 (61)	209 (68)	
Sergeant. Lieutenant, or Captain	27 (19)	41 (13)	0.11
Detective	13 (9)	30 (10)	
Other	16 (11)	28 (9)	
Metabolic Syndrome (n,%)			
Yes	39 (28)	87 (28)	0.87
No	102 (72)	219 (72)	
Smoking Status (n,%)			
Current	18 (12)	55 (18)	
Former	31 (21)	85 (28)	0.04
Never	98 (67)	165 (54)	
Age (years, mean SD)	42.44 ± 8.33	42.12 ± 8.34	0.71
Systolic Blood Pressure (mmHG, mean ± SD)	123.41 ± 13.13	120.40 ± 12.07	0.02
Physical Activity Score (score, mean ± SD)	21.94 ± 16.82	20.73 ± 18.50	0.49
Drinks Per Week (number, mean ± SD)	6.91 ± 12.42	4.89 ± 7.71	0.66
BMI (kg/m^2, mean ± SD)	29.54 ± 4.87	29.15 ± 4.70	0.42

Column percentages may not equal 100% due to rounding. Stratum numbers may not equal column total due to missing data. All categorical variable p-values based on chi-squared test and all continues p-values are based on t-tests or Wilcoxon rank sums test. **Abbreviations**: BCOPS=The Buffalo Cardio-Metabolic Occupational Police Stress, BMI=Body Mass Index.

Table 4.3 Distribution of PSQI Components

Subjective Sleep Measures	Total
	(n=457)
Global PSQI (n,%)	
Good Sleep	224 (49)
Bad sleep	233 (51)
Sleep Quality (n,%)	
0	47 (11)
1	228 (51)
2	139 (31)
3	30 (7)
Sleep Latency (n,%)	
0	142 (32)
1	159 (36)
2	84 (19)
3	57 (13)
Sleep Duration (n,%)	
0	162 (37)
1	141 (32)
2	100 (22)
3	37 (8)
Daytime Dysfunction (n,%)	
0	159 (36)
1	215 (48)
2	59 (13)
3	13 (3)

Column percentages may not equal 100% due to rounding. Stratum numbers may not equal column total due to missing data. **Abbreviations**: PSQI=Pittsburgh Sleep Quality Index. **Cut points:** good sleep<5 PSQI Global, bad sleep>=5 PSQI Global.

Table 4.4 Distribution of Actigraph Measures of Sleep

Objective Sleep Measures	Total
	(n=308)
Sleep Duration (hours, mean ± SD)	6.25 ± 1.38
Sleep Efficiency (%, mean ± SD)	84.85 ± 10.06
Sleep onset latency (minutes, mean ± SD)	3.57 ± 3.25
Wake After Sleep Onset (minutes, mean ± SD)	54.19 ± 46.65

Table 4.5 Distribution of Actigraph Measures of Sleep by Shiftwork

Objective Sleep Measures	Day Shift	Evening/Night Shift
	(n=124)	(n=165)
Sleep Duration (hours, mean ± SD)	6.36 ± 1.47	6.18 ± 1.26
Sleep Efficiency (%, mean ± SD)	85.06 ± 10.40	84.86 ± 9.92
Sleep onset latency (minutes, mean ± SD)	4.01 ± 3.40	3.35 ± 3.23
Wake After Sleep Onset (minutes, mean ± SD)	53.74 ± 60.22	53.83 ± 34.74

Table 4.6. Adjusted Mean Inflammation Markers by PSQI Components

	CRP mg/L	p-value	TNF-α pg/L	p-value
PSQI Global				
Good Sleep (n=216)	2.40 (2.11, 2.69)	ref	5.13 (4.88, 5.38)	ref
Bad sleep (n=212)	2.32 (2.03, 2.61)	0.70	5.30 (5.05, 5.55)	0.34
PSQI Global Continuous	-0.001 (0.03)	0.97	-0.01 (0.03)	0.71
Sleep Quality				
0 (n=41)	2.46 (1.80, 3.11)	ref	5.03 (4.47, 5.59)	ref
1 (n=218)	2.46 (2.17, 2.75)	0.99	5.30 (5.06, 5.55)	0.38
2 (n=128)	2.22 (1.84, 2.59)	0.53	5.18 (4.87, 5.50)	0.64
3 (n=30)	2.36 (1.58, 3.14)	0.85	5.01 (4.33, 5.70)	0.97
Sleep Latency				
0 (n=132)	2.25 (1.88, 2.62)	ref	5.03 (4.72, 5.35)	ref
1 (n=148)	2.50 (2.14, 2.84)	0.35	5.34 (5.03, 5.64)	0.17
2 (n=134)	2.38 (2.01, 2.84)	0.64	5.28 (4.97, 5.60)	0.27
Sleep Duration				
0 (n=134)	2.51 (2.16, 2.86)	0.41	5.32 (5.02, 5.62)	0.57
1 (n=149)	2.29 (1.92, 2.66)	ref	5.20 (4.88, 5.51)	ref
2 (n=129)	2.38 (2.01, 2.75)	0.75	5.15 (4.83, 5.47)	0.83
Day time dysfunction				
0 (n=144)	2.63 (2.28, 2.99)	ref	5.25 (4.95, 5.56)	ref
1 (n=220)	2.33 (2.04, 2.61)	0.18	5.20 (4.96, 5.72)	0.79
2 (n=54)	1.94 (1.36, 2.52)	0.04	5.22 (4.72, 5.72)	0.91

Values represent least-square means and 95% confidence intervals via general linear models. Continuous variables values represent beta coefficient and standard error via general linear models. **Abbreviations**: PSQI=Pittsburgh Sleep Quality Index. **Cut points:** good sleep<5 PSQI Global, bad sleep>=5 PSQI Global. **Adjustments**: All models adjusted for age, systolic blood pressure, and total drinks per week.

Table 4.6. (Continued) Adjusted Mean Inflammation Markers by PSQI Components

	IL-6 pg/mL	p-value	Fibrinogen mg/dL	p-value
PSQI Global				
Good Sleep (n=220)	1.86 (1.72, 2.01)	ref	318.37 (309.20, 327.53)	ref
Bad sleep (n=211)	1.96 (1.81, 2.11)	0.36	307.92 (298.63, 317.22)	0.12
PSQI Global Continuous	0.01 (0.02)	0.59	-2.15 (1.03)	0.04
Sleep Quality				
0 (n=42)	2.00 (1.67, 2.33)	ref	323.32 (302.85, 343.80)	ref
1 (n=217)	1.94 (1.80, 2.09)	0.76	316.83 (307.65, 326.01)	0.57
2 (n=133)	1.88 (1.69, 2.07)	0.53	306.20 (294.59, 317.81)	0.15
3 (n=28)	1.76 (1.34, 2.17)	0.37	305.89 (280.67, 331.12)	0.29
Sleep Latency				
0 (n=134)	1.85 (1.66, 2.04)	ref	320.30 (308.68, 331.91)	ref
1 (n=151)	1.87 (1.69, 2.05)	0.87	312.40 (301.17, 323.63)	0.34
2 (n=132)	2.03 (1.84, 2.22)	0.19	308.65 (297.05, 320.25)	0.17
Sleep Duration				
0 (n=133)	1.93 (1.75, 2.11)	0.49	319.23 (308.03, 330.42)	0.21
1 (n=151)	1.84 (1.65, 2.03)	ref	308.80 (297.17, 320.44)	ref
2 (n=131)	1.99 (1.80, 2.18)	0.27	312.62 (300.66, 324.58)	0.65
Daytime Dysfunction				
0 (n=145)	2.00 (1.82, 2.18)	ref	318.32 (307.09, 329.54)	ref
1 (n=220)	1.89 (1.75, 2.04)	0.34	311.52 (302.41, 320.64)	0.36
2 (n=56)	1.79 (1.50, 2.08)	0.22	311.08 (292.58, 329.49)	0.51

Values represent least-square means and 95% confidence intervals via general linear models. Continuous variables values represent beta coefficient and standard error via general linear models. **Abbreviations**: PSQI=Pittsburgh Sleep Quality Index. **Cut points:** good sleep<5 PSQI Global, bad sleep>=5 PSQI Global. **Adjustments**: All models adjusted for age, systolic blood pressure, and total drinks per week.

Table 4.7. Adjusted Inflammation Markers by Actigraph Measures of Sleep

	CRP mg/L	p-value	TNF-α pg/mL	p-value
Sleep Duration				
$\geq$ 7 hours (n=109)	2.71 (1.8, 3.63)	0.98	5.16 (4.37, 5.94)	0.58
7-6 hours (n=94)	2.54 (1.64, 3.43)	ref	5.25 (4.40, 6.09)	ref
$\leq$ 6 hours (n=94)	2.72 (1.82, 3.62)	0.53	5.01 (4.19, 5.83)	0.73
Sleep Efficiency	-0.03 (0.01)	0.02	0.002 (0.01)	0.87
SOL	0.07 (0.03)	0.05	0.03 (0.03)	0.37
WASO	0.006 (0.002)	<0.01	-0.0004 (0.002)	0.87

Values represent beta coefficients and standard errors via general linear models. Categorical values represent least-square means and 95% confidence intervals via general linear models**. Abbreviations**: SOL= Sleep onset latency, WASO=Wake after sleep onset. **Adjustments**: All models were adjusted for metabolic syndrome and age. Sleep Duration models additional adjusted for systolic blood pressure, total physical activity score, and rank. Models with TNF-α additional adjusted for race and gender. Models with CRP additional adjusted for rank.

Table 4.7. (Continued) Adjusted Inflammation Markers by Actigraph Measures of Sleep

	IL-6 pg/mL	p-value	Fibrinogen mg/dL	p-value
Sleep Duration				
$\geq$ 7 hours (n=108)	2.33 (1.7, 2.98)	0.92	362.06 (322.5, 401.62)	0.13
7-6 hours (n=92)	2.17 (1.51, 2.83)	ref	349.88 (309.16, 390.6)	ref
$\leq$ 6 hours (n=94)	2.32 (1.68, 2.97)	0.31	348 (308.16, 387.83)	0.21
Sleep Efficiency	-0.004 (0.006)	0.51	-0.50 (0.38)	0.19
SOL	-0.03 (0.02)	0.11	1.68 (1.14)	0.14
WASO	0.0004 (0.001)	0.75	0.11 (0.08)	0.18

Values represent beta coefficients and standard errors via general linear models. Categorical values represent least-square means and 95% confidence intervals via general linear models**. Abbreviations**: SOL= Sleep onset latency, WASO=Wake after sleep onset. **Adjustments**: All models were adjusted for metabolic syndrome and age. Sleep Duration models additional adjusted for systolic blood pressure, total physical activity score, and rank. Models with TNF-α additional adjusted for race and gender. Models with CRP additional adjusted for rank.

Table 4.8. Adjusted Mean Inflammation Markers by PSQI Components Stratified by BMI Status

	CRP mg/L	p-value	TNF-α pg/mL	p-value
Normal Weight (18.5-24.9 BMI)				
PSQI Global				
Good Sleep (n=35)	1.86 (1.15, 2.57)	ref	4.53 (3.92, 5.15)	ref
Bad sleep (n=48)	1.71 (1.11, 2.31)	0.75	4.54 (4.00, 5.07)	0.99
PSQI Global Continuous	-0.07 (0.06)	0.25	-0.0003 (0.06)	0.99
Sleep Quality				
0 (n=13)	2.61 (1.46, 3.75)	ref	5.89 (4.90, 6.87)	ref
1 (n=28)	1.77 (0.97, 2.56)	0.24	4.02 (3.34, 4.70)	<0.01
2 (n=32)	1.52 (0.77, 2.26)	0.12	4.57 (3.93, 5.21)	0.03
3 (n=8)	1.75 (0.29, 3.20)	0.36	4.74 (3.48, 5.99)	0.16
Sleep Latency				
0 (n=21)	1.73 (0.83, 2.64)	ref	4.58 (3.80, 5.36)	ref
1 (n=34)	1.77 (1.04, 2.50)	0.96	4.73 (4.08, 5.38)	0.77
2 (n=26)	1.91 (1.10, 2.72)	0.77	4.50 (3.79, 5.20)	0.88
Sleep Duration				
0 (n=23)	2.34 (1.56, 3.12)	0.07	4.76 (4.07, 5.45)	0.55
1 (n=29)	1.25 (0.37, 2.13)	ref	4.45 (3.68, 5.21)	ref
2 (n=28)	1.68 (0.91, 2.46)	0.46	4.58 (3.88, 5.28)	0.80
Daytime Dysfunction				
0 (n=24)	2.41 (1.54, 3.28)	ref	4.78 (4.01, 5.55)	ref
1 (n=42)	1.64 (1.01, 2.28)	0.16	4.26 (3.70, 4.82)	0.28
2 (n=15)	1.32 (0.27, 2.38)	0.12	5.29 (4.35, 6.22)	0.41
Overweight (25.0-29.9 BMI)				
PSQI Global				
Good Sleep (n=98)	2.10 (1.68, 2.52)	ref	4.98 (4.62, 5.34)	
Bad sleep (n=80)	2.05 (1.58, 2.51)	0.86	5.16 (4.77, 5.56)	0.5
PSQI Global Continuous	0.02 (0.05)	0.64	0.05 (0.04)	0.25
Sleep Quality				
0 (n=17)	1.66 (0.66, 2.66)	ref	3.64 (2.82, 4.45)	ref
1 (n=96)	2.14 (1.71, 2.56)	0.39	5.29 (4.92, 5.65)	<0.01
2 (n=49)	1.98 (1.39, 2.57)	0.59	5.23 (4.74, 5.72)	<0.01
3 (n=12)	2.42 (1.17, 3.66)	0.35	4.90 (3.84, 5.97)	0.06
Sleep Latency				
0 (n=65)	2.13 (1.62, 2.65)	ref	4.82 (4.38, 5.27)	ref
1 (n=55)	2.02 (1.46, 2.58)	0.77	4.95 (4.47, 5.44)	0.7
2 (n=52)	2.01 (1.43, 2.58)	0.74	5.50 (5.01, 5.99)	0.05
Sleep Duration				
0 (n=54)	2.13 (1.63, 2.64)	0.34	5.10 (4.67, 5.54)	0.63
1 (n=68)	1.77 (1.21, 2.33)	ref	4.94 (4.45, 5.43)	ref
2 (n=50)	2.34 (1.76, 2.93)	0.16	5.14 (4.63, 5.65)	0.58
Daytime Dysfunction				
0 (n=65)	2.34 (1.84, 2.85)	ref	5.03 (4.60, 5.46)	ref
1 (n=91)	1.93 (1.50, 2.36)	0.22	5.06 (4.68, 5.43)	0.94
2 (n=18)	1.64 (0.67, 2.61)	0.21	5.23 (4.37, 6.09)	0.69
Obese (≥30 BMI)				

PSQI Global				
Good Sleep (n=83)	2.95 (2.50, 3.41)	ref	5.96 (5.57, 6.35)	ref
Bad sleep (n=84)	2.97 (2.51, 3.43)	0.96	5.44 (5.04, 5.83)	0.06
PSQI Global Continuous	0.02 (0.06)	0.74	-0.07 (0.05)	0.13
Sleep Quality				
0 (n=11)	3.43 (2.19, 4.67)	ref	6.23 (5.20, 7.25)	ref
1 (n=94)	3.01 (2.57, 3.44)	0.53	5.69 (5.32, 6.06)	0.33
2 (n=47)	2.92 (2.32, 3.52)	0.47	5.50 (5.01, 5.99)	0.21
3 (n=10)	2.92 (1.60, 4.23)	0.58	5.42 (4.28, 6.55)	0.29
Sleep Latency				
0 (n=46)	2.61 (1.99, 3.22)	ref	5.48 (4.97, 5.99)	ref
1 (n=59)	3.34 (2.80, 3.89)	0.08	6.00 (5.53, 6.46)	0.14
2 (n=56)	2.98 (2.42, 3.53)	0.38	5.46 (4.98, 5.95)	0.96
Sleep Duration				
0 (n=57)	3.04 (2.46, 3.61)	0.64	5.88 (5.38, 6.38)	0.66
1 (n=52)	3.22 (2.67, 3.78)	ref	5.72 (5.25, 6.20)	ref
2 (n=51)	2.84 (2.26, 3.42)	0.35	5.47 (4.97, 5.97)	0.46
Daytime Dysfunction				
0 (n=55)	3.11 (2.55, 3.67)	ref	5.72 (5.24, 6.20)	ref
1 (n=87)	3.08 (2.63, 3.52)	0.93	5.80 (5.41, 6.18)	0.81
2 (n=21)	2.56 (1.65, 3.47)	0.32	5.08 (4.31, 5.84)	0.16

Values represent least-square means and 95% confidence intervals via general linear models. Continuous variables values represent beta coefficient and standard error via general linear models. **Abbreviations**: PSQI=Pittsburgh Sleep Quality Index. **Cut points:** good sleep<5 PSQI Global, bad sleep>=5 PSQI Global. **Adjustments**: All models adjusted for age, systolic blood pressure, and total drinks per week

Table 4.8. (Continued) Adjusted Mean Inflammation Markers by PSQI Components Stratified by BMI Status

	IL-6 pg/mL	p-value	Fibrinogen mg/dL	p-value
Normal Weight (18.5-24.9 BMI)				
PSQI Global				
Good Sleep (n=36)	1.49 (1.13, 1.86)	ref	303.12 (279.90, 326.35)	ref
Bad sleep (n=45)	1.84 (1.52, 2.16)	0.16	290.98 (270.87, 311.09)	0.43
PSQI Global Continuous	0.01 (0.04)	0.71	-2.10 (2.08)	0.32
Sleep Quality				
0 (n=13)	1.83 (1.23, 2.42)	ref	316.90 (279.18, 1354.62)	ref
1 (n=27)	1.71 (1.28, 2.13)	0.74	285.63 (259.55, 311.71)	0.18
2 (n=31)	1.80 (1.41, 2.20)	0.94	300.23 (275.74, 324.73)	0.46
3 (n=8)	1.22 (0.46, 1.98)	0.22	291.90 (244.08, 339.71)	0.42
Sleep Latency				
0 (n=21)	1.49 (1.02, 1.96)	ref	312.96 (283.78, 342.14)	ref
1 (n=33)	1.41 (1.02, 1.79)	0.79	279.72 (255.34, 304.10)	0.08
2 (n=25)	2.27 (1.84, 2.69)	0.02	303.15 (276.64, 329.65)	0.62
Sleep Duration				
0 (n=24)	1.64 (1.22, 2.05)	0.74	308.37 (282.41, 334.33)	0.18
1 (n=28)	1.74 (1.29, 2.19)	ref	282.34 (253.64, 311.05)	ref
2 (n=26)	1.77 (1.35, 2.19)	0.92	295.25 (268.87, 321.63)	0.51
Daytime Dysfunction				
0 (n=23)	2.04 (1.58, 2.51)	ref	327.49 (298.93, 356.05)	ref
1 (n=41)	1.66 (1.33, 2.00)	0.19	284.78 (263.90, 305.65)	0.02
2 (n=15)	1.37 (0.82, 1.92)	0.07	284.36 (249.68, 319.04)	0.06
Overweight (25.0-29.9 BMI)				
PSQI Global				
Good Sleep (n=98)	1.80 (1.59, 2.02)	ref	318.83 (305.7, 332.49)	ref
Bad sleep (n=81)	1.97 (1.73, 2.21)	0.31	307.07 (292.02, 322.12)	0.26
PSQI Global Continuous	0.01 (0.03)	0.71	-3.21 (1.64)	0.05
Sleep Quality				
0 (n=17)	2.11 (1.59, 2.63)	ref	318.85 (287.75, 349.95)	ref
1 (n=95)	1.86 (1.63, 2.08)	0.38	320.81 (306.91, 334.71)	0.91
2 (n=52)	1.88 (1.59, 2.18)	0.45	303.04 (284.29, 321.82)	0.39
3 (n=12)	1.75 (1.10, 2.40)	0.39	292.18 (251.36, 332.99)	0.13
Sleep Latency				
0 (n=65)	1.64 (1.22, 2.05)	ref	310.02 (293.34, 326.69)	ref
1 (n=56)	1.74 (1.29, 2.19)	0.44	314.26 (296.07, 332.45)	0.74
2 (n=53)	1.77 (1.35, 2.19)	0.40	314.45 (296.19, 332.71)	0.73
Sleep Duration				
0 (n=52)	1.92 (1.66, 2.18)	0.57	322.81 (306.38, 339.24)	0.13
1 (n=71)	1.80 (1.50, 2.10)	ref	303.99 (285.67, 322.30)	ref
2 (n=51)	1.94 (1.64, 2.25)	0.52	310.28 (290.97, 329.60)	0.64
Daytime Dysfunction				
0 (n=66)	1.96 (1.70, 2.22)	ref	326.69 (310.55, 342.84)	ref
1 (n=92)	1.88 (1.66, 2.11)	0.67	306.71 (292.63, 320.78)	0.07

2 (n=18)	1.59 (1.09, 2.10)	0.13	297.44 (265.70, 329.18)	0.11
Obese (≥30 BMI)				
PSQI Global				
Good Sleep (n=86)	2.07 (1.84, 2.30)	ref	323.35 (308.71, 337.99)	ref
Bad sleep (n=85)	2.02 (1.79, 2.26)	0.77	318.18 (303.47, 332.90)	0.62
PSQI Global Continuous	0.002 (0.02)	0.93	-1.00 (1.74)	0.57
Sleep Quality				
0 (n=12)	2.01 (1.39, 2.63)	ref	336.30 (397.18, 375.42)	ref
1 (n=95)	2.09 (1.87, 2.32)	0.80	321.69 (307.61, 335.76)	0.49
2 (n=50)	1.92 (1.62, 2.22)	0.79	312.80 (294.16, 331.44)	0.29
3 (n=8)	2.34 (1.57, 3.10)	0.52	333.81 (290.57, 377.05)	0.93
Sleep Latency				
0 (n=48)	2.10 (1.79, 2.41)	ref	336.26 (317.12, 355.40)	ref
1 (n=62)	2.06 (1.78, 2.33)	0.84	327.19 (309.87, 344.51)	0.49
2 (n=54)	2.01 (1.72, 2.31)	0.68	306.49 (288.48, 324.50)	0.03
Sleep Duration				
0 (n=57)	2.10 (1.80, 2.40)	0.40	319.31 (300.5, 338.13)	0.75
1 (n=52)	1.92 (1.63, 2.21)	ref	323.55 (305.78, 341.33)	ref
2 (n=54)	2.15 (1.85, 2.45)	0.26	324.04 (305.44, 342.63)	0.97
Daytime Dysfunction				
0 (n=56)	2.05 (1.76, 2.34)	ref	305.23 (287.35, 323.12)	ref
1 (n=87)	2.01 (1.78, 2.24)	0.83	328.78 (314.58, 342.98)	0.04
2 (n=23)	2.22 (1.77, 2.67)	0.54	339.11 (310.57, 367.67)	0.05

Values represent least-square means and 95% confidence intervals via general linear models. Continuous variables values represent beta coefficient and standard error via general linear models. **Abbreviations**: PSQI=Pittsburgh Sleep Quality Index. **Cut points:** good sleep<5 PSQI Global, bad sleep>=5 PSQI Global. **Adjustments**: All models adjusted for age, systolic blood pressure, and total drinks per week

Table 4.9 Adjusted Inflammatory Markers by Actigraph Measures of Sleep Stratified by BMI Status

	CRP mg/L	p-value	TNF-α pg/mL	p-value
Normal Weight (18.5-24.9 BMI)				
Sleep Duration				
≥ 7 hours (n=17)	2.28 (1.06, 3.51)	0.34	4.64 (3.49, 5.79)	0.90
7-6 hours (n=27)	1.74 (0.63, 2.84)	ref	4.71 (3.64, 5.78)	ref
≤ 6 hours (n=18)	2.32 (1.12, 3.52)	0.31	4.88 (3.71, 6.05)	0.76
Sleep Efficiency	-0.03 (0.02)	0.15	0.02 (0.02)	0.37
SOL	0.10 (0.08)	0.24	0.008 (0.07)	0.91
WASO	0.01 (0.008)	0.10	-0.01 (0.007)	0.10
Overweight (25.0-29.9 BMI)				
Sleep Duration				
≥ 7 hours (n=37)	2.29 (1.26, 3.32)	0.61	4.72 (3.75, 5.69)	0.23
7-6 hours (n=41)	2.51 (1.54, 3.48)	ref	5.23 (4.26, 6.2)	ref
≤ 6 hours (n=45)	2.55 (1.57, 3.54)	0.91	4.76 (3.83, 5.69)	0.24
Sleep Efficiency	0.02 (0.02)	0.46	0.02 (0.03)	0.38
SOL	0.07 (0.08)	0.39	0.14 (0.08)	0.08
WASO	-0.002 (0.007)	0.74	-0.008 (0.007)	0.29
Obese (≥30 BMI)				
Sleep Duration				
≥ 7 hours (n=55)	3.34 (2.35, 4.33)	0.98	5.47 (4.63, 6.3)	0.88
7-6 hours (n=26)	3.33 (2.23, 4.43)	ref	5.40 (4.38, 6.42)	ref
≤ 6 hours (n=31)	3.19 (2.12, 4.26)	0.78	5.15 (4.16, 6.13)	0.60
Sleep Efficiency	-0.02 (0.02)	0.34	0.002 (0.02)	0.92
SOL	0.01 (0.05)	0.77	-0.02 (0.04)	0.67
WASO	0.004 (0.003)	0.12	0.00003 (0.003)	0.99

Values represent beta coefficients and standard errors via general linear models. **Abbreviations**: SOL= Sleep onset latency, WASO=Wake after sleep onset. **Adjustments**: All models were adjusted for metabolic syndrome and age. Sleep Duration models additional adjusted for systolic blood pressure, total physical activity score, and rank. Models with TNF-α additional adjusted for race and gender. Models with CRP additional adjusted for rank

Table 4.9 (Continued) Adjusted Inflammatory Markers by Actigraph Measures of Sleep Stratified by BMI Status

	IL-6 pg/mL	p-value	Fibrinogen mg/dL	p-value
Normal Weight (18.5-24.9 BMI)				
Sleep Duration				
≥ 7 hours (n=16)	2.02 (1.21, 2.83)	0.58	327.44 (278.0, 376.88)	0.80
7-6 hours (n=25)	1.83 (1.05, 2.61)	ref	322.15 (274.58, 369.73)	ref
≤ 6 hours (n=18)	2.36, 1.56, 3.17)	0.11	348.77 (299.98, 398.15)	0.19
Sleep Efficiency	-0.007 (0.02)	0.67	-0.22 (0.85)	0.80
SOL	-0.005 (0.06)	0.92	3.65 (2.84)	0.20
WASO	0.002 (0.006)	0.74	0.22 (0.29)	0.46
Overweight (25.0-29.9 BMI)				
Sleep Duration				
≥ 7 hours (n=36)	2.45 (1.72, 3.17)	0.50	367.23 (323.95, 412.51)	0.40
7-6 hours (n=41)	2.28 (1.58, 2.97)	ref	355.37 (312.43, 398.32)	ref
≤ 6 hours (n=44)	2.23 (1.54, 2.92)	0.85	346.28 (304.22, 388.34)	0.53
Sleep Efficiency	-0.01 (0.01)	0.41	0.05 (0.87)	0.96
SOL	-0.008 (0.05)	0.87	4.70 (2.64)	0.08
WASO	0.003 (0.004)	0.44	0.03 (0.24)	0.91
Obese (≥30 BMI)				
Sleep Duration				
≥ 7 hours (n=56)	2.34 (1.68, 3.01)	0.77	364.7 (323.97, 405.42)	0.52
7-6 hours (n=26)	2.27 (1.51, 3.02)	ref	354.86 (308.76, 400.97)	ref
≤ 6 hours (n=32)	2.37 (1.64, 3.1)	0.72	340.96 (296.2, 385.72)	0.41
Sleep Efficiency	0.003 (0.008)	0.70	-0.67 (0.5)	0.19
SOL	-0.05 (0.02)	0.01	-0.10 (1.41)	0.95
WASO	-0.0006 (0.001)	0.67	0.09 (0.09)	0.33

Values represent beta coefficients and standard errors via general linear models. **Abbreviations**: SOL= Sleep onset latency, WASO=Wake after sleep onset. **Adjustments**: All models were adjusted for metabolic syndrome and age. Sleep Duration models additional adjusted for systolic blood pressure, total physical activity score, and rank. Models with TNF-α additional adjusted for race and gender. Models with CRP additional adjusted for rank

Table 4.10. Adjusted Mean Inflammation Markers by PSQI Components Stratified by Shiftwork Status

	CRP mg/L	p-value	TNF-α pg/mL	p-value
Day				
PSQI Global				
Good Sleep (n=104)	2.59 (1.90, 3.28)	ref	5.45 (4.85, 6.04)	ref
Bad sleep (n=74)	2.31 (1.72, 2.89)	0.52	5.23 (4.72, 5.73)	0.59
PSQI Global Continuous	-0.07 (0.07)	0.35	-0.003 (0.06)	0.95
Sleep Quality				
0 (n=22)	3.06 (0.95, 5.16)	ref	4.66 (2.98, 6.34)	ref
1 (n=87)	2.37 (1.74, 3.00)	0.54	5.38 (4.82, 5.94)	0.42
2 (n=46)	2.50 (1.79, 3.21)	0.62	5.35 (4.76, 5.94)	0.45
3 (n=14)	1.68 (-0.05, 3.40)	0.32	5.20 (3.66, 6.74)	0.64
Sleep Latency				
0 (n=61)	2.46 (1.53, 3.38)	ref	5.46 (4.71, 6.21)	ref
1 (n=61)	2.63 (1.87, 3.38)	0.78	5.04 (4.37, 5.70)	0.41
2 (n=48)	2.15 (1.45, 2.84)	0.60	5.37 (4.77, 5.98)	0.86
Sleep Duration				
0 (n=53)	2.71 (1.84, 3.58)	0.60	5.18 (4.43, 5.92)	0.93
1 (n=69)	2.41 (1.68, 3.13)	ref	5.22 (4.59, 5.85)	ref
2 (n=47)	2.17 (1.41, 2.92)	0.66	5.51 (4.85, 6.16)	0.53
Daytime Dysfunction				
0 (n=70)	3.23 (2.45, 4.00)	ref	5.49 (4.8, 6.17)	ref
1 (n=78)	1.98 (1.36, 2.60)	0.01	5.12 (4.58, 5.65)	0.40
2 (n=22)	2.15 (1.12, 3.18)	0.10	5.63 (4.71, 6.55)	0.81
Evening/Night				
PSQI Global				
Good Sleep (n=98)	2.45 (2.11, 2.78)	ref	5.32 (5.03, 5.61)	ref
Bad sleep (n=131)	2.39 (2.04, 2.73)	0.81	5.10 (5.03, 5.61)	0.30
PSQI Global Continuous	0.01 (0.04)	0.73	-0.02 (0.03)	0.56
Sleep Quality				
0 (n=18)	2.45 (1.75, 3.15)	ref	5.06 (4.45, 5.67)	ref
1 (n=118)	2.56 (2.22, 2.89)	0.79	5.33 (5.03, 5.62)	0.45
2 (n=78)	2.19 (1.74, 3.64)	0.54	5.13 (4.74, 5.52)	0.86
3 (n=14)	2.57 (1.66, 3.47)	0.85	4.89 (4.09, 5.69)	0.73
Sleep Latency				
0 (n=64)	2.23 (1.81, 2.65)	ref	4.94 (4.58, 5.31)	ref
1 (n=80)	2.53 (2.12, 2.94)	0.32	5.43 (5.07, 5.78)	0.06
2 (n=81)	2.56 (2.12, 2.99)	0.29	5.28 (4.9, 5.67)	0.21
Sleep Duration				
0 (n=76)	2.59 (2.19, 2.93)	0.41	5.38 (5.03, 5.73)	0.60
1 (n=71)	2.34 (1.90, 2.77)	ref	5.24 (4.59, 5.63)	ref
2 (n=78)	2.41 (1.96, 2.84)	0.83	5.01 (4.62, 5.39)	0.39
Daytime Dysfunction				
0 (n=64)	2.54 (2.12, 2.95)	ref	5.19 (4.83, 5.55)	ref
1 (n=134)	2.49 (2.16, 2.82)	0.86	5.25 (4.96, 5.54)	0.79
2 (n=30)	1.93 (1.21, 2.65)	0.15	5.11 (4.47, 5.75)	0.84

Values represent least-square means and 95% confidence intervals via general linear models. Continuous variables values represent beta coefficient and standard error via general linear models. **Abbreviations**: PSQI=Pittsburgh Sleep Quality Index. **Cut points:** good sleep<5 PSQI Global, bad sleep>=5 PSQI Global. **Adjustments**: All models adjusted for age, systolic blood pressure, and total drinks per week

Table 4.10 (Continued) Adjusted Mean Inflammation Markers by PSQI Components Stratified by Shiftwork Status

	IL-6 pg/mL	p-value	Fibrinogen mg/dL	p-value
Day				
PSQI Global				
Good Sleep (n=102)	1.99 (1.66, 2.33)	ref	321.79 (299.62, 343.96)	ref
Bad sleep (n=74)	2.33 (2.03, 2.62)	0.14	314.09 (295.64, 332.55)	0.60
PSQI Global Continuous	0.001 (0.04)	0.97	-3.08 (2.49)	0.22
Sleep Quality				
0 (n=22)	2.88 (1.93, 3.82)	ref	323.69 (262.33, 385.05)	ref
1 (n=85)	1.95 (1.63, 2.27)	0.07	320.1 (299.43, 340.78)	0.91
2 (n=47)	2.31 (1.97, 2.66)	0.27	311.74 (290.1, 333.38)	0.72
3 (n=13)	2.49 (1.63, 3.36)	0.56	323.79 (267.56, 380.03)	0.99
Sleep Latency				
0 (n=58)	2.39 (1.94, 2.83)	ref	330.38 (302.13, 358.63)	ref
1 (n=63)	2.08 (1.70, 2.46)	0.30	318.02 (293.56, 342.49)	0.51
2 (n=47)	1.96 (1.73, 2.19)	0.42	310.86 (288.65, 333.07)	0.28
Sleep Duration				
0 (n=51)	2.43 (2.01, 2.85)	0.03	332.33 (304.48, 360.18)	0.16
1 (n=69)	1.81 (1.45, 2.18)	ref	306.75 (283.55, 329.95)	ref
2 (n=47)	2.37 (1.99, 2.74)	0.04	317.24 (293.32, 341.16)	0.53
Daytime Dysfunction				
0 (n=68)	2.35 (1.96, 2.75)	ref	324.98 (299.7, 350.27)	ref
1 (n=78)	2.15 (1.85, 2.46)	0.43	312.45 (292.66, 332.23)	0.44
2 (n=22)	1.96 (1.44, 2.48)	0.24	315.82 (281.98, 349.65)	0.67
Evening/Night				
PSQI Global				
Good Sleep (n=103)	1.83 (1.66, 2.00)	ref	316.72 (306.06, 327.38)	ref
Bad sleep (n=130)	1.81 (1.63, 1.98)	0.85	306.52 (295.33, 317.71)	0.19
PSQI Global Continuous	0.004 (0.02)	0.84	-2.01 (1.18)	0.09
Sleep Quality				
0 (n=19)	1.84 (1.49, 2.20)	ref	323.94 (301.64, 346.24)	ref
1 (n=118)	1.93 (1.76, 2.10)	0.66	314.73 (303.83, 325.63)	0.47
2 (n=82)	1.70 (1.48, 1.93)	0.51	305.26 (290.9, 319.62)	0.17
3 (n=13)	1.50 (1.03, 1.98)	0.26	298.79 (269.44, 328.14)	0.18
Sleep Latency				
0 (n=68)	1.72 (1.51, 1.93)	ref	316.54 (303.15, 329.92)	ref
1 (n=81)	1.83 (1.61, 2.02)	0.50	310.66 (297.48, 323.85)	0.54
2 (n=80)	1.96 (1.73, 2.19)	0.13	309.29 (295.08, 323.49)	0.47
Sleep Duration				
0 (n=76)	1.84 (1.64, 2.04)	0.87	318.07 (305.23, 330.90)	0.41
1 (n=73)	1.81 (1.59, 0.03)	ref	310.10 (296.06, 324.13)	ref
2 (n=80)	1.85 (1.62, 2.07)	0.83	307.90 (293.66, 322.14)	0.83
Daytime Dysfunction				
0 (n=67)	1.86 (1.65, 2.07)	ref	315.72 (302.33, 329.1)	ref
1 (n=134)	1.82 (1.66, 1.99)	0.79	311.53 (300.85, 322.2)	0.63
2 (n=31)	1.75 (1.39, 2.11)	0.61	308.1 (284.6, 331.59)	0.58

Values represent least-square means and 95% confidence intervals via general linear models. Continuous variables values represent beta coefficient and standard error via general linear models. **Abbreviations**: PSQI=Pittsburgh Sleep Quality Index. **Cut points:** good sleep<5 PSQI Global, bad sleep>=5 PSQI Global. **Adjustments**: All models adjusted for age, systolic blood pressure, and total drinks per week

Table 4.11 Adjusted Inflammatory Markers by Actigraph Measures of Sleep Stratified by Shiftwork Status

	CRP mg/L	p-value	TNF-α pg/mL	p-value
Day				
Sleep Duration				
$\geq$ 7 hours (n=39)	2.46 (1.44, 3.49)	0.13	5.01 (4.14, 5.88)	0.35
7-6 hours (n=40)	3.10 (2.08, 4.120	ref	5.41 (4.44, 6.39)	ref
$\leq$ 6 hours (n=39)	2.78 (1.83, 3.85)	0.46	4.73 (3.76, 5.70)	0.10
Sleep Efficiency	-0.06 (0.03)	0.04	-0.009 (0.03)	0.73
SOL	0.20 (0.10)	0.04	0.12 (0.08)	0.16
WASO	0.02 (0.009)	0.08	0.00002 (0.008)	0.99
Evening/ Night				
Sleep Duration				
$\geq$ 7 hours (n=63)	3.19 (2.19, 4.18)	0.02	5.38 (4.44, 6.32)	0.71
7-6 hours (n=48)	2.34 (1.36, 3.32)	ref	5.24 (4.25, 6.23)	ref
$\leq$ 6 hours (n=39)	2.83 (1.81, 3.85)	0.21	5.38 (4.43, 6.33)	0.72
Sleep Efficiency	-0.02 (0.01)	0.05	0.002 (0.01)	0.88
SOL	0.04 (0.04)	0.26	0.02 (0.04)	0.68
WASO	0.006 (0.003)	0.01	-0.0003 (0.003)	0.89

Values represent beta coefficients and standard errors via general linear models. **Abbreviations**: SOL= Sleep onset latency, WASO=Wake after sleep onset. **Adjustments**: All models were adjusted for metabolic syndrome and age. Sleep Duration models additional adjusted for systolic blood pressure, total physical activity score, and rank. Models with TNF-α additional adjusted for race and gender. Models with CRP additional adjusted for rank

Table 4.11 (Continued) Adjusted Inflammatory Markers by Actigraph Measures of Sleep Stratified by Shiftwork Status

	IL-6 pg/mL	p-value	Fibrinogen mg/dL	p-value
Day				
Sleep Duration				
≥ 7 hours (n=39)	2.16 (1.49, 2.84)	0.75	357.43 (315.84, 399.02)	0.56
7-6 hours (n=39)	2.24 (1.51, 2.97)	ref	366.34 (321.93, 410.75)	ref
≤ 6 hours (n=38)	2.26 (1.57, 2.94)	0.95	351.45 (309.22, 393.69)	0.32
Sleep Efficiency	-0.02 (0.02)	0.22	-0.58 (0.92)	0.53
SOL	-0.01 (0.05)	0.84	-0.13 (3.11)	0.97
WASO	0.006 (0.005)	0.25	0.14 (0.27)	0.61
Evening/ Night				
Sleep Duration				
≥ 7 hours (n=62)	2.78 (2.06, 3.50)	0.16	377.89 (334.15, 421.62)	0.04
7-6 hours (n=47)	2.48 (1.76, 3.20)	ref	351.27 (307.04, 395.51)	ref
≤ 6 hours (n=88)	2.75 (2.03, 3.47)	0.21	355.80 (311.51, 400.09)	0.74
Sleep Efficiency	-0.00008 (0.007)	0.99	-0.53 (0.43)	0.22
SOL	-0.03 (0.02)	0.15	2.07 (1.27)	0.10
WASO	-0.00002 (0.001)	0.99	0.11 (0.09)	0.23

Values represent beta coefficients and standard errors via general linear models. **Abbreviations**: SOL= Sleep onset latency, WASO=Wake after sleep onset. **Adjustments**: All models were adjusted for metabolic syndrome and age. Sleep Duration models additional adjusted for systolic blood pressure, total physical activity score, and rank. Models with TNF-α additional adjusted for race and gender. Models with CRP additional adjusted for rank

Table 4.12. Crude and Adjusted Odds Ratio of CRP by PSQI and Actigraph Measures of Sleep

	Present (n,%)	Absent (n,%)	Crude (Odds Ratio, 95% CI)	Adjusted (Odds Ratio, 95% CI)
Actigraph Sleep Measures				
Sleep Duration				
≥ 7 hours	42 (43)	72 (34)	0.82 (0.46, 1.45)	1.22 (0.64, 2.32)
7-6 hours	25 (25)	73 (35)	Referent	Referent
≤ 6 hours	31 (32)	65 (31)	0.59 (0.33, 1.06)	1.17 (0.60, 2.28)
Sleep Efficiency			0.97 (0.94,0.99)	0.97 (0.95, 0.99)
SOL			1.11 (1.03, 1.20)	1.08 (1.00, 1.17)
WASO			1.01 (1.00, 1.02)	1.01 (1.00, 1.02)
PSQI Sleep Measures				
PSQI Global				
Good Sleep	74 (51)	159 (51)	Referent	Referent
Bad sleep	70 (49)	154 (49)	0.98 (0.67, 1.45)	0.91 (0.60, 1.36)
PSQI Global Continuous			1.00 (0.94, 1.07)	0.99 (0.93, 1.05)
Sleep Quality				
0	15 (11)	32 (11)	Referent	Referent
1	73 (52)	155 (51)	1.01 (0.51, 1.97)	0.92 (0.46, 1.84)
2	43 (31)	96 (32)	0.96 (0.47, 1.95)	0.84 (0.41, 1.76)
3	9 (6)	21 (7)	0.91 (0.34, 2.47)	0.74 (0.27, 2.07)
Sleep Latency				
0	47 (34)	95 (31)	Referent	Referent
1	47 (34)	112 (37)	0.85 (0.52, 1.38)	0.86 (0.52, 1.42)
2	45 (32)	96 (32)	0.95 (0.58, 1.56)	0.85 (0.51, 1.41)
Sleep Duration				
0	53 (38)	109 (36)	1.15 (0.70, 1.87)	1.30 (0.79, 2.15)
1	42 (30)	99 (23)	Referent	Referent
2	46 (33)	91 (30)	1.19 (0.72, 1.98)	1.16 (0.69, 1.94)
Day time dysfunction				
0	58 (41)	101 (33)	Referent	Referent
1	67 (47)	161 (53)	0.73 (0.47, 1.12)	0.68 (0.44, 1.06)
2	17 (12)	42 (14)	0.71 (0.37, 1.35)	0.76 (0.39, 1.48)

Column percentages may not equal 100% due to rounding. Stratum numbers may not equal column total due to missing data. Odds ratios obtained through simple logistic regression. **Abbreviations**: PSQI=Pittsburgh Sleep Quality Index. **Cut points:** good sleep<5 PSQI Global, bad sleep>=5 PSQI Global. **Adjustments for Subjective**: All models adjusted for age, systolic blood pressure, and total drinks per week. **Adjustments for Objective**: All models were adjusted for metabolic syndrome and age. Sleep Duration models additional adjusted for systolic blood pressure, total physical activity score, and rank. Models with TNF-α additional adjusted for race and gender. Models with CRP additional adjusted for rank.

CHAPTER 5

Discussion

We found that CRP levels were significantly higher in individuals with the most daytime dysfunction compared to those with the least dysfunction. We also found that as the global PSQI scores increased, fibrinogen levels significantly decreased. After stratifying by BMI, sleep quality levels 1 and 2 (the middle levels of sleep quality) were statistically significantly associated with TNF-α in normal-weight and overweight individuals compared to sleep level 0 (the best level of sleep quality). Normal-weight individuals with mid-level daytime dysfunction (level 1) and obese individuals with any daytime dysfunction (levels 1 and 2) had significantly higher fibrinogen levels compared to individuals with the least daytime dysfunction (level 0). As global PSQI score increased, fibrinogen levels decreased in overweight individuals. Overweight individuals with the worst sleep latency (level 2) had significantly higher levels of TNF-α compared to those with the least sleep latency (level 0). In addition, obese individuals with the worst sleep latency also had the highest levels of fibrinogen. After stratification by BMI, actigraph measures showed significant associations in the obese category only. As sleep-onset latency increased, IL-6 levels significantly decreased in obese individuals.

After stratifying by shift work, we found that day shift workers with mid-level daytime dysfunction (level 1) had significantly increased CRP levels compared to those with the least daytime dysfunction (level 0). For day shift workers, a sleep duration of 5-6 hours was significantly associated with higher IL-6 levels compared to a sleep duration of >7 hours. There was no significant association between inflammation markers and PSQI components for evening/night shift workers. Some significant associations between CRP and objective measures of sleep were seen when analyses were stratified by shiftwork. As sleep duration increased, CRP levels significantly decreased in day shift workers. In addition, as sleep-onset latency increased in day shift workers, CRP also significantly increased. For evening/night shift workers, as wake after sleep onset increased, CRP also significantly increased. After categorizing CRP into high and low risk clinical cut point, we found that every one-unit increase in sleep efficiency led to an odds ratio of 0.97 (0.95, 0.99) for a CRP >3.0.

Both the Heart and Soul Study and a cross-sectional study using 2005-2006 National Health and Nutrition Examination Survey (NHANES) data investigated the associations between sleep quality using subjective measures of sleep and inflammation (18, 28). These studies found no association between sleep quality and IL-6, CRP, or fibrinogen. The study using NHANES data did, however, find a significant association for all three inflammatory markers using the PSQI when looking at women over a 5-year period (28). This study found a J-shaped relationship between sleep quality, assessed using the Sleep Disorders

Questionnaire, and CRP (28). Two additional gender-restricted studies also examined sleep quality and inflammatory markers, with some similarities to our study: these studies each showed increased levels of CRP in individuals with poor sleep or low sleep quality (55, 56), which is consistent with our finding that as sleep efficiency increased, CRP levels decreased.

However, some of our findings contrasted with those of previous research studies on inflammation markers and sleep. The 2000 and 2006 Social Environment and Biomarkers of Aging Study performed in Taiwan by Dowd et al. showed no association between inflammation markers and overall sleep quality but did find that longer sleep durations (>8 hours) were associated with higher levels of CRP, IL-6, and fibrinogen (20). The sleep measures used by Dowd et al. were collected using a modified PSQI, making them comparable to our study's use of subjective markers. Although Dowd et al. found no association between sleep quality and inflammation, we did find a statistically significant association between sleep quality and fibrinogen when we stratified our analyses by BMI. In their analysis, Dowd et al. controlled for waist circumference, which is generally highly correlated with BMI. Dowd et al. found that sleep quality differed depending on the individual's waist circumference, although they may have masked the effect of sleep quality by not stratifying their analyses (20). It is possible that waist circumference lies on the causal pathway between sleep and inflammation, and it would therefore would be inappropriate to adjust for waist circumference. Our findings regarding PSQI measurements were consistent with those of Dowd and

colleagues. We found statistically significant associations between sleep duration, as a PSQI component, and IL-6, but only among day shift workers after stratifying by shiftwork status. Using actograph sleep measures after stratifying by shiftwork, the day shift group showed a significant negative association between sleep duration and CRP levels in the current study. This, is in contrast to what was found by Dowd et al. in their Taiwanese population (20).

An ancillary study to the Netherlands Study of Depression and Anxiety showed similar results to those of the Dowd et al. study mentioned above. In this ancillary study, significantly higher levels of CRP and IL-6 were found in individuals with longer sleep durations (19). Prather et al. used subjective sleep measures to obtain individuals' sleep exposure and controlled for BMI. The study population comprised individuals diagnosed with depression or anxiety. In this analysis, depression (CESD) and anxiety (PSS) affected the association between inflammation markers and sleep. Although our analysis did not have a high enough sample size to justify stratifying by these measures, the Prather et al. study did, which may partially explain our contradictory results with regard to CRP (19).

A study using both subjective and objective measures of sleep found positive associations between sleep duration and CRP, as well as sleep duration and IL-6 (25). Using an objective measure of sleep, Patel et al. showed that sleep duration and TNF-α were inversely related. However, the analysis using actigraph data showed no significant relationship between TNF-α and sleep measures. This analysis did find that compared to the lowest level of sleep quality, PSQI-assessed

sleep quality at every level but the highest was significantly associated with TNF-α in normal-weight and overweight individuals. The discrepancy in sleep duration results between our study and Patel et al. could be due to the differing study populations used. Patel et al. used individuals enrolled in the Cleveland Family Clinic, a longitudinal cohort designed to study the genetics of obstructive sleep apnea (OSA) (25). Although police officers and individuals with sleep apnea do have comparable traits in sleep habits, there are key factors that burden police officers that are different from those factors at play in the Patel et al. study (25). However, the results of our logistic regression analysis are consistent with what was found by Patel et al. in patients with OSA, indicating that poor sleep is associated with higher levels of CRP (57). These results show that there are effect modifiers for the relationship between sleep and inflammation markers.

When comparing our results to these previous studies, there are two major aspects that differ. First, we used both subjective measures of sleep from the PSQI and objective measures of sleep from actigraphy. Most sleep studies use a self-reported questionnaire, such as the PSQI. Relying on self-reported information can cause misclassification of exposure because the participant must recall sleeping patterns from the last month or longer. Objective measures of sleep are reliant on the accuracy of the measurement tool used, for example, the actiwatch. Participants do not need to try to remember how long it took them to fall asleep once they got into bed because the actiwatch can monitor heart rate and electronically record when sleep begins. Objective measurements are the more

reliable option but can be unrealistic and expensive in large cohort studies or nested studies (103).

A key difference between this study and previous studies of sleep and inflammation is our use of police officers as the study population. Police officers have a different lifestyle compared to people in other occupations. Police officers are exposed to a higher level of occupational stress and varying work shifts, both of which are strong contributors to sleep disruption. Occupational stress occurs when the stimuli an individual is exposed to in his or her work environment cause psychological changes. The more an individual is exposed to this stimulus, the more likely it is that psychological stress will cause physiological changes (17). The physiological changes brought about by stress can cause individuals to lose sleep or experience poor sleep. This effect may be exacerbated by poor stress management frequently found among police officers (13). Shiftwork also has a role in police officers' sleep patterns. The purpose of shiftwork is to provide services 24 hours a day; this is important in professions that need continuous coverage (e.g., healthcare and law enforcement). Shift workers may consistently work one of the three 8-hour shifts that makes up the 24 hours in a day (day shift, evening shift, or night shift), or they may be on a rotating shift schedule in which their shift is not fixed, longer than 8 hours, and/or rotates between day and evening/night shifts. Working at night, while an individual's circadian clock is in sleep mode, can cause disrupted circadian rhythms, which are associated with many health risks (80). The differences between police officers and the populations

examined in previous studies are vast and should be considered when we compare the results of our study to those of others.

There is a strong link between the immune system and the quality of sleep an individual receives. This is because the immune system is regulated by a circadian cycle that modifies the function of the immune system over the course of the day (104). Cytokines, or inflammation markers, are at their highest levels in the blood at night and their lowest levels in the morning (104). The immune system causes inflammation by releasing pro-inflammatory cytokines when an infection or injury occurs (104). Inflammation can then be turned off by the immune system once the infection or injury has been repaired (104). Inflammation can persist past the time of injury or infection for a number of reasons. It has been observed that poor sleep can cause an increase in pro-inflammatory cytokines (104). If sleep does not occur at the length or level needed, the body will try to offset this disruption by increasing sleep-wake regulation cytokines. Because cytokines such as TNF-α and IL-6 are pro-inflammatory and are involved in sleep-wake regulation, it makes biological sense that a person's sleep duration shortens or sleep quality lessens when these cytokines becomes elevated (105).

The other inflammatory markers analyzed were CRP and fibrinogen. C-reactive protein is an indicator for cardiovascular disease (CVD), as those at risk for CVD present higher levels of CRP (91). Because CRP is regulated independently from circadian rhythms, it is easy to see how sleep affects this inflammation marker

directly (104). Increased CRP can indicate long-term effects of sleep on inflammation, whereas fibrinogen can measure short-term acute effects (106).

Body mass index has shown to have an inverse association with sleep duration (107). This association has been researched extensively because of the rising obesity epidemic (107). There is some dispute as to whether sleep is the cause or a consequence of obesity. Studies involving children have shown a strong relationship between sleep duration and weight gain, whereas studies involving adults showed poor sleep as both a cause and consequence of weight gain (107).

The link between body fat and inflammation is better understood. The inflammatory response caused by obesity is very different from the normal inflammatory response during injury or infection (108). The trigger for this response occurs in adipose tissue and is due to an excess consumption of food. When excess macronutrients are consumed over a long period of time, metabolic signals engage with inflammatory pathways to introduce low levels of inflammatory cytokines. The adipose tissue then becomes altered to favor high levels of pro-inflammatory cytokines. Once this change occurs, the metabolic rate decreases, and the inflammatory state in adipose tissue becomes persistent (108).

When stratified by BMI, our findings are consistent with hypotheses presented in previous studies. When using BMI as an effect modifier, we found significant results related to sleep latency rather than sleep duration, as had been found in previous studies (107). Here, decreases in sleep quality and poor sleep overall were associated with increases of inflammatory markers in normal and

overweight individuals but not in the obese population. Most of the associations between sleep measures and inflammatory markers were found in the overweight group. The sample sizes for the overweight (n=187) and obese (n=180) groups were almost equal, so the reason for the increased associations with inflammatory markers seen in the overweight group could be due to processes occurring at a cellular level in obese individuals. Adipose tissue is associated with inflammation, and obese individuals have larger amounts of adipose tissue than overweight or normal-weight individuals. The presence of this large amount of adipose tissue may mask the effect of poor sleep (109).

Another factor influencing sleep and inflammatory markers is shift work. Shift work is associated with a host of chronic diseases, as well as disrupted sleep and increased fatigue (75). This disruption in sleep is caused by displaced work hours that can change frequently for individuals employed in shiftwork jobs. Environmental light can cause phase changes in the body's circadian rhythm, where evening light causes a delay and morning light causes an advancement (110). When an individual transitions from a normal sleep-wake schedule to working an evening/night shift, he or she must adapt to a different sleep-wake schedule. Therefore, individuals working evening/night shifts or switching between day and evening/night shifts will suffer from circadian disruption, and their sleep quality and duration will suffer (110). Because of this circadian disruption, we expect people working evening/night shifts to have higher levels of daytime dysfunction and lower sleep quality.

Shiftwork is associated with increased risk of cardiovascular disease (111). Just as sleep is affected by shiftwork, inflammation also is affected by shiftwork (112). Studies indicate that evening/night and alternating shiftwork cause an increase in inflammatory markers that are not seen in people working normal day shifts (82). A study performed using BCOPS data examined the association between shiftwork and immune cells and demonstrated that night shifts are associated with elevated levels of leukocytes (80). This association between shiftwork and immune cells suggests that there might be an elevation of inflammatory markers in night shift workers (43).

Here we found results for the PSQI measures that were contradictory to those in previous studies. We found that compared to the lowest level of daytime dysfunction, a moderate level of daytime dysfunction was significantly associated with CRP in day shift workers. We also found that a sleep duration of 6-7 hours was significantly associated with IL-6 levels in day shift workers but not in night shift workers compared to sleep duration of >7 hours. As sleep duration increased among day shift workers, CRP levels decreased, and as sleep-onset latency increased, CRP levels increased. We found that among evening/night shift workers, wake after sleep onset was positively associated with CRP. The association between sleep duration and CRP for day shift workers might indicate that these individuals tend to sleep longer, leading to more opportunity to observe the effect of sleep on inflammation. This could also signify that the time participants are sleeping during the night might have more of a restorative effect.

Stress also affects sleep and inflammation. Stress is present in all individuals and can cause problems with sleep such as difficulties falling asleep and large WASO intervals (113). Difficulty falling asleep is caused by increased arousal with delayed sleep onset (113). Individuals in high-stress situations experience shorter duration of sleep compared to those in low-stress situations (113). We would expect police officers, in general, to have elevated levels of stress. Stress is a risk factor for depression, and inflammatory markers are one mechanism by which depression occurs (114). According to the social signal transduction theory of depression, stress causes an upregulation of the immune system, and pro-inflammatory cytokines specifically. An increase in pro-inflammatory cytokines has a role in behavior and can cause changes that include depressive symptoms (114). Using this theory, we would expect police officers to have elevated levels of inflammatory markers and worse sleep as scores on stress measures and depression tests increase.

We investigated stress as an effect modifier but only found three significant associations. Sleep-onset latency was statistically associated with CRP in people with a high CESD score but not for individuals with a low CESD score. Wake after sleep onset latency was statistically associated with fibrinogen, but not among individuals with a low CESD score. A sleep duration of 6-7 hours was statistically associated with TNF-α in individuals with a high PSS score but not those with a low PSS score. These findings reinforce the theory of stress and inflammatory markers, but not for all levels of CESD score. It is possible that we did not see

associations at all levels of CESD score because all police officers are exposed to high levels of occupational stress, so there was no reference group that had no exposure to stress.

A major strength of this study was the use of both subjective and objective measures of sleep. This allowed for a measure of sleep that was not subject to recall bias, making it more reliable. Using both measures also allowed us to understand participants' perception of their sleep (PSQI), in conjunction with their actual objective sleep characteristics (actigraph). Another strength was the use of electronic payroll records for classification of shiftwork because it allowed for calculation of total hours worked per shift and placed people in their most-worked category. Using four different inflammatory markers allowed us to observe the impact of sleep on two inflammatory markers that are sleep regulators and two that are not sleep regulators. We were also able to examine differences in associations with CRP and fibrinogen between long-term and short-term shiftwork. Previous studies have looked at all four of these markers in relation to sleep but have seldom investigated all four together.

Along with the strengths, there were limitations in this study. The BCOPS population is not generalizable to other occupational groups because of the stress and shiftwork present in these occupations (17, 84). Blood was only drawn once, in the morning, meaning we had to assume that inflammatory markers collected at a single timepoint were characteristic of chronically elevated levels. In addition, inflammatory markers are at their lowest in the morning, which could have

prevented us from capturing chronic elevation of some inflammatory markers and may be responsible for the lack of associations found (104). There also is the possibility of a healthy worker effect within the police population. The healthy worker effect describes the phenomenon that employed individuals are usually healthier than the general population (115). In this case, there are primary components to the healthy worker effect. First, individuals must undergo a medical examination to become employed as police officers. Those too sick to pass the examination could not be hired as police officers and therefore could not be part of our study population. Second, the environment in which police officers work can cause people to leave because of disease or health complaints (115). It could be that the police officers that work the night shift do so because they have increased coping skills, and people that did not have these skills quit or switched to the day shift. Night shift workers could be healthier in this regard, drawing our results towards the null. This could have influenced the association between sleep and inflammation by shiftwork categories (115).

CHAPTER 6

Conclusion

Significant associations were found between different inflammation markers and sleep exposures. This study's findings indicate that sleep can affect police officers' health and potentially lead to an increased risk of disease. Future longitudinal research should be done on this association, which would allow researchers to examine changes in inflammation over time. This type of study could help capture chronic inflammation and explain its temporality. A more diverse population should be used because police officers experience high levels of occupational stress and are not generalizable to the overall population. With a large diverse population, the findings would have a larger clinical impact. The actigraphy data also could be measured more frequently and for longer periods of time.

The findings from this study support evidence that can be translated into public health practice. If sleep is found to be associated with inflammation in a longitudinal study, especially among high-stress occupations, education and intervention programs could be designed to target high-risk populations, such as police officers. For example, police officers could be made aware of the risk of poor sleep among shift workers, and officers could be urged to follow sleep duration

guidelines and not try to follow the sleep-wake schedule mandated by their assigned shifts on their days off. Regular tracking of blood inflammation levels among police officers may help identify individuals in need of additional assistance in improving their sleep patterns to reduce risk of future disease.

REFERENCES

1. Kolla BP, Mansukhani S, Mansukhani MP. Consumer sleep tracking devices: a review of mechanisms, validity and utility. Expert Rev Med Devic. 2016;13(5):497-506.
2. Zisapel N. Sleep and sleep disturbances: biological basis and clinical implications. Cell Mol Life Sci. 2007;64(10):1174-86.
3. Curtis AM, Bellet MM, Sassone-Corsi P, O'Neill LA. Circadian clock proteins and immunity. Immunity. 2014;40(2):178-86.
4. Vgontzas AN, Zoumakis E, Bixler EO, Lin HM, Follett H, Kales A, et al. Adverse effects of modest sleep restriction on sleepiness, performance, and inflammatory cytokines. J Clin Endocrinol Metab. 2004;89(5):2119-26.
5. Berger J. A two-clock model of circadian timing in the immune system of mammals. Pathol Biol (Paris). 2008;56(5):286-91.
6. Lange T, Dimitrov S, Born J. Effects of sleep and circadian rhythm on the human immune system. Ann N Y Acad Sci. 2010;1193:48-59.
7. Ryan GB, Majno G. Acute inflammation. A review. Am J Pathol. 1977;86(1):183-276.
8. Melnicoff MJ, Horan PK, Morahan PS. Kinetics of changes in peritoneal cell populations following acute inflammation. Cell Immunol. 1989;118(1):178-91.
9. Doherty DE, Downey GP, Worthen GS, Haslett C, Henson PM. Monocyte retention and migration in pulmonary inflammation. Requirement for neutrophils. Lab Invest. 1988;59(2):200-13.
10. Gabay C. Interleukin-6 and chronic inflammation. Arthritis Res Ther. 2006;8 Suppl 2:S3.
11. Bastard JP, Maachi M, Lagathu C, Kim MJ, Caron M, Vidal H, et al. Recent advances in the relationship between obesity, inflammation, and insulin resistance. Eur Cytokine Netw. 2006;17(1):4-12.
12. Wirth M, Vena JE, Smith EK, Bauer SE, Violanti J, Burch J. The epidemiology of cancer among police officers. Am J Ind Med. 2013;56(4):439-53.
13. Lucas T, Weidner N, Janisse J. Where does work stress come from? A generalizability analysis of stress in police officers. Psychol Health. 2012;27(12):1426-47.
14. Miller PR, Partrick MS, Hoth JJ, Meredith JW, Chang MC. A practical application of practice-based learning: development of an algorithm for empiric antibiotic coverage in ventilator-associated pneumonia. J Trauma. 2006;60(4):725-9; discussion 9-31

15. Depner CM, Stothard ER, Wright KP, Jr. Metabolic consequences of sleep and circadian disorders. Curr Diab Rep. 2014;14(7):507.
16. Sookoian S, Gemma C, Fernandez Gianotti T, Burgueno A, Alvarez A, Gonzalez CD, et al. Effects of rotating shift work on biomarkers of metabolic syndrome and inflammation. J Intern Med. 2007;261(3):285-92.
17. Violanti JM, Burchfiel CM, Miller DB, Andrew ME, Dorn J, Wactawski-Wende J, et al. The Buffalo Cardio-Metabolic Occupational Police Stress (BCOPS) pilot study: methods and participant characteristics. Ann Epidemiol. 2006;16(2):148-56.
18. Prather AA, Epel ES, Cohen BE, Neylan TC, Whooley MA. Gender differences in the prospective associations of self-reported sleep quality with biomarkers of systemic inflammation and coagulation: findings from the Heart and Soul Study. J Psychiatr Res. 2013;47(9):1228-35.
19. Prather AA, Vogelzangs N, Penninx BW. Sleep duration, insomnia, and markers of systemic inflammation: results from the Netherlands Study of Depression and Anxiety (NESDA). J Psychiatr Res. 2015;60:95-102.
20. Dowd JB, Goldman N, Weinstein M. Sleep duration, sleep quality, and biomarkers of inflammation in a Taiwanese population. Ann Epidemiol. 2011;21(11):799-806.
21. Grandner MA, Buxton OM, Jackson N, Sands-Lincoln M, Pandey A, Jean-Louis G. Extreme sleep durations and increased C-reactive protein: effects of sex and ethnoracial group. Sleep. 2013;36(5):769-79E.
22. Irwin MR, Wang M, Campomayor CO, Collado-Hidalgo A, Cole S. Sleep deprivation and activation of morning levels of cellular and genomic markers of inflammation. Arch Intern Med. 2006;166(16):1756-62.
23. Vgontzas AN, Papanicolaou DA, Bixler EO, Lotsikas A, Zachman K, Kales A, et al. Circadian interleukin-6 secretion and quantity and depth of sleep. J Clin Endocrinol Metab. 1999;84(8):2603-7.
24. Meier-Ewert HK, Ridker PM, Rifai N, Regan MM, Price NJ, Dinges DF, et al. Effect of sleep loss on C-reactive protein, an inflammatory marker of cardiovascular risk. J Am Coll Cardiol. 2004;43(4):678-83.
25. Patel SR, Zhu X, Storfer-Isser A, Mehra R, Jenny NS, Tracy R, et al. Sleep duration and biomarkers of inflammation. Sleep. 2009;32(2):200-4.
26. Janko KA, Comella, C.L., Morrissey, M. Two measures of nocturnal sleep in Parkinson's disease: Correlation of actigraph measures and the Pittsburgh Sleep Quality Index. Neurology. 2001;56(8):A21.
27. Youngstedt SD, Goff EE, Reynolds AM, Kripke DF, Irwin MR, Bootzin RR, et al. Has adult sleep duration declined over the last 50+years? Sleep Med Rev. 2016;28:69-85.
28. Kanagasabai T, Ardern CI. Inflammation, Oxidative Stress, and Antioxidants Contribute to Selected Sleep Quality and Cardiometabolic Health Relationships: A Cross-Sectional Study. Mediators Inflamm. 2015;2015:824589.
29. Jean-Louis G, Kripke DF, Ancoli-Israel S. Sleep and quality of well-being. Sleep. 2000;23(8):1115-21.

30. Pilcher JJ, Ginter DR, Sadowsky B. Sleep quality versus sleep quantity: relationships between sleep and measures of health, well-being and sleepiness in college students. J Psychosom Res. 1997;42(6):583-96.
31. Bryant PA, Trinder J, Curtis N. Sick and tired: Does sleep have a vital role in the immune system? Nat Rev Immunol. 2004;4(6):457-67.
32. Hastings MH, Maywood ES, Reddy AB. Two decades of circadian time. J Neuroendocrinol. 2008;20(6):812-9.
33. Majde JA, Krueger JM. Links between the innate immune system and sleep. J Allergy Clin Immunol. 2005;116(6):1188-98.
34. Beersma DG. Models of human sleep regulation. Sleep Med Rev. 1998;2(1):31-43.
35. Maquet P. The role of sleep in learning and memory. Science. 2001;294(5544):1048-52.
36. Yaggi HK, Araujo AB, McKinlay JB. Sleep duration as a risk factor for the development of type 2 diabetes. Diabetes Care. 2006;29(3):657-61.
37. Gangwisch JE, Heymsfield SB, Boden-Albala B, Buijs RM, Kreier F, Pickering TG, et al. Short sleep duration as a risk factor for hypertension: analyses of the first National Health and Nutrition Examination Survey. Hypertension. 2006;47(5):833-9.
38. Ayas NT, White DP, Manson JE, Stampfer MJ, Speizer FE, Malhotra A, et al. A prospective study of sleep duration and coronary heart disease in women. Arch Intern Med. 2003;163(2):205-9.
39. Roth T, Ancoli-Israel S. Daytime consequences and correlates of insomnia in the United States: results of the 1991 National Sleep Foundation Survey. II. Sleep. 1999;22 Suppl 2:S354-8.
40. Dijk DJ, Lockley SW. Integration of human sleep-wake regulation and circadian rhythmicity. J Appl Physiol (1985). 2002;92(2):852-62.
41. Labrecque N, Cermakian N. Circadian Clocks in the Immune System. J Biol Rhythms. 2015;30(4):277-90.
42. Kizaki T, Sato S, Shirato K, Sakurai T, Ogasawara J, Izawa T, et al. Effect of Circadian Rhythm on Clinical and Pathophysiological Conditions and Inflammation. Crit Rev Immunol. 2015;35(4):261-75.
43. Scheiermann C, Kunisaki Y, Frenette PS. Circadian control of the immune system. Nat Rev Immunol. 2013;13(3):190-8.
44. Wirth M, Burch J, Violanti J, Burchfiel C, Fekedulegn D, Andrew M, et al. Association of the Period3 clock gene length polymorphism with salivary cortisol secretion among police officers. Neuro Endocrinol Lett. 2013;34(1):27-37.
45. Huang XL, Fu CJ, Bu RF. Role of circadian clocks in the development and therapeutics of cancer. J Int Med Res. 2011;39(6):2061-6.
46. Chrousos GP. Stress and disorders of the stress system. Nat Rev Endocrinol. 2009;5(7):374-81.
47. Opp MR. Sleep and psychoneuroimmunology. Immunol Allergy Clin North Am. 2009;29(2):295-307.

48. Haus E, Smolensky MH. Biologic rhythms in the immune system. Chronobiol Int. 1999;16(5):581-622.
49. Petrovsky N. Towards a unified model of neuroendocrine-immune interaction. Immunol Cell Biol. 2001;79(4):350-7.
50. Hermann C, von Aulock S, Dehus O, Keller M, Okigami H, Gantner F, et al. Endogenous cortisol determines the circadian rhythm of lipopolysaccharide-- but not lipoteichoic acid--inducible cytokine release. Eur J Immunol. 2006;36(2):371-9.
51. Lange T, Dimitrov S, Fehm HL, Born J. Sleep-like concentrations of growth hormone and cortisol modulate type1 and type2 in-vitro cytokine production in human T cells. Int Immunopharmacol. 2006;6(2):216-25.
52. Xing Z, Braciak T, Jordana M, Croitoru K, Graham FL, Gauldie J. Adenovirus-mediated cytokine gene transfer at tissue sites. Overexpression of IL-6 induces lymphocytic hyperplasia in the lung. J Immunol. 1994;153(9):4059-69.
53. Atreya R, Mudter J, Finotto S, Mullberg J, Jostock T, Wirtz S, et al. Blockade of interleukin 6 trans signaling suppresses T-cell resistance against apoptosis in chronic intestinal inflammation: evidence in crohn disease and experimental colitis in vivo. Nat Med. 2000;6(5):583-8.
54. Haack M, Sanchez E, Mullington JM. Elevated inflammatory markers in response to prolonged sleep restriction are associated with increased pain experience in healthy volunteers. Sleep. 2007;30(9):1145-52.
55. Okun ML, Coussons-Read M, Hall M. Disturbed sleep is associated with increased C-reactive protein in young women. Brain Behav Immun. 2009;23(3):351-4.
56. Almeida OP, Alfonso H, Yeap BB, Hankey G, Flicker L. Complaints of difficulty to fall asleep increase the risk of depression in later life: the health in men study. J Affect Disord. 2011;134(1-3):208-16.
57. Li K, Wei P, Qin Y, Wei Y. Is C-reactive protein a marker of obstructive sleep apnea?: A meta-analysis. Medicine (Baltimore). 2017;96(19):e6850.
58. de Heredia FP, Gomez-Martinez S, Marcos A. Obesity, inflammation and the immune system. Proc Nutr Soc. 2012;71(2):332-8.
59. Marti A, Marcos A, Martinez JA. Obesity and immune function relationships. Obes Rev. 2001;2(2):131-40.
60. Hotamisligil GS. Inflammation and metabolic disorders. Nature. 2006;444(7121):860-7.
61. Cappuccio FP, Taggart FM, Kandala NB, Currie A, Peile E, Stranges S, et al. Meta-analysis of short sleep duration and obesity in children and adults. Sleep. 2008;31(5):619-26.
62. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the United States, 2011-2012. JAMA. 2014;311(8):806-14.
63. Ogilvie RP, Patel SR. The epidemiology of sleep and obesity. Sleep Health. 2017;3(5):383-8.

64. Meyer KA, Wall MM, Larson NI, Laska MN, Neumark-Sztainer D. Sleep duration and BMI in a sample of young adults. Obesity (Silver Spring). 2012;20(6):1279-87.
65. Cohen S, Kessler, R.C., Gordon, L.U. Measuring Stress. New York: Oxford University Press. 1997

3-28.
66. Chrousos GP, Gold PW. The concepts of stress and stress system disorders. Overview of physical and behavioral homeostasis. JAMA. 1992;267(9):1244-52.
67. Violanti JM. Predictors of police suicide ideation. Suicide Life Threat Behav. 2004;34(3):277-83.
68. Hodgins GA, Creamer M, Bell R. Risk factors for posttrauma reactions in police officers: a longitudinal study. J Nerv Ment Dis. 2001;189(8):541-7.
69. Violanti JM, Vena JE, Petralia S. Mortality of a police cohort: 1950-1990. Am J Ind Med. 1998;33(4):366-73.
70. Williams MA, Petratis MM, Baechle TR, Ryschon KL, Campain JJ, Sketch MH. Frequency of physical activity, exercise capacity, and atherosclerotic heart disease risk factors in male police officers. J Occup Med. 1987;29(7):596-600.
71. Franke WD, Cox DF, Schultz DP, Anderson DF. Coronary heart disease risk factors in employees of Iowa's Department of Public Safety compared to a cohort of the general population. Am J Ind Med. 1997;31(6):733-7.
72. Rosmond R, Bjorntorp P. Endocrine and metabolic aberrations in men with abdominal obesity in relation to anxio-depressive infirmity. Metabolism. 1998;47(10):1187-93.
73. Rosmond R, Dallman MF, Bjorntorp P. Stress-related cortisol secretion in men: relationships with abdominal obesity and endocrine, metabolic and hemodynamic abnormalities. J Clin Endocrinol Metab. 1998;83(6):1853-9.
74. Gibson EL, Checkley S, Papadopoulos A, Poon L, Daley S, Wardle J. Increased salivary cortisol reliably induced by a protein-rich midday meal. Psychosom Med. 1999;61(2):214-24.
75. Akerstedt T. Shift work and disturbed sleep/wakefulness. Occup Med (Lond). 2003;53(2):89-94.
76. Straif K, Baan R, Grosse Y, Secretan B, El Ghissassi F, Bouvard V, et al. Carcinogenicity of shift-work, painting, and fire-fighting. Lancet Oncol. 2007;8(12):1065-6.
77. Violanti JM, Burchfiel CM, Hartley TA, Mnatsakanova A, Fekedulegn D, Andrew ME, et al. Atypical work hours and metabolic syndrome among police officers. Arch Environ Occup Health. 2009;64(3):194-201.
78. Puttonen S, Harma M, Hublin C. Shift work and cardiovascular disease - pathways from circadian stress to morbidity. Scand J Work Environ Health. 2010;36(2):96-108.
79. Arble DM, Bass J, Laposky AD, Vitaterna MH, Turek FW. Circadian timing of food intake contributes to weight gain. Obesity (Silver Spring). 2009;17(11):2100-2.

80. Wirth MD, Andrew ME, Burchfiel CM, Burch JB, Fekedulegn D, Hartley TA, et al. Association of shiftwork and immune cells among police officers from the Buffalo Cardio-Metabolic Occupational Police Stress study. Chronobiol Int. 2017;34(6):721-31.
81. Lu LF, Wang CP, Tsai IT, Hung WC, Yu TH, Wu CC, et al. Relationship between shift work and peripheral total and differential leukocyte counts in Chinese steel workers. J Occup Health. 2016;58(1):81-8.
82. Puttonen S, Viitasalo K, Harma M. Effect of shiftwork on systemic markers of inflammation. Chronobiol Int. 2011;28(6):528-35.
83. Kim SW, Jang EC, Kwon SC, Han W, Kang MS, Nam YH, et al. Night shift work and inflammatory markers in male workers aged 20-39 in a display manufacturing company. Ann Occup Environ Med. 2016;28:48.
84. Rajaratnam SM, Barger LK, Lockley SW, Shea SA, Wang W, Landrigan CP, et al. Sleep disorders, health, and safety in police officers. JAMA. 2011;306(23):2567-78.
85. Ambulatory Monitoring, INC. Ardsley, NY.
86. Shrivastava D, Jung S, Saadat M, Sirohi R, Crewson K. How to interpret the results of a sleep study. J Community Hosp Intern Med Perspect. 2014;4(5):24983.
87. Grandner MA, Kripke DF, Yoon IY, Youngstedt SD. Criterion validity of the Pittsburgh Sleep Quality Index: Investigation in a non-clinical sample. Sleep Biol Rhythms. 2006;4(2):129-39.
88. Knutson KL, Rathouz PJ, Yan LL, Liu K, Lauderdale DS. Stability of the Pittsburgh Sleep Quality Index and the Epworth Sleepiness Questionnaires over 1 year in early middle-aged adults: the CARDIA study. Sleep. 2006;29(11):1503-6.
89. Buysse DJ, Reynolds CF, 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989;28(2):193-213.
90. Lawrence T, Gilroy DW. Chronic inflammation: a failure of resolution? Int J Exp Pathol. 2007;88(2):85-94.
91. Pearson TA, Mensah GA, Alexander RW, Anderson JL, Cannon RO, 3rd, Criqui M, et al. Markers of inflammation and cardiovascular disease: application to clinical and public health practice: A statement for healthcare professionals from the Centers for Disease Control and Prevention and the American Heart Association. Circulation. 2003;107(3):499-511.
92. Dade Behring Inc. Deerfield, IL.
93. R&D Systems. Minneapolis, MN.
94. Linco Research, Inc. St Charles, MO.
95. Spielberger CD, Westberry, L.G., Grier, K.S., Greenfield, G. The Police Stress Survey: sources of stress in law enforcement Human Resources Institute Monograph Series Three, No 6 1981.
96. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. J Health Soc Behav. 1983;24(4):385-96.

97. Hewitt P, Flett, G., Mosher, S., . The Perceived Stress Scale: Factor structure and relation to depression symptoms in a psychiatric sample. Journal of Psychopathology. 1992;14(3):247-57.
98. Weathers FW LB, Herman DS, Huska JA, Keane TM. The PTSD Checklist (PCL): reliability, validity, and diagnostic utility. Presented at the Annual meeting of the International Society of Traumatic Stress Studies. 1993.
99. I M. The center for epidemiologic studies depression scale (CES-D). . 2006:305-8.
100. LS R. The CES-D scale: A self-report depression scale for research in the general population. Applied Psychological Measurements. 1977;1(3):385-401.
101. Wirth MD, Burch J, Shivappa N, Violanti JM, Burchfiel CM, Fekedulegn D, et al. Association of a dietary inflammatory index with inflammatory indices and metabolic syndrome among police officers. J Occup Environ Med. 2014;56(9):986-9.
102. Martelli TA, Waters LK, Martelli J. The police stress survey: reliability and relation to job satisfaction and organizational commitment. Psychol Rep. 1989;64(1):267-73.
103. Sadeh A, Hauri PJ, Kripke DF, Lavie P. The role of actigraphy in the evaluation of sleep disorders. Sleep. 1995;18(4):288-302.
104. Simpson N, Dinges DF. Sleep and inflammation. Nutr Rev. 2007;65(12 Pt 2):S244-52.
105. Motivala S, Irwin, M. Sleep and Immunity: Cytokine Pathways Linking Sleep and Health Outcomes. Current Directions in Psychological Science. 2007;16(1):21-5.
106. Matthews KA, Zheng H, Kravitz HM, Sowers M, Bromberger JT, Buysse DJ, et al. Are inflammatory and coagulation biomarkers related to sleep characteristics in mid-life women?: Study of Women's Health across the Nation sleep study. Sleep. 2010;33(12):1649-55.
107. Patel SR, Hu FB. Short sleep duration and weight gain: a systematic review. Obesity (Silver Spring). 2008;16(3):643-53.
108. Gregor MF, Hotamisligil GS. Inflammatory mechanisms in obesity. Annu Rev Immunol. 2011;29:415-45.
109. Rakotoarivelo V, Lacraz G, Mayhue M, Brown C, Rottembourg D, Fradette J, et al. Inflammatory Cytokine Profiles in Visceral and Subcutaneous Adipose Tissues of Obese Patients Undergoing Bariatric Surgery Reveal Lack of Correlation With Obesity or Diabetes. EBioMedicine. 2018.
110. Drake CL, Roehrs T, Richardson G, Walsh JK, Roth T. Shift work sleep disorder: prevalence and consequences beyond that of symptomatic day workers. Sleep. 2004;27(8):1453-62.
111. Vyas MV, Garg AX, Iansavichus AV, Costella J, Donner A, Laugsand LE, et al. Shift work and vascular events: systematic review and meta-analysis. BMJ. 2012;345:e4800.

112. Viitasalo K, Puttonen S, Kuosma E, Lindstrom J, Harma M. Shift rotation and age - interactions with sleep-wakefulness and inflammation. Ergonomics. 2015;58(1):65-74.
113. Sadeh A, Keinan G, Daon K. Effects of stress on sleep: the moderating role of coping style. Health Psychol. 2004;23(5):542-5.
114. Slavich GM, Irwin MR. From stress to inflammation and major depressive disorder: a social signal transduction theory of depression. Psychol Bull. 2014;140(3):774-815.
115. Meijers JM, Swaen GM, Volovics A, Lucas LJ, van Vliet K. Occupational cohort studies: the influence of design characteristics on the healthy worker effect. Int J Epidemiol. 1989;18(4):970-5.