

**SLEEP, HEALTH-RELATED BIOLOGICAL FUNCTION AND  
WELL-BEING**

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**This thesis is submitted for the Degree of Doctor of Philosophy, UCL**

## **STUDENT DECLARATION**

I, Marta Jackowska, confirm that the work presented in this thesis is my own.

Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Signed:

Date:

## **ABSTRACT**

Sleep patterns are linked to cardiovascular outcomes and psychological well-being, but gaps in knowledge remain. This thesis tested four aspects of the relationships between sleep, cardiovascular risk and well-being using different methods of investigation; an analysis of a large population dataset (the English Longitudinal Study of Aging (Study 1), an investigation of affective and biological responses in everyday life of working women (Studies 2, 3), and a short-term well-being intervention (Study 4).

Studies 1 and 2 tested whether direct biological dysregulation may be in part responsible for higher risk of cardiovascular outcomes in poor sleepers. Study 1 found that in older adults longer sleep was correlated with elevated inflammation, while short sleep was associated with low haemoglobin. Disturbed sleep was more prevalent among those with higher inflammation, lower dehydroepiandrosterone sulfate and haemoglobin as well as anaemia. These relationships were found mostly in men, but nonetheless they emphasise that self-reported sleep has important biological correlates in older adults. Study 2 extended data from experimental studies to real life settings, and found that disturbed sleep is related to lower heart rate variability (HRV). This suggests that lower HRV, a marker of dysfunctional autonomic activity, may be another pathway contributing towards higher risk of cardiovascular outcomes in poor sleepers.

Study 3 compared objective and subjective measures of sleep efficiency and discovered that psychosocial characteristics including work stress and social support are related to underestimations of sleep efficiency, in comparison with objective measures. Thus

associations between self-reported sleep and health-related factors may be overestimated in studies based on self-report.

Study 4 aimed to induce positive well-being in a randomised controlled trial, to test whether this would lead to improvements in sleep. Well-being was increased post-intervention, but improvements in sleep were marginal. Importantly, changes in well-being were correlated with beneficial alternations in subjective sleep, tentatively suggesting that positive well-being may exert protective effects on (self-reported) sleep.

In combination, these studies contribute to the research literature relating sleep problems with cardiovascular risk and poor psychological well-being.

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I dedicate this PhD to my parents and in particular my dearest father. From a very young age he instilled a thirst for knowledge and independent thinking in me that have both served me very well indeed. My dad's belief in me has made me believe in myself. Thank you.

I hope I will be forgiven for writing this dedication in Polish as well: Ta praca doktorancka jest zadedykowana moim rodzicom, a zwłaszcza mojemu ojcu. Od bardzo młodego wieku moj ojciec zakorzenił we mnie głód wiedzy i niezależnego myślenia, które posłużyły mi bardzo dobrze w życiu. Wiara mojego taty we mnie pozwoliła mi uwierzyć w siebie. Dziękuję.



## **LIST OF ABBREVIATIONS**

AHI apnoea-hypopnoea index

ANCOVA analysis of covariance

ANOVA analysis of variance

ANS autonomic nervous system

APA American Psychiatric Association

ARIC Atherosclerosis Risk in Communities (study)

ATRAMI Autonomic Tone and Reflexes After Myocardial Infarction (study)

BMI body mass index

CAPI computer assisted personal interview

CARDIA Coronary Artery Risk Development in Young Adults (study)

CES-D Centre for Epidemiologic Studies Depression scale

CHD coronary heart disease

C.I. Confidence Interval

CRP C-reactive protein

CVD cardiovascular disease

DHEA dehydroepiandrosterone

DHEAS dehydroepiandrosterone sulfate

DRM Day Reconstruction Method

DSM-IV Diagnostic and Statistical Manual of Mental Disorders –Fourth Edition

ECG electrocardiograph

EEG electroencephalogram

ELSA English Longitudinal Study of Ageing

EMG electromyogram

EOG electrooculogram

GHQ-12 12 item-General Health Questionnaire

GQ-6 Gratitude Questionnaire-6

HADS Hospital Anxiety and Depression Scale

HPA hypothalamic-pituitary-adrenal (axis)

HR heart rate

HR hazard ratio

HRV heart rate variability

HUNT Nord-Trøndelag Health Study

HR hazard ratio

IL-6 interleukin-6

ISEL Interpersonal Support Evaluation List

JACC Japan Collaborative Cohort

LSD least-significant (test)

LVET left ventricular ejection time

MI myocardial infarction

MIDUS Mid-life in the US survey

MORGEN Monitoring Project on Risk factors for Chronic Diseases (study)

N-N normal to normal (intervals)

NREM non-rapid eye movement

OR odds ratio

OSA obstructive sleep apnoea

PA parasympathetic activity

PANAS Positive and Negative Affect Schedule

PEP pre-ejection period

PPIs positive psychology intervention studies

PSG polysomnography

PSQI Pittsburgh sleep quality index

REM rapid eye movement

RLS restless leg syndrome

RMSSD root mean square of the successive standard differences

RR Risk Ratio

SA sympathetic activity

SDB sleep disordered breathing

SEM standard error of the mean

SES socio-economic status

SOF Study of Osteoporotic Fractures

SPANES Scale of Positive and Negative Experience

SPSS Statistical Packages for the Social Sciences

SWAN Study of Women's Health Across the Nation

SV stroke volume

SWS slow wave sleep

TNF- $\alpha$  tumour necrosis factor- $\alpha$

WASO wake time after sleep onset

WHO World Health Organization

WHR waist-hip ratio

# **CHAPTER 1: SLEEP AND HEALTH**

## **1.1 Introduction**

This literature review will be preceded by a brief description of sleep physiology and sleep function, which will be followed by a section on sleep disorders. The next sections will draw upon the prevalence of short and long sleep hours and sleep disturbance in the general population, followed by a section on age-related changes in sleep. Next I will present epidemiological and experimental evidence relating sleep duration and disturbance with all-cause mortality, cardiovascular disease (CVD) and CVD mortality. I will also outline three possible pathways that might translate insufficient and disturbed sleep into cardiovascular outcomes. In the final section of the literature review I will discuss the issues relating sleep measurement.

This thesis describes a series of studies relating sleep with health-related physiology and well-being. The present chapter provides an introduction to the research literature relevant to Studies 1, 2 and 3. Study 4 is a short-term intervention study designed to discover whether modifying affective well-being will have an impact on sleep. The literature related to this study is reviewed in Chapter 5.

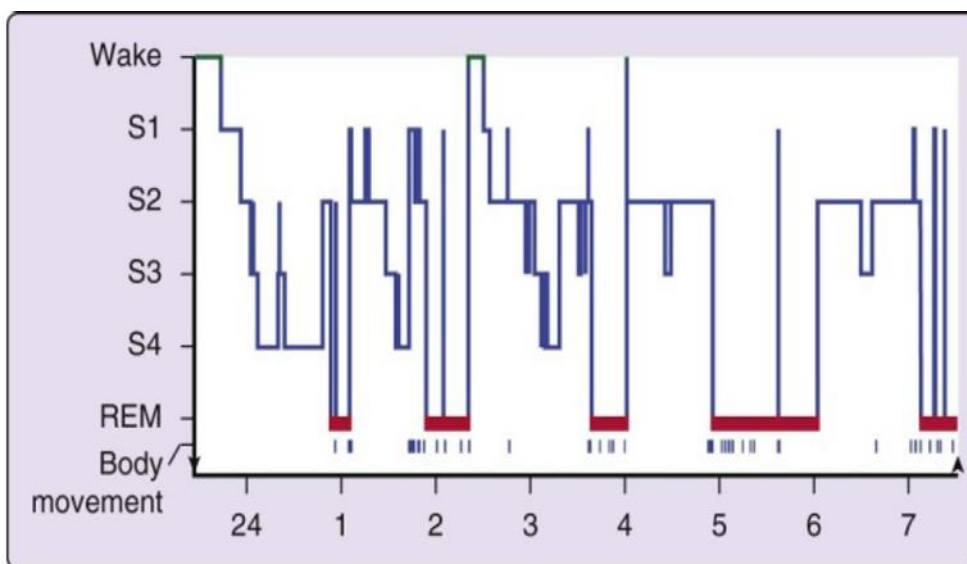
## **1.2 Defining sleep**

### **1.2.1 The physiology of sleep**

Sleep is a behaviour characterised by a lessened consciousness, greatly reduced skeletal muscles movement and slowed-down metabolism (Carlson, 2002; Zisapel, 2007). Based on the changes of central nervous activity sleep of a healthy adult can be divided into non-rapid eye movement (NREM) and rapid eye movement (REM) sleep, which alternate cyclically

(Zisapel, 2007). Each cycle lasts approximately 90 minutes and typically begins in NREM sleep and ends in REM sleep (see Figure 1.1 for the progression of sleep stages across the night). Based on the electroencephalogram (EEG) patterns NREM sleep is further divided into four stages. Briefly, the transition from wakefulness to sleep occurs in stage 1. In stage 2 the EEG activity remains irregular, but the arousal threshold is higher than in stage 1. These two sleep stages are often termed as light sleep (Carlson, 2002; Siegel, 2005). Stages 3 and 4 are characterised by the occurrence of high-amplitude delta activity and are often referred to as deep or slow wave sleep (SWS) (Carskadon & Dement, 2011; Zisapel, 2007). On the other hand, REM sleep is characterised by desynchronised EEG activity, a loss of muscle tone and rapid eye movements. REM sleep is also associated with dreaming (Carlson, 2002; Siegel, 2005). Interestingly, dreams also occur in NREM sleep, but they tend to be shorter and less vivid so they are more difficult to recall (Blagrove, 2009). Finally, in normal, healthy sleep the first part of the night is dominated by SWS (NREM sleep stages 3 and 4), whereas the second part of the night is dominated by REM sleep (Zisapel, 2007). Interestingly, while the amount of REM sleep does not diminish markedly as people age, SWS might disappear after the age of 60 years, in particular among men (Carskadon & Dement, 2011). The associations between sleep parameters and older age will be discussed in greater detail in the forthcoming sections of this chapter.

**Figure 1.1 The progression of sleep stages across a single night in a healthy, young adult (adapted from Carskadon & Dement, 2011).**

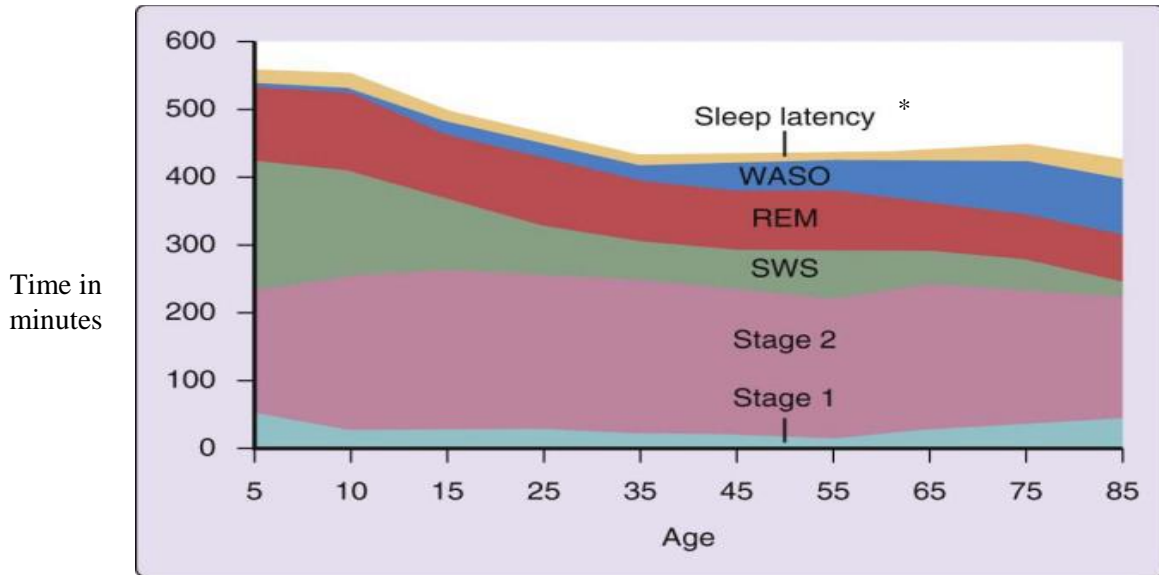


S1 to S4 indicate sleep stages from 1 to 4. Red thick lines at the bottom of the graph mark the presence of REM sleep. As the graphs shows, S3 and S4 (deep sleep stages) sleep stages occur in the first part of the night, while REM sleep becomes longer in the later part of the night.

The literature relating sleep in children and adolescents is beyond the scope of this thesis, but it is important to note that their sleep patterns differ markedly from those of adults. Very young babies spend about half of their total sleep time in REM sleep, while in adults REM is between 20 and 25% of sleep. This is because the length of REM sleep is strongly correlated with immaturity at birth, and REM sleep is thought to be involved in brain development (Siegel, 2005). In addition, new born babies begin their sleep cycle from REM sleep (adults do so from NREM sleep) and have much shorter sleep cycles. Sleep stages are typically established as the brain develops in the first two years of life (Carskadon & Dement, 2011). As can be seen in Figure 1.2 children spend considerably longer in deep sleep (SWS) and have better sleep continuity as indicated by a very short wake time after sleep onset

(WASO) when compared with adults. Young children also spend more time in REM sleep than, for example, middle aged adults, but the difference is less pronounced.

**Figure 1.2 Changes in sleep architecture from age 5 to 85 years (adapted from Carskadon & Dement, 2011).**



\*Sleep latency refers to the time needed to fall asleep. WASO=wake up time after sleep onset.

### 1.2.2 The role of sleep

The general consensus is that sleep is vital for the regulation of physical health and emotional well-being, and NREM and REM sleep are thought to be important for different functions of the brain and body. NREM sleep appears to be essential for energy conservation, especially among newborns (Siegel, 2005). In adults NREM sleep, and in particular the deep sleep stages are implicated in energy recovery. This is supported by experimental sleep deprivation studies showing a significant increase in deep sleep after one or a few nights of sleep deprivation (Bonnet, 2011). Deep sleep stages are also thought to be pivotal for the



regulation of glucose metabolism (Spiegel, Tasali, Leproult, & Van Cauter, 2009). In addition, NREM sleep might be important for proliferation and generation of new neurons in the brain. For example, 56 hours of sleep deprivation was associated with a 36% reduction of cell proliferation in an adult rat's dentate gyrus (Tung, Takase, Fornal, & Jacobs, 2005). The changes in sleep architecture seen during infection, as indicated by suppressed REM and fragmented NREM sleep, suggest that sleep is implicated in the generation of fever as well, which is induced to fight bacterial pathogens (Imeri & Opp, 2009).

REM sleep is thought to be involved in emotional regulation (Siegel, 2005; Zisapel, 2007), and chronic partial sleep deprivation in rats has been associated with alterations of neurotransmitter systems responsible for the regulation of emotional responses (Meerlo, Sgoifo, & Suchecki, 2008). The fact that new born babies spend about 50% of their total sleep in REM sleep additionally suggests that this sleep stage is involved in brain development. In adults, on the other hand, REM sleep is thought to stimulate the brain in order to facilitate alertness upon waking up. This is supported by the fact that REM sleep becomes a dominant sleep stage as the night progresses, and by a high brain neural activity associated with REM sleep. The notion that humans are far less alert if they wake up during NREM sleep further supports this hypothesis (Carskadon & Dement, 2011; Siegel, 2011). REM sleep has also been implicated in memory consolidation (Zisapel, 2007), however, its precise role in memory and learning processes remains to be elucidated (Maquet, 2001), and currently the evidence supporting this hypothesis is poor (Siegel, 2011). Moreover, a number of medications, such as monoamine oxidase inhibitors or tricyclic antidepressants suppress REM sleep, yet individuals who take these drugs for prolonged periods of time do not report memory loss or deficit. Along the same lines, people who suffered brain injuries resulting in a permanent loss of REM

sleep also do not suffer from memory problems, or learning deficits (Siegel, 2005; Siegel, 2011).

In addition to exploring the distinct functions of NREM and REM sleep in the brain and body processes, researchers have investigated the role of sleep duration and continuity by using different methods of investigations. For example, observational studies in birds and mammals have documented that sleep is a dynamic behaviour and length can be reduced without major consequences on performance, in particular to facilitate mating and seasonal migration, or to enable survival during food shortages (Siegel, 2012). On the other hand, experimental studies with rodents have shown that long-term sleep deprivation leads to skin lesions, hypothermia and eventually death (Rechtschaffen, 1998; Siegel, 2005). In addition, animal research suggests that sustained sleep deprivation impairs brain areas involved in stress reactivity by changing the basal activity of neuroendocrine systems, as illustrated, for instance, by reduced serotonin receptor sensitivity. This in turn impacts the responses to environmental challenges (Meerlo et al., 2008).

Experimental studies in humans reported that total and partial sleep deprivation result in alterations of metabolic, hormonal and neural responses as well (Leproult, Copinschi, Buxton, & VanCauter, 1997; McEwen, 2006; Meerlo et al., 2008; Mullington, Haack, Toth, Serrador, & Meier-Ewert, 2009; Spiegel, Leproult, & Van Cauter, 1999). In addition, experimentally induced sleep deprivation in humans has been associated with reduced vigilance, impaired logical reasoning, increased negative and decreased positive mood (Blagrove & Akehurst, 2001; Blagrove, Alexander, & Horne, 1995; Franzen, Siegle, & Buysse, 2008; Minkel et al., 2012; Talbot, McGlinchey, Kaplan, Dahl, & Harvey, 2010). It has been suggested that these

changes in mood and cognitive function reflect the impact of sleep deprivation on the prefrontal cortex (Killgore, Balkin, & Wesensten, 2006).

Data from naturalistic and observational studies have been another valuable source of information about the role of sleep. For example, there is growing evidence linking sleep measures, in particular short sleep duration, with breast cancer (Kakizaki et al., 2008) and cancer (von Ruesten, Weikert, Fietze, & Boeing, 2012). Moreover, population studies indicate that sleeping regularly 5 or fewer hours per night is prospectively associated with increased risk of all-cause mortality (Cappuccio, D'Elia, Strazzullo, & Miller, 2010) and cardiovascular outcomes (Cappuccio, Cooper, D'Elia, Strazzullo, & Miller, 2011). Poor sleep quality is also prospectively related to cardiovascular outcomes and mortality (Dew et al., 2003; Laugsand, Vatten, Platou, & Janszky, 2011). Because this part of the sleep literature is particularly relevant to this thesis it will be discussed in the subsequent sections of this chapter.

Taken together, although many functions of sleep are yet to be delineated (Naidoo, 2009; Siegel, 2011) there is substantive evidence suggesting that sleep has multiple functions ranging from its involvement in brain development in new born babies, cognitive performance, emotional and physical health, among others. However, this PhD thesis is going to focus on the implications of sleep duration and quality on cardiovascular health with the aim of exploring the possible mechanisms that might be contributing towards this prospective association. Therefore in the subsequent sections of this chapter I will discuss in greater detail the literature relating sleep measures with cardiovascular outcomes. I will then focus on three possible pathways that are thought to be translating sleep duration and poor sleep quality into CVD and CVD mortality. Namely, I will review the evidence suggesting that mood disturbance (pathway 1), health behaviours (pathway 2), and direct biological dysregulation

(pathway 3) might in part be responsible for the higher risk of CVD and CVD mortality among individuals with deviant sleep patterns. All three mechanisms are important, but it is beyond the scope of this PhD to explore each one in detail. My interests lie particularly in the pathway relating direct biological dysregulation therefore this field of research will be reviewed in greater detail in order to highlight the gaps of the literature that this PhD was set out to address.

### **1.3 Sleep disorders**

The studies that I have conducted to fulfil this PhD were based on data from healthy individuals and not on populations with sleep disorders. Nonetheless, because findings from studies in sleep disordered samples will be discussed in this document it is important to briefly describe the most prevalent sleep disorders, namely, insomnia, obstructive sleep apnoea and restless leg syndrome. There are other sleep disorders such as narcolepsy, periodic limb movement disorder, circadian sleep disorders or REM sleep behaviour disorders, but they will not be described here due to space constraints.

#### **1.3.1 Insomnia**

Insomnia is the most common sleep disorder characterised by sleep complaints such as inability to fall sleep, stay asleep or nonrestorative sleep. In addition, insomnia patients often report fatigue and reduced daytime functioning (Harvey, 2002). The prevalence of insomnia varies between studies from 5% to 50%, but if insomnia is diagnosed with the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition (text revision) (DSM-IV) (2000) the prevalence is about 6% (Lichstein, Taylor, Mccrae, & Ruitter, 2011; Morin, LeBlanc, Daley, Gregoire, & Merette, 2006). A most recent report commissioned by the American Academy of Sleep Medicine (Edinger et al., 2004) concluded that to be diagnosed with chronic insomnia

an individual must report sleep problems such as inability to fall asleep, stay asleep, or nonrestorative sleep at least 3 times a week for 6 months or longer. These sleep complaints must be present despite the opportunity for sleep in the night. In addition, individuals must also report impairments in daytime functioning such as fatigue, low mood, impaired attention or memory, among others. Polysomnography (PSG), a gold standard sleep measure, is not required to diagnose chronic insomnia since insomnias do not always have disturbed sleep when measured objectively (Fernandez-Mendoza et al., 2010; Rosa & Bonnet, 2000).

Insomnia has various manifestations, durations and aetiologies, so it remains a poorly understood sleep disorder. For instance, insomnia can be a separate sleep disorder (primary insomnia) and as a symptom of many chronic diseases (comorbid insomnia), or both. Insomnia lasting up to 4 weeks or less is defined as acute insomnia, while insomnia lasting longer than 6 months is defined as chronic; insomnia occurring more than 4 weeks but less than 6 months is often referred to as intermittent insomnia (Ellis, Gehrman, Espie, Riemann, & Perlis, 2012; Lichstein et al., 2011). Different manifestations of insomnia include sleep-onset insomnia, sleep maintenance insomnia, or early morning awakening insomnia. Insomnia is thought to be a disorder of hyper-arousal, as indicated by increased heart rate or sympathetic nervous system dominance in the night, but causal pathways are yet to be delineated (Bonnet & Arand, 2010; Harvey, 2002; Lichstein et al., 2011). The most prevalent risk factors for insomnia are female sex, ethnicity (e.g., in the US more Black Americans than White have insomnia), lower SES as indicated by income and educational attainment, and mood disorders such as depression and anxiety (Lichstein et al., 2011; Ohayon, 2002). Older age has been frequently reported as a risk factor for insomnia, but this seems to be the case from the age of 45 onwards but not among the elderly, where insomnia is more often a comorbid disorder

(Ancoli-Israel, Ayalon, & Salzman, 2008; Lichstein et al., 2011; Ohayon, 2002). Interestingly, there is some suggestion that genetic factors might predispose to this sleep disorder, albeit the evidence is weak at present (Bonnet & Arand, 2010; Lichstein et al., 2011). In addition to being a symptom of many mood and medical disorders it is important to note that insomnia is a risk factor for depression and CVD as well (Bonnet & Arand, 2010).

### 1.3.2 Sleep apnoea

Obstructive sleep apnoea (OSA) (also referred to as sleep disordered breathing) is another prevalent sleep disorder in which sleep is disrupted by a frequent total or partial collapse of the upper airway. Individuals diagnosed with this disorder suffer from poor sleep quality, as indicated by low levels of deep sleep and sleep fragmentation, reduced sleep duration, fatigue and daytime somnolence; due to breathing difficulties snoring is prevalent too (Bradley & Floras, 2009; Institute Of Medicine, 2006; Spiegel et al., 2009). In middle-aged men and women the prevalence of OSA has been estimated to be approximately 4% and 2%, respectively (Young et al., 1993). A more recent review suggested the prevalence of OSA to be between 3% and 7% (Punjabi, 2008). The most common risk factors for this sleep disorder are older age, male gender and smoking (Kasai, Floras, & Bradley, 2012; Punjabi, 2008; Young, Skatrud, & Peppard, 2004). Higher body mass index (BMI) is associated with OSA in cardiac populations, but the relationship is weaker in the general population; BMI also seems to be unrelated to apnoea severity (Kasai et al., 2012). OSA appears to be more frequent among ethnic minority groups, in particular Asian and Black populations. This is thought to be driven by different levels of obesity and differences in craniofacial morphology between Caucasian, Black and Asian populations (see Sutherland, Lee, & Cistulli, 2012 for a recent review of the literature in this area). In women the risk of OSA is greater among those

who are pregnant and suffer from polycystic ovary syndrome and hypothyroidism (Punjabi, 2008; Spiegel et al., 2009). In addition, OSA is more prevalent among individuals with diabetes mellitus, but the causal pathway has not yet been documented (Spiegel et al., 2009). Genetic factors might predispose to OSA, but currently the evidence is inconsistent as well (Kasai et al., 2012)

OSA is diagnosed with overnight PSG which provides information about apnoeas and hypopnoeas amongst other sleep variables including EEG. An apnoea refers to a complete obstruction of the upper airway lasting for at least 10 seconds, while hypopnoea to a partial (25%-50%) obstruction of the air flow (Punjabi, 2008). The frequency of apnoeas/hypopnoeas per hour is used to compute the apnoea-hypopnoea index (AHI) which provides information about OSA severity. The cut-off of  $AHI \geq 5$  is used to diagnose the presence of sleep apnoea. AHI between 5 and 15 refers to mild, 15-30 to moderate while  $AHI > 30$  to severe sleep apnoea (Bradley & Floras, 2009). In addition, apnoeas can be divided into obstructive, central and mixed (Punjabi, 2008). In OSA patients experience disruptions of the air flow due to a collapse of the upper airway, but the drive to breathe is present, while in central sleep apnoea the drive of respiratory muscles is absent (Kasai et al., 2012). Central sleep apnoeas are more prevalent in individuals with CVD than in the general population (Kasai et al., 2012).

A recent review concluded that OSA is a risk factor for cardiovascular outcomes such as hypertension, heart failure, arrhythmias and stroke, in particular among men. Importantly, the relationship between OSA and cardiovascular outcomes, such as hypertension or heart failure, is thought to be bi-directional. Individuals with hypertension or heart failure are often prone to sodium and water retention. In the night, due to a change in body position, the retained fluids are shifted from the legs to the upper parts of the body including the neck where the

fluids can contribute to the narrowing of the air passage (i.e. hypopnoea) or its collapse (i.e. apnoea). Hypopnoeas and apnoeas stimulate releases of cortisol and autonomic activation, which over time can additionally contribute towards the severity of hypertension and heart failure (Kasai et al., 2012). However, it is currently unclear whether OSA contributes towards CVD independently of other CVD risk factors (Kasai et al., 2012).

### 1.3.3 Restless leg syndrome

Restless leg syndrome (RLS) is a neurologic disorder in which individuals feel the urge to move their legs to relieve unpleasant symptoms or feelings described as “creepy-crawly, jittery, itchy or burning” (Institute Of Medicine, 2006, p. 97). Approximately half of RLS patients report their symptoms as painful (Montplaisir, Allen, Walters, & Ferini-Strambi, 2011). The symptoms are often felt over large parts of the thigh or the calve, and sometimes on both. Some individuals also experience symptoms on their arms. RLS is associated with sleep disturbance since the unpleasant sensations and subsequently the need to move legs or arms intensify during periods of rest or inactivity. Therefore RLS patients often report difficulty falling asleep or staying asleep. Unsurprisingly, RLS is associated with fatigue, daytime somnolence and reduced quality of life as well (Montplaisir et al., 2011). Overnight PSG is a standard diagnostic tool in this disorder.

The prevalence of RLS has been estimated to be between 5% and 10%, making it one of the most common sleep and movement disorders (Allen & Earley, 2001). The aetiology of RLS is not well understood at present, but genetic factors are thought to be important (Montplaisir et al., 2011). RLS is more prevalent in end-stage renal disease patients, musculoskeletal disorders and pregnant women (Institute Of Medicine, 2006; Ohayon & Roth, 2002), and it is thought to be a risk factor for CVD (Trotti, Bhadriraju, & Becker, 2012).



There has been extensive research linking RLS and anaemia, and iron deficiency is thought to contribute to this disorder through its effects on dopamine signalling (Institute Of Medicine, 2006; Montplaisir et al., 2011). However, causality is yet to be delineated since a recent review failed to establish whether iron therapy is an effective treatment for this disorder (Trotti et al., 2012).

#### **1.4 Sleep duration and sleep disturbance: definitions and prevalence**

Before focusing on the associations between sleep measures and cardiovascular outcomes I will briefly discuss possible determinants of sleep duration and quality. I will also define what is meant by sleep disturbance, short and long sleep duration, and I will discuss the literature relating the prevalence of these sleep measures in the general population.

Diurnal preference (the morningness-eveningness disposition), sleep quality and duration are likely to be determined by both genetic and environmental factors. For instance, early twin studies demonstrated that genetic influences accounted for approximately 30 to 40% of the variance in sleep patterns including sleep duration (Heath, Kendler, Eaves, & Martin, 1990; Partinen, Kaprio, Koskenvuo, Putkonen, & Langinvainio, 1983). More recently, de Castro (2002) reported that in a US sample of 86 identical twins, 78 fraternal same-sex and 51 fraternal mixed-sex twins hereditary factors accounted for 21 to 41% of the variance in sleep parameters such as duration, bed time, WASO, or the alertness upon waking up. In an Australian study the hereditary component of sleep disturbance and duration was substantial as well, but personality characteristics such as neuroticism and recent anxiety and depressive symptoms also explained a significant proportion of variance in these sleep measures, and in particular in sleep disturbance (Heath, Eaves, Kirk, & Martin, 1998). A

recent study in the UK reported that genes explained a large proportion of variance in sleep measures such as sleep latency (21%), quality (41%) or habitual sleep efficiency (30%) (typically defined as the proportion of total sleep time to the time spent in bed), but not in sleep duration, which was to some extent explained by shared environment (26%). The authors suggested that the lack of genetic influence on sleep duration in their data might be explained by a relatively young age of their participants (mean age=20 years), when compared with other studies, who might have had more variable bed time and wake up schedules than older individuals (Barclay, Eley, Buysse, Rijdsdijk, & Gregory, 2010). These studies suggest that hereditary factors explain a significant proportion of variance in sleep duration and disturbance, but sleep was assessed with subjective measures that might differ from objective indices of sleep (Lauderdale, Knutson, Yan, Liu, & Rathouz, 2008; van den Berg et al., 2009).

Genetic factors account for less than half of the variance in sleep parameters and in recent years sleep curtailment and disturbance have become widespread, and it is expected that this trend will continue to grow (Meerlo et al., 2008). For example, an investigation of sleep diaries extracted from eight US studies conducted between 1975 and 2008 established that the odds ratio (OR) of short sleep (<6 hours) over the 31 years period was 1.19 (CI:1.0-1.42) (P-value=0.05), but the trend was present only in people working full-time. Interestingly, workers sleeping fewer than 6 hours also had longer work hours (Knutson, Van Cauter, Rathouz, DeLeire, & Lauderdale, 2010). Data from the National Health Interview Survey in the US also suggest that sleep duration has decreased in the last 20 years (Luckhaupt, Tak, & Calvert, 2010). However, a survey conducted with 1997 British men and women found little support for the contention that habitual sleep duration decreased in the last 40 years (Groeger, Zijlstra, & Dijk, 2004). Findings from two recent reviews that investigated changes in sleep

duration since the 1970s also found mixed support that short sleep hours became more prevalent (Bin, Marshall, & Glozier, 2012; Bin, Marshall, & Glozier, 2013). For example, while the prevalence of short sleep ( $\leq 6$  hours) increased in Italy and Norway, in countries such as the UK, US and Sweden short sleep became less common. Interestingly, long sleep hours (defined as  $\geq 9$  hours) became more widespread (Bin et al., 2013).

Insufficient or poor quality sleep might also be a consequence of a sleep or medical disorder, as observed in people with OSA or insomnia, or among those with chronic health conditions such as heart failure or hypertension (Hall, 2010; Institute Of Medicine, 2006). Importantly, people's sleep duration might also be influenced by a subjective sleep need. For example, a study of nearly 9000 Norwegian men and women (age range 40-45 years) revealed that subjective sleep need was positively correlated with sleep duration in both sexes (Ursin, Bjorvatn, & Holsten, 2005). However, aspects associated with modern life, such as extended working hours, shift work, TV and Internet usage and leisure activities, are thought to be a major trigger to reduced sleep duration or poor sleep quality in the general population (Institute Of Medicine, 2006; Luckhaupt et al., 2010; Ohayon, Lemoine, Arnaud-Briant, & Dreyfus, 2002).

#### **1.4.1 Sleep duration**

##### **1.4.1.1 Short sleep duration**

Sleeping between 6 and 8 hours a night appears to be optimal for health while shorter sleep hours, typically defined as  $< 5$ ,  $< 6$  and sometimes  $< 7$  hours, are associated with negative health outcomes (Cappuccio et al., 2010; Cappuccio et al., 2011). The literature suggests that in many developed countries up to 1/3 of adults report short sleep. For example, Kripke et al., (2002) found that approximately 15% men and women aged 30-102 years from the Cancer

Prevention Study II (N=1.1 million) reported sleeping 6 hours on average, while 3.5% women and 2.9% men slept 5 hours. More recently a US survey of 110,441 middle-aged adults revealed that over 28% of the respondents reported sleeping 6 or fewer hours on average (Krueger & Friedman, 2009). A similar statistic was reported by Luckhaupt et al., (2010) where in a sample of 66,099 participants from the National Health Interview Survey in the US 29.9% reported sleeping  $\leq 6$  hours. People aged 46-55 years were more likely to be short sleepers than their younger or older counterparts. Short sleep duration (defined as  $< 7$  hours) was somewhat less prevalent (15.2%) in the baseline data from the Alameda County Health and Ways of Living Study, but the probability of short sleep did increase with each subsequent follow-up conducted in 1974,1983,1994 and 1999 (Stamatakis, Kaplan, & Roberts, 2007). In an Australian survey of middle-aged men and women 16.6% of the sample reported short sleep duration (defined as  $<7$  hours) (Magee, Iverson, & Caputi, 2009).

Short sleep duration is prevalent in European countries as well. For example, a representative survey of healthy people aged 55 years or older in seven European countries (UK, France, Spain, Italy, Germany, Portugal, and Finland) found that British people tended to have the lowest median sleep duration ranging from 6 hours 30 minutes in the 74-84 years age group to 6 hours 50 minutes in the 55-64 and 64-74 years age groups (Ohayon, 2004). However, a representative survey of British men and women aged 16-93 years (N=1997) reported that only 5% of the sample slept less than 5 hours (Groeger et al., 2004). A recent survey of 3218 Spanish people found that approximately 15% of the sample reported sleeping less than 7 hours (Ohayon & Sagales, 2010). A cross-sectional telephone survey in France revealed that out of 1004 men and women 18% reported sleeping less than 6 hours on an average week day (Leger et al., 2011).

Taken together, short sleep duration is common in developed countries and depending on the definition used (<5 hours, <6 hours or <7 hours) is reported by approximately 5 to 30% of the general population. Sleep curtailment is also prevalent among young adults and children (Meerlo et al., 2008). For example, a multi-national survey conducted among students aged 17 to 30 years revealed that 6% of the sample reported sleeping less than 6 hours and 15% reported sleeping between 6 and 7 hours on average (Steptoe, Peacey, & Wardle, 2006).

#### 1.4.1.2 Long sleep hours

Long sleep duration, which is usually defined as being greater than 8 or 9 hours (e.g., Ferrie et al., 2007; Stranges et al., 2008) is another form of an abnormal sleep pattern. The precise link between longer sleep duration and health is unclear at present (Mullington et al., 2009). It has been suggested, however, that prolonged sleep duration might be a consequence rather than a cause of ill health (Cappuccio et al., 2010; Gangwisch et al., 2007; Stranges et al., 2008).

The study by Kripke et al., (2002) found that approximately 6% of men and women from the Cancer Prevention Study II reported sleeping 9 hours, while 1.5% women and 2% men slept 10 hours or more on average. This is in agreement with a representative survey of British people where 6% of the sample slept more than 9 hours (Groeger et al., 2004). Similarly, just over 5% of participants from the Nurses Health Study II reported long sleep hours (defined as  $\geq 9$  hours) (Patel, Malhotra, Gottlieb, White, & Hu, 2006). Findings from a recent, large population-based survey in the US revealed that 8.5% of the sample reported sleeping 9 hours or longer (Krueger & Friedman, 2009). In Australia long sleep hours were somewhat more prevalent since 13.9% of men and women aged 45-65 reported sleeping 9

hours or more on average (Magee et al., 2009). Ohayon (2004) explored sleep patterns in adults aged 55-101 years in seven countries in Europe and found that long sleep hours ( $\geq 9$  hours) were more prevalent in France, Portugal and Spain than in the UK, Germany or Finland. More recently a cross-sectional survey of the general population in Spain reported that just over 9% of the sample reported sleeping 9 hours or longer, while 45.6% slept from 8 hours to 8 hours 59 minutes (Ohayon & Sagales, 2010).

Taken together, the prevalence of long sleep duration differs across the studies, and depending on the definition used varies from 1.5 to 45.6%. However, the variation in prevalence could also be influenced by the age of studied populations since younger and very old individuals might sleep longer hours than their middle-aged counterparts (Bliwise, 2011). Cultural differences and the climate/geographical region might be important as well (Ohayon, 2004). Finally, it is worth to reiterate that while recent reviews provided mixed support for the contention that sleep duration has decreased in the last 30-40 years, long sleep hours have become more widespread, at least in developed countries such as the UK or US (Bin et al., 2012; Bin et al., 2013).

#### 1.4.2 **Sleep disturbance**

Sleep studies have traditionally focused on measuring sleep duration, and the seminal paper by Kripke et al., (2002) was one of the first major studies linking sleep hours with increased mortality, but it has been recognised that the quality of sleep might be more important (Ekstedt, Akerstedt, & Soderstrom, 2004; Meerlo et al., 2008; Spiegel et al., 2009; Zisapel, 2007). In addition, sleep duration provides no information about sleep fragmentation or sleep depth (Hall, 2010).

Sleep quality is a broad term that tends to encompass a number of sleep measures and definitions, and poor sleep quality has been described with terms such as sleep problems, disturbance or insomnia symptoms. Individuals who have impaired sleep quality report a wide range of sleep complaints. For instance, they might experience difficulties falling sleep, staying asleep, or they tend to wake up too early. Feeling tired upon waking up and daytime sleepiness are also common complaints associated with poor sleep quality (Ohayon, 2002). The Pittsburgh sleep quality index (PSQI) is the most widely used self-reported measure of sleep quality (Buysse, Reynolds III, Monk, Berman, & Kupfer, 1989). It is important to recognise that measures of sleep continuity (e.g., sleep latency, WASO, sleep efficiency) or of sleep architecture/depth (e.g., NREM sleep stages) might also fall under the umbrella term of sleep quality, and have been found related to health outcomes (Hall, 2010). However, associations between sleep continuity or architecture and health have been studied less frequently, possibly because they require objective sleep assessment (in particular sleep architecture) that is often not feasible in larger population studies.

The literature suggests that sleep disturbances are common in developed countries. For instance, a large US survey of 79,625 men and women aged 18 years old or older established that over 25% of the respondents reported disturbed sleep (Strine & Chapman, 2005). In addition, Ohayon (2005) looked at the prevalence of nonrestorative sleep (defined as a poor quality sleep which might occur despite the maintenance of a normal sleep duration) across seven European countries including the UK. The UK had the highest prevalence of nonrestorative sleep (16.1%) followed by Germany (15.5%). That disturbances of sleep are prevalent in the UK was also reported by a survey of nearly 2000 British people, in which, for example, 36% of the sample reported difficulties falling asleep (Groeger et al., 2004). In

France a survey of 12,778 people found that nearly 30% of the respondents reported having at least one sleep complaint three times a week (Leger, Guilleminault, Dreyfus, Delahaye, & Paillard, 2000), and more recent data suggested that 12% of French men and women aged 25-45 years had insomnia, as defined by DSM-IV revised criteria (American Psychiatric Association (APA), 2000) (Leger et al., 2011). Data from the Augsburg Cohort Study in Germany (N=6896) revealed that 22% of women and 10% of men had problems with falling asleep, while 29.4% of women and 20% of men struggled with staying sleep (Meisinger, Heier, Lowel, Schneider, & Doring, 2007). A recent cross-sectional investigation conducted among over 22,000 respondents from five European countries (France, the UK, Germany, Italy and Spain) revealed that 31.2% of the sample reported being awake after sleep onset at least 3 days per week. Nearly 8 per cent of these respondents also reported difficulties getting back to sleep (Ohayon, 2010). Another survey assessed the prevalence of sleep problems in Western Europe (with the inclusion of the UK), the US and Japan. While the Japanese respondents reported the lowest prevalence of disturbed sleep (23%), the US respondents had the highest prevalence (56%). Among the Western European countries the prevalence of sleep problems was the highest in the UK (36%) (Leger, Poursain, Neubauer, & Uchiyama, 2008).

In summary, a number of large national and cross-national surveys conducted in the last decade or so have documented that sleep complaints are very prevalent in developed countries, and depending on a definition used can range from 10% (e.g., Meisinger et al., 2007) to as high as 56% (Leger et al., 2008). However, in the literature described above sleep problems were measured with self-report since it is often impractical or financially prohibitive to use objective sleep indicators in large surveys or population-based cohorts. Thus bearing in mind that people might over-report their sleep problems, when compared with an objective sleep



measure (van den Berg et al., 2009; Vitiello, Larsen, & Moe, 2004), it is possible that the prevalence of sleep complaints could have been somewhat lower had, for instance, wrist actigraphy been used instead. I will focus on the issues related to sleep measurement in later sections of this chapter.

## **1.5 Age-related changes in sleep patterns**

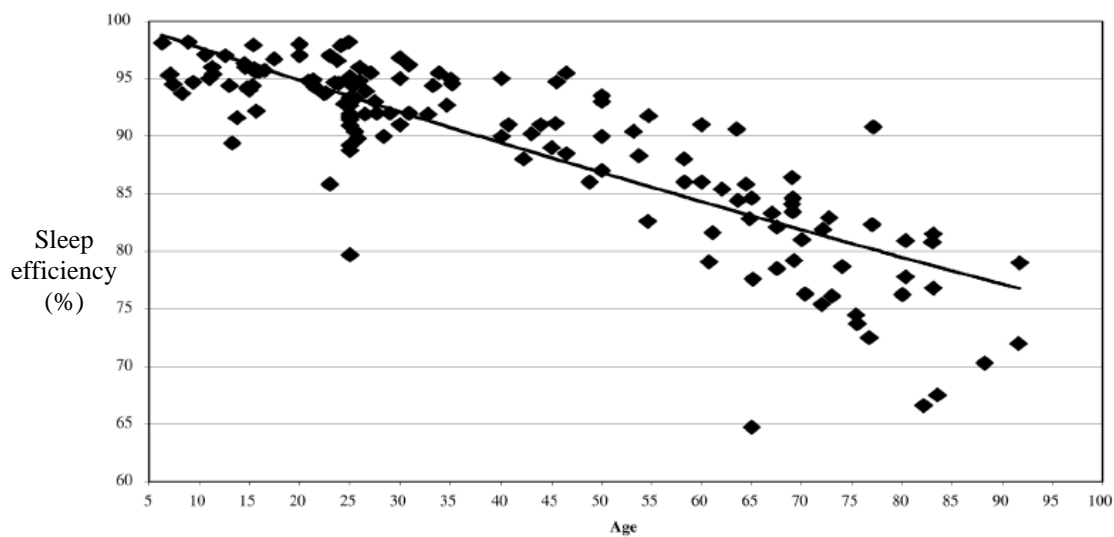
The age-related changes in sleep are noteworthy. In this section I will illustrate the alterations of sleep architecture occurring with advancing age and factors comorbid with sleep measures, in particular mood disturbances and medical disorders. I will then briefly address the issue of napping, and its associations with performance and health in older people. This will be followed by a discussion highlighting the importance of studying sleep parameters in older individuals.

### **1.5.1 Changes in sleep architecture in older people**

The most comprehensive meta-analysis to date, which assessed objective sleep parameters from childhood to old age in 3,577 healthy participants from 65 studies, concluded that apart from the reduction of sleep efficiency the most pronounced changes in sleep occur before the age of 60 years. To recapitulate, sleep efficiency is typically calculated as the proportion of total sleep time to the time spent in bed. Specifically, while sleep efficiency continues to decrease in the elderly (60-70 years) and “old” elderly ( $\geq 70$  years) (see Figure 1.3) total sleep time does not significantly decline in people older than 60 years (Ohayon, Carskadon, Guilleminault, & Vitiello, 2004). Time spent awake after sleep onset increases markedly with advancing age, but the change is no longer significant after the age of 60 years; the increase in sleep latency is modest as well (Ohayon et al., 2004). Sleep architecture also shows aged-related changes since both SWS and REM sleep decrease with age, but the

changes after the age of 60 years are again not significant. The review also uncovered sex differences in sleep parameters suggesting that older women have better sleep than men. Namely, women tend to have longer total sleep time and spend more time in deep sleep and less time in Stage 2, but take longer to fall asleep (Ohayon et al., 2004). That older women have better objective sleep than men have been subsequently reported by a number of studies (Bixler et al., 2009; Redline et al., 2004; van den Berg et al., 2009). To date it remains unclear why there is a greater reduction in the duration of SWS in men but not in women. This issue is further complicated by large individual variations in deep sleep seen in the male gender as a whole, which are greater than differences in SWS seen between men and women (Bliwise, 2011).

**Figure 1.3 Changes in sleep efficiency across the life span (adapted from Ohayon et al., 2004).**



### 1.5.2 Factors comorbid with sleep parameters in older age

Although objective sleep measures indicate that after the age of 60 years most sleep parameters do not change substantively, between 20 and 40% of older people frequently report insomnia symptoms, in particular the inability to maintain sleep (Bliwise, 2011). Comorbid medical disorders are thought to be an important trigger to this phenomenon (Ancoli-Israel, 2009; Ancoli-Israel et al., 2008; Ohayon et al., 2004). For example, in the Established Populations for Epidemiologic Studies of the Elderly (N>9000 of men and women aged 65 years or older) over 50% of respondents reported at least 3 sleep complaints occurring most of the time, with inability to stay asleep and fall asleep being particularly prevalent. However, statistical analysis revealed that sleep complaints were related to the presence of a number of health conditions including depressive symptoms, respiratory problems and poor subjective health (Foley, Monjan, Brown, & Simonsick, 1995). A more recent US survey of men and women aged 55-84 years reported a strong association between the number of chronic conditions and poor sleep quality. Specifically, 10% of respondents who were in good health rated their sleep as poor, while as many as 40% of those with comorbid conditions endorsed poor sleep rating. For example, bodily pain and heart disease were associated with difficulty falling asleep, fragmented sleep and waking up too early (Foley, Ancoli-Israel, Britz, & Walsh, 2004). Moreover, a higher prevalence of sleep disordered breathing (SDB) seen in the elderly has also been associated with disturbed sleep (Bliwise, 2011). For example, in the Sleep Heart Health study (N=2685, mean age 61.9 years) SDB was associated poorer sleep architecture, as indicated by shorter SWS and REM sleep, lower sleep efficiency as well as longer time spent in sleep stages 1 and 2 (Redline et al., 2004). Frequent trips to the bathroom in the night (nocturia) and side effects of medications such as  $\beta$ -blockers, corticosteroids or

diuretics, which a large proportion of the elderly takes daily, are also associated with poorer sleep and daytime somnolence (Ancoli-Israel, 2009; Bliwise, 2011; Foley et al., 2007; Pack et al., 2006).

Mood impairments are thought to be another significant contributor to the higher prevalence of disturbed sleep in older people (Bliwise, 2011). For instance, data from more than 3000 men aged 67 years or older revealed that compared with non-depressed men those who were depressed had nearly four times higher odds of poor sleep quality, as defined by the PSQI (Buysse et al., 1989). In addition, objective sleep latency, as indicated by wrist actigraphy, was also positively associated with depressive symptoms (Paudel et al., 2008). Kochar et al., (2007) explored cross-sectional associations between depressive symptoms and sleep problems (difficulty falling sleep, staying sleep and waking up too early) in nearly 700 non-caregivers and 375 caregiver older women from the Study of Osteoporotic Fractures (SOF) in the US. Interestingly, both non- and caregivers with elevated depressive symptoms had higher odds of sleep problems, in particular of maintaining sleep and waking up too early, but caregivers with low depressive symptoms did not have more disturbed sleep than non-caregivers with low depressive symptoms.

### 1.5.3 **Napping**

Daytime napping and somnolence are also more frequent in older adults when compared with younger individuals (Bliwise, 2011; Buysse et al., 1992), but the increase in the duration of naps is smaller than the increase in their frequency (Kamel & Gammack, 2006). This is thought to be a consequence of changes in sleep architecture, such as increased sleep fragmentation, age-related disturbances of circadian rhythms (Kamel & Gammack, 2006; Zisapel, 2007), and a correlate of psychiatric and medical disorders. The 2003 Sleep in

America Poll conducted amongst 1506 adults aged 55-84 years revealed, for instance, that 15% of the sample napped regularly and the prevalence of napping was positively related to age. Regular napping was predicted by daytime sleepiness, depression, pain and frequent trips to the bathroom in the night, but was unrelated to gender (Foley et al., 2007). Pack and colleagues (2006) conducted a case-control study comparing older adults reporting daytime sleepiness (N=149) with those who did not (N=144) across a range of medical, demographic and behavioural factors. Sleep was measured with the PSQI (Buysse et al., 1989) and two nights of PSG. Excessive daytime sleepiness was predicted by SDB, poor subjective sleep, shorter REM latency, pain (the best predictor), prescribed medication and male gender. It is also worth mentioning that cases with the highest number of risk factors for daytime sleepiness were most likely to suffer from it (Pack et al., 2006).

A relevant question in this context is whether napping and daytime sleepiness are associated with negative health outcomes or impaired daytime functioning in the elderly. To date, however, the evidence has been mixed (Bliwise, 2011). An experimental study conducted with young men and women found that a night of total sleep deprivation followed by a 2-hour mid-afternoon nap was associated with improvements of alertness, cognitive performance and favourable biological profiles, as indicated by reduced interleukin-6 and cortisol levels (Vgontzas et al., 2007). These data cannot be extrapolated to older populations but nonetheless suggest a restorative effect of napping in sleep deprived subjects. Interestingly, an earlier study described by Campbell et al., (2004) reported beneficial effects of napping on older people's performance as well. The participants, who were 32 men and women (mean age 68.5 years) free of a major medical, psychiatric or sleep disorder, provided 3 nights of PSG-based sleep data and nights 2 and 3 were followed by a mid-afternoon nap or

a sedentary interval. The results revealed that although napping was associated with longer sleep latency in the night, sleep duration, efficiency and architecture were not negatively affected. Moreover, having a nap resulted in improved cognitive and psychomotor performance (Campbell, Murphy, & Stauble, 2004).

Napping and sleepiness have been found related to health outcomes, but findings have been inconsistent with protective and harmful effects being reported. This might in part be explained by differences in studied populations in terms culture, geographical location or age, and by the differences in how napping was defined (Bliwise, 2011). For example, a large study in Greece (N=23,681) reported that taking a midday nap was protective against coronary heart disease (CHD) mortality; namely napping at least 3 times a week was associated with a 37% reduction of CHD mortality compared with no napping, after adjustment for a range of covariates (e.g., age, smoking, BMI). This prospective association was particularly prevalent in working men (Naska, Oikonomou, Trichopoulou, Psaltopoulou, & Trichopoulos, 2007). Recent evidence from a cohort study of over 1000 older people (age range 75-94 years) in Israel suggested that short sleep hours were predictive of lower risk of mortality among respondents who were taking daily naps, but the association was present only for those older than 84 years (Cohen-Mansfield & Perach, 2012). In contrast, findings from the Study of Osteoporotic Fractures (SOF) in the US revealed that older women (mean age 77 years) who reported napping every day had a 44% increased risk of all-cause mortality and a 58% increased risk of CVD mortality in comparison with women who did not nap. These findings were independent of a number of covariates including BMI, depression, cognitive impairment and the presence of at least one medical condition (Stone et al., 2009).

#### 1.5.4 **The importance of studying sleep in older people**

Life expectancy is steadily increasing (Oeppen & Vaupel, 2002) while the probability of disease and disability in old age is rising (Franco et al., 2009). This is associated with a huge burden on social and healthcare services. Sleep disturbance is a common consequence of medical and mood disorders and poor sleep in such populations is likely to exacerbate the severity of a medical or psychiatric illness (Zee & Turek, 2006), and additionally add to the social and economic burden. Disturbed sleep is also prospectively associated with cognitive decline (Ancoli-Israel, 2009; Bliwise, 2011) that is a serious issue in ageing populations. On the other hand, representative data of older people and findings from a meta-analytic review have indicated that individuals who are free of serious health problems can enjoy good sleep (Ohayon et al., 2004; Redline et al., 2004). Growing evidence also suggests that older people who are otherwise relatively healthy have reduced homeostatic drive for sleep, as indicated by shorter deep sleep in the night and reduced daytime sleep propensity (Dijk, Groeger, Stanley, & Deacon, 2010). However, a hypothesis that remains unexplored to date is whether too short or disturbed sleep have more deleterious impact on health with advancing age. Gene expression studies in mammals and birds (e.g., rat, mice, sparrow) have shown that at the subcellular level the adaptive stress response, referred to as the unfolded protein response, to sleep deprivation is smaller in older animals suggesting more harmful effects of sleep loss with advancing age (see Naidoo, 2009 for the most recent review in this area). Sleep deprivation in aged animals has also been found associated with lower levels of anti-apoptotic proteins and higher levels of the caspase cascade, which mediates programmed cells death (Naidoo, 2009). These findings must be replicated in humans and if confirmed the study of sleep and health in older age might be more important than previously acknowledged.

Past studies have predominantly explored sleep parameters as risk factors for disease and mortality (e.g., Cappuccio et al., 2010; Gallicchio & Kalesan, 2009; Gangwisch et al., 2007), and research on the correlates of healthy ageing, in particular good sleep, remains largely unexplored (Franco et al., 2009; Phelan, Love, Ryff, Brown, & Heidrich, 2010). There is some evidence suggesting that good sleep is related to better biological profiles. For example, a study of 74 elderly women showed that good sleep quality was associated with lower levels of interleukin-6 (IL-6), which is a pro-inflammatory cytokine involved in sleep-wake regulation and inflammatory responses (Friedman et al., 2005). These data were cross-sectional so the temporal relationship between IL-6 and sleep is uncertain. A longitudinal investigation of 184 older men and women found that diurnal cortisol outputs were lower among participants who had good sleep quality measured 2 years earlier (Wrosch, Miller, Lupien, & Pruessner, 2008). A further follow-up of these data 2 years later (N=157) revealed that (1) shorter sleep at baseline and reduction of sleep duration between baseline and time 2 predicted higher cortisol 4 years later and (2) an increase in sleep duration from baseline to time 2 was related to no change in cortisol levels 4 years later. However, baseline cortisol levels and changes in cortisol concentration from baseline to time 2 were unrelated to sleep duration at a 4-year follow-up (Rueggeberg, Wrosch, & Miller, 2012). More research exploring the protective role of sleep is warranted, but the studies described above indicate that good sleep is related to better biological outcomes in older people. Therefore it is timely to explore factors that promote better sleep that might particularly benefit elderly cohorts, where the accumulation of risk factors might increase the risk of mortality and morbidity (Gruenewald, Seeman, Ryff, Karlamangla, & Singer, 2006).



## **1.6 Implications of sleep deprivation and disturbance**

The consequences of poor sleep are wide-reaching and affect, both directly and indirectly, many aspects of public health. For example, sleep-related fatigue contributes to medical errors (Institute Of Medicine, 2006). Motor vehicle accidents and work-related injuries resulting from tiredness, errors in judgement and decreased psychomotor performance are another consequences of deviant sleep patterns (Hillman, Murphy, Antic, & Pezzullo, 2006; Rajaratnam & Arendt, 2001). Sleep loss and disturbance are also associated with large costs to the economy due to their impact on productivity and absenteeism. Sleep deprivation and disturbance are linked to cognitive deficit and impairment as well (Institute Of Medicine, 2006; Zisapel, 2007), causing slower reaction time and reduced psychomotor vigilance performance (Franzen et al., 2008). Finally, mood impairments, decreased quality of life and poor self-rated health have also been associated with sleep loss and/or disturbance (Pilcher & Huffcutt, 1996; Steptoe et al., 2006; Stranges et al., 2008; Strine & Chapman, 2005).

Sleep duration and sleep disturbance are also related to a number of health outcomes including cancer, CVD, CVD mortality and all-cause mortality. I have already mentioned on page 27 that in my PhD thesis I will focus on the literature relating sleep measures with cardiovascular outcomes and mortality, which will be discussed in the following sections.

### **1.6.1 Sleep duration and overall mortality**

Sleep duration has been implicated in all-cause mortality by over 20 prospective cohort studies to date (Gallicchio & Kalesan, 2009), and the relationship is U-shaped with hours between 7 and 8 typically being associated with lowest mortality while those shorter and longer than that with excess mortality. The U-shaped relationship was reported as early as in 1964 where men sleeping 5 or fewer hours and 10 or more hours, in comparison with 7 hours,

had significantly higher mortality rates (Hammond, 1964). A follow-up of these data suggested that relative to 7-7.9 hours men and women sleeping less than 4 or 10 or more hours had increased risk of mortality (Kripke, Simons, Garfinkel, & Hammond, 1979). Mortality has also been associated with short and long sleep hours in the Alameda County Study in California, US (Kaplan, Seeman, Cohen, Knudsen, & Guralnik, 1987).

Nonetheless, the interest in sleep duration as a risk factor for mortality has been stimulated by findings from the Cancer Prevention Study II of over 1 million American men and women (Kripke, Garfinkel, Wingard, Klauber, & Marler, 2002). Specifically, respondents sleeping less than 7 hours were at a greater risk of mortality, in particular those sleeping 3.5 or 4.5 hours on average. However, in both men and women sleeping over 10 hours was a stronger predictor of mortality than short sleep, as compared with the 7 hours reference category (Kripke et al., 2002). Results from another US prospective investigation conducted among female nurses revealed that in comparison with sleep duration of 7 hours sleeping 5 or fewer hours was related to increased risk of all-cause mortality. However, in line with Kripke et al., (2002) the risk of mortality was highest among women sleeping longer hours (9 or more) (Patel et al., 2004). More recently longitudinal analyses of the first National Health and Nutrition Examination Survey (NHANES I) also revealed a U-shaped association between sleep duration and mortality (Gangwisch et al., 2008). Namely, in comparison with the 7 hours category respondents sleeping  $\leq 5$  hours or  $\geq 9$  hours had significantly increased hazard ratios (HRs). However, this trend was only found in older (60-86 years) but not younger (32-59 years) participants. In the study of Osteoporotic Fractures in the US older women (mean age 77 years) sleeping between 9-10 hours, as compared with 8-9 hours, had significantly

higher HRs, independently of major confounders such as age, BMI, smoking, diabetes, depression or cognitive impairment (Stone et al., 2009).

A number of investigations conducted with Asian populations have also reported a prospective association between sleep duration and mortality. For example, sleeping less than 7 hours was associated with greater likelihood of all-cause mortality among Japanese women, but not men. Long sleep hours were predictive of higher mortality in both sexes though (Tamakoshi & Ohno, 2004). A more recent Japanese cohort study reported that in both sexes sleep duration shorter than 7 and longer than 10 hours predicted all-cause mortality, independently of potential confounders (Ikehara et al., 2009). Suzuki et al., (2009), on the other hand, reported that in a population-based cohort of elderly Japanese men and women only long sleep hours ( $\geq 10$ ) predicted mortality from all causes. Similarly, in Taiwan only long sleep duration ( $\geq 9$  hours) was predictive of all-cause mortality in a sample of middle- and early-old aged men and women followed for approximately 16 years (Chien et al., 2010).

A 22-year follow-up of the Finish Twin Cohort showed that in comparison with the 7-8 hours sleep category short ( $< 7$  hours) and long ( $> 8$  hours) sleep hours were associated with increased risk of mortality in men and women. These findings were independent of relevant covariates (e.g., age, marriage, BMI, physical activity, smoking) and were stronger in men (Hublin, Partinen, Koskenvuo, & Kaprio, 2007). A recent longitudinal investigation of the FINRISK data in Finland found that relative to the reference group (7-8 hours) sleep of 5 or fewer hours was predictive of total mortality in men and women. Moreover, sleep duration of 9 hours was related to higher mortality risk, but men and women sleeping 10 hours or more had the highest risk of total mortality in this study (Kronholm, Laatikainen, Peltonen, Sippola, & Partonen, 2011). An investigation of the Bambui Health and Ageing Study in Brazil

revealed that long sleep hours (>9 hours) were associated with a 53% increase in the risk of all-cause mortality in comparison with sleep duration of 7 hours. Short sleep hours were unrelated to mortality in these data (Castro-Costa et al., 2011). A recent 20-year follow-up study of older Jewish men and women (mean age at follow-up 83 years) from Israel found that only long sleep hours (>9 hours), relative to 7-9 hours, predicted higher mortality. Short sleep (< 7 hours) was unrelated to mortality in these data (Cohen-Mansfield & Perach, 2012).

The association between sleep hours and all-cause mortality has been reported in the UK as well. For example, a follow-up study of Scottish men and women, who provided information on sleep hours at baseline and 4 to 7 years later, reported that sleep duration of less than 7 hours at both time points predicted all-cause mortality 25 years later. Long sleep duration was unrelated to mortality in these data (Heslop, Smith, Metcalfe, Macleod, & Hart, 2002). However, in the Whitehall II study of British civil servants short ( $\leq 5$  hours) and long sleep hours ( $\geq 9$  hours) were both prospectively related to higher mortality from all causes, independently of sociodemographic characteristics, health behaviours and major chronic illnesses (Ferrie et al., 2007). Interestingly, an increase from sleep duration of 7 or 8 hours, in comparison with those who retained sleep of 7 hours, was related to higher mortality risk at the follow-up as well.

In summary, in the last decade or so a considerable number of studies reported that self-reported short and long sleep duration prospectively predict all-cause mortality, with long sleep hours being a stronger risk factor, especially in older people (Cappuccio et al., 2010). Importantly, the U-shaped association between sleep duration and mortality has been supported by two meta-analytic reviews (Cappuccio et al., 2010; Gallicchio & Kalesan, 2009). However, in a more recent review of prospective studies relating sleep duration with all-cause

mortality only 14 out of 42 studies lent support for this relationship (Kurina et al., 2013). The main limitation of this literature is the reliance on a self-reported measure of sleep duration since people are often not accurate in estimating their sleep hours in the night (e.g., Lauderdale et al., 2008; van den Berg et al., 2008). However, a study comparing self-reported and actigraphy-based measures of sleep parameters reported reasonable agreement between subjective and objective indices of sleep duration ( $r=0.57$ ) (Lockley, Skene, & Arendt, 1999). Population-based studies relating objective measures of sleep duration with mortality are rare (Kurina et al., 2013), but have been conducted in insomnia patients (Vgontzas et al., 2010). Interestingly, a recent follow-up of the observational study of Women's Health Initiative reported that short (<5 hours) and long (>6.5 hours) sleep, as defined objectively by wrist actigraphy, were predictive of mortality (Kripke, Langer, Elliott, Klauber, & Rex, 2011). The finding that sleep hours greater than 6.5 were associated with excess mortality in these data suggests that the cut off values for long sleep duration as a risk factor might differ depending on whether subjective or objective sleep measure is used. Indeed, in Kripke et al's study (2011) objective sleep durations were up to 52 minutes shorter than subjective durations. This is in line with data from the Coronary Artery Risk Development in Young Adults (CARDIA) study where self-reported sleep duration was approximately 48 minutes longer than duration based on wrist actigraphy (Lauderdale et al., 2008). In addition, residual confounding in the association between sleep duration and mortality cannot always be ruled out (Kurina et al., 2013). For example, in the meta-analysis carried out by Gallicchio and Kalesan (2009) out of 23 reviewed studies 7 did not adjust their statistical models for comorbid conditions. However, when these 7 studies were excluded from the analysis the pooled risk ratios for short and long sleep hours remained largely unchanged. It is also important to mention that the

associations between sleep duration and all-cause mortality seem to vary little by socioeconomic circumstances and gender (Cappuccio et al., 2010).

### 1.6.2 Sleep disturbance and overall mortality

Disturbances of sleep are linked to all-cause mortality as well, but this association has been explored to a lesser extent than the relationship between sleep duration and mortality, and the findings are less consistent. For instance, Dew et al., (2003) reported that objectively measured greater sleep latency and reduced sleep efficiency were associated with increased risk of all-cause mortality in a small sample (N=185) of elderly adults, independently of covariates including gender, age and medical disorders. Results from a large prospective study (N=22933) of middle-aged men and women in Sweden revealed that difficulty falling asleep and waking up too early predicted all-cause mortality in men, whereas in women this relationship was present for difficulty falling asleep. These findings were independent of age, BMI, smoking, alcohol consumption, cholesterol levels, or blood pressure (Nilsson, Nilsson, Hedblad, & Berglund, 2001). In a sample of over 3000 Taiwanese middle-aged men and women insomnia symptoms experienced nearly every day, relative to never, were associated with a 70% higher all-cause mortality, independently of age, sex, BMI, smoking and a range of medical disorders present at baseline (Chien et al., 2010).

However, a number of studies failed to find a prospective association between disturbed sleep and all-cause mortality. For example, insomnia (assessed with ‘On the average, how many times a month do you have insomnia’) was unrelated to mortality risk in the Cancer Prevention Study II described by Kripke et al., (2002). Similarly, disturbed sleep did not predict mortality in a cohort study of elderly Japanese adults (Suzuki et al., 2009). Insomnia symptoms of inability to fall asleep and stay asleep were associated with total mortality in

Swedish men, independently of age, but after further adjustment for economic circumstances, health behaviours and medical conditions both sleep complaints were no longer predictive of mortality. In women in the age-adjusted model inability to fall asleep was predictive of higher mortality, but the relationship did not survive additional adjustment for other confounders (Mallon, Broman, & Hetta, 2002). Sleep problems (difficulties falling asleep, staying asleep and waking up feeling exhausted) were prevalent in the Atherosclerosis Risk in Communities (ARIC) study in the US, but after adjustment for confounders they were unrelated to all-cause mortality (Phillips & Mannino, 2005).

It is uncertain why there has been mixed support for the prospective association between sleep disturbances and all-cause mortality. One possible explanation is the difference in indices used to assess sleep disturbance. For example, Dew and co-workers (2003) used PSG, a gold-standard sleep measure, to assess sleep while Kripke et al., (2002) relied on just one item ('On the average, how many times a month do you have insomnia'). This is a crude sleep measure, and that particular sentence seems vague so could have been interpreted differently by different respondents. However, the study described by Kripke et al., (2002) was based on over 1 million respondents and the statistical analyses were adjusted for 32 possible confounding factors. Thus another possibility is that perhaps the association between disturbed sleep or poor sleep quality and mortality from all causes is weaker than that of sleep duration. Moreover, the literature seems to suggest that poor sleep quality might be a better predictor of cardiovascular outcomes and mortality rather than total mortality. This will be discussed in the following sections. Interestingly, sleep disturbances have been associated with all-cause mortality in clinical populations including insomnia patients (Vgontzas et al.,

2010), haemodialysis patients (Elder et al., 2008) or those undergoing rehabilitation following stroke, bone fracture or medical surgery (Martin et al., 2011).

## **1.7 Sleep parameters and CVD**

### **1.7.1 CVD**

CVD is the main cause of death in developed countries including the UK, where it accounts for nearly 198,000 deaths per year (British Heart Foundation, 2012). The most common forms of CVD are CHD (also referred to as ischemic heart disease or coronary artery disease) and stroke. CHD is the most common cause of premature death in the UK (British Heart Foundation, 2012). As can be expected the economic and social cost of CVD in the UK is vast, since it is associated not only with high mortality, but also with healthcare costs, loss of productivity and earnings and informal health care costs, among others (Luengo-Fernandez, Leal, Gray, Petersen, & Rayner, 2006). CVD is also associated with impaired quality of life and significant mood impairments, in particular depression and anxiety (Nicholson, Kuper, & Hemingway, 2006; Tully, Cosh, & Baune, 2013). The majority of CHD is caused by atherosclerosis, a long-term process whereby progressive narrowing of coronary arteries leads to impaired blood flow to the heart muscle.

Traditional risk factors for CVD are well-established and include non-modifiable risk factors (e.g., age, gender, or family history) and modifiable risk factors including lifestyle choices (smoking, physical inactivity, alcohol consumption) and medical disorders, such as diabetes, hypertension, raised cholesterol levels, obesity and metabolic syndrome, among others (Roth & Mindell, 2008). Psychosocial risk factors have also been implicated in the development and progression of CVD and include, for example, low socio-economic status (SES), low social support, work stress and mood disorders (Hemingway & Marmot, 1999;



Rozanski, Blumenthal, Davidson, Saab, & Kubzansky, 2005). In the last decade or so evidence has accumulated to suggest that extreme durations of sleep (short and long) and impaired sleep quality are also prospective risk factors for CVD and CVD mortality.

## 1.7.2 **Observational studies and cardiovascular outcomes**

### 1.7.2.1 **Sleep duration**

Population studies suggest that both short and long sleep duration predict cardiovascular mortality and morbidity (Cappuccio et al., 2011; Gallicchio & Kalesan, 2009; Mezick, Hall, & Matthews, 2011). For example, in the Nurses' Health Study in the US sleeping 5 or fewer hours per night, relative to 8 hours, was associated with a 39% increase in risk of total CHD (including nonfatal myocardial infarction (MI) and CHD death). Long sleep hours were a prospective predictor of total CHD as well (Ayas et al., 2003). However, a different investigation of the Nurses' Health Study revealed that, in comparison with 7 hours, women sleeping 8 or  $\geq 9$  hours had higher risk of CVD mortality, but no association was found with short sleep (6 or  $\leq 5$  hours) (Patel et al., 2004). In Singapore short ( $\leq 5$  hours) and long ( $\geq 9$  hours) sleep were associated with higher risk of CHD mortality, when compared with 7 hours, after adjustment for relevant confounders (Shankar, Koh, Yuan, Lee, & Yu, 2008). Findings from the Japan Collaborative Cohort (JACC) study (N=98,634) also indicated that, in comparison with 7 hours, short sleep ( $\leq 4$  and 5 hours) predicted CHD in women while long ( $\geq 10$  hours) sleep was associated with increased cardiovascular mortality in both sexes (Ikehara et al., 2009). However, a smaller study of 1255 Japanese older men and women reported a prospective association only between short sleep hours ( $< 7$  hours) and CVD mortality, as compared with the 7.5 hours reference category (Eguchi et al., 2008). In addition, a cohort study in Germany found that women sleeping 5 or fewer hours were more likely to

suffer MI than those sleeping 8 hours, but no such association was found in men, and long sleep hours were unrelated to MI in both sexes (Meisinger et al., 2007). More recent findings also from Germany revealed that after adjustment for multiple covariates, relative to 7-8 hours, short (<6 hours) and long sleep ( $\geq 9$  hours) predicted stroke (von Ruesten et al., 2012). Finally, evidence from Finland suggested that in women but not men, relative to 7-8 hours, sleep of  $\leq 5$  hours and sleep of  $\geq 10$  hours were a significant predictor of CVD mortality, independently of relevant covariates. In women long sleep hours were also a prospective risk factor for stroke and MI (Kronholm et al., 2011).

While the studies discussed above assessed sleep duration only at one time point, some authors explored whether a change in sleep duration between baseline and follow-up is also associated with cardiovascular outcomes. For example, in the Whitehall II study respondents sleeping 6, 7 or 8 hours at baseline who reduced their habitual sleep duration, in comparison with those who retained sleep of 7 hours, had increased cardiovascular mortality up to 17 years later. Interestingly, an increase in sleep duration from baseline levels of 7 or 8 hours was not predictive of higher CVD mortality (Ferrie et al., 2007) (see Table 1.1 for an overview of the above studies).

**Table 1.1 Overview of prospective population-based studies linking sleep hours with CVD and CVD mortality.**

Reference, year published, journal	Sample characteristics	Reference category, short & long sleep definition	Main results*
<b>Ayas et al., 2003,</b> Archives of internal medicine	71,617 females from the Nurses' Health Study, US, age range at follow-up 50-75 years	<b>Ref: 8 h</b> Short s. 7,6 and $\leq 5$ h Long s. $\geq 9$ h	$\leq 5$ and $\geq 9$ h predicted $\uparrow$ risk of total CHD (including nonfatal MI and CHD death)
<b>Patel et al., 2004,</b> SLEEP	82,969 females from the Nurses' Health Study, US, age range at follow-up 40-65 years	<b>Ref: 7 h</b> Short s. 6 and $\leq 5$ h Long s. 8 and $\geq 9$ h	8 and $\geq 9$ h predicted $\uparrow$ risk of CVD mortality, 6 and $\leq 5$ h unrelated to CVD mortality
<b>Shankar et al., 2008,</b> American journal of epidemiology	58,044 men and women from the Singapore Chinese Health Study, age at follow-up approx. 57 years	<b>Ref: 7 h</b> Short s. 6 and $\leq 5$ h Long s. 8 and $\geq 9$ h	$\leq 5$ and $\geq 9$ h predicted $\uparrow$ risk of CHD mortality
<b>Ikehara et al., 2009,</b> SLEEP	98,634 men and women from the JACC study, Japan, age at follow-up 40-79 years	<b>Ref: 7 h</b> Short s. $\leq 4,5,6$ and $<7$ h Long s. 8,9 and $\geq 10$ h	$\leq 4$ and 5 h predicted $\uparrow$ risk of CHD in women; $\geq 10$ predicted $\uparrow$ risk of CVD mortality in both sexes
<b>Eguchi et al., 2008,</b> Archives of internal	1255 men and women, Japan, mean age at follow-up 70 years	<b>Ref: 7.5 h</b> Short s. $<7$ h	$<7$ h predicted $\uparrow$ risk of CVD mortality; $>7$ h unrelated to CVD

medicine		Long s. >7 h	mortality
<b>Meisinger et al., 2007,</b> SLEEP	6896 men and women from The MONICA/KORA Augsburg cohort study, Germany, baseline age 45-74 years (age at follow-up not given)	<b>Ref. 8 h</b> Short s. ≤5, 6, 7 Long s. >8 and 9≥	≤5 predicted ↑ risk of MI (women only), >8 and 9≥ unrelated to MI in both sexes
<b>Von Ruesten et al., 2012,</b> PLoS ONE	23,620 men and women from EPIC-Potsdam study, Germany, age at follow-up approx. 58 years	<b>Ref. ≥7 &lt;8 h</b> Short s. <6, ≥6 and <7, Long s. ≥8 <9 and ≥9	<6 and ≥9 predicted ↑ risk of stroke
<b>Kronholm et al., 2011,</b> Sleep medicine	23,290 men and women from the FINRISK surveys, Finland, approx. age at baseline 45 years (age at follow-up not given)	<b>Ref. 7-8 h</b> Short s. ≤5, 6 Long s. 9, and ≥10 h	≤5 and ≥ 10 h predicted ↑ risk of CVD mortality (women only), ≥10 h predicted ↑ risk of MI and stroke (women only)
<b>Ferrie et al., 2007,</b> SLEEP	7,729 men and women from the Whitehall II study, UK, age at follow-up approx. 50 years	<b>Ref: 7 h</b> Short s. 6 and ≤5 h Long s. 8 and ≥9 h	Decrease from 6,7,8 h at baseline predicted ↑ risk of CVD mortality

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\* Main results were derived from fully adjusted models. Approx.=approximately, ref=reference, h=hours, s.=sleep, ↑=higher.

However, not all population-based studies supported the U-shaped association between sleep hours and cardiovascular outcomes. For instance, a cohort study of working Scottish men and women found that sleeping less than 7 hours, relative to 7-8 hours, at baseline and 3-7 years later predicted CVD mortality in men in the age-adjusted models. However, the prospective relationship did not survive additional adjustment for sociodemographic characteristics and medical disorders, and no consistent relationships were found in women (Heslop et al., 2002). Sleep duration was also unrelated to CHD mortality (in both age-adjusted and multivariable models) in a middle-aged sample of Swedish men (N=906) and women (N=964) (Mallon et al., 2002). In the US Study of Osteoporotic Fractures (SOF) (N=8101) night-time sleep hours were unrelated to CVD mortality as well. Interestingly though, a total 24-hour sleep duration (inclusive of night-time sleep hours and daytime naps) of 10 or more hours, relative to 8-9 hours, was associated with a 77% increase in CVD mortality (Stone et al., 2009). Findings from a sample of older Japanese men and women revealed that in comparison with 7 hours neither short nor long sleep hours predicted CVD mortality in multivariable statistical models (Suzuki et al., 2009). Recent data from the Chin-Shan Community Cardiovascular Cohort Study in Taiwan (N=3,430m) revealed that in middle- and early-old aged adults CVD incidence was positively associated with sleep hours in the age and gender adjusted models, with higher risk of CVD being related to increasing sleep hours. However, further adjustment for socio-economic and lifestyle factors (e.g., smoking) reduced the association to a non-significant level (Chien et al., 2010). In the Monitoring Project on Risk factors for Chronic Diseases (MORGEN) study (N=20,432) of Dutch men and women aged 20-65 years followed for up to 15 years 6 or fewer hours of habitual sleep predicted CVD incidence and CHD, relative to 7 hours. Additional adjustment

for SES, lifestyle and biological factors, however, reduced these relationships to a non-significant level. Long sleep hours were unrelated to CVD outcomes in the basic (age and gender adjusted) as well as multivariable models in these data (Hoevenaar-Blom, Spijkerman, Kromhout, van den Berg, & Verschuren, 2011).

In summary, most of the studies reviewed above support the hypothesis that short and/or long sleep hours are predictive of cardiovascular outcomes and mortality, but in some investigations the associations were only found in unadjusted models. A recent meta-analysis reported that short sleep duration was prospectively associated with CHD incidence and death (Risk Ratio (RR)=1.48, Confidence Interval (C.I.) 1.22-1.80) and stroke (RR=1.15, C.I. 1.00-1.31), but not with CVD mortality (RR=1.03, C.I. 0.93-1.15). On the other hand, long sleep hours were found prospectively associated with all of the above outcomes (CHD: RR=1.38, C.I. 1.15-1.66; stroke: RR=1.65, C.I. 1.45-1.87; CVD mortality: RR=1.41, C.I. 1.19-1.68) (Cappuccio et al., 2011). This is broadly in line with the results of a meta-analysis published a year earlier, which found that only long sleep was a significant prospective predictor of cardiovascular-related mortality (RR=1.38, C.I. 1.13-1.69) (Gallicchio & Kalesan, 2009).

One possible reason why sleep hours have not been related to CVD and CVD mortality in some of the studies discussed above might be due to residual confounding, since the type and number of included covariates differ between studies. Different definitions of short and long sleep and well as of the reference group might also contribute to the heterogeneity of findings (Grandner, Hale, Moore, & Patel, 2010). The literature relating sleep duration and CVD and sleep duration and CVD mortality is further limited by the reliance on subjective sleep measures. Given that people often overestimate their night-time sleep hours, as illustrated in the CARDIA (Lauderdale et al., 2008) and Rotterdam studies (van den Berg et

al., 2008), self-reports are less reliable than objective sleep indicators. Another important issue is that except for two investigations conducted in the UK (Ferrie et al., 2007; Heslop et al., 2002) the remaining studies assessed sleep duration only at one time point. This might be unrepresentative of respondents' sleep duration since it does not take into account the fact that people might subsequently start sleeping more or fewer hours, in particular if the follow-up is conducted a long time after the initial assessment. Finally, although the prospective associations between sleep duration and cardiovascular outcomes differed by gender in some studies (e.g., Kronholm et al., 2011; Meisinger et al., 2007), a recent meta-analytic review reported no sex differences in the pooled RRs (Cappuccio et al., 2011).

Despite of the limitations of the literature discussed above there is substantial evidence documenting that short sleep hours are a prospective predictor of CVD while long sleep duration is a risk factor for both CVD and CVD mortality, independently of sociodemographic characteristics and medical conditions. Therefore, building on this evidence, more research is warranted to elucidate the mechanisms through which sleep duration might increase the risk of cardiovascular outcomes.

#### **1.7.2.2 Sleep disturbance**

Sleep disturbances have been another sleep parameter linked to cardiovascular outcomes. In Sweden Nilsson et al., (2001) reported that in a large sample (N=22933) of men and women a combination of two sleep disturbances (difficulty falling asleep and waking up too early) predicted CVD mortality in men, whereas in women difficulty falling asleep was found to be related to increased CVD mortality. Another prospective cohort study of 1870 Swedish men and women found that difficulty falling sleep was associated with increased CHD mortality as well, but only in men (Mallon et al., 2002). That difficulty falling asleep is

a prospective risk factor for cardiovascular outcomes and mortality was also reported in a sample of 774 women aged 45-64 years from the Framingham study, US (Eaker, Pinsky, & Castelli, 1992). In the Caerphilly cohort of older men living in Wales, UK, relative to good sleep frequent insomnia symptoms (a combination of difficulties falling asleep and waking up in the night) were prospectively associated with stroke, after adjustment for age, SES, smoking, alcohol consumption and BMI. The association between insomnia symptoms and MI approached significance (OR=1.47, C.I.0.98-2.21) (Elwood, Hack, Pickering, Hughes, & Gallacher, 2006). In the Chin-Shan Community Cardiovascular Cohort Study in Taiwan, a prospective investigation of middle-aged men and women, insomnia symptoms (assessed with ‘How frequent is your insomnia complaint?’) occurring nearly every day, as compared to never, predicted CVD events. This finding was independent of SES, age, gender and medical conditions at baseline (Chien et al., 2010). A recent investigation in Norway linking insomnia symptoms with acute MI reported that independently of a range of confounders including biological risk factors and mood disorders difficulty falling asleep, staying asleep and waking up unrefreshed were independent predictors of MI. In addition to the independent association between each insomnia symptom and MI, the risk of MI was associated with the number of insomnia symptoms in a dose-dependent manner (Laugsand et al., 2011).

The prospective association between disturbances of sleep and cardiovascular outcomes has not been supported by some studies. For instance, findings from the Augsburg Cohort Study described by Meisinger et al., (2007) suggested that problems falling asleep and staying asleep were unrelated to MI in men. In women difficulties maintaining sleep were weakly associated with MI risk (HR=1.53, C.I. 0.99-2.37), after adjustment for covariates. Relatedly, in the ARIC study of nearly 12,000 middle-aged men and women reporting either difficulties



falling asleep or maintaining sleep at baseline was unrelated to CVD; the combination of either of these sleep complaints with nonrestorative sleep was also not predictive of CVD. Only the presence of all three sleep problems at baseline predicted higher risk of CVD at a 6-year follow-up (Phillips & Mannino, 2007).

A number of studies have explored the combined effects of sleep duration and quality on CVD and CVD mortality. In the Taiwanese study described on the previous page respondents reporting sleep of 9 hours or more and frequent insomnia (measured with ‘How frequent is your insomnia complaint?’) had a two-fold increased risk of CVD compared with those who slept 7-8 hours and reported no insomnia symptoms (Chien et al., 2010). In Japan findings from a prospective cohort study of elderly men and women revealed that while neither sleep duration nor disturbance were related to CVD mortality, respondents with long sleep ( $\geq 10$  hours) and at least one sleep complaint had a significantly higher risk of mortality (Suzuki et al., 2009). A longitudinal investigation conducted among British civil servants established that participants who reported having restless and disturbed sleep were at a greater risk of CHD, independently of sleep duration. Interestingly, short sleep duration ( $\leq 6$  hours) also predicted increased risk of CHD, but only among those individuals who also reported disturbed sleep (Chandola, Ferrie, Perski, Akbaraly, & Marmot, 2010). This is to some extent in line with recent evidence from Holland. Namely, in the MORGEN study short sleep ( $\leq 6$  hours), compared with 7-8 hours, predicted CVD and CHD incidence only among respondents who also reported poor sleep quality. These findings were independent of a number of covariates including medical conditions at baseline. However, sleep quality did not predict cardiovascular outcomes independently of sleep duration (Hoevenaer-Blom et al., 2011). These findings are important since they suggest that information on sleep duration might be, at

least among some individuals, insufficient to indicate increased risk of cardiovascular outcomes. This is because sleep duration offers no information on sleep depth or fragmentation that have been found related to CVD risk factors such as type 2 diabetes (Mezick et al., 2011), or higher blood pressure (Ekstedt et al., 2004). Therefore to broaden our understanding of how sleep relates to cardiovascular outcomes studies should explore both the role of sleep duration and its quality.

In summary, there is growing evidence from population-based studies suggesting that, in addition to sleep duration, disrupted sleep is also a prospective risk factor for cardiovascular outcomes including mortality. However, to date very few studies have explored whether sleep disturbances predict cardiovascular outcomes independently of sleep duration, and findings are mixed. For example, while in the Whitehall II study (Chandola et al., 2010) disturbed sleep remained a significant predictor of CHD after sleep duration was added into the statistical model, this was not the case in the MORGEN study conducted in Holland (Hoevenaar-Blom et al., 2011). More studies are warranted to explore this issue further. Importantly, the risk of CVD or CVD mortality appears stronger in those who report both disturbed and short (e.g., Chandola et al., 2010) or long sleep hours (e.g., Chien et al., 2010), suggesting a synergistic effect of poor sleep quality and extremes of sleep duration on cardiovascular health.

Further limitations of the literature relating sleep disturbance with cardiovascular outcomes must also be addressed. For example, the definition of sleep complaints differs across studies making comparisons of data difficult. For example, while Laugsand et al., (2011) defined sleep complaints as difficulty falling asleep, staying asleep and waking up unrefreshed, in the MORGEN study sleep disturbance was assessed with one item ('Do you

usually rise rested’) (Hoevenaar-Blom et al., 2011). It is also important to emphasise that the findings discussed above were based on self-reported ratings of sleep quality, which could mean different things to different people and be affected by memory biases and current mood (Krystal & Edinger, 2008). Although objective sleep assessments are often infeasible in large population studies recent findings from 459 women aged 50-81 years suggested that sleep efficiency, measured with wrist actigraphy, was inversely associated with mortality (total) (Kripke et al., 2011).

In contrast to the literature relating sleep duration with cardiovascular health fewer population-based studies have explored whether disturbed sleep is prospectively associated with CVD and CVD mortality. However, growing evidence supports this hypothesis and more work is needed to study the mechanisms that might in part be responsible for the higher risk of cardiovascular outcomes among individuals with disturbed sleep.

### **1.8 Mechanisms linking sleep loss and disturbance to CVD**

So far I have discussed evidence that both sleep hours (short and long) and disturbed sleep are prevalent in the US, Europe, Asia and Australia. I have then discussed the literature relating the implications of deviant sleep patterns on all-cause mortality, CVD and CVD mortality. There are convincing data that, independently of relevant confounders including medical conditions, short and long sleep are risk factors for death from all causes and CVD (long sleep) as well as for CVD. There is also growing evidence that sleep problems, such as inability to fall asleep, prospectively increase the risk of cardiovascular outcomes including mortality. In this section I will discuss possible pathways through which sleep parameters might lead to CVD and CVD mortality.

Although I have outlined evidence suggesting that short and long sleep hours are predictive of future CVD and CVD mortality, the mechanisms linking these two extremes of sleep duration with health indicators are thought to be distinct. While short sleep hours might predispose to higher CVD incidence and mortality, long sleep is thought to be a marker of ill health rather than a risk factor (Cappuccio et al., 2011). For instance, unadjusted analyses of the first National Health and Nutrition Examination Survey revealed that in comparison with 7 hours short ( $\leq 5$  hours) and long sleep ( $\geq 9$  hours) were predictive of higher mortality. However, after adjustment for potential confounders including BMI, diabetes, hypertension, general health and cancer, the U-shaped association between sleep duration and mortality was only confirmed in participants aged 60-86 years old, but not among those 32-59 years old. The authors hypothesised that long sleep hours rather than being a risk factor might be a consequence of, for instance, inflammatory responses to medical conditions such as diabetes or cancer (Gangwisch et al., 2008). Interestingly, an earlier review of the literature in this area suggested that because long sleep hours are more prevalent with increasing age they might be part of the deterioration of function that presages death in the elderly (Youngstedt & Kripke, 2004).

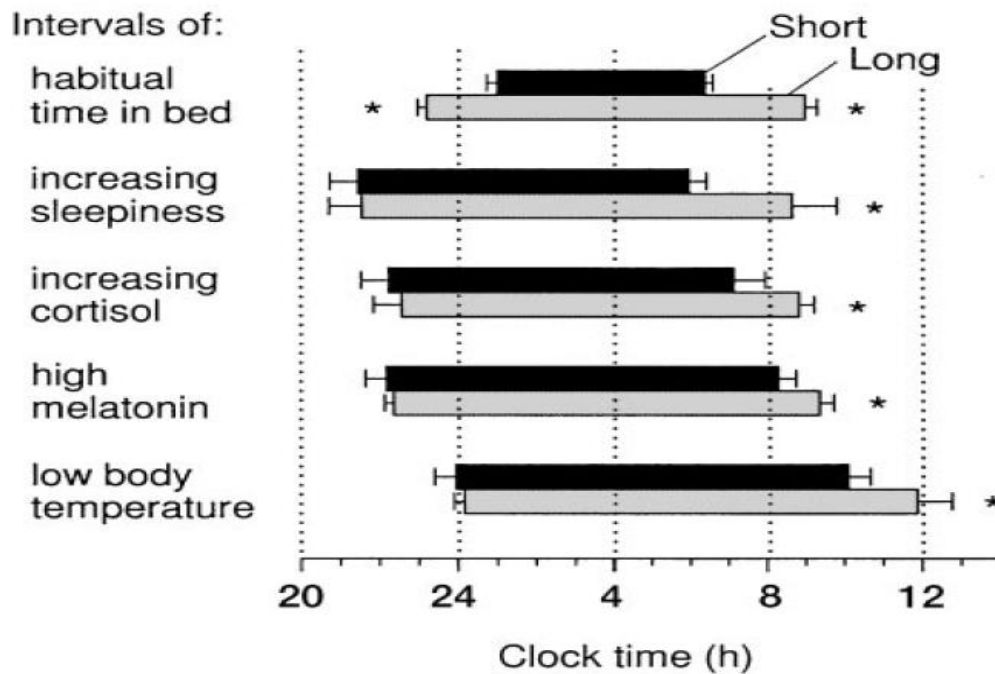
In addition, both long sleep duration and CVD are associated with a number of factors that could act as potential mediators, or confounders of the long sleep-CVD relationship. For example, in the Nurses' Health Study of 85,700 women long sleep (defined as  $\geq 9$  hours and reported by 5.3% of the sample) was associated with depressive symptoms (OR=1.9, C.I. 1.7-2.0), antidepressant medication (OR=3.1, C.I. 2.9-3.3), being unemployed (OR=2.4, C.I. 2.3-2.6), divorced and never married (OR=1.21, C.I. 1.10-1.32; OR=1.37, C.I. 1.22-1.37, respectively), low SES (OR=4.46, C.I. 3.36-5.92) as well as multiple sclerosis (OR=3.7, C.I.

3.0-4.5), among others (Patel et al., 2006). Patel et al., (2006, p. 883) further computed the confounding rate ratio (a statistic calculating to what degree a given factor (e.g., depression) is responsible for the association between long sleep and mortality) and reported that from among the correlates of long sleep listed above, depression and socioeconomic circumstances accounted for the largest proportion of variance in the relationship between long sleep and mortality in these data. It was concluded that while SES and depression are likely act as confounders, it is plausible that depression, at least to some extent, partly mediates the long sleep-mortality relationship.

A review of the literature relating long sleep duration with mortality supported these findings and further suggested that long sleep hours are associated with physical inactivity, anxiety, poor coping strategies and sleep disorders including sleep apnoea (Grandner & Drummond, 2007). In addition, long sleepers have poorer sleep quality, as suggested by objective and subjective sleep indicators, and the relationship is likely to be bidirectional. It is possible that people with fragmented sleep might try to sleep longer hours to compensate for their poor quality of sleep. On the other hand, prolonged sleep might result in sleep fragmentation, which increases in frequency as the period spent in bed increases (Grandner & Drummond, 2007). However, in some individuals longer sleep hours are not a marker of their health status (mental or physical), but a reflection of their longer biological night. Namely, a comparison of young, healthy men and women who were either habitual short (<6 hours) or long (>9 hours) sleepers suggested that the latter group had (1) longer period of high levels of plasma melatonin (a hormone involved in sleep propensity), (2) longer interval of low body temperature, (3) longer night-time period of increasing cortisol (resulting in approximately 2.5 hours later peak of morning cortisol) (4) longer interval of the circadian rhythm in the night

(Aeschbach et al., 2003) (see Figure 1.4 for a graphic depiction of these physiological differences).

**Figure 1.4 Physiological nocturnal differences between healthy, young long and short sleepers (adapted from Aeschbach et al., 2003).**



\* Indicate significant difference ( $P < 0.05$ ) between short and long sleepers in terms of sleep duration, night-time sleepiness (measure of the circadian rhythm), night-time cortisol and melatonin levels as well as night-time temperature.

Given that the aetiological pathways linking short and long sleep with health outcomes are likely to be distinct, the majority of studies relating sleep hours with cardiovascular outcomes have predominantly focused on short sleep duration. Therefore in the remainder of this section I will also discuss evidence from observational and experimental studies of sleep loss/insufficiency.

The literature suggests that three broad sets of pathways might be involved in translating sleep disturbance and duration into cardiovascular outcomes and mortality. As already specified at the beginning of this chapter (page 27), these relationships could be mediated through mood disturbance, in particular depression. Lifestyle factors such as cigarette smoking, eating habits and physical inactivity might also potentially mediate the sleep-CVD relationship. Experimental studies have suggested that disturbances and loss of sleep lead to changes in neuroendocrine, autonomic and inflammatory processes. Therefore a direct biological dysregulation is likely to be another pathway through which impaired sleep might be linked with CVD. Each of these three pathways will be discussed in more detail below, with particular focus on the biological mechanisms.

### **1.8.1 Pathway 1: Sleep and mood disturbances**

According to the (revised) guidelines of DSM-IV (2000) deviant sleep patterns, such as restless sleep, are a diagnostic criterion for depression. Therefore most questionnaires designed to measure depression or depressive symptoms, such as the Centre for Epidemiologic Studies Depression Scale described by (Radloff, 1977) include questions on sleep. That mood disorders, in particular depression, are related to disturbances of sleep has also been supported by meta-analytic reviews. For example, a meta-analysis of 177 studies conducted among 7151 psychiatric patients and controls reported that affective disorders, in particular depression, are strongly associated with poor sleep. Specifically, relatively to controls individuals with mood disorders had lower sleep efficiency, shorter SWS and sleep duration and longer sleep latency, as indicated by PSG (Benca, Obermeyer, Thisted, & Gillin, 1992). Population-based studies also suggest that sleep disturbances are associated with depressive symptoms. A cross-

sectional study of 5,201 elderly people (age range 65-100 years) in the US reported that sleep disturbances, such as difficulty falling asleep or fragmented sleep, were strongly associated with depressive symptoms (Newman, Enright, Manolio, Haponik, & Wahl, 1997). Similarly, Foley et al., (2004) explored the prevalence of sleep disturbances in a sample of elderly people (N=1506) aged 65-84 years and reported that sleep complaints were more common among depressed participants. Namely, depression was significantly associated with difficulty falling asleep, waking up in the night, waking up too early and waking up feeling unrefreshed, after adjustment for age, sex and the presence of a sleep disorder. Another US cross-sectional survey of nearly 80,000 men and women aged 18 years and older found that 20% of respondents who reported disturbed sleep also reported frequent depressive symptoms. On the other hand, only 4.4% of respondents with good sleep reported suffering from depression (Strine & Chapman, 2005). However, Foley et al., (2004) and Strine and Chapman (2005) assessed depression with one item (e.g., “Have you ever been told by the doctor to have depression”), while Newman et al., (1997) provided no information whether questions concerning sleep were removed from the scale used to assess depressive symptoms in their study. This raises the possibility that the questions used to assess sleep in these studies shared common method variance with depressive symptoms questionnaires/items.

Sleep duration has also been found associated with depression. An Australian cross-sectional study of middle- and early-old aged men and women (N=49,405) reported that short (6 hours) and long sleep duration ( $\geq 6$  hours) was strongly associated with depression (Magee et al., 2009). These findings were corroborated by a large US study of 110,441 adults (Krueger & Friedman, 2009) as well. Finally, Stranges and colleagues (2008) investigated factors associated with sleep duration in a sample of British civil servants (N=6,472) and in a



sample drawn from the Western New York Health Study (N=3,027). In both samples respondents who were depressed were approximately three times more likely to report short sleep duration ( $\leq 6$  hours) when compared with those who were not depressed. Long sleep hours were unrelated to depressive symptoms in both samples (Stranges et al., 2008).

The data described above come from cross-sectional studies, thus it is not possible to establish the direction of the relationship between poor sleep and disturbed mood. Given that between 50 and 90% of people with depression experience disturbed sleep (Mezick et al., 2011) it was originally believed that depression precedes insomnia, but growing evidence suggests this is not the case (Benca & Peterson, 2008). For instance, a study of over 14,000 middle-aged men and women from four European countries including the UK found that in over 40% of respondents with mood disorders insomnia preceded mood disturbances (Ohayon & Roth, 2003). In the Alameda County Study in the US participants who reported disturbed sleep (a combination of difficulties falling asleep, staying asleep and sleeping too long) were over two times more likely to be depressed a year later, after adjustment for a range of sociodemographic factors and health behaviours (Roberts, Shema, Kaplan, & Strawbridge, 2000). In the Wisconsin Sleep Cohort study of 555 men and women (mean age 54.0 years) followed for up to 4 years insomnia symptoms predicted depression, independently of a number of covariates (Szklo-Coxe, Young, Peppard, Finn, & Benca, 2010). A recent study of over 40,000 men and women in Finland revealed that sleep problems predicted subsequent depression treatment at a mean follow-up of 3.5 years. Specifically, moderate (experienced 2-4 times a week) and severe (experienced 5-7 times a week), as compared to never, difficulties with falling asleep, staying asleep, waking up too early and having a non-refreshing sleep all predicted subsequent depression. In addition, there was a dose-dependent relationship

between the number of sleep complaints and depression risk with those reporting all four sleep complaints having the highest likelihood of future depression, independently of covariates (Salo et al., 2012).

Disturbed sleep has also been linked with depression recurrence. For example, in the study by Ohayon and Roth (2003) mentioned earlier insomnia preceded recurring mood disorders in over 50% of respondents. Another prospective study of 351 elderly adults conducted in the US reported that depressed participants with sleep problems at baseline were three times more likely to suffer from depression two years later, independently of comorbidities, other depressive symptoms and medication (Cho et al., 2008)

Taken together, there is growing evidence suggesting that disturbed sleep is prospectively related with depression, but causality has yet to be proven (Mezick et al., 2011). Depression has been implicated in CHD as well (Hemingway & Marmot, 1999; Steptoe, 2006). A meta-analytic review of 21 prospective studies with a mean follow-up period of 10.8 years reported that depression was associated with a 1.81 greater risk of future CHD (Nicholson et al., 2006). It has also been documented that depression is particularly prevalent among cardiac patients, and it is a strong risk factor for cardiac events and mortality (Nicholson et al., 2006; van Melle et al., 2004). For instance, a review established nearly 20% of patients with acute MI meet criteria for a major depressive disorder (Thombs et al., 2006).

An extended discussion of the potential pathways linking depression with CVD is beyond the scope of this thesis, but it should be mentioned that this relationship is a multifaceted one (Frasure-Smith & Lesperance, 2010; Steptoe, 2006). For example, a review by Steptoe (2006) suggested that biological processes such as inflammation, autonomic or neuroendocrine dysregulation, among others, are likely to be involved. Importantly, deviant

sleep patterns have also been associated with disruptions of these biological pathways (e.g., McEwen, 2006; Meerlo et al., 2008; Mullington, Simpson, Meier-Ewert, & Haack, 2010). For example, in patients with acute major depression objectively measured (longer) sleep latency, REM sleep density and depressive symptoms were significantly associated with higher levels of IL-6 (proinflammatory cytokine) in bivariate correlation analyses. However, once sleep measures were adjusted for depressive symptoms were no longer related to IL-6 levels (Motivala, Sarfatti, Olmos, & Irwin, 2005). This suggests that, at least in these data, sleep parameters might contribute to elevations of inflammatory markers in depressed individuals. An important question in this context is, therefore, whether sleep measures and depression are independent or overlapping risk factors for CVD. A recent review found that sleep continuity (difficulties falling or staying sleep) and depression predict future CVD independently of each other; however it remains less clear whether this is also the case with sleep duration (short and long) (Mezick et al., 2011).

### **1.8.2 Pathway 2: Sleep and health behaviours**

In addition to biological pathways behavioural factors have been implicated in the development and pathogenesis of CVD as well. In particular, there is strong evidence relating obesity, physical inactivity and smoking to cardiovascular outcomes (Pi-Sunyer, 1993; Thompson et al., 2003; Visscher & Seidell, 2001). Importantly, these health behaviours have also been associated with sleep duration and disturbance.

#### **1.8.2.1 Obesity**

It has been suggested that changes in sleep patterns, in particular chronic sleep deprivation, might have contributed in part to the increasing prevalence of obesity (Knutson,

Spiegel, Penev, & Van Cauter, 2007). A systematic review established that in children short sleep duration was both cross-sectionally and prospectively associated weight gain. In adult populations the cross-sectional association was less consistent, but short sleep predicted weight increase in three longitudinal studies (Patel & Hu, 2008). A meta-analysis of 30 cross-sectional studies (634,511 participants) reported that short sleep was associated with higher risk of obesity in children (OR=1.98, C.I.1.46-2.43) and adults (OR=1.55, C.I. 1.43-1.68) (Cappuccio et al., 2008). More recently in the CARDIA study in the US researchers assessed cross-sectional and longitudinal relationships between objectively measured sleep duration and BMI, but only a cross-sectional relationship was found (Lauderdale et al., 2009). Large cross-sectional studies in Australia and US also reported an association between short sleep hours and obesity that was independent of relevant covariates such as age, sex, SES or health behaviours (Altman et al., 2012; Krueger & Friedman, 2009; Magee et al., 2009).

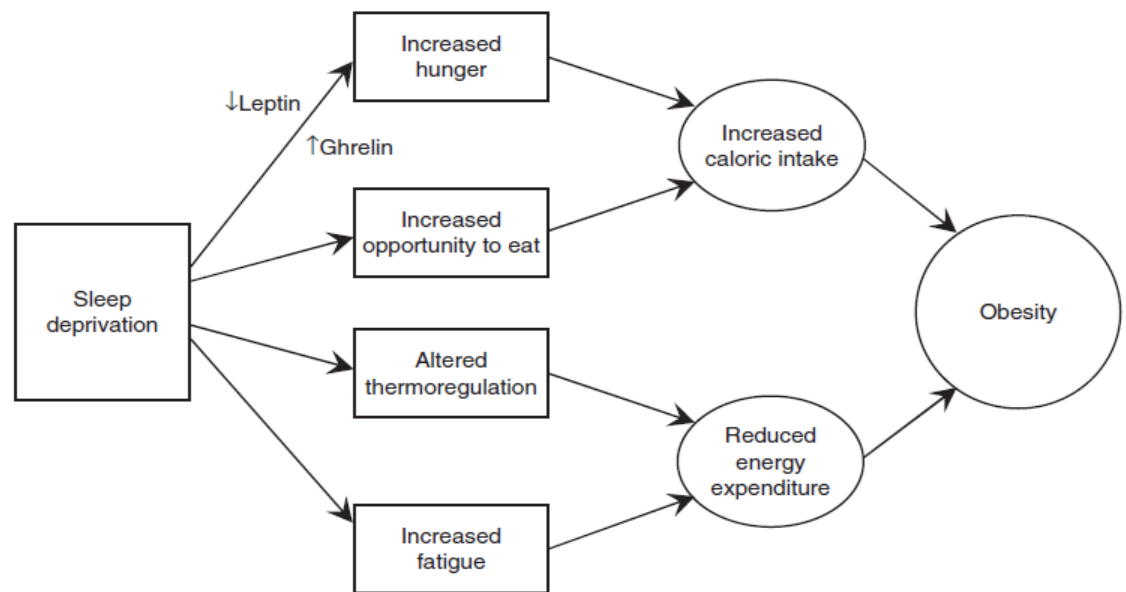
One possible explanation why not all studies support cross-sectional and/or longitudinal associations between short sleep and obesity could be due to residual confounding, in particular mood disorders (Horne, 2008; Horne, 2011; Spiegel et al., 2009). For example, in the Penn State Cohort study of 1300 men and women short sleep hours were more prevalent in obese respondents, but only if they also reported sleep disturbances or emotional distress. There was no significant difference in sleep duration between obese and non-obese respondents with good quality of sleep. The authors concluded that in obese individuals short sleep hours are more likely to be a marker of poor sleep quality or mood disturbances rather than a risk factor for weight gain (Vgontzas et al., 2008).

Interestingly, obesity has been associated with disturbed sleep as well. For instance, an analysis of the 2003 Sleep in America Poll (N=1506) revealed that waking up after sleep onset

and waking up unrefreshed were both positively associated with obesity (Foley et al., 2004). A cross-sectional investigation of nearly 80,000 US men and women aged 18 years and older reported that obese respondents (defined as those having  $BMI \geq 30$ ) were significantly more likely to report insufficient sleep (Strine & Chapman, 2005). Relatedly, impaired sleep quality was associated with a significantly greater waist-hip ratio (WHR) in a sample of middle-aged British people (Lasikiewicz, Hendrickx, Talbot, & Dye, 2008).

The possible mechanisms linking short sleep and obesity are multifaceted, and their detailed discussion is beyond the scope of this PhD thesis. Briefly, experimental data suggest that dysregulation of hormones involved in appetite regulation, such as leptin or ghrelin, and reduced physical activity (due to fatigue and tiredness caused by insufficient/poor sleep) are likely to be involved (Knutson et al., 2007; Mullington et al., 2009; Spiegel et al., 2009; Van Cauter et al., 2007) (see Figure 1.5 for a graphic illustration of the probable pathways translating sleep loss into obesity). In addition to these mechanisms emerging experimental evidence in humans suggests that fragmented sleep has detrimental effects on glucose metabolism, as indicated by lower insulin sensitivity and decreased glucose effectiveness, so could also contribute to the increased risk of obesity (Stamatakis & Punjabi, 2010; Tasali, Leproul, Ehrmann, & Van Cauter, 2008). Importantly, in these data the changes in glucose metabolism caused by microarousals from sleep occurred despite no reduction of respondents' sleep duration. This could be another explanation why not all studies support the association between sleep loss and obesity.

**Figure 1.5 Potential mechanisms relating sleep loss with increased obesity risk (adapted from Patel & Hu, 2008).**



### 1.8.2.2 Physical inactivity

Numerous studies have documented associations between physical inactivity and sleep parameters. For instance, the study by Strine and Chapman (2005) described above (page 77) reported that independently of covariates such as age, ethnicity, marital status or education insufficient sleep was more frequently reported by participants who also reported to be physically inactive. This was corroborated by another US investigation carried out among 1506 participants aged 55-84 years, where engaging in physical exercise less than once a week was related to sleep disturbances such as difficulty falling asleep, or sleep fragmentation. As above, these associations were independent of relevant confounders (Foley et al., 2004). In the UK a positive association between sleep duration and physical activity (low levels-shorter sleep) was also discovered in an analysis of the Whitehall II study (Stranges et al., 2008).

Similarly, a study conducted among 434 young adults (mean age 17.2 years) established that adolescents who do not engage in physical exercise are more likely to have more disturbed sleep than those who have higher levels of physical activity. These effects were particularly pronounced among males (Brand et al., 2010). A recent study of 48 young men and women reported a positive association between habitual sleep duration and physical activity, which were both assessed over 13 days with wrist actigraphy (Booth et al., 2012). Specifically, relative to sleep of 6 hours or more, short sleepers were significantly less likely to engage in moderate or vigorous physical activity, and spent a greater proportion of the day in sedentary activities. This study suggests that too short sleep might contribute towards adoption of a sedentary lifestyle. However, sedentary lifestyle or the way people spend their leisure time nowadays, such as TV watching, browsing the Internet or using social media (e.g., Facebook) to socialise, could also contribute towards reduced levels of physical activity or shorter sleep, as demonstrated by findings from the Nurses' Health Study in the US (Hu, Li, Colditz, Willett, & Manson, 2003). That the association between sleep duration and physical activity is likely to be bi-directional is supported by evidence from intervention studies suggesting that promoting physical activity might lead to longer sleep duration, increased deep sleep (Driver & Taylor, 2000; Naylor et al., 2000), and an overall better sleep quality (Physical Activity Guidelines Advisory Committee, 2008).

### 1.8.2.3 **Smoking**

A number of investigations have suggested that smoking is associated with sleep parameters. For example, a study of 258 insomniacs and 258 controls matched in terms of sex and age reported that 40.7% of respondents with insomnia smoked, while only 22.9% of controls were regular smokers (Jefferson et al., 2005). The study by Stranges et al., (2008)

mentioned earlier, which compared UK and US samples, reported that US smokers were more likely to report short sleep duration (defined as  $\leq 6$  hours). A different investigation by the same research group revealed that being a smoker was correlated with short sleep duration at both baseline and follow-up among female civil servants as well (Ferrie et al., 2007). A nationally representative survey of over 110,000 US adults also reported that current smoking status was related to short sleep duration (Krueger & Friedman, 2009). Similarly, a cross-sectional study conducted in Australia (N=49,405) showed that short sleep duration was more prevalent among respondents who also reported to be current smokers (Magee et al., 2009).

While the studies discussed above used self-reported sleep indices, research comparing objective sleep measures of smokers and never smokers also supports the notion that smoking is associated with abnormal sleep patterns. For example, findings from the Sleep Heart Health Study suggested that in comparison with never smokers (N=2,916) current smokers (N=779) had significantly longer sleep latency and shorter sleep duration (14 minutes on average). Current smokers also spent more time in shallow sleep, as indicated by greater proportion of Stage 1 and shorter deep sleep. These relationships were independent of sex, age, BMI, CVD or respiratory disease. Interestingly, former smokers did not have more disturbed or shorter sleep than respondents who never smoked (Zhang, Samet, Caffo, & Punjabi, 2006), suggesting that the detrimental effects of smoking on sleep might be reversible. These findings are partly supported by a recent study of healthy, young men and women from Germany (Jaehne et al., 2012), where in comparisons with non-smokers those who smoked took more time to fall asleep and spent less time asleep (13 minutes on average). In contrast, there were no differences in terms of slow-wave sleep, but smokers had higher REM sleep density. Importantly, smokers had significantly higher apnoea/hypopnea index supporting the notion



that tobacco smoking is a risk factor for sleep apnoea (Kasai et al., 2012; Punjabi, 2008). It has been suggested that one mechanism explaining why smokers experience poor and shorter sleep is due to the effects of nicotine on a range of neurotransmitters including dopamine, serotonin and norepinephrine (Zhang et al., 2006).

The studies relating smoking and sleep measures discussed above were cross-sectional (with the exception of Ferrie et al., 2007), so the temporal relationship between smoking and sleep cannot be established based on these data. Smoking negatively impacts sleep continuity, duration and architecture, which is supported by findings from the Whitehall II study where women who smoked at baseline had shorter sleep duration at follow-up (Ferrie et al., 2007). However, disturbed and/or short sleep is a stressor in itself (McEwen, 2006), which might result in more cigarettes than usual being smoked the next day. Insufficient and poor quality sleep are both associated with fatigue (Thomas, Motivala, Olmstead, & Irwin, 2011), and this could also increase the number of cigarettes smoked given the moderately stimulating effects of nicotine (Zhang et al., 2006).

In summary, I have presented evidence illustrating that sleep parameters are associated with obesity, physical inactivity and smoking. These behaviours are also well-established CVD risk factors. However, the mechanisms relating sleep measures and health behaviours with CVD are likely to be very complex. Short sleep is prospectively associated with weight gain, which might subsequently contribute towards increased CVD risk. There is emerging evidence that sleep curtailment might result in reduced levels of physical activity, which could also increase the risk of future CVD, for example, through higher levels of obesity or diabetes mellitus. Finally, smoking is an independent risk factor for CVD, but it might also increase

the risk of cardiovascular outcomes indirectly through its detrimental effects on sleep duration, continuity and architecture.

### **1.8.3 Pathway 3: Sleep and biological mechanisms**

Findings from experimental research and emerging evidence from population-based studies have shed light on the probable physiological mechanisms through which parameters of sleep might lead to CVD and CVD mortality. In this section I will discuss inflammatory, autonomic and neuroendocrine pathways with a particular focus on the first two pathways since these will be explored in Studies 2 and 3, respectively.

#### **1.8.3.1 Inflammatory pathways**

Inflammatory processes play a key role in the development of CVD (Libby, Ridker, & Hansson, 2011; Steptoe & Brydon, 2007), and low-grade inflammation might be one pathway through which insufficient and/or disturbed sleep contribute towards CVD. To review the literature supporting this contention I will first present experimental evidence followed by data from population-based studies.

#### **Experimental studies**

A study of healthy men and women described by Vgontzas et al., (2004) found that a week of a modest sleep deprivation (6 hours per night) was associated with increased secretion of IL-6 and tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ). Both inflammatory markers have been implicated in the development of CVD (Papanicolaou, Wilder, Manolagas, & Chrousos, 1998; Ridker et al., 2000). In another investigation sleep reduced to 4 hours over one night also resulted in elevated levels of both IL-6 and TNF- $\alpha$  (Irwin, Wang, Campomayor, Collado-

Hidalgo, & Cole, 2006). A study of 18 healthy men and women described by Haack and co-workers (2007) reported that 12 days of partial sleep loss (4 hours per night) resulted in a significantly higher IL-6 levels as well. However, one night of total sleep deprivation was unrelated to changes in IL-6 or TNF- $\alpha$  in a sample of ten males (Born, Lange, Hansen, Molle, & Fehm, 1997). Interestingly, a study described by Shearer et al., (2001) found that 4 days of total, but not partial, sleep deprivation was related to greater concentrations of TNF- $\alpha$  receptor 1 (thought to be involved in sleep regulation) and IL-6. More recently a study of 19 healthy men and women reported that 40 hours of total sleep loss led to significantly reduced IL-6 concentrations (Frey, Fleshner, & Wright, 2007).

C-reactive protein (CRP) is another inflammatory biomarker, which secretion is stimulated by proinflammatory cytokines, in particular IL-6. CRP is one of the most widely studied inflammatory markers (Stephens & Poole, 2010), and it has been implicated in CVD (Danesh et al., 2000; Libby et al., 2011). Sleep deprivation might also lead to elevated levels of CRP. For instance, in a study of 10 healthy young men 10 days of partial (4.2 hours per night) and 88 hours of total sleep deprivation resulted in an increase in CRP levels (Meier-Ewert et al., 2004). A recent study involving 13 healthy young men reported that sleep restriction to 4 hours over 5 days resulted in a 145% increase of CRP; interestingly following two nights of sleep recovery CRP levels remained elevated and were higher than immediately after sleep loss (van Leeuwen et al., 2009). In another study partial sleep loss (4 hours per night) over 10 days was associated with elevated levels of CRP as well, but the difference was not statistically significant in comparison with respondents who slept 8 hours per night (Haack, Sanchez, & Mullington, 2007). Similarly, two nights of sleep fragmentation by acoustic and mechanical stimuli were unrelated to changes in CRP (Stamatakis & Punjabi,

2010). A recent study in France also found no association between one night of total sleep deprivation and CRP concentration (Chennaoui et al., 2011). Interestingly, a study by Frey et al., (2007), in which 19 healthy young men and women were kept awake for 40 hours, found that in comparison with baseline CRP levels following sleep loss were significantly lower.

Taken together, there is considerable experimental evidence that acute total and partial sleep loss lead to raised concentrations of inflammatory markers such as CRP, IL-6 or TNF- $\alpha$ . In addition, sleep loss has been related to higher levels of other inflammatory cytokines, such as interleukin-1b, intracellular adhesion molecule- or interleukin-17 (Frey et al., 2007; van Leeuwen et al., 2009), but the three biomarkers discussed herein have been studied most extensively in relation to sleep deprivation, and their prospective association with CVD and in particular atherosclerosis is well established (Libby et al., 2011; Libby, Ridker, & Maseri, 2002). Not all studies discussed in this section supported the hypothesis that partial or total sleep loss lead to higher levels of CRP (Chennaoui et al., 2011; Haack et al., 2007) or IL-6 and TNF- $\alpha$  (Born et al., 1997; Chennaoui et al., 2011). This might be in part explained by differences in methodology including the number of nights of total or partial sleep loss (e.g., one versus ten), or whether participants spent the first or the second part of the night awake (in partial sleep loss protocols). The frequency of blood collection, the presence or absence of light and circadian phase has been cited as well (Frey et al., 2007). Finally, individual differences in basal levels of inflammatory markers and in physiological responses to sleep loss were also likely to contribute towards the divergent findings (Motivala, 2011; Mullington et al., 2009).

## **Population-based studies**

The association of short sleep duration and disturbance with elevated levels of inflammatory markers has been reported in population studies, but findings remain inconsistent (Mullington et al., 2010). I have already mentioned in the section on sleep and ageing (page 48) that better sleep has been cross-sectionally associated with lower IL-6 levels in older women (Friedman et al., 2005). On the other hand, in the Whitehall II study women who slept 8 hours, as compared to 7 hours, had significantly lower levels of IL-6, after adjustment for relevant covariates. Moreover, women who reported sleeping 5 hours or less on average had elevated high sensitivity CRP concentrations (Miller et al., 2009). A more recent investigation based on the Whitehall II data found that short sleep duration was prospectively associated with higher IL-6, but not CRP, independently of demographic and health-related covariates (e.g., age, blood pressure) (Ferrie et al., 2013). A small US study of 70 young healthy men and women (Hong, Mills, Loreda, Adler, & Dimsdale, 2005) reported that raised levels of IL-6 also appear to be associated with poor sleep efficiency. However, in the Wisconsin Sleep Cohort study of 907 men and women (mean age 52.8 years) sleep duration was unrelated to CRP levels (Taheri et al., 2007). Sleep hours were not linked to CRP in the Chicago Health, Aging and Social Relations study as well, but respondents with longer sleep latency ( $\geq 30$  minutes) had significantly elevated levels of this biomarker (McDade, Hawkey, & Cacioppo, 2006). Sleep problems and short sleep duration were unrelated to inflammatory markers in a study of middle- and early-old aged Taiwanese adults, but long sleep hours predicted raised levels of CRP, IL-6 and fibrinogen (another marker of inflammation implicated in the development and pathogenesis of CVD (Danesh, Lewington, Thompson, Lowe, & Collins, 2005) (Dowd, Goldman, & Weinstein, 2011). Insomnia

symptoms (defined as difficulties falling or staying sleep and non-restorative sleep) were also unrelated to CRP concentrations in middle-aged men and women from the Nord-Trøndelag Health Study (HUNT study) in Norway (Laugsand, Vatten, Bjørngaard, Hveem, & Janszky, 2012). In Finland disturbed sleep was prospectively associated with higher CRP concentrations, but only among men (average age 31 years) (Liukkonen et al., 2007). In contrast, Suarez (2008) found that CRP and IL-6 were higher in women who reported disturbed sleep, but no association was found in men, and sleep duration was unrelated to inflammatory markers in either sex. Complex relationships between sleep measures and markers of inflammation were also found in the Study of Women's Health Across the Nation (SWAN) (Matthews et al., 2010). For example, subjective and objective sleep duration was unrelated to inflammatory markers in the full sample, but African-American women with short objective sleep had higher levels of CRP, while fibrinogen was higher only among African-American women with poor sleep continuity. Finally, a recent study of older men and women with established CHD found that sleep problems (e.g., difficulties falling asleep) were associated with higher levels of CRP, fibrinogen and IL-6, albeit only in women (Prather, Epel, Cohen, Neylan, & Whooley, 2013).

It is uncertain why findings relating sleep measures with markers of inflammation are inconsistent in population-based research. One probable explanation might be due to the difference in sleep measures used in experimental and population-based studies. For example, data from the Cleveland Family study revealed that PSG-defined short sleep was related to higher TNF- $\alpha$ , while self-reported sleep was positively associated with CRP and IL-6 concentrations (Patel et al., 2009). This suggests that self-report and PSG could be measuring distinct phenomena. Depending on the study's protocol PSG provides a measure of sleep

across 1, 2 or 3 nights, while self-reported sleep measure usually refers to habitual sleep duration, typically in the last month or so (Patel et al., 2009). Differences in populations studied in terms of ethnicity or age might be another explanation. In addition, some studies treated gender as a covariate (Taheri et al., 2007) while others analysed men and women separately (Liukkonen et al., 2007). This is important since sex differences in responses to acute sleep loss have been reported, with higher levels in inflammatory markers being found in women (Irwin, Carrillo, & Olmstead, 2010). It has thus been suggested that gender might moderate the relationship between sleep curtailment and inflammation (Mullington et al., 2010; Mullington et al., 2009). Another explanation for the somewhat weaker and less consistent findings in observational studies, when compared with the experimental sleep literature, could be that the associations between sleep measures and inflammatory markers are relatively small at the population level, so very large samples might be necessary to detect these effects (Mullington et al., 2010). Clearly more research in this area of the sleep literature is needed. In particular, given the emerging evidence that poor or insufficient sleep might be more detrimental to health in older individuals (Naidoo, 2009), and the fact that the accumulation of risk factors for mortality increases with advancing age (Gruenewald et al., 2006) suggest that elderly cohorts might particularly benefit from further research in this area. There is some evidence linking sleep indices with biological markers including inflammatory factors in older people, but the existing studies were either based on small and unrepresentative samples, or comprised only women (e.g., Friedman et al., 2005; McDade et al., 2006). This limitation will be addressed in Study 1 (Chapter 2) where I will analyse associations between biological factors including inflammatory markers and sleep measures using a large representative study of British men and women aged 50 years or older.

### 1.8.3.2 **Autonomic pathways**

Reduced heart rate variability (HRV), which indicates an imbalance between sympathetic and parasympathetic modulation of the heart, has been implicated in the long-term development of CVD and mortality (Thayer, Hansen, & Johnsen, 2010; Thayer & Lane, 2007). In normal, healthy sleep sympathetic tone is generally lower while parasympathetic modulation of the heart is higher than during wakefulness, in particular during deep sleep. Sympathetic modulation increases in REM sleep and during night-time awakenings (Stein & Pu, 2012; Trinder et al., 2001; Viola et al., 2002). Sleep deprivation might potentially increase the dominance of sympathetic activity over parasympathetic modulation (Meerlo et al., 2008). However, this area of the sleep literature received considerably less attention than the associations relating sleep measures with inflammatory or endocrine processes, and the experimental data have been inconsistent (Stein & Pu, 2012).

### **Experimental studies**

An Australian investigation reported that 30 hours of sleep deprivation was coupled with a decrease in sympathetic activity, but no change of parasympathetic modulation (Holmes, Burgess, & Dawson, 2002). On the other hand, in the US a study involving 16 men and 2 women found that while acute sleep deprivation was associated with augmented sympathetic activity, parasympathetic activity was reduced (Zhong et al., 2005). These data are supported by findings from a French study in which 40 hours of total sleep loss resulted in a significant decrease of parasympathetic modulation, while the sympathetic activity was markedly higher (Sauvet et al., 2010). Similarly, in Brazil 5 nights of sleep lasting between 3 and 5 hours were associated with a significantly higher sympathetic tone and a significantly lower



parasympathetic tone (Dettoni et al., 2012). However, two different investigations of the effects of one night of sleep deprivation on autonomic regulation found that sleep loss predicted an increase in vagal tone (Pagani et al., 2009; Vaara, Kyrolainen, Koivu, Tulppo, & Finni, 2009) (see Table 1.2 for an overview of the above studies).

**Table 1.2 Characteristics of experimental studies of sleep deprivation and HRV.**

<b>Authors, country, journal, published year</b>	<b>Sample description</b>	<b>Details of experimental manipulation</b>	<b>Measures of sympathetic activity (SA) and parasympathetic activity (PA)</b>	<b>Main findings</b>
<b>Holmes et al.</b> , 2002, Australia, Journal of applied physiology	12 healthy subjects (6 men and 6 women), mean age: 23 years	30 hours of total sleep deprivation spent in a recumbent position	SA: pre-ejection period via impedance cardiography; PA: power spectral analysis (frequency domain)	Decline in SA; no change in PA
<b>Zhong et al.</b> , 2005, US, Journal of applied physiology	18 healthy subjects (16 men, 2 women), mean age:26 years	36 hours of total sleep deprivation in recumbent and seated positions, plus vigilance and executive function tests on a computer	SA and PA both measured with power spectral analysis	Increase in SA in recumbent, sitting and vigilance test conditions; decrease in PA in sitting and vigilance test conditions
<b>Pagani et al.</b> , 2009, Italy, Autonomic neuroscience: basic & clinical	24 healthy subjects (12 men, 12 women), age range: 27-45 years	24 hours of total sleep deprivation	SA and PA both measured with power spectral analysis	No change in SA, increase in PA

<b>Vaara et al.,</b> 2009, Finland, European journal of applied physiology	20 healthy military cadets (17 men, 3 women), mean age: 26 years	60 hours of total sleep deprivation while maintaining normal military tasks apart from rigorous physical activity	SA and PA both measured with power spectral analysis	Increase in SA, increase in PA
<b>Sauvet et al.,</b> 2010, France, Journal of applied physiology	12 healthy subjects (12 males), mean age: 29 years	40 hours of total sleep deprivation	SA and PA both measured with power spectral analysis	Increase in SA, decrease in PA
<b>Dettoni et al.,</b> 2012, Brazil, Journal of applied physiology	13 healthy men, mean age: 31 years	5 days of partial sleep deprivation (4.5 hours on average) in natural settings (at home)	SA and PA both measured with power spectral analysis	Increase in SA, decrease in PA

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Sleep fragmentation has been found related to changes in autonomic activity as well. For instance, a study involving healthy young men (N=9) and women (N=2) reported that two nights of fragmented sleep were associated with a significant increase of sympathetic and a significant decrease of parasympathetic nervous activity. Interestingly, sleep duration was not experimentally reduced in that study (Stamatakis & Punjabi, 2010). Similarly, in a sample of 9 men and women 3 nights of suppression of SWS, but maintenance of normal sleep duration, also resulted in a significant shift of autonomic activity towards sympathetic modulation of the heart (Tasali et al., 2008). Acute stress is another factor associated with reduced HRV during sleep. An analysis described by Hall et al., (2004) illustrated, for instance, that experiencing acute stress immediately prior bedtime (being asked to give an oral speech upon waking up) resulted in augmented sympathetic and reduced parasympathetic modulation of the heart during the night.

It is unclear why the effects of sleep loss on autonomic nervous system differ across studies, but methodological consideration might be one possible explanation. For instance, body posture (whether participants spent their sleep deprivation period sitting or lying down), food or nutrients content, room temperature, the presence of a cognitive challenge or emotional stress associated with spending one/few nights in the sleep laboratory could be relevant (Stein & Pu, 2012).

### **Clinical studies**

There is extensive research relating cardiac autonomic regulation with sleep apnoea and specific clinical problems such as chronic fatigue syndrome, irritable bowel syndrome or chronic heart failure (e.g., Burton, Rahman, Kadota, Lloyd, & Vollmer-Conna, 2010; Robert, Elsenbruch, & Orr, 2006; Ueno et al., 2011). It has been well documented that

OSA is associated with reduced HRV, as indicated by lower parasympathetic and higher sympathetic modulation of the heart. These alterations of autonomic function were detected in individuals free of hypertension or heart failure, and they seem to be linked to the severity of OSA (Narkiewicz et al., 1998). This suggests that reduced HRV might be one pathway through which OSA increases the risk of cardiovascular outcomes (Stein & Pu, 2012). HRV has also been studied in individuals with chronic insomnia (e.g., Spiegelhalder et al., 2011), but findings have been inconsistent (Stein & Pu, 2012).

### **Population-based studies**

To date research relating sleep measures with autonomic modulation of the heart remains sparse in healthy population samples (Stein & Pu, 2012). For example, in university students aged 22 years on average self-reported sleep deprivation (defined as sleep reduced by at least 80%) experienced during final exams was associated with a significantly reduced HRV, when compared with HRV measured before the exam period. At both times HRV was measured for 1 hour between 4 and 6 PM (Takase et al., 2004). Shift and night-time work are associated with disturbed sleep, and Chung et al., (2009) studied HRV of nurses working only during the day and of those working only at night. HRV was assessed during sleep in this investigation. Nurses with regular night-time shifts had longer sleep latencies, less deep sleep and a significantly higher sympathetic modulation of the heart than nurses working only during the day.

The above two studies tentatively suggest that poor/insufficient sleep might be associated with lower HRV in everyday life. However, these data cannot be extrapolated to the general population since shift work and university examination period do not reflect the lives of the majority of people. Moreover, the validity of the sleep deprivation measure in the study described by Takase et al., (2004) is questionable. More importantly though,

although all respondents in that investigation reported having their sleep duration reduced by at least 80%, the changes seen in HRV might have been driven by sleep deprivation, stress associated with undergoing final university exams, or a combination of both. The authors did not explore the independent effects of these variables. It therefore remains unclear whether sleep disturbance or loss would be associated with impaired HRV in real life settings. I will address this gap in the sleep literature in Study 2 (Chapter 3) by exploring relationships between sleep disturbances and HRV in a sample of 199 healthy, working women.

Another relevant issue in this context is whether disturbed sleep is associated with lower HRV during the day, at night or both. To date the link between impaired sleep and HRV has been measured at night (Chung et al., 2009), in the early evening (Takase et al., 2004) or during experimentally induced sleep deprivation (e.g., Zhong et al., 2005). There have been no naturalistic studies of disturbed sleep and HRV assessed both during the day and at night. This limitation of the literature will also be addressed in Study 2 by analysing the relationship between sleep and HRV measured over a 24-hour period.

### 1.8.3.3 **Neuroendocrine pathways**

The hypothalamic-pituitary-adrenal (HPA) axis is part of a neuroendocrine system implicated in the stress response. Briefly, in a response to a stressful event or stimuli hypothalamus releases corticotrophin-releasing hormone, which induces the release of adrenocorticotrophic hormone from the pituitary glands. Adrenocorticotrophic hormone, on the other hand, stimulates the release of glucocorticoids in the adrenal cortex (Meerlo et al., 2008).

Cortisol is a well-established stress hormone, which has been implicated in various diseases including CVD (Dekker et al., 2008; McEwen, 2007). Cortisol levels show a pronounced diurnal rhythm with highest concentrations in the morning and lowest in the

night. Cortisol plays multiple functions in humans, for instance, it is involved in energy regulation via its effects on insulin and glucose metabolism. Cortisol is also implicated in inflammatory processes, and levels are generally negatively associated with IL-6 (Motivala, 2011).

### **Experimental studies**

Studies in humans have shown that optimal sleep (in terms of duration and quality) is associated with a healthy diurnal profile of cortisol release. This has led to the hypothesis that abnormal sleep patterns might contribute to increases of cortisol secretion, but experimental data have been mixed (Meerlo et al., 2008; Mullington et al., 2009). While some studies of sleep deprivation (partial and total) found no increases in cortisol levels (Akerstedt, Palmblad, Delatorre, Marana, & Gillberg, 1980; Born et al., 1997; Follenius, Brandenberger, Badesapt, Libert, & Ehrhart, 1992; Shearer et al., 2001), more recent investigations showed that total and/or partial sleep deprivation (e.g., 4 hours per night) were associated with raised cortisol concentrations in the evening (Leproult et al., 1997; Reynolds et al., 2012; Spiegel et al., 2004; Spiegel et al., 1999). In a study conducted by Vgontzas et al., (2004) the association between sleep curtailment (6 hours per night over 1 week) and cortisol levels was complex, since although cortisol values were higher in the second part of the night, the morning peak of cortisol was lower when compared with cortisol concentrations when sleep was not restricted. In a sample of young women one night of partial sleep deprivation (3 hours) resulted in a significantly lower morning cortisol levels and higher afternoon/evening values, suggesting a slower decline of cortisol concentrations throughout the day (Omisade, Buxton, & Rusak, 2010). However, a study of 13 healthy young men in Finland found no association between 5 nights of sleep restricted to 4 hours and cortisol levels (van Leeuwen et al., 2009).

Interestingly, there is evidence suggesting that poor sleep quality is associated with elevated cortisol concentrations as well. A study of healthy men (N=9) and women (N=2) found that experimentally induced sleep fragmentation throughout all sleep stages over 2 nights was associated with a 12.5% increase in morning cortisol levels. Importantly, sleep duration was not experimentally reduced in this study (Stamatakis & Punjabi, 2010).

### **Population-based studies**

Evidence from population-based studies supporting the hypothesis that sleep disturbance and loss are linked to deregulated cortisol secretion has been inconsistent (Motivala, 2011; Mullington et al., 2009). I have already mentioned on page 48 that in older men and women good sleep quality has been prospectively linked with lower diurnal cortisol outputs (Wrosch et al., 2008), while short sleep at baseline predicted higher cortisol levels at a 4-year follow-up (Rueggeberg et al., 2012). Poor sleep quality was also associated with blunted cortisol profiles in a sample (N=147) of middle-aged British people (Lasikiewicz et al., 2008). Furthermore, a study conducted among 2751 British civil servants revealed that sleep disturbances and short sleep duration (<5 hours) were predictive of a flatter cortisol profile. Short sleep duration was also related to a steeper morning rise in cortisol. These findings were independent of potential covariates such as age, smoking or waist circumference (Kumari et al., 2009). A recent study of 4066 Danish civil servants found no cross-sectional association between sleep duration and cortisol, but disturbed sleep in the last month was linked to lower morning and evening cortisol levels. Moreover, a 3-month follow-up of 387 participants revealed that sleep problems including frequent morning awakenings predicted a flatter cortisol profile, as indicated by a lower cortisol awakening response and a reduced cortisol slope (Hansen et al., 2012). Sleep problems were unrelated to cortisol measures in a recent study conducted in Sweden, but



symptoms of tiredness and non-refreshing sleep were associated with a higher cortisol awakening response, in particular amongst women (Eek, Karlson, Garde, Hansen, & Orabeak, 2012). An observational study of 96 community-dwelling Chinese men and women reported no association between cortisol awakening response and measures of sleep duration and quality (defined with wrist actigraphy) (Zhang et al., 2011). Similarly, a study described by Garde et al., (2011) of 265 working men and women from Denmark found no relationship between sleep problems and morning cortisol levels as well.

Taken together, physiological mechanisms by which parameters of sleep might be associated with CVD and CVD mortality are only beginning to be discovered, and experimental sleep studies have contributed substantively to this area of the sleep literature. Research conducted in a laboratory setting enables the measurement of a number of physiological functions and biomarkers, which are usually not feasible in larger studies or population-based surveys (Steptoe & Poole, 2010). In addition, the experimental studies discussed above were conducted with carefully selected young and healthy respondents so the changes seen in inflammatory markers, cortisol levels or HRV can be attributed to short or fragmented sleep, and are unlikely to be confounded by underlying medical or mood disorders.

However, experimental sleep studies are associated with a number of caveats. Due to ethical reasons and/or financial constraints experimental sleep studies are usually conducted over very few days, so the long-term consequences of disturbed or short sleep on human physiology remain uncertain (Meerlo et al., 2008). Moreover, a number of experimental studies reviewed in this chapter tested the effects of total sleep deprivation, or of sleep restricted to just 4 hours, on human biology, but such sleep conditions are rarely present in real life. Indeed, evidence suggests that most people are not able to sustain wakefulness or cognitive function for long periods of time while sleeping just 4 hours per

night (Blagrove et al., 1995). Interestingly, the development of activity-based measures has facilitated the objective investigation of sleep parameters in ordinary life, without the need for staying in sleep laboratories. In addition, advances in technology have also opened up an opportunity to assess biological markers, for instance heart rate, in real life settings (Steptoe & Poole, 2010). This is important as the major advantage of measuring both sleep and biomarkers in everyday life is that these measures have greater ecological validity than those obtained in the sleep laboratory. Naturalistic studies might therefore be suitable to further explore the autonomic, neuroendocrine and inflammatory mechanisms described in this section. For instance, as pointed out above, associations between sleep loss, disturbance and HRV have been mainly investigated in clinical or experimental studies, and remain largely unexplored in healthy population samples. In addition, associations between sleep measures and inflammatory markers have not been systematically studied in representative cohorts of older men and women. Another limitation of the experimental literature discussed in this section is that the majority of studies were either conducted with men or involved too few women. This is problematic because sex differences in inflammatory responses to sleep loss have been reported (Irwin et al., 2010). In addition, the recruitment of young and healthy samples to experimental studies limits the generalizability of these data to the general population, and in particular to older individuals. These limitations can be addressed with well-designed population-based studies.

It should be mentioned that due to space constraints only autonomic, neuroendocrine and inflammatory pathways that might relate sleep parameters with CVD and CVD mortality were outlined in this section. However, other mechanisms, for example, appetite regulation or glucose metabolism, are also thought to be contributing towards the increased risk of cardiovascular outcomes in people with poor and/or short sleep (Knutson, 2010;

Knutson et al., 2007; Mullington et al., 2009; Spiegel et al., 2009; Van Cauter et al., 2007). Moreover, in the forthcoming studies I will explore relationships between sleep measures, inflammatory factors and HRV. Research relating sleep indices with cortisol has yield inconclusive findings so it warrants further investigation, but time constraints do not allow me to investigate this field of the sleep literature as well.

#### 1.8.3.4 **Sleep and psychosocial risk factors**

I have so far presented evidence suggesting that sleep duration and disturbance might contribute towards higher risk of CVD and CVD mortality through at least three pathways: disordered mood, unhealthy lifestyle choices and direct biological dysregulation. However, it ought to be acknowledged that sleep abnormalities are associated with a number of psychosocial factors, which might impact cardiovascular health through their detrimental effects on sleep. In other words, sleep might also be on the intermediate pathway between psychosocial characteristics and CVD. Although this area of sleep research is not the focus of this thesis, it is an important topic, and in this section I will discuss studies relating sleep measures with socioeconomic characteristics, social support and work stress.

Lower SES is a strong risk factor for CVD and CVD mortality (Hemingway & Marmot, 1999; Rozanski et al., 2005), and it has been documented that individuals from disadvantaged socio-economic groups are more likely to have poorer sleep quality and/or shorter sleep duration (Van Cauter & Spiegel, 1999). For example, in the Detroit Area Study (N=1139) Moore et al., (2002) reported that poor sleep quality was more prevalent among respondents with lower education and income, after adjustment for age, sex and health status. Sleep duration was unrelated to SES in this study. Data from a representative survey of over 8,000 British men and women aged 16-74 years revealed that independently of age, sex, having children, marital status and depression low or no

qualification (relative to degree) and being unemployed (relative to full-time employment) were significantly associated with higher ORs of disturbed sleep (Arber, Bote, & Meadows, 2009). In addition, in a sample of older US women socioeconomic characteristics were associated with poor sleep quality, defined both with the PSQI (Buysse et al., 1989) and home-based PSG (Friedman et al., 2007). Specifically, independently of demographic factors (age, marital status) or smoking, fewer years of education and lower income were associated with longer objective sleep latency, while lower income was related to poorer subjective sleep quality. In the Whitehall II study lower SES, indexed by employment grade, was associated with higher ORs of short sleep hours (<6 hours), relative to 6-8 hours (Stranges et al., 2008). A study of working Japanese men and women (N=3684) reported that men in a lower SES group (assessed with employment grade) had a significantly poorer sleep quality than men in higher SES groups. Importantly, the association between SES and physical health was reduced by 21.1% after a global rating of sleep quality was added to the statistical model (Sekine, Chandola, Martikainen, Marmot, & Kagamimori, 2006).

Low social support is a well-established risk factor for ill health (Uchino, Cacioppo, & KiecoltGlaser, 1996), and it has been found prospectively associated with the progression of atherosclerosis (Wang, Mittleman, & Orth-Gomer, 2005). Interestingly, there is evidence suggesting that low or lack of social support might be related to sleep measures too. For example, infrequent contact with friends and low emotional support were found to be risk factors for insomnia among elderly Swedish men (Hanson & Ístergren, 1987). A more recent cross-sectional Swedish investigation of 6231 men and women established that low network support mediated the relationship between sleep disturbances and MI in women, but not in men (Nordin, Knutsson, & Sundbom, 2008). A study of older adults with insomnia (N=79) and controls (N=40), who were matched for

sex and age, reported that in both groups higher levels of social support were correlated with shorter objective sleep latency (assessed with wrist actigraphy). Other sleep parameters, such as duration or subjective sleep quality, were unrelated to social support in these data (Troxel, Buysse, Monk, Begley, & Hall, 2010).

Social support in the workplace is also a correlate of sleep. For example, a Swedish study (N=5231) suggested that respondents reporting higher social support at work were less likely to have disturbed sleep, while those with low social support had awakening difficulties, such as waking up too early or waking up feeling unrefreshed (Akerstedt et al., 2002). Relatedly, low social support at work was linked to poor sleep quality in a sample of 351 Swedish pilots (Runeson, Lindgren, & Wahlstedt, 2011).

The studies discussed above were all cross-sectional thus it is possible that low social supports engenders poor sleep, and/or that poor sleep impacts negatively on social interactions with others. Indeed, this was reported in an earlier study of older men and women (Dew et al., 1994), in which PSG-assessed inefficient sleep at baseline predicted lower instrumental support from family members and friends at a 12-month follow-up.

High levels of social support are associated with a lower prevalence of morbidity and mortality including better cardiovascular health. The pathways through which social support exerts its protective effects on health include endocrine and immune function as well as autonomic activity (Uchino et al., 1996). To date the mechanisms relating sleep and social support with negative health outcomes have not been investigated. Interestingly, a study of 74 older women reported that high objective sleep efficiency and positive relationships with others (e.g., “I feel I can get a lot out of my friendships”) were both independent predictors of lower IL-6 concentrations, after adjustment for relevant confounders (Friedman et al., 2005). IL-6 concentrations were highest in women who had low sleep efficiency and weak social relationships. However, respondents who had poor

sleep efficiency but good relationships with others, or those with high sleep efficiency but inadequate relationships also had low levels of IL-6. More recently analysis of the Survey of Mid-life in the US (MIDUS) revealed that objective sleep efficiency and subjective sleep quality moderated the effects of poor relationships with others on IL-6, but only in men. As in the earlier study by Friedman et al., (2005), in these data good social relationships buffered the impact of poor sleep on IL-6 as well (Friedman, 2011). Although these studies were based on a cross-sectional design and did not directly assess social support they nonetheless suggest that depending on their quality social relationships might either buffer or exacerbate the impact of sleep on health.

Work stress has also been implicated in CVD. The literature in this area has been dominated by the demand-control model (Karasek & Theorell, 1990), which posits that a combination of low decision latitude, demanding work characteristics and low social support from co-workers and supervisors elicit stress in the workplace. Stressful working conditions assessed with the demand-control model (Karasek & Theorell, 1990) have been found associated with adverse health outcomes including CHD. For example, a cross-sectional study of 5231 Swedish men and women established that in comparison with participants reporting low demands at work, those with high demands were significantly more likely to report disturbed and unrefreshed sleep. There was no association between low decision latitude and sleep parameters in that study (Akerstedt et al., 2002). A prospective cohort study in Japan explored whether job strain (defined as a combination of high demands and low control) and social support in the workplace were associated with future onset and maintenance of insomnia. Results revealed that while job strain was related to a new episode of insomnia, low social support was associated with its maintenance (Ota et al., 2009). Another recent prospective investigation explored the relationships between job control, job demands and sleep quality, and reported that at a 1-

year follow-up both stress measures were linked to a decrease in sleep quality (De Lange et al., 2009).

Siegrist (1996) developed an alternative model termed the effort-reward imbalance model, which defines work stress as a lack of reciprocity between efforts and rewards. In addition, the model distinguishes between extrinsic and intrinsic effort. The former reflects a person's perception of efforts needed to deal with work demands. The latter refers to a personal coping style, referred to as "overcommitment", with challenges in the workplace. Overcommitted individuals tend to exaggerate their efforts due to their desire for approval and/or social recognition, and are often unable to withdraw from work obligations (Siegrist, 1996). Effort/reward imbalance and/or overcommitment have been found to prospectively predict CVD (Kivimaki et al., 2002; Kuper, Singh-Manoux, Siegrist, & Marmot, 2002; Lynch, Krause, Kaplan, Tuomilehto, & Salonen, 1997). Effort/reward imbalance and/or overcommitment are also associated with disturbed sleep. For example, sleep problems were positively associated with overcommitment in a cross-sectional study of British civil servants (Steptoe, Siegrist, Kirschbaum, & Marmot, 2004). In addition, a cross-sectional analysis of data from a study of German employees showed that overcommitment was associated with sleep disturbances in men, whereas lower reward and overcommitment predicted sleep disturbances in women (Kudielka, Von Kanel, Gander, & Fischer, 2004). Finally, a cross-sectional investigation in Sweden established that higher overcommitment and greater effort/reward imbalance were associated with sleep disturbances in both sexes (Fahlen et al., 2006).

To date there have been few longitudinal studies relating effort/reward imbalance, overcommitment and sleep parameters. Rugulies and colleagues (2009) analysed cross-sectional and longitudinal associations between effort/reward imbalance and sleep disturbances in a sample of Danish men and women. While effort/reward imbalance was

related to disturbed sleep in both sexes at baseline, at a 5-year follow-up work stress predicted the onset of sleep disturbances only among males. A study described by Ota et al., (2009) reported that effort/reward imbalance at baseline was related to the maintenance of insomnia at a 2-year follow-up, whereas among participants without insomnia symptoms at baseline overcommitment predicted the onset of a new episode of insomnia. Although more longitudinal studies relating effort/reward imbalance and overcommitment with impaired sleep are warranted, these data suggest that work stress is a risk factor for sleep problems.

Taken together, the evidence discussed above raises the possibility that links between psychosocial factors and CVD might be mediated in part through disturbances of sleep. I have discussed SES, social support and work stress as examples of psychosocial characteristics, but other factors such as loneliness (Cacioppo et al., 2002) might also be relevant.

## **1.9 Sleep measurement**

Experimental and observation studies have suggested that insufficient sleep duration is detrimental to health. Findings from population studies indicate that long sleep duration is associated with ill health as well (Cappuccio et al., 2010; Gallicchio & Kalesan, 2009), albeit, as already discussed, long sleep is thought to be a marker of ill health rather than a risk factor. There is increasing evidence that impaired sleep quality is also related to adverse health outcomes (Chandola et al., 2010; Ekstedt et al., 2004; Hoevenaar-Blom et al., 2011; Laugsand et al., 2011; Meerlo et al., 2008; Spiegel et al., 2009; Zisapel, 2007), including mortality (Dew et al., 2003). This highlights the importance of assessing both sleep quality and duration as possible risk factors for ill health. However, I have already pointed out on a number of occasions that accurate sleep measurement is difficult, and consequently poses a number of challenges to researchers and health professionals. This

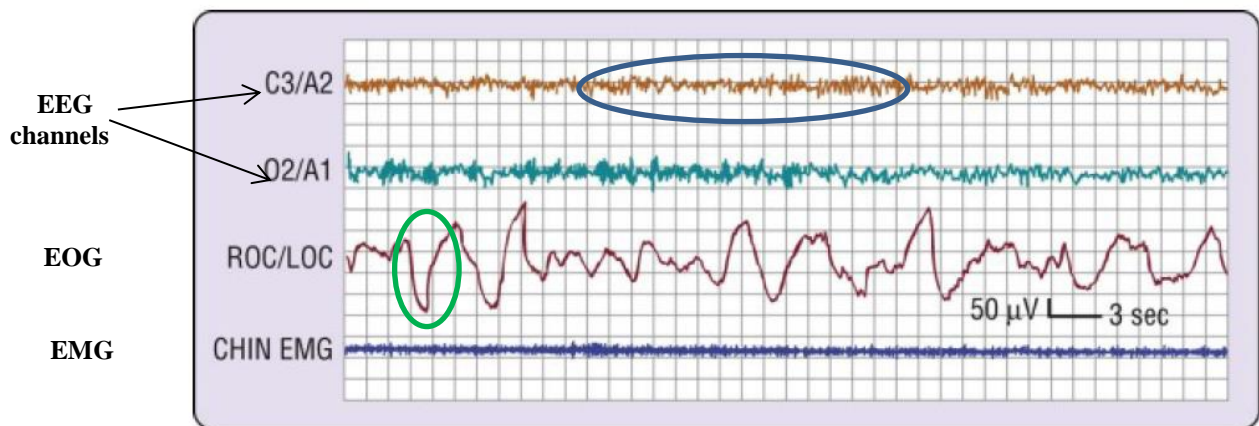


section will therefore focus on the measures used to assess sleep parameters and the limitations associated with this field of the sleep literature.

### 1.9.1 Polysomnography (PSG)

PSG is the gold standard objective measure of sleep which records physiological data during sleep (Ancoli-Israel et al., 2003; Institute Of Medicine, 2006). The advantage of this method over other sleep measures is that sleep is assessed by incorporating data from at least three polysomnographic measures: the electroencephalogram (EEG), the electrooculogram (EOG) and the electromyogram (EMG) (see Figure 1.6 for an example of data provided by each of the three measures).

**Figure 1.6 The transition from wakefulness to Stage 1 of sleep (adapted from Carskadon & Dement, 2011).**



C3/A2 and O2/A1 refer to two different EEG channels. ROC refers to right outer canthus (eye corner) and LOC refers to left outer canthus and both provide information about slow eye movements. The transition from wakefulness to Stage 1 can be observed on the C3/A2 and O2/A1 channels where rhythmic alpha activity (synonymous with a state of relaxation) seen on the left changes into a low-voltage, mixed frequency pattern approximately in the middle of the figure (marked by the blue circle). The ROC/LOC channel indicates slow eye movements (marked by the green circle) that occur before the change in EEG pattern. As suggested by Carskadon and Dement (2011) both EEG change and slow eye movements are usually required to confirm the transition from wakefulness to sleep. Finally, as indicated by EMG, muscle tone seems minimal here.

EEG is attached to the skull and measures cortical activity (brainwave), EOG provides information about eye movements while EMG is attached to the chin and records muscle tone (Ancoli-Israel et al., 2003; Carskadon & Dement, 2011). Data from these three channels are used to score sleep stages. PSG also provides accurate information on sleep parameters such as total sleep time, sleep onset latency, sleep efficiency (usually defined as the ratio of the time spent asleep to the total time spent in bed) and wake up time after sleep onset. In addition, studies using PSG often measure heart activity (with electrocardiogram), chest and abdominal excursion, body position and air flow (Blackwell et al., 2008). PSG is useful for assessing pathological sleep patterns including sleep disordered breathing (Hirshkowitz & Kryger MH, 2011; Young et al., 1993) and periodic

leg movements (Krystal & Edinger, 2008). PSG might be used to diagnose insomnia as well, but the obtained data should be supported by information from sleep questionnaires, sleep diaries and a clinical consultation. This is because insomnia has a number of different manifestation, and it might be a symptom of many medical conditions and/or a sleep disorder (i.e. primary insomnia) (Spielman, Yang, & Glovinsky, 2011).

To measure sleep participants are required to spend one or more nights in the sleep laboratory (in contrast to ambulatory PSG which is discussed below). This enables to control for various biases and personal characteristics (Steptoe & Poole, 2010), so it is a major advantage of PSG. However, spending a night in the sleep laboratory might impact on sleep quality and/or duration due to a “first-night effect” (Toussaint et al., 1995) and, as a consequence, lead to spurious results. For example, Lorenzo and Barbanoj (2002) compared polysomnographic sleep data of healthy young men and women across 12 nights and found a significantly reduced sleep quality during the first night. This was driven by a longer REM latency (people taking longer to enter REM sleep) and shorter time spent in REM. There was no significant difference in sleep between the remaining nights (Lorenzo & Barbanoj, 2002). This underscores the importance of the inclusion of an adaptation night in a study protocol, which has been done by some authors (Dijk et al., 2010; Mills, Von Kanel, Natarajan, Ziegler, & Dimsdale, 2007; Sivertsen et al., 2006), but not others (Johnson et al., 2007). In addition, PSG requires trained technicians to score and interpret sleep data, which makes it labour-intensive so it is often impractical in a clinical setting (van de Water, Holmes, & Hurley, 2011). Along the same lines, high financial cost and participant burden often make PSG prohibitive in large population studies.

### **1.9.2 Ambulatory sleep measures**

Ambulatory sleep measures, such as home-based PSG (Blackwell et al., 2008; Ekstedt et al., 2004; Silva et al., 2007) or actigraphy (Stone & Ancoli-Israel, 2011), are an

alternative approach to objective sleep assessment. Home-based PSG was used, for instance, in the Sleep Heart Health Study, a large prospective cohort study set out to investigate the association between sleep disordered breathing and cardiovascular outcomes (Quan et al., 1997). The advantage of this objective method is that it records rich sleep data in a natural setting, so it has a greater ecological validity than PSG. However, the equipment (e.g., EEG, EOG, EMG, airflow or heart rate monitors) needs to be fitted by trained technicians during a home visit at about one or two hours before bedtime. This is likely to be costly, and could also be burdensome for participants. Because PSG sensors might be uncomfortable to wear the “first-night effect” could impact sleep measures such as duration or latency (Silva et al., 2007).

Another possibility is to measure sleep with actigraphy. The device is usually worn on a wrist (wrist actigraphy), but it is possible to fit it on an ankle or trunk instead (Ancoli-Israel et al., 2003). While in PSG or home-based PSG at least three sources of information are used to infer sleep, an actigraph contains an accelerometer measuring the arm, leg or torso’s movements per epoch (1 epoch=30 or 60 seconds), which are then used to calculate sleep and wake periods. It therefore does not assess sleep in the same sense as PSG since the activity pattern is an approximation of sleep, and not sleep itself (Krystal & Edinger, 2008; Morgenthaler et al., 2007a). The validity and reliability of actigraphy has been established by comparing it against the gold standard sleep measure -PSG (Ancoli-Israel et al., 2003; Sadeh, 2011; van de Water et al., 2011). The general agreement is that actigraphy performs best at measuring total sleep time, and in normal subjects the reliability coefficients range between 0.89 to 0.98 when compared with PSG-assessed total sleep time (Stone & Ancoli-Israel, 2011). While earlier reviews (Sadeh, Hauri, Kripke, & Lavie, 1995) recommended actigraphy for sleep assessment mainly in healthy populations, advances in technology has made actigraphy suitable for a clinical setting as well. For

example, in insomnia actigraphy might be useful for the assessment of total sleep time or sleep variability across several nights (Sadeh, 2011; Stone & Ancoli-Israel, 2011). Actigraphy can also be used to record periodic limb movement during sleep, sleep fragmentation in patients with sleep apnoea (Stone & Ancoli-Israel, 2011), or to study sleep patterns in individuals with circadian rhythm sleep disorders (Morgenthaler et al., 2007b). Actigraphy is unobtrusive and less cumbersome than PSG, so it is recommended for objective sleep assessment in paediatric and elderly populations, and in particular among elderly living in nursing homes or those suffering from dementia (Ancoli-Israel et al., 2003; Stone & Ancoli-Israel, 2011).

There are numerous advantages of measuring sleep with actigraphy, for instance, in contrast with PSG or home-based PSG it is less costly and easier to use. Actigraphy has a higher ecological validity than PSG since it is less obtrusive and participant burden is greatly reduced. Because an actigraph can record sleep data for many nights it is particularly useful for studying sleep variability in insomnia or circadian sleep disorders. Such data can also be used to assess the severity of these sleep disorders (Sadeh, 2011; Stone & Ancoli-Israel, 2011). Nonetheless, the major limitation of actigraphy is its tendency to overestimate sleep and underestimate wake (often referred to as low specificity) since the lack of motion may or may not be an indication of sleep. This results in underestimated sleep latency and overestimations of total sleep time and sleep efficiency (Krystal & Edinger, 2008; Paquet, Kawinska, & Carrier, 2007; Stone & Ancoli-Israel, 2011; van de Water et al., 2011). Despite the improvements in the design of the actigraph (some devices can measure ambient light, skin temperature or sound) this tool still performs best in healthy individuals with normal sleep, and its specificity is greatly reduced if sleep is disturbed (Sadeh, 2011; van de Water et al., 2011). For instance, Paquet et al., (2007) compared three nights of sleep recorded by wrist actigraphy and PSG, and

noted that the agreement between the devices was good if participants slept well, since good quality of sleep is associated with markedly reduced/minimal body movement. However, when sleep became fragmented the ability of wrist actigraphy to distinguish between sleep and wake fell to 50%, when compared with PSG. This is because people often lie motionless even if they are not asleep (Krystal & Edinger, 2008), and a lack of movement is often recorded as sleep by actigraphy. Similarly, data from the Study of Osteoporotic Fractures revealed that in women with poor PSG-assessed sleep efficiency (less than 70%), actigraphy overestimated total sleep time by up to 31 minutes (Blackwell et al., 2008). Although actigraphy might provide useful data on altered sleep patterns for individuals with sleep disorders such as insomnia, periodic limb movement or sleep disordered breathing, it is not appropriate for the diagnosis of these disorders, and it should be supported by information from a clinical assessment, participants' subjective sleep reports or PSG, as appropriate (Ancoli-Israel et al., 2003; Sadeh, 2011).

Another important issue is that a number of different actigraphs have been used to measure sleep (e.g., Actillum, MotionLogger, Actiwatch), often recording different types of data and using different algorithms to calculate sleep (Krystal & Edinger, 2008; Paquet et al., 2007; Sadeh, 2011). Therefore, it is possible that two different actigraphs and/or two different sleep algorithms can have different levels of agreement in the same population when compared against PSG (Blackwell et al., 2008; van de Water et al., 2011).

In addition to home-based PSG and actigraphy, which are the most widely used ambulatory sleep measures, there are other objective sleep indices available, for example, bed actigraphy or a non-contact biomotion sensor designed to detect chest movements. These measures have been recently reviewed by van de Water et al., (2011) who concluded that actigraphy remains the most validated ambulatory sleep measure while the remaining

tools were deemed as “promising”, but “at a prototype phase” (van de Water et al., 2011: 198). Further discussion about these sleep measures is beyond the scope of this thesis.

### 1.9.3 Subjective sleep indices

Subjective measures of sleep are typically obtained by a questionnaire such as the PSQI (Buysse et al., 1989), and the Jenkins Sleep Problems Scale (Jenkins, Stanton, Niemcryk, & Rose, 1988). The PSQI is a widely used self-reported measure of sleep that has a good reliability (Cronbach’s  $\alpha=0.83$ ) and validity, as demonstrated by the scale’s ability to distinguish between poor and good sleepers (Buysse et al., 1989). The questionnaire consists of 19 items assessing 7 components of sleep in the last month including sleep disturbance, duration, habitual sleep efficiency, or daytime dysfunction. The answers to these questions can be summed to produce a global score ranging from 0 to 21. A score  $\geq 5$  is indicative of poor sleep, and has a diagnostic sensitivity of 89.6% and specificity of 86.5% in distinguishing between good (scores $<5$ ) and poor sleepers (Buysse et al., 1989). In addition to providing a global sleep score, the PSQI can be used to measure distinct sleep problems (e.g., sleep efficiency). The PSQI can be used in a wide range of settings. For instance, in a clinical setting it might provide information about the presence of disturbed sleep or its severity, or to determine if a psychiatric condition is comorbid with disturbed sleep. The scale has also been used in epidemiological cohort studies (e.g., Dowd et al., 2011; Matthews et al., 2010), smaller-scale observational studies (Suarez, 2008), or to evaluate interventions aimed at improving sleep (Irwin, Olmstead, & Motivala, 2008; Li, Chen, Li, Gau, & Huang, 2011).

The Jenkins Sleep Problems Scale (Jenkins et al., 1988) is another frequently used self-reported sleep questionnaire, which has a good reliability (Cronbach’s  $\alpha=0.79$ ) and validity. The scale measures sleep problems in the past month and comprises of 4 items (e.g., “Have trouble falling asleep”, “Wake up several times per night?”). To compute a

global sleep score scores are either totalled or averaged and higher scores are indicative of worst sleep. Because the Jenkins Sleep Problems Scale (Jenkins et al., 1988) is brief it might be more convenient to use than the PSQI (Buysse et al., 1989), especially if participant burden is an issue, but it should be pointed out that it is less comprehensive a measure. Nonetheless, the scale has been used in clinical samples (Jenkins, Stanton, & Jono, 1994), observational studies of healthy people (Kudielka et al., 2004), and in large epidemiological cohorts (Kumari et al., 2009; Lallukka et al., 2012).

Karolinska sleep diary (Akerstedt, Hume, Minors, & Waterhouse, 1994b) has also been used to assess sleep. The questionnaire was developed in Sweden and provides valid measures of sleep quality (e.g., “how did you sleep”, [are you] “feeling well rested after awakening”) and duration. Sleep quality items are rated on a 5-point Likert scale and higher scores indicate better sleep quality. The measure has been frequently used to compare subjective and objective indices of sleep quality (Akerstedt, Hume, Minors, & Waterhouse, 1994a; Akerstedt et al., 1994b; Akerstedt, Kecklund, & Axelsson, 2008; Kecklund & Akerstedt, 1997).

Sleep parameters, in particular duration, have also been assessed with a one-item question (e.g., “On average, how many hours do you sleep each night?”), which due to its brevity is suitable for very large population-based surveys (e.g., Kripke et al., 2002; Magee et al., 2009; Steptoe et al., 2006). Sleep duration can also be determined with sleep diaries and logs (e.g., van den Berg et al., 2008), where respondents are typically required to report their bed and wake up times, or estimated sleep duration. Sleep logs are often used in studies relying on actigraphy since self-reported wake and bed time are needed to calculate sleep parameters. One- or two-items indices have been used to assess sleep disturbance as well. For example, Chandola et al., (2010) used two items (“Have you recently lost much sleep over worry” and “Have you recently been having restless,



disturbed sleep”) from the General Health Questionnaire (Goldberg et al., 1997) to measure sleep problems in relation to CHD risk.

The major shortcoming of self-reported sleep measures is that participants’ evaluations of sleep can be affected by mood, memory biases and demand characteristics (Bliwise & Young, 2007; Krystal & Edinger, 2008), or personality (Fernandez-Mendoza et al., 2010; Tsuchiyama, Nagayama, Kudo, Kojima, & Yamada, 2003; Vanable, Aikens, Tadimeti, Caruana-Montaldo, & Mendelson, 2000).

In addition, it remains uncertain what people mean when they report their habitual sleep duration (Bliwise & Young, 2007). Indeed, studies that compared objective and subjective indices of sleep duration suggest that misperceptions of sleep duration are common. For example, a laboratory-based study compared PSG-assessed and subjective sleep latency and awakenings in twenty healthy men and women (mean age 25 years), and reported that participants overestimated their latency and underestimated the number of times they woke up in the night (Baker, Maloney, & Driver, 1999). This is in line with the findings from over 2000 older men and women from the Sleep Heart Health Study where subjective measures of sleep latency and total sleep time were overestimated when compared with home-based PSG (Silva et al., 2007). Sex differences were unrelated to the discrepancy of measures in both studies, but a lower education level was associated with overestimations of total sleep time in the study of Silva et al., (2007). In the Rotterdam study comparisons of subjective and actigraphic measures of sleep duration in nearly 1000 men and women (mean age 69 years) indicated that 34% of the sample reported sleeping an hour longer than indicated by wrist actigraphy. Interestingly, respondents who slept between 7-8 hours, as indicated by actigraphy, reported their sleep duration most accurately (van den Berg et al., 2008). On the other hand, poorer cognitive function, functional disability and male gender were related to less accurate perceptions of sleep

duration in these data. In the CARDIA study Lauderdale et al., (2008) compared actigraphic and subjective measures of sleep duration in over 600 males and females (average age 43 years) and found significant discrepancies in sleep assessments. Participants tended to overestimate their sleep duration by up to 60 minutes, and the correlation between objectively and subjectively assessed sleep duration was 0.47 in that study; this was considered as “moderate” by the authors (Lauderdale et al., 2008). Greater tendency to overestimate was associated with poor self-rated health, lower sleep efficiency and lower SES as indicated by education and income.

A relevant question in this context is whether the disagreement between objective and self-reported measures of sleep duration is reduced if subjective sleep duration is assessed soon after awakening, since this is likely to have greater accuracy of recall than habitual sleep duration. This has not been the case either in the CARDIA (Lauderdale et al., 2008) or the Sleep Heart Health studies (Silva et al., 2007).

To date little work has been done to explain why people’s ratings of sleep duration are incongruent with objective data, albeit as noted above, certain factors such as lower SES, gender, poorer self-reported health or cognitive decline have been implicated in this phenomenon. Studies conducted with insomnia patients suggest that psychological characteristic, for example, rumination or poor coping strategies, impact sleep perceptions as well (Fernandez-Mendoza et al., 2010), but these data cannot be extrapolated to the general population. Another limitation of this literature is that apart from the CARDIA study (Lauderdale et al., 2008), the Rotterdam (van den Berg et al., 2008) and the Sleep Heart Health studies (Silva et al., 2007) comprised older individuals, and given the well documented changes in sleep seen in the elderly (Ancoli-Israel, 2009; Carskadon & Dement, 2011) these data should not be extrapolated to younger individuals.

The PSQI (Buysse et al., 1989) and the Jenkins Sleep Problems scale (Jenkins et al., 1988) were developed to measure global sleep quality, and have been used extensively in sleep research. However, there is still no consensus what good quality sleep actually entails, and different authors have used different definitions of this sleep parameter (Harvey, Stinson, Whitaker, Moskovitz, & Virk, 2008). More importantly, discrepancies between subjective and objective measures of sleep quality have received less attention in the sleep literature than those relating sleep duration, and they remain little understood at present. For instance, Vitiello et al., (2004) explored correlations between sleep quality defined by the PSQI (Buysse et al., 1989) and PSG in 150 healthy older men and women. Data revealed that men were more accurate than women in their subjective sleep perceptions since men with PSQI scores  $\geq 5$  (a cut off indicating sleep disturbance) had disturbed sleep across numerous PSG-based sleep measures, while women with PSQI scores  $\geq 5$  had less disturbed objective sleep than men scoring  $\geq 5$ . However, both men and women with PSQI scores  $\geq 5$  had significantly lower objective sleep efficiency than men and women with scores  $< 5$  (Vitiello et al., 2004). A similar pattern of findings was reported in the Rotterdam study, a population-based cohort of older people, where women despite having higher scores on the PSQI (Buysse et al., 1989) than men (4.6 vs. 2.6, respectively) also had higher objective sleep efficiency (79.0% vs. 77.8%), as defined by wrist actigraphy (van den Berg et al., 2009).

It is uncertain why discrepancies in sleep measures between men and women were found in these studies, but the authors speculated that differences in sex hormones, women's greater vigilance to and awareness of their bodies, or more realistic sleep expectations might be partly responsible (van den Berg et al., 2009).

Interestingly, in the Sleep Heart Health Study data from over 5,000 men and women (mean age 63 years) showed no association between PSG-defined sleep efficiency, or deep

sleep, and subjective measures of sleep quality such as feeling tired upon waking up, or having troubles falling asleep (Unruh et al., 2008). The authors were unable to explain this lack of an association. However, objective sleep was measured only over one night, so this might not have represented participants' overall sleep quality since the first night of PSG, even if measured at participants' home, as was done in this study, could still impact sleep quality and/or duration (Silva et al., 2007). Indeed, Akerstedt et al., (2008) found that subjective quality was predicted by objective sleep parameters measured with home-based PSG, but in that study participants rated their sleep after each night of objective sleep monitoring. In contrast, in the study described by Unruh et al., (2008) respondents provided global ratings of sleep quality, so this could explain in part why they were unrelated to one night of PSG-defined sleep quality.

Taken together, similarly to the literature relating sleep duration population-based studies indicate that self-reported and objective indicators of sleep quality are often incongruent. It is unclear why these discrepancies occur, or why men and women differ in their judgments of sleep quality. Although studies in insomnia patients have reported that maladaptive personality characteristics and affective responses, such as tension, dysphoric mood, anxiety or poor coping styles, are associated with discrepancies between subjective and objective indices of sleep duration (Fernandez-Mendoza et al., 2010), it is uncertain whether this is also the case with sleep quality. In particular, the psychosocial and affective correlates of over- or under-reporting of sleep problems remain unexplored in healthy samples. The population-based studies relating measures of sleep quality discussed here were based on elderly populations, which is problematic given the pronounced age-related changes in sleep architecture seen in older people (Ancoli-Israel, 2009). This issue has already been raised while discussing the discrepancies between measures of sleep duration. However, because sleep duration seems to be less affected by

ageing process than sleep parameters such as SWS (Ohayon et al., 2004), findings relating comparisons of sleep quality indicators in older people might be even less generalizable than those exploring differences in sleep duration measures. Therefore, to address this gap in the literature in Study 3 (Chapter 4) I will compare subjective and objective measures of sleep quality in a sample of healthy young women, and explore whether the discrepancies in measures differ by psychosocial or affective factors.

### **1.10 Summary**

Disturbed and insufficient sleep pose a serious public health burden. CVD is the main cause of death in the UK (British Heart Foundation, 2012), therefore in my literature review I have focused on the implications of sleep quantity and disturbance on CVD and CVD mortality. I have outlined three plausible pathways through which sleep parameters might be associated with cardiovascular outcomes. However, there are still many areas in the sleep literature that require further investigation. Specifically, the literature relating sleep measures and inflammation is inconsistent, and has not been systematically studied in representative samples of older men and women. I will address this issue in Study 1 (Chapter 2). Experimental and clinical studies suggest that short and disturbed sleep exert deleterious effects on the autonomic modulation of the heart, but it remains unclear whether sleep disturbances are associated with autonomic imbalance in real life. I will endeavour to fill this gap in the sleep literature in Study 2 (Chapter 3). Sleep measurement poses a serious issue. It has been well established that people are not accurate in estimations of sleep duration when compared with objective measures, but it is less certain whether subjective and objective indicators of sleep quality are also incongruent. In addition, it is currently unclear which psychosocial or affective characteristics are

associated with misperceptions of sleep quality. I will address these important questions in Study 3 (Chapter 4).

## **CHAPTER 2: SELF-REPORTED SLEEP MEASURES AND BIOLOGICAL MARKERS OF HEALTH AND DISEASE IN OLDER PEOPLE (Study 1)**

### **2.1 Introduction**

Chapter 1 showed that there is convincing evidence that sleep duration is important for cardiovascular health. Briefly, too short (usually <5 or <6 hours per night) and too long sleep hours (usually >8 or ≥9 hours) have been implicated in cardiovascular outcomes such as MI, stroke, and cardiovascular mortality. There is growing support for the contention that disturbed sleep is a prospective risk factor for CVD, albeit the evidence remains somewhat inconsistent at present. Sleep parameters are associated with type 2 diabetes, obesity and hypertension, which in addition to being pathological conditions in themselves are well-established CVD risk factors.

This body of evidence provides a sound rationale to explore which pathways are likely to be responsible for translating abnormal sleep patterns into cardiovascular outcomes. In the previous chapter I have suggested that at least three mechanisms might be involved: (1) mood disturbances, (2) health behaviours and (3) direct biological dysregulation. In this chapter I will focus on the pathway regarding direct biological dysregulation, and in particular on the cross-sectional associations between sleep measures and inflammatory factors (CRP, fibrinogen), and between sleep measures and dehydroepiandrosterone sulfate and haemoglobin.

Numerous population-based studies and meta-analytic reviews documented that low grade chronic inflammation is a prospective risk factor for CVD (Libby et al., 2011). In particular, there is considerable evidence suggesting that raised concentrations of CRP

(Buckley, Fu, Freeman, Rogers, & Helfand, 2009), fibrinogen (Danesh et al., 2005), IL-6 and TNF- $\alpha$  (Papanicolaou et al., 1998; Ridker et al., 2000) are prospectively linked with cardiovascular outcomes. Importantly, as noted in Chapter 1, experimental studies have reported that sleep deprivation increases levels of these inflammatory factors, thus raising the possibility that abnormal sleep patterns might be contributing towards higher risk of CVD through their negative impact on inflammation. However, not all studies have lent support to the contention that experimentally induced sleep loss (total or partial) results in higher levels of the above inflammatory factors. This is thought to be explained in part by differences in methodology in terms of the number of nights of partial/total sleep deprivation, frequency of blood collection, or by individual differences in basal levels of inflammatory markers, among others (Frey et al., 2007; Motivala, 2011; Mullington et al., 2009). In addition, experimental sleep studies usually last only for a few days, so their implications for long-term CVD risk are uncertain. Large scale population studies provide complementary data concerning biomarkers related to sleep.

As noted in Chapter 1 (see page 86) associations between inflammatory markers and sleep parameters have been inconsistent in population-based studies as well (Motivala, 2011) (it might be interesting to note that CRP has been studied most extensively in relation to sleep measures while fewer investigations have focused on fibrinogen, IL-6 or TNF- $\alpha$ ). For example, CRP has been related to sleep parameters in young (Liukkonen et al., 2007), middle-aged (Matthews et al., 2010; Miller et al., 2009; Suarez, 2008) and elderly populations (Dowd et al., 2011; Prather et al., 2013) in some studies, but not in others (Ferrie et al., 2013; Laugsand et al., 2012; Taheri et al., 2007). Poor sleep quality has been linked with raised fibrinogen in American middle-aged (Matthews et al., 2010; Suarez, 2008) and older women (Prather et al., 2013), while long sleep was associated higher levels of this biomarker in older Taiwanese individuals (Dowd et al., 2011) and



older American women (Hale et al., 2013), but not among British civil servants (Miller, Kandala, Kumari, Marmot, & Cappuccio, 2010). A number of studies found an association between higher IL-6 and sleep parameters as well (Ferrie et al., 2013; Friedman et al., 2005; Miller et al., 2009). In addition, greater variability in sleep-related behaviours, such as later wake up time or longer time in bed, were linked with higher levels of IL-6 and TNF- $\alpha$  in community-dwelling elders (mean age 73.7 years) (Okun et al., 2011).

The reasons why findings relating sleep measures with markers of inflammation have been equivocal in population-based research could be, for instance, due to reliance on different measures of sleep (objective vs. subjective), differences in the studied populations in terms of age and ethnicity, or due to insufficient sample sizes (Mullington et al., 2010; Patel et al., 2009). Moreover, gender differences in associations between sleep indices and inflammation have not been systematically addressed, since some authors adjusted their statistical models for gender (Dowd et al., 2011; Ferrie et al., 2013; Taheri et al., 2007), others analysed men and women separately (Liukkonen et al., 2007; Miller et al., 2009; Suarez, 2008), while some studies were based exclusively on women (Hale et al., 2013; Matthews et al., 2010). This is important as emerging evidence suggests that sleep deprivation impacts inflammatory pathways differently in men and women. For instance, Irwin et al., (2010) reported that one night of partial sleep loss resulted in higher morning levels of IL-6 and TNF- $\alpha$  in both sexes, but in the evening the inflammatory markers increased in women and decreased in men. Clearly more research is warranted to study gender differences in the context of sleep indices and inflammation.

The cardiovascular and metabolic problems associated with sleep duration and quality, such as obesity, hypertension or type 2 diabetes, are more common among older people. Sleep duration does not differ markedly between younger and older adults, but sleep efficiency and continuity deteriorate with increasing age (Ancoli-Israel, 2009;

Ohayon et al., 2004). However, research on biomarkers in representative cohorts of older people has been limited (Steptoe, 2011). In addition, little is known about associations between biological measures and sleep parameters in elderly populations since the majority of studies have predominantly focused on younger or middle-aged individuals. This may be important for at least two reasons. First, exploring associations between biomarkers and sleep parameters could particularly benefit elderly cohorts, where the accumulation of risk factors increases the risk of mortality and morbidity (Gruenewald et al., 2006), and disturbed or inadequate sleep might be more disadvantageous to health than among younger individuals (Naidoo, 2009). Second, sleep duration and disturbance are potentially amenable to modification (Irwin et al., 2008; King, Oman, Brassington, Bliwise, & Haskell, 1997), so could provide an opportunity to ameliorate health risk at older ages. Therefore, the first aim of this study was to investigate the relationship between sleep measures and inflammatory markers (CRP and fibrinogen) in a representative, large sample of older men and women. I hoped that this investigation would add to the limited literature relating sleep measures and inflammatory factors in older populations as well as further explore gender differences in these associations.

To date a substantive number of experimental and population studies linking sleep with objective indicators of health have focused on inflammatory markers, endocrine pathways or glucose metabolism (Knutson, 2010; Mullington et al., 2009), largely because these mechanisms are also implicated in CVD or other chronic conditions such as type 2 diabetes. However, the English Longitudinal Study of Ageing (ELSA), on which this study is based on, contains a number of unexplored yet potentially important biomarkers in relation to sleep and health that could shed more light on how sleep parameters relate to biological function in elderly populations. Therefore, I also decided to explore associations with dehydroepiandrosterone sulfate (DHEAS) and haemoglobin.

Dehydroepiandrosterone (DHEA) and its sulfate form DHEAS are the most abundant endogenous steroid hormones in elderly populations, though levels decline with age (Labrie et al., 1998). DHEAS has been implicated in cardiovascular health with low levels being associated with CVD and all-cause mortality in older men (Barrett-Connor, Khaw, & Yen, 1986; Ohlsson et al., 2010). On the other hand, higher concentrations are related to better health outcomes such as lower risk of metabolic syndrome in men (Phillips et al., 2010), and higher bone mineral density and lower risk of breast cancer in women (Labrie et al., 1998). However, research relating associations between sleep parameters and steroid hormones has been limited. For example, a study in Austria found no association between DHEAS and sleep quality in a sample of 375 men (age range 45-85 years) (Ponholzer et al., 2005). Sleep duration was also unrelated to DHEAS concentrations in 531 Singaporean Chinese men (age range 29-72 years) (Goh, Tong, Mok, & Said, 2007).

Haemoglobin is the iron-containing molecule responsible for carrying oxygen from the respiratory organs to the rest of the body, and low levels are usually indicative of anaemia. Low levels of haemoglobin and anaemia are prevalent in the elderly (Nilsson-Ehle, Jagenburg, Landahl, & Svanborg, 2000), and anaemia is associated with a host of negative outcomes including longer hospitalization, cognitive decline, greater risk of mortality and CVD (Culleton et al., 2006; Eisenstaedt, Penninx, & Woodman, 2006). In addition, anaemia has been cross-sectionally associated with depressive symptoms in older adults (Hamer & Malloy, 2009; Onder et al., 2005), and fatigue in clinical populations (Cella, 2002; Fink, Sullivan, Zerwic, & Piano, 2009). As in the case of DHEAS, associations between haemoglobin, anaemia and sleep parameters remain largely unexplored in the general or elderly population, but have been extensively studied in children (Peirane et al., 2010) and clinical samples (Pai et al., 2007; Zilberman et al., 2007).

Taken together, DHEAS and haemoglobin levels have important implications for health and disease in the elderly, but their relationships with sleep indices in healthy, community-dwelling older men and women received little attention to date. Therefore, in addition to inflammatory pathways, the second aim of this study was to address this gap in the literature.

## **2.2 Hypotheses**

Based on the limitations of the sleep literature identified above I formulated the following hypotheses that this study was set out to test:

- 1.** There would be a curvilinear association with sleep duration, with both short and long sleep duration being related to higher levels of CRP and fibrinogen.
- 2.** Greater sleep disturbances would be associated with raised levels of CRP and fibrinogen.

Given that low levels of both DHEAS and haemoglobin are related to adverse health outcomes I also hypothesised that:

- 3.** Short and long sleep duration would be associated with lower levels of DHEAS, haemoglobin, and greater likelihood of anaemia.
- 4.** Higher sleep disturbances would be associated with lower levels of DHEAS, haemoglobin, and greater likelihood of anaemia.

## **2.3 Method**

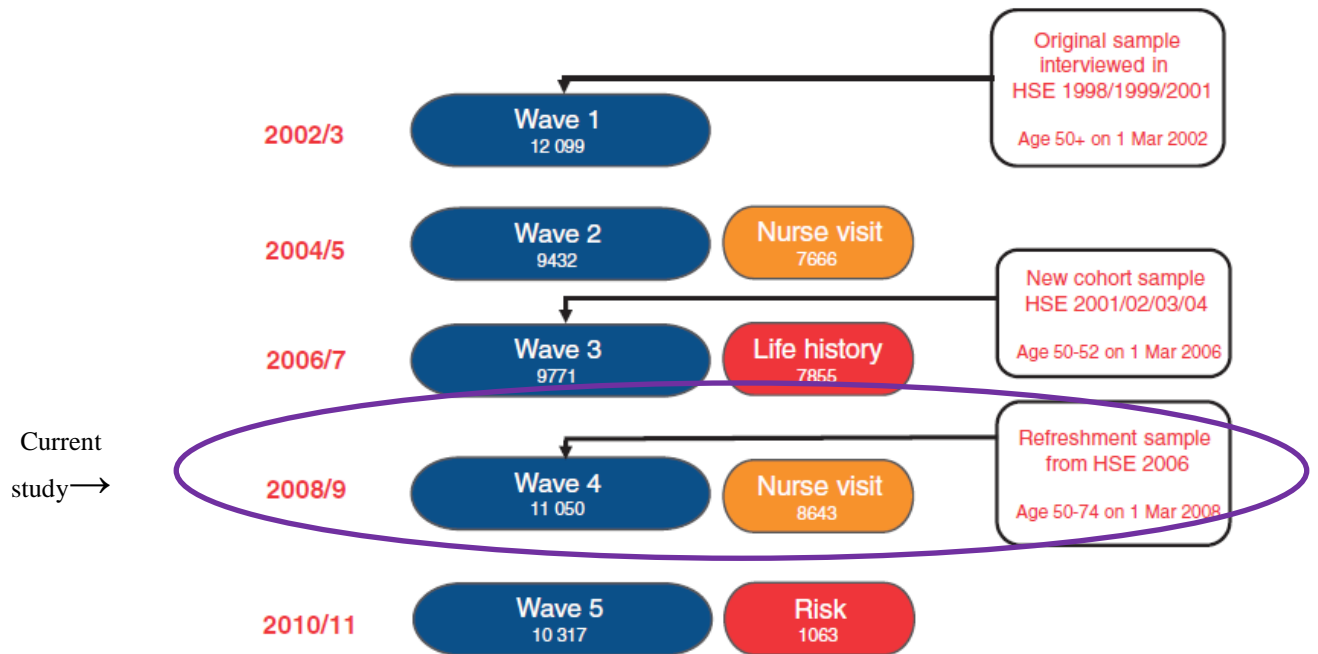
### **2.3.1 Study design**

The cross-sectional analyses described here are based on data from wave 4 of ELSA collected between 2008 and 2009. ELSA is a prospective cohort study representative of men and women aged 50 years and older living in England (Marmot et al., 2003; Steptoe,

Breeze, Banks, & Nazroo, 2012). The study began in 2002 and participants have been seen biannually since then, and to date there have been 5 waves of data collection (see Figure 2.1 for an overview of data collection to date). Participants in the first wave of ELSA were drawn from 3 waves of Health Survey for England (1998, 1999, 2001), which is a cross-sectional study conducted every year to determine trends in health of the general population (Mindell et al., 2012). To ensure that there were enough participants aged 50-53 years a refreshment sample was added in wave 3; in wave 4 new people aged 50-75 also entered the study (see Figure 2.1) (Stephoe et al., 2012).

ELSA is a multidisciplinary investigation designed to gain a better understanding of the lives of people aged 50 years and above who live in England. In particular, to provide an insight into factors that determine life trajectories in older age ELSA contains rich information on physical health, well-being as well as economic and social circumstances (Marmot et al., 2003). Since the first wave of ELSA new measures have been added to the subsequent waves of data collection, such as sleep indices in wave 4 or accelerometry in wave 6 (currently in fieldwork). To date there have been more than 130 peer-reviewed publications based on data from this cohort study (Stephoe et al., 2012).

**Figure 2.1 Waves 1 to 5 of ELSA and complete sample size for each wave (adapted from Steptoe et al., 2012).**



### 2.3.2 Participants

Respondents in wave 4 included members of the core sample assessed in wave 1 (2002), supplemented by refreshment samples in wave 3 (2006/7) and wave 4 (Banks et al., 2010). Participants were eligible to take part in wave 4 if they lived in a private residential address during data collection, and if they were living within the household (as opposed to an institution such as care home) during wave 3 of data collection. The response rate in wave 4 was 74%, and the main reason for nonparticipation was refusal (Hussey et al., 2010).

### 2.3.3 Procedure

Data collection consisted of a computer assisted personal interview (CAPI) and a separate nurse assessment carried out a few days later (Hussey, Lessof, Ward, & Wood, 2010). Both were conducted face-to-face in the participants' homes. This way of data

collection, in comparison with pencil and paper tests or online surveys, greatly reduces missing data since all questions are asked verbally by a trained interviewer who types the answers immediately after each question. Respondents are allowed to refuse answering to any question, should they wish to do so. CAPI was used to provide measures of socioeconomic characteristics, demographic information, housing situation, self-reported health (e.g., disability, chronic conditions (cancer, cardiovascular disease), eyesight, pain, difficulties with daily activities, sleep duration and disturbance), and cognitive function, among others. At the end of CAPI each ELSA participant was given a self-completion questionnaire which included, for instance, measures of quality of life, social participation, life satisfaction, participation in and attitudes towards voluntary work as well as fruit, vegetable and alcohol consumption. Upon completion the questionnaire was returned by post. The nurse visit was used to obtain numerous objective measures of physical health, such as blood samples (to provide information on inflammatory markers, lipids, fasting glucose, iron levels and genetics, among others), lung function, blood pressure or anthropometric measures (Hussey et al., 2010). More detailed information on blood sampling will be provided in the Measures section below. All participants provided signed consent, and ethical approval was granted by the London Multi-Centre Research Ethics Committee.

#### **2.3.4 Measures**

##### **2.3.4.1 Demographic variables**

Participants' age and gender were assessed during a face-to-face visit in the home. For the purpose of the analyses described here continuous age data were re-coded into 4 categories: "50-59", "60-69", "70-79" and "80+" years. Respondents aged 80 years or

more were grouped together because of a relatively small number of very old participants, for example, there were only 44 participants aged 87 years or only 61 aged 90 or older.

ELSA was one of the first surveys to collect very detailed information on its respondents' socioeconomic characteristics (Banks, Karlsen, & Oldfield, 2003; Steptoe et al., 2012). Thus in this study socioeconomic status (SES) was indexed by total household wealth, including financial wealth (savings and investments), the value of any home and other property (less mortgage), the value of any business assets and physical wealth such as artwork and jewellery, net of debt. Wealth is the most robust indicator of socioeconomic circumstances in ELSA (Banks et al., 2003). ELSA sample consists of people aged 50 to 100 years so respondents' economic circumstances are likely to differ; younger participants, especially those below the age of 60 or 65 years, are more likely to rely on full- or part-time employment, while older individuals rely on pensions (state and/or private) (Banks et al., 2003). To take account of this wealth was divided into age-related quintiles for the purposes of analysis.

#### 2.3.4.2 Sleep measures

Sleep parameters were assessed during the CAPI. Sleep duration was measured by an open-ended question asking participants to report how many hours they slept on an average weeknight (Kumari, Green, & Nazroo, 2010). This is a frequently used method of sleep duration assessment in large population-based surveys (e.g., Kripke et al., 2002; Magee et al., 2009; Steptoe et al., 2006). Responses were coded into "<5 hours" (short sleep duration), "5-6 hours", "6-7 hours", "7-8 hours" (optimal sleep duration) and ">8 hours" (long sleep duration). The cut-offs for short, optimal and long sleep hours were based on the sleep literature (Cappuccio et al., 2010; Cappuccio et al., 2011; Kripke et al., 2002; Stranges et al., 2008). Sleep disturbance was assessed with three questions derived from the Jenkins Sleep Problems Scale (Jenkins et al., 1988), which referred to the most



common symptoms of insomnia. Specifically, participants were requested to indicate how often in the past month they had difficulties falling sleep, staying asleep, and whether they felt tired upon waking up in the morning. These items were rated on a 4-point scale (ranging from 1="Not during the last month" to 4="Three or more times a week"). The scores were averaged, with higher scores corresponding to greater sleep disturbances (range 1-4). The Cronbach's  $\alpha$  in this sample was .62. Sleep disturbance scores were divided into tertiles prior to analysis to check for non-linear associations with biomarkers, as in the case of sleep duration. Because in these data women reported more frequent sleep problems than men, which is in line with the literature (van den Berg et al., 2009; Vitiello et al., 2004), I computed sex-specific tertiles. In women the 1<sup>st</sup> tertile (best sleep) ranged from 1 to 1.8, the 2<sup>nd</sup> (intermediate sleep problems) ranged from 1.81 to 2.8 and the 3<sup>rd</sup> tertile (poorest sleep) ranged from 2.81 to 4. In men the 1<sup>st</sup> tertile's range was 1 to 1.8, the 2<sup>nd</sup> tertile's range was 1.81 to 2.4 and the 3<sup>rd</sup> tertile ranged from 2.41 to 4.

#### 2.3.4.3 **Biological measures**

Blood samples were collected during the nurse's visit. Exclusion criteria for providing a blood sample were refusal, clotting (e.g., low platelets) or bleeding disorder (e.g., haemophilia), taking anti-coagulant medication, such as warfarin therapy, and ever having had a fit (de Oliveira, Shankar, Kumari, Nunn, & Steptoe, 2010). Viable blood samples were obtained from 6188 respondents (75.6% of wave 4 participants). Unless participants were older than 80 years, had diabetes, reported ever having had a fit, were frail or seemed unwell, the nurse collected fasting blood samples, which were defined as not eating or drinking at least 5 hours prior to the blood test (4149 respondents provided fasting blood samples) (de Oliveira et al., 2010).

CRP was measured using the *N* Latex CRP mono immunoassay on the Behring Nephelometer II analyser. Fibrinogen was analysed using a modification of the Clauss

thrombin clotting method on the Organon Teknika MDA 180 analyser. Haemoglobin levels were measured with two Abbott Diagnostics Cell-Dyn 4000 analysers (Craig, Deverill, & Pickering, 2006). DHEAS measures were performed on the DPC Immulite 2000 analyser. All blood samples were analysed in the Royal Victoria Infirmary laboratory in Newcastle upon Tyne, UK.

#### 2.3.4.4 **Health-related variables**

Participants were requested to indicate whether they had any chronic illnesses or disability (“have you got any long-standing illness, disability or infirmity?”). This information was obtained during the CAPI (Hussey et al., 2010). Those who indicated having an illness/disability were further asked whether their condition(s) limited their activities. The response was then stratified into “yes” for limiting long-standing illness and “no” for the absence of limiting long-standing illness. Height and weight, which were assessed by a nurse, were used to calculate body mass index (BMI,  $\text{kg/m}^2$ ). Smoking was assessed by asking participants whether they had ever smoked, and those who stated that they had were further required to indicate whether they still smoked. The responses were then categorised as “yes” for current smoker and “no” for non-smoker. Physical activity was assessed by asking participants how often they engaged in vigorous, moderate or mild physical activity; the response options were “hardly ever or never”, “one to three times a month”, “once a week” and “more than once a week”. For the purpose of the current analysis physical activity was categorised into engaging in moderate or vigorous physical activity at least once per week or less than once a week.

#### 2.3.4.5 **Other measures**

Depressive symptoms were assessed during the CAPI with a shortened version (8 items) of the Centre for Epidemiologic Studies Depression scale (CES-D) devised for the

Health and Retirement Study in the US (Steffick, 2000). The CES-D is a well-established measure of depressive symptoms and it has been widely used in population-based research (e.g., Hamer, Batty, & Kivimaki, 2011; Heisler, 2007; Shankar, McMunn, Banks, & Steptoe, 2011). For the purpose of this study I removed the item concerning sleep from the CES-D (“Much of the time during the past week, your sleep was restless?”) as to minimise the risk of shared variance with sleep disturbance measure. The scale comprised 7 items (e.g., “Much of the time during the past week, you felt depressed?”, “Much of the time during the past week, you felt that everything you did was an effort?”) that were answered with a “yes” or “no” response. A total score was computed (ranging from 0 to 7), with higher scores corresponding to more depressive symptoms. The Cronbach’s  $\alpha$  in this sample was .80. Using a validated cut-off point described by Steffick (2000) scores were categorized into “no depressive symptoms” (3 or fewer symptoms) and “elevated depressive symptoms” (4 or more symptoms).

## **2.4 Statistical analysis**

Fibrinogen (N=5928), haemoglobin (N=5995) and DHEAS (N=6028) were treated as continuous variables in these analyses. Based on a well-recognized cut-off of 3 mg/L, CRP (N=6061) was divided into low/normal levels (< 3 mg/L) and raised levels ( $\geq 3$  mg/L) (Pearson et al., 2003). In line with past studies relating sleep parameters and inflammation (e.g., Dowd et al., 2011; Matthews et al., 2010; Miller et al., 2009) I analysed CRP as a continuous variable as well. A number of studies relating associations between sleep measures and CRP cited in this PhD thesis (e.g., Laugsand et al., 2012; Matthews et al., 2010; McDade et al., 2006) have excluded from their analyses participants with CRP >10 mg/L since this may reflect an acute inflammatory response (infection), as suggested by Pearson et al., (2003). However, a more recent study of 3971 men and women aged 65 years or older reported that CRP>10 mg/L is an important risk factor for CHD, whereby

after adjustment for relevant covariates respondents with CRP>10 mg/L had a nearly double risk of CHD when compared with those with lower levels of this biomarker (Cushman et al., 2005). In addition, in a recent study of older men and women (mean age 66 years) associations between sleep measures and CRP concentrations were unchanged when respondents with CRP>10 mg/L were removed from analysis (Dowd et al., 2011). Therefore I have decided not to remove participants with CRP>10 mg/L (7.2% of the sample) from the data set used in this study. To obtain anaemia status (no/yes) haemoglobin levels were divided based on the WHO guidelines (<13 g/dL for men and <12 g/dL for women) (World Health Organization, 1968).

Associations between sleep disturbance and biomarkers were tested with logistic regression models for binary variables (anaemia, CRP), and with analysis of covariance (ANCOVA) and linear regressions for continuous measures (fibrinogen, CRP, DHEAS and haemoglobin). Where ANCOVA result was significant the least-significant (LSD) multiple comparison test was performed to explore post-hoc differences in biomarkers by different sleep duration categories or sleep tertiles. Haemoglobin and fibrinogen data were normally distributed, but DHEAS data were skewed thus a square root transformation was performed to normalise the distribution. All analyses were adjusted for age, wealth, BMI, current smoking, physical activity, limiting long-standing illness and depressive symptoms, since these are associated with sleep parameters (Arber et al., 2009; Lauderdale et al., 2006; Stranges et al., 2008). Models relating sleep measures with CRP and fibrinogen were additionally adjusted for the use of statins and arthritis medication since these are likely to impact inflammation (Albert, Danielson, Rifai, & Ridker, 2001). To calculate sample characteristics and to assess associations between sleep measures and covariates I performed univariate analysis of variance (ANOVA), *t*-tests, cross-tabulations with Chi-squared test and bivariate correlations, as appropriate. Curvilinear associations with sleep

duration were tested using the 7-8 hour category as the reference group. I chose this reference category based on the sleep literature, as stated earlier in the Measures section. Each sleep measure was treated as a predictor variable and separate analyses were performed for each biomarker. To explore sex differences in the relationships tested in this study men and women were analysed separately. Analyses were carried out using weighted data, applying a weighting factor relating to non-participation in blood sampling, in order to ensure that survey data matched population estimates in terms of age, sex, housing tenure, ethnicity, educational qualifications, marital status, and region of the country (Hussey et al., 2010). Weighting factors are computed for each wave of ELSA by the National Centre for Social Research based on the most recent Census data (Hussey et al., 2010; Marmot et al., 2003).

Results are presented as odds ratio (OR) and 95% confidence intervals (C.I.) for logistic regression models, unstandardized regression coefficients (*B*), 95% C.I. and P-values for linear regressions, and F-statistics with P-values for ANCOVA. All analyses were conducted using Statistical Packages for the Social Sciences (SPSS) version 18.

## **2.5 Results**

### **2.5.1 Sample characteristics**

Participants' characteristics stratified by gender are depicted in Table 2.1. 2916 men and 3549 women provided data on at least one biomarker. There were more women than men in the sample. Men tended to have greater wealth, and were more likely to engage in moderate or vigorous physical activity at least once a week. More women reported limiting long-standing illness and had elevated depressive symptoms (12.7% and 6.2%, respectively).

As shown in Table 2.1 there were also significant differences in sleep duration and disturbance regarding gender ( $P < 0.001$ ,  $P < 0.001$ , respectively). More women than men reported short sleep duration (14.7% and 10.3%, respectively) and disturbed sleep (34.2% and 28.1%, respectively). This is in line with the sleep literature (Ohayon, 2004; van den Berg et al., 2009; Vitiello et al., 2004).

In addition, optimal sleep duration (7-8 hours) was reported by nearly 30% of men and 27.8% of women, while sleep between 6 and 7 hours was the most prevalent sleep duration in these data with 34.7% of male and 29.8% of female respondents reporting sleeping such hours. In other words, approximately 60% of the sample slept between 6 and 8 hours. This is broadly in agreement with a study of older men and women from Taiwan, where 64% of the sample slept 6-8 hours (Dowd et al., 2011). Finally, in ELSA a similar percentage of men (6.6) and women (7.1) were long sleepers. A similar statistic has been reported in the sleep literature as well (Kripke et al., 2002; Ohayon, 2004; Patel et al., 2006).

**Table 2.1 Sample characteristics.**

Variable	Mean (SD) /frequency (%)		P-value
	Men (N=2916)	Women (N=3549)	
<b>Age</b>			0.019
50-59 years	874 (30.0)	1101 (31.0)	
60-69 years	1137 (39.0)	1308 (36.9)	
70-79 years	686 (23.5)	805 (22.7)	
80+ years	219 (7.5)	335 (9.4)	
<b>Wealth quintiles</b>			0.001
Poorest quintile	485 (16.6)	687 (19.4)	
2 <sup>nd</sup> quintile	500 (17.1)	693 (19.5)	
3 <sup>rd</sup> quintile	565 (19.4)	679 (19.1)	
4 <sup>th</sup> quintile	610 (20.9)	676 (19.0)	
Richest quintile	626 (21.5)	671 (18.9)	
<b>Current smoking status</b>			0.517
No	2524 (86.6)	3047 (85.9)	
Yes	375 (12.9)	475 (13.4)	
<b>Moderate or vigorous physical activity</b>			<0.001
Less than once per week	850 (29.1)	1306 (36.8)	
At least once per week	2066 (70.9)	2242 (63.3)	
<b>Limiting long-standing illness</b>			0.001
No	2085 (71.5)	2401 (67.7)	
Yes	831 (28.5)	1147 (32.3)	
<b>Depressive symptoms</b>			<0.001
No	2715 (93.1)	3074 (86.6)	
Yes	180 (6.2)	451 (12.7)	
<b>BMI</b>	27.99 (4.33)	28.06 (5.55)	0.537
<b>Sleep duration</b>			<0.001
< 5 hours	300 (10.3)	520 (14.7)	
5-6 hours	538 (18.4)	720 (20.3)	
6 -7 hours	1013 (34.7)	1059 (29.8)	
7-8 hours	872 (29.9)	958 (27.8)	
>8 hours	192 (6.6)	252 (7.1)	

<b>Sleep disturbance</b>			<0.001
Low sleep disturbance	1131 (38.8)	951 (26.8)	
Intermediate sleep disturbance	965 (33.1)	1383 (39.0)	
High sleep disturbance	819 (28.1)	1215 (34.2)	

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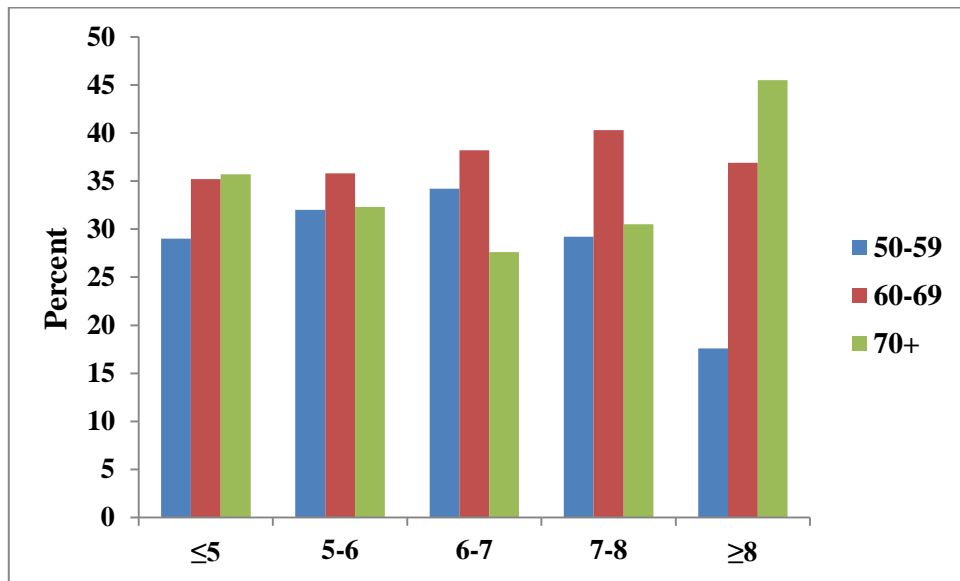
SD=standard deviation; BMI=body mass index.

### 2.5.2 Associations between sleep measures and covariates

Sleep duration was positively related to age ( $P < 0.001$ ), as depicted in Figure 2.2, where long sleep ( $\geq 8$  hours) was most prevalent among the oldest ELSA's participants. Sleep  $\geq 8$  hours was least common in the youngest age group. Wealth was also significantly associated with sleep duration ( $P < 0.001$ ), with wealthier individuals reporting longer (optimal) sleep hours, while those in the poorest wealth quintile being more likely to be short sleepers (see Figure 2.3).

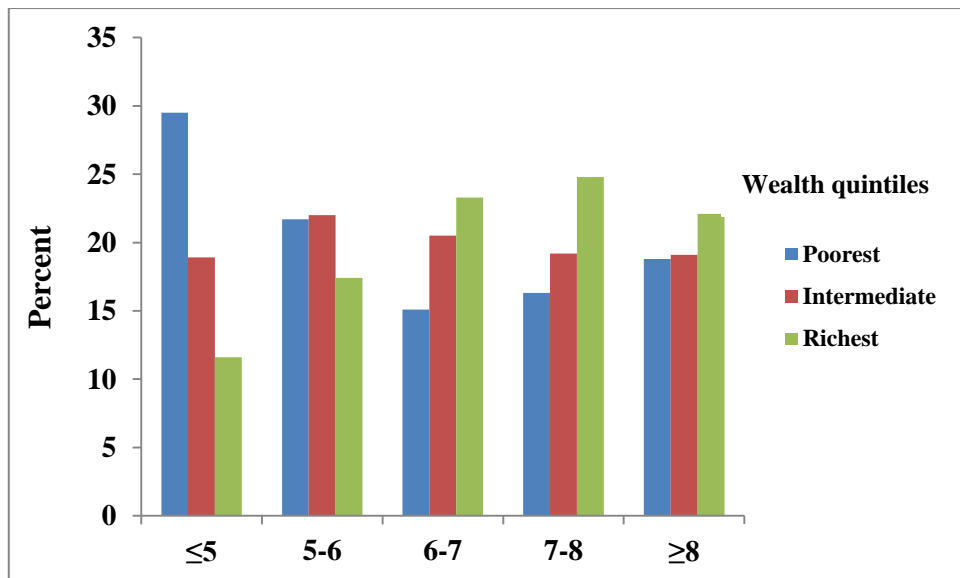


**Figure 2.2 Distribution of sleep duration categories across age groups.**



For presentation purposes age groups '70-79' and '80+' were reclassified into '70+'.

**Figure 2.3 Distribution of sleep duration categories across poorest, intermediate and richest wealth quintiles.**

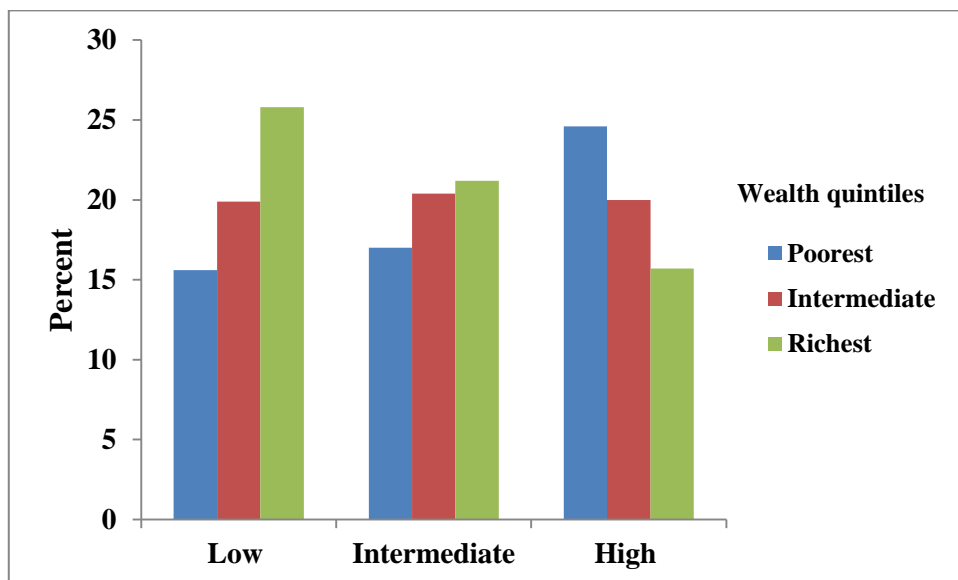


For presentation purposes only poorest (first), intermediate (third) and richest (fifth) wealth quintiles are depicted here.

Sleep duration was shorter among participants with limiting long-standing illness ( $P<0.001$ ), smokers ( $P<0.001$ ), those with elevated depressive symptoms ( $P<0.001$ ), and higher BMI ( $P<0.001$ ). Individuals who reported short and long sleep duration were less likely to engage in moderate or vigorous physical activity more than once a week than those who slept 7-8 hours ( $P<0.001$ ).

Sleep disturbance was unrelated to age, but was more prevalent in the lowest wealth quintile ( $P<0.001$ ) (see Figure 2.4), as well as among current smokers ( $P<0.001$ ), respondents with limiting long-standing illness ( $P<0.001$ ), those who had higher BMI ( $P<0.001$ ), and respondents who took part in moderate or vigorous physical activity less than once a week ( $P<0.001$ ). Respondents with elevated depressive symptoms also had more disturbed sleep ( $P<0.001$ ). The findings relating sleep measures and covariates discussed herein are consistent with the sleep literature (Arber et al., 2009; Benca & Peterson, 2008; Foley et al., 2004).

**Figure 2.4 Sleep disturbance tertiles across poorest, intermediate and richest wealth quintiles.**



For presentation purposes only poorest (first), intermediate (third) and richest (fifth) wealth quintiles are depicted here. Sleep disturbance tertiles are plotted on the horizontal axis.

## 2.6 Biological data characteristics

Mean levels of biological markers are depicted in Table 2.2. To obtain these results a weighting factor relating to non-participation in blood sampling was applied. Mean CRP concentrations were 3.63 mg/L while fibrinogen levels were 3.39 g/l on average. Thirty five per cent of the sample had CRP levels  $\geq 3$  mg/L (N=2159). Average haemoglobin levels were 14.07 g/dL and mean DHEAS concentrations were 2.43  $\mu\text{mol/L}$  (untransformed data; mean DHEAS levels for transformed data were 1.47  $\mu\text{mol/L}$ ). Nearly 7% of respondents had anaemia (N=424).

**Table 2.2 Biological data: means and standard deviations.**

<b>Biomarker</b>	<b>N</b>	<b>Mean</b>	<b>SD</b>
CRP (continuous data)	6061	3.63 mg/L	5.1
Fibrinogen	5928	3.39 g/l	0.6
Haemoglobin	5995	14.07 g/dL	1.33
DHEAS	6028	2.43 $\mu\text{mol/L}$ *	1.81
DHEAS	6028	1.47 $\mu\text{mol/L}$ **	0.53

SD =standard deviation. \*Untransformed data. \*\* Transformed data.

Next I will present associations of each biomarker with the covariates used in my analyses (age, wealth, BMI, current smoking, physical activity, limiting long-standing illness and depressive symptoms) and with gender. Results as presented as means and SD for *t*-tests and ANOVA-s, Pearson correlation coefficients and frequencies, as appropriate.

## **CRP**

CRP concentrations were higher in women than men (3.85 mg/L, SD=5.17 vs. 3.37 mg/L, SD=4.94, mg/L,  $P<0.001$ ) and in older respondents ( $r=0.09$ ,  $P<0.001$ ). CRP was significantly (negatively) associated with wealth ( $P<0.001$ ), for example mean levels of CRP in the poorest wealth quintile were 4.45 mg/L (SD=5.66), while those in the richest wealth quintile were 2.58 mg/L (SD=3.56) on average. In comparison with a non-smoking category smokers had higher CRP levels (3.42 mg/L, SD=4.89 vs. 4.70 mg/L, SD=5.79,  $P<0.001$ ). Higher BMI ( $r=0.22$ ,  $P<0.001$ ), elevated depressive symptoms, relative to 3 or fewer depressive symptoms (4.74 mg/L, SD=6.45 vs. 3.42 mg/L, SD=4.82,  $P<0.001$ ) and limiting standing illness, relative to none (4.73 mg/L, SD=6.16 vs. 2.99 mg/L, SD=4.25  $P<0.001$ ) were also correlated with raised levels of this inflammatory marker. In comparison with respondents engaging in moderate or vigorous physical activity more than once a week, those who did so less than once a week had greater CRP concentrations as well (2.96 mg/L, SD=4.21 vs. 4.60 mg/L, SD=6.05,  $P<0.001$ ).

## **Fibrinogen**

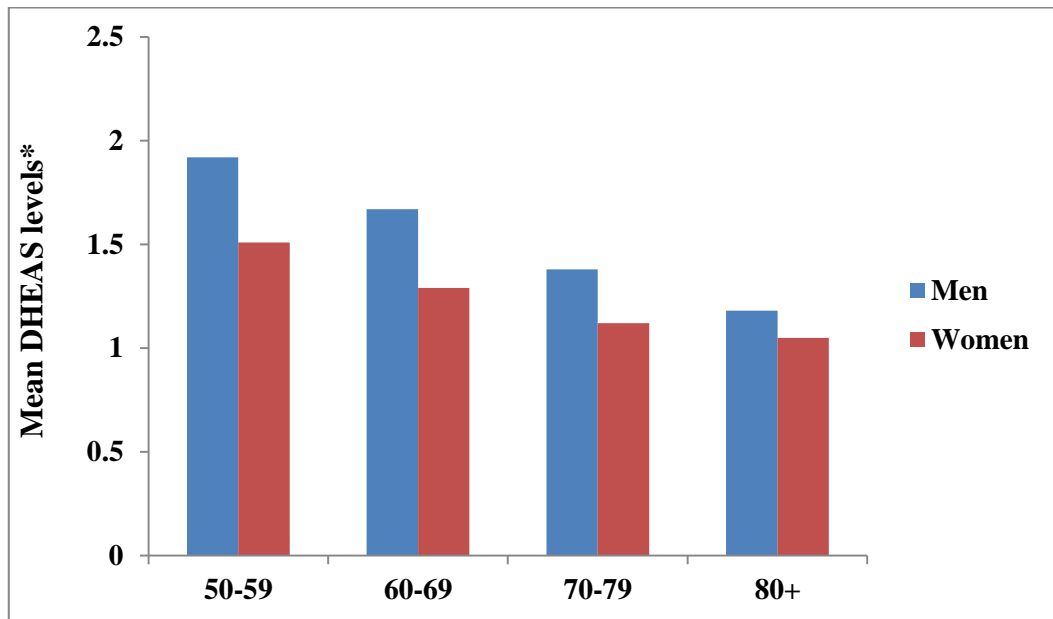
Similarly to CRP, fibrinogen was higher in females than males (3.44 g/l, SD=0.56 vs. 3.33 g/l, SD=0.59,  $P<0.001$ ) and in older respondents ( $r=0.14$ ,  $P<0.001$ ). Those with a less advantageous SES had significantly higher fibrinogen as well ( $P<0.001$ ). Specifically, individuals in the poorest wealth quintile had mean concentrations of fibrinogen of 3.48 g/l (SD=0.61), while in the wealthiest quintile average concentrations of this inflammatory marker were 3.26 g/l (SD=0.52). Participants with higher BMI ( $r=0.17$ ,  $P<0.001$ ) and smokers, relative to non-smokers, also had raised levels of fibrinogen (3.61 g/l, SD=0.60 vs. 3.35 g/l, SD=0.56,  $P<0.001$ ). The presence of elevated depressive symptoms, compared with 3 or fewer symptoms and of a limiting long-standing illness, relative to

none, were also associated with higher levels of this biomarker (3.53 g/l, SD=0.66 vs. 3.36 g/l, SD=0.55,  $P<0.001$ ; 3.52 g/l, SD=0.62 vs. 3.32 g/l, SD=0.53,  $P<0.001$ , respectively). ELSA respondents who engaged in moderate or vigorous physical activity less than once a week also had elevated concentrations of fibrinogen, when compared with those who were physically active at least once a week (3.51 g/L, SD=0.60 vs. 3.31 g/L, SD=0.54,  $P<0.001$ ).

## **DHEAS**

DHEAS was higher in men than women (1.66  $\mu\text{mol/L}$ , SD=0.56 vs. 1.30  $\mu\text{mol/L}$ , SD=0.45,  $P<0.001$ ), younger ELSA participants ( $r=-0.41$ ,  $P<0.001$ ) (see Figure 2.5 for mean DHEAS levels across age group categories stratified by sex), as well as among wealthier respondents ( $P<0.001$ ), and those who smoked (DHEAS in non-smokers was 1.45  $\mu\text{mol/L}$ , SD=0.53 while in smokers it was 1.57  $\mu\text{mol/L}$ , SD=0.57,  $P<0.001$ ). DHEAS levels were lower in heavier respondents, but only slightly so ( $r=-0.03$ ,  $P=0.009$ ). Respondents with greater depressive symptoms, relative to no elevated symptoms (1.34  $\mu\text{mol/L}$ , SD=0.50 vs. 1.48  $\mu\text{mol/L}$ , SD=0.53,  $P<0.001$ ), limiting long-standing illness, compared with none (1.33  $\mu\text{mol/L}$ , SD=0.51 vs. 1.53, SD=0.53,  $P<0.11$ ), and those not engaging in moderate or vigorous physical activity at least once a week, compared with being physically active at least once per week (1.34  $\mu\text{mol/L}$ , SD=0.49 vs. 1.53  $\mu\text{mol/L}$ , SD=0.54,  $P<0.001$ ) also had lower DHEAS concentrations.

**Figure 2.5 Mean DHEAS levels across age groups stratified by sex.**



\*DHEAS transformed data were used to plot this graph.

### **Haemoglobin**

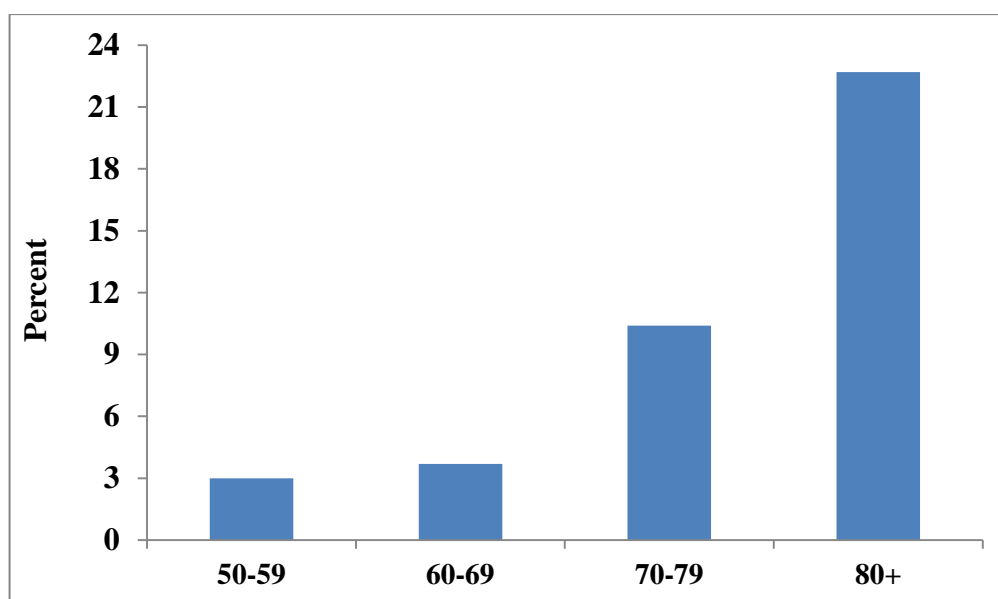
Plasma haemoglobin was lower in women than in men (13.50 g/dL, SD=1.10 vs. 14.74 g/dL, SD=1.26,  $P<0.001$ ) and in older participants ( $r=-0.24$ ,  $P<0.001$ ). Individuals in poorer wealth quintiles also had lower concentrations of this biomarker ( $P<0.001$ ); for instance mean concentrations of haemoglobin in the poorest wealth quintile were 13.91 g/dL (SD=1.47), while in the richest wealth quintile the levels were 14.23 g/dL (SD=1.18) on average. Respondents who smoked had higher haemoglobin levels than their counterparts who were non-smokers (14.45 g/dL, SD=1.42 vs. 14.01 g/dL, SD=1.30,  $P<0.001$ ). Haemoglobin was higher in respondents with higher BMI, but the relationship was very small ( $r=0.04$ ,  $P=0.003$ ). Concentrations of haemoglobin were lower in individuals with higher depressive symptoms and those with limiting long-standing illnesses, when compared with those without elevated depressive symptoms and limiting long-standing illness (13.77 g/dL, SD=1.38 vs. 14.13 g/dL, SD=1.31,  $P<0.001$ ; 13.82 g/dL,

SD=1.41, vs. 14.22 g/dL, SD=1.25,  $P<0.001$ , respectively). Persons who engaged in moderate or vigorous physical activity less than once a week, relative to those who did so at least once a week, had lower haemoglobin concentrations as well (13.82 g/dL, SD=1.43 vs. 14.25 g/dL, SD=1.22,  $P<0.001$ ).

## **Anaemia**

Anaemia was more prevalent in older participants since mean age in respondents with this condition was 75 years (SD=9.83), while participants without anaemia were 64 years old on average (SD=12.79) ( $P<0.001$ ). Figure 2.6 depicts the distribution of anaemia across age groups, where it can be seen, for instance, that anaemia was more than seven times more prevalent in participants aged 80 years and over compared with those in the 50-59 years category. Anaemia was unrelated to gender in these data ( $P=0.446$ ). Wealthier respondents were less likely to suffer from anaemia since 11.4% of participants in the poorest wealth quintile had anaemia in comparison with only 3.5% in the richest quintile ( $P<0.001$ ). However, smokers had slightly lower levels of anaemia than non-smokers (5.2% and 7.3%, respectively) ( $P=0.018$ ), but there was no association with BMI ( $P=0.997$ ). Participants with limiting long-standing illness and elevated depressive symptoms, when compared with those who did not have a limiting condition or elevated depressive symptoms, were more likely to have anaemia (11.7% relative to 4.6%,  $P<0.001$  and 12.1% relative to 6.4%,  $P<0.001$ , respectively). The percentage of individuals with anaemia was nearly three times higher among respondents who engaged in moderate or vigorous physical activity less than once a week when compared with those who were physically active more than once a week (11.8% vs. 4.1%,  $P<0.001$ ).

**Figure 2.6 Distribution of anaemia across age groups.**



### 2.6.1 Sleep duration and biological data

In men nearly 38% of long sleepers had CRP  $\geq 3$  mg/L while only 31.1% of optimal sleepers (7-8 hours) had raised levels of this biomarker (see Table 2.3). Logistic regression analysis confirmed that sleep of longer than 8 hours was associated with elevated CRP levels compared with those sleeping 7-8 hours (OR: 1.50, C.I. 1.05-2.14). This finding was independent of age, wealth, BMI, smoking status, moderate or vigorous activity at least once per week, limiting longstanding illness and depressive symptoms. There were no differences in CRP between the shorter sleep periods. Inflammation levels are likely to be affected by some medications, particularly statins, which have anti-inflammatory properties (Albert et al., 2001). Since ELSA comprises of older people who are quite likely to be on cholesterol-lowering medications, I repeated these analyses additionally controlling for the use of statin medication. Similarly, arthritis medication is also likely to impact inflammation due to its anti-inflammatory properties, so was added as an additional



covariate. 949 of the 6061 participants in the CRP analysis reported being on cholesterol-lowering medication, and 205 were currently taking medication for arthritis. In men following adjustment for both types of medication the association between CRP and long sleep (>8 hours) was unchanged (OR: 1.50, C.I. 1.05-2.15), and short sleep remained unrelated to CRP concentration (OR: 0.87, C.I. 0.64-1.18) (see Table 2.3). Because some past studies relating sleep parameters and inflammation (e.g., Dowd et al., 2011; Miller et al., 2009) analysed CRP as a continuous variable I repeated the analysis treating CRP as continuous data. ANCOVA revealed that sleep duration was no longer associated with CRP ( $F(4,2910)=0.816$ ,  $P=0.515$ ), but the association was in the same direction, with highest levels among men sleeping longest hours (mean levels for 7-8 hours were 3.18 mg/L while for those in the >8 hours category mean levels were 3.76 mg/L, independently of covariates).

Mean concentrations of fibrinogen were highest in men sleeping more than 8 hours, and ANCOVA revealed that sleep duration was significantly associated with fibrinogen ( $F(4,2845)=5.007$ ,  $P=0.001$ ). The LSD multiple comparisons test showed that in comparison with 7-8 hours men sleeping <5 hours had significantly lower fibrinogen concentrations ( $P=0.003$ ) (which is contrary to the first hypothesis), while men sleeping >8 hours had significantly higher fibrinogen ( $P=0.028$ ). Sleep duration remained associated with fibrinogen following adjustment for the use of statins and arthritis medication ( $F(4,2843)=5.079$ ,  $P<0.001$ ), and the LSD multiple comparisons test confirmed that short sleepers (<5 hours) still had significantly lower fibrinogen than those sleeping 7-8 hours ( $P=0.003$ ), while long sleepers (>8 hours) had significantly higher concentrations ( $P=0.028$ ). These results are depicted in Table 2.3.

As shown in Table 2.3 DHEAS levels virtually did not vary by sleep duration in men ( $F(4,2897)=0.108$ ,  $P=0.980$ ). However, haemoglobin levels were lower in shorter

sleepers independently of covariates ( $B=0.052$ , C.I. 0.01-0.09,  $P=0.015$ ). In comparison with the 7-8 hours sleep category anaemia levels were highest in men sleeping 5-6 hours (5.6% vs. 7.2%), but logistic regression analysis revealed no significant association between anaemia and sleep duration in men.

As shown in Table 2.3 in women CRP levels were higher in short and long sleepers (37.9%, 37.7%, respectively) when compared with optimal sleepers (35.0%), but logistic regression analysis was not significant (OR: 1.16, C.I. 0.90-1.49, OR: 1.17, C.I. 0.84-1.63, respectively). These results were virtually unchanged after additional adjustment for the use of statins and arthritis medication since for short sleep the OR was: 1.16, C.I. 0.90-1.49, while for long sleep it was 1.17, C.I. 0.84-1.64 (see Table 2.3). When CRP was treated as a continuous variable the association with sleep duration remained non-significant ( $F(4,3365)=0.290$ ,  $P=0.885$ ). There was little variation in fibrinogen levels by sleep duration categories and ANCOVA result was not significant ( $F(4,3278)=0.406$ ,  $P=0.805$ ). The ANCOVA result remained non-significant following additional adjustment for the use of statins and arthritis medication ( $F(4,3276)=0.405$ ,  $P=0.805$ ). In comparison with optimal sleepers DHEAS levels were lowest in short sleepers (1.30  $\mu\text{mol/L}$  vs. 1.26  $\mu\text{mol/L}$ , respectively), and ANCOVA revealed that the relationship between sleep duration and this biomarker approached a significant level ( $F(4,3335)=2.329$ ,  $P=0.054$ ). Post hoc comparisons, however, showed that DHEAS levels in short sleepers were not significantly lower from those of optimal sleepers ( $P=0.088$ ). Haemoglobin concentrations differed very slightly by sleep duration and linear regression analysis yielded a non-significant result ( $B=0.015$ , C.I. -0.02- 0.05,  $P=0.351$ ). The association between anaemia and sleep duration was not curvilinear since this condition was more prevalent only in long (10%), but not short (5.7%) sleepers, when compared with the 7-8 hour sleep category (6.1%).

Although the logistic regression analysis confirmed the direction of this association it was not statistically significant (OR: 1.54 C.I. 0.91-2.62).

**Table 2.3 Associations between sleep duration and biomarkers in men and women.**

	Percent / adjusted means (SD) <sup>1</sup>	Adjusted odds ratio <sup>1,2</sup> (95% C.I.)/ P value for continuous data	Percent / adjusted means (SD) <sup>1</sup>	Adjusted odds ratio <sup>1,2</sup> (95% C.I.)/ P value for continuous data
	Men		Women	
<b><i>C-reactive protein (<math>\geq 3</math> mg/L)</i></b>				
< 5 hours	28.4%	0.87 (0.64-1.18)	37.9%	1.16 (0.90-1.49)
5-6 hours	33.2%	1.18 (0.92-1.51)	35.5%	1.07 (0.85-1.36)
6 -7 hours	31.3%	1.07 (0.86-1.34)	35.5%	1.05 (0.84-1.31)
7-8 hours	31.1%	1 (reference)	35.0%	1 (reference)
>8 hours	37.9%	1.50 (1.05-2.15)	37.7%	1.17 (0.84-1.64)
<b><i>Plasma fibrinogen (g/L)</i></b>				
< 5 hours	3.23 (0.59)	<0.001	3.42 (0.56)	0.805
5-6 hours	3.34 (0.55)		3.44 (0.56)	
6 -7 hours	3.30 (0.57)		3.41 (0.54)	
7-8 hours	3.34 (0.58)		3.41 (0.54)	
>8 hours	3.44 (0.60)		3.43 (0.57)	
<b><i>DHEAS (<math>\mu\text{mol/L}</math>)</i></b>				
< 5 hours	1.66 (0.56)	0.980	1.26 (0.43)	0.054
5-6 hours	1.66 (0.55)		1.30 (0.44)	
6 -7 hours	1.66 (0.54)		1.33 (0.45)	
7-8 hours	1.66 (0.55)		1.30 (0.45)	
>8 hours	1.68 (0.61)		1.32 (0.49)	

***Plasma haemoglobin (g/dL)***

< 5 hours	14.71 (1.37)	0.015	13.49 (1.13)	0.351
5-6 hours	14.68 (1.20)		13.52 (1.11)	
6 -7 hours	14.79 (1.21)		13.60 (1.00)	
7-8 hours	14.80 (1.19)		13.58 (1.05)	
>8 hours	14.87 (1.40)		13.43 (1.17)	

***Anaemia (below***

***haemoglobin threshold)***

< 5 hours	5.7%	0.97 (0.56-1.69)	5.7%	0.97 (0.61-1.55)
5-6 hours	7.2%	1.40 (0.87-2.24)	6.4%	0.98 (0.63-1.52)
6 -7 hours	5.8%	1.05 (0.67-1.64)	4.6%	0.64 (0.40-1.03)
7-8 hours	5.6%	1 (reference)	6.1%	1 (reference)
>8 hours	5.3%	1.01 (0.53-1.94)	10.0%	1.54 (0.91-2.62)

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<sup>1</sup> Adjusted for age, wealth, BMI, smoking status, moderate or vigorous activity at least once per week, limiting longstanding illness and depressive symptoms. <sup>2</sup> Models relating CRP and fibrinogen are additionally adjusted for the use of statins and arthritis medication.

In summary, in men long sleep hours, but not short, were associated with higher concentrations of CRP and fibrinogen. On the other hand, short sleep was linked with lower haemoglobin levels. These findings were independent of age, wealth, BMI, smoking status, moderate or vigorous activity at least once per week, limiting longstanding illness and depressive symptoms. In the analyses relating sleep duration with inflammatory markers the results were virtually the same after additional adjustment for the use of statins and arthritis medication. DHEAS and anaemia were unrelated to sleep duration in men.

In women no biomarker was associated with sleep duration independently of covariates.

### 2.6.2 Sleep disturbance and biological data

Associations between sleep disturbance and biomarkers are depicted in Table 2.4. In men, in comparison with low disturbances of sleep, CRP was higher in the intermediate sleep disturbance tertile (30.9% vs. 34.6%, respectively), but not in the highest one (29.5%). Logistic regression, after adjustment for covariates, confirmed that men reporting intermediate levels of disturbed sleep had elevated CRP concentrations (OR: 1.29, C.I. 1.05-1.59). This association was largely unchanged after the use of statins and arthritis medication was additionally adjusted for (OR: 1.30, C.I. 1.06-1.59) (see Table 2.4). The same relationship was found when CRP was treated as a continuous variable ( $F(2,2912)=7.420$ ,  $P=0.001$ ), and post hoc comparisons confirmed that CRP was elevated in the intermediate sleep tertile, when compared with the low sleep disturbance category ( $P=0.002$ ). As shown in Table 2.4 fibrinogen concentrations did not vary by sleep disturbance tertiles, and ANCOVA confirmed that there was no association between sleep disturbance and fibrinogen in men ( $F(2,2847)=2.496$ ,  $P=0.083$ ). The F-statistic was largely unchanged following additional adjustment for the use of statins and arthritis medication ( $F(2,2845)=2.558$ ,  $P=0.078$ ). Men with the most disturbed sleep had lower levels of DHEAS than those with good sleep (1.62  $\mu\text{mol/L}$  vs. 1.69  $\mu\text{mol/L}$ , respectively), and ANCOVA confirmed that sleep disturbance was significantly associated with DHEAS in these data ( $F(2,2899)=4.126$ ,  $P=0.016$ ). Post hoc test revealed that indeed men in the high sleep disturbance tertile had significantly lower DHEAS concentrations than men in the best sleep tertile ( $P=0.004$ ). Disturbed sleep was linked with low haemoglobin ( $F(2,2882)=3.239$ ,  $P=0.039$ ) as well, and post hoc test confirmed that levels of this biomarker were significantly lower in the intermediate ( $P=0.038$ ) and high sleep disturbance tertile ( $P=0.026$ ), when compared with the low disturbance tertile. As shown in Table 2.4 anaemia levels were higher in men with intermediate (7.2%) and high sleep

disturbances (6.3%), when compared with those with low disturbances (4.7%). Logistic regression confirmed this, but the difference was only significant for those in the intermediate sleep disturbance tertile (OR: 1.73, C.I. 1.13-2.65), independently of age, wealth, BMI, smoking, limiting long-standing illness, physical activity and depressive symptoms.

In women CRP levels were slightly higher in the intermediate and high sleep disturbance tertile, when compared with the low sleep disturbance tertile, but logistic regression analysis showed that the differences in CRP concentrations were non-significant (OR: 1.08, C.I. 0.88-1.33, OR: 1.07, C.I. 0.86-1.33, respectively). As shown in Table 2.4 sleep disturbance tertiles remained unrelated to CRP following additional adjustment for the use of statins and arthritis medication (intermediate tertile: OR: 1.08, C.I. 0.88-1.33, high tertile: OR: 1.06, C.I. 0.85-1.32). When CRP was treated as a continuous variable the association remained non-significant ( $F(2,3379)=0.833$ ,  $P=0.435$ ). Fibrinogen levels were virtually unchanged across sleep disturbance tertiles ( $F(2,3292)=0.124$ ,  $P=0.883$ ), and additional adjustment for the use of statins and arthritis medication did not alter this finding ( $F(2,3290)=0.123$ ,  $P=0.884$ ). DHEAS was lowest in women with high sleep disturbance, when compared with those with good sleep (1.29  $\mu\text{mol/L}$  vs. 1.33  $\mu\text{mol/L}$ , respectively), but ANCOVA result was non-significant ( $F(2,3349)=1.923$ ,  $P=0.146$ ). Plasma haemoglobin did not differ across sleep disturbance tertiles and ANCOVA result was non-significant ( $F(2,3340)=0.694$ ,  $P=0.499$ ). However, 6.6% of women with intermediate sleep disturbance had anaemia, while only 4.5% of those with low sleep disturbances had this condition. Logistic regression confirmed this finding (OR: 1.59 (1.02-2.46), independently of age, wealth, BMI, smoking, limiting long-standing illness, physical activity and depressive symptoms.

In summary, in comparison with low sleep disturbance tertile, men in the intermediate sleep tertile had significantly higher CRP levels, but there was no association with fibrinogen. Men with intermediate disturbances of sleep also had lower DHEAS and haemoglobin concentrations, and greater likelihood of anaemia, independently of covariates.

Women with disturbed sleep were more likely to suffer from anaemia, independently of covariates, but the remaining biomarkers were unrelated to sleep disturbance measure.

**Table 2.4 Associations between sleep disturbance tertiles and biomarkers in men and women.**

	Percent / adjusted means (SD) <sup>1</sup>	Adjusted odds ratio <sup>1,2</sup> (95% C.I.)/ P value for continuous data	Percent / adjusted means (SD) <sup>1</sup>	Adjusted odds ratio <sup>1,2</sup> (95% C.I.)/ P value for continuous data
	Men		Women	
<i>C-reactive protein (≥ 3 mg/L)</i>				
Low sleep disturbance	30.9%	1 (reference)	34.8%	1 (reference)
Intermediate sleep disturbance	34.6%	1.30 (1.06-1.59)	36.5%	1.08 (0.88-1.33)
High sleep disturbance	29.5%	0.97 (0.78- 1.21)	36.6%	1.06 (0.86-1.32)
<i>Plasma fibrinogen (g/L)</i>				
Low sleep disturbance	3.32 (0.56)	0.078	3.42 (0.54)	0.884
Intermediate sleep disturbance	3.35 (0.59)		3.43 (0.54)	
High sleep disturbance	3.29 (0.58)		3.41 (0.57)	
<i>DHEAS (μmol/L)</i>				
Low sleep disturbance	1.69 (0.55)	0.016	1.33 (0.45)	0.146
Intermediate sleep disturbance	1.67 (0.54)		1.30 (0.43)	
High sleep disturbance	1.62 (0.56)		1.29 (0.46)	
<i>Plasma haemoglobin (g/dL)</i>				
Low sleep disturbance	14.84 (1.10)	0.039	13.58 (1.01)	0.499
Intermediate sleep disturbance	14.73 (1.31)		13.55 (1.09)	
High sleep disturbance	14.71 (1.30)		13.52 (1.10)	
<i>Anaemia (below haemoglobin threshold)</i>				
Low sleep disturbance	4.7%	1 (reference)	4.5%	1 (reference)
Intermediate sleep disturbance	7.2%	1.73 (1.13-2.65)	6.6%	1.59 (1.02-2.46)
High sleep disturbance	6.3%	1.49 (0.95-2.35)	6.2%	1.49 (0.95-2.33)

<sup>1</sup> Adjusted for age, wealth, BMI, smoking status, moderate or vigorous activity at least once per week, limiting longstanding illness and depressive symptoms. <sup>2</sup> Models relating CRP and fibrinogen are additionally adjusted for the use of statins and arthritis medication.



## 2.7 Discussion

This study found gender differences in the associations between sleep measures and biological data, since with the exception of the relationship between disturbed sleep and anaemia the effects were present only in men. The hypothesis that there might be a curvilinear association between sleep duration and markers of inflammation was partly supported. Men sleeping long hours had elevated CRP and fibrinogen levels compared with the 7-8 hours category. There was a limited support for the hypothesis that disturbed sleep would be associated with raised levels of inflammatory markers because only the association between sleep disturbance and CRP was significant, and there was no relationship with fibrinogen. The third hypothesis was only partly supported as although short sleep was associated with low haemoglobin concentrations, there was no relationship between sleep duration and DHEAS, or between sleep duration and anaemia. The fourth hypothesis was more strongly supported by the data as disturbed sleep was associated with lower DHEAS levels, lower haemoglobin concentrations, and increased risk of anaemia, independently of covariates.

The findings relating to inflammation are partly consistent with previous studies. The observation that long (>8 hours) sleep duration was related to elevated levels of CRP has also been reported in a study of older Taiwanese men and women (Dowd et al., 2011). However, other population-based studies of men and women (Suarez, 2008) or of middle-aged women (Matthews et al., 2010) failed to find an association between self-reported sleep duration and this inflammatory marker. Objective sleep duration was also unrelated to CRP in middle-aged men and women from the Wisconsin sleep cohort study (Taheri et al., 2007). In the Whitehall II study CRP was higher in women sleeping fewer than 5 hours, but not among those sleeping more than 9 hours, and unlike in this study no association was found in men (Miller et al., 2009). A more recent analysis of data from the

Whitehall II study revealed that although short sleep was prospectively associated with higher CRP levels in the statistical models adjusted for age, sex and occupational position, this relationship was no longer significant after chronic conditions and CVD risk factors (e.g., BMI) were added into the model. Long sleep hours were unrelated to CRP in these data (Ferrie et al., 2013). It is important to note that in my study the association with sleep duration was only significant when CRP was treated as a dichotomous variable, and not as a continuously distributed measure. This suggests that in these data the relationship is not a graded one, but is only apparent when potentially clinically significant levels of systemic inflammation are present.

Fibrinogen was unrelated to sleep duration in previous studies (Matthews et al., 2010; Miller et al., 2010; Suarez, 2008), but my data suggest that long sleep hours are related to higher levels of this biomarker in men. Sampling differences between this study and those of Suarez (2008) and Matthews et al., (2010) could be one explanation for the lack of this association in their data since the former study was not based on an older population, while the latter comprised only women. The Whitehall II study (Miller et al., 2010) compared men and women, but the mean age was approximately 49 years, while in these data participants were 65 years on average. A recent longitudinal investigation reported that higher fibrinogen was linked to longer sleep hours, but the sample included only older women (Hale et al., 2013). However, the finding in this study supports data from elderly Taiwanese adults where sleep longer than 8 hours, but not short sleep, was related to higher fibrinogen concentrations. The mean age in that cohort was 66 years (Dowd et al., 2011). Therefore since my study comprised older participants, who are more likely to suffer from chronic medical conditions than younger individuals, this might partly explain why my findings are congruent with a cohort of older, but not middle-aged population studies.

Insufficient sleep, if prolonged, is thought to contribute towards systemic low-level inflammation that might in turn increase the risk of cardiovascular outcomes, but in this study I found that only long sleep hours were associated with raised levels of inflammatory markers. While the link between short sleep and inflammation has received a considerable attention in the literature, associations with long sleep remain uncertain. By the same token, mechanisms relating long sleep duration with health outcomes are not well understood at present (Gangwisch et al., 2008; Stranges et al., 2008), but as emphasised in the previous chapter (pages 68-69), pathways linking short and long sleep hours with health are likely to be distinct. For example, in the Whitehall II cohort authors studied changes in sleep duration over time in relation to CVD mortality and all-cause mortality. Respondents who reduced their baseline sleep duration of 6, 7, or 8 hours, relative to those who retained sleep of 7 hours, had higher cardiovascular mortality at follow-up. However, those who subsequently increased their baseline sleep duration of 7 or 8 hours, again compared to those who reported sleeping 7 hours both at baseline and follow-up, had elevated risk of all-cause mortality, but not of CVD mortality (Ferrie et al., 2007). It has been argued that long sleep hours are secondary to pre-existing illness, whereas short sleep precedes ill-health (Cappuccio et al., 2011; Gangwisch et al., 2008; Stranges et al., 2008). If this is the case, then perhaps greater inflammation is an indicator of pre-existing illness. I did not include specific measures of CHD, diabetes, or cancer in these analyses, although the presence of a limiting long-standing illness was taken into account. Sleep apnoea might be another pathway translating long sleep duration into adverse health outcomes (Foley, 2004). Sleep apnoea was not measured in ELSA, but all analyses were adjusted for BMI, age, and smoking, which are well-established risk factors for this sleep disorder (Kasai et al., 2012; Punjabi, 2008). Sleep apnoea has also been found more prevalent among ethnic minority groups (Sutherland et al., 2012), in particular in Asian and Black

populations, but these data comprise largely white participants (96.3%). Family history of sleep apnoea is another risk factor (Kasai et al., 2012), but there is no information on this variable in ELSA. Polycystic ovary syndrome and pregnancy are risk factors for sleep apnoea in women (Punjabi, 2008). Women in this study were aged 50 years or more and none were pregnant, and analyses were adjusted for limiting long-standing illnesses that would have taken into account the presence of polycystic ovaries. Data from over 85,000 women from the Nurses' Health Study suggested that the association between long sleep duration and mortality might be confounded by depression and lower SES (Patel et al., 2006), but in the present study the associations with biomarkers were independent of depressive symptoms and socio-economic circumstances as defined by participants' wealth.

These data support the association between elevated CRP levels and disturbed sleep (Matthews et al., 2010; Prather et al., 2013; Suarez, 2008), but the association was modest and was found only in men. This is in line with the findings from the Northern Finland 1966 Birth Cohort (Liukkonen et al., 2007). CRP was also associated with insomnia symptoms (difficulties falling asleep and nonrestorative sleep) in male respondents from the HUNT study in Norway, albeit only in age-adjusted models (Laugsand et al., 2012). Although sleep disturbances have been related to elevated fibrinogen among women (Matthews et al., 2010; Prather et al., 2013; Suarez, 2008), my analyses support this association only in men. It is uncertain why this study do not support data previously reported in females, but as already noted in relation to the association between long sleep and fibrinogen, differences in the populations studied may in part explain these divergent findings. For example, the study described by Prather et al., (2013) was exclusively based on participants with established CHD, while in my analytical sample only 331 participants (5.4%) were diagnosed with this chronic condition. In addition to the issues of age and

gender discussed earlier, Matthews et al., (2010) found associations between measures of sleep disturbance and fibrinogen only among African American women, and the study described by Suarez (2008) was also based on a multi-ethnic sample. ELSA, as already mentioned, comprises of largely white participants.

Higher levels of DHEAS have been associated with advantageous health outcomes including lower prevalence of metabolic syndrome in men (Phillips et al., 2010). To date there have been few studies relating sleep parameters with DHEAS, but an Austrian study of middle-aged and elderly men failed to find an association between sleep quality and DHEAS (Ponholzer et al., 2005), and DHEAS was also unrelated to sleep duration in a sample of men from Singapore (aged 29-72 years) (Goh et al., 2007). In this study I found an inverse relationship between sleep disturbance and DHEAS in men, independently of confounders. It has been reported that men tend to have higher DHEAS levels than women (Vermeulen, 1995), and this was also the case in these data (DHEAS was 1.66  $\mu\text{mol/L}$  in men and 1.30  $\mu\text{mol/L}$  in women (transformed data),  $P < 0.001$ ). That could explain in part gender differences in the relationship between sleep disturbance and DHEAS in this study. Nonetheless, this novel finding suggests that fewer sleep complaints are associated the higher DHEAS among older people. Since DHEAS concentration declines markedly with age, this might be a mechanism through which better sleep promotes health at older ages. However, because this study is cross-sectional it might also be the case that greater DHEAS levels promote better sleep. Future studies are needed to test the temporal relationship between sleep quality and DHEAS.

Low haemoglobin and anaemia are serious issues in elderly populations, which have been implicated in adverse health outcomes and mortality (Culleton et al., 2006). Little is known about associations between sleep parameters and haemoglobin levels in elderly community-dwelling individuals. These data indicate that in men, greater sleep problems

and short sleep hours are associated with lower haemoglobin levels, independently of covariates including depressive symptoms. More sleep problems were also related to higher odds of having anaemia in both sexes. Given that approximately 34% of anaemias in the elderly have unexplained causes (Guralnik, Ershler, Schrier, & Picozzi, 2005) this is potentially an important finding; it suggests that, in addition to nutritional deficiencies or chronic illnesses, behavioural factors such as poor sleep might be implicated in this condition. Short sleep duration was marginally related to lower haemoglobin levels as well (but not to higher odds of anaemia). However, because these data are cross-sectional, it is uncertain whether disturbed and short sleep are risk factors or consequences of lower haemoglobin levels and anaemia in this elderly cohort. Anaemia is related to fatigue (Beghe, Wilson, & Ershler, 2004), which has also been associated with poor sleep (Thomas et al., 2011), so it is possible that fatigue in part drove the associations between sleep parameters and haemoglobin levels in this study. There is evidence that iron deficiency, which might cause low haemoglobin and anaemia, leads to disturbed sleep. For instance, iron deficiency and anaemia have been associated with alterations of sleep architecture in paediatric populations (both cross-sectionally and prospectively) (Peirane et al., 2010). Iron deficiency is also associated with restless leg syndrome, which ranges between 5 to 15% in the general population (Trotti et al., 2012). Information about sleep disorders is not collected in ELSA, but all analyses were adjusted for a limiting long-standing illness. Longitudinal studies are required to explore these associations further.

It is notable that in this study nearly 30% of the sample slept 7-8 hours, while sleep duration of 6-7 hours was most prevalent. This is to some extent in agreement with findings from a study conducted with men and women from seven European countries including the UK, who were at a similar age (55-101 years) to ELSA's participants (Ohayon, 2004). In particular, from among 1612 British respondents 25% slept 7.5 hours

(Ohayon, 2004). In addition, as already mentioned in the Results section, the prevalence of sleep duration of 6-7 and 7-8 hours in my data is similar to those reported in a study of older Taiwanese men and women (Dowd et al., 2011).

Longer sleep duration was more prevalent with increasing age in these data. It has been well documented that sleep efficiency and continuity diminish markedly as people age, with men showing more pronounced changes than women (Carskadon & Dement, 2011; Ohayon et al., 2004). This does not always seem to be the case with sleep duration. A meta-analytic review of sleep parameters across the lifespan showed that while in healthy adults sleep duration is negatively associated with age, the trend is no longer significant among individuals over 60 years old (Ohayon et al., 2004). More recently data from over 1000 men and women aged 60 years and above revealed that the average sleep duration was 7 hours 8 minutes (Ohayon & Vecchierini, 2005), which does not markedly differ from sleep duration reported by middle-aged individuals (Magee et al., 2009). Older age has also been associated with longer sleep duration in a large US study (Krueger & Friedman, 2009).

This study has several strengths. These analyses are based on a large and well-characterized sample of older individuals living in England. I was able to take advantage of the extensive economic and health data available in ELSA, and to study a range of biomarkers. Because the variables studied were collected within a larger study protocol, there is little chance that participants were aware of the specific interests of the investigators in sleep and biological function.

These data also have several limitations. Sleep duration and disturbance were assessed with self-report, which may be affected by memory biases and affective states (Bliwise & Young, 2007; Krystal & Edinger, 2008). In addition, sleep disturbance was measured with a short scale based on the Jenkins Sleep Problems Scale (Jenkins et al.,

1988) rather than a more elaborate measure such as the PSQI (Buysse et al., 1989). However, the items overlap with those included in longer measures, and the Jenkins Sleep Problems Scale has previously been used to investigate outcomes such as sickness absence, weight gain, and recovery from surgery (Jenkins et al., 1994; Lallukka et al., 2012; Lyytikäinen, Rakhonen, Lahelma, & Lallukka, 2011), as well as cardiovascular and neuroendocrine function (Kudielka et al., 2004; Kumari et al., 2009). The use of self-report is common in large community-based research studies, where the expense of using objective sleep measures may be prohibitive. However, it cannot be concluded that the associations observed here would necessarily be replicated with objective indicators, as shown in the Cleveland Family study where objective short sleep was related to higher TNF- $\alpha$ , while self-reported sleep was positively associated with CRP and IL-6 concentrations (Patel et al., 2009). The cross-sectional design did not allow me to establish the temporal precedence between sleep parameters and biological measures in this study. Deviant sleep patterns might lead to poor health, for example through inflammatory responses, but poor health is also likely to impair sleep (Zee & Turek, 2006). Therefore it should be recognised that the biological measures described in this study could mediate the relationship between poor sleep and ill health, but also be risk factors for disordered sleep. Sleep measures were introduced to ELSA in wave 4, thus it is not yet possible to study longitudinal associations between sleep parameters and biological measures. CRP and fibrinogen are acute phase proteins that may be stimulated by a number of different processes including inflammatory cytokine release from a variety of tissues. It would have been informative to explore relationships between sleep and IL-6, TNF- $\alpha$  or other inflammatory markers, but these were not measured in ELSA.

In conclusion, disturbed sleep was associated with higher odds of anaemia in women, but there was no relationship between sleep measures and other biomarkers. The findings



in male respondents support the growing body of evidence that low grade inflammation, as indicated by CRP and fibrinogen, is associated with long sleep duration. Further I found for the first time, to the best of my knowledge, an association of DHEAS with sleep disturbance. I have also extended findings relating low haemoglobin and anaemia with sleep parameters to a representative sample of older adults. These results support the hypothesis that sleep is an important marker of physical health in the elderly. A better understanding of these relationships, preferably using longitudinal cohort studies, will broaden our understanding of risk factors for ill health in elderly populations.

## **CHAPTER 3: DISTURBED SLEEP AND HEART RATE**

### **VARIABILITY IN EVERYDAY LIFE (Study 2)**

#### **3.1 Introduction**

The autonomic nervous system (ANS) is responsible for many physiological functions including heart rate (HR) (Thayer & Lane, 2007). Briefly, the ANS consists of two major branches. The sympathetic branch is involved in energy mobilization and is typically activated during stress and the fight-or-flight responses. The parasympathetic branch, on the other hand, is involved in physiological functions that occur when the organism is at rest, for example, digestion. The heart is dually innervated by the ANS, which means that an increase in sympathetic modulation typically leads to a faster HR, while an increase in parasympathetic modulation slows it down (Thayer et al., 2010). In healthy individuals the relationship between both branches of the ANS system is dynamic reflecting the flexibility of the brain's responses to environmental stimuli. Interestingly, experimental studies documented that when the main nerves controlling both branches of the ANS were blocked by a drug (e.g., atropine and propranolol - often referred to as double blockade) the resting HR was lower than the intrinsic one, suggesting that HR is dominated by the parasympathetic branch. In addition, the variability in beat-to-beat changes of HR is also under the dominance of the parasympathetic branch (Thayer et al., 2010; Thayer & Lane, 2007). It should further be mentioned that the parasympathetic and sympathetic branches of the ANS differ in how fast they can change HR. While the former branch alters HR in milliseconds, the latter one does so in seconds (Thayer et al., 2010).

There are a number of methods to assess the autonomic modulation of the heart, and heart rate variability (HRV) is a useful and non-invasive measure based on the electrocardiograph (ECG) data. Other measures of autonomic influences on the heart include, for instance, pre-ejection period (PEP), stroke volume (SV) and left ventricular

ejection time (LVET), however because neither of them was used in this study and due to space constraints I will not discuss them further in this thesis (see Thayer et al., 2010 for a recent review in this area). Short-term HRV (0.5-5 minutes) reflects the balance between sympathetic and parasympathetic innervation, with reduced HRV being indicative of heightened sympathetic activity and/or vagal withdrawal. Reduced HRV has been implicated in the development of CVD and mortality (Sztajzel, 2004; Thayer & Lane, 2007). For example, two separate investigations of the data from the ARIC study revealed that low HRV predicted CHD incidence and mortality in initially healthy populations (Dekker et al., 2000; Liao et al., 1997). Impaired HRV is also predictive of mortality among cardiac patients, as reported in the Autonomic Tone and Reflexes After Myocardial Infarction (ATRAMI) study, where patients with reduced HRV who suffered MI (N=1284) were over 3 times more likely to die within 8 months of follow-up (RR=3.2, C.I. 1.42-7.36), when compared with those who did not have lower HRV (La Rovere et al., 2003). Reduced HRV has been associated with mortality among patients with congestive heart failure as well (Ponikowski et al., 1997).

Sleep in healthy humans is associated with a decrease in HR, blood pressure and sympathetic activity, whereas parasympathetic modulation of the heart increases, especially during deep sleep stages (Meerlo et al., 2008; Stein & Pu, 2012). Experimental data have suggested that sleep curtailment could result in adverse physiological responses such as an increase in blood pressure, or in HR (Meerlo et al., 2008). Sleep problems might also result in autonomic imbalance, for instance, by increasing the dominance of sympathetic activity over parasympathetic modulation (Meerlo et al., 2008). There is extensive research relating cardiac autonomic regulation with sleep apnoea and specific clinical problems such as chronic fatigue syndrome (Burton et al., 2010), irritable bowel syndrome (Robert et al., 2006) or chronic heart failure (Ueno et al., 2011), but studies in

healthy population samples have been limited and findings remain inconsistent (Stein & Pu, 2012). Since the literature relating sleep measures and HRV has been reviewed in Chapter 1 (pages 88-94) it will only be briefly summarised here. For example, 30 hours of total sleep deprivation resulted in a decrease in sympathetic activity, but no change of parasympathetic modulation (Holmes et al., 2002). On the other hand, more recent studies reported that total (Sauvet et al., 2010; Zhong et al., 2005) and partial sleep deprivation (Dettoni et al., 2012) were associated with increased sympathetic activity and decreased parasympathetic activity. Finally, sleep deprivation has also been associated with an increase in vagal tone (Pagani et al., 2009; Vaara et al., 2009). Experimentally induced sleep fragmentation (but maintenance of participants' typical sleep duration) has been linked to reduced HRV as well (Stamatakis & Punjabi, 2010; Tasali et al., 2008).

It is uncertain what accounts for the heterogeneity of these experimental findings, but one explanation might be differences in methodology in terms of duration of sleep deprivation, whether or not participants were required to perform cognitive tests, and the presence of light, among others (Stein & Pu, 2012). In addition, because the above studies have been conducted in sleep laboratories, with the exception of the work described by Dettoni et al., (2012) where induced sleep loss took place at participants' home, it is not clear whether impaired sleep might also be related to alterations of cardiac autonomic activity in everyday life. Observational research into associations between sleep measures and HRV has been rare, and the existing evidence comes from populations known to experience severe sleep disturbances or deprivation, for instance, university students undergoing final exams (Takase et al., 2004), or nurses working only at nights (Chung et al., 2009). Although both studies reported impaired HRV among their participants, the generalizability of their data to the general population is limited. In addition, although studies which measured HRV during normal (healthy) sleep revealed that changes in

autonomic modulation of the heart are primarily driven by changes in sleep stages (Trinder et al., 2001), it remains unclear whether in everyday life disturbed sleep would be associated with lower HRV during the day, at night or both.

It is plausible that the impact of disturbed sleep might be more prominent under certain conditions that are themselves related to impaired HRV. For instance, in the Whitehall II study stressful working conditions, defined with the demand-control model (Karasek & Theorell, 1990), have been found associated with lower HRV, independently of covariates including age, sex or health behaviours (Chandola et al., 2008). In Netherlands a study of 820 middle-aged working men and women reported a trend ( $P=0.059$ ) between work stress, measured with the effort-reward imbalance model described by Siegrist (1996), and lower HRV (Vrijkotte, van Doornen, & de Geus, 2000). More recently Loerbroks et al., (2010) also found an inverse association between work stress (again measured with the model by Siegrist (1996) and HRV in 581 German employees. This raises the possibility that the effects of disturbed sleep might be greater when HRV is measured during the working day rather than in less demanding circumstances during leisure activities, or at weekends. In addition, an experimental study showed that participants who were exposed to acute physiological stress before bedtime (being asked to give an oral speech the next day) had significantly lower HRV during sleep than subjects in the control group (Hall et al., 2004).

Bearing in mind the limitations of the sleep literature discussed herein, the first aim of this study was to integrate the evidence from population studies that impaired HRV is related to stressful working conditions, and results from experimental studies indicating that sleep loss predicts lower HRV, by exploring the link between sleep problems and cardiac autonomic regulation measured over a 24-hour period. However, this relationship could be explained by two possible mechanisms. First, it might be the result of enduring

individual biobehavioural differences between individuals who do and do not experience sleep problems, and if so it would be present both at night and during the day. Secondly, it could arise from the specific demands of work, and could thus be present during the working day, but not at night. To test these two possibilities associations between both night-time and daytime HRV with sleep problems were explored.

In addition to work stress another explanation for an association between sleep problems and HRV might be concurrent or prior affective states since reduced HRV is associated with anxiety (Friedman, 2007) and depression (Kemp et al., 2010; Rottenberg, 2007). For instance, a Dutch study (N=2059) found that, in comparison with controls, respondents diagnosed with anxiety disorders had significantly lower HRV, albeit the association was only statistically significant among those on antidepressant medication (Licht, de Geus, van Dyck, & Penninx, 2009). More recently lower HRV has also been reported among patients with major depressive disorder (medium effect size), and in particular among respondents suffering from depression comorbid with anxiety disorder (large effect size), when compared with controls matched in terms of age and sex (Kemp, Quintana, Felmingham, Matthews, & Jelinek, 2012). On the other hand, negative emotional states are correlated with sleep problems (Benca et al., 1992), while positive affective states are related to good sleep and to greater HRV. For example, Steptoe et al., (2008) found that positive affect (e.g., feelings of happiness or excitement) and psychological well-being (e.g., purpose of life, autonomy) were associated with fewer disturbances of sleep, after adjustment for relevant covariates. Positive affect has been found related to fewer insomnia symptoms in the MIDUS study as well (Hamilton et al., 2007a). Finally, cardiac patients who experienced greater positive affect had significantly higher parasympathetic modulation of the heart, while the sympathetic dominance was decreased, when compared with those with lower positive affect. These relationships were

independent of sex, age, medication, coronary artery disease status (definite vs. absent), and health behaviours (Bhattacharyya, Whitehead, Rakhit, & Steptoe, 2008). Therefore, the second aim of this study was to explore whether the associations between sleep problems and HRV were in part accounted for by perceived stress and affective states.

### **3.2 Hypotheses**

Based on the limitations of the sleep literature identified herein this study was set out to test two hypotheses.

1. The main hypothesis was that sleep problems would be associated with reduced HRV over the working day. If this association was the result of enduring individual biobehavioural differences between individuals who do and do not experience sleep problems similar relationships would be present both during the day and at night. If the association arises from the specific demands of work, it might be present during the working day, but not at night.

To determine whether the inverse association between sleep problems and HRV was explained, at least to some extent, by experienced affect or stress I also hypothesised that:

2. Greater perceived stress and lower positive affect on the evening before work, or during the work period itself, would account in part for the associations between sleep problems and HRV.

### **3.3 Method**

#### **3.3.1 Study design**

The work described here is based on the data from the Daytracker study, which was a cross-sectional investigation of relationships between affective states and biological responses in everyday life of working women. The project was funded by the National

Institute on Aging and the Economic and Social Research Council. The data were collected by researchers from the Psychobiology Group, UCL, between spring 2007 and summer 2008. Participants were asked to complete two 24-hour periods of ambulatory measurement of HR (one full work and one full leisure day), together with other biological, psychosocial and affective measures, but only the measures relevant to this PhD will be described in this study. To date a number of peer-reviewed articles have been published based on the Daytracker study (e.g., Dockray & Steptoe, 2011; Dockray et al., 2010)

### **3.3.2 Participants**

The sample comprised 199 women employed at UCL and neighbouring institutions, who were recruited through advertisement (posters and emails). Participants were deemed eligible if they met the following criteria: aged 18 to 65 years, in full-time, paid employment, not taking any medication except for oral contraception or hormone replacement therapy, Internet access at home, not being pregnant, no history of sleep problems, and free from any serious illness (e.g., cancer, CVD) within the last two years. Women interested in the study contacted the research team via an e-mail, and were then sent information sheet and a short questionnaire to establish their eligibility. Participants who fulfilled the study criteria were scheduled for two appointments at a UCL research laboratory. The study was approved by UCL Research Ethics Committee. Women who completed the study received a small honorarium.

### **3.3.3 Procedure**

Participants provided ambulatory measures of HR and HRV for one work and one leisure day. Only the work day is presented here, since the focus in this study was on sleep and HRV during work. HR/HRV measurement periods began approximately at 5:00pm and lasted 24 hours. The work day monitoring session was scheduled for any day between



Monday and Thursday, while the leisure period (not described here) always began on a Friday. During the first appointment in the research laboratory participants signed the consent form, and were given a set of measures to complete assessing socio-economic and demographic characteristics, as well as health-related factors including sleep. A member of the research team measured participants' weight and height, which were later used to calculate body mass index (BMI, kg/m<sup>2</sup>). Participants were also instructed how to complete the Day Reconstruction Method (DRM) (Kahneman, Krueger, Schkade, Schwarz, & Stone, 2004), which was used to assess experienced affect during the study period (the DRM will be explained in the Measures section). HR and HRV were monitored using an Actiheart device (Actiheart, Cambridge Neurotechnology Ltd, Papworth, UK) for 24 hours. Participants wore the Actiheart and completed the DRM in the same 24-hour monitoring period.

### **3.3.4 Measures**

#### **3.3.4.1 Background measures**

Participants' age, ethnicity, marital status, family situation, education and economic status were measured by questionnaire, in which from among a range of possible answers respondents selected those that most closely described their demographic and economic circumstances. For example, educational attainment was assessed by asking participants to select a category representing their highest qualification (e.g., "GCSEs", "GNVQ", "Diploma" or "Postgraduate degree"). Due to a small number of participants with qualifications lower than a degree (e.g., GCSEs: N=1, diploma: N=10) educational attainment was reclassified into "Less than a degree" and "Degree or higher". In this study I used personal income as a measure of socioeconomic status, with annual income being assessed in 8 income bands (e.g., "Less than £9,999"; "£10,000 - £14,999"; up to "More

than £70,000”), which for the purpose of analyses described here were divided into tertiles (<£25,000, £25,000-£35,000 and >£35,000).

#### **3.3.4.2 Sleep assessment**

Sleep problems were assessed the Jenkins Sleep Problems Scale (Jenkins et al., 1988), a widely used self-reported measure of sleep (Kudielka et al., 2004; Kumari et al., 2009; Lyytikainen et al., 2011). The questionnaire comprises 4 items (e.g., “Have trouble falling asleep”, “Have trouble staying asleep”) and participants are requested to indicate how often in the past month they experienced each sleep problem (see Appendix 1). Items were rated on a 6-point scale (ranging from 0=“not at all” to 5=“22-31 days”). The scores were averaged, with higher scores corresponding to greater sleep problems (range 0.0 to 1.66). The Cronbach’s  $\alpha$  in this sample was .71.

#### **3.3.4.3 DRM assessment**

The Day Reconstruction Method (DRM) (Kahneman et al., 2004) was used to assess affect during the evening and following day, so as to provide measures of experienced affect during the study period. In the Daytracker study the DRM was administered online. Participants were requested to recall all activities they engaged in over the past 24 hours as a continuous series of episodes. The start and end time of each activity or episode was recorded. After the 24-hour monitoring period was reconstructed, participants were asked to answer a number of questions about each activity or episode, for example, their location and with whom they were interacting (see Figure 3.1 for a screenshot depicting an online version of the DRM). In addition, participants indicated how they felt during each episode (e.g., “impatient for it to end”, “happy”, “frustrated”) using a series of 7-point scales anchored at 0=“not at all” to 6=“very much” (see Figure 3.2). To account for the fact that affective states are likely to differ throughout the day in terms of duration and intensity

separate duration-weighted averages were computed for each state. For example, for the feeling of frustration a rating of 6 over a 1-hour episode and a rating of 1 over a 5-hour episode would have an average of 3.5  $((6+1)/2)$ , yet this would not accurately reflect that feeling over the monitoring period. So in this case the duration-weighted mean would be calculated by taking an average of  $6*1$  and  $1*5$  divided by their total time of 6 hours (1.8).

For the purpose of this study two DRM-derived affective states were computed: positive affect, computed through aggregating ratings of happiness, feeling warm and friendly, and enjoyment, and stress (an average of frustration, feeling hassled, and feeling criticised). In addition, separate duration-weighted averages were created for the evening period (from the beginning of the study at about 5:00pm until bed time), and the work day itself. This was performed in order to obtain periods of affective states corresponding with daytime and night-time HRV.

**Figure 3.1** A screenshot of an online version of the DRM used in the Daytracker study.

DayTracker
UCL

1	17 : 00	Socialising	Pub/club/bar/restaurant	<input type="text" value="Friends"/> <input type="text" value="Colleagues"/> <input type="text" value="Spouse/partner"/>
2	20 : 00	Eating	Pub/club/bar/restaurant	<input type="text" value="Spouse/partner"/> <input type="text" value="Friends"/> <input type="text"/>
3	23 : 00	Socialising	Pub/club/bar/restaurant	<input type="text" value="Friends"/> <input type="text" value="Spouse/partner"/> <input type="text"/>
4	01 : 00	Travelling/Commuting	Public transport	<input type="text" value="Spouse/partner"/> <input type="text"/> <input type="text"/>
5	02 : 00	Sleeping	Your home	<input type="text" value="Spouse/partner"/> <input type="text"/> <input type="text"/>
6	11 : 00	Dressing/showering	Your home	<input type="text" value="Spouse/partner"/> <input type="text"/> <input type="text"/>
7	11 : 30	Eating	Your home	<input type="text" value="Spouse/partner"/> <input type="text"/> <input type="text"/>
8	12 : 00	Travelling/Commuting	Public transport	<input type="text" value="Spouse/partner"/> <input type="text"/> <input type="text"/>

Start  :

◀ BACK
DAY COMPLETE ▶
NEXT EPISODE ▶

**Figure 3.2 Affect measurement of one episode captured by the DRM.**

DayTracker
UCL

Episode 1

Between 16:00 and 17:00 you were travelling/commuting on public transport with no-one.

During this time please rate each feeling on the scale given. A rating of 0 means that you did not experience this feeling at all. A rating of 6 means that this feeling was a very important part of the experience. Please click the number between 0 and 6 that best describes how you felt.

	Not at all						Very much
	(0)	(1)	(2)	(3)	(4)	(5)	(6)
Impatient for it to end	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Happy	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Frustrated	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Depressed	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Competent	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Hassled	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Warm / Friendly	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Angry	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Worried / Anxious	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Enjoying Myself	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Criticized	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Tired	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

NEXT EPISODE ▶

#### 3.3.4.4 Heart rate and heart rate variability assessment

Heart rate and HRV were recorded continuously for 24 hours from approximately 5:00 pm on a work day by the Actiheart monitor, which was attached to participants' chests with two electrodes. The Actiheart has been designed to assess HR and motor movement, and is suitable to measure physical activity in population-based studies. The reliability and validity of the device has been established by Brage et al., (2005) at the University of Cambridge. At the end of the 24-h monitoring period beat-to-beat HR was screened by visual inspection to remove artefacts, and converted to normal-to-normal (N-N) intervals. HRV was indexed by the root mean square of the successive standard differences (RMSSD) of N-N intervals expressed in milliseconds since this is known to relate to vagal activity (Task Force of the European Society of Cardiology and the North

American Society of Pacing Electrophysiology, 1996). RMSSD is a frequently used time domain measure of HRV (Thayer et al., 2010). HRV can also be measured with frequency domain indices where power spectral analysis is used to obtain information on different frequency bands reflecting, for instance, the parasympathetic modulation (the high frequency band), or the sympathetic modulation of the heart (the low frequency band) (Thayer et al., 2010). However, this method of HRV assessment was not used in this study since there were doubts about the fine-grained temporal resolution of the instrument, so it will not be described in greater detail here.

Data processing was carried out using Kubios HRV Analysis Software version 2.226.001 (Biosignal Analysis and Medical Imaging Group, Dept. Of Applied Physics, University of Kuopio, Finland). All analyses were carried out in 5 min blocks. HR and RMSSD for the night-time were derived by averaging the 5 min blocks from the time each participant reported going to bed to their reported waking time, while values for the working day were computed from the reported waking time until the end of the recording period.

#### 3.3.4.5 **Other measures**

Habitual physical activity may be related to greater HRV (Borresen & Lambert, 2008) and is associated with fewer sleep problems (Physical Activity Guidelines Advisory Committee, 2008), so was included in these analyses as a potential confounder. Physical activity was assessed with an abridged version of the scale used in the Whitehall II study (Marmot & Brunner, 2005), in which participants were asked how often on average they engaged in moderately energetic and vigorous physical activity each. The scores ranged from 0 = ‘never/hardly ever’ to 3 = ‘three or more times a week’. Examples of activities were provided for each category. For instance, cycling, dancing or leisurely swimming were given as examples of moderate physical activity, while running, tennis or squash

were possible examples of vigorous activity. Scores were summed to generate a combined measure ranging from 0 to 6, with higher values reflecting greater physical activity.

Smoking has been associated with both lower HRV (Kuch et al., 2001) and impaired sleep (Jaehne et al., 2012), so was included as a covariate as well, and was assessed by self-report. Namely, participants were required to indicate whether they smoked, and current smokers were further asked to indicate the number of cigarettes they smoked a day.

Although the Actiheart is a small and unobtrusive device it was nonetheless possible that it could have impacted sleep quality in some women. To account for this possibility, following the night during which the device was worn, participants were requested to indicate whether their sleep was typical, and the responses available were “much better”, “better”, “typical”, somewhat worse” and “much worse”.

### 3.3.5 Statistical analysis

Sleep problems and HRV data were skewed thus logarithmic transformations were used to normalise the distributions. The quality of HRV data varied because of loss of electrode contact and movement artefacts, reducing the number of participants from whom reliable data were available. Satisfactory work day data were obtained from 123 participants, whereas from the night-time period data from 112 participants were available. There were no differences between women who did and did not complete daytime HRV assessments in terms of age ( $P=0.516$ ), marital status ( $P=0.672$ ), ethnicity ( $P=0.475$ ), education ( $P=0.152$ ), personal income ( $P=0.152$ ), smoking ( $P=0.822$ ), BMI ( $P=0.459$ ), sleep problems ( $P=0.540$ ), habitual physical activity ( $P=0.839$ ), or experienced affect measures (daytime positive affect ( $P=0.055$ ), daytime stress ( $P=0.307$ ), evening positive affect ( $P=0.200$ ), evening stress ( $P=0.244$ )).

Women whose HRV measurements failed in the night period had higher mean levels of evening positive affect (3.55,  $SD=1.09$ ) than those whose recordings were successful

(3.14, SD=1.13, P=0.014). However, there was no significant difference with regard to age (P=0.407), BMI (P=0.723), sleep problems (P=0.129), marital status (P=0.966), ethnicity (P=0.144), education (P=0.165), smoking status (P=0.839), personal income (P=0.212), or physical activity (P=0.464). Women who did and did not have night-time HRV recordings also did not differ in their ratings of daytime positive affect and stress (P=0.399, P=0.698, respectively), or of evening stress (P=0.487).

The associations between sleep problems and potential covariates were examined with bivariate correlations, *t*-tests and univariate analysis of variance, as appropriate.

The associations between sleep problems and DRM-derived positive affect and stress were explored first with bivariate correlation analyses, and then with multivariable linear regression analyses adjusting for sociodemographic characteristics (age, marital and parental status, personal income), health behaviours (smoking, habitual physical activity) and BMI. These factors have been found associated with sleep measures (Arber et al., 2009; Stranges et al., 2008). Since DRM assessment was performed at the end of the 24-hour monitoring period it is plausible that reporting of affect might have been biased by the quality of sleep during the preceding night. Therefore the variable whether a participant's sleep was typical during the night of the monitoring period was also included as a covariate.

The associations between sleep problems and HRV were assessed with bivariate correlations analyses followed by multivariable linear regressions. Separate models were carried out on day and night RMSSD measures. Three models were tested in each case to explore changes in the regression coefficient for sleep problems after covariates were added to the model, and most importantly to see whether adding experienced affect would reduce the regression coefficient for sleep. In model 1, the regression of sleep problems on HRV was adjusted for demographic factors identified in the literature as relevant



covariates, namely, age, marital status, having children, and income (Arber et al., 2009; Lauderdale et al., 2006). Sleep and HRV have been found associated with BMI, smoking and physical activity (Bernardi, Valle, Coco, Calciati, & Sleight, 1996; Driver & Taylor, 2000; Knutson et al., 2007; Kuch et al., 2001), so these factors were entered in model 2. Finally, to test whether the relationships between sleep problems and HRV were mediated by DRM-derived affective states, model 3 included positive affect and stress measures. The regressions on HRV over the working day included daytime experienced affect and stress measures, while the regressions on night-time HRV involved affect ratings from the previous evening. All results are presented as Pearson correlation coefficients ( $r$ ), P-values and unstandardised regression coefficients ( $B$ ), 95% confidence intervals (C.I.) and P-values, as appropriate. The analyses were performed with SPSS package version 18.

### **3.4 Results**

#### **3.4.1 Sample characteristics**

Participants' characteristics are depicted in Table 3.1. The mean age was 33.8 years and a half of participants were married. The majority were of White European background, and reported being in good health, while two thirds were university educated. Participants reported going to bed at 11:27pm on average, and waking at 6:53am.

As shown in Table 3.2 mean HR was substantially lower at night than during the day (67.35 (SD=10.35) vs. 80.27 (SD=11.60),  $P=0.001$ ), but HRV did not differ between the day and night periods (4.32 (SD=0.42) vs. 4.32 (SD=0.31),  $P=0.932$ ). Affect measures derived from the DRM confirmed that participants experienced significantly greater positive affect and less stress in the evening period (3.32 (SD=1.12), 0.67 (SD=0.68),

respectively) than in the subsequent working day (3.01 (SD=1.14), 1.02 (SD=0.93), respectively).

Heart rate variability was lower among participants with higher HR ( $r=-0.35$ ,  $P<0.001$ ), and night-time HRV was also lower among those with higher HR ( $r=-0.21$ ,  $P=0.024$ ). Daytime HRV ( $r=0.09$ ,  $P=0.305$ ), night-time HRV ( $r=0.17$ ,  $P=0.079$ ) and daytime HR ( $r=-0.15$ ,  $P=0.077$ ) were unrelated to physical activity, but night-time HR was inversely associated with physical activity ( $r=-0.27$ ,  $P=0.003$ ).

**Table 3.1 Characteristics of study participants.**

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<b>Variable</b>	<b>Mean (SD) /frequency (%)</b>
Age	33.8 (9.3)
Marital status	
Married/cohabiting	100 (50.3%)
Single	85 (42.7%)
Separated/divorced	11 (5.5%)
Children	
Yes	29 (14.6%)
No	168 (84.4%)
Ethnicity	
White European	160 (80.4%)
Other	37 (18.6%)
Education	
Less than degree	71 (35.7%)
Degree or higher	126 (63.3%)
Personal income	
<£25,000	64 (32.2%)
£25,000-35,000	87 (43.7%)
>£35,000	46 (23.1%)
Self-rated health	
Excellent	27 (13.6%)
Very good	74 (37.2%)
Good	65 (32.7%)
Fair	26 (13.1%)
Poor	3 (1.5%)
Current smoker	
Yes	31 (15.6%)
No	164 (82.4%)
Body mass index (kg/m <sup>2</sup> )	23.5 (4.2)
Sleep problems questionnaire ( range 0.0-1.66)	0.88 (0.39)
Bed-time (Hr:min)	23:27 (64)
Wake time (Hr:min)	6:53 (87)

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Physical activity	2.83 (1.77)
Daytime/evening DRM positive affect	3.0 (1.1)/ 3.3 (1.1)
Daytime/evening DRM stress	1.01 (0.9)/0.7 (0.7)

SD= standard deviation.

**Table 3.2 Cardiovascular activity and affect.**

	<b>Night-time</b>	<b>Day time</b>	<b>P</b>
Heart rate (bpm)	67.35 ± 10.35	80.27 ± 11.6	0.001
RMSSD (log) (ms)	4.32 ± 0.31	4.32 ± 0.42	0.932
Positive affect	3.32 ± 1.12 <sup>1</sup>	3.01 ± 1.14	0.001
Stress	0.67 ± 0.68 <sup>1</sup>	1.02 ± 0.93	0.001

<sup>1</sup> Measures obtained on the evening before the night assessment period. Results are presented as means and standard deviations (±).

### 3.4.2 Sleep problems and covariates

Sleep problems were not associated with marital status (P=0.744), education (P=0.350), ethnicity (P=0.502), or personal income (P=0.533). Sleep problems were also unrelated to health behaviours including physical activity (P=0.082), smoking (P=0.796) and BMI (P=0.137). However, rather surprisingly, participants without children reported greater sleep disturbances ( $F(1,192)=9.766$ ,  $P=0.002$ , controlling for age). The positive association between sleep problems and age approached statistical significance ( $r=0.14$ ,  $P=0.052$ ).

### 3.4.3 Sleep problems and affect

Sleep problems were consistently related to positive affect and stress measured using the DRM. Specifically, fewer sleep problems were reported by women with higher

daytime and evening positive affect ( $r=-0.28$ ,  $P<0.001$ ,  $r=-0.25$ ,  $P=0.001$ , respectively), and by those with lower daytime and evening stress ( $r=0.33$ ,  $P<0.001$ ,  $r=0.20$ ,  $P=0.009$ , respectively).

Table 3.3 depicts a summary of four separate regression models where sleep problems were regressed on DRM affective states. After adjustment for age, marital status, having children, income, BMI, smoking, physical activity and whether last night's sleep was typical fewer sleep problems remained strongly associated with higher daytime ( $B=-0.878$ , C.I. -1.374 to -0.3821,  $P=0.001$ ) and evening positive affect ( $B=-0.713$ , C.I. -1.188 to -0.239,  $P=0.003$ ). The positive association with daytime ( $B=0.696$ , C.I. 0.281 to 1.111,  $P=0.001$ ) and evening stress ( $B=0.376$ , C.I. 0.090 to 0.633,  $P=0.010$ ) was also significant after adjustment for the covariates.

**Table 3.3 Associations between sleep problems and affect.**

<b>Regression of sleep problems on affect<sup>1</sup></b>			
	<b>B</b>	<b>95% C.I.</b>	<b>P</b>
Positive affect – work day	-0.878	(-1.374 to -0.3821)	0.001
Positive affect – evening	-0.713	(-1.188 to -0.239)	0.003
Stress – work day	0.696	(0.281 to 1.111)	0.001
Stress – evening	0.376	(0.090 to 0.633)	0.010

Results are presented as unstandardized regression coefficients (B) and 95% confidence intervals (C.I.). <sup>1</sup>Adjusted for age, marital status, children, income, BMI, physical activity, smoking, and whether last night's sleep was typical.

#### **3.4.4 Sleep problems, HR and HRV**

There were no significant associations between sleep problems and HR either during the work day ( $r=0.06$ ,  $P=0.473$ ) or at night ( $r=-0.05$ ,  $P=0.588$ ).

##### **3.4.4.1 Sleep problems and daytime HRV**

Bivariate correlations showed that sleep problems were significantly associated with lower daytime HRV ( $r=-0.23$ ,  $P=0.013$ ).

The regressions of sleep problems on daytime HRV are summarised in Tables 3.4 (model 1), 3.5 (model 2) and 3.6 (model 3). As shown in Table 3.4 the association between sleep problems and reduced HRV was significant for the work day after adjustment for age, marital status, having children, and personal income ( $B= -0.296$ , C.I. -0.54 to -0.06,  $P=0.016$ ). Additional adjustment for physical activity, smoking and BMI in model 2 reduced the regression coefficient for sleep problems by 8.1%, but the association with reduced HRV remained significant ( $B=-0.272$ , C.I.-0.52 to -0.03,  $P=0.031$ ) (see Table

3.5). Finally, as depicted in Table 3.6, additional adjustment for daytime positive affect and stress in model 3 did not lead to further reductions in the association between sleep problems and reduced HRV over the work day ( $B=-0.309$ , C.I.  $-0.57$  to  $-0.05$ ,  $P=0.022$ ).

One possible reason why DRM-assessed affect did not explain the inverse association between disturbed sleep and daytime HRV is because experienced affect was not related to daytime HRV. The regressions of experienced daytime positive affect and stress on daytime HRV ranged from  $B=-0.008$ , C.I.  $-0.09$  to  $0.08$ ,  $P=0.855$  to  $B=-0.024$ , C.I.  $-0.15$  to  $0.10$ ,  $P=0.702$ , respectively.

The association between sleep problems and daytime HRV is also illustrated in Figure 3.3, where for the presentation purposes sleep problems were divided into quartiles.

#### 3.4.4.2 Sleep problems and night-time HRV

Bivariate correlations suggested that sleep problems were significantly associated with lower night-time HRV ( $r=-0.23$ ,  $P=0.015$ ).

The regressions of sleep problems on night-time HRV are summarised in Tables 3.4 (model 1), 3.5 (model 2) and 3.6 (model 3). As can be seen in Table 3.4 sleep problems were no longer related to lower HRV during the night after adjustment for socio-demographic characteristics ( $B=-0.157$ , C.I.  $-0.33$  to  $0.02$ ,  $P=0.079$ ). In model 2 health behaviours were added to the statistical analysis, but the association remained non-significant ( $B=-0.149$  C.I.  $-0.33$  to  $0.03$ ,  $P=0.098$ ) (see Table 3.5). In the third model evening positive affect and stress were added, but sleep problems were still unrelated to night-time HRV ( $B=-0.147$ , C.I.  $-0.33$  to  $0.04$ ,  $P=0.120$ ) (see Table 3.6).

As in the case of DRM-derived daytime affective states and daytime HRV, evening stress and positive affect were not associated with night-time HRV, and the regressions ranged from  $B=-0.023$ , C.I.  $-0.13$  to  $0.08$ ,  $P=0.663$  to  $B=0.007$ , C.I.  $-0.05$  to  $0.07$ ,  $P=0.818$ , respectively.

**Table 3.4 Associations between sleep problems and HRV: Model 1.**

	Daytime HRV			Night-time HRV		
	B	95% C.I.	P	B	95% C.I.	P
Sleep problems	-0.296	(-0.54 to -0.06)	0.016	-0.157	(-0.33 to 0.02)	0.079
Age	0.000	(-0.01 to 0.01)	0.966	-0.003	(-0.01 to 0.01)	0.536
Marital status	-0.086	(-0.27 to 0.10)	0.349	-0.070	(-0.21 to 0.07)	0.312
Children	-0.155	(-0.43 to 0.12)	0.271	0.025	(-0.19 to 0.24)	0.821
Personal income	-0.040	(-0.19 to 0.11)	0.587	-0.022	(-0.13 to 0.09)	0.690

Results are presented as unstandardized regression coefficients (B) and 95% confidence intervals (C.I.). Model 1: Analyses adjusted for age, marital status, children and personal income.



**Table 3.5 Associations between sleep problems and HRV: Model 2.**

	Daytime HRV			Night-time HRV		
	B	95% C.I.	P	B	95% C.I.	P
Sleep problems	-0.272	(-0.52 to -0.03)	0.031	-0.149	(-0.33 to 0.03)	0.098
Age	-0.003	(-0.02 to 0.01)	0.649	-0.003	(-0.01 to 0.01)	0.605
Marital status	-0.088	(-0.27 to 0.10)	0.345	-0.059	(-0.20 to 0.08)	0.401
Children	-0.173	(-0.45 to 0.11)	0.221	0.003	(-0.22 to 0.22)	0.979
Personal income	-0.044	(-0.19 to 0.11)	0.560	-0.030	(-0.14 to 0.08)	0.590
Smoking	-0.242	(-0.56 to 0.07)	0.129	-0.043	(-0.25 to 0.16)	0.680
BMI	0.012	(-0.01 to 0.04)	0.353	0.004	(-0.01 to 0.02)	0.632
Physical activity	-0.013	(-0.07 to 0.04)	0.621	0.024	(-0.02 to 0.07)	0.238

Results are presented as unstandardized regression coefficients (B) and 95% confidence intervals (C.I.). Model 2: Analyses adjusted for age, marital status, children, personal income, smoking, BMI, physical activity.

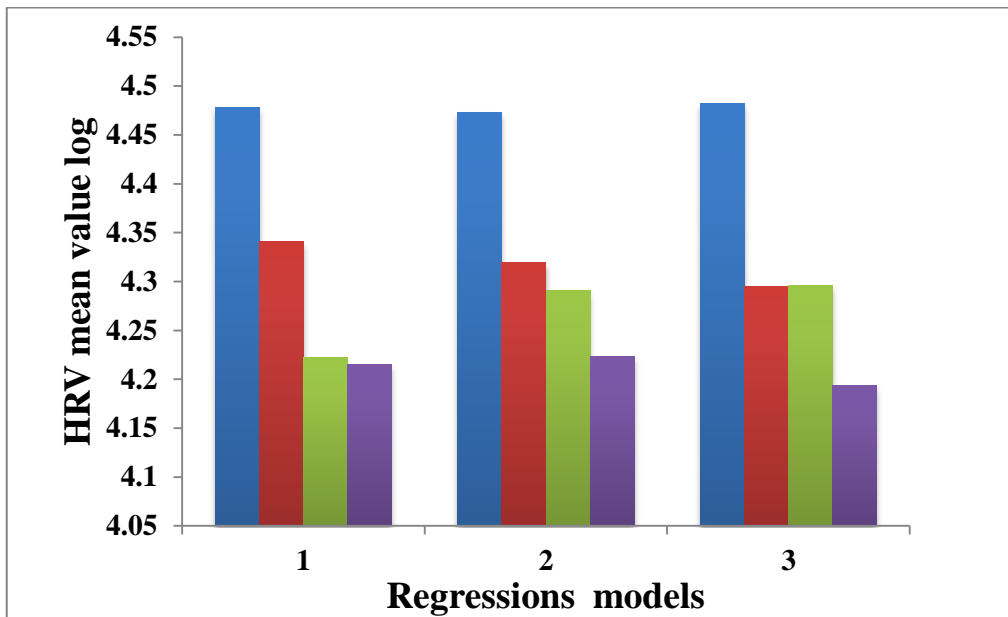
**Table 3.6 Associations between sleep problems and HRV: Model 3.**

	Daytime HRV			Night-time HRV		
	B	95% C.I.	P	B	95% C.I.	P
Sleep problems	-0.309	(-0.57 to -0.05)	0.022	-0.147	(-0.33 to 0.04)	0.120
Age	-0.004	(-0.02 to 0.01)	0.546	-0.002	(-0.01 to 0.01)	0.622
Marital status	-0.076	(-0.26 to 0.11)	0.417	-0.059	(-0.20 to 0.08)	0.407
Children	-0.152	(-0.44 to 0.13)	0.294	0.005	(-0.22 to 0.23)	0.964
Personal income	-0.046	(-0.20 to 0.10)	0.542	-0.032	(-0.15 to 0.09)	0.593
Smoking	-0.214	(-0.54 to 0.11)	0.191	-0.044	(-0.26 to 0.17)	0.683
BMI	0.012	(-0.02 to 0.04)	0.389	0.004	(-0.01 to 0.02)	0.643
Physical activity	-0.017	(-0.07 to 0.04)	0.542	0.024	(-0.02 to 0.07)	0.243
Positive affect	-0.043	(-0.14 to 0.05)	0.349	0.000	(-0.07 to 0.07)	0.993
Stress	-0.008	(-0.13 to 0.12)	0.901	-0.008	(-0.12 to 0.11)	0.898

Results are presented as unstandardized regression coefficients (B) and 95% confidence intervals (C.I.).

Model 3: Fully adjusted model including DRM-derived daytime or evening (as appropriate) positive affect and stress.

**Figure 3.3 Associations between sleep problems and daytime HRV.**



The blue bars refer to few sleep problems quartile, the red and green bars correspond to intermediate sleep problems quartiles, and the purple bars to high sleep problems quartile. Model 1 is adjusted for age, marital status, having children, and personal income. Model 2 is in addition adjusted for smoking, BMI and physical activity, and model 3 is also adjusted for daytime positive affect and daytime stress.

### 3.5 Discussion

The first aim of this study was to test the hypothesis that in a healthy sample assessed under everyday life conditions sleep problems would be associated with reduced HRV over the working day. My data supported this hypothesis. To explore whether the relationship between HRV and sleep problems would be present at night, during the day or both I tested two possibilities. If the association was the result of enduring biobehavioural differences between those with and without disturbed sleep it would be present both at night and during the day. However, if the inverse association between sleep problems and HRV was due to low-level chronic stress, such as demands at work, I conjectured that it would only be present during daytime hours. The results supported the second contention since participants reporting disturbed sleep had reduced daytime HRV independently of

relevant confounders, and the association between disturbed sleep and reduced night-time HRV was not significant. There was little evidence suggesting that greater stress or lower positive affect explained the inverse association between disturbed sleep and HRV, so the second hypothesis was rejected.

To date the associations between disturbed sleep and HRV have been extensively explored in patient populations, such as those with chronic fatigue syndrome or heart failure (Burton et al., 2010; Ueno et al., 2011), and research in healthy samples has been dominated by experimental studies (e.g., Holmes et al., 2002; Zhong et al., 2005). There have been some observational investigations that found lower HRV among respondents with severely disturbed sleep, but they were conducted with unrepresentative samples including nurses working night-shifts (Chung et al., 2009), or university students undergoing final exams (Takase et al., 2004). The current findings are consistent with past experimental studies (Dettoni et al., 2012; Sauvet et al., 2010; Zhong et al., 2005), which showed that acute sleep deprivation was associated with decreased parasympathetic and increased sympathetic modulation of the heart. This study extends these observations to HRV in naturalistic settings, namely into the working day, as well as to a more representative sample of working women. Since reduced HRV is a risk factor for cardiovascular morbidity and all-cause mortality (Thayer & Lane, 2007) it could be a potential pathway linking sleep problems with CVD.

I attempted to address the issue of whether the association between sleep problems and HRV was a persistent effect, or related to the specific demands of the working day, by testing relationships both over the day and at night. The results were inconclusive. Although the relationship between sleep problems and reduced HRV was only significant for the working day, the association was in the same direction for the night-time. One explanation might be that this study lacked the statistical power to detect an association

between sleep problems and night-time measure of HRV, since for the night-time period data were available from only 112 participants. On the other hand, it is also plausible that the more pronounced impact of disturbed sleep on daytime HRV could have been present due to a third variable unmeasured in this study. Another factor that may be relevant is that, unexpectedly, HRV was not reduced on average in the night compared with the day, despite differences in HR. It is unclear why this was the case.

I found that self-reported sleep problems were associated with greater perceived stress and less positive affect over the evening and working day, after controlling for relevant covariates. Perceived stress and positive affect were measured using the DRM, so provided indications of experienced affect in everyday life. Although the DRM is a retrospective measure it overcomes some of the limitations associated with conventional affect questionnaires, since recalling the events of the last 24 hours in a sequential order retrieves specific and recent memories, and subsequently reduces current mood and memory biases (Kahneman et al., 2004:1777). This helps to resolve the problem of using retrospective questionnaire measures, which share common method variance with sleep problems questionnaires. The administration of the DRM online ensured that the measure was completed at the end of the 24-hour monitoring period, and not filled in on another occasion. However, even though sleep problems were associated with experienced affect, differences in affect did not account for reduced HRV. This suggests that it might not be the case that people with sleep problems had worse mood over the monitoring period, which in turn drove variations in HRV. It is possible that sleep problems have a more direct relationship with the autonomic modulation of the heart that is not mediated through experienced affective states. However, it was also apparent that HRV was not related to affect assessed with the DRM in this study. Previous investigations have documented associations between reduced HRV and depressed mood (Kemp et al., 2010), but

associations with affective measures have been less consistent under everyday life conditions. For example, a study of 76 men and women with suspected heart disease showed that while higher positive affect, assessed with the DRM, was associated with a lower sympathetic and a higher parasympathetic modulation of the heart, experienced depressed mood was not (Bhattacharyya et al., 2008).

These data must be interpreted with caution since the cross-sectional design used in this study precludes any causal conclusions from being drawn. Experimental evidence suggests that total or partial sleep deprivation lead to autonomic imbalance, for example, by increasing sympathetic modulation of the heart (e.g., Zhong et al., 2005). However, patients with insomnia tend to have increased levels of physiological arousal including augmented sympathetic activity, and sleep problems appear to be secondary to autonomic imbalance (Bonnet & Arand, 2010). Although in this study the sample comprised healthy women who were not diagnosed with any medical or psychological conditions including insomnia, it is possible that increased physiological arousal engendered disturbed sleep. Longitudinal investigations with healthy samples would help to clarify the direction of this relationship.

In addition to the cross-sectional design this study has a number of further limitations. There was a considerable loss of HRV data due to the poor quality of many recordings. Although the research team made a considerable effort to position the ActiHearts on participants' chests correctly and secure them firmly, there were numerous artefacts in the N-N intervals data that reduced the statistical power of this study. Sleep problems were assessed with self-report, which may be influenced by mood, memory biases and demand characteristics (Bliwise & Young, 2007; Krystal & Edinger, 2008), as well as by personality (Tsuchiyama et al., 2003). All analyses, however, were adjusted for relevant confounders including socio-demographic characteristics, health behaviours and

experienced affect. Nonetheless, there are a number of time-varying lifestyle factors, such as consumption of caffeinated beverages and alcohol intake, that might negatively impact on sleep quality that were not taken into account in the analyses. Physical activity and sleep were assessed with global measures, whereas HRV data were obtained for a 24-hour period only. However, when the analyses exploring associations between sleep problems and HRV were additionally adjusted for whether participants' sleep was typical on the monitoring night the relationship remained statistically significant ( $B=-0.340$ , C.I.  $-0.61$  to  $-0.08$ ,  $P=0.013$ ). Finally it should be pointed out that the generalizability of these data is limited by the fact that the sample comprised mainly young women of whom over 60% were university-educated.

Notwithstanding, this study extends a growing body of experimental evidence suggesting that disturbed sleep is also associated with reduced HRV over the working day. Diminished HRV could, therefore, be a potential pathway linking sleep problems with CVD. More naturalistic studies in this area of sleep research are warranted.

## **CHAPTER 4: PSYCHOSOCIAL FACTORS AND SLEEP**

### **EFFICIENCY: DISCREPANCIES BETWEEN SUBJECTIVE AND OBJECTIVE EVALUATIONS OF SLEEP (Study 3)**

#### **4.1 Introduction**

In Chapter 1 I argued that sleep measurement remains an important issue in the literature. To recapitulate, polysomnography (PSG), the “gold standard” objective measure of sleep, is typically carried out in the sleep laboratory and it provides very rich sleep data. However, PSG is often too expensive and impractical in population-based studies, but home-based PSG is beginning to be applied on a larger scale (Blackwell et al., 2008; Silva et al., 2007). Community-based studies of objective sleep are more feasible using actigraphy, which has been endorsed by the American Academy of Sleep Medicine for assessing sleep patterns in community studies (Morgenthaler et al., 2007a).

Self-reported sleep ratings remain the most widely used measure in population-based research as they are brief, easy to use and inexpensive, but can be affected by mood and memory biases (Bliwise & Young, 2007; Krystal & Edinger, 2008), as well as personality characteristics (Blagrove & Akehurst, 2001; Tsuchiyama et al., 2003). Moreover, as discussed in Chapter 1, people are not accurate in their estimations of sleep duration (Lauderdale et al., 2008; Silva et al., 2007; van den Berg et al., 2008). However, since those studies were primarily conducted to test whether subjective and actigraphic (Lauderdale et al., 2008; van den Berg et al., 2008), or subjective and home-based PSG (Silva et al., 2007) measures of sleep duration are congruent, they provided limited data on factors that might influence people’s estimations of sleep duration, though gender, SES, cognitive decline, poor subjective health and depressive symptoms have been implicated.



Interestingly, discrepancies between subjective and objective measures of sleep duration have been extensively studied in clinical population samples. For instance, early studies in insomnia patients suggested that the majority of insomniacs under-report their sleep duration and over-report sleep latency (Carskadon, Dement, Mitler, Guilleminault, & Zarcone, 1976; Frankel, Coursey, Buchbinder, & Snyder, 1976), but subsequent research has challenged this notion since (1) not all insomniacs misreport their sleep durations, (2) and some insomniacs tend to overestimate the number of hours slept (Edinger & Krystal, 2003). For example, a study of 5 sub-types of insomnia (N=104) (including insomnia associated with depressive disorder, sleep state misperception or insomnia with periodic limb movement) reported a range of discrepancies between subjective and PSG-based sleep latency and duration (Vanable et al., 2000). For example, insomniacs with better sleep continuity (reported and objective) were most accurate in their sleep perceptions, while those who underestimated total sleep time and overestimated sleep latency spent more time awake during their night in the sleep laboratory, and reported shorter habitual sleep hours than those with more congruent sleep measures. Notably, under-reporting of total sleep hours was associated with cognitive rumination, somatic symptoms of tension/anxiety and catastrophic thoughts about sleep. Overestimations of sleep duration were detected in this study as well, albeit less frequently (Vanable et al., 2000).

More recently Fernandez-Mendoza et al., (2010) explored the role of objective sleep duration (assessed with PSG) and psychological characteristics in sleep perceptions in a large sample of insomniacs and controls. Insomniacs with normal sleep duration ( $\geq 6$  hours) significantly underestimated their sleep hours, and were characterised by depressive mood, poor coping styles, anxiety and a tendency to ruminate. Insomniacs with short sleep ( $< 6$  hours) were more likely to overestimate sleep duration and reported higher depressive symptoms, fatigue, and a range somatic complains.

A recent review exploring reasons for misperceptions of sleep duration and latency in insomnia suggested that the most probable explanations for this phenomenon are the interpretation of sleep as wake, worrying about not being about to sleep or fall asleep, and frequent brief awakenings (lasting from 3 seconds to 30) in the night (Harvey & Tang, 2012).

Sleep misperceptions have been studied in depressed patients as well, where over- and under-reporting of sleep hours were reported. Rotenberg et al., (2000) found that in patients with major depression underestimation of sleep duration was more common than overestimation (42% vs. 32%, respectively), and underestimation of night-time awakenings was also frequent when compared with healthy controls. Data from 23 patients diagnosed with major depression also revealed that in comparison with patients who overestimated their sleep duration, those who underestimated it had shorted objective sleep duration and less deep sleep, were older and tended to be less extraverted (Tsuchiyama et al., 2003). A study of 40 men and women with moderate to severe depression also reported that more participants underestimated than overestimated their sleep duration, albeit the differences between PSG-assessed and subjective sleep hours were small (Argyropoulos et al., 2003). Participants' recall of night-time awakenings was poor in these data too, as compared with PSG. Armitage et al., (1997) also found a lack of congruence between subjective and PSG-assessed number of awakenings, but in contrast with the above studies there was a high level of agreement between self-reported and objective sleep duration.

To date it remains uncertain why depressed patients make poorer judgements than healthy individuals regarding their sleep measures (Mayers, Grabau, Campbell, & Baldwin, 2009), but one underlying mechanism could be the significantly reduced amount of deep sleep (SWS) seen in this population, and/or changes in REM activity (Rotenberg, Indursky, Kayumov, Sirota, & Melamed, 2000).

In summary, although the above studies were based on clinical samples (which were often small) and their findings should not be generalised to healthy populations, they nonetheless suggest that psychological factors, such as poor coping styles, anxiety, a tendency to ruminate, or catastrophic thoughts about sleep influence people's perception of their sleep duration.

Discrepancies in measures of subjective and objective sleep quality in the general population are less understood than those of sleep duration. The existing population-based studies, which have been reviewed in Chapter 1, comprised older populations and were mainly concerned with exploring sex differences in self-reported versus objective sleep quality measures (Unruh et al., 2008; van den Berg et al., 2009; Vitiello et al., 2004). Given the age-related alterations in sleep architecture, in particular the reduced amount of deep sleep (Ohayon et al., 2004), these data cannot be extrapolated to younger adults. Another important reason for broadening our understanding of sleep quality is supported by the emerging evidence that disturbed sleep, in particular sleep fragmentation, can be as deleterious to health as short sleep duration (Meerlo et al., 2008; Tasali et al., 2008). Finally, there are also data that in otherwise healthy individuals sleep quality may be a better predictor of affective states, such as anger, tension, depressed mood, than sleep duration (Pilcher, Ginter, & Sadowsky, 1997).

The comparisons of subjective and objective measures of sleep quality have been, however, studied in clinical populations, in particular in patients with insomnia (Akerstedt et al., 2008). For example, results from a study of 47 older adults with primary insomnia revealed that higher sleep satisfaction (assessed with "pick one number below to indicate your overall quality rating or satisfaction with your sleep") was related to longer periods of deep sleep and shorter sleep latency. Namely, insomniacs satisfied with their sleep spent about 60 minutes in deep sleep and 26 minutes in light sleep (Stage 1), whereas those who

were unsatisfied (with their sleep) had deep sleep of approximately 24 minutes and light sleep of 46 minutes, as determined by PSG (Riedel & Lichstein, 1998). Rosa & Bonnet (2000) studied subjective (measured with one item) and PSG-defined sleep of insomniacs (N=121) and controls (N=56) and found that participants with insomnia did not have significantly poorer objective sleep quality than those in the control group. Notably though, poor PSG-defined sleep quality of insomniacs was predicted by tension, self-reported time awake after sleep onset, older age and male sex.

Interestingly, a recent study of depressed and never-depressed college students found that while there were no differences in actigraphy-based measures of sleep between these two groups of participants, those who were depressed reported significantly more sleep problems (Karlson, Stevens, Olson, & Hamilton, 2010).

It is worth mentioning that the correlations between objective and subjective sleep quality indicators have also been explored in healthy samples by a number of small studies conducted in Sweden. For example, data from eight women, who had irregular sleep schedules over 9 days as to provide a variation in sleep quality, revealed that objective sleep efficiency accounted for the highest proportion of variance ( $R^2=53\%$ ) in self-reported sleep quality (Akerstedt et al., 1994a). Slow wave sleep, total sleep time and sleep latency were also related to subjective sleep quality, albeit weakly when compared with efficiency. A naturalistic study by the same research group compared sleep assessed with home-based PSG and the Karolinska sleep diary (Akerstedt et al., 1994b); the sample (N=47) consisted of men and women who began their jobs either very early in the morning, or in the later morning, as to provide a variation of different sleep patterns (Keklund & Akerstedt, 1997). Subjective quality of sleep was positively correlated with time spent in SWS (deep sleep) and sleep efficiency, but there was no relationship with sleep duration. Age was unrelated to these associations, and gender differences were not explored (Keklund & Akerstedt,

1997). More recently, in a sample of healthy men and women (N=33, age range 28-69 years) sleep parameters assessed with home-based PSG were used to predict subjective sleep quality, which was measured with the Karolinska sleep diary (Akerstedt et al., 1994b). Poor subjective sleep quality was predicted by Stage 0 (a state of being awake/stage wake) and lower sleep efficiency, albeit to a lesser extent. Deep sleep was not related to sleep quality in the whole sample, but in the intraindividual analysis (an analysis conducted separately for each participant) poor quality sleep was associated with 32 minutes of deep sleep, while good sleep with almost 40 minutes of deep sleep (Akerstedt et al., 2008). Age and gender were unrelated to subjective sleep quality.

Taken together, studies with clinical and healthy populations suggest that good self-reported sleep quality is associated with objective parameters of sleep continuity, such as shorter sleep latency, longer deep sleep, and higher sleep efficiency, as defined by PSG. These findings are useful for broadening our understanding of sleep quality, but the evidence discussed above comes from studies predominantly conducted in sleep laboratories. This enables to take into account confounding variables, but simultaneously such studies lack ecological validity. Although some of the studies described by Akerstedt and co-workers (e.g., Akerstedt et al., 2008; Keklund & Akerstedt, 1997) were naturalistic, their small and selective samples severely restrict the generalizability of these data to the general population. In addition, different definitions (e.g., sleep satisfaction vs. sleep quality) and measures of sleep quality (sleep questionnaire vs. one sleep item) make comparisons across studies difficult. Most importantly, however, these studies were designed to explore the correlations between subjective and objective indices of sleep quality, but they have not addressed the issue of whether global ratings of sleep quality are congruent with objective sleep data, and if the degree of agreement between these measures is associated with affective or psychological responses.

In Chapter 1 I have discussed evidence that short and long sleep duration and disturbances of sleep are independent risk factors for CVD and CVD mortality. I also argued that sleep parameters might increase the risk of cardiovascular outcomes indirectly through their associations with psychosocial risk factors. For instance, infrequent contact with friends and low emotional support are risk factors for insomnia among elderly men (Hanson & Ístergren, 1987), while low network support has been shown to mediate the relationship between sleep disturbances and myocardial infarction in women (Nordin et al., 2008). Sleep problems are also associated with lower SES (Arber et al., 2009), a major risk factor for CVD (Rozanski et al., 2005).

Work stress is another psychosocial factor implicated in cardiovascular disorders. As outlined in Chapter 1 (pages 102-103) the most widely used models of work stress in the literature have been the demand-control model (Karasek & Theorell, 1990) and the effort-reward imbalance model (Siegrist, 1996), which is the focus in this study. Briefly, according to Siegrist (1996) people exert extrinsic and intrinsic efforts at work. The former reflect their perceptions of efforts needed to deal with work demands, whereas the latter refer to a personal coping style with challenges in the workplace, which is termed “overcommitment”. Individuals characterised by this coping style often enhance their efforts in the pursuit of approval and/or social recognition, and struggle to withdraw from work obligations (Siegrist, 1996). Greater sleep problems have been cross-sectionally associated with overcommitment in British (Steptoe et al., 2004) and German workers (Kudielka et al., 2004), while effort/reward imbalance prospectively predicted the onset of sleep disturbances in a study of Danish men (Rugulies, Norborg, Sorensen, Knudsen, & Burr, 2009).

Positive and negative affective states are linked with physical health outcomes including CVD (Chida & Steptoe, 2008; Nicholson et al., 2006). As noted in Chapter 1

(page 71) there is also substantial evidence for negative affective states, in particular depressive symptoms, being associated with both sleep duration and quality (Benca et al., 1992). The causal associations have not always been clear, but prospective studies suggest that sleep problems at baseline can predict future depression (Szklo-Coxe et al., 2010) as well as its recurrence (Cho et al., 2008). Relatively little work has related positive affective responses and sleep, but in the MIDUS study insomnia symptoms were inversely related to subjective well-being, independently of relevant socio-demographic and clinical confounders including emotional disorders (Hamilton et al., 2007a). This finding was corroborated by a British study showing that after adjustment for traditional confounders associated with sleep, sleep problems were less prevalent among respondents reporting greater levels of positive affect (Stephoe, O'Donnell, Marmot, & Wardle, 2008).

At this stage it ought to be acknowledged that although it is currently unclear whether objective and subjective measures of sleep quality are congruent, this does not indicate that perceptions of sleep quality should be discredited. This is because irrespectively of whether one has good objective sleep quality or not, the perceptions of sleep are likely to have implications for people's future behaviour, and individual differences in subjective sleep need have been reported (Ursin et al., 2005).

In summary, self-reported disturbed sleep has been associated with low social support, work stress and negative mood. In contrast, positive affective states are correlated with fewer sleep complaints. Importantly, there has been no research investigating whether these factors are also linked to discrepancies between subjective and objective evaluations of sleep quality. Therefore, the aim of this study was to address this gap in the literature by evaluating whether differences in subjective and objective indices of sleep quality differ by work stress, social support, depressive symptoms and happiness. In addition, since poorer ratings of physical health have been found related to discrepancies

between subjective and objective indices of sleep duration (Lauderdale et al., 2008; van den Berg et al., 2008), I decided to explore whether poor self-reported health would also be associated with incongruence between subjective and objective measures of sleep quality.

Objective sleep efficiency was the measure of objective sleep quality in this study (defined as the proportion of total sleep period during which the person was asleep), and was assessed with the Actiheart monitor (Actiheart, Cambridge Neurotechnology Ltd, Papworth, UK). Subjective sleep quality was assessed with a standardized sleep questionnaire. For clarity I will refer to the two sleep measures used in this study as self-reported and objective sleep efficiency.

## **4.2 Hypotheses**

Based on the literature discussed above I formulated the following hypotheses:

- 1.** Higher work stress would be associated with greater discrepancy between subjective and objective measures of sleep efficiency.
- 2.** Lower social support would be associated with greater discrepancy between subjective and objective measures of sleep efficiency.
- 3.** Lower levels of happiness and higher depressive symptoms would be associated with greater discrepancy between subjective and objective measures of sleep efficiency.
- 4.** Poorer self-rated health would be associated with greater discrepancy between subjective and objective measures of sleep efficiency.

Evaluations of sleep might be affected by negative affectivity (Krystal & Edinger, 2008) thus the above hypotheses were tested adjusting for negative affect.



## **4.3 Method**

### **4.3.1 Study design**

This cross-sectional study used data from the Daytracker, a naturalistic investigation of biological and affective responses in everyday life, which has already been described in Study 2 (page 167) that is also based on the Daytracker.

### **4.3.2 Participants**

One hundred and ninety nine women working at UCL and neighbouring institutions took part in the current study. Participants' details have been described in Study 2, however to recapitulate, participants were eligible if they fulfilled the following criteria: aged 18 to 65 years, in full-time, paid employment, not taking any medication except for oral contraception or hormone replacement therapy, Internet access at home, not being pregnant, and free from any serious illness (e.g. cancer) within the last two years.

### **4.3.3 Procedure**

Participants were asked to wear the Actiheart monitor over two 24-hour periods (one full work and one full leisure day), as to provide an ambulatory measure of sleep efficiency. On both days the monitoring session began at around 5:00pm, and to avoid order effects half of the study participants began measurement on a work day, and the other half on a leisure day. During the first visit informed consent and anthropometric measures (weight and height) were obtained, and body mass index (BMI,  $\text{kg/m}^2$ ) was computed. Participants were given a set of questionnaires to complete, measuring socio-economic, demographic, psychosocial and affect variables, as well as subjective evaluations of sleep and health-related variables.

#### 4.3.4 Measures

##### 4.3.4.1 Background measures

Information about age, marital and parental status, ethnicity, education, and smoking was obtained by questionnaire. Education status and personal income were used as markers of SES. Personal income was divided into tertiles (<£25,000, £25,000-£35,000 and >£35,000), while educational attainment was categorised into “Less than a degree” and “Degree or higher”.

##### 4.3.4.2 Psychosocial and affective measures

###### *Work stress*

Work stress was measured according to the effort–reward imbalance model (Siegrist, 1996), which has been widely used in the literature (Bellingrath & Kudielka, 2008; Kudielka et al., 2004; Steptoe et al., 2004). The model’s components (work effort, reward and overcommitment) were assessed with a series of items that were rated on a 4-point scale.

Work effort was assessed with six items (e.g., “I have constant time pressure due to a heavy work load”, “Do you have enough time to do everything”). The scale ranged from 6 to 30 with higher scores corresponding to greater effort. The internal consistency in the present study was 0.82.

Reward was measured with four items (e.g., “I receive the respect I deserve from my superiors and colleagues”, “How satisfied are you with your usual take-home pay?”). Higher scores indicated greater reward (range 4 to 24), and the internal consistency of the reward scale was 0.66.

Effort/reward imbalance was computed by standardizing, then dividing the effort by the reward score. Values equal to 1 indicated a balance between effort and reward, whereas scores above 1 indicated a disproportionate effort at work.

Overcommitment (i.e. intrinsic effort) was measured with five items (e.g., “People close to me say I sacrifice myself too much for my job”). Scores could range from 5 to 20, and high overcommitment corresponded to a high score on this scale. The internal consistency was 0.88.

### ***Depressive symptoms***

Depressive symptoms were measured with the Centre for Epidemiologic Studies Depression scale (CES-D) (Radloff, 1977), a well-established and widely used (Knight, Williams, McGee, & Olaman, 1997) self-reported measure of depressive symptoms over the past week. In this study the CES-D consisted of 20 items (e.g., “I felt fearful”, “I could not get going”), which were rated on a 4-point scale ranging from 0 “Rarely or none of the time” to 3 “Most or all of the time”. Ratings were summed and higher scores corresponded to a greater number of symptoms (range 0-60). The Cronbach’s  $\alpha$  in this sample was 0.88.

### ***Negative affect***

Negative affect was assessed with the negative items from the Positive and Negative Affect Schedule (PANAS) (Watson, Clark, & Tellegen, 1988). PANAS has been used extensively in the literature to measure affective states (e.g., Steptoe, Gibson, Hamer, & Wardle, 2007; Steptoe, Wright, Kunz-Ebrecht, & Iliffe, 2006). The scale, which measures affective states over the past week, included 10 negative items (e.g., “nervous”, “guilty”, “irritable”) rated on 5-point scales anchored at 1 “very slightly, not at all” to 5

“extremely”. The scores were totalled and could range from 10 to 50, with higher scores indicating greater negative affect. The Cronbach’s  $\alpha$  was 0.86.

### ***Social support***

Social support was measured with a shortened version of the Interpersonal Support Evaluation List (ISEL) (Peirce, Frone, Russell, & Cooper, 1996) consisting of 12 items (e.g., “There is someone I can turn for advice about handling problems with my family”, “I feel there is no one I can share my most private worries and fears”). This is a validated and widely used measure of social support (e.g., Widows, Jacobsen, Booth-Jones, & Fields, 2005). The items were rated on 4-point scales. Ratings were totalled to create a summary score (range 0-36), and higher scores indicated greater social support. The internal consistency of the scale in this study was 0.87.

### ***Happiness***

Happiness was assessed with Lyubomirsky’s happiness scale (Lyubomirsky & Lepper, 1999). This scale consists of four items (e.g., “Compared to most of my peers, I consider myself...”) rated on 7-point scales anchored from 0 “not a very happy person” to 6 “a very happy person”. Ratings were totalled, with higher scores reflecting greater happiness (range 0-24). The Cronbach’s  $\alpha$  in this sample was .90.

### ***Subjective health status***

Participants were asked to rate their health status on a 5-point scale (ranging from “excellent” to “poor”), with greater scores indicating poorer health. This measure has been found to be a reliable predictor of mortality across numerous studies (Idler & Benyamini, 1997).

### ***Other measures***

The Actiheart software requires information on bed time and wake up time to calculate sleep parameters including sleep efficiency. These data were therefore collected during work and leisure monitoring periods.

The information whether sleep on both monitoring nights was typical was also collected, and the responses available were “much better”, “better”, “typical”, “somewhat worse” and “much worse”.

#### **4.3.4.3 Sleep measures**

##### ***Objective sleep efficiency***

Objective sleep data were recorded by the Actiheart monitor, a combined electrocardiogram (ECG) and accelerometer (Brage, Brage, Franks, Ekelund, & Wareham, 2005). The Actiheart was used to measure heart rate variability (HRV) in Study 2, where it has already been described in detail. However, to recapitulate, the monitor consists of a pair of electrodes that are attached to the left side of the chest using adhesive pads. One electrode incorporates a uniaxial accelerometer, battery and solid state memory. The device was programmed to record beat by beat heart rate (HR) along with activity (in 15 second bins) for 24 hours. The HR and activity signals were used in combination with reported bed and wake up time to define sleep parameters with the Actiheart software (version 2.226.001). Several sleep parameters were assessed, such as sleep duration, latency, mean awake time, but since my analyses focus on sleep efficiency, defined as the proportion of the total sleep period that the person was asleep, these will not be described here.

To ensure that sleep data were recorded properly, the Actiheart device was attached to a participant’s chest by a member of the research team prior to each recording period. If

the measurement period was on a week night the Actiheart was removed by a member of the research team on the following day. If the measurement period was on a leisure night, participants were instructed to remove the device themselves. Since sleep times are likely to differ between work and leisure periods I aggregated sleep data from the two nights of recording as to provide a more robust estimate of objective sleep efficiency.

### ***Subjective sleep efficiency***

The Jenkins Sleep Problems Scale was used to assess participants' evaluations of sleep efficiency (Jenkins et al., 1988) (see Appendix 1). This scale has a well-established validity and reliability and has been previously used in many sleep studies (Kudielka et al., 2004; Kumari et al., 2009; Lallukka et al., 2012; Lyytikainen et al., 2011). The questionnaire consists of 4 items where respondents are asked to report on a 6-point scale how often in the past month they experienced the following sleep problems: (1) trouble falling asleep, (2) waking up in the night, (3) trouble staying asleep, and (4) waking up after the usual amount of sleep feeling tired and worn out. To obtain a self-reported measure of sleep efficiency that would be as compatible as possible with the objective measure of sleep efficiency, I used a revised scale with item 4 removed. The scores were averaged, with higher scores corresponding to poorer sleep efficiency (range 0.0 to 1.67). The Cronbach's  $\alpha$  in this sample was .68.

## **4.4 Statistical analysis**

Self-reported sleep efficiency data were positively skewed while objective sleep efficiency data were negatively skewed, so both were logarithmically transformed. Objective sleep efficiency data were lost for 20 individuals due to poor quality of ECG recordings, device errors, or displacement of electrodes, so statistical analyses were based

on 179 recordings. There was no difference between those for whom I had and did not have objective sleep efficiency with regard to age ( $P=0.890$ ), relationship ( $P=0.831$ ) and parental status ( $P=0.807$ ), personal income ( $P=0.618$ ), education ( $P=0.444$ ) and ethnicity ( $P=0.810$ ). Participants with and without the objective measure of sleep also did not differ in terms of health-related variables (BMI:  $P=0.540$ , smoking:  $P=0.148$ , self-rated health:  $P=0.485$ ), work stress (efforts:  $P=0.949$ , rewards:  $P=0.184$ , effort-reward imbalance:  $P=0.431$ , overcommitment:  $P=0.680$ ), social support ( $P=0.648$ ) and affective variables (depressive symptoms:  $P=0.790$ , happiness:  $P=0.973$ , and negative affect (PANAS):  $P=0.905$ ).

To create the sleep discrepancy measure, which is an indication of the extent to which self-reported sleep efficiency matches objective sleep efficiency, differences between self-reported sleep problems and objective sleep efficiency were computed (it may be worth to reiterate that objective sleep efficiency was calculated by aggregating sleep data from work and leisure nights). First I reversed the scores on the sleep questionnaire so higher ratings indicated greater subjective sleep efficiency. Next both sleep efficiency measures were converted into z-scores, and in the final step subjective sleep efficiency ratings were subtracted from the objective efficiency data. Positive sleep discrepancy scores indicated under-estimation of sleep efficiency, while negative scores reflected over-estimation of sleep efficiency.

To determine whether there was a difference in associations between separate discrepancy scores for work and leisure days and psychosocial and affect variables I also computed work and leisure day discrepancy scores.

The associations between sleep measures (self-reported and objective) and potential covariates were examined with bivariate correlations, *t*-tests and univariate analysis of variance, as appropriate.

Before testing my hypotheses I analysed the associations between self-reported sleep efficiency and psychosocial and affect variables. This was performed with bivariate correlation analyses and multivariable linear regression models. In the regression analyses self-reported sleep efficiency scores were treated as the outcome variable and all models were adjusted for age, having children, personal income, marital status, BMI and negative affect since these have been related to sleep experience (Arber et al., 2009; Benca & Peterson, 2008; Ohayon et al., 2004; Stranges et al., 2008). Separate models were performed for each psychosocial and affect measure. A similar approach was used for analysing associations between objective sleep efficiency and psychosocial and affect measures. Separate models were performed for work and leisure night efficiency measures. In addition, although the Actiheart is a small and unobtrusive device it was nonetheless possible that it could have impacted sleep quality in some women. To account for this possibility, the regression models were repeated additionally controlling for whether last night's sleep was typical.

The associations between the sleep discrepancy measure and psychosocial factors (work stress, social support) and affect (depressive symptoms, happiness) were assessed with bivariate correlation analyses followed by multivariable linear regression analyses. In the regression analyses sleep discrepancy was treated as an outcome measure, and separate regressions were conducted for each psychosocial and affect measure. All analyses were adjusted for age, having children, personal income, marital status, and BMI. All models were also repeated controlling for negative affect since, as mentioned above, there is extensive literature relating these variables with sleep measures. In these analyses a positive B coefficient would be an indication that a given predictor is associated with under-estimation of sleep efficiency, whereas a negative B coefficient would be an



indication that a given psychosocial or affect measure is associated with over-estimation of sleep efficiency.

All results are presented as Pearson correlation coefficients ( $r$ ), unstandardised regression coefficients ( $B$ ), 95% C.I. and P-values, as appropriate. The analyses were performed with SPSS package version 18.

## **4.5 Results**

### **4.5.1 Sample characteristics**

Descriptive characteristics of the participants are summarised in Table 4.1. The mean age was 33.8 years, half of the sample was married and nearly 1/3 had children. Women who took part in this study were healthy since 37.2% reported being in very good health, and further 32.7% rated their health as good. The average BMI was 23.5 and over 80% of respondents were non-smokers.

**Table 4.1 Participants characteristics.**

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<b>Variable</b>	<b>Mean (SD) /frequency (%)</b>
Age	33.8 (9.3)
Marital status	
Married/cohabiting	100 (50.3%)
Single	85 (42.7%)
Separated/divorced	11 (5.5%)
Children	
Yes	29 (14.6%)
No	168 (84.4%)
Ethnicity	
White European	160 (80.4%)
Other	37 (18.6%)
Education	
Less than degree	71 (35.7%)
Degree or higher	126 (63.3%)
Personal income	
<£25,000	64 (32.2%)
£25,000-35,000	87 (43.7%)
>£35,000	46 (23.1%)
Self-rated health	
Excellent	27 (13.6%)
Very good	74 (37.2%)
Good	65 (32.7%)
Fair /poor	29 (14.6%)
Current smoker	
Yes	31 (15.6%)
No	164 (82.4%)
Body mass index (kg/m <sup>2</sup> )	23.5 (4.2)
Self-reported sleep efficiency ( range 0-1.67 )	0.82 (0.43)
Objective sleep efficiency (work day) (%)	90.6 (6.9)
Objective sleep efficiency (leisure day) (%)	91.8 (7.3)
Effort	11.5 (4.3)

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Reward	17.4 (2.9)
Effort-reward imbalance	0.7 (0.5)
Overcommitment (range 5-20)	11.2 (2.4)
Social support (range 0-36)	26.5 (6.5)
Depressive symptoms (CES-D; range 0-60)	12.1 (8.6)
Negative affect (range 10-50)	19.5 (7.1)
Happiness (range 0-24)	15.9 (5.0)

SD=standard deviation; CES-D=Centre for Epidemiological Studies Depression scale.

#### 4.5.2 Sleep measures and covariates

##### 4.5.2.1 Self-reported sleep efficiency

Preliminary analyses revealed that self-reported sleep efficiency was unrelated to education ( $P=0.840$ ), ethnicity ( $P=0.309$ ), personal income ( $P=0.712$ ), marital status ( $P=0.993$ ), BMI ( $P=0.265$ ) or smoking ( $P=0.950$ ). The association between self-reported sleep efficiency and age was statistically significant, with older participants reporting lower sleep efficiency ( $r=0.18$ ,  $P=0.012$ ). In addition, controlling for age, I found that individuals who did not have children reported lower sleep efficiency (mean=0.83, SD=0.44) than those who had children (mean=0.73, SD=0.38) ( $F(1,191)=8.552$ ,  $P<0.001$ ). Participants with higher levels of negative affect also reported lower sleep efficiency ( $r=0.18$ ,  $P=0.015$ ).

##### 4.5.2.2 Objective sleep efficiency

Work and leisure night objective sleep efficiency values ranged from 51.1 to 99.1% on the work night, and from 31.9 to 99.8% on the leisure night.

Work night sleep efficiency was not related to participants' age ( $P=0.118$ ), their income ( $P=0.307$ ), educational attainment ( $P=0.147$ ), marital status ( $P=0.517$ ), or whether they smoked ( $P=0.439$ ). A lower work night sleep efficiency was associated with a higher

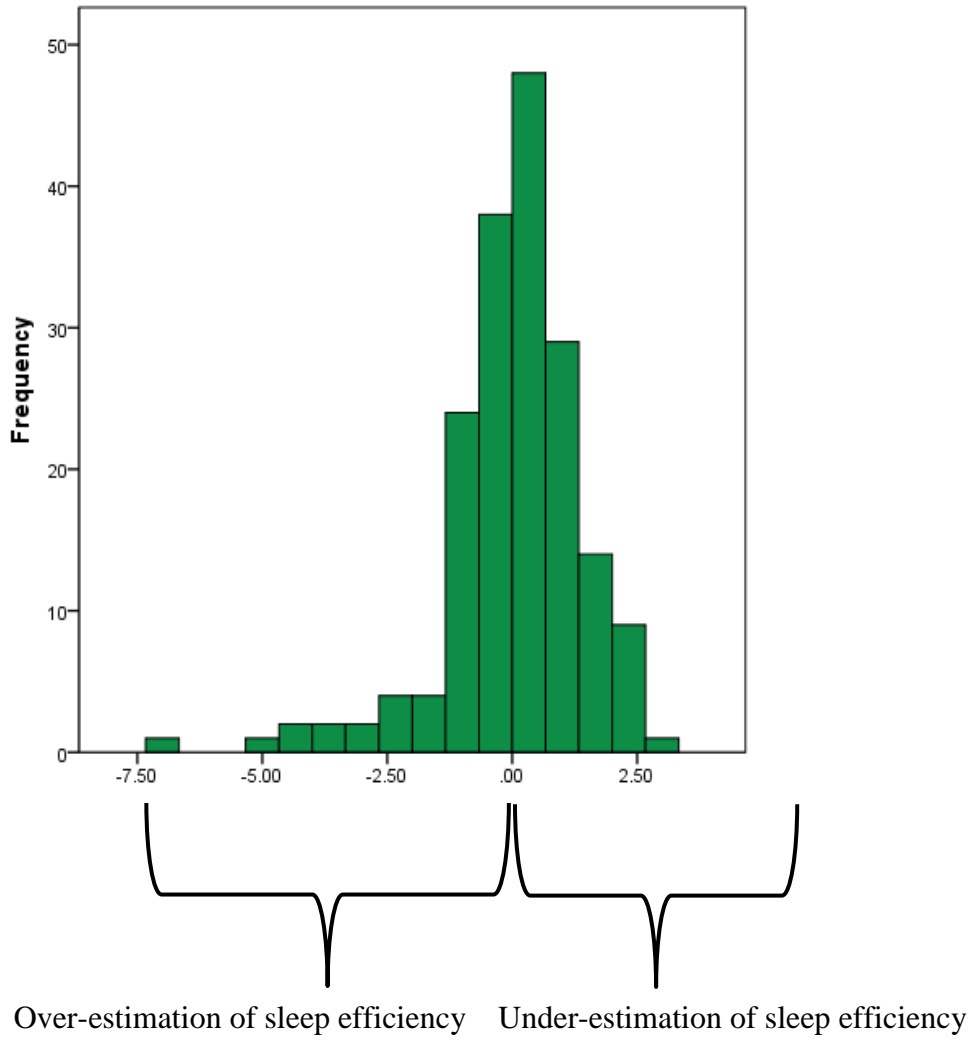
BMI ( $r=-0.25$ ,  $P=0.002$ ). Participants of ethnic minority background had lower work night sleep efficiency (mean=86.68, SD=10.89) than white participants (mean=91.34, SD=5.71) ( $P=0.027$ ). Women who had children also had lower sleep efficiency (mean=87.78, SD=9.53) than those who did not have children (mean=90.91, SD=6.65) ( $P=0.049$ ), but the relationship was no longer significant after I adjusted for age ( $F(1,159)=1.728$ ,  $P=0.191$ ). There was no association with negative affect ( $P=0.636$ ).

Leisure night sleep efficiency was unrelated to age ( $P=0.571$ ), marital status ( $P=0.779$ ), having children ( $P=0.293$ ), income ( $P=0.512$ ), education ( $P=0.381$ ), and ethnicity ( $P=0.575$ ). Health-related factors (BMI:  $P=0.150$ , smoking:  $P=0.840$ ) and negative affect ( $P=0.541$ ) were also not associated with this sleep measure.

#### 4.5.2.3 Sleep discrepancy measure

Sleep discrepancy measure scores ranged from -7.11 to 2.72 (mean=0.04, SD=1.41) (see Figure 4.1 for a graphic depiction of the measure).

**Figure 4.1 Distribution of sleep disturbance measure scores.**



The sleep discrepancy measure was unrelated to participants' age ( $P=0.160$ ), education ( $P=0.807$ ), ethnicity ( $P=0.170$ ), personal income ( $P=0.652$ ), marital status ( $P=0.826$ ), smoking ( $P=0.738$ ), or BMI ( $P=0.341$ ). However, participants without children were more likely to under-estimate their sleep efficiency than those with children (mean=0.13, SD=1.37; mean=-0.49, SD=1.52, respectively) ( $P=0.035$ ). After adjustment for age the relationship remained statistically significant ( $F(1,176)=12.170$ ,  $P=0.001$ ). The association with negative affect was positive ( $r=0.15$ ,  $P=0.048$ ), suggesting that higher negative affect was related to under-estimation of sleep efficiency.

#### 4.5.3 Self-reported sleep efficiency and psychosocial and affect measures

Bivariate correlations between self-reported sleep efficiency and psychosocial characteristics and affect are depicted in Table 4.2. There was no association with effort ( $P=0.206$ ) or effort-reward imbalance ( $P=0.164$ ), but lower rewards ( $r=-0.17$ ,  $P=0.020$ ) and higher overcommitment at work ( $r=0.24$ ,  $P=0.001$ ) were linked to lower subjective sleep efficiency. Lower social support ( $r=-0.24$ ,  $P=0.001$ ), greater depressive symptoms ( $r=0.22$ ,  $P=0.003$ ), lower happiness ( $r=-0.26$ ,  $P<0.001$ ) and poorer subjective health ( $r=0.33$ ,  $P<0.001$ ) were related to lower self-reported sleep efficiency as well.

Next I conducted regression analyses that are depicted in Table 4.3. Effort and effort-reward imbalance remained unrelated to subjective sleep efficiency ( $B=0.004$ , C.I. -0.01 to 0.02,  $P=0.651$ ,  $B=0.015$ , C.I. -0.12 to 0.15,  $P=0.823$ , respectively), and the relationship with reward was no longer statistically significant ( $B=-0.012$ , C.I. -0.04 to 0.01,  $P=0.320$ ). However, overcommitment was associated with lower self-reported sleep efficiency ( $B=0.036$ , C.I. 0.01 to 0.06,  $P=0.009$ ), independently of age, having children, personal income, marital status, BMI and negative affect. Reduced sleep efficiency was also reported by those with lower social support ( $B=-0.011$ , C.I. -0.02 to -0.001,  $P=0.030$ ), and greater depressive symptoms ( $B=0.011$ , C.I. 0.000 to 0.02,  $P=0.048$ ). There was a

significant negative association between self-reported sleep efficiency and happiness as well ( $B=-0.017$ , C.I.  $-0.03$  to  $-0.003$ ,  $P=0.016$ ), with greater sleep efficiency among happier participants. The relationship between self-reported sleep efficiency and self-reported health status also remained statistically significant after adjustment for covariates ( $B=0.138$ , C.I.  $0.07$  to  $0.21$ ,  $P<0.001$ ), with those in poorer health reporting lower efficiency.

**Table 4.2 Bivariate correlations between sleep measures and psychosocial characteristics and affect.**

	<b>Self-reported sleep efficiency</b>	<b>P</b>	<b>Objective sleep efficiency (work day)</b>	<b>P</b>	<b>Objective sleep efficiency (leisure day)</b>	<b>P</b>	<b>Sleep discrepancy</b>	<b>P</b>
Effort	0.09	0.206	-0.01	0.873	0.13	0.115	0.12	0.107
Reward	-0.17	0.020	0.05	0.531	-0.09	0.239	-0.17	0.025
Effort-reward imbalance	0.10	0.164	-0.01	0.886	0.11	0.173	0.17	0.026
Overcommitment	0.24	0.001	0.002	0.977	0.08	0.328	0.22	0.003
Social support	-0.24	0.001	0.03	0.735	-0.09	0.271	-0.22	0.003
Depressive symptoms	0.22	0.003	-0.05	0.558	0.02	0.795	0.16	0.034
Happiness	-0.26	<0.001	0.08	0.322	-0.08	0.317	-0.18	0.017
Self-reported health	0.33	<0.001	-0.09	0.278	-0.01	0.865	0.22	0.004

Results are presented as Pearson correlation coefficients ( $r$ ) and P-values.



**Table 4.3 Associations between self-reported sleep efficiency and psychosocial characteristics and affect.**

Predictors	Self-reported sleep efficiency		
	B <sup>1</sup>	95% C.I.	P
Effort	0.004	(-0.01 to 0.02)	0.651
Reward	-0.012	(-0.04 to 0.01)	0.320
Effort-reward imbalance	0.015	(-0.12 to 0.15)	0.823
Overcommitment	0.036	(0.01 to 0.06)	0.009
Social support	-0.011	(-0.02 to -0.001)	0.030
Depressive symptoms	0.011	(0.000 to 0.02)	0.048
Happiness	-0.017	(-0.03 to -0.003)	0.016
Self-reported health	0.138	(0.07 to 0.21)	<0.001

Results are presented as unstandardized regression coefficients (B) and 95% confidence intervals (C.I.).

<sup>1</sup> Models are adjusted for age, having children, personal income, marital status, BMI and negative affect.

#### 4.5.4 Objective sleep efficiency and psychosocial and affect measures

Bivariate correlations between objective sleep efficiency, psychosocial characteristics and affect are summarized in Table 4.2. Work day sleep efficiency was unrelated to work stress measures (effort:  $P=0.873$ , reward:  $P=0.531$ , effort-reward imbalance:  $P=0.886$ , overcommitment:  $P=0.977$ ), psychosocial and affective variables (social support:  $P=0.735$ , depressive symptoms:  $P=0.558$ , happiness:  $P=0.322$ ), and a subjective health rating ( $P=0.278$ ).

Similarly, sleep efficiency assessed on the leisure night was not related to work stress (effort:  $P=0.115$ , reward:  $P=0.239$ , effort-reward imbalance:  $P=0.173$ , overcommitment:  $P=0.328$ ), psychosocial and affective variables (social support:  $P=0.271$ , depressive symptoms:  $P=0.795$ , happiness:  $P=0.317$ ) as well as self-reported health status ( $P=0.865$ ) (see Table 4.2).

As can be seen in Table 4.4 regression analyses confirmed that the above associations were not statistically significant. Work stress measures (effort:  $B=0.063$ , C.I. -0.20 to 0.33,  $P=0.635$ , reward:  $B=-0.013$ , C.I. -0.42 to 0.40,  $P=0.952$ , effort-reward imbalance:  $B=0.810$ , C.I. -1.79 to 3.41,  $P=0.539$ , and overcommitment:  $B=0.324$ , C.I. -0.12 to 0.77,  $P=0.151$ ), social support ( $B=0.025$ , C.I. -0.15 to 0.20,  $P=0.777$ ), affective variables (happiness:  $B=0.141$ , C.I. -0.09 to 0.37,  $P=0.229$ , depressive symptoms:  $B=-0.136$ , C.I. -0.32 to 0.05,  $P=0.145$ ), and self-rated health ( $B=-0.728$ , C.I. -1.90 to 0.44,  $P=0.220$ ) remained unrelated to work night objective sleep efficiency.

Leisure night sleep efficiency was also not associated with work stress (effort:  $B=0.168$ , C.I. -0.14 to 0.48,  $P=0.283$ , reward:  $B=-0.238$ , C.I. -0.72 to 0.25,  $P=0.335$ , effort-reward imbalance:  $B=1.468$ , C.I. -1.65 to 4.58,  $P=0.353$ , and overcommitment:  $B=0.234$ , C.I. -0.31 to 0.78,  $P=0.397$ ), psychosocial and affective responses (social support:  $B=-0.034$ , C.I. -0.24 to

0.18,  $P=0.748$ , happiness:  $B=-0.044$ , C.I.-0.31 to 0.22,  $P=0.739$ , depressive symptoms:  $B=-0.106$ , C.I.-0.32 to 0.11,  $P=0.337$ ) as well as self-reported health ( $B=-0.257$ , C.I.-1.67 to 1.15,  $P=0.719$ ) (see Table 4.4).

As shown in Table 4.5 when models were additionally adjusted for whether last night's sleep was typical the regressions between objective sleep efficiency on both the work and leisure days and psychosocial and affective responses were still not significant.

**Table 4.4 Associations between objective sleep efficiency and psychosocial characteristics and affect.**

Predictors	Objective sleep efficiency (work day)			Objective sleep efficiency (leisure day)		
	B <sup>1</sup>	95% C.I.	P	B <sup>1</sup>	95% C.I.	P
Effort	0.063	(-0.20 to 0.33)	0.635	0.168	(-0.14 to 0.48)	0.283
Reward	-0.013	(-0.42 to 0.40)	0.952	-0.238	(-0.72 to 0.25)	0.335
Effort-reward imbalance	0.810	(-1.79 to 3.41)	0.539	1.468	(-1.65 to 4.58)	0.353
Overcommitment	0.324	(-0.12 to 0.77)	0.151	0.234	(-0.31 to 0.78)	0.397
Social support	0.025	(-0.15 to 0.20)	0.777	-0.034	(-0.24 to 0.18)	0.748
Depressive symptoms	-0.136	(-0.32 to 0.05)	0.145	-0.106	(-0.32 to 0.11)	0.337
Happiness	0.141	(-0.09 to 0.37)	0.229	-0.044	(-0.31 to 0.22)	0.739
Self-reported health	-0.728	(-1.90 to 0.44)	0.220	-0.257	(-1.67 to 1.15)	0.719

Results are presented as unstandardized regression coefficients (B) and 95% confidence intervals (C.I.).

<sup>1</sup>Models are adjusted for age, having children, personal income, marital status, BMI, and negative affect.

**Table 4.5 Associations between objective sleep efficiency and psychosocial characteristics and affect additionally adjusted for whether last night’s sleep was typical.**

Predictors	Objective sleep efficiency (work day)			Objective sleep efficiency (leisure day)		
	B <sup>1</sup>	95% C.I.	P	B <sup>1</sup>	95% C.I.	P
Effort	0.039	(-0.26 to 0.33)	0.796	0.287	(-0.08 to 0.65)	0.119
Reward	0.049	(-0.41 to 0.50)	0.832	-0.298	(-0.86 to 0.27)	0.299
Effort-reward imbalance	0.476	(-2.71 to 3.66)	0.768	2.740	(-1.21 to 6.69)	0.172
Overcommitment	0.373	(-0.10 to 0.85)	0.124	0.400	(-0.19 to 0.99)	0.178
Social support	0.030	(-0.17 to 0.23)	0.762	-0.043	(-0.30 to 0.21)	0.737
Depressive symptoms	-0.139	(-0.34 to 0.06)	0.165	-0.049	(-0.30 to 0.20)	0.698
Happiness	0.137	(-0.11 to 0.39)	0.277	-0.030	(-0.33 to 0.27)	0.846
Self-reported health	-0.704	(-1.96 to 0.55)	0.268	-0.159	(-1.73 to 1.41)	0.841

Results are presented as unstandardized regression coefficients (B) and 95% confidence intervals (C.I.). <sup>1</sup>Models are adjusted for age, having children, personal income, marital status, BMI, negative affect and whether last night’s sleep was typical.

#### 4.5.5 Sleep discrepancy and psychosocial and affect measures

Before analysing associations between the sleep discrepancy measure, psychosocial factors and affect I first explored whether there was a difference in associations between separate discrepancy scores for work and leisure days, and psychosocial and affect variables. The scores were correlated ( $r=0.61$ ,  $P<0.001$ ), and the associations were broadly similar for overcommitment, social support, depressive symptoms and self-rated health (see Table 4.6). However, the association with happiness was stronger for the leisure day discrepancy measure ( $r=-0.33$ ,  $P<0.001$ ) than for the work day measure ( $r=-0.15$ ,  $P=0.056$ ). The leisure day discrepancy measure was also more strongly associated with effort ( $r=0.15$ ,  $P=0.062$ ), reward ( $r=-0.22$ ,  $P=0.006$ ) and effort-reward imbalance ( $r=0.19$ ,  $P=0.016$ ) than the work day discrepancy measure (effort:  $r=0.04$ ,  $P=0.583$ , reward:  $r=-0.08$ ,  $P=0.299$  and effort-reward imbalance:  $r=0.08$ ,  $P=0.302$ ).

**Table 4.6 Bivariate correlations between work and leisure day discrepancy measures, psychosocial and affect variables.**

	<b>Work day discrepancy</b>	<b>P</b>	<b>Leisure day discrepancy</b>	<b>P</b>
Effort	0.04	0.583	0.15	0.062
Reward	-0.08	0.299	-0.22	0.006
Effort-reward imbalance	0.08	0.302	0.19	0.016
Overcommitment	0.20	0.014	0.22	0.005
Social support	-0.19	0.015	-0.23	0.004
Depressive symptoms	0.17	0.028	0.28	<0.001
Happiness	-0.15	0.056	-0.33	<0.001
Self-reported health	0.22	0.006	0.31	<0.001

Results are presented as Pearson correlation coefficients ( $r$ ) and P-values.

Next I analysed relationships between the discrepancy measure, psychosocial and affective variables. As depicted in Table 4.2 on page 216 the sleep discrepancy measure was correlated with all psychosocial and affect measures except effort at work ( $P=0.107$ ). Specifically, lower reward ( $r=-0.17$ ,  $P=0.025$ ), effort-reward imbalance ( $r=0.17$ ,  $P=0.026$ ) and higher overcommitment ( $r=0.22$ ,  $P=0.003$ ) were linked to under-estimations of sleep efficiency. Respondents reporting lower social support ( $r=-0.22$ ,  $P=0.003$ ), more depressive symptoms ( $r=0.16$ ,  $P=0.034$ ) and less happiness ( $r=-0.18$ ,  $P=0.017$ ) were also more likely to perceive their sleep efficiency to be lower than indicated by the objective data. Poorer self-reported health was similarly associated with a higher discrepancy between sleep efficiency measures ( $r=0.22$ ,  $P=0.004$ ).

The regression models for sleep discrepancy and psychosocial and affect variables are summarised in Table 4.7. Effort remained unrelated to the discrepancy measure ( $B=0.042$ , C.I.  $-0.01$  to  $0.09$ ,  $P=0.119$ ). Reward and effort-reward imbalance were associated with discrepancies between self-reported and objective sleep measures ( $B=-0.080$ , C.I.  $-0.16$  to  $-0.01$ ,  $P=0.036$ ,  $B=0.559$ , C.I.  $0.05$  to  $1.07$ ,  $P=0.032$ , respectively), and after negative affectivity was additionally controlled for the regression of effort/reward imbalance on sleep discrepancy only approached statistical significance ( $B=0.516$ , C.I.  $-0.01$  to  $1.05$ ,  $P=0.056$ ), but the relationship with reward was no longer significant ( $B=-0.072$ , C.I.  $-0.15$  to  $0.01$ ,  $P=0.074$ ). There was a significant positive association between overcommitment and sleep discrepancy ( $B=0.137$ , C.I.  $0.06$  to  $0.22$ ,  $P=0.001$ ), and after additional adjustment for negative affect  $B$  remained virtually unchanged ( $B=0.139$ , C.I.  $0.05$  to  $0.23$ ,  $P=0.002$ ). This suggests that overcommitted individuals and those experiencing a disproportionate effort at work under-estimated their sleep efficiency.

Low social support was also significantly associated with under-estimations of sleep efficiency ( $B=-0.039$ , C.I.  $-0.07$  to  $-0.01$ ,  $P=0.025$ ), and the association remained statistically significant after including negative affect into the model ( $B=-0.035$ , C.I.  $-0.07$  to  $0.000$ ,  $P=0.049$ ). However, there was no association between the discrepancy measure and depressive symptoms in both model 1 ( $B=0.024$ , C.I.  $-0.001$  to  $0.05$ ,  $P=0.063$ ) and model 2 ( $B=0.021$ , C.I.  $-0.02$  to  $0.06$ ,  $P=0.266$ ). Similarly, there was no association with happiness in both regression models ( $B=-0.035$ , C.I.  $-0.08$  to  $0.01$ ,  $P=0.100$ ,  $B=-0.030$ , C.I.  $-0.07$  to  $0.02$ ,  $P=0.187$  respectively).

Finally, there was a significant association between sleep discrepancy and self-reported health ( $B=0.302$ , C.I.  $0.08$  to  $0.52$ ,  $P=0.008$ ), with those in poor self-rated health under-estimating their sleep efficiency. The association was only slightly reduced after negative affect was added to the regression model ( $B=0.276$ , C.I.  $0.05$  to  $0.51$ ,  $P=0.020$ ).



**Table 4.7 Associations between sleep discrepancy measure and psychosocial characteristics and affect.**

Predictors	Sleep discrepancy (Model 1)			Sleep discrepancy (Model 2)		
	B	95% C.I.	P	B	95% C.I.	P
Effort	0.043	(-0.01 to 0.10)	0.100	0.042	(-0.01 to 0.09)	0.119
Reward	-0.080	(-0.16 to -0.01)	0.036	-0.072	(-0.15 to 0.01)	0.074
Effort-reward imbalance	0.559	(0.05 to to1.07)	0.032	0.516	(-0.01 to 1.05)	0.056
Overcommitment	0.137	(0.06 to 0.22)	0.001	0.139	(0.05 to 0.23)	0.002
Social support	-0.039	(-0.07 to -0.01)	0.025	-0.035	(-0.07 to 0.000)	0.049
Depressive symptoms	0.024	(-0.001 to 0.05)	0.063	0.021	(-0.02 to 0.06)	0.266
Happiness	-0.035	(-0.08 to 0.01)	0.100	-0.030	(-0.07 to 0.02)	0.187
Self-reported health	0.302	(0.08 to 0.52)	0.008	0.276	(0.05 to 0.51)	0.020

Results are presented as unstandardized regression coefficients (B) and 95% confidence intervals (C.I.).

Model 1: Adjusted for age, having children, personal income, marital status, and BMI.

Model 2: Additionally adjusted for negative affect (PANAS).

## 4.6 Discussion

This study set out to test four hypotheses. As predicted in the first hypothesis, higher work stress was associated with greater discrepancy between sleep measures. Specifically, overcommitted individuals and those experiencing a disproportionate effort at work reported lower sleep efficiency than indicated by the objective measure of sleep efficiency. This relationship was independent of age, having children, marital status, personal income, BMI and negative affect. Under-estimation of sleep efficiency was also more prevalent among individuals who reported lower social support and poorer self-rated health, thus the second and fourth hypotheses were supported by the data. However, the third hypothesis was rejected since neither lower happiness nor depressive symptoms were related to the sleep discrepancy measure. Notably, while objective sleep efficiency was unrelated to any of the psychosocial and affect indicators, reduced self-reported sleep efficiency was greater among overcommitted and less happy individuals, as well as among those reporting lower social support and more depressive symptoms, after adjustment for relevant confounding variables. These associations were also independent of negative affect, suggesting that they are not simply due to plaintive set, or a negative affectivity reporting bias.

Most population-based studies comparing subjective and objective sleep measures have investigated discrepancies in sleep duration (Lauderdale et al., 2008; Silva et al., 2007; van den Berg et al., 2008). For example, in a sample of healthy elderly persons over one third misreported sleep duration when compared with actigraphy-based measure (van den Berg et al., 2008). Under-estimation of sleep duration was associated with depressive symptoms, poor subjective sleep quality and using sleep medication, whereas over-estimation of sleep duration was related to lower objective sleep efficiency, shorter objective sleep duration, older age, and

poorer cognitive function. Another population-based study found that more educated and obese participants were more likely to under-estimate their sleep duration (Silva et al., 2007). A study of middle-aged adults found that over-estimation of sleep duration was related to poorer health status, depressive symptoms, obesity and sleep apnoea risk as well (Lauderdale et al., 2008). In addition, there is some evidence from studies in elderly cohorts that although men have poorer objective sleep than women, women are more likely to perceive their sleep quality as poor (Unruh et al., 2008; van den Berg et al., 2009; Vitiello et al., 2004).

My study extends these observations by demonstrating that self-reported and objective measures of sleep efficiency also seem to be incongruent; and that this phenomenon appears to be present not only in older, but also in younger adults. The findings that those reporting work stress, low social support and poor health reported lower sleep efficiency than was warranted by the objective measure of sleep have important implications. Specifically, they suggest that the magnitude of the relationship between self-reported sleep efficiency and health-related psychosocial factors may be over-estimated in studies based on self-report.

It is notable that none of the psychosocial or affect indicators were related to objective sleep efficiency. Similar findings have been observed in past studies. For instance, in a sample of young women self-reported sleep quality was found associated with perceived stress whereas actigraphic sleep quality was not (Tworoger, Davis, Vitiello, Lentz, & McTiernan, 2005). Perceived stress has been weakly associated with PSG-defined sleep parameters in middle-aged women with insomnia (Shaver, Johnston, Lentz, & Landis, 2002), and was only correlated with subjective, but not actigraphic, sleep quality in older adults with chronic insomnia (Friedman, Brooks, Bliwise, Yesavage, & Wicks, 1995). These results suggest that subjective and objective indicators of sleep quality might be measuring, at least to some

extent, different phenomena. This underscores the importance of using both objective and subjective measures of sleep quality in research. However, an important consideration is whether in my study the nights of objective sleep monitoring were representative for the individual, since if they were not typical, this might account for failure to observe associations with psychosocial factors. This seems not to be case, since when I repeated the regression models additionally adjusting for whether sleep on the work or leisure night was typical the affective and psychosocial variables remained unrelated to objective sleep efficiency.

I found that higher overcommitment was associated with reduced self-reported sleep efficiency. This is in agreement with findings from the Whitehall II cohort (Steptoe et al., 2004), as well as with studies conducted with German (Kudielka et al., 2004) and Swedish workers (Fahlen et al., 2006). The negative association between social support and self-reported sleep efficiency also corroborates previous findings (Hanson & Ístergren, 1987; Nordin et al., 2008). Reduced self-reported sleep efficiency was less prevalent among happy individuals, and this relationship was independent of negative affect and other relevant confounders. This finding is consistent with results from previous studies in the US and UK (Hamilton et al., 2007a; Steptoe et al., 2008). This study replicates the well-established association between self-reported sleep problems and depressive symptoms as well (Foley et al., 2004; Strine & Chapman, 2005). It might be argued that reports of overcommitment to work, poor social support, greater depressive symptoms and less happiness are manifestations of negative affectivity, and that associations with reduced self-reported sleep efficiency were due to the measures being completed around the same period. However, the regressions remained statistically significant after negative affect had been taken into account. This

indicates that the associations may reflect more fundamental perceptions of sleep efficiency among women with more adverse psychosocial profiles.

My study has several strengths. First, because sleep duration and/or quality may vary between week and weekend nights, sleep was measured on one work and one leisure night. Second, sleep was assessed with an Actiheart monitor, which allows measurement of sleep objectively without altering normal sleep habits. Further, in contrast to wrist actigraphy, which relies on motor activity to establish wake and sleep patterns (Ancoli-Israel et al., 2003), this instrument used the combination of activity monitored from the torso and heart rate as an indicator of sleep. Finally, my findings complement the existing data on sleep duration and suggest that subjective and objective measures of sleep efficiency are also incongruent, and vary by psychosocial stress.

However, my study also has several limitations. The cross-sectional design of this investigation precludes any causal conclusions from being drawn, and because the study's participants were young women, caution is needed in extrapolating the findings to older women or the male population. The relatively small sample size and the preponderance of university-educated participants further limit the generalizability of the findings. In the Daytracker study self-reports were used to establish if participants were free of any serious medical condition, but it would have been valuable to corroborate this information with scrutiny of medical records. To minimize data loss the Actiheart monitor was fitted to participants' chests by a member of the research team prior to each night of assessment, and for practical reasons the leisure night assessment began on a Friday night. It might be argued that a Saturday night would have been more appropriate to capture a "weekend" night sleep. Subjective sleep efficiency was measured with the Jenkins Sleep Problems Scale (Jenkins et

al., 1988), which in common with other sleep questionnaires such as the PSQI (Buysse et al., 1989), asks for information about sleep over the previous month, while my objective sleep measures were obtained only over two nights. This raises the possibility that the nights of objective sleep monitoring might not have reflected participants' typical sleep, and were therefore unrelated to affect and psychosocial factors. Sleep data were not collected on other nights in the Daytracker study. However, when the statistical models were additionally adjusted for whether last night's sleep was typical the results relating objective sleep efficiency, psychosocial and affective responses remained non-significant. While the Actiheart is an unobtrusive, objective sleep measure it does not provide as reliable or informative data as PSG, a "gold standard" sleep measure. In addition, because this is the first study, to the best of my knowledge, that measured sleep with the Actiheart, these data are still preliminary and further studies are warranted to corroborate the current findings.

Notwithstanding, my study may have important implications for the sleep literature. People's judgements of sleep efficiency are associated with psychosocial stress and affective responses, and this may result in under-estimation of sleep efficiency. My findings suggest that the magnitude of associations between sleep and psychosocial factors may be augmented by self-report biases. The finding that only self-reported, but not objective sleep efficiency, was related to affect and psychosocial factors also further suggests that objective and subjective sleep indices might to some extent be measuring distinct phenomena.

## **CHAPTER 5: A POSITIVE WELL-BEING INTERVENTION STUDY TO IMPROVE SUBJECTIVE AND OBJECTIVE SLEEP MEASURES IN HEALTHY YOUNG WOMEN (Study 4)**

### **5.1 Introduction**

This chapter describes a short-term intervention study designed to discover whether modifying affective well-being will have a beneficial impact on subjective and objective sleep indices. The introduction to Study 4 consists of 4 subsections. In the first subsection I will provide an overview of the well-being literature and its main constructs. In subsection 2 I will focus on the associations between well-being and physical health, and more importantly I will argue that positive well-being has a beneficial impact on physical functioning and longevity. This will be followed by subsection 3 in which the literature relating positive well-being with better sleep will be discussed. In this subsection I will also outline the gaps in current knowledge that Study 4 was set out to address. In particular I will argue that one way to improve disturbed sleep might be through increased positive well-being. In subsection 4 I first discuss possible determinants of well-being, and next I will outline a number of approaches previously used to enhance positive well-being as to introduce the reader to the experimental paradigm that Study 4 was based on. Subsection 4 will be followed by research hypotheses.

#### **5.1.1 Well-being literature and its main constructs**

Research into well-being has been concerned with two broad constructs: eudaimonic well-being and hedonic well-being (Ryan & Deci, 2001). Eudaimonic well-being, also termed flourishing, refers to the realization of one's true potential. Importantly, the eudaimonic well-

being paradigm does not perceive happiness and bodily pleasures as synonymous with true well-being (Ryan & Deci, 2001; Ryff & Keyes, 1995). For instance, Ryff and Keyes (1995) defined eudaimonic well-being as a construct encompassing six dimensions including autonomy, environmental mastery, personal growth, positive relationships with others, purpose in life, and self-acceptance. Briefly, autonomy refers to self-determination and the ability to follow personal principles. Environment mastery has been conceptualised as effective coping with the demands of everyday life, and life in general. Personal growth is the recognition that one's potentials and talents are being fulfilled and are able to develop with time, while purpose of life is the feeling that one's life is meaningful and full of purpose. Self-acceptance refers to the recognition of one's virtues and shortcomings, and finally positive relationships with others reflect the ability to have intimate, positive and meaningful relations with other people (Ryff & Keyes, 1995; Ryff, Singer, & Love, 2004).

Hedonic well-being, often also termed affective well-being or positive affect, is concerned with feelings and emotions such as happiness, anger, sadness, life satisfaction and pleasure (Keyes, Shmotkin, & Ryff, 2002; Ryan & Deci, 2001). Researchers studying hedonic well-being have focused predominantly on two interrelated but independent dimensions, namely, life satisfaction and happiness. Happiness reflects a combination of high positive and low negative affect, and refers to emotional evaluations of more immediate events in people's lives (Keyes et al., 2002). Life satisfaction, on the other hand, is concerned with cognitive-judgmental appraisals of peoples' lives (Diener, Emmons, Larsen, & Griffin, 1985; Diener, Oishi, & Lucas, 2003). More contemporary research, however, suggests that life satisfaction is an evaluative measure of well-being and not part of hedonic well-being (Dolan, Layard, & Metcalfe, 2011). For example, data from the Gallup-Healthways Well-Being Index survey



(N=1000) revealed that measures of hedonic well-being (e.g., stress, enjoyment) and life satisfaction were associated with different aspects of people's lives. While higher life satisfaction was linked to education and income, hedonic well-being was more strongly correlated (and negatively) with health behaviours such as smoking, caregiving and loneliness (Kahneman & Deaton, 2010).

Although eudaimonic and hedonic constructs are related, each represents a unique aspect of well-being. For example, research has documented that some people perceive their life as unfulfilling but nonetheless rate themselves as happy, while others report low levels of happiness or affect despite pursuing their life goals (McGregor & Little, 1998; Ryan & Deci, 2001; Ryff & Keyes, 1995). However, some authors have argued that the distinction between eudaimonic and hedonic well-being is not always clear since the constructs tend to overlap conceptually, and might be part of a shared psychological mechanism (Kashdan, Biswas-Diener, & King, 2008).

### **5.1.2 Positive well-being and physical health**

Traditionally research has focused on associations between emotional distress, in particular depression and anxiety, with health outcomes, but it is becoming increasingly recognised that positive affect and eudaimonic well-being are associated with better health and longevity. An important issue, however, is whether the presence of happiness or eudaimonic well-being is simply synonymous with the absence of depression, anxiety or negative affectivity. If that is the case than studying hedonic and eudaimonic well-being in relation to health might reiterate what is already known. Growing evidence suggests that well-being measures are independent predictors of better health outcomes. For example, a meta-analytic review of prospective cohort studies with healthy (N=26) and disease (N=28) populations by

Chida and Steptoe (2008) tested associations between positive well-being and mortality. Positive affective states (e.g., joy) and dispositions (e.g., life satisfaction) were predictive of reduced mortality among both healthy (combined HR=0.82, C.I. 0.76-0.89, P<0.001) and disease populations, albeit the protective effects in the latter group were smaller (combined HR=0.98, C.I. 0.95,-1.00, P=0.030). Importantly, the protective impact of positive states and dispositions on mortality was independent of negative affect.

Since the aforementioned meta-analysis a number of prospective studies relating positive well-being with mortality and morbidity, in particular cardiovascular health, have been published. For example, a population-based study of 1739 Canadian men and women reported that participants with greater levels of positive affect at baseline were less likely to have CHD incident ten years later (HR=0.78, C.I. 0.63-0.96, P=0.020). This finding was independent of negative affect and depressive symptoms (Davidson, Mostofsky, & Whang, 2010). In the Whitehall II study (N=7956) a mean score of satisfaction with eight domains of respondents' life (e.g., job, health, family life, marital or love relationship) was prospectively associated with reduced risk of CHD incidence, independently of relevant covariates including mood disturbances (Boehm, Peterson, Kivimaki, & Kubzansky, 2011). In the English Longitudinal Study of Ageing (ELSA) higher experienced positive affect, relative to low positive affect, was associated with lower mortality risk (HR=0.65, C.I. 0.44-0.96, P=0.030) up to 5 years later. This finding was independent of a number of covariates including depressive symptoms (Steptoe & Wardle, 2011). Another recent investigation of ELSA revealed that enjoyment of life (a component of hedonic well-being) was predictive of lower mortality rate up to 7 years after the initial assessment, independently of a host of covariates such as health behaviours, health indicators and depressive symptoms (Steptoe & Wardle,

2012). Finally, a recent review concluded that independently of depressive symptoms or negative mood both eudaimonic and hedonic well-being are prospectively associated with better cardiovascular health in initially healthy populations. In patient populations the effects of well-being constructs were summarised as protective as well, albeit the evidence is less consistent at present (Boehm & Kubzansky, 2012).

Taken together, there is now substantive (prospective) evidence that individuals reporting higher levels of hedonic as well as eudaimonic well-being enjoy longer and healthier lives, and that these effects are present over and above mood disturbances. The discussion of mechanisms relating well-being with better health outcomes is beyond the scope of this PhD, but it should be mentioned that more than one pathway is likely to be involved. For example, positive affective states and eudaimonic well-being might contribute towards better health through health behaviours such as higher levels of physical activity, lower risk of being a smoker, healthier diets, moderate alcohol consumption and better sleep (Boehm & Kubzansky, 2012). Another plausible mechanism is (healthier) biological activation or function as indicted, for instance, by autonomic activation, inflammation, neuroendocrine and immune processes (Boehm & Kubzansky, 2012; Steptoe, Dockray, & Wardle, 2009). Positive affective states, eudaimonic well-being and health risk might also share genetic factors, but this hypothesis has not been tested thus far (Boehm & Kubzansky, 2012; Steptoe et al., 2009).

### **5.1.3 Sleep measures and positive well-being**

The literature relating sleep measures with mood disturbances, in particular depressive symptoms, is extensive and has already been reviewed in Chapter 1. However, despite the growing interest in the relationship between well-being and health there have been few studies exploring associations between positive well-being and sleep. For example, in a sample of

275 middle-aged men and women sleep satisfaction was positively associated with quality of well-being, which was assessed with questions on mobility, physical activity and social functioning. Interestingly, actigraphic sleep quality was unrelated to well-being in that study (Jean-Louis, Kripke, & Ancoli-Israel, 2000). An analysis of the National Survey of Midlife Development (MIDUS) (N=3643) revealed that insomnia symptoms, defined as difficulty falling asleep and staying asleep in the last month, were inversely related to subjective well-being that was conceptualised as low negative affect, high positive affect and life satisfaction. Eudaimonic well-being, which was measured with the scale by Ryff et al., (1989), was also negatively associated with insomnia symptoms, albeit the size of the association was nearly two times smaller than that between disturbed sleep and subjective well-being. Importantly, these associations were independent of relevant socio-demographic and clinical confounders including emotional disorders (Hamilton et al., 2007a). Using Whitehall II data (N=736) Steptoe and co-workers (2008) explored associations between positive affect, eudaimonic well-being and sleep problems, and found that disturbed sleep was less prevalent among respondents reporting greater levels of positive affect and eudaimonic well-being, independently of psychological distress. In addition to the direct associations with sleep, positive well-being attenuated the relationship between psychosocial risk factors (e.g., financial strain or low emotional support) and sleep, suggesting that feelings of happiness and purpose of life may buffer the negative impact of daily life stressors. Finally, a more recent study conducted with depressed participants (N=60) and controls (N=36) reported that lower sleep quality predicted lower positive affect independently of depression diagnosis or anxiety. Interestingly, poor sleep quality did not predict higher negative affect once the presence of

depression diagnosis was statistically adjusted for (Bower, Bylsma, Morris, & Rottenberg, 2010).

There is some evidence that sleep quantity is associated with well-being as well. For example, in 502 US community dwelling men and women (mean age 45 years) optimal sleep duration, defined as equal or higher than 6 hours and shorter than 8.5 hours, was associated with higher levels of eudaimonic well-being. When the analyses were repeated after the exclusion of respondents with depressive symptoms eudaimonic well-being remained statistically associated with optimal sleep hours (Hamilton, Nelson, Stevens, & Kitzman, 2007b). However, in an earlier study by Jean-Louis et al., (2000) sleep duration assessed with self-report and actigraphy was unrelated to the quality of well-being.

The studies discussed herein relied on cross-sectional designs thus the direction of the relationship between sleep and well-being could not be established. Positive affective states might promote good sleep, but it is also plausible that people with good sleep experience greater levels of well-being. To date there have been only two prospective investigations of sleep and well-being. Phelan et al., (2010) found that in a sample of 115 elderly women greater eudaimonic well-being and lower depression were associated with a decreased likelihood of disturbed sleep ten years later. A 10-year follow-up of data from the MIDUS described earlier revealed that insomnia symptoms were prospectively related to greater psychological distress, but not to well-being. Interestingly, the presence of insomnia symptoms at both baseline and follow-up was associated with reduced levels of hedonic and eudaimonic well-being (Karlson, Gallagher, Olson, & Hamilton, 2013).

However, based on these two studies the temporal precedence of sleep and well-being is still uncertain since these investigations had different exposure and outcome variables.

Specifically, in the study by Phelan et al., (2010) well-being was the exposure factor and sleep the outcome variable, whereas in Karlson et al.'s investigation (2013) the exposure factor was insomnia symptoms and the outcome well-being measures. Nonetheless, if supported by further research, the findings described by Phelan et al., (2010) tentatively suggest that one possible way of improving sleep might be through interventions aimed at increasing positive and/or eudaimonic well-being. Improved sleep might then contribute towards reducing the public health burden associated with abnormal sleep patterns, in particular CVD and CVD mortality (Cappuccio et al., 2010; Cappuccio et al., 2011).

#### 5.1.4 Positive well-being interventions

##### *Determinants of well-being*

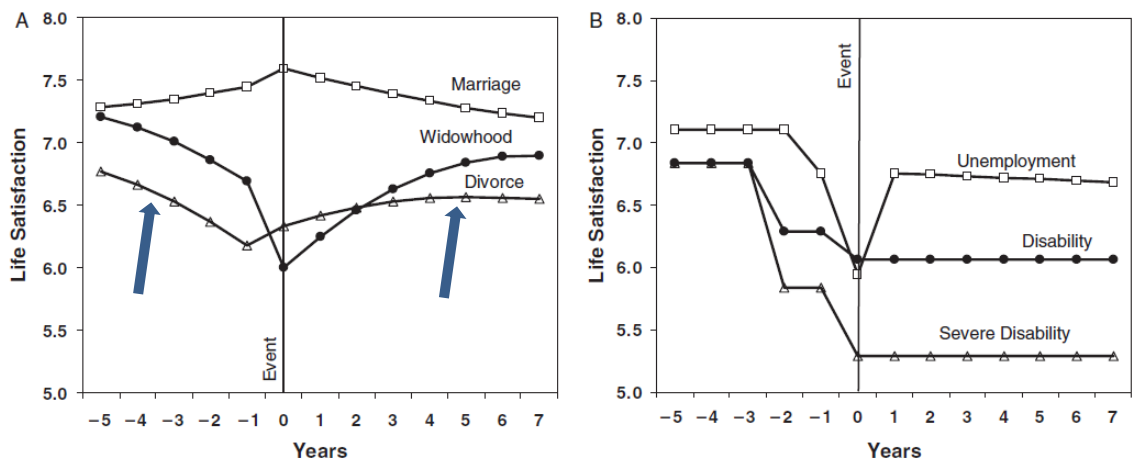
Before discussing the literature concerned with experimental approaches aimed at increasing positive well-being is it important to consider what makes people happy and fulfilled, and whether it is actually possible to enhance hedonic, evaluative and/or eudaimonic well-being in the long term. It should be mentioned that authors exploring the possible causes of positive well-being have largely focused on hedonic and evaluative well-being, in particular life satisfaction and global happiness, and less so on eudaimonic well-being. For example, early research on positive well-being (e.g., Wilson, 1967) stipulated that happiness is largely determined by personality characteristics and dispositions, such as extraversion, neuroticism and optimism, which are heritable (Diener, Suh, Lucas, & Smith, 1999). Indeed, large twin studies revealed that approximately 50% of the variance in well-being is explained by genetic factors (e.g., Lykken & Tellegen, 1996). However, it has been argued that the true proportion is likely to be somewhat lower (Diener et al., 1999). For example, a study of identical and fraternal twins reported that genetic factors explained 16% of the variance in total depression

scores (assessed with the CES-D (Radloff, 1977), but when the authors looked separately at the CES-D items relating depressed mood and well-being the variance explained by hereditary factors was minimal (7%). On the other hand, the effects of non-shared environment explained a large proportion of the variance in well-being items (74-80%) (Gatz, Pederson, Plomin, & Nesselroade, 1992). Similarly, Baker et al., (1992) found that although hereditary factors explained a large proportion of the variance in negative affectivity, this was not the case with positive affect where shared environment was more important. It has been suggested that one explanation for the low influence of genetic factors on positive affect might be because it is strongly influenced by current situations or circumstances (Gatz et al., 1992). Findings from these earlier studies are, however, at odds with more contemporary research. For example, a study of over 5,000 twins and their siblings (age range 13-28 years) reported that hereditary components explained between 36 and 50% of the variance in well-being, which was a combined measure of quality of life, satisfaction with life and happiness (Bartels & Boomsma, 2009).

In addition, Headey and Wearing (1989) postulated in their dynamic equilibrium model that happiness levels are anchored around a genetically determined set point, and although both favourable and adverse life events lead to fluctuations in well-being people eventually return to their baseline happiness levels. If that is the case then interventions studies aimed at increasing happiness could be a futile endeavour. Interestingly, a more recent review of large, prospective studies suggested that certain life events, such as unemployment or divorce, lead to long-lasting changes in life satisfaction and happiness (see Figure 5.1 for a graphic depiction of this phenomenon). There also appears to be substantial individual differences in the degree to which people adapt to both negative and positive life events (Lucas, 2007). For

example, pre- and post-divorce life satisfaction scores plotted in the figure on the left (marked by two blue arrows) are based on findings from a longitudinal investigation of over 30,000 German people followed for approximately 18 years (Lucas, 2005). As can be seen, following the divorce life satisfaction eventually increases, but it does not return to its pre-divorce values staying between 0.22 to 0.34 points lower. However, the figure on the left also depicts that there are baseline differences in life satisfaction between people who divorce and stay married. This, on the other hand, is suggestive of selection effects to either of this group of people (Lucas, 2005).

**Figure 5.1 Changes in life satisfaction following major life events (adapted from Lucas, 2007).**



The figure on the left depicts levels of life satisfaction before and after marriage, widowhood and divorce, while the figure on the right shows changes in life satisfaction following unemployment, and disability. As can be seen in the figure on left life satisfaction increases after getting married but eventually returns to its pre-married levels. By contrast, the figure on the left and on the right both show that life satisfaction drops markedly following adverse life events and that the decline appears to be permanent, in particular following unemployment and disability.



In addition to being determined by a hereditary component, well-being is influenced by life circumstances and demographic characteristics. For example, it is well-documented that higher income, better self-reported health, being married, and having a satisfying job are associated with greater life satisfaction and happiness (Diener et al., 1999). Interestingly, life satisfaction and negative affect appears to fluctuate little with age, albeit positive affect declines with advancing age (Diener & Suh, 1998; Stone, Schwartz, Broderick, & Deaton, 2010). More women than men suffer from depression (Hankin & Abramson, 2001), and women report stronger negative and positive mood than men (Fujita, Diener, & Sandvik, 1991). However, there appears to be none or very small gender differences in life satisfaction or global happiness (Diener et al., 1999; Fujita et al., 1991; Stone et al., 2010).

Importantly, depending on a study's design (cross-sectional versus longitudinal) or its methodological quality, life circumstances explain only between 8 and 15% of the variance in happiness levels (Diener et al., 1999; Lyubomirsky, Sheldon, & Schkade, 2005). One possible reason why life events, such as getting married or receiving a pay rise, explain only a modest proportion of the variance in well-being is because despite resulting in a temporary increase in life satisfaction or happiness most people, but not all, adapt to new circumstances and return to their initial well-being levels (Lucas, Clark, Georgellis, & Diener, 2003) (for example, see Figure 5.1 for changes in life satisfaction following marriage). By contrast, as already mentioned, adverse life events such as disability result in long-lasting decrements in happiness (Lucas, 2007).

To summarise, hereditary factors and life circumstances account for between 58 and 65% of the variance in happiness levels. This leaves at least 35% of the variance unexplained. In other words, although these two factors are important determinants of well-being they

cannot fully elucidate what makes people happy and satisfied with their lives, or why people differ in their emotional reactions to both positive and negative life events. This has led to the recognition that well-being is also likely to be influenced by psychological processes that additionally enhance happiness, and/or allow people to continuously derive satisfaction from, for instance, their marriage or profession (Diener et al., 1999; Lyubomirsky et al., 2005). Moreover, the substantive proportion of the variance in happiness that is not accounted for by one's genetic make-up, demographic profile and lifestyle, all of which are impossible or difficult to change, suggests that it might be indeed possible to improve people's well-being.

### ***Experimental approaches aimed at increasing positive well-being***

The field of positive psychology, which is concerned with the study of positive emotions, adaptive personality characteristics and personal growth (Seligman, Steen, Park, & Peterson, 2005), has provided empirical evidence and guidance for the development of intervention studies aimed at promoting eudaimonic well-being and happiness. Importantly, a recent meta-analytic review of 51 positive psychology intervention studies (PPIs) concluded that such interventions can indeed enhance well-being, at least in the short-term. The review further suggested that although PPIs are primarily concerned with boosting happiness or promoting personal development, rather than with treating mood disorders or helping people to deal with traumas, they also seem to be effective in reducing depressive symptoms and improving positive well-being of depressed individuals (Sin & Lyubomirsky, 2009).

A number of techniques have been used to enhance well-being, and for ease of reference I will discuss each paradigm separately.

### **Goal attainment**

For example, a study by Sheldon et al., (2002) set out to promote short-term personal growth, which was operationalized with Ryff and Keyes's eudaimonic well-being scale (1995). The intervention included one group-based and one individual session with a counsellor who helped participants to identify the most important personal goals (e.g., to make new friends), as well as the possible ways to achieve them. Working towards realisation of these goals was meant to subsequently facilitate personal growth. At follow-up approximately 3 months later, relative to the control group, participants in the intervention group reported higher eudaimonic well-being and lower negative mood. However, this intervention seemed to benefit mostly those participants who reported high personal growth as baseline.

### **Best possible selves**

Visualising best possible selves is another example of a PPI that is concerned with promoting an optimistic outlook on life and focusing on the future rather than the past. Specifically, in studies that use this approach participants are typically asked to imagine (and consequently write down) that due to their hard work and decisions they have made their dreams, both in terms of personal and professional life, have been fulfilled. In other words, participants are requested to imagine that their lives have turned out as best as they possibly could (e.g., Boehm, Lyubomirsky, & Sheldon, 2011). For example, it has been shown that in comparison with participants who for over one month wrote about the details of their day those who wrote about their best possible future selves reported significantly higher levels of positive affect as well as significantly reduced negative mood (Sheldon & Lyubomirsky, 2006). Notably though, the improvements in well-being measures were only evident among respondents who (1) enjoyed this particular writing task, and (2) invested a considerable effort

into their writing exercises. More recently, visualising ideal future selves over the period of 6 weeks was found to significantly increase satisfaction with life when compared with the control group, who focused on the events that happened in the previous week (Boehm et al., 2011). Another investigation also provided empirical support that this PPI, practised over a 2 month-period, increased hedonic well-being (Lyubomirsky, Dickerhoof, Boehm, & Sheldon, 2011). Interestingly, to test whether self-selection influenced the extent to which well-being improved in this study, prior to the receipt of the writing task, participants were required to indicate whether they wanted to take part in either ‘happiness’ or ‘cognitive’ intervention. Analysis of the data revealed that despite being given the same writing exercise participants who self-selected into the ‘happiness intervention’ showed significantly larger improvements in well-being than those in the ‘cognitive intervention’ (Lyubomirsky et al., 2011). This suggests that PPIs might be more effective amongst individuals who are more motivated to improve their well-being, or in other words, that PPIs might not benefit those people who might need them most.

### **Expressing gratitude**

Expressing gratitude has been shown to successfully improve mood as well. In a first series of studies of this kind Emmons and McCullough (2003) showed that writing about five things or people ones feels grateful for resulted in increases of positive affect and life satisfaction as well as reduced negative affect, when compared with not doing any writing exercises, or with writing about daily hassles. Notably, the beneficial effects of expressing gratitude on well-being were only present if the exercise was practised over a two- or three-week period, but not after one week. More recent intervention studies have also reported that expressing gratitude can lead to increases in positive well-being (operationalized as a

composite score of happiness, satisfaction with life and positive affect) (Layous, Lee, Choi, & Lyubomirsky, 2013; Lyubomirsky et al., 2011), reduced negative affect (Sheldon & Lyubomirsky, 2006) and higher life satisfaction (Boehm et al., 2011). It is important to note that as in the case of the best possible selves paradigm there is evidence that expressing gratitude seems more effective in boosting positive well-being in those individuals who are also more motivated to improve their happiness levels (Lyubomirsky et al., 2011).

### **Behavioural approaches to increase positive well-being**

While the studies discussed above relied on cognitive activities to boost well-being, there is evidence that behavioural approaches might bolster mood and/or eudaimonic well-being as well. Using signature strengths is one such approach, where participants are first asked to identify a few positive (e.g., five) features of their personality, or themselves, and are then encouraged to use them in a novel way. For instance, Seligman et al., (2005) reported that participants encouraged to use their signature (i.e. unique) strengths of character over seven consecutive days reported higher levels of happiness and fewer depressive symptoms, when compared with controls who wrote about their early memories. Interestingly, the beneficial effects of this intervention on mood were present up to six months. Performing five acts of kindness (e.g., blood donation, paying a visit to an older member of one's family), relative to none, over one day has also been found to enhance well-being. However, doing five acts of kindness over a 1- or 3-week period did not enhance well-being (Lyubomirsky et al., 2005).

Taken together, growing empirical evidence suggests that it is possible to increase both hedonic and eudaimonic well-being. Nonetheless, the intervention studies discussed herein followed-up their participants for a maximum period of 6 months (e.g., Seligman et al., 2005)

and more evidence is needed to demonstrate whether the cognitive and behavioural activities advocated by PPIs can improve well-being in the long term. Another important issue to bear in mind is that PPIs appear to be more effective in improving well-being amongst individuals who are motivated to increase their happiness and/or personal growth as well as prepared to invest a considerable effort into the assigned exercises, thus suggesting that these approaches are not suitable for everyone.

***Improving sleep: are positive psychology paradigms suitable?***

To recapitulate, hedonic and eudaimonic well-being are correlated with higher sleep quality and possibly longer sleep hours, and emerging evidence suggests that positive well-being is prospectively linked with better sleep quality as well (Phelan et al., 2010). Thus, as already pointed out, one way to improve sleep might be through enhancing positive affect and/or eudaimonic well-being. Although a number of PPIs have successfully increased positive well-being, it remains uncertain whether this type of interventions can also be used to promote better sleep. Simultaneously it ought to be acknowledged that other non-pharmacological techniques exist to treat insomnia and sleep problems including cognitive-behaviour therapy (Morin, Kowatch, Barry, & Walton, 1993), expressive writing (Mooney, Espie, & Broomfield, 2009), or physical exercise (King et al., 1997). Since none of these methods aims to improve sleep through increasing positive well-being I will not discuss them further in this study.

Interestingly, findings from an intervention study that has already been described above (Emmons & McCullough, 2003) revealed that expressing gratitude not only led to improvements in well-being measures, but also in sleep. Specifically, relative to controls who

did not do any writing exercises, participants who wrote gratitude diaries for 21 days reported longer sleep hours and more refreshing sleep. Analysis of the data revealed that expressing gratitude elicited positive emotions that then had favourable effects on sleep. This is the only intervention study published to date that reported beneficial effects of expressing gratitude on sleep, and it should be pointed out that in addition to a small sample size (N=65) this project was based on a group of adults suffering from neuromuscular diseases; thus the generalizability of these findings is limited. Nonetheless, these data are promising one and suggest that a relatively simple and brief writing exercise might improve sleep.

The finding that gratitude is associated with better sleep is supported by emerging non-experimental evidence as well. For example, in 401 British community-dwelling men and women higher gratitude was cross-sectionally associated with better sleep quality, longer sleep duration and shorter sleep latency, independently of neuroticism and social desirability. Interestingly, the relationships between sleep indices and gratitude were mediated by pre-sleep cognitive thoughts (assessed with a list of 60 different positive and negative thoughts), whereby more grateful participants had less worrying and more positive thoughts than their less grateful counterparts (Wood, Joseph, Lloyd, & Atkins, 2009). On the other hand, a cross-sectional study in chronic pain patients (N=224) reported that sleep problems mediated the relationship between gratitude and anxiety, with 45.5% of the effects of gratitude on anxiety symptoms being explained by disturbed sleep (Ng & Wong, 2013). Since both of these studies were based on a cross-sectional design the precise relationship between sleep quality and gratitude cannot be certain. Nonetheless, these data suggest that the association could be indirect, as reported by Wood et al., (2009), direct (Ng & Wong, 2013), or both. More studies are warranted to explore this issue further.

### ***Gratitude: definition***

Observational and experimental evidence suggests that gratitude is associated with better sleep quality and longer (healthier) sleep duration, so in the present study we decided to use a gratitude intervention in order to test its impact on well-being and sleep. At this stage it is important, therefore, to explain what gratitude is. Gratitude has been conceptualised both as a disposition and a state (McCullough, Emmons, & Tsang, 2002; Wood, Froh, & Geraghty, 2010). While it was previously stipulated that gratitude is primarily associated with the appreciation and recognition of an altruistic gift or help from other people (Emmons & McCullough, 2003; McCullough et al., 2002), subsequent research has suggested that grateful individuals display a much broader appreciation of life and the world in general (Wood et al., 2010). Gratitude correlates positively with many adaptive personality characteristics (e.g., altruism, dutifulness, competence, gregariousness), life satisfaction and positive emotions. Relatedly, grateful individuals are less likely to be characterised by maladaptive personality traits and experience negative emotions including depression, envy, or anxiety. Grateful individuals also seem to attach less value to materialistic goals in life and display more prosocial behaviour (McCullough et al., 2002; Wood et al., 2010). Finally it is important to add that, firstly, gratitude is associated with positive well-being measures, for instance life satisfaction, over and above other personality characteristics (Wood, Joseph, & Maltby, 2008), and secondly, that it is distinct from other dispositional measures such as optimism or hope (McCullough et al., 2002).



## *Summary*

Taken together, growing evidence suggests that hedonic and eudaimonic well-being are correlated with healthier sleep, but it is less certain whether positive well-being leads to better sleep or is just its epiphenomenon. Therefore this study aimed to address this important issue by exploring whether modifying well-being would have a beneficial impact on sleep. Because to date the only positive psychology paradigm that has successfully improved (self-reported) sleep duration and quality was expressing gratitude exercise, I decided to use this technique in this study. The literature suggests that objective and self-report sleep measures are not always congruent (Lauderdale et al., 2008; Silva et al., 2007), and in Study 3 I concluded that objective and subjective sleep indices might to some extent be measuring distinct phenomena. Therefore I also aimed to establish whether expressing gratitude would improve sleep perceptions as well as the actual sleep behaviour.

Past gratitude interventions have been criticised for not including a true control group (Wood et al., 2010). For example, controls have been asked to write about early memories (Seligman et al., 2005), their typical day (Sheldon & Lyubomirsky, 2006) or experiences of the past week (Lyubomirsky et al., 2011). This is problematic as participants in any of these control groups could have potentially increased their well-being by simply expecting it to improve (the so-called demand effects) (Wood et al., 2010). To address this limitation I decided to have two control groups in my study: a waitlist control group and daily events group. I will discuss the intervention conditions in more detail in the Method section.

## **5.2 Hypotheses**

Based on the literature discussed above I formulated the following two hypotheses:

1. Participants reporting moderate distress and sleep problems randomised to a two week gratitude intervention would report greater improvements in well-being when compared with those in the waitlist or daily events conditions.

Since there is evidence that gratitude is directly associated with sleep (Ng & Wong, 2013) I also hypothesised that:

2. Randomisation to a two week gratitude programme would lead to greater improvements in subjective and objective sleep in individuals with moderate distress and sleep problems at baseline, in comparison with control conditions.

In this study eudaimonic well-being was assessed with the Flourishing Scale (Diener et al., 2010), while hedonic well-being was measured with The Scale of Positive and Negative Experience (Diener et al., 2010), and the Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983). Gratitude was assessed with the Gratitude Questionnaire-6 (McCullough et al., 2002). These measures will be described in more detail in the Method section.

## **5.3 Method**

### **5.3.1 Study design**

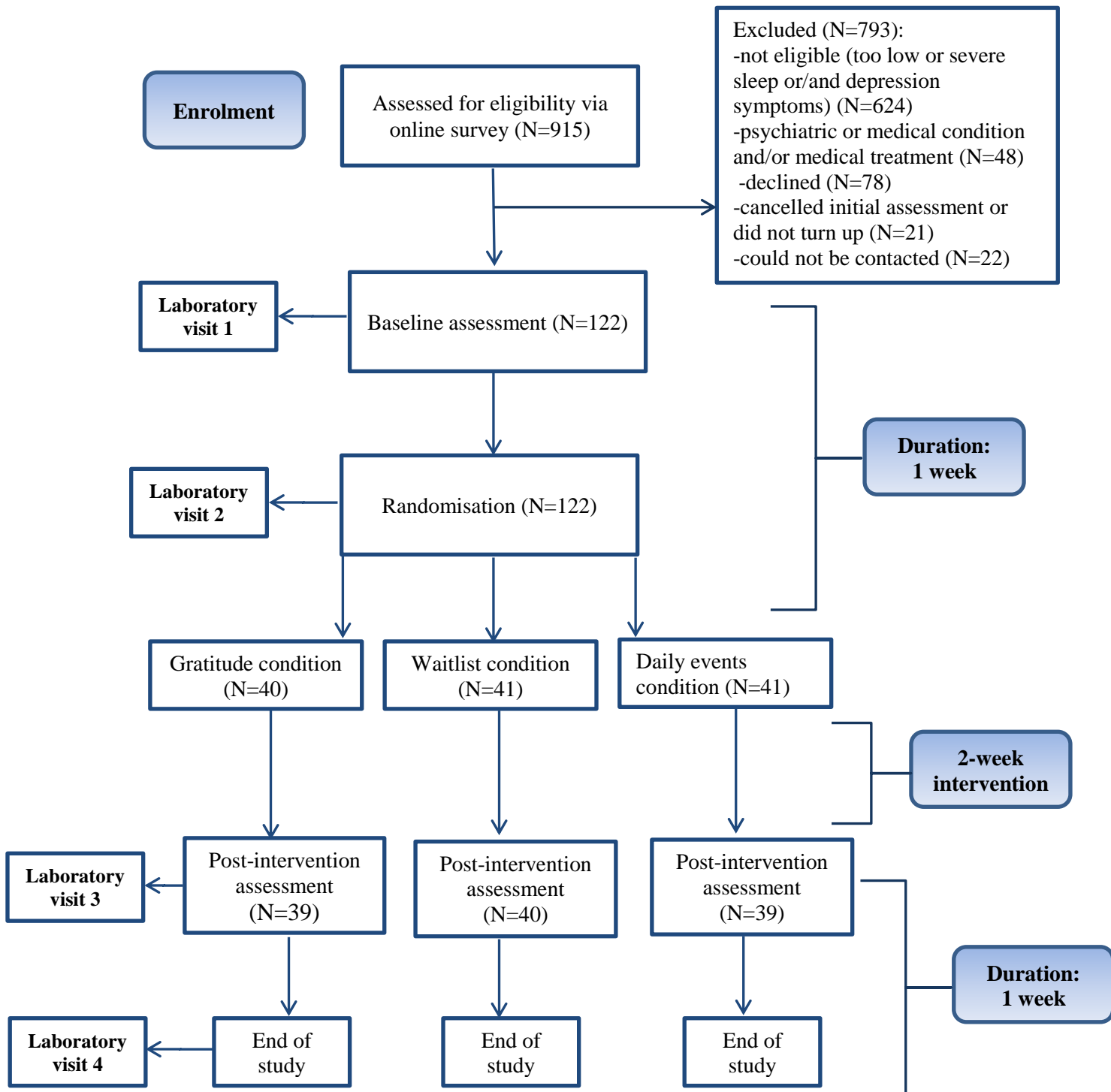
This study was a single-blinded randomised control intervention, which included two control conditions (waitlist and daily events) and the experimental condition –the gratitude group.

The study lasted four weeks and participants in all conditions attended the research laboratory four times in total (see Figure 5.2 for the CONSORT flow diagram depicting the study's design). During the initial visit, which was the start day of the baseline monitoring week, informed consent was obtained, and participants provided anthropometric measures and were given a set of questionnaires to complete at home, as well as a wrist accelerometer to assess their sleep. The accelerometer was worn for 7 nights as to provide a measure of objective sleep during both the week and weekend. All participants also provided ambulatory blood pressure and cortisol measures, which were both assessed over one full working day. The second visit took place one week later during which participants returned completed questionnaires and the accelerometer, and were informed about the study condition to which they had been randomly allocated. The gratitude and daily events groups were given paper diaries in which they were asked to practice their writing exercises. The intervention lasted two full weeks. The third meeting was the start day of the post-intervention monitoring week, and except for not taking anthropometric measures it was the same as the first session. Participants in the gratitude and daily events conditions were requested to bring their completed diaries to the third meeting, and were not asked to practice their writing exercises during the post-intervention monitoring week. During the final visit to the research laboratory participants returned completed questionnaires and the accelerometer, and were thanked for their participation.

This intervention study was conducted with another PhD student who collected ambulatory blood pressure and cortisol data as part of her PhD thesis. Both biological variables were collected over one day before and after the experimental/control tasks. Since neither of the measures is part of this study they will not be described here in detail. Similarly,

psychological and any other measures that were not part of this study will not be detailed here as well.

**Figure 5.2 CONSORT flow diagram.**



### 5.3.2 Participants

One hundred and twenty two women from UCL and University of London were recruited to this study through advertisement (emails and posters) (see Appendix 2 and 3). The recruitment took place between October 2011 and April 2013.

The initial eligibility criteria were being a healthy female, aged 18 to 45 years who was in full/part-time employment or/and a postgraduate student. Due to practical limitations men were not recruited to this study. Firstly, there were only small blood pressure cuffs available, which would not fit men with larger arms. Secondly, although past gratitude interventions included both sexes (Emmons & McCullough, 2003; Sheldon & Lyubomirsky, 2006) we anticipated that the nature of this intervention (i.e. improving well-being) might seem less appealing to men, and as a result could significantly lengthen the recruitment process.

Volunteers who showed an interest in participation were emailed the study's information sheet (see Appendix 4), and those who were still willing to take part were requested to complete a short online survey (see Appendix 5) to further establish their eligibility. The survey contained two questionnaires to screen for emotional distress and sleep disturbance as well as questions about regular medications, pregnancy, and the presence of a serious illness, for instance, heart disease, depression or insomnia in the last two years. Volunteers were also requested to provide their name, contact details and date of birth.

The 12-item General Health Questionnaire (GHQ-12) (Goldberg et al., 1997) was the measure of emotional distress, and the Jenkins Sleep Problems Scale (Jenkins et al., 1988) was the measure of potential sleep problems at the screening selection stage. I decided to use these scales because both have good psychometric properties and are relatively brief. The internal consistency of the GHQ-12 (Goldberg et al., 1997) and the Jenkins Sleep Problems Scale

(Jenkins et al., 1988) was .79 and .83, respectively. Based on the literature (Goldberg et al., 1997; Vahtera, Pentti, Helenius, & Kivimaki, 2006) I used cut-off points between 2 and 9 as an indication of emotional distress, and a mean score between 1.5 and 4 on the sleep questionnaire as an indication of moderate sleep problems. Thus participants with no symptoms of disturbed sleep and/or emotional distress, or those with severely disturbed mood and/or sleep (GHQ-12>10, mean sleep problems>4) were excluded from participation. To reduce variability in sleep data I decided not to recruit women older than 45 years since sleep patterns change with age (Ohayon et al., 2004). This also helped to ensure that women undergoing menopause were excluded. This is important since many women, but not all, experience disrupted sleep in the periods preceding and during the menopause (Manber & Armitage, 1999). Since pregnancy is often associated with disturbed sleep (Balsarak & Lee, 2011) women who were pregnant were excluded from participation as well.

Potential participants who scored within the above mentioned cut-off points on the emotional distress and sleep questionnaires, were currently not pregnant, not on any medications apart from the contraceptive pill and free of any medical or psychiatric condition in the last two years were telephoned to be recruited.

The study was approved by UCL Research Ethics Committee. Women who completed the study received a small honorarium.

### 5.3.3 Procedure

Participants provided ambulatory measures of blood pressure, cortisol, physical activity and sleep, but since only sleep is the focus in this study assessment of the remaining three variables is not described in detail here.

The first visit to the research laboratory was scheduled for any day between Monday and Thursday. After ensuring participants understood the study and had an opportunity to ask questions the informed written consent (see Appendix 6) was sought. Next participants' weight and height were measured, which were later used to calculate body mass index (BMI,  $\text{kg/m}^2$ ) (see Table 5.1 for all measures and the duration of their assessment). Following instructions participants were given two questionnaires to complete at home as well as the wrist accelerometer to wear for 7 days and nights. The ActiGraph GT3X (ActiGraph, Pensacola, Florida, US) was the accelerometer used for objective sleep assessment in this study. During the first session in the laboratory participants were also fitted with an ambulatory blood pressure monitor and were given a set of 7 plastic tubes to collect their saliva, as to obtain a measure of ambulatory cortisol. Both variables were assessed over one full day.

The second visit to the research laboratory took place a week after the initial one, during which participants returned completed questionnaires and the accelerometer, and were informed about the condition (waitlist, daily events or gratitude) to which there had been randomly assigned. In total 40 participants were randomly allocated to the gratitude condition, 41 to the daily events condition and 41 to the waitlist condition. Participants in the daily events and gratitude conditions were provided with a paper diary for writing their exercises. Both groups were instructed to practice their writing tasks for 2 weeks. During the next two weeks respondents in both conditions received two emails reminding them to continue doing their writing exercises. Participants in the waitlist condition were informed that they would receive their writing task in three weeks time, and they were asked to go on about their lives as usual in the next two weeks.



The third visit to the research laboratory was scheduled two weeks later. Participants in the daily events and gratitude conditions returned their writing tasks and participants in all study groups were given two questionnaires to complete at home, as well as the wrist accelerometer to wear for 7 days and nights, so apart from not taking the anthropometric measures this visit was the same as the initial session in the laboratory.

The last visit to the research laboratory took place a week later during which questionnaires and the wrist accelerometer were returned. Participants were debriefed, thanked for their time and received a £30 honorarium. To ensure a fair treatment participants in the waitlist condition received their payment at this time as well. They were then given the gratitude writing task to complete and return in two weeks time. Since the waitlist condition was the control condition reminder emails were not sent to these participants, and those who did not return their gratitude diaries were not followed-up.

**Table 5.1 List of measures and their duration of assessment.**

	Baseline monitoring period			Post-intervention monitoring period		
	Timeline			Timeline		
	Once	One full day	One full week	Once	One full day	One full week
Anthropometric measures	√					
Sociodemographic characteristics	√					
Health-related variables <sup>1</sup>	√					
Well-being measures	√			√		
Sleep disturbance (PSQI)	√			√		
Daily sleep quality and duration			√			√
Objective sleep measures			√			√
Ambulatory cortisol		√			√	
Ambulatory blood pressure		√			√	

<sup>1</sup>=Refers to smoking and physical activity; PSQI=Pittsburgh sleep quality index.

### 5.3.4 Measures

#### 5.3.4.1 Background measures

Participants' age, ethnicity, marital status, family situation, education and economic status were measured by a self-completion questionnaire, in which from among a range of possible answers respondents selected those that most closely described their demographic and economic circumstances (see Appendix 7, section 1). Occupation was assessed by asking participants to select the category that best described their current employment, for example "Administrative/clerical", "Manual and craft" (e.g., cleaner, security), "Non-clinical research" (e.g., research associate, research nurse), "Postgraduate student". However, because only 16 participants were employed with the rest being a postgraduate student, in this study current occupation was reclassified into "Employed" and "Postgraduate student".

Educational attainment was assessed with 8 possible categories (see Appendix 7, section 1) ranging from "No qualifications", "GCSE/'O'Levels" to "Postgraduate qualification". Only 1 person reported "A or AS level" qualification, while 70 respondents selected an "Undergraduate degree" category, and the remaining 51 chose "Postgraduate degree". Therefore educational attainment was reclassified into "Undergraduate degree or less" and "Postgraduate degree".

Since participants were recruited mostly from among UCL and University of London postgraduate students ethnicity was assessed with 16 possible categories (see Appendix 7, section 1), to account for the fact that both institutions have multi-ethnic and multi-national student populations. Seventy three per cent of respondents were White Caucasians (including White British, White Irish and any other White background), 9% were Chinese, 6.5% were

Asian and approximately 4% were Black. Since the majority was White Caucasians ethnicity was reclassified into “White” and “Other”.

Given that the majority of participants were students I decided to use annual household income (as opposed to annual personal income) as the measure of socioeconomic status (SES). Annual household income was assessed in 10 income bands (e.g., “Less than £9,999”; “£10,000 - £14,999”; up to “More than £200,000”). For the purpose of analyses described here this variable was reclassified into 3 groups: “<£25,000”, “£25,000-£49,000” and “>£50,000”.

#### 5.3.4.2 **Objective sleep assessment**

Objective sleep was measured with the ActiGraph GT3X (ActiGraph, Pensacola, Florida, US) over 7 nights before and after the intervention/control tasks. The GT3X is a light (27 grams) and small device that looks like a watch (see Figure 5.3 below). Although traditionally it was recommended that a wrist actigraph should be worn on the non-dominant wrist, more recent studies suggested that sleep can be reliably measured on both wrists (Stone & Ancoli-Israel, 2011). Therefore participants were permitted to wear the actigraph on either wrist, but were requested to use the same one during both assessment periods.

As mentioned, participants were requested to wear the accelerometer for 7 nights, but in exceptional circumstances (e.g., travel, shortage of actigraphs) the actigraph was worn for 6 nights.

**Figure 5.3 GT3X ActiGraph used in the study.**



In addition to wearing the accelerometer participants were instructed to complete a sleep diary providing information about bed and wake up time (see Appendix 8). To maximise the accuracy of recall respondents were encouraged to fill in the diary in the morning. This information was collected in order to process sleep data with sleep software.

ActiLife software version 5.8.3 (ActiGraph, Pensacola, Florida, US) was the sleep scoring software utilised in this study. Using bed and wake up time provided by participants and recorded wrist movements the sleep software calculated the following sleep variables: time of sleep onset, sleep latency (time needed to fall asleep), total sleep time, time spent awake after initial sleep onset, number of night-time awakenings, average time spent awake, and sleep efficiency (the proportion of total sleep period during which the person was asleep). Sleep scoring was performed with the Cole-Kripke algorithm that is recommended for adult and young populations (Cole, Kripke, Gruen, Mullaney, & Gillin, 1992). After sleep parameters were calculated baseline and post-intervention sleep outputs were visually inspected to remove artefacts. Sleep efficiency of 100%, zero or very few total movement

counts, and no awakenings were an indication that the wrist actigraph was not worn on a given night, so was treated as missing data (see Figure 5.4 below for an example of this).

**Figure 5.4 Sleep output from the ActiLife software.**

Sleep Scores									
In Bed	Out Bed	Sleep Onset	Latency	Total Sleep Time	Time Awake	Awakenings	Avg Awakening	Total Counts	Efficiency
08/03/2013 01:30	08/03/2013 12:00	08/03/2013 01:30	0 min	577 min	53 min	21	2.52 min	26659	91.56%
09/03/2013 01:40	09/03/2013 11:30	09/03/2013 01:40	0 min	547 min	43 min	17	2.53 min	32723	92.71%
10/03/2013 00:45	10/03/2013 11:00	10/03/2013 00:45	0 min	563 min	52 min	29	1.79 min	27982	91.54%
11/03/2013 00:30	11/03/2013 10:30	11/03/2013 00:30	0 min	600 min	0 min	0	0 min	326	100%
12/03/2013 01:15	12/03/2013 09:40	12/03/2013 01:15	0 min	466 min	39 min	23	1.7 min	26495	92.28%
13/03/2013 00:20	13/03/2013 07:15	13/03/2013 00:20	0 min	386 min	29 min	19	1.53 min	16808	93.01%
14/03/2013 01:00	14/03/2013 09:00	14/03/2013 01:00	0 min	453 min	27 min	15	1.8 min	16036	94.38%

Sleep data highlighted in yellow are an indication that the actigraph was not worn on that night.

In this study I focused on 4 measures: sleep latency, total sleep time, sleep efficiency and number of night-time awakenings. To calculate these sleep measures I averaged values across nights 2-6 at baseline and post-intervention. Data from the first night of both assessments periods were excluded to account for the fact that this night of sleep monitoring might have been unusual to some participants. Although the wrist actigraph used in this study was a relatively small device it was nonetheless possible that it could have impacted sleep quality and/or duration in some women. Because not all respondents wore the actigraph for 7 nights data from the last night of sleep monitoring were excluded as well.

### 5.3.4.3 Subjective sleep assessment

The Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989), one of the most widely used sleep questionnaires, was the subjective sleep measure in this study (please see Chapter 1

page 111 for a more detailed description of the scale). The PSQI comprises of 19 items assessing various aspects of sleep, for example, sleep latency, sleep duration or sleep efficiency. Apart from sleep duration, sleep latency, bed and wake up time the remaining sleep items are rated on a 4-point Likert scale ranging from 0="Not during the past week" to 3="Three or more times per week" (see Appendix 7, section 3). During both monitoring periods participants completed this scale with reference to the past week. Raw questionnaire responses were entered into the PSQI scoring database downloaded from University of Pittsburgh Sleep Medicine Institute (<http://www.sleep.pitt.edu/content.asp?id=1484&subid=2316>) (see Appendix 9). After scores were entered for each participant the database, which is a Microsoft Access document, automatically calculated various subjective sleep measures, such as sleep latency, sleep efficiency, or sleep disturbance as well as a total sleep score. Greater total scores are indicative of more disturbed sleep, and in this study the scores ranged from 1 to 15 at baseline, and from 0 to 15 post-intervention. The scale's internal consistency both at baseline and post-intervention was .76.

#### 5.3.4.4 Other sleep measures

In addition to the two sleep measures described above I also asked participants to provide daily sleep quality ratings (ranging from 0="Very good", 1="Fairly good", 2="Fairly bad" to 3="Very bad") and daily sleep duration. This information was recorded in sleep diaries (see Appendix 8) along with bed and wake up time over the baseline and post-intervention monitoring week. These data were collected to assess daily variations in sleep perceptions that were less likely to be captured by the PSQI (Buysse et al., 1989), which was administered once at baseline and once post-intervention.

Average baseline daily sleep quality and duration scores were computed by taking a mean of sleep ratings from nights 2 to 6. I excluded ratings for night 1 since sleep on the first night might have been unusual for participants. Participants who did not wear the actigraph on night 7 also did not complete the sleep diary, so to account for this I excluded information on daily sleep quality and duration for night 7 for all participants. Post-intervention daily sleep ratings were computed in the same fashion. With regard to sleep quality, higher scores were reflective of more disturbed sleep. For clarity I will refer to these two measures as daily sleep quality and daily sleep duration.

#### 5.3.4.5 Eudaimonic well-being

##### *Flourishing*

The Flourishing Scale described by Diener et al., (2010) was used to measure eudaimonic well-being in this study. This recently developed scale has a good internal reliability (Cronbach's alpha .87), and was designed to assess aspects of people's lives such as positive relationships with others, purpose in life, or competence (see Appendix 7, section 6). The scale consists of 8 items rated on a 7-point Likert scale ranging from 1="Strongly disagree" to 7="Strongly agree". The scores were totalled with higher scores reflecting greater eudaimonic well-being, and during both monitoring weeks the scale was completed without a specific time frame. At baseline the scale ranged from 12 to 56, while the range at post-intervention was 24-56. The Cronbach's alpha at baseline and post-intervention was as follows: .85 and .84, respectively.



## ***Gratitude***

The Gratitude Questionnaire-6 (GQ-6) was the measure of gratitude in this study (McCullough et al., 2002). I decided to use this scale since it has high internal consistency (Cronbach's  $\alpha=.82$ ) (McCullough et al., 2002), it is brief, and it has been widely used (Wood et al., 2010). The GQ-6 comprises of 6 items (see Appendix 7, section 5) measuring intensity and frequency of grateful affect towards life in general (e.g., "I have so much in life to be thankful for"), as well as towards other people (e.g., "I am grateful to a wide variety of people"). The items are rated on a 7-point Likert scale, which greater scores indicating higher gratitude. During both monitoring periods participants completed this scale with reference to the past week. In this study scores were averaged and ranged from 3.5 to 7 at baseline and from 2.83 to 7 at post-intervention. The internal consistency at baseline and post-intervention was acceptable and was as follows: .67 and .74, respectively.

### **5.3.4.6 Hedonic well-being**

#### ***Positive and negative affect***

The Scale of Positive and Negative Experience (SPANE) (Diener et al., 2010) was used to assess positive and negative affect in this study (see Appendix 7, section 4). The scale has a very good internal consistency (.87 for positive affect, .81 for negative affect and .89 for the overall scale) (Diener et al., 2010). The SPANE consists of 12 items, of which 6 measure positive affect (e.g., "Positive", "Good", "Joyful") and 6 negative affect (e.g., "Negative", "Unpleasant", "Angry"). The items are rated on a 5-point Likert anchored from 1="Very rarely or never" to 5="Very often or always", and higher scores reflect greater frequency of positive/negative emotions. In this study, during baseline and post-intervention monitoring weeks, respondents completed this questionnaire with reference to the past week. Scores on

each sub-scale were averaged and mean positive affect ranged from 1.83 to 4.83 at baseline, and from 1.50 to 5 post-intervention. Baseline and post-intervention negative affect mean scores ranged from 1 to 4.17 and from 1 to 4.33, respectively. The internal consistency for baseline positive scale was .87 while for post-intervention it was .90. The internal consistency for negative affect scales was somewhat lower since at baseline it was .77 and at post-intervention it was .82.

### ***Emotional distress***

Emotional distress was assessed with the Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983). The scale has very good psychometric properties, and although it was originally developed to be used in a clinical setting it is a reliable measure of depressive and anxiety symptoms in non-clinical samples as well. Since the HADS (Zigmond & Snaith, 1983) does not include items assessing physical symptoms of emotional distress (e.g., loss of appetite) it is capable of detecting lower levels of distress (Herrmann, 1997). The HADS (Zigmond & Snaith, 1983) consists of 14 items (see Appendix 7, section 10) of which 7 refer to anxiety symptoms (e.g., “I feel tense or wound up”, “I get a sort of frightened feeling as if something awful is about to happen”), and the remaining half to depressive symptoms (“I feel as I am slowed down”, “I have lost interest in my appearance”). The items were rated on a 4-point Likert scale (ranging from 0 to 3), and during both monitoring weeks participants completed the HADS with reference to the past week. In this study I computed (by totalling) an overall baseline (range 3-26) and post-intervention (range 1-34) emotional distress score. Higher scores reflected greater emotional distress. The internal consistency of the total scale at baseline and post-intervention was .81, and .84, respectively.

#### 5.3.4.7 **Intervention writing tasks**

Details relating the content of the writing tasks, their duration and frequency were decided by myself and the other PhD student with whom this intervention was carried out.

To recapitulate, expressing gratitude was the intervention condition, and the daily events and waitlist groups were both control conditions. As already mentioned in the Introduction, past gratitude interventions have been criticised for lacking a true control group (Wood et al., 2010), so to address this serious limitation this study had a waitlist condition as well. The main rationale for having a waitlist as a control, as opposed to not offering anything to this group, was to reduce attrition rate. We anticipated that the prospect of being given a writing task after week 4 as opposed to after week 1 would motivate participants to complete the post-intervention assessment.

Participants in the gratitude and daily events conditions were given oral instructions about their writing tasks during the second visit to the research laboratory; both conditions were also provided with written instructions in their diaries (the diaries were the size of an A4 paper). The instructions for both writing tasks were an abridged version of those used in a study by Sheldon and Lyubomirsky (2006) (see Figures 5.5 and 5.6 below). Briefly, participants in the gratitude condition were asked to express gratitude towards people, as well as other things in their life regardless of whether they were large or small. To ensure participants understood the task examples were provided, and respondents were encouraged to express gratitude about previously unappreciated things or persons.

Participants in the daily events condition were requested to record things that happened to them, and/or things that they noticed during each day they completed the paper diary. To keep the task neutral respondents were encouraged to notice things and/or events irrespectively

of whether they were pleasant, neutral or unpleasant. To ensure the task was understood examples of possible things/events were provided.

### **Figure 5.5 Gratitude writing exercise instructions.**

*You have been randomly assigned to try to cultivate a sense of gratitude now, and during the next few weeks. "Cultivate a sense of gratitude" means that you make an effort to think about the many things in your life, both large and small, that you have to be grateful for. These might include particular supportive relationships, sacrifices or contributions that others have made for you, facts about your life such as your advantages and opportunities, or even gratitude for life itself, and the world that we live in.*

*For example: I am grateful... 'To my husband for paying me a compliment on my new dress', 'That I found the strength to deal with a difficult situation at work', 'That I finally cleaned my flat', 'for the kindness of my parents', 'I am grateful that the trees are finally green', 'I am grateful I was given a seat in the bus this morning', 'I am grateful my cat is no longer unwell', 'After watching this evening news I am grateful I live in a peaceful country'...*

*In all of these cases you are identifying previously unappreciated aspects of your life, for which you can be thankful. You may not have thought about yourself in this way before, but research suggests that doing so can have a positive effect on your mood and life satisfaction.*

*When you get home, we'd like you to write about 3 things you are grateful for. We would like you to do this 3 times per week. You should spread out your writing exercises e.g. every other day such as Monday, Wednesday, Friday. We would like you to do this for 2 weeks (6 writing exercises in total). Please try to write something different every time.*

*We have provided boxes for you to write your sentences on the next 2 pages, you do not have to fill the entire space. Please provide the day of the week you wrote your exercise, so that you can keep track."*

### **Figure 5.6 Daily events writing exercise instructions.**

*"You have been randomly assigned to write about events that have happened during your day. We want you to start focusing your attention on everyday events, and become more aware of what is happening around you. For example, on your way to work instead of rushing to a bus stop, or a train station, try not to think about or plan your day, but pay attention to your surroundings. Perhaps listen if birds are singing, look at the flowers in people's front gardens, or just simply observe the things around you. You may not have thought about yourself in this way before, but research suggests that doing so can have a positive effect on your mood and life satisfaction.*

*For example, today I noticed... 'The wind rustling in the trees', 'The colours of the flowers', 'My neighbour's children playing in the garden', 'The noise of the traffic', 'The first signs of autumn', 'The smell of grass after the rain', 'Other people talking in the train', 'The building opposite my office was being cleaned'.*

*When you get home, we'd like you to write about 3 different events that happened that day. We would like you to do this 3 times per week. You should spread out your writing exercises e.g. every other day such as Monday, Wednesday, Friday. We would like you to do this for 2 weeks (6 writing exercises in total). Please try to write something different every time.*

*We have provided boxes for you to write your sentences on the next 2 pages, you do not have to fill the entire space. Please provide the day of the week you wrote your exercise, so that you can keep track. "*

In the past studies the duration of expressing gratitude varied from 2 (Emmons & McCullough, 2003) to 8 weeks (Lyubomirsky et al., 2011). However, the main difference between the current and previous gratitude interventions is that in this study in addition to expressing gratitude participants were also required to provide a week of baseline and a week of post-intervention ambulatory measures. This lengthened the study's duration considerably, so we decided that two weeks of writing exercises would be most feasible. We hoped that this would make participation more attractive as well as reduce attrition. To compensate for the relatively short period of experimental manipulation we asked participants to practice their gratitude exercises 3 times a week, on every other day, so in total they were required to complete 6 writing exercises. In the studies where gratitude exercises were practiced for up to 6 or 8 weeks (Boehm et al., 2011; Lyubomirsky et al., 2011) participants were required to express gratitude once a week. So although the experimental manipulation lasted longer in these studies than in this intervention, the number of required gratitude exercises was very similar.

In order to standardise the number of times a given writing task was performed we asked participants in the gratitude condition to express gratitude about three things or towards three people each day they wrote in their diary, while those in the daily events condition were requested to write about three events and/or things they noticed on that particular day (see Appendix 10).

Emails reminding participants to continue with their writing tasks as instructed (see Appendix 11) were sent in the middle of the second and third week of the study. The content of the emails was the same for both groups. As already mentioned in the Procedure subsection participants in the waitlist condition were not sent reminder emails.

#### 5.3.4.8 Other measures

##### *Effort invested in the intervention tasks*

To assess how much effort participants in the gratitude and daily events conditions had invested into their writing tasks both groups were required to answer the following two questions: “How many times did you do the writing exercises?” (answers could range from “Once” to “6 times”), and “How much effort did you put into the writing task overall?” with the possible responses being “Very little effort”, “Quite a bit of effort” and “A lot of effort”.

##### *Health behaviours*

Physical inactivity (Driver & Taylor, 2000; Physical Activity Guidelines Advisory Committee, 2008), smoking (Stranges et al., 2008; Zhang et al., 2006), and alcohol consumption have been found relevant to sleep experience (Magee et al., 2009), so were measured in this study (see Appendix 7, section 2).

Physical activity was assessed with an amended version of the scale previously used in the Whitehall II cohort study (Marmot & Brunner, 2005). Participants were asked how often they engaged in mild (e.g., walking, general household chores), moderate (e.g., leisurely swimming, cycling) and vigorous (e.g., running, tennis) physical activity. The responses could range from 0=“Never/hardly ever” to 3=“Three times or more a week”. Scores were summed (range 0-6) with higher scores reflecting more frequent physical activity.

Smoking was measured by asking participants to indicate whether they smoked, and those who reported they were smokers were further asked to indicate how many cigarettes they smoked a day.

Information on alcohol consumption was obtained in the same fashion. Participants were requested to answer a question: “Do you drink alcohol”, and those who responded positively were also requested to state on how many days in the past two weeks they consumed alcohol, and to provide a number of alcoholic drinks they had on those days.

## **5.4 Statistical analysis**

### **5.4.1 Attrition of participants**

To recapitulate, 122 women were recruited but 4 dropped out after the first week, so in total 118 completed the study. Those who did and did not complete the study did not differ in terms of age ( $P=0.462$ ), relationship status ( $P=0.422$ ), parental status ( $P=0.844$ ), SES (household income) ( $P=0.273$ ), ethnicity ( $P=0.705$ ), educational attainment ( $P=0.558$ ), and current occupation (employment vs. postgraduate student) ( $P=0.566$ ). Women who dropped out of the study also did not differ from those who completed the study with regard to health-related variables (BMI ( $P=0.255$ ), smoking ( $P=0.655$ ), alcohol consumption ( $P=0.519$ ), physical activity ( $P=0.411$ ), and affective responses including emotional distress (HADS total score) ( $P=0.629$ ), and negative affect ( $P=0.655$ ).

### **5.4.2 Objective sleep data loss**

Due to technical difficulties with the sleep software (e.g., incurred whilst initializing the actigraphs) and failure of the actigraphs there were objective sleep data available for 115 participants at baseline, and for 116 respondents at post-intervention (see Table 5.2 below for the distribution of missing sleep data across the conditions). There were no differences between participants who did and did not have objective sleep data in terms of age ( $P=0.468$ ), relationship and parental status ( $P=0.329$ ,  $P=0.740$ , respectively), current occupation



( $P=0.229$ ), educational attainment ( $P=0.377$ ), ethnicity ( $P=0.611$ ), household income ( $P=0.276$ ), or health-related variables (smoking ( $P=0.528$ ), alcohol consumption ( $P=0.088$ ), physical activity ( $P=0.611$ ), BMI ( $P=0.456$ ). Respondents for whom objective sleep information was unavailable reported higher baseline negative affect (mean=3.0; SD=0.8) than those who provided these data (mean=2.4; SD=0.6) ( $P=0.033$ ), but there were no differences with regard to emotional distress ( $P=0.443$ ). It is unclear why participants without objective sleep data had higher negative affect, but one explanation might be a chance finding.

**Table 5.2 Distribution of missing objective sleep data across the study's conditions.**

Condition	Baseline assessment	Post-intervention assessment
	N*=7	N=6
Gratitude	2	2
Daily events	4	3
Waitlist	1	1

\*Number of participants without objective sleep data.

#### 5.4.3 Distribution of data

The distribution of data was determined by plotting histograms and by looking at the values of kurtosis and skewness, and if needed was logarithmically transformed. Subjective sleep disturbance (PSQI scores) (post-intervention), objective sleep duration (baseline and post-intervention), and number of night-time awakenings (baseline and post-intervention) were normally distributed. However, baseline subjective sleep disturbance (PSQI scores) and objective sleep latency (baseline and post-intervention) data were positively skewed, while

sleep efficiency (baseline and post-intervention) data were negatively skewed, thus these variables' distribution was log transformed prior to analyses. Daily ratings of sleep quality and duration (baseline and post-intervention) were normally distributed.

Eudaimonic and hedonic well-being measures were normally distributed as well.

#### 5.4.4 **Statistical approach to explore possible covariates**

Univariate analysis of variance (ANOVA) and Chi-squared tests were used to determine whether there were any baseline differences across the study's conditions in terms of socio-demographic characteristics, health-related variables, as well as sleep and well-being measures. The associations between baseline measures of sleep (self-reported and objective) and well-being with potential covariates were examined with Pearson product-moment correlations, *t*-tests and ANOVAs, as appropriate.

#### 5.4.5 **Main analyses**

The first research hypothesis was tested with a repeated measures ANOVA where the eudaimonic and hedonic well-being measures taken before and after the intervention were the within-subject factor, and the condition (waitlist, daily events, gratitude) was the between-subject factor. A separate repeated measures ANOVA was performed for each of the eudaimonic and hedonic well-being measure. Since the repeated measures (i.e. eudaimonic and hedonic well-being) were assessed only twice the assumption of sphericity was not an issue in this study (Field, 2009, p. 451), but the homogeneity of variance was explored for each of the three conditions by looking at the Levene's test of equality of error of variances table in SPSS output. To avoid repetition unless the homogeneity of variance was violated the results of the Levene's test will not be reported here. If the results of a repeated measures ANOVA revealed a significant interaction term between the condition and a given well-being

measure this was then further explored with a post hoc test, or separate repeated measures ANOVAS for the different conditions, as appropriate. In this study I used the least-significance difference (LSD) pairwise comparison test as post hoc. For the purpose of these tests I calculated a change score ( $\Delta$ ) in well-being measures by subtracting baseline values from those at post-intervention (absolute change), so higher scores indicated greater improvements in positive well-being, while lower scores were suggestive of reduction in negative affect and emotional distress.

The second research hypothesis was tested in two steps. First I conducted a repeated measures ANOVA where baseline and post-intervention sleep scores or values (for objective sleep measures) were the within-subject factor, and the condition was the between-subject factor. The homogeneity of variance was explored for each of the three conditions, but to avoid repetition unless it was violated the results of the Levene's test will not be reported here. Next, an interaction term between a sleep measure and the condition, if statistically significant, was followed-up with a post hoc test (LSD pairwise comparisons test) to determine whether the change in sleep ( $\Delta$ sleep) in the gratitude condition was significantly different from the control groups. The  $\Delta$ sleep was computed by subtracting baseline values from post-intervention values. A higher/positive  $\Delta$ sleep was an indication of an increase in sleep duration (objective and daily duration) and sleep efficiency, while a negative  $\Delta$ sleep was suggestive of reduced sleep disturbance on the PSQI scale (Buysse et al., 1989), shortened sleep latency, fewer night-time awakenings and improved daily sleep quality post-intervention.

All results are presented as F-statistics and P-values, Pearson correlation coefficients ( $r$ ) and P-values, and means and standard deviations, as appropriate. The analyses were performed with SPSS package version 20.

## **5.5 Results**

### **5.5.1 Sample characteristics**

Descriptive statistics stratified by the condition are depicted in Table 5.3. There were no statistically significant differences in terms of socio-demographic, economic or health-related variables between the study's three conditions. This suggests that based on these variables the randomisation was successful. The average age was 26 years old, with the majority of women being single and White. In all 3 conditions over 85% of participants were currently undertaking a postgraduate degree, while the remainder of the sample was either in full- or part-time employment. In terms of health-related variables the majority of respondents reported drinking alcohol, but there were few smokers and the average BMI was 22, which suggests a normal, healthy weight.

**Table 5.3 Participants characteristics stratified by the condition.**

Variable	Mean (SD) /frequency (%)			P-value
	Gratitude (N=40)	Daily events (N=41)	Waitlist (N=41)	
Age	26.0 (4.8)	26.8 (5.0)	26.0 (4.9)	0.711
Relationship status				0.648
Married/cohabiting	13 (32.5%)	12 (29.3%)	16 (39.0%)	
Single	25 (62.5%)	29 (70.7%)	25 (61.0%)	
Children				0.805
Yes	2 (5.0%)	2 (4.9%)	1 (2.4%)	
No	38 (95.0%)	39 (95.1%)	40 (97.6%)	
Ethnicity				0.639
White Caucasian	27 (67.5%)	31 (75.6%)	31 (75.6%)	
Other	13 (32.5%)	10 (24.4%)	10 (24.4%)	
Educational attainment				0.666
Undergraduate degree or less	23 (57.5%)	22 (53.7%)	26 (63.4%)	
Postgraduate degree	17 (42.5%)	19 (46.3%)	15 (36.6%)	
Current occupation				0.939
Full/part-time employment	5 (12.5%)	5 (12.2%)	6 (14.6%)	
Postgraduate student	35 (87.5%)	36 (87.8%)	35 (85.4%)	
Household income				0.292
<£25,000	18 (45.0%)	20 (48.8%)	19 (46.3%)	
£25,000-£49,000	7 (17.5%)	13 (31.7%)	11 (26.8%)	
>£50,000	10 (25.0%)	4 (9.8%)	11 (26.8%)	
Current smoker				0.138
Yes	5 (12.5%)	1 (2.4%)	6 (14.6%)	
No	34 (85%)	40 (97.6%)	35 (85.4%)	
BMI (kg/m <sup>2</sup> )	22.4 (3.7)	22.3 (2.8)	22.4 (3.0)	0.980
Habitual physical activity	2.9 (1.9)	2.7 (1.5)	3.5 (1.8)	0.119

Alcohol consumption				0.217
Yes	35 (87.5%)	31 (75.6%)	35 (85.4%)	
No	4 (10.0%)	10 (24.4%)	6 (14.6%)	

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SD=standard deviation; BMI=body mass index.

### 5.5.2 Baseline sleep measures

Table 5.4 depicts baseline sleep measures calculated separately for each condition. As can be seen in all 3 conditions mean baseline PSQI scores (Buysse et al., 1989) were greater than 5, which suggests that women recruited to this study reported disturbed sleep. However, objective sleep assessment suggested that sleep efficiency was good, and the average objective sleep duration ranged from 6.8 (gratitude condition) to 7.3 hours (waitlist condition). These objective sleep data are similar to those reported in another study of young women (mean age 30 years old) (Tworoger et al., 2005).

More importantly, there were few differences between the study's conditions in terms of sleep parameters. There were no significant differences between sleep disturbance scores on the PSQI (Buysse et al., 1989) ( $P=0.436$ ), and there was also no difference in daily sleep quality across the study's conditions ( $P=0.304$ ). However, there was a significant difference in daily sleep duration between the conditions ( $P=0.045$ ), and a post hoc test (LSD pairwise comparison test) revealed that the average sleep duration was shorter in the gratitude condition (7.3 hours,  $SD=0.9$ ) than in the waitlist condition (7.8 hours,  $SD=1.0$ ) ( $P=0.018$ ).

In terms of objective sleep data participants in the three conditions did not differ with regard to average night-time awakenings ( $P=0.979$ ), sleep latency ( $P=0.240$ ) and sleep efficiency ( $P=0.508$ ). There was a significant difference in sleep duration across the conditions ( $P=0.034$ ), and post hoc analysis (LSD pairwise comparison test) showed that mean

sleep duration in the gratitude condition (6.8 hours, SD=1.0) was shorter than the duration in the waitlist condition (7.3 hours, SD=0.8) (P=0.019). Thus the self-report difference in sleep duration was corroborated by the objective measure. There were no other differences in sleep duration between the study's conditions.

**Table 5.4 Baseline sleep measures stratified by the condition.**

Sleep measure	Mean (SD)			P-value
	Gratitude (N=40)	Daily events (N=41)	Waitlist (N=41)	
Sleep disturbance (PSQI)	6.3 (2.2)	6.3 (2.7)	7.0 (3.3)	0.436
Daily sleep quality <sup>1</sup>	1.1 (0.4)	1.0 (0.4)	0.9 (0.4)	0.304
Daily sleep duration	7.3 (0.9)	7.4 (1.0)	7.8 (1.0)	<b>0.045</b>
Objective sleep measures:				
Duration	6.8 (1.0)	6.9 (0.9)	7.3 (0.8)	<b>0.034</b>
Latency <sup>2</sup>	6.9 (6.9)	5.1 (5.4)	4.8 (5.3)	0.240
Night-time awakenings	16.6 (6.7)	16.3 (5.8)	16.6 (6.1)	0.979
Efficiency <sup>2</sup>	87.2 (8.4)	88.9 (5.6)	88.4 (5.9)	0.508

SD=standard deviation; PSQI=Pittsburgh sleep quality index; <sup>1</sup>= higher scores reflect poorer sleep quality; <sup>2</sup>= untransformed data.

### 5.5.3 Baseline well-being measures

Baseline well-being measures (stratified by the condition) are presented in Table 5.5. There was no difference between the study's conditions with regard to flourishing scores

( $P=0.682$ ) and positive affect ( $P=0.454$ ). Importantly, there were also no baseline differences in gratitude scores ( $P=0.638$ ), negative affect ( $P=0.704$ ) and emotional distress (HADS total score) ( $P=0.963$ ). HADS ratings were high on average, confirming the emotional distress of the participants in the study.

**Table 5.5 Baseline well-being measures stratified by the condition.**

Well-being measure	Mean (SD)			P-value
	Gratitude (N=40)	Daily events (N=41)	Waitlist (N=41)	
Flourishing	42.2 (7.8)	41.9 (8.2)	43.2 (5.8)	0.682
Gratitude	5.6 (0.8)	5.6 (0.8)	5.8 (0.8)	0.638
Positive affect (SPANE)	3.4 (0.7)	3.3 (0.7)	3.4 (0.6)	0.454
Negative affect (SPANE)	2.4 (0.6)	2.4 (0.7)	2.5 (0.6)	0.704
Emotional distress (HADS)	13.4 (6.2)	13.6 (5.4)	13.2 (5.5)	0.963

SD=standard deviation; SPANE=the scale of positive and negative experience; HADS=the hospital anxiety and depression scale.

In summary, the results presented above indicate that except for objective and daily sleep duration there were no baseline differences in sleep and well-being measures across the study's conditions. Respondents in the gratitude condition had longer reported and actual sleep hours than those in the waitlist condition, but overall the randomization process was successful.



## 5.5.4 Baseline sleep measures and covariates

### 5.5.4.1 Subjective sleep disturbance (PSQI)

Subjective sleep disturbance was unrelated to age, relationship and parental status, ethnicity, educational attainment, current occupation (employment vs. postgraduate student) and household income. PSQI scores were unrelated BMI, physical activity, alcohol consumption and smoking as well. In terms of affective responses greater sleep disturbance was more prevalent among respondents with higher emotional distress ( $r=0.49$ ,  $P<0.001$ ) and negative affect ( $r=0.47$ ,  $P<0.001$ ). This is in line with the sleep literature (Benca et al., 1992; Benca & Peterson, 2008).

### 5.5.4.2 Daily sleep ratings

#### *Daily sleep duration*

Participants with a postgraduate degree reported slightly shorter sleep hours (mean=7.3, SD=1.0) than those with an undergraduate degree (mean=7.7, SD=0.9) ( $P=0.015$ ), but there was no association with age, marital and parental status, respondents' household income, ethnicity or current occupation. Similarly, smoking, alcohol consumption, BMI and physical activity were not linked to this measure of sleep duration. Neither emotional distress ( $P=0.181$ ) nor negative affect ( $P=0.446$ ) were correlated with daily sleep duration as well.

#### *Daily sleep quality*

Daily sleep quality was unrelated to age, relationship and parental status, ethnicity, educational attainment, household income, or current occupation. Smokers reported lower sleep quality (mean=1.4, SD=0.4) than non-smokers (mean=1.0, SD=0.4) ( $P=0.002$ ), but alcohol consumption, BMI and physical activity were unrelated to this sleep variable. Finally,

lower sleep quality was more likely to be reported by respondents with higher emotional distress ( $r=0.29$ ,  $P=0.001$ ) and higher negative affect ( $r=0.18$ ,  $P=0.044$ ).

Taken together, PSQI scores and daily sleep quality were positively associated with emotional distress and negative affect, while daily sleep duration and daily sleep quality were linked to educational attainment and smoking, respectively.

#### 5.5.4.3 Objective sleep measures

##### *Sleep duration*

Sleep duration was not associated with respondents' age, their relationship status, having children, ethnicity, educational attainment, current occupation, or household income. Health-related variables including BMI, physical activity, alcohol consumption and smoking were unrelated to this sleep measure as well. Sleep duration was also unrelated to emotional distress and negative affect

##### *Sleep efficiency*

Mean sleep efficiency was higher among single participants (mean=0.99 (log transformed data),  $SD=0.2$ ) than those who were married/cohabiting (mean=0.84,  $SD=0.3$ ),  $P=0.013$ ), but was unrelated to age, parental status, household income, ethnicity, educational attainment, and current occupation. Similarly, there was no association with BMI, physical activity, alcohol consumption, and smoking status. Emotional distress and negative affectivity were unrelated to sleep efficiency as well.

### *Sleep latency*

Mean sleep latency was longer among participants with children (mean=0.76 (log transformed data), SD=0.4) than those without (mean=0.44, SD=0.3) ( $P=0.040$ ), however it was not associated with age, relationship status, ethnicity, household income, current occupation, and educational attainment. Physical activity, BMI, smoking status and alcohol consumption were all unrelated to sleep latency as well. As in the case of the above objective sleep measures there was no association with emotional distress and negative affectivity.

### *Number of night-time awakenings*

Average number of awakenings was unrelated to respondents' age, having children, relationship status, household income, ethnicity, educational attainment, and current occupation. None of the health-related variables were associated with this sleep measure as well. Higher emotional distress was linked to a lower number of average number of awakenings ( $r=-0.20$ ,  $P=0.033$ ), but there was no relationship with negative affect.

In summary, with the exception of the associations with relationship and parental status and emotional distress objective sleep measures were unrelated to participants' socio-demographic or affective characteristics.

### **5.5.5 Baseline well-being measures and covariates**

The measures of well-being (i.e. flourishing, gratitude, positive affect, negative affect and emotional distress) were unrelated to age, relationship status, having children, household income, educational attainment, ethnicity, or current occupation. Health-related variables including drinking alcohol, smoking and BMI were not associated with well-being measures

as well. There was, however, an association with physical activity since participants who reported more frequent habitual physical activity also reported higher flourishing ( $r=0.21$ ,  $P=0.022$ ) and more gratitude ( $r=0.22$ ,  $P=0.015$ ). As could be expected, flourishing, gratitude and positive affect were lower among respondents with higher negative affect and emotional distress (see Table 5.6 below).

**Table 5.6 Bivariate correlations between baseline well-being measures.**

	Negative affect <sup>1</sup>	P-value	Emotional distress <sup>2</sup>	P-value
Flourishing	-0.36	<0.001	-0.50	<0.001
Gratitude	-0.29	0.001	-0.40	<0.001
Positive affect <sup>1</sup>	-0.65	<0.001	-0.63	<0.001

Results are presented as Pearson correlation coefficients ( $r$ ) and P-values. <sup>1</sup>SPANE=the scale of positive and negative experience; <sup>2</sup>HADS=the hospital anxiety and depression scale.

### 5.5.6 Compliance with experimental manipulation

The average number of completed writing tasks in the gratitude condition was 5.4 (SD=1.1) (range 1-6), and out of 39 participants in this group 29 (72.5%) completed all writing exercises, and only one person did one writing task. The mean effort invested into those tasks was 2.1 (SD=0.5) (range 1-3).

In the daily events condition the average number of completed writing tasks was 5.3 (SD=1.2) (range 2-6), and out of 40 participants 26 (63.4%) did all 6 writing tasks, while only one person did just two exercises. The mean effort invested into the tasks was 2.1 (SD=0.6) (range 1-3).

## 5.5.7 Main analyses

### 5.5.7.1 Eudaimonic well-being

To explore whether participants in the gratitude condition would report higher levels of eudaimonic and/or hedonic well-being following the intervention than those in the control groups I conducted a series of repeated measures ANOVAS. Significant interaction terms were followed up with a post hoc analysis (LSD pairwise comparison test), or separate ANOVAS for the different groups, as appropriate. In view of the exploratory nature of these analyses, I decomposed these effects if the interaction was significant at  $P < 0.1$  instead of the usual  $P < 0.05$ . In these analyses the main effects of time will only be reported if significant. Baseline and post-intervention means and standard deviations for well-being measures (stratified by the condition) are depicted in Table 5.7 below.

**Table 5.7 Baseline and post-intervention well-being measures for the gratitude, daily events and waitlist conditions.**

Well-being measure	Gratitude <sup>1</sup>		Daily events		Waitlist	
	Baseline	Post-intervention	Baseline	Post-intervention	Baseline	Post-intervention
Flourishing	42.0 (7.8)	43.9 (7.0)	42.0 (8.4)	43.6 (6.0)	43.3 (5.8)	42.9 (6.7)
Gratitude	5.6 (0.8)	5.8 (0.9)	5.7 (0.7)	5.7 (0.8)	5.7 (0.8)	5.5 (1.0)
Positive affect (SPANE)	3.4 (0.7)	3.5 (0.7)	3.3 (0.7)	3.5 (0.7)	3.4 (0.6)	3.3 (0.7)
Negative affect (SPANE)	2.4 (0.6)	2.3 (0.6)	2.4 (0.7)	2.3 (0.6)	2.5 (0.6)	2.6 (0.8)
Emotional distress (HADS)	13.5 (6.2)	11.6 (5.4)	13.3 (5.1)	13.5 (6.4)	13.3 (5.5)	14.2 (6.2)

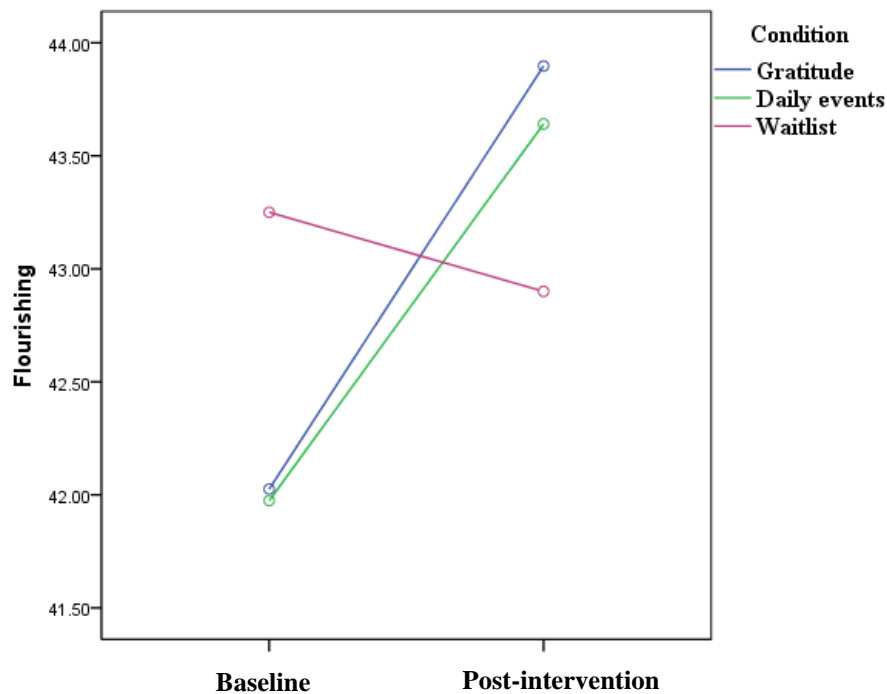
<sup>1</sup> Results are presented as means and standard deviations (in brackets). SPANE=the scale of positive and negative experience; HADS=the hospital anxiety and depression scale.

### *Flourishing*

A repeated measures ANOVA revealed that there was no interaction between experimental condition and time ( $F(2,115)=2.630$ ,  $P=0.076$ ), suggesting that flourishing levels did not change differently between the conditions (see Figure 5.7 for a graphic depiction of this finding). However, there was a main effect of time ( $F(1,115)=5.863$ ,  $P=0.017$ ) and flourishing increased from baseline (mean=42.4, standard error of the mean (SEM)=0.68) to post-intervention (mean=43.5, SEM=0.61). Follow-up analyses (justified by the near significant interaction) assessed changes in flourishing in the three conditions separately. The results revealed that there was a significant increase in flourishing scores from baseline to post-intervention in the gratitude ( $P=0.023$ ), but not in the waitlist condition ( $P=0.567$ ). Although there seemed to be an increase in the daily events condition, this was not significant ( $P=0.063$ ). It appears from these results that the gratitude intervention produced the largest improvement in scores on the flourishing scale.

Interestingly, the change score in flourishing ( $\Delta$ flourishing) in the gratitude condition was unrelated to the effort invested into the writing task ( $P=0.474$ ), and to the number of completed tasks ( $P=0.958$ ).

**Figure 5.7 Condition by time interaction (flourishing).**



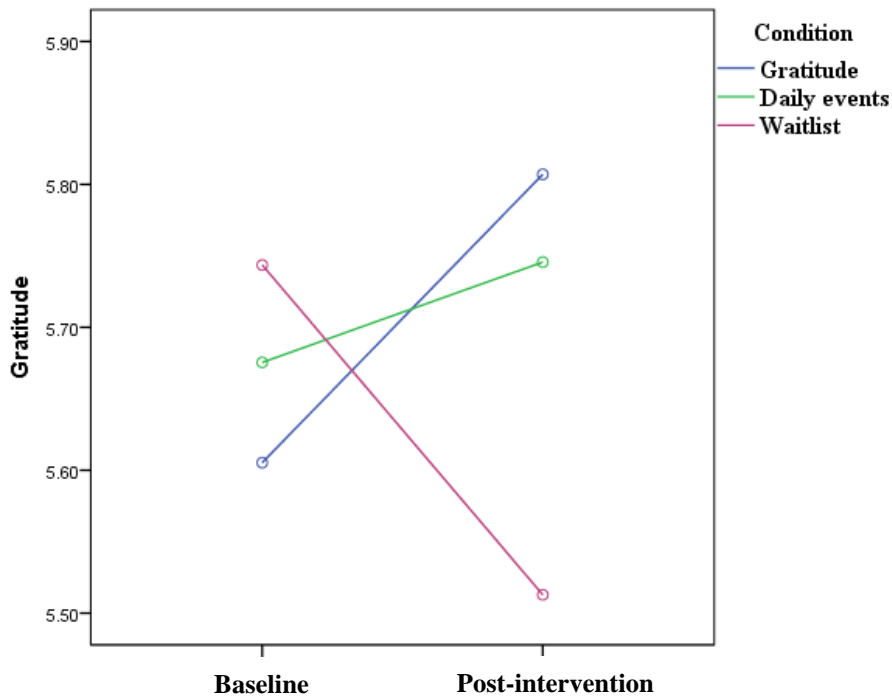
### *Gratitude*

The condition by time interaction was significant ( $F(2,112)=3.222, P=0.044$ ) indicating that gratitude levels changed differently between the conditions. As shown in Figure 5.8, over time gratitude increased in the gratitude condition and to some extent in the daily events condition, while its levels were reduced in the waitlist group. To determine whether the change in gratitude levels ( $\Delta$ gratitude) was significantly greater in the gratitude condition than in the control conditions I run a post hoc test. The results revealed that indeed  $\Delta$ gratitude was larger in the gratitude condition (mean=0.20, SEM=0.12) than in the daily events condition (mean=0.07, SEM=0.12), but this difference was not statistically significant ( $P=0.456$ ). As shown in Figure 5.8,  $\Delta$ gratitude score in the waitlist condition was negative (mean=-0.23, SEM=0.12) confirming that participants in this group reported lower gratitude post-intervention. Unsurprisingly, the difference in  $\Delta$ gratitude scores between the gratitude and



waitlist conditions was statistically significant ( $P=0.015$ ). However, the change score in gratitude (in the experimental condition) was not associated with the number of completed writing tasks ( $P=0.151$ ), or with the effort invested into those tasks ( $P=0.441$ ).

**Figure 5.8 Condition by time interaction (gratitude).**



#### 5.5.7.2 Hedonic well-being

##### *Positive affect*

The condition by time interaction was not significant ( $F(2,113)=1.925$ ,  $P=0.151$ ) suggesting there were no changes in positive affect that differed between the groups. Nor was there a significant main effect of time ( $P=0.158$ ), indicating that the positive affect scale was not sensitive to this intervention.

### 5.5.7.3 Negative affectivity and emotional distress

Since expressing gratitude has resulted in lower negative affect (Emmons & McCullough, 2003; Sheldon & Lyubomirsky, 2006) I explored this possibility in this study as well. These data are described below.

#### *Negative affect*

The condition by time interaction was not significant ( $F(2,113)=1.470$ ,  $P=0.234$ ) indicating that there was no change in this variable that was different between the conditions. The main effect of time was also not significant ( $P=0.397$ ), so the negative affect scale was not sensitive to this intervention.

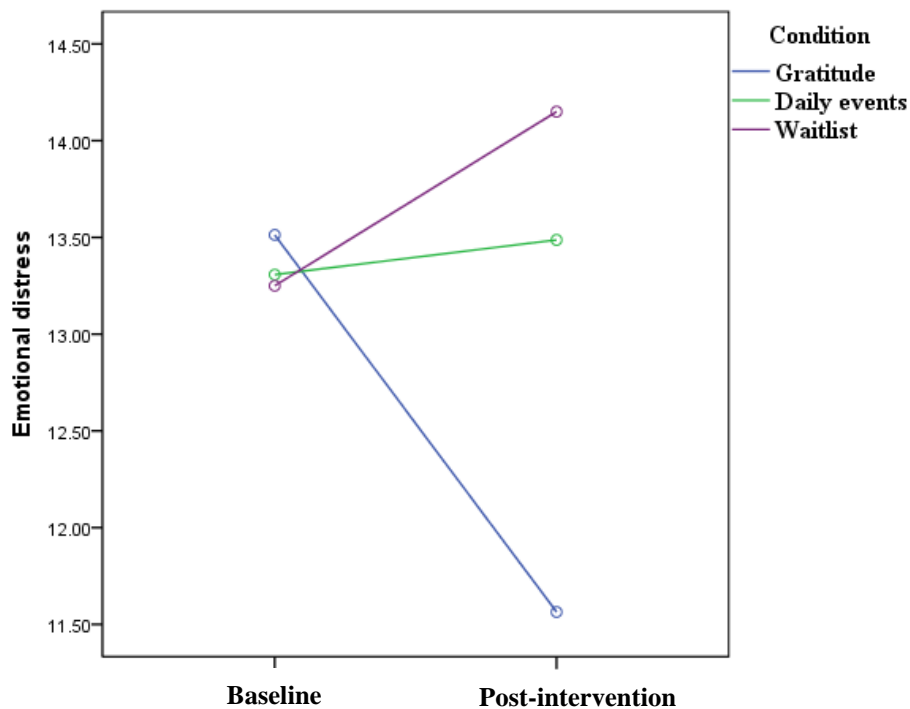
#### *Emotional distress (HADS total score)*

The condition by time interaction was significant in the analysis of the HADS ( $F(2,115)=3.630$ ,  $P=0.030$ ), suggesting that emotional distress changed over time differently between the study's conditions. As depicted in Figure 5.9, emotional distress was reduced between baseline and post-intervention assessments in the gratitude condition, while its levels remained virtually unchanged in the daily events condition, and increased slightly in the waitlist condition. To determine whether these changes in emotional distress ( $\Delta$ emotional distress) were statistically different from each other I performed a post hoc analysis. The test confirmed that  $\Delta$ emotional distress score was the largest in the gratitude condition (mean=-1.9, SEM=0.8), and that it differed significantly from the waitlist condition (mean=0.9, SEM=0.8) ( $P=0.011$ ), and marginally from the daily events condition (mean=0.2, SEM=0.8) ( $P=0.056$ ). In other words, the post hoc test confirmed that in

comparison with the control conditions participants in the gratitude group had significantly lower emotional distress post-intervention.

To explore the interaction further, I ran a repeated measures ANOVA for each of the conditions. The ANOVA for the gratitude condition confirmed that emotional distress was significantly reduced from baseline to post-treatment ( $P=0.019$ ), while there were no significant changes either in the daily events ( $P=0.831$ ) or waitlist conditions ( $P=0.207$ ). However, as in the case of flourishing and gratitude, the significant reduction of emotional distress in the gratitude condition was not linked to the effort invested into the writing task ( $P=0.905$ ), or to the number of completed tasks ( $P=0.634$ ).

**Figure 5.9 Condition by time interaction (emotional distress).**



In summary, following the 2-week intervention participants in the gratitude condition reported significantly higher eudaimonic well-being and reduced emotional distress, but no

such associations were found in the control conditions. These results confirm hypothesis 1. However, there was no change in positive or negative affect between baseline and post-intervention.

#### **5.5.7.4 Sleep measures**

To test the second hypothesis that participants in the gratitude condition would report fewer sleep problems post-intervention, and/or experience better objective sleep, in comparison with those in the control conditions, I performed a series of repeated measures ANOVAS. Means and standard deviations stratified by the condition for baseline and post-intervention sleep measures are depicted in Table 5.8 below.

**Table 5.8 Baseline and post-intervention sleep measures for the gratitude, daily events and waitlist conditions.**

Sleep measure	Gratitude*		Daily events		Waitlist	
	Baseline	Post-intervention	Baseline	Post-intervention	Baseline	Post-intervention
Sleep disturbance (PSQI) <sup>1</sup>	6.3 (2.2)	5.6 (2.8)	6.3 (2.7)	6.0 (2.7)	7.0 (3.4)	6.2 (3.2)
Sleep disturbance (PSQI) <sup>2</sup>	0.8 (0.1)	0.8 (0.2)	0.8 (0.2)	0.8 (0.2)	0.9 (0.2)	0.8 (0.2)
Daily sleep quality <sup>3</sup>	1.1 (0.4)	1.0 (0.4)	1.0 (0.5)	0.9 (0.5)	0.9 (0.4)	1.1 (0.5)
Daily sleep duration	7.3 (0.9)	7.3 (0.7)	7.4 (1.0)	7.1 (1.1)	7.8 (1.0)	7.5 (1.1)
Objective sleep measures:						
Sleep duration	6.8 (1.0)	6.8 (1.0)	6.8 (0.9)	6.8 (0.9)	7.3 (0.8)	7.1 (1.2)
Sleep latency <sup>1</sup>	7.0 (7.1)	5.6 (5.4)	5.2 (5.4)	5.0 (5.3)	4.6 (5.2)	5.3 (4.2)
Sleep latency <sup>2</sup>	0.5 (0.3)	0.5 (0.3)	0.4 (0.3)	0.5 (0.3)	0.4 (0.4)	0.5 (0.3)
Sleep efficiency <sup>1</sup>	87.1 (8.6)	87.5 (5.4)	88.7 (5.5)	89.9 (4.1)	88.8 (5.5)	89.9 (4.1)
Sleep efficiency <sup>2</sup>	1.0 (0.3)	1.0 (0.2)	0.9 (0.3)	0.9 (0.3)	0.9 (0.2)	0.9 (0.2)
Night-time awakenings	16.4 (6.9)	16.6 (6.3)	16.6 (5.7)	15.9 (6.6)	16.4 (5.9)	15.7 (5.7)

\*Results are presented as means and standard deviations (in brackets). PSQI=Pittsburgh sleep quality index; <sup>1</sup>=raw vales; <sup>2</sup>=log transformed values; <sup>3</sup>= higher scores reflect poorer sleep quality.

## **Subjective sleep data**

### ***Subjective sleep disturbance (PSQI total score)***

Since the distribution of baseline sleep disturbance scores was already log transformed, for the purpose of this analysis post-intervention sleep disturbance scores were logarithmically transformed as well. A repeated measures ANOVA revealed that the condition by time interaction was not significant ( $F(2,115)=0.471$ ,  $P=0.626$ ), suggesting that there was no change in sleep disturbance that differed across the conditions. However, the main effect of time was significant ( $F(1,115)=8.311$ ,  $P=0.005$ ) since sleep disturbance decreased from baseline (mean=0.85, SEM=0.02) to post-intervention (mean=0.80, SEM=0.02). Because the interaction term was not significant no further analysis was conducted.

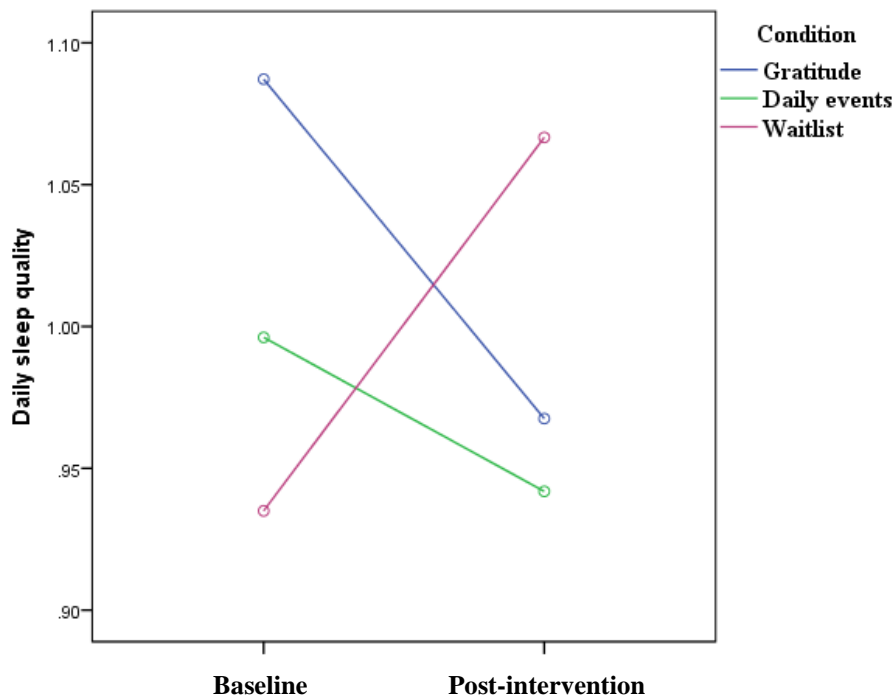
### ***Daily sleep quality***

The condition by time interaction was significant for daily sleep quality ratings ( $F(2,115)=3.434$ ,  $P=0.036$ ), suggesting that daily sleep quality changed over time differently between the study's conditions (see Figure 5.10 for a graphic depiction of this interaction).

In order to understand the nature of this interaction, I ran a univariate ANOVA with a post hoc pairwise comparison test to determine whether the change in daily sleep quality in the gratitude condition was significantly different from that in the control conditions. In this analysis I used  $\Delta$ sleep quality. The post hoc test revealed that  $\Delta$ sleep quality scores were negative in the gratitude (mean=-0.120, SEM=0.07) and daily events (mean=-0.054, SEM=0.07) conditions and positive in the waitlist condition (mean=0.132, SEM=0.07), suggesting that sleep quality improved in both the gratitude and daily events conditions, but that it worsened in the waitlist group. The difference in  $\Delta$ sleep quality scores was significant

between the gratitude and waitlist conditions ( $P=0.013$ ), but not between the gratitude and daily events conditions ( $P=0.516$ ). This analysis therefore provides support for hypothesis 2, in that daily sleep quality ratings were improved to a greater extent in the gratitude than control conditions.

**Figure 5.10 Condition by time interaction (daily sleep quality).**



### ***Daily sleep duration***

The condition by time interaction was not significant ( $F(2,115)=1.187$ ,  $P=0.309$ ) suggesting that self-reported sleep duration did not change differently across the study's three groups. The main effect of time was significant ( $F(1,115)=5.265$ ,  $P=0.024$ ), and daily sleep duration decreased between baseline (mean=7.50, SEM=0.09) and post-intervention (mean=7.32, SEM=0.09).

## **Objective sleep data**

### ***Sleep latency***

The condition by time interaction was not significant, so changes in sleep latency were not different across the conditions ( $F(2,107)=0.838$ ,  $P=0.435$ ). Due to a non-significant interaction term no further tests were performed for this sleep measure.

### ***Sleep duration***

The condition by time interaction was not significant ( $F(2,107)=0.201$ ,  $P=0.818$ ) indicating that sleep duration did not change with time differently across the groups, thus no follow-up tests were conducted.

### ***Sleep efficiency***

The condition by time interaction was not significant ( $F(2,107)=0.550$ ,  $P=0.579$ ), so sleep efficiency did not change differently between the study's three conditions.

### ***Night-time awakenings***

The condition by time interaction was not significant ( $F(2,107)=0.263$ ,  $P=0.769$ ), so the average number participants woke-up in the night did not change differently between the conditions. As in the case of the above objective sleep measures, no further tests were performed on this sleep variable.

In summary, these analyses showed partial support for hypothesis 2, but only in daily ratings of sleep quality. Neither the standard self-report measure (PSQI) nor the objective



measures showed any effect of the intervention. There was a significant difference between the conditions in the daily rating analysis, since the gratitude condition was the only group to show an improvement following the intervention period. However as can be seen in Figure 5.10, ratings of poor daily sleep quality were also slightly higher at baseline in the gratitude condition (albeit the difference was not statistically significant), so the post-intervention ratings were not strikingly different between groups.

#### 5.5.7.5 Sleep and well-being measures change scores

Next I conducted bivariate correlation analyses exploring the associations between change scores in well-being ( $\Delta$ well-being) and change scores in sleep ( $\Delta$ sleep), as to see whether improved well-being was linked to better sleep. To recapitulate, higher  $\Delta$ positive well-being scores were indicative of an increase in a given positive well-being measure, while lower negative  $\Delta$ well-being scores were indicative of reduced negative affect and emotional distress. In terms of sleep measures, higher  $\Delta$ sleep values were an indication of an increase in sleep duration (objective and daily (subjective) and sleep efficiency, while negative  $\Delta$ sleep values were suggestive of reduced sleep disturbance on the PSQI scale (Buysse et al., 1989), shortened sleep latency, fewer night-time awakenings and improved daily sleep quality post-intervention.

Table 5.9 shows bivariate correlations for the whole sample while Table 5.10 just for the gratitude condition. As can be seen in Table 5.9, increases in positive affect were correlated with reduced sleep disturbance ( $P=0.001$ ), improved daily sleep quality ( $P=0.006$ ) as well as longer daily ( $P<0.001$ ) and objective ( $P=0.032$ ) sleep duration. On the other hand, reduced negative affect was correlated with reduced sleep disturbance ( $P=0.037$ ) and longer daily sleep

duration ( $P=0.002$ ), while reduced emotional distress was linked to lower sleep disturbance on the PSQI (Buysse et al., 1989) ( $P=0.001$ ). When I repeated these analyses only for the gratitude condition (see Table 5.10) increased positive affect remained associated with reduced sleep disturbance ( $P=0.043$ ), improved daily sleep quality ( $P<0.001$ ) and longer daily sleep duration ( $P=0.007$ ), while reduced negative affect was linked to longer daily sleep duration ( $P=0.018$ ).

**Table 5.9 Bivariate correlations between well-being and sleep change scores (whole sample).**

$\Delta$ Subjective sleep measures							$\Delta$ Objective sleep measures							
$\Delta$ Well-being measure	Sleep disturbance (PSQI)	<i>P</i>	Daily sleep quality	<i>P</i>	Daily sleep duration	<i>P</i>	Sleep duration	<i>P</i>	Sleep latency	<i>P</i>	Sleep efficiency	<i>P</i>	Night-time awakenings	<i>P</i>
Flourishing	-0.07	0.482	-0.11	0.234	0.002	0.983	-0.01	0.881	-0.03	0.767	-0.09	0.371	-0.03	0.795
Gratitude	-0.05	0.585	-0.07	0.473	0.01	0.934	-0.04	0.664	-0.10	0.316	0.09	0.344	0.01	0.926
Positive affect <sup>1</sup>	-0.30	<b>0.001</b>	-0.25	<b>0.006</b>	0.32	<b>&lt;0.001</b>	0.21	<b>0.032</b>	-0.5	0.612	-0.004	0.970	0.22	<b>0.020</b>
Negative affect <sup>1</sup>	0.19	<b>0.037</b>	0.14	0.139	-0.29	<b>0.002</b>	-0.16	0.099	0.06	0.557	-0.09	0.356	-0.10	0.296
Emotional distress <sup>2</sup>	0.31	<b>0.001</b>	0.14	0.126	-0.09	0.319	-0.03	0.762	0.04	0.676	-0.13	0.173	-0.13	0.138

Results are presented as Pearson correlation coefficients (*r*) and P-values. PSQI=Pittsburgh sleep quality index; <sup>1</sup> SPANE= the scale of positive and negative experience; <sup>2</sup> HADS=the hospital anxiety and depression scale.

**Table 5.10 Bivariate correlations between well-being and sleep change scores (gratitude condition only).**

ΔSubjective sleep measures							ΔObjective sleep measures							
ΔWell-being measure	Sleep disturbance (PSQI)	<i>P</i>	Daily sleep quality	<i>P</i>	Daily sleep duration	<i>P</i>	Sleep duration	<i>P</i>	Sleep latency	<i>P</i>	Sleep efficiency	<i>P</i>	Night-time awakenings	<i>P</i>
Flourishing	-0.27	0.098	-0.01	0.943	0.04	0.826	0.04	0.807	-0.04	0.816	-0.13	0.456	0.06	0.735
Gratitude	-0.04	0.817	0.002	0.991	-0.04	0.798	-0.01	0.967	-0.16	0.374	-0.08	0.652	-0.03	0.868
Positive affect <sup>1</sup>	-0.33	<b>0.043</b>	-0.59	<b>&lt;0.001</b>	0.43	<b>0.007</b>	0.31	0.072	0.19	0.282	-0.30	0.082	0.17	0.329
Negative affect <sup>1</sup>	0.21	0.196	0.21	0.199	-0.38	<b>0.018</b>	-0.27	0.111	-0.25	0.156	0.09	0.603	-0.14	0.428
Emotional distress <sup>2</sup>	0.19	0.254	0.26	0.111	-0.14	0.387	0.01	0.971	-0.05	0.773	-0.09	0.606	-0.15	0.396

Results are presented as Pearson correlation coefficients (*r*) and P-values. PSQI= Pittsburgh sleep quality index; <sup>1</sup> SPANE= the scale of positive and negative experience; <sup>2</sup> HADS=the hospital anxiety and depression scale.

## **5.6 Discussion**

This study aimed to discover whether modifying well-being would have a beneficial impact on subjective and objective sleep. The first hypothesis, that participants reporting moderate distress and sleep problems randomised to a two week gratitude intervention would report greater improvements in well-being, when compared with those in the waitlist or daily events conditions, was partly supported by my data. Specifically, participants in the gratitude condition reported greater flourishing, gratitude and reduced emotional distress post-intervention, when compared with control conditions. However, levels of positive and negative affect were unchanged following the two-week gratitude intervention. The second hypothesis was supported by my data, albeit very weakly since participants in the gratitude condition, compared with the controls, had slightly improved daily ratings of sleep quality, but there was no change in the global measure of sleep disturbance (PSQI), in daily ratings of sleep duration, or in any of the objective sleep indicators. Additionally, there were positive correlations between improvements in well-being and improvements in sleep measures, providing supportive evidence for the hypothesis that the changes in well-being were responsible for the improvements in sleep.

### **5.6.1 Well-being measures**

My study suggests that expressing gratitude just over a 2-week period can significantly increase eudaimonic well-being. To the best of my knowledge this finding has not been reported before since the majority of past research based on this paradigm explored its effects on positive and negative affect (e.g., Emmons & McCullough, 2003; Sheldon & Lyubomirsky, 2006), satisfaction with life (Boehm et al., 2011; Emmons & McCullough, 2003), global happiness (Lyubomirsky et al., 2011) or depressive symptoms (Seligman et al., 2005). However, other positive psychology paradigms have been found

associated with increases of eudaimonic well-being. For example, college students who during one academic semester were encouraged by a counsellor to realise a number of previously identified personal goals, such as to make a new friend, reported significantly higher eudaimonic well-being (Sheldon, Kasser, Smith, & Share, 2002). A more recent positive well-being psychotherapy in adolescents (mean age 14.4 years) used a number of techniques (e.g., teaching how to recognise discrete emotions, demonstrating how emotions interact with cognitions, asking students to identify their positive attitudes/characteristics) to increase eudaimonic well-being. At a 6-month follow-up, relative to controls, students in the experimental condition reported significantly higher personal growth (Ruini et al., 2009). A forgiveness therapy, aimed to teach participants how to refrain from negative reactions to the person/persons they feel hurt by and simultaneously to promote positive responses to that person (Reed & Enright, 2006, p. 921) resulted in a significantly increased environmental mastery, as defined by Ryff and Singer's scale (1996). This intervention was delivered over an 8-month period, and the sample comprised of adult women.

My intervention study significantly increased gratitude. It is difficult to compare this finding with the literature since gratitude has rarely been assessed in intervention studies based on this paradigm. The only study to date that measured gratitude was the intervention by Emmons and McCullough (2003, study 3 in that manuscript), where, in line with my data, the authors reported a significant increase in gratitude from baseline to post-treatment, and increases in gratitude mediated increases in positive affect. Interestingly though, a recent review of the literature concluded that there is currently limited evidence to suggest that a gratitude intervention induces positive well-being through increases in gratitude (Wood et al., 2010). Instead, for example, it is thought that gratitude interventions might increase well-being through cognitive biases since grateful

individuals perceive help received from others as more valuable than their less grateful counterparts, which then subsequently has a beneficial impact on their emotions. The second plausible pathway is based on the principles of the broaden-and-build theory (Fredrickson, 2001) stipulating that each positive emotion has its unique evolutionary determined purpose, and people who are grateful are more likely to have stronger social bonds that not only have a positive impact on their current well-being, but also become invaluable during periods of crisis or adversity (Emmons & McCullough, 2003; Wood et al., 2010).

Analysis of my data further revealed that expressing gratitude significantly reduced emotional distress. Similarly to eudaimonic well-being emotional distress (i.e. anxiety and/or depressive symptoms) has been rarely evaluated in studies based on this paradigm. One explanation for this could be because authors using PPIs might have been primarily interested in boosting positive emotions or happiness, and less so in eliminating depressed mood. However, my finding corroborates results from an intervention described by Seligman et al., (2005), in which writing and subsequently delivering a letter of gratitude to a person who had not been previously thanked for their kindness was associated with reduced depressive symptoms up to a one month following the intervention, but not at a 6-month follow-up. Interestingly, a number of other positive psychology paradigms have successfully reduced emotional distress. These approaches include, for example, the forgiveness (Reed & Enright, 2006) and positive well-being psychotherapies (Ruini et al., 2009) described above, as well as using signature (i.e. unique) personality characteristics in a novel way (Seligman et al., 2005). It is worth mentioning that these three approaches resulted in long-term decrements of emotional distress ranging from 6 (Ruini et al., 2009; Seligman et al., 2005) to approximately 8 months after the experimental manipulation finished (Reed & Enright, 2006). A meta-analytic review of 25 well-being interventions,

which measured emotional distress, also concluded that PPIs can lead to moderate decreases in depressive symptoms (Sin & Lyubomirsky, 2009).

Interestingly, the significant changes in flourishing, gratitude and emotional distress were unrelated to the effort invested into the gratitude task, or to the number of completed tasks. This is in contrast with a recently published gratitude intervention (Lyubomirsky et al., 2011). However, while in my study compliance with the experimental task and effort invested into this task were rated by the participants themselves, in the aforementioned study the invested effort was assessed by two researchers who read the completed gratitude diaries paying particular attention to the length of each task as well as its content. The difference in assessment of compliance might therefore in part explain the divergent findings.

However, my data revealed that neither positive nor negative affect ratings were changed following the intervention. This is in contrast with past studies. For example, expressing gratitude daily over the period of 2 or 3 weeks led to significant increases in positive affect (Emmons & McCullough, 2003, studies 2 and 3, respectively), while negative affect was significantly reduced following 3 weeks of gratitude exercises (Emmons & McCullough, 2003, study 3). In my study the actual intervention period was 2 weeks and participants were required to write 3 times a week about 3 people/events/things they felt grateful for, so one plausible explanation why my data do not support those of Emmons and McCullough (2003) could be a shorter duration of my intervention, and a fewer number of completed exercises. Moreover, sample characteristics could have to some extent moderated the effects of gratitude intervention on well-being. Specifically, Emmons and McCullough's study 3 (2003) comprised individuals with neuromuscular diseases, and although it can only be speculated perhaps this group of people responded more strongly (i.e. positively) to gratitude exercises than



my sample. These participants were also considerably older (mean age=49 years) than those in my study, and it has been reported that older individuals gain more benefits from PPIs than younger people (Sin & Lyubomirsky, 2009). However, Emmons and McCullough's study 2 (2003) (published in the same manuscript) involved university students. Another PPI reported that expressing gratitude once a week for 4 weeks resulted in lower negative affect, but similarly to my study, positive affect remained unchanged (Sheldon & Lyubomirsky, 2006). This intervention was based on a student sample. It is difficult to compare my findings with two recently published gratitude investigations since positive and negative affect responses were not explored on its own, but as part of a composite measure also including happiness and life satisfaction (Lyubomirsky et al., 2011) or life satisfaction scores (Layous et al., 2013).

It is notable that in the daily events condition some of the well-being measures changed between baseline and post-intervention, and although not significant, these alterations mirrored those in the gratitude condition. In particular, flourishing and positive affect were both increased while negative affect was lower post-intervention. Although we aimed to keep this condition as neutral as possible, by instructing participants to focus on negative as well as positive events or things in a given day, it is nonetheless possible that by simply being given something active to do participants' mood or eudaimonic well-being improved. Alternatively, by asking participants to pay attention to their immediate surroundings and things happening around them we might have increased their mindfulness, which is an awareness of "moment-to-moment experiences" (Bishop et al., 2004, p. 230). Mindfulness, which originates from Buddhism, can be achieved through meditation (Bishop et al., 2004), and it has been found to reduce anxiety, depressive symptoms and stress (Fjorback, Arendt, Ornbol, Fink, & Walach, 2011). My study did not involve any meditation, but it is plausible that the daily events task impacted well-being in

a similar way to a mindfulness meditation, where by paying attention to things happening around them participants might have been simultaneously less likely to focus on negative aspects of their life, which subsequently improved their well-being. It might be therefore argued that expressing gratitude is only marginally more beneficial for eudaimonic and hedonic well-being than focusing on one's immediately surroundings. Importantly though, expressing gratitude reduced emotional distress, while no such effect was found for the daily events task.

### 5.6.2 Sleep measures

My study was set out to establish whether positive well-being is a precursor of good sleep, or its epiphenomenon. The results were inconclusive since although participants in the experimental condition had modestly improved daily ratings of sleep quality post-intervention, the remaining sleep measures were unchanged. To date there has been only one (published) gratitude intervention that successfully improved sleep, and my data partly support these earlier findings. Specifically, 3 weeks of daily gratitude exercises led to significantly improved self-reported measures of sleep quality and quantity in a sample of adults with neuromuscular diseases (Emmons & McCullough, 2003, study 3). However, expressing gratitude daily over the period of 2 weeks was unrelated to subjective sleep ratings in a sample of undergraduate students (Emmons & McCullough, 2003, study 2). The reasons for why sleep measures were so modestly changed in my study are likely to be similar to those that I already discussed with relation to the well-being measures, and might include too short and/or not intensive enough experimental manipulation and differences in sample characteristics (e.g., students vs. middle-aged adults, healthy women vs. people with a disability), when compared with study 3 described by Emmons and McCullough (2003).

Another possibility to consider in this context is that perhaps a PPI might impact sleep perceptions more strongly than the actual sleep behaviour. Indeed, in Study 3 (Chapter 4) I have found that while subjective sleep efficiency (assessed with the Jenkins Sleep Problems Scale (Jenkins et al., 1988) was correlated with a number of psychosocial and affective measures including social support, happiness and depressive symptoms, the objective measure of sleep efficiency was not. That objective sleep parameters are weakly associated with affective measures and psychosocial factors has been reported by earlier research as well (Friedman et al., 1995; Shaver et al., 2002; Tworoger et al., 2005).

It is also important to acknowledge that although all women recruited to this study reported disturbed sleep at baseline, as indicated by the PSQI (Buysse et al., 1989), baseline objective sleep parameters were, by contrast, indicative of healthy sleep. For example, across the 3 conditions women had on average good sleep efficiency (above 85%), short sleep latency and 'healthy' sleep duration ranging from 6.8 hours in the gratitude condition to 7.3 hours in the waitlist condition. So since objective sleep was good at baseline it might be argued that perhaps there was not much room for improvement.

Alternatively, even if it is possible to improve sleep behaviour perhaps the changes in well-being in my study were too modest to elicit any alterations in sleep, since although flourishing was significantly higher and distress was reduced post-intervention, both positive and negative affect remained unchanged. The same issue applies to subjective sleep indicators in my study. It is notable that although both flourishing and emotional distress were changed following the experimental manipulation, change scores of these two measures were actually unrelated to change scores in any of the subjective sleep indices. On the other hand, change scores in positive affect were correlated with change scores in the PSQI (Buysse et al., 1989) and daily measures of sleep duration and quality, while negative affect change score was associated with increased daily sleep duration. This

raises the possibility that if my intervention had successfully increased positive affect and/or reduced negative affect perhaps this would have improved sleep measures, at least the self-reported ones.

It is unclear why change scores in eudaimonic well-being and emotional distress in the gratitude condition were unrelated to change scores in sleep measures. One possibility is that eudaimonic well-being might be less strongly associated with sleep than positive affect, as discovered in the MIDUS (Hamilton et al., 2007a). However, the opposite was reported in the Whitehall II study, where associations with sleep were stronger for eudaimonic well-being (Steptoe et al., 2008). The link between emotional distress, in particular depression, and disturbed sleep is well documented (Benca et al., 1992; Benca & Peterson, 2008; Szklo-Coxe et al., 2010), yet in my study the significant reduction of emotional distress (in the gratitude condition) was unrelated to improved sleep. It could only be speculated, but it is plausible that this change was still too modest to promote better sleep.

Taken together, more research is still needed to establish the temporal precedence of sleep and well-being measures. Nonetheless, the finding that daily sleep quality ratings were slightly improved in the gratitude condition; and that despite the lack of a significant modification of positive and negative affect changes in these measures were correlated with favourable alterations of self-reported sleep indices tentatively suggest that positive well-being might indeed predict better sleep, at least with regard to self-report. This is still important since people's perceptions of sleep, regardless of its objective quality or quantity, are likely to impact their future behaviour.

### **5.6.3 Strengths of the study**

My study has several strengths. In contrast with past well-being interventions (Boehm et al., 2011; Lyubomirsky et al., 2011; Sheldon & Lyubomirsky, 2006), and to

address the critique of the gratitude literature (Wood et al., 2010) my study had a true control group (the waitlist condition), so the changes in well-being and sleep in the gratitude condition could be compared against no treatment. For instance, as already pointed out, similarly to participants in the gratitude condition those in the daily events condition also showed increases in flourishing post-intervention (see Table 5.7), while no such pattern was apparent in the waitlist condition. Had my study only included the daily events condition it could have been less certain whether expressing gratitude induces stronger increases of eudaimonic well-being than writing about events/people/things noticed on a particular day. It might therefore be puzzling why my study involved two control conditions instead of the waitlist group only. The main advantage of including the daily events condition was that this group was matched with the experimental condition in terms of attention from the researchers as well as the materials given (i.e. both conditions received paper diaries to complete). This subsequently allowed to test whether expressing gratitude is more beneficial for well-being than writing about neutral daily events. As previously acknowledged, while both writing exercises had a similar effect on the flourishing scale (Diener et al., 2010), only the gratitude condition successfully reduced emotional distress.

Another strength of my study is the minimal attrition rate since out of 122 recruited volunteers only 4 did not finish the study, and the attrition was evenly distributed across the study's conditions. Participants in the three conditions were also well matched in terms of socio-demographic, well-being and sleep measures, with the exception of objective and self-report sleep duration which was shorter in the gratitude condition. Finally, my study extends the well-being literature relating PPIs and suggests that in addition to approaches such as goal attainment (Sheldon et al., 2002), forgiveness therapy (Reed & Enright, 2006),

or using signature strength in a novel way (Seligman et al., 2005), expressing gratitude paradigm can increase eudaimonic well-being as well as reduce emotional distress.

#### 5.6.4 Limitations of the study

A number of limitations have to be discussed. The sample comprised mostly white and university educated participants, so it cannot be concluded whether expressing gratitude would be associated with higher eudaimonic well-being or reduced emotional distress in less educated or more ethnically diverse populations. However, there is evidence from studies in community-dwelling adults that expressing gratitude is associated with increased well-being (Boehm et al., 2011; Seligman et al., 2005), thus suggesting that this paradigm can benefit people from the general population and not just highly educated women. The literature relating cultural differences in the effectiveness of PPIs in bolstering well-being remains relatively unexplored, but a recent study reported that expressing gratitude had a minimal impact on life satisfaction among community-dwelling Americans of Asian descent (Boehm et al., 2011). Another investigation tested the effects of expressing gratitude and performing acts of kindness on positive well-being among university students from US and South Korea. Results revealed that while US participants benefited from both interventions, in the South Korean sample well-being was significantly increased only among those who did acts of kindness (Layous et al., 2013). Therefore, it is important to acknowledge that people from individualistic societies, such as the UK or US, might benefit more from PPIs than those from collectivist cultures (e.g., China, Japan, South Korea) partly because they place more value on personal happiness (Lyubomirsky & Layous, 2013). The generalizability of my data is further limited by a solely female sample. As already outlined in the Methods section men were not recruited to this study due to practical constraints (lack of larger blood pressure cuffs). Moreover, this intervention was jointly designed and conducted with another PhD student who had a

shorter time-frame within which she needed to complete her thesis, and we anticipated that the nature of this study (i.e. well-being intervention) might generate less interest amongst men, which would consequently lengthen the recruitment process.

My data suggest that following two weeks of expressing gratitude participants reported significantly higher flourishing post-intervention, when compared with the control conditions. However, this finding must be interpreted with caution since there was no time frame with regard to which the flourishing scale (Diener et al., 2010) was answered (see Appendix 7, section 6). So although when people complete well-being scales their answers are often influenced by their most recent experiences, it cannot be certain whether post-treatment flourishing scores reflect how participants felt in the last two weeks, or in general. Importantly, the remaining scales described in this study were completed with reference to the previous week.

The significant changes in eudaimonic and affective well-being as well as in daily evaluations of sleep quality reported by the participants in the gratitude condition were assessed immediately after the experimental manipulation, so my data shed no light on more long-term effects of this paradigm on well-being and sleep measures.

Relatedly, the experimental manipulation lasted only two weeks and participants were not requested to continue their gratitude exercises during the post-intervention assessment week. This might have contributed towards the inconclusive findings in my study since the changes in well-being were relatively modest. In the same vein, except for daily sleep quality the remaining objective and self-report sleep measures were not improved post-intervention, but changes in positive and negative affect were nonetheless correlated with beneficial alterations in self-reported sleep measures. If participants had continued with their gratitude task throughout the post-intervention assessment week this could have possibly bolstered my findings.

Due to time constraints and to reduce participant burden I collected objective sleep information over one week before and after the experimental manipulation. However, a relevant question in this context is whether one week can provide a reliable approximation of one's sleep. Past studies designed to compare objective and subjective sleep indices, where it was therefore paramount to obtain an accurate measure of objective sleep, recorded sleep information over 4 (Lauderdale et al., 2008) or 6 nights only (van den Berg et al., 2008), which is not very different from my study.

#### 5.6.5 Conclusion

Following two weeks of expressing gratitude participants in the gratitude condition had significantly higher eudaimonic well-being and reduced emotional distress, when compared with controls. Similarly, relative to controls, participants in the experimental condition had modestly improved daily ratings of sleep quality post-intervention. More importantly, my study provides evidence that experimentally increased hedonic well-being is associated with improved sleep ratings. This sheds light on the cross-sectional evidence relating positive well-being with sleep (Hamilton et al., 2007a; Steptoe et al., 2008) and tentatively suggests that well-being exerts a protective effect on (subjective) sleep, as previously reported by Phelan et al., (2010). However, positive and negative affect was unchanged following the intervention, so were the remaining measures of subjective sleep and objective sleep indicators. More gratitude intervention studies, possibly with a longer and more intensive experimental period, are still required to rectify the temporal precedence of the relationship between positive well-being and good sleep. Notwithstanding, my study suggests that a relatively short and easy well-being intervention can successfully improve eudaimonic well-being and reduce emotional distress.



## CHAPTER 6: MAIN DISCUSSION

This PhD thesis consists of 4 studies, which tested 4 broad aims by using different methods of investigation including a large epidemiological cohort (Study 1), a more intensive investigation of affective states and biological responses in everyday life of working women (Studies 2 and 3), as well as a short-term intervention (Study 4).

The literature concerned with the implications of sleep duration and quality on cardiovascular health has grown in recent years, but many gaps in knowledge still remain. Disturbed, insufficient and too long sleep prospectively predict adverse cardiovascular outcomes and at least three pathways might be responsible for this phenomenon: mood disturbance, health behaviours, and direct biological dysregulation. All three mechanisms are important, but it was beyond the scope of my PhD to explore each one in detail, and since my interests lie particularly in the pathway relating direct biological dysregulation Studies 1 and 2 aimed to test whether inflammation (Study 1) and autonomic modulation of the heart (Study 2) could be in part responsible for poorer cardiovascular health among sleepers with too short or too long sleep duration, and in those with disturbed sleep.

Sleep measurement is challenging. The majority of studies relating sleep indices with cardiovascular health, or with other physical health outcomes, have relied on subjective sleep information. This is problematic since people are not accurate in reporting their sleep duration or quality, when compared with objective sleep indicators. Current understanding of the reasons for the discrepancy between subjective and objective sleep parameters is limited, so I aimed to explore this issue in Study 3.

Growing evidence suggests that depression is a prospective risk factor for disturbed sleep and chronic insomnia, while positive affect and eudaimonic well-being are cross-sectionally linked to better sleep. What is less understood, however, is whether positive

well-being can prospectively predict healthier sleep. If confirmed by further research, this could have important implications for improving sleep and subsequently physical health. Therefore, in Study 4 I aimed to test whether experimentally induced positive well-being would beneficially impact sleep.

I will now briefly summarise my studies' aims and hypotheses as well as the main findings, and show how my studies have advanced understanding of sleep, well-being, and health.

## **6.1 Main findings and their implications**

### **6.1.1 Study 1**

In Study 1, based on wave 4 of the English Longitudinal Study of Ageing (ELSA) (N=6465), I explored the possibility that direct biological dysregulation might be translating deviant sleep patterns into cardiovascular outcomes. The literature relating sleep parameters with inflammation, a well-established CVD risk factor (Libby et al., 2011), is inconsistent and has not been explored systematically in representative cohorts of older adults. Moreover, dehydroepiandrosterone sulfate (DHEAS), which is the most abundant endogenous steroid hormone in the elderly, and haemoglobin both decline with age and lower levels are linked to adverse health outcomes including mortality. However, their associations with sleep measures remain unexplored in ageing populations.

Therefore, four hypotheses were tested relating inflammatory markers (C-reactive protein (CRP), fibrinogen), DHEAS, haemoglobin and anaemia with self-reported sleep duration and disturbance, as detailed on page 124. The hypotheses were only partly supported by the data, and I found gender differences in the associations between sleep measures and biomarkers, since with the exception of the relationship between disturbed sleep and anaemia the effects were present only in men. Specifically, hypothesis 1, that

there might be a curvilinear association between sleep duration and markers of inflammation was partly supported since men sleeping long hours (>8 hours) had raised CRP and fibrinogen levels, compared with the 7-8 hours category, but there was no association with short sleep (<5 hours). Hypothesis 2, that disturbed sleep would be associated with elevated concentrations of CRP and fibrinogen, was only partly supported as well since only the association with CRP was significant. The data provided a weak support for the third hypothesis as although short sleep was associated with low haemoglobin concentrations, there was no relationship between sleep duration and DHEAS, or between sleep duration and anaemia. However, hypothesis 4 was more strongly supported since disturbed sleep was associated with lower DHEAS levels, lower haemoglobin concentrations, and increased risk of anaemia, independently of covariates.

My study corroborates the evidence (Dowd et al., 2011) that in older adults long sleep hours, but not short, are linked to elevated levels of inflammation, namely CRP and fibrinogen. This is important given that long sleep hours, but not short, have become more widespread in developed countries in the last 30 or so years (Bin et al., 2013). Recent data from a cohort of older women also revealed that fibrinogen partly mediated (by approximately 8%) the prospective association between long sleep and incident CHD (Hale et al., 2013).

Moreover, in Study 1, taking advantage of the rich information available in ELSA, I addressed the gap in the literature relating self-reported sleep measures with DHEAS and haemoglobin and found that disturbed sleep was linked to lower DHEAS levels in men, while lower haemoglobin was more prevalent in men sleeping short hours. Both men and women reporting disturbed sleep were more likely to suffer from anaemia as well. These cross-sectional data need to be corroborated by further research, but to the best of my

knowledge, these are novel findings emphasising that sleep is an important marker of health and disease in ageing adults.

### 6.1.2 Study 2

Study 2 was based on an intensive cross-sectional investigation of ambulatory biological responses and affective characteristics in a sample (N=199) of healthy young women. As in Study 1, this study also explored the possibility that direct biological dysregulation might be in part responsible for higher risk of CVD and CVD mortality amongst poor sleepers.

Reduced heart rate variability (HRV), which is an indication of heightened sympathetic activity and/or vagal withdrawal, is a risk factor for CVD and mortality (Thayer & Lane, 2007). Experimentally induced total and partial sleep deprivation are also related to lower HRV (Stein & Pu, 2012). However, in contrast to neuroendocrine or inflammatory pathways, this area of research has rarely been studied outside the sleep laboratory except for very few studies including participants with irregular sleep patterns, such as university students undergoing final exams and nurses working night shifts (Chung et al., 2009; Takase et al., 2004). To address this gap in the literature I set out to test the hypothesis that sleep problems would be associated with reduced HRV over the working day, as described on page 167. If this association was the result of enduring individual biobehavioural differences between individuals who do and do not experience sleep problems, similar relationships would be present both during the day and at night. If the association arises from low-level chronic stress, such the specific demands of work, it might be present during the working day, but not at night. This hypothesis was supported by my data since independently of covariates disturbed sleep was associated with reduced HRV, but only over the working day and not at night.

In Study 2 I also aimed to determine whether the inverse association between sleep problems and HRV was explained, at least to some extent, by experienced affect or stress. However, hypothesis 2, that greater perceived stress and lower positive affect on the evening before work, or during the work period itself, would account in part for associations between sleep problems and HRV was unsupported by my data.

This study adds to the literature in showing that under naturalistic conditions in otherwise healthy young women disturbed sleep is associated with lower daytime HRV, independently of covariates. My data, therefore, corroborate previous experimental and observational findings and extend them to a more representative sample of community-dwelling women. The results indicate that even in the general population there is an association between sleep problems and reduced HRV. Both sleep and HRV measures are linked to adverse affective and psychosocial characteristics, raising the possibility that they could be part of a pathway through which disturbed sleep might exert a negative impact on HRV. This was not the case in my data suggesting that disturbances of sleep could have a more direct association with HRV.

### 6.1.3 **Study 3**

Study 3 was based on the same data set as Study 2, and focused on the differences between self-reported and objectively measured sleep. Self-reported short and long sleep increase the risk of cardiovascular outcomes, but it is becoming increasingly recognised that sleep quality might be equally important for optimal health. Self-reported sleep disturbances are common in the UK (Groeger et al., 2004), but research exploring whether global ratings of sleep quality are congruent with objective sleep data is sparse. Furthermore, self-reported sleep quality is related to a number of psychosocial and affective characteristics, but it remains uncertain whether we can rely on self-reported measures to understand these processes.

Therefore, the aim of this study was to evaluate whether subjective and objective indices of sleep quality would show similar relationships with work stress, social support, depressive symptoms, happiness and subjective health status. Objective sleep efficiency was the measure of objective sleep quality in this study. Four hypotheses were tested, as detailed on page 200. The data supported hypothesis 1 since greater work stress was associated with underestimation of sleep efficiency than warranted by the objective sleep measure. Hypotheses 2 and 4 were also supported by my data as lower social support and poorer self-reported health were both associated with underestimations of sleep efficiency. Importantly, these findings were independent of negative affect. However, hypothesis 3 was rejected since neither happiness nor depressive symptoms were linked to the discrepancies between subjective and objective sleep efficiency indicators.

Study 3 also uncovered that while subjective sleep efficiency was associated with affective and psychosocial characteristics, the objective sleep measure was not.

These findings have important implications for the sleep literature. Objective and subjective indices of sleep duration are often incongruent, and in Study 3 I extended these data to global sleep quality since I found that people are also inaccurate in estimations of their sleep quality, when compared with the objective sleep measure. Both over-estimation (worse self-reported than objective sleep disturbance) and under-estimation (better self-reported than objective sleep disturbance) occur. More importantly, my data revealed that psychosocial characteristics including work stress, lower social support and poor subjective health were more prevalent in participants who perceived their sleep quality to be lower than otherwise warranted by the objective sleep measure. These novel findings underscore the need for researchers studying sleep quality as a plausible risk factor for ill health to be aware that the magnitude of the relationship between self-reported sleep

quality and health-related psychosocial factors may be over-estimated in studies based on self-report.

In Study 3 I also corroborated previous findings (Friedman et al., 1995; Shaver et al., 2002; Tworoger et al., 2005) that only subjective, but not objective, sleep quality was associated with psychosocial factors and affective responses. This suggests that to some extent sleep behaviour and sleep perceptions are distinct phenomena. However, this should not be interpreted as a support for the notion that subjective sleep information is unimportant or invalid. On the contrary, how people feel about their sleep, whether it is objectively good or not, is likely to impact on their future health behaviour and well-being. This is demonstrated in insomnia, which is the most prevalent sleep disorder, where polysomnography (PSG) (a gold standard sleep measure) is not required to diagnose this disorder since insomniacs do not always have disturbed sleep when measured objectively (Fernandez-Mendoza et al., 2010; Rosa & Bonnet, 2000).

#### 6.1.4 **Study 4**

Study 4 (N=122) was a short-term intervention designed to discover whether modifying well-being would have a beneficial impact on subjective and objective sleep.

Positive well-being measures are cross-sectionally associated with better sleep quality (Hamilton et al., 2007a; Steptoe et al., 2008) and possibly quantity (Hamilton et al., 2007b). To date only one prospective study (Phelan et al., 2010) has found that higher hedonic and eudaimonic well-being predicted better self-reported sleep, and more research is needed to corroborate these data, as well as to establish whether this pattern of findings can be replicated for objective sleep. If confirmed it could offer a new avenue for intervention aimed at improving sleep.

Observational and experimental evidence suggest that gratitude is associated with better sleep quality and longer (healthier) sleep duration, so in Study 4 I decided to use a

gratitude intervention in order to test its impact on well-being and sleep. Two hypotheses were tested, as described on page 250. Hypothesis 1 was that participants reporting moderate distress and sleep problems randomised to a two week gratitude intervention would report greater improvements in well-being, when compared with those in control conditions. My data lent partial support to this hypothesis since participants in the experimental condition reported significantly higher eudaimonic well-being and reduced emotional distress, but positive and negative affect were unchanged. There was a weak support for hypothesis 2, as although daily sleep quality was improved post-intervention, when compared with controls, global ratings of sleep disturbance, self-reported sleep duration and objective sleep data were not. However, importantly, changes in affective responses were correlated with beneficial alterations in self-reported sleep measures lending support to the contention that the changes in well-being were responsible for the improvements in sleep.

My short-term intervention supported previous findings that expressing gratitude can significantly increase grateful affect (Emmons & McCullough, 2003). My study extends the beneficial effects of expressing gratitude to eudaimonic well-being (i.e. flourishing) and emotional distress as well. It is noteworthy that although flourishing was increased, albeit not significantly, in one of the control conditions (i.e. the daily events), emotional distress was significantly reduced only in the gratitude condition. More importantly though, changes in positive and negative affect were correlated with improvements in self-reported sleep, thus tentatively supporting the contention that positive well-being might exert protective effects on sleep. Indeed, Study 4 found a modest improvement in subjective sleep since following two weeks of gratitude exercises participants reported significantly higher daily sleep quality, in comparison with controls.



Objective sleep data were not improved post-intervention. As already acknowledged in the discussion section of Chapter 5 (pages 306-7), this could be due to too brief and/or not intensive enough experimental manipulation, or due to the fact that the improvements in well-being measures were too modest to drive changes in sleep. However, another possibility is that interventions based on positive psychology paradigms might be more suitable to impact sleep perceptions rather than sleep behaviour, partly because they target eudaimonic and affective responses that are themselves more strongly linked with self-reported sleep, as reported in Study 3. One might therefore wonder whether positive psychology interventions, and in particular the gratitude paradigm, can be used to improve subjective sleep ratings. The changes in sleep in my study were very modest, so it is premature to conclude that expressing gratitude can increase quality of sleep. However, if confirmed by future studies, this positive psychology paradigm can offer a new avenue for non-pharmacological sleep intervention research.

Taken together, not all hypotheses in my studies were supported by the data, and some were supported only partially. Nonetheless, I believe that my work has shed light on previously unexplored associations between sleep and biomarkers, in particular DHEAS and haemoglobin (Study 1), as well as extended data previously reported in experimental research to observational settings (Study 2). I also hope that I tentatively improved our understanding of the issues associated with self-reported measures of sleep quality (Study 3), and provided some support that positive well-being might exert a beneficial role on sleep (Study 4).

## **6.2 Methodological issues and limitations**

My findings have to be interpreted in light of their limitations. Since I have already discussed in detail caveats of all my studies here I will only focus on the most important issues.

First of all, Studies 1 and 2 were based on cross-sectional data so although they suggest that disturbed, too short and too long sleep are associated with adverse biological outcomes including lower HRV, raised inflammation or anaemia, it cannot be ruled out that poor sleep could also be a consequence of these biological processes. Similarly, in Study 3 I found that self-reported sleep problems were associated with adverse psychosocial and affective responses, but it is also plausible that these factors engender poorer sleep.

Studies 1 and 2 were based on subjective sleep information. People are not accurate in their ratings of sleep duration and quality, and objective and subjective sleep indices could to some extent be measuring different phenomena. Therefore it has to be acknowledged that the findings reported in these two studies would not necessary be replicated if objective sleep indices were used instead, as established previously (Patel et al., 2009).

While Study 1 was based on a large and representative cohort of older men and women, Studies 2, 3 and 4 were based on a sample of healthy, young and predominantly university-educated women, so findings might not generalise to those less educated, older or male individuals.

Although in Study 4 I have demonstrated that the gratitude intervention led to increases in eudaimonic well-being as well as decreases in emotional distress, the changes in sleep were very modest limiting the conclusions that could be drawn from these data.

Whilst the above limitations relate mainly to the methodological issues it is also important to discuss the limitations of my PhD thesis as a whole. I have emphasised throughout this thesis that abnormal sleep patterns might increase the risk of CVD and CVD mortality via at least 3 pathways: mood disturbances, health behaviours and direct biological dysregulation. In Studies 1 and 2 I focused on the last pathway, but I only explored two possible biological mechanisms, namely inflammation and autonomic modulation of the heart, which could both be increasing CVD risk in poor sleepers. However, it would have been valuable to study other biological pathways such as glucose metabolism or neuroendocrine processes as well.

A further limitation of my thesis is that in Studies 1-3 I adjusted my statistical analyses for factors related to sleep experience, such as physical activity, smoking and BMI, but I have not explored how these variables themselves are related to the higher CVD risk among poor sleepers. In particular, whilst the association between obesity and (short) sleep duration has received considerable attention in the literature (Cappuccio et al., 2008; Horne, 2008; Patel & Hu, 2008), less is known about the relationship between poor sleep quality and obesity. Similarly, the contribution of physical inactivity or sedentary behaviour towards greater preponderance of CVD in individuals with disturbed or insufficient sleep also remains uncertain.

In Study 3 I have found that adverse psychosocial factors (e.g., low social support) are associated with over-reporting of sleep problems. However, in this study I have only looked at a limited number of variables that might be potentially related to how people rate their sleep. It would also be interesting to investigate how more favourable psychosocial characteristics or dispositions impact sleep behaviour or its perceptions. For example, there is an extensive prospective evidence relating optimism with better health outcomes

(Chida & Steptoe, 2008; Rasmussen, Scheier, & Greenhouse, 2009), but the association between this personality characteristic and sleep remains little explored to date.

### **6.3 Suggestions for future research**

Each of the studies included in this thesis suggests a number of different avenues for future research. It has been argued that long sleep hours are a marker of poor health rather than a risk factor, particularly in the elderly. However, this contention remains more speculative than data driven. The biological mechanisms relating long sleep hours and cardiovascular health have received little attention to date, but emerging observational evidence including my data in Study 1 suggests that in older people long sleep hours, but not short, are linked to low-grade inflammation. Fibrinogen has recently been found to partly mediate the prospective association between long sleep and CHD incident (Hale et al., 2013). Given that in developed countries, including the UK, the number of long sleepers is increasing more research is urgently needed to delineate the direction of the relationship between long sleep and biological risk factors for CVD, such as inflammation.

Low haemoglobin and anaemia are a serious issue in the elderly, but approximately 30% of anaemias have unexplained causes (Guralnik et al., 2005). In Study 1 I have found a cross-sectional association between short and disturbed sleep with low haemoglobin and anaemia. Longitudinal data would help to establish whether low haemoglobin and/or anaemia are a risk factor for poor sleep, as tentatively suggested in paediatric populations (Peirane et al., 2010). Relatedly, prospective studies are warranted to explore the association between sleep measures and DHEAS.

It is notable that in Study 1 apart from the association between disturbed sleep and anaemia, all relationships between the studied biomarkers and sleep measures were found only in men. In particular, gender might moderate the relationship between sleep parameters and inflammation (Mullington et al., 2010; Mullington et al., 2009). Although

in my data short sleep was unrelated to inflammatory responses in either sex, experimental evidence suggests that women have higher levels of inflammatory markers following sleep deprivation (Irwin et al., 2010). Past studies relating sleep and inflammation have either included only female samples (Hale et al., 2013; Matthews et al., 2010), or treated gender as a covariate (Ferrie et al., 2013; Taheri et al., 2007). More systematic approach to gender in sleep studies will help to delineate this issue.

The observational literature relating lower HRV and deviant sleep patterns is still in its infancy. In Study 2 I found that disturbed sleep was cross-sectionally associated with lower daytime HRV, but my sample was relatively small and included only women, so this finding needs to be corroborated by larger prospective studies including both genders. Since sleep was assessed with self-report it would also be informative to test whether similar results would emerge with objective sleep measures. Furthermore, I was only able to demonstrate that daytime, but not night-time, HRV was related to sleep problems. It is unclear whether this is a genuine finding or a reflection of an insufficient statistical power, thus this also deserves further investigation.

Disturbed sleep is common in the UK and has negative consequences on health, in particular in short and long sleepers. Thus it is vital that information on sleep quality is collected in population-based research. However, it is also important to be aware that people's ratings of sleep quality might be influenced by factors other than sleep itself. In Study 3 I found that, independently of negative affect, women reporting higher work stress, lower social support and poor self-reported health underestimated their sleep quality, when compared with the objective sleep quality measure. These women were young, healthy and well-educated, so the next step should be to establish whether this pattern of findings can be replicated in the general population, or more importantly amongst men and women

from less advantageous socio-economic backgrounds, who are at a higher risk of poor sleep (Arber et al., 2009).

Relatedly, due to advances in technology, objective sleep measures (e.g., wrist actigraphy) are becoming more feasible in population-based research. This should stimulate prospective studies to simultaneously assess objective and subjective sleep to establish which measure is more informative. This could help to clarify whether relying on either subjective or objective sleep information is sufficient to explain future health risk.

My short-term intervention (Study 4) increased eudaimonic well-being and reduced emotional distress, and in line with past research it also (slightly) improved daily ratings of sleep quality. My data further suggested that changes in well-being can predict changes in sleep, but on the whole my findings were modest. Longer experimental manipulation, for example 4 weeks, and possibly greater frequency of gratitude exercises are now required to replicate and bolster my findings. It is also important to determine the feasibility of delivering the gratitude paradigm to other populations of people, such as those less educated, male or the elderly.

#### **6.4 Final conclusions**

I hope the studies in this PhD thesis have filled some important gaps in the literature. Using representative and large data of older adults I supported growing evidence relating low-grade inflammation and long sleep hours. I found for the first time, to the best of my knowledge, an association of DHEAS with sleep disturbance, and extended data relating low haemoglobin and anaemia with sleep parameters to a representative sample of older adults. My work has corroborated experimental findings that disturbed sleep is associated with reduced HRV, but more importantly, I discovered that this association can be observed in naturalistic settings as well as in a more representative sample of working women. Furthermore, my PhD has revealed that objective and subjective indicators of

sleep quality are incongruent, a finding previously reported mainly in relation to sleep duration, and that their level of agreement is associated with adverse psychosocial characteristics. Finally, my work has lent tentative support that expressing gratitude can increase positive well-being, which might then have a beneficial impact on subjective sleep ratings.

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## APPENDICES

### Appendix 1. The Jenkins Sleep Problem Scale used in the Daytracker study.

The next series of questions relate to your usual sleep habits in the past month only. Your answers should indicate the most accurate response for the majority of days and nights in the past month. Please tick one answer for each question.

1. How often in the past month did you...

		Not at all	1 – 3 days	4 – 7 days	8-14 days	15-21 days	22-31 days
1.	Have trouble falling asleep?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
2.	Wake up several times per night?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3.	Have trouble staying asleep (including waking up too early).	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4.	Wake up after your usual amount of sleep feeling tired and worn out?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

**Appendix 2. Recruitment email sent to UCL graduate students.**

Email Subject: **Paid female volunteers wanted for well-being study**

**Well-being intervention Study**

**Do you want to improve your mental well-being, and get more from your life?**

We are looking for healthy **female** participants aged 18 to 45 years old, who are either working or are postgraduate students.

The study involves a series of short writing exercises over a 2 week period. We will be collecting questionnaire measures of well-being, plus biological measures (saliva samples, blood pressure, heart rate and physical activity), before and after the writing task.

We compensate each participant **£30** for their time.

If you are interested in taking part, please contact us for more details about the study:

[wellbeingstudy@yahoo.com](mailto:wellbeingstudy@yahoo.com)

Thank you very much, and hope to see you soon!

Best wishes

Marta Jackowska & Amy Ronaldson  
Psychobiology group  
Research Department of Epidemiology and Public Health  
1-19 Torrington Place  
UCL

Appendix 3. Poster used to recruit participants to the study.



## Wellbeing Intervention Study

**Do you want to improve your mental wellbeing, and get more from your life?**

We are looking for healthy **female** participants aged **18 to 45** years old, who are either working or are postgraduate students.

The study involves a series of short writing exercises over a 2-week period. We will be collecting questionnaire measures of wellbeing plus biological measures (saliva samples, blood pressure, physical activity), before and after the writing task.

**Each participant gets £30 for their time.**



If you are interested in taking part, contact us:  
**[wellbeingstudy@yahoo.com](mailto:wellbeingstudy@yahoo.com)**

Thank you very much, and hope to see you soon!  
Jennie & Marta

Psychobiology group  
Dept of Epidemiology and Public Health  
1-19 Torrington Place

Wellbeing Study ☎ 020 7679 8248 ✉ <a href="mailto:wellbeingstudy@yahoo.com">wellbeingstudy@yahoo.com</a>	Wellbeing Study ☎ 020 7679 8248 ✉ <a href="mailto:wellbeingstudy@yahoo.com">wellbeingstudy@yahoo.com</a>	Wellbeing Study ☎ 020 7679 8248 ✉ <a href="mailto:wellbeingstudy@yahoo.com">wellbeingstudy@yahoo.com</a>	Wellbeing Study ☎ 020 7679 8248 ✉ <a href="mailto:wellbeingstudy@yahoo.com">wellbeingstudy@yahoo.com</a>	Wellbeing Study ☎ 020 7679 8248 ✉ <a href="mailto:wellbeingstudy@yahoo.com">wellbeingstudy@yahoo.com</a>	Wellbeing Study ☎ 020 7679 8248 ✉ <a href="mailto:wellbeingstudy@yahoo.com">wellbeingstudy@yahoo.com</a>	Wellbeing Study ☎ 020 7679 8248 ✉ <a href="mailto:wellbeingstudy@yahoo.com">wellbeingstudy@yahoo.com</a>	Wellbeing Study ☎ 020 7679 8248 ✉ <a href="mailto:wellbeingstudy@yahoo.com">wellbeingstudy@yahoo.com</a>
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## Appendix 4. Participants information sheet.

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**UCL PSYCHOBIOLOGY GROUP**  
RESEARCH DEPARTMENT OF EPIDEMIOLOGY AND  
PUBLIC HEALTH



### Well-being intervention study

#### **PARTICIPANT INFORMATION SHEET (Confidential)**

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

#### **What is the purpose of the study?**

Positive psychological states and emotions are associated with better health and longer lifespan. Psychological studies have shown that regularly practising activities designed to increase positive feelings or behaviours can improve well-being. In our project, we want to see whether improving well-being is associated with healthier biological measures. This intervention study is part of two PhD projects supervised by Professor Andrew Steptoe from the Research Department of Epidemiology and Public Health, UCL.

#### **Who can take part?**

This study is being carried out with healthy women aged 18 to 45 years old who are working, or studying at UCL and nearby institutions. Volunteers should not be on any regular medicines or medications except for oral contraceptives. If you have suffered from a serious illness such as heart disease or cancer over the past two years, you will not be suitable for the study.

#### **What will happen during the study?**

The study lasts for 4 weeks in total. During the first week we will ask you to complete a short daily questionnaire on your mood and sleeping habits plus one longer questionnaire booklet that includes measures of lifestyle factors such as smoking and various psychological measures. During this first week, we will also take some biological measurements from you over one day. These measures include blood pressure, heart rate and saliva samples to look at the stress hormone cortisol. We will also ask you to wear a small activity monitor on your wrist for the first week.

Then you will be allocated to a group who will be asked to complete short writing tasks *either* immediately after week one, or after week four.

If you will be asked to do your writing tasks *immediately* after week one we will ask you to complete short writing tasks over week two and three. These writing tasks will ask you to

reflect on your everyday life. You will be given one of two different writing tasks, each looking at different aspects of how you think about your life. During the final (fourth) week, we will ask you to repeat the questionnaire and biological measurements as in week 1. This is so that we can look for changes in these measures to evaluate any effects of the writing tasks.

If you will be asked to do your writing tasks *after week four* there will be a two weeks break after your first week in the study followed by the same questionnaire and biological measurements as in week 1. At the end of your second measurement period we will ask you to complete short writing tasks. These writing tasks will ask you to reflect on your everyday life. You will be given one of two different writing tasks, each looking at different aspects of how you think about your life. You will be asked to practice your writing task for 2 weeks, and return it to us once you finish.

On the first day of the study you will need to come to our research laboratory at the Research Department of Epidemiology and Public Health, UCL, situated at 1-19 Torrington Place before work. When you arrive in the building, one of our team members will take you to an office on the 3<sup>rd</sup> floor. If you happen to have a cold or flu or have had to take any medicines shortly before, please get in touch so that we can reschedule the appointment.

At the beginning of the first session we will measure your height and weight. Next, we will fit you with an activity monitor and a blood pressure monitor. You should wear the activity monitor for the next 7 days and nights, whereas the blood pressure monitor should be kept on for the rest of that day. The blood pressure monitor consists of an arm cuff, and a small monitor attached to your belt (it might be more comfortable for you if you wear a pair of trousers on that day). The blood pressure cuff and monitor are connected by a thin tube that is worn underneath a shirt/top. This device is not uncomfortable, but it will automatically inflate every 30 minutes to measure your blood pressure. It is important that you do not remove the device until you go to bed. We would like to ask you to refrain from taking a bath or shower on the day you will be wearing the blood pressure device. Should you need to take a shower/bath please remove the device.

We will also ask you to give us some samples of saliva over a 24 hour period, so that we can measure the stress hormone cortisol. The saliva samples are taken by chewing gently on a cotton roll for two minutes, then putting the wet cotton roll into a test tube. We want to collect 5 saliva samples over the day and 2 the next morning. We will ask you to come back to the research laboratory to return the blood pressure monitor and saliva samples, but we would be equally happy to collect them from your work place if that is going to be more convenient for you.

The collected information is completely confidential. Results will not be available to anyone outside the study group and will only be used anonymously.

**What if I change my mind during the study?**

If at any point for any reason you do not want to carry on, then you may stop. There are no consequences of withdrawal from the study, other than forfeiting the honorarium payment (see below).

**What happens to the information?**

All the information we get from this study about you, including your name, will be confidential and will only be used for research purposes. The data will be collected and stored in accordance with the 1998 Data Protection Act. The data we collect from all volunteers will be combined, and it will not be possible to identify any individual within published results.



**What happens at the end of the study?**

Provided you have completed all the parts of the study we will give you an honorarium of £30. When the study is complete and all the results are analysed, we will send you a summary of our findings.

**Can I take part if I am pregnant?**

There are no risks to taking part in the study because you are pregnant. However, because pregnancy has effects on some of measures, we do not wish pregnant women to participate.

We hope you are able and willing to take part in our study. If you have any questions, please contact Marta Jackowska ([marta.jackowska.09@ucl.ac.uk](mailto:marta.jackowska.09@ucl.ac.uk)) or Amy Ronaldson ([a.ronaldson@ucl.ac.uk](mailto:a.ronaldson@ucl.ac.uk)), Tel. 020 7679 8328 (internal 48328).

Psychobiology Group, Research Department of Epidemiology and Public Health, 1-19 Torrington Place, London WC1E 6BT.

## Appendix 5. Online eligibility questionnaire (screen shots).

### WELLBEING STUDY: SUITABILITY QUESTIONNAIRE

We would like to know a little about how you have been feeling recently. This is so that we can assess whether or not you are suitable to participate in our study.

If you are suitable, we will contact you to arrange a time to meet. However, if you do not hear from us within three months, please assume you have not been invited to take part.

All answers will be kept strictly private and confidential, and will only be used for the purposes of assessing your suitability for the study.

[Start](#)

Powered by  
[Opinio Survey Software](#)

We should like to know if you have had any medical complaints and how your health has been in general over the **past few weeks**. Please answer **ALL** questions by selecting the answer which you think most nearly applies to you. Remember that we want to know about present and recent complaints, not those you had in the past. It is important that you try to answer ALL the questions.

### Have you recently...

1. been able to concentrate on whatever you are doing?

Better than usual   Same as usual   Less than usual   Much less than usual

2. lost much sleep over worry?

Not at all   No more than usual   Rather more than usual   Much more than usual

3. felt that you are playing a useful part in things?

More so than usual   Same as usual   Less useful than usual   Much less useful

4. felt capable of making decisions about things?

More so than usual   Same as usual   Less so than usual   Much less capable

5. felt constantly under strain?

Not at all   No more than usual   Rather more than usual   Much more than usual

6. felt you couldn't overcome your difficulties?

Not at all   No more than usual   Rather more than usual   Much more than usual







## Appendix 6. The study consent form.

**UCL PSYCHOBIOLOGY GROUP**  
DEPARTMENT OF EPIDEMIOLOGY AND PUBLIC  
HEALTH



### **Confidential** **Informed Consent Form**

**Project title: Well-being intervention study**

- |   |          |
|---|----------|
| Have you read the information sheet about this study?   | Yes / No |
| Have you had the opportunity to ask questions and discuss the study?  | Yes / No |
| Have you received satisfactory answers to all your questions?   | Yes / No |
| Have you received enough information about the study?   | Yes / No |
| Do you understand that you are free to withdraw from the study at any time, without giving a reason for withdrawal?<br>/ No | Yes      |
| Do you agree with the publication of the results of this study in appropriate outlets?<br>Yes / No                          |          |
| Do you agree to take part in this study?<br>/ No  | Yes      |

Signature of participant:

Signature of investigator:

Date:

If you have any further questions about the study, please contact:  
Marta Jackowska ([marta.jackowska.09@ucl.ac.uk](mailto:marta.jackowska.09@ucl.ac.uk)) or Amy Ronaldson  
([a.ronaldson@ucl.ac.uk](mailto:a.ronaldson@ucl.ac.uk))  
Psychobiology Group, Research Department of Epidemiology and Public Health,

1-19 Torrington Place, London WC1E 6BT. Tel. 020 7679 8328 (internal 48328).

If you wish to complain about any aspect of the way you have been approached or treated during the course of the study, you should email the Chair of the UCL Committee for the Ethics of Non-NHS Human Research ([gradschoolhead@ucl.ac.uk](mailto:gradschoolhead@ucl.ac.uk)) or send a letter to: The Graduate School, North Cloisters, Wilkins Building, UCL, Gower Street, London WC1E 6BT.



**Appendix 7. Baseline questionnaire assessing sociodemographic, economic, eudaimonic and affective characteristics of study participants.**

**Well-being study**

**QUESTIONNAIRE BOOKLET**

**PLEASE FILL OUT ONCE DURING THE FIRST WEEK**

*Week 1*

Date \_\_\_\_\_ Project ID \_\_\_\_\_

**Instructions:**

In this booklet we will be asking you questions related to your personal circumstances, your regular behaviour and your health and well-being. We will give you a similar questionnaire booklet to fill out during the last week of the study.

Please answer every question in the booklet, and read instructions carefully at the start of each set of questions, as they may differ. You should indicate your answers by either circling one answer or ticking a box as instructed.

If you have any questions on how to fill out any part of this booklet, please contact either Jennie or Marta for guidance:

**Amy:** a.ronaldson@ucl.ac.uk

**Marta:** marta.jackowska.09@ucl.ac.uk

**Phone number: 020 7679 8248**

We would like to assure you that all your answers are strictly confidential. It will not be possible to identify your responses from the reports we prepare. We will use the information to conduct statistical analyses and to write academic articles, but it will not be possible to identify your responses from any reports or publications. None of the information will be made available to anyone else apart from the research group.

Thank you very much again for your participation.

## **SECTION 1**

This section has a series of questions that ask about you and your current situation.

1. Today's date? / /
2. What is your date of birth? DD/MM/YYYY / /
3. Please indicate what is your relationship status at the moment?
  - Married & living together, or living with someone in marital-like relationship
  - Single
  - Separated / Divorced / Formerly lived with someone in a marital-like relationship
  - Widowed
4. Please indicate your ethnic background.

<input type="radio"/> White British	<input type="radio"/> White and Black Caribbean	<input type="radio"/> Indian
<input type="radio"/> White Irish	<input type="radio"/> White and Black African	<input type="radio"/> Pakistani
<input type="radio"/> Any other white background	<input type="radio"/> White and Asian	<input type="radio"/> Bangladeshi
<input type="radio"/> Caribbean	<input type="radio"/> Any other Mixed background	<input type="radio"/> Any other Asian background
<input type="radio"/> African	<input type="radio"/> Chinese	<input type="radio"/> Any other
5. What is your religion?

<input type="radio"/> Buddhist	<input type="radio"/> Jewish	<input type="radio"/> No religion
<input type="radio"/> Christian (Catholic)	<input type="radio"/> Moslem	<input type="radio"/> Other? <i>(please specify)</i>
<input type="radio"/> Christian (Protestant)	<input type="radio"/> Sikh	

---

**6.** Which category best describes your employment?

- Administrative/clerical
  - Manual & craft (e.g. cleaner, security)
  - Non clinical research (e.g. research associate/assistant)
  - Medical/clinical (e.g. clinical research associate, research nurse)
  - Technician (e.g. lab technician, IT)
  - Managerial
  - Non clinical academic/teaching (e.g. lecturer, teaching assistant)
  - Postgraduate student
  - Other, please describe:
- 

**7.** How many hours a week do you work, on average?

- 1-20 hours per week
- 21-34 hours per week
- 35-45 hours per week
- 46+ hours per week

8. What educational qualifications do you have? Please mark the circle next to your highest qualification.

- |   |  |
|---|--|
| <input type="radio"/> No qualifications                     | <input type="radio"/> Higher National Certificate (HNC) or Diploma (HND) |
| <input type="radio"/> CSE, GCSE or 'O' Level                | <input type="radio"/> Undergraduate degree                               |
| <input type="radio"/> Vocational qualification (GNVQ, BTEC) | <input type="radio"/> Postgraduate qualification (Masters, PhD)          |
| <input type="radio"/> 'A' or 'AS' level                     | <input type="radio"/> Other (please specify)                             |
- 

9. Do you have children? No  Yes

10. ↪ If yes, how many? \_\_\_\_\_

11. ↪ If yes, how old are your children?

---

12. ↪ How many of your children live with you? \_\_\_\_\_

13. What is the total current yearly amount you receive from your wage, benefit allowances, annual salary or other sources (e.g. investments) *before* tax is deducted? Please mark one circle.

- |   |   |
|---|---|
| <input type="radio"/> Less than £9,999  | <input type="radio"/> £25,000 - £34,999 |
| <input type="radio"/> £10,000 - £14,999 | <input type="radio"/> £35,000 - £49,999 |
| <input type="radio"/> £15,000 - £19,999 | <input type="radio"/> £50,000 - £69,999 |
| <input type="radio"/> £20,000 - £24,999 | <input type="radio"/> More than £70,000 |

14. What total income (including your own) has your household received in the last 12 months *before* tax is deducted?

- |   |   |
|---|---|
| <input type="radio"/> Less than £9,999  | <input type="radio"/> £35,000 - £49,999   |
| <input type="radio"/> £10,000 - £14,999 | <input type="radio"/> £50,000 - £69,999   |
| <input type="radio"/> £15,000 - £19,999 | <input type="radio"/> £70,000 - £99,999   |
| <input type="radio"/> £20,000 - £24,999 | <input type="radio"/> £100,000 - £199,999 |
| <input type="radio"/> £25,000 - £34,999 | <input type="radio"/> More than £200,000  |

## **SECTION 2**

This section asks you about your habits and lifestyle.

How often do you take part in sports or activities that are mildly energetic, moderately energetic or vigorous? (Circle one answer only for each item).

		<b>Never / hardly ever</b>	<b>About once to three times a month</b>	<b>Once to twice a week</b>	<b>Three times or more a week</b>
1.	Mildly energetic ( <i>e.g. walking, woodwork, weeding, general housework</i> )	0	1	2	3
2.	Moderately energetic ( <i>e.g. cycling, dancing, scrubbing, golf, decorating, lawn mowing, leisurely swimming</i> )	0	1	2	3
3.	Vigorous ( <i>e.g. running, hard swimming, tennis, squash, digging, cycle racing</i> )	0	1	2	3

4. Do you smoke cigarettes regularly? (*Please mark only one circle*)

- No
- Yes

5. If yes, about how many cigarettes a day do you usually smoke? \_\_\_\_\_

The next questions are about drinking alcohol, including beer, wine, spirits and any other alcoholic drink.

6. Do you drink alcohol?

- No
- Yes

7. If yes, on how many days over the past two weeks (14 days) did you have a drink?  
\_\_\_\_\_ *days*

8. On the days that you did drink, how many drinks did you have, on average?  
(One drink = one small glass of wine, half a pint of beer or cider, a single measure of spirits)  
\_\_\_\_\_ *drinks*

**SECTION 3**

The following questions relate to your usual sleep habits during the **past week**. Your answers should indicate the most accurate replay for the majority of days and nights in the past week. It is important that you answer all questions.

1. During the past week, what time have you usually gone to bed at night?

BED TIME \_\_\_\_\_

2. During the past week, how long (in minutes) has it usually taken you to fall asleep each night?

NUMBER OF MINUTES \_\_\_\_\_

3. During the past week, what time have you usually got up in the morning?

GETTING UP TIME \_\_\_\_\_

4. During the past week, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spent in bed).

HOURS OF SLEEP PER NIGHT \_\_\_\_\_

For each of the remaining questions, please circle the response that best describes your sleep. Please answer all questions.

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

a	Cannot get to sleep within 30 minutes			
	Not during the past week	Less than once a week	Once or twice a week	Three or more times a week
b	Wake up in the middle of the night or early morning			
	Not during the past week	Less than once a week	Once or twice a week	Three or more times a week



c	Have to get up to use the bathroom			
	Not during the past week	Less than once a week	Once or twice a week	Three or more times a week
d	Cannot breathe comfortably			
	Not during the past week	Less than once a week	Once or twice a week	Three or more times a week
e	Cough or snore loudly			
	Not during the past week	Less than once a week	Once or twice a week	Three or more times a week
f	Feel too cold			
	Not during the past week	Less than once a week	Once or twice a week	Three or more times a week
g	Feel too hot			
	Not during the past week	Less than once a week	Once or twice a week	Three or more times a week
h	Had bad dreams			
	Not during the past week	Less than once a week	Once or twice a week	Three or more times a week
i	Have pain			
	Not during the past week	Less than once a week	Once or twice a week	Three or more times a week
j	Other reason(s), please describe _____			
	How often during the past week have you had trouble sleeping because of this?			
	Not during the past week	Less than once a week	Once or twice a week	Three or more times a week
6.	During the past week, how would you rate your overall sleep quality?			
	Very good	Fairly good	Fairly bad	Very bad

7.	<p data-bbox="347 197 1391 271">During the past week, how often have you taken medicine to help you sleep (prescribed by the doctor or “over the counter”)?</p> <table data-bbox="347 309 1391 383"> <tr> <td data-bbox="347 309 603 383">Not during the past week</td> <td data-bbox="603 309 858 383">Less than once a week</td> <td data-bbox="858 309 1114 383">Once or twice a week</td> <td data-bbox="1114 309 1391 383">Three or more times a week</td> </tr> </table>	Not during the past week	Less than once a week	Once or twice a week	Three or more times a week
Not during the past week	Less than once a week	Once or twice a week	Three or more times a week		
8.	<p data-bbox="347 450 1391 524">During the past week, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?</p> <table data-bbox="347 562 1391 636"> <tr> <td data-bbox="347 562 603 636">Not during the past week</td> <td data-bbox="603 562 858 636">Less than once a week</td> <td data-bbox="858 562 1114 636">Once or twice a week</td> <td data-bbox="1114 562 1391 636">Three or more times a week</td> </tr> </table>	Not during the past week	Less than once a week	Once or twice a week	Three or more times a week
Not during the past week	Less than once a week	Once or twice a week	Three or more times a week		
9.	<p data-bbox="347 674 1391 748">During the past week, how much of a problem has it been for you to keep up enough enthusiasm to get things done?</p> <table data-bbox="347 786 1391 898"> <tr> <td data-bbox="347 786 826 824">No problem at all</td> <td data-bbox="826 786 1391 824">Only a very slight problem</td> </tr> <tr> <td data-bbox="347 862 826 898">Somewhat of a problem</td> <td data-bbox="826 862 1391 898">A very big problem</td> </tr> </table>	No problem at all	Only a very slight problem	Somewhat of a problem	A very big problem
No problem at all	Only a very slight problem				
Somewhat of a problem	A very big problem				
10.	<p data-bbox="347 927 1391 965">Do you have a bed partner or room mate?</p> <table data-bbox="347 1003 1391 1122"> <tr> <td data-bbox="347 1003 954 1041">No bed or room mate</td> <td data-bbox="954 1003 1391 1041">Partner/room mate in other room</td> </tr> <tr> <td data-bbox="347 1079 954 1117">Partner in same room, but not same bed</td> <td data-bbox="954 1079 1391 1117">Partner in same bed</td> </tr> </table>	No bed or room mate	Partner/room mate in other room	Partner in same room, but not same bed	Partner in same bed
No bed or room mate	Partner/room mate in other room				
Partner in same room, but not same bed	Partner in same bed				

#### **SECTION 4**

Please think about what you have been doing and experiencing during the **past week**. Please report how much you experienced each of the following feelings, using the scale below. For each item, select a number from 1 to 5 that best describes your feelings.

		<b>Very rarely or never</b>	<b>Rarely</b>	<b>Sometimes</b>	<b>Often</b>	<b>Very often or always</b>
1.	Positive	1	2	3	4	5
2.	Negative	1	2	3	4	5
3.	Good	1	2	3	4	5
4.	Bad	1	2	3	4	5
5.	Pleasant	1	2	3	4	5
6.	Unpleasant	1	2	3	4	5
7.	Happy	1	2	3	4	5
8.	Sad	1	2	3	4	5
9.	Afraid	1	2	3	4	5
10.	Joyful	1	2	3	4	5
11.	Angry	1	2	3	4	5
12.	Contented	1	2	3	4	5

## **SECTION 5**

For each of the following items, indicate how often you have felt like this in the **past week** by circling the number for each item, using the response choices listed just below.

		<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>
		<b>Strongly disagree</b>	<b>Disagree</b>	<b>Slightly disagree</b>	<b>Neutral</b>	<b>Slightly agree</b>	<b>Agree</b>	<b>Strongly agree</b>
1.	I have so much in life to be thankful for	1	2	3	4	5	6	7
2.	If I had to list everything that I felt grateful for, it would be a very long list	1	2	3	4	5	6	7
3.	When I look at the world, I don't see much to be grateful for	1	2	3	4	5	6	7
4.	I am grateful to a wide variety of people	1	2	3	4	5	6	7
5.	As I get older I find myself more able to appreciate the people, events, and situations that have been part of my life history	1	2	3	4	5	6	7
6.	Long amounts of time can go by before I feel grateful to something or someone	1	2	3	4	5	6	7

## **SECTION 6**

Below are eight statements with which you may agree or disagree. Using the 1–7 scale below, indicate your agreement with each item by indicating that response for each statement.

		<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>
		<b>Strongly disagree</b>	<b>Disagree</b>	<b>Slightly disagree</b>	<b>Neither agree nor disagree</b>	<b>Slightly agree</b>	<b>Agree</b>	<b>Strongly agree</b>
1.	I lead a purposeful and meaningful life	1	2	3	4	5	6	7
2.	My social relationships are supportive and rewarding	1	2	3	4	5	6	7
3.	I am engaged and interested in my daily activities	1	2	3	4	5	6	7
4.	I actively contribute to the happiness and well-being of others	1	2	3	4	5	6	7
5.	I am competent and capable in the activities that are important to me	1	2	3	4	5	6	7
6.	I am a good person and live a good life	1	2	3	4	5	6	7
7.	I am optimistic about my future	1	2	3	4	5	6	7
8.	People respect me	1	2	3	4	5	6	7

## **SECTION 7**

Below is a list of statements of how people might think and feel. For each of the following sentences, *indicate how much you agree* by circling the most honest and accurate response. Try not to let your response to one statement influence your other responses.

		<b>I disagree a lot</b>	<b>I disagree a little</b>	<b>I neither agree nor disagree</b>	<b>I agree a little</b>	<b>I agree a lot</b>
1.	In uncertain times, I usually expect the best	0	1	2	3	4
2.	It's easy for me to relax	0	1	2	3	4
3.	If something can go wrong for me, it will	0	1	2	3	4
4.	I'm always optimistic about my future	0	1	2	3	4
5.	I enjoy my friends a lot	0	1	2	3	4
6.	It's important for me to keep busy	0	1	2	3	4
7.	I hardly ever expect things to go my way	0	1	2	3	4
8.	I don't get upset too easily	0	1	2	3	4
9.	I rarely count on good things happening to me	0	1	2	3	4
10.	Overall, I expect more good things to happen to me than bad	0	1	2	3	4

## **SECTION 8**

Below are five statements with which you may agree or disagree. Using the 1-7 scale below, please indicate your agreement with each item by circling the appropriate number.

	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>			
	<b>Strongly disagree</b>	<b>Disagree</b>	<b>Slightly disagree</b>	<b>Neither agree nor disagree</b>	<b>Slightly agree</b>	<b>Agree</b>	<b>Strongly agree</b>			
1.	In most ways my life is close to my ideal			1	2	3	4	5	6	7
2.	The conditions of my life are excellent			1	2	3	4	5	6	7
3.	I am satisfied with my life			1	2	3	4	5	6	7
4.	So far I have got the important things I want in life			1	2	3	4	5	6	7
5.	If I could live my life over, I would change almost nothing			1	2	3	4	5	6	7

## **SECTION 9**

The questions in this scale ask you about your feelings and thoughts over the **past week**. In each case, you will be asked to indicate by circling *how often* you felt or thought a certain way.

		<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>
		<b>Never</b>	<b>Almost never</b>	<b>Sometimes</b>	<b>Fairly often</b>	<b>Very often</b>
1.	How often have you been upset because of something that happened unexpectedly?	0	1	2	3	4
2.	How often have you felt that you were unable to control the important things in your life?	0	1	2	3	4
3.	How often have you felt nervous and “stressed”?	0	1	2	3	4
4.	How often have you felt confident about your ability to handle your personal problems?	0	1	2	3	4
5.	How often have you felt that things were going your way?	0	1	2	3	4
6.	How often have you found that you could not cope with all the things that you had to do?	0	1	2	3	4
7.	How often have you been able to control irritations in your life?	0	1	2	3	4
8.	How often have you felt that you were on top of things?	0	1	2	3	4



0	1	2	3	4
Never	Almost never	Sometimes	Fairly often	Very often

9.	How often have you been angered because of things that were outside of your control?	0	1	2	3	4
10.	How often have you felt difficulties were piling up so high that you could not overcome them?	0	1	2	3	4

### **SECTION 10**

Please read each item and circle the reply which comes closest to how you have been feeling in the **past week**. Don't take too long over your replies: your immediate reaction to each item will probably be more accurate than a long thought out response.

<b>1</b>	<b>I feel tense or 'wound up':</b>			
	Most of the time	A lot of the time	From time to time, occasionally	Not at all
<b>2</b>	<b>I still enjoy the things I used to enjoy:</b>			
	Definitely as much	Not quite so much	Only a little	Hardly at all
<b>3</b>	<b>I get a sort of frightened feeling as if something awful is about to happen:</b>			
	Very definitely and quite badly	Yes, but not too badly	A little, but it doesn't worry me	Not at all

<b>4</b>	<b>I can laugh and see the funny side of things:</b>			
	As much as I always could	Not quite so much now	Definitely not so much now	Not at all
<b>5</b>	<b>Worrying thoughts go through my mind:</b>			
	A great deal of the time	A lot of the time	From time to time, but not too often	Only occasionally
<b>6</b>	<b>I feel cheerful:</b>			
	Not at all	Not often	Sometimes	Most of the time
<b>7</b>	<b>I can sit at ease and feel relaxed:</b>			
	Definitely	Usually	Not Often	Not at all
<b>8</b>	<b>I feel as if I am slowed down:</b>			
	Nearly all the time	Very often	Sometimes	Not at all
<b>9</b>	<b>I get a sort of frightened feeling like 'butterflies' in the stomach:</b>			
	Not at all	Occasionally	Quite Often	Very Often
<b>10</b>	<b>I have lost interest in my appearance:</b>			
	Definitely	I don't take as much care as I should	I may not take quite as much care	I take just as much care as ever
<b>11</b>	<b>I feel restless as I have to be on the move:</b>			
	Very much indeed	Quite a lot	Not very much	Not at all

<b>12</b>	<b>I look forward with enjoyment to things:</b>			
	As much as I ever did	Rather less than I used to	Definitely less than I used to	Hardly at all
<b>13</b>	<b>I get sudden feelings of panic:</b>			
	Very often indeed	Quite often	Not very often	Not at all
<b>14</b>	<b>I can enjoy a good book or radio or TV program:</b>			
	Often	Sometimes	Not often	Very seldom

**15.** In general, how would you say that your health has been in the **past week**? Please circle the answer which best describes your health.

Poor                  Fair                  Good                  Very good                  Excellent

That was the final section in this questionnaire; please check you have completed all the sections before returning it to us. If you have any comments, or you would like to add anything to what you have told us, please add them in the space below.

Thank you very much for taking the time to participate in this research project, we appreciate the contribution you have made to our research on wellbeing and health.

*Additional comments.*

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**Appendix 8. Sleep diary (night 1).**

**DAY 2**

**Today's date is:** \_\_\_\_\_

**Sleep record:**

Below are questions referring to your sleep ***last night***.

---

1     What time did you go to sleep last night?

---

2     What time did you wake up this morning?

---

3     Please circle the answer that best describes your sleep *quality* last night:

Very good

Fairly good

Fairly bad

Very bad

---

4     How *long* did you sleep for last night? Please state in hours and minutes:

Hours.....Minutes.....

---

**Appendix 9. PSQI database for entering raw data (top figure) and calculated subjective sleep measures (bottom figure) (screen shots).**

A\_PSQI

Study ID

Assessment Date

Q1-Bed Time

Q2-Fall Asleep

Q3-Getting Up

Q4-Hours Of Sleep

Q5A-Cannot Sleep

Q5B-Wake Up

Q5C-Bathroom

Q5D-Breathe

Q5E-Cough Or Snore

Q5F-Cold

Q5G-Hot

Q5H-Bad Dreams

Q5I-Pain

Q5JComment-Other Reason

Q5J-Troubling Sleep

Q6-Sleep Quality

Q7-Medicine-Induced Sleep

Q8-Trouble Staying Awake

Q9-Enthusiasm

Q10-Bed Partner/Roommate

Q10A-Loud Snoring

Q10B-Long Pauses

Q10C-Legs Twitching

Q10D-Disorientation

Q10EComment-Other Restlessness

Q10E-Restlessness

Record: 1 of 122 No Filter Search

A\_PSQI\_S

Study ID	Assessment	nq2	DURAT	nq5j	tmpsd	DISTB	tmpsl	LATEN	tmpdd
1	23/10/2011	1	0	0	2	1	3	2	2
2	24/10/2011	1	1	0	4	1	3	2	5
3	24/10/2011	0	0	0	4	1	0	0	3
4	21/10/2011	1	0	2	10	2	2	1	2
5	26/10/2011	0	0	3	9	1	3	2	4
6	25/10/2011	2	3	0	5	1	5	3	1
7	26/10/2011	2	1	0	4	1	5	3	3
8	26/10/2011	2	0	3	13	2	5	3	2
9	26/10/2011	0	2	3	7	1	0	0	3
10	03/11/2011	2	1	0	9	1	5	3	2
11	31/10/2011	0	2	2	10	2	2	1	3
12	01/11/2011	0	1	0	7	1	0	0	0
13	06/11/2011	1	0	0	12	2	1	1	0
14	02/11/2011	0	0	0	9	1	2	1	3
15	04/11/2011	0	1	0	11	2	1	1	3
16	03/11/2011	1	1	0	13	2	2	1	1
17	08/11/2011	0	0	2	9	1	2	1	3
18	10/11/2011	1	0	0	6	1	4	2	1
19	14/11/2011	1	0	0	2	1	3	2	1

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**Appendix 10. Paper diary used in the gratitude and daily events conditions (week 1).**

**Week 1**

Exercise 1: Today's date is.....

1.
2.
3.

Exercise 2: Today's date is.....

1.
2.
3.

Exercise 3: Today's date is.....

1.
2.
3.

**Appendix 11. Reminder email sent to participants in the gratitude and daily events conditions.**

**Subject: Wellbeing study - writing task reminder**

Dear ,

I hope you are getting on OK with the writing task. Just a quick reminder that we would like you to please do the writing exercises 3 times per week over the 2 weeks (6 times in total). You should try to spread out when you do the exercises if possible e.g. every other day.

If you have any problems or questions, please do not hesitate to contact me. I'll send you another reminder next week and to arrange when to meet for the final part of the study.

## LIST OF PUBLICATIONS

Studies 1, 2, 3 presented in this thesis have already been published and Study 4 is currently being prepared for publication. Some of my work has also been presented at scientific conferences.

- Waller J, Bartoszek\* M, Marlow L, Wardle J. (2009). Barriers to cervical cancer screening attendance in England: a population-based survey. *Journal of Medical Screening*, 16, 199-204.
- Jackowska M, Dockray S, Hendrickx H, Steptoe A. (2011). Psychosocial factors and sleep efficiency: Discrepancies between subjective and objective evaluations of sleep. *Psychosomatic Medicine*, 73,810-816.
- Waller J, Jackowska M, Marlow L, Wardle J. (2012). Exploring age differences in reasons for non-attendance for cervical screening: a qualitative study. *An International Journal of Obstetrics & Gynaecology*, 119, 26-32.
- Jackowska M, von Wagner C, Wardle J, Juszczuk D, Luszczynska A, Waller J. (2012). Cervical screening among migrant women: a qualitative study of Polish, Slovak and Romanian women in London, UK. *Journal of Family Planning and Reproductive Health Care*, 38,229-38.
- Jackowska M, Dockray S, Endrighi R, Hendrickx H, Steptoe A. (2012). Sleep problems and heart rate variability over the working day. *Journal of Sleep Research* 21,434-440.
- Jackowska M, Hamer M, Carvalho LA, Erusalimsky JD, Butcher L, Steptoe A. (2012). Short Sleep Duration Is Associated with Shorter Telomere Length in Healthy Men: Findings from the Whitehall II Cohort Study. *Plos One* 7,e47292.
- Jackowska M, Kumari M, Steptoe A. (2013). Sleep and biomarkers in the English Longitudinal Study of Ageing: Associations with C-reactive protein, fibrinogen, dehydroepiandrosterone sulfate and hemoglobin. *Psychoneuroendocrinology* (In Press).

\* name changed from Bartoszek to Jackowska in 2010 due to marriage.



## CONFERENCE PRESENTATIONS

### Posters:

- 1." Predictors of well-being in the English Longitudinal Study of Ageing (ELSA)". The 64th Annual Scientific Meeting of the Gerontological Society of America, New Orleans, US, November 2010.
- 2."Psychosocial factors and sleep problems: Discrepancies between subjective and objective evaluations of sleep".UK Society for Behavioural Medicine conference, Leeds, December 2010.
- 3."The relationship between sleep and health-related biomarkers; an analysis from the English Longitudinal Study of Ageing (ELSA)".The 25th European Health Psychology Conference, Crete, Greece, September 2011.
4. "Positive Affect and related psychological characteristics are associated with subjective but not objective sleep measures in a sample of young women". The 71st Annual Scientific Meeting of American Psychosomatic Society, Miami, US, March 2013.

### Oral presentations:

- 1."Well-being in relation to socio-demographic and health-related variables in a nationally representative sample of British people age 50+".University of Michigan, US, March 2010.
- 2."The relationship between sleep and health-related biomarkers: an analysis from the English Longitudinal Study of Ageing (ELSA)". UCL-NIMR Student Seminar Day at the National Institute for Medical Research, London, May 2011.
- 3."Sleep and Biomarkers in the English Longitudinal Study of Ageing: Associations with C-Reactive Protein, Fibrinogen, Dehydroepiandrosterone Sulfate and Hemoglobin".The 70th Annual Scientific Meeting of American Psychosomatic Society, Athens, Greece, March 2012.