SLEEP AND ITS ASSOCIATION WITH METABOLIC FUNCTION ACROSS THE LIFESPAN

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ABSTRACT

Obesity and accompanied metabolic dysfunction are global public health problems. A better understanding of factors contributing to obesity and metabolic disease development is needed, particularly lifestyle behaviours including sleep. Sleep duration has been suggested to be a contributor to obesity and metabolic dysfunction development. This thesis examines the relationships between sleep, obesity, and metabolic function in different age groups and ethnicities. The thesis also presents a model for experimental sleep manipulation that can be used to understand the underlying mechanisms for the associations among sleep duration, obesity, and metabolic dysfunction. The studies and findings were as follows:

1. Cross-sectional data from young South Asian children in Birmingham showed that 'inadequate' sleep duration, unlike findings from different population studies, was not associated with overweight/obesity.
2. Cross-sectional data from a population of adolescents in the Midlands showed that short sleep duration was associated with increased odds of overweight/obesity.
3. Cross-sectional data from older Chinese from Guangzhou, China, showed that total long sleep duration was associated with increased odds of the metabolic syndrome.
4. Data from the experimental sleep model revealed that reducing sleep over a prolonged period is more achievable than sleep extension.

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Abbreviations

AASM	American Academy of Sleep Medicine
BEACHeS	Birmingham healthy Eating and Active lifestyle for Children Study
BIA	Bioelectrical Impedance Analysis
BMI	Body Mass Index
BF	Body Fat
BF%	Body Fat Percentage
CDC	Centers for Disease Control and Prevention
CHD	Coronary Heart Disease
CI	Confidence Interval
CPU	Cellular Phone Use
CSHQ	Children's Sleep Habits Questionnaire
CT	X-ray computed tomography
CVD	Cardiovascular Disease
DXA	Dual-energy X-ray Absorptiometry
DSPS	Delayed Sleep Phase Syndrome
ECG	Electrocardiogram
EDS	Excessive Daytime Sleepiness
EEG	Electroencephalography
ESS	Epworth Sleepiness Scale
FM	Fat Mass
FFM	Fat Free Mass
GBCS	Guangzhou Biobank Cohort Study
HC	Hip Circumference
HDL-C	High Density Lipoprotein-Cholesterol
HOMA-IR	Homeostasis Model Assessment-Insulin Resistance
HR	Hazard Ratio
HSE	Health Survey for England
IDF	International Diabetes Federation
IFG	Impaired Fasting Glucose
IOTF	International Obesity Task Force
LDL-C	Low Density Lipoprotein-Cholesterol
MASSES	Midlands Adolescent Schools Sleep Education Study
MT	Mobile Telephones
MUAC	Mid Upper Arm Circumference
NCEP	U.S. National Cholesterol Education Program
NHS	National Health Service
NREM	Non-REM Sleep
NSF	National Sleep Foundation
OR	Odds Ratio
PC	Personal Computer
PDSS	Paediatric Daytime Sleepiness Scale
PSG	Polysomnography

PSQI	Pittsburgh Sleep Quality Index
REM	Rapid Eye Movement sleep
ROR	Risk odds ratio
SCN	Suprachiasmatic Nucleus
SES	Socioeconomic Status
SOL	Sleep Onset Latency
SSHS	Schools Sleep Habits Survey
SWS	Slow Wave Sleep
T2DM	Type 2 Diabetes Mellitus
TBFM	Total Body Fat Mass
TIB	Time In Bed
TSD	Total Sleep Deprivation
TST	Total Sleep Time
TV	Television
VG	Video Games
VGD	Video Game Dependency
WASO	Wake After Sleep Onset
WC	Waist Circumference
WHO	World Health Organisation

1 INTRODUCTION

Sleep is an integral part of human biology and the most prevalent form of human behaviour.[1] Sleep occupies around a third of adult life but the need for sleep alters across the lifespan. Unlike other essential needs for survival, such as water and food, which individuals can withhold, with the potential to eventually result in death, the urge to sleep cannot be resisted. This is indicative of a strong biological drive. The importance of sleep to survival has been previously demonstrated in a, now outdated, rodent model of total sleep deprivation (TSD) where exposure to TSD resulted in death.[2] Human population studies have also observed an association between sleep duration and mortality.[3] Thus, sleep is essential for survival. The precise physiological functions of sleep and what adequate sleep is, however, remain unclear and warrant further investigation. Apart from the possible relationship with survival, it is increasingly recognised that sleep has an impact on physical and mental health. Recent evidence also suggests an important link between sleep and metabolic function but mechanisms underlying this association are largely undetermined.

The sections below provide a brief overview of the history of sleep and its measurement, sleep stages and the currently accepted views regarding adequate sleep duration. Sleep duration across the human lifespan is reviewed followed by data linking sleep and metabolism.

1.1 Sleep and its measurements

Despite sleep intriguing mankind throughout history, sleep research is a relatively young scientific discipline. Several methods have been used to collect data regarding sleep and its disorders. These include self-reported questionnaires and diaries, actigraphy and polysomnography (PSG). Prior to development of the electroencephalogram (EEG) and PSG, however, little was known about physiological alterations during sleep. The EEG was invented in the 1920's, allowing measurement of human brain activity. Subsequently, PSG, a complete recording of biophysiological alterations that take place during sleep, was developed with definitions of sleep stages determined by consensus.[4] PSG monitors brain, eye, muscle, breathing and heart activity through use of strategically positioned electrodes, transducers and monitors.

Prior to the invention of EEG, it was believed that brain activity was diminished during sleep but we now know that sleep is a highly complex behaviour accompanied by cyclical alterations in brain activity. An intriguing discovery was that of Rapid Eye Movement (REM) sleep by Aserinsky[5] in the early 1950's, which not only generated great interest amongst sleep researchers but also allowed the complete PSG staging of sleep to be defined.

Polysomnographic sleep is divided into four defined sleep stages according to the current American Academy of Sleep Medicine (AASM) criteria.[6] There are two different types of sleep: rapid eye movement (REM; Stage R) sleep and non-rapid eye movement (NREM) sleep (Stages N1-N3). NREM is further divided into three different stages (N1-N3), based

on characteristics of EEG patterns. All stages and types of sleep alternate cyclically.[7] A typical night's sleep consists of 4-5 sleep cycles (Figure 1.1). EEG activity is defined according to frequency bands of alpha, beta, delta and theta activity. During normal wakefulness beta activity is present (Figure 1.2). Conversely, alpha and theta activity is representative of N1 sleep (Figure 1.3), usually the transitional period between wakefulness and sleep, lasting a few minutes. N2 is also characterised by theta waves along with two specific brain wave patterns: K complexes and sleep spindles, a single sudden strong wave or brief bursts of waves both lasting less than a second, respectively (Figure 1.4). The EEG then signals high amplitude (>75 microvolts) and low frequency waves (<4Hz), known as delta activity indicating N3 sleep stage (Figure 1.5). This sleep stage is classified as deep or slow wave sleep (SWS) and is accompanied by profound muscle relaxation and is believed to be the most restorative stage. Approximately 90 minutes after sleep onset, delta waves vanish, theta waves reappear and the brain becomes highly active, similar to what is observed during active wakefulness. The eyes move rapidly back and forth under closed eyelids, muscle tone is lost and the individual becomes paralysed, with the exception of the eye and respiratory muscles (diaphragm). This stage is REM or Stage R sleep where pulse, metabolic rates, blood pressure and brain temperature become elevated and erratic. EEG activity REM sleep is similar to that of wakefulness (hence the use of the term "paradoxical sleep") but muscle tone reduces, detected by the electromyography (EMG) and the rapid eye movements are shown through the electro-oculography (EOG) channels (Figure 1.6).

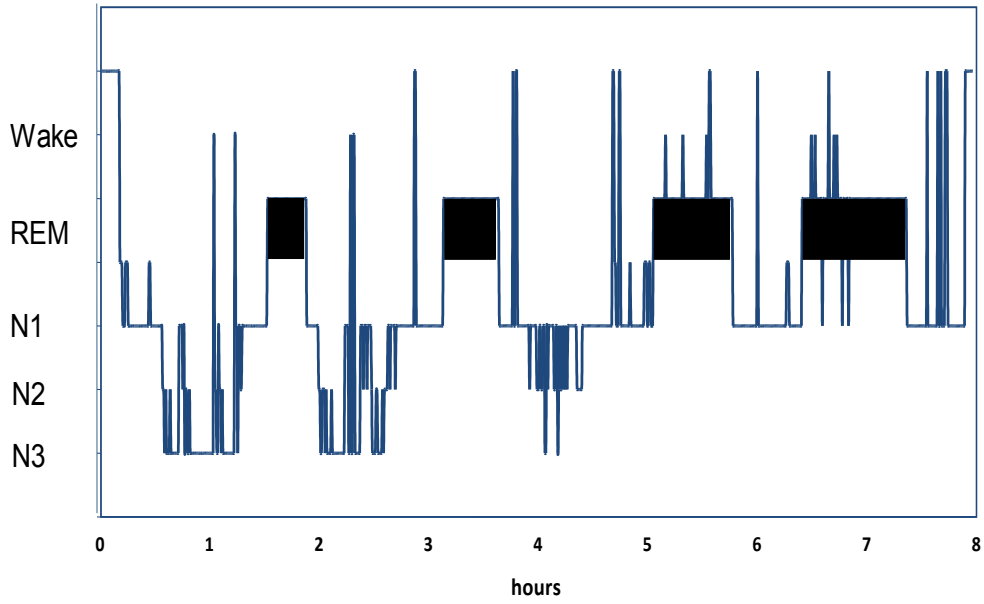

Figure 1.1: A hypnogram showing the sleep stages and cycles of a healthy and normal adult over 1 night.

One night of sleep is usually comprised of 4-5 sleep cycles, each approximately 90 minutes in duration. The majority of slow wave sleep (SWS; N3) occurs in the first two sleep cycles whereas the majority of rapid eye movement (REM; R) sleep occurs mainly in the last few sleep cycles. REM sleep is associated with an increased propensity of dreaming, hence the likelihood of waking up remembering a dream in the morning after the longest bout of REM. With each progressive sleep cycle, SWS decreases and REM sleep increases.

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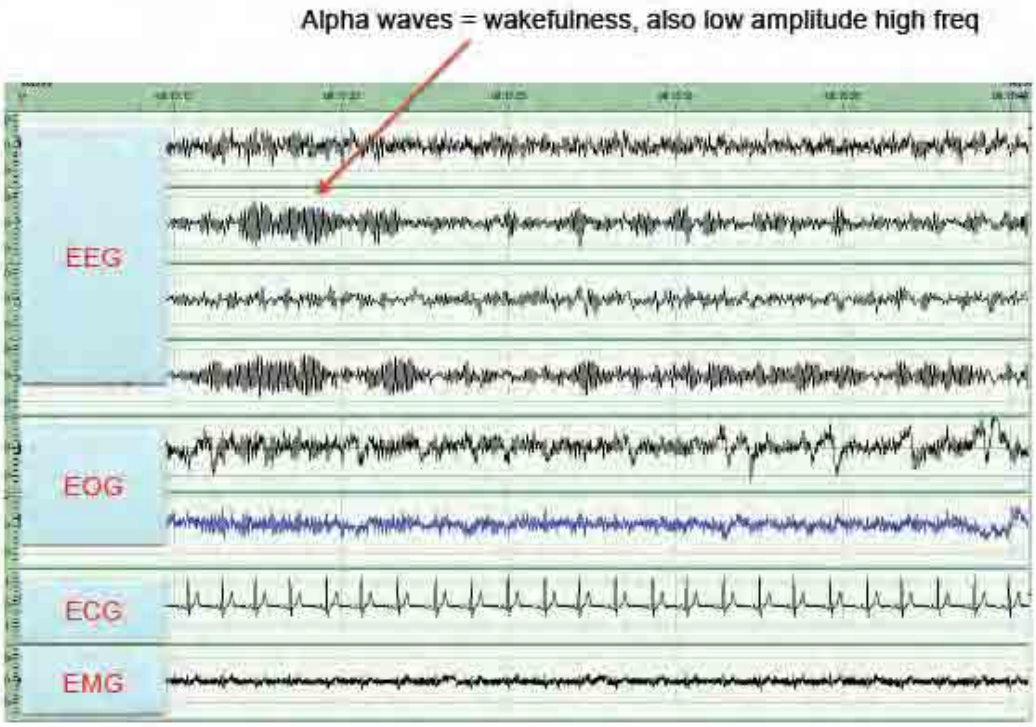

Figure 1.2: PSG output showing brain activity during wakefulness.

Alpha waves are present during wakefulness with low amplitude and high frequency waves. Although the EEG shows wakefulness through the presence of alphas waves, the individual's eyes are closed, as shown from the EOG activity (no blinking).

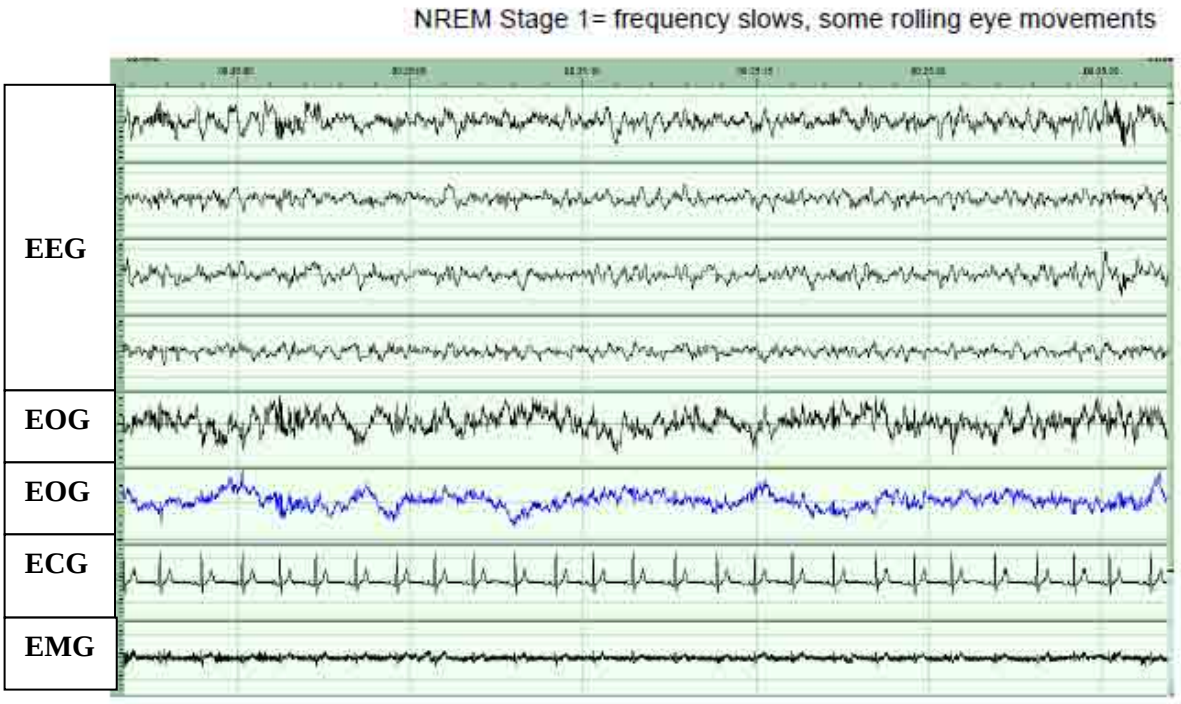

Figure 1.3: PSG output showing brain activity during N1 sleep.

The EEG frequency reduces and the EOG activity shows rolling eye movements as the individual 'drifts' into N1 sleep.

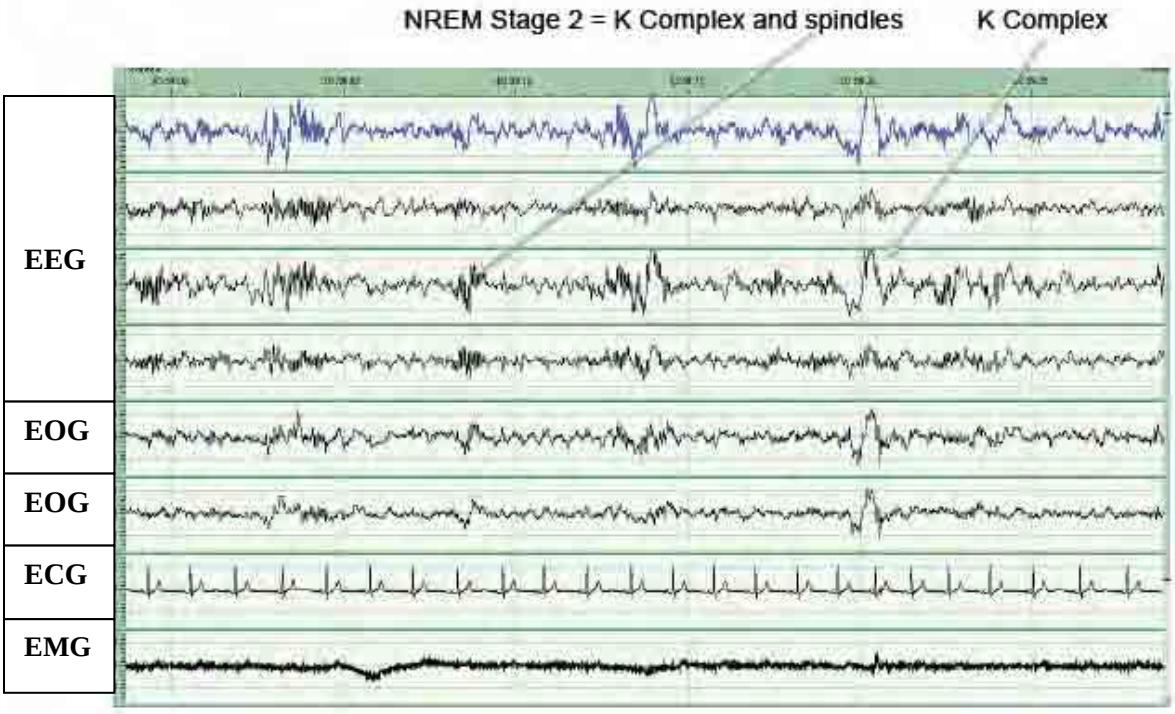

Figure 1.4: PSG output showing brain activity during N2 sleep with sleep spindles and K-complexes.

K-complexes are brief but sudden sharp waveforms with a negative high-voltage peak with a subsequent slower positive complex followed by a negative peak. The EEG activity then normalises. K-complexes are often followed by bursts of brain activity, called sleep spindles. Sleep spindles consist of 12-14 Hz waves, which occur for a minimum of 0.5 seconds and can occur 2-5 times per minute.

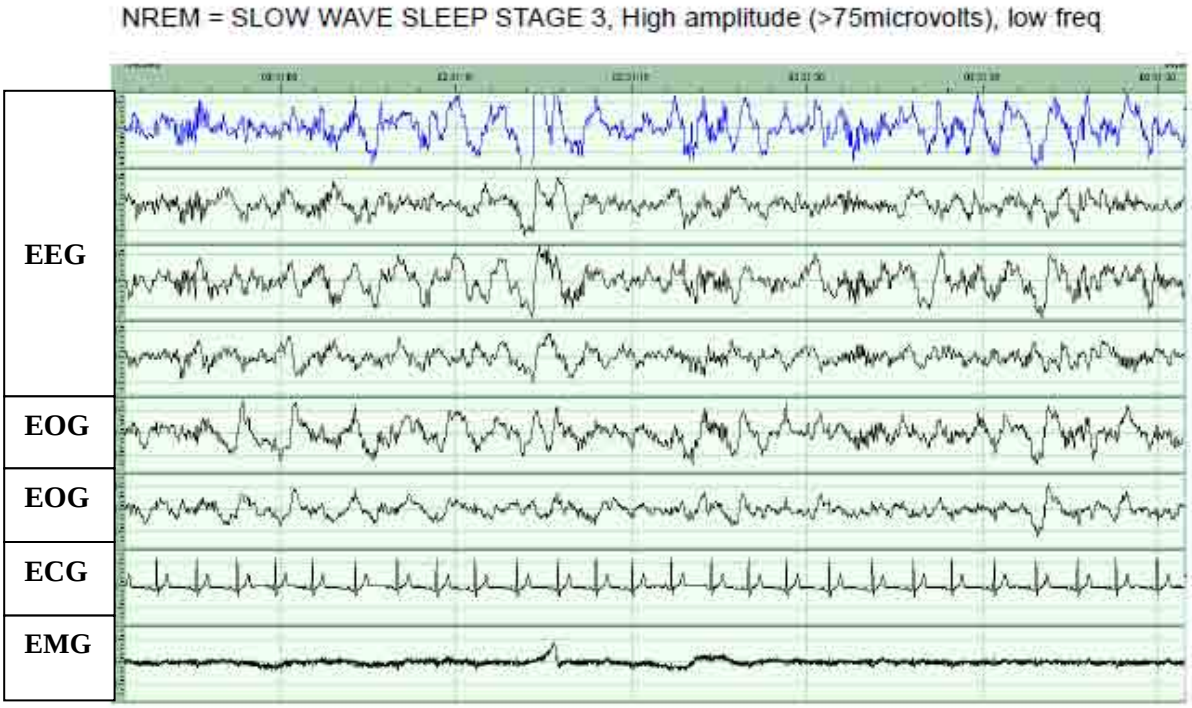

Figure 1.5: PSG output showing EEG activity during N3 sleep with high amplitude, low frequency delta activity.

N3 sleep is also known as slow wave sleep (SWS) where individuals enter deeper stages of sleep. N3 sleep is scored when a 30 second epoch is comprised of at least 20% of delta waves. Previously, N3 was divided into stages 3 and 4 with Stage 4 classified as a 30 second epoch with at least 50% of delta activity.

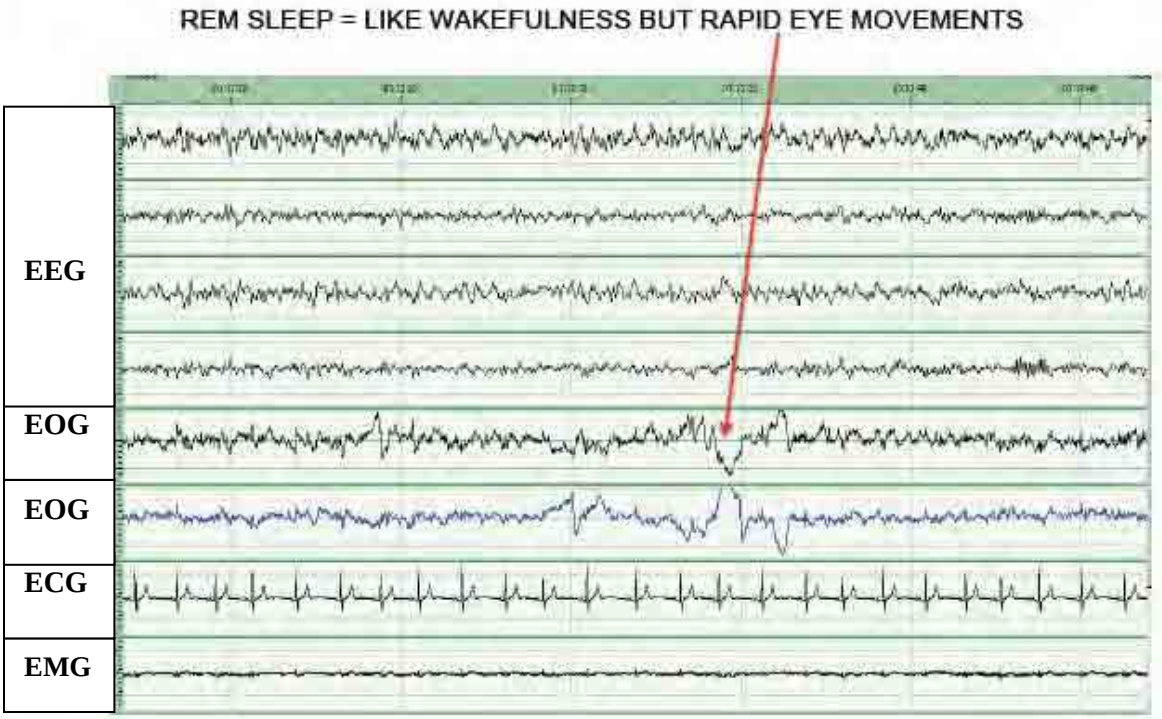

Figure 1.6: PSG output showing brain activity and eye movements during REM sleep.

The EEG activity is similar to that of wakefulness where the brain activity is heightened, despite being in REM sleep. The body becomes paralyzed with the EMG showing minimal muscle tone. The EOG shows burst of rapid eye movements.

During successive sleep cycles, episodes of REM become progressively longer; in contrast, longest periods of SWS occur at the beginning of the night and become shorter with each cycle of sleep, as shown in Figure 1.1. REM sleep is associated with an increased propensity of dreaming, hence the likelihood of waking up remembering a dream in the morning after the longest bout of REM.

PSG is widely used and is considered to be the gold standard for in depth objective evaluation of sleep and its disorders. This is, however, impractical for large-scale studies and so currently, there is increasing use of accelerometry (actigraphy). Actigraphy is a wrist-worn device used to measure sleep and waking activity, in the absence of sleep laboratory attendance and in the individual's own environment. It is accurate and cost-effective but does not offer a full in depth output compared to PSG and lacks resolution for detection of most sleep disorders. Sleep can also be obtained through self-report or parental report through utilisation of questionnaires and/or sleep diaries. Table 1.1 shows the different types of measures used to determine sleep highlighting the advantages and limitations of each technique.

Table 1.1: The advantages and limitations of the various techniques used to measure sleep.

Sleep measure	Advantages	Limitations
Polysomnography (PSG)	• Accurate for various sleep parameters • Objective • Defines sleep architecture • Determines brain activity and other physiological measures • Can determine sleep disorders • Can be combined with other physiological measures (hormone sampling under controlled conditions)	• Expensive • May not capture usual sleep due to equipment and/or environment (1st night effect) • Requires experienced technicians to score • Invasive • Uncomfortable • Unsuitable for long-term assessment • Inter/intra observer variation
Actigraphy	• Objective • Can be used in free-living conditions • Can provide data over prolonged period • Inexpensive compared to PSG • Non-invasive	• Does not determine sleep architecture • Only provides sleep estimates • Some are not waterproof • No physiological measures to determine sleep • Needs accompanying accurate sleep diary • May overestimate sleep because of inactivity • Several different software and cut-points for analysis
Actiheart	• Objective • Includes additional physiological measures (heart rate) for determination of sleep • Can be used in free-living conditions • Can provide data over prolonged period • Non-invasive	• Not validated against polysomnography • Expensive • Does not determine sleep architecture • Only provides estimates of sleep parameters • Needs an accompanying accurate sleep diary • May overestimate sleep during inactive periods • Can be uncomfortable • May result in rash with ECG electrodes • Can lose signal if contacts are poor

Table 1.1 cont'd

Sleep measure	Advantages	Limitations
Self-reported questionnaire	• Inexpensive • Quick to administer • Can be administered to large populations • Less labour intensive • Some have been validated against objective sleep techniques • Can enquire about numerous sleep parameters	• Subjective • Recall bias • Variable response rates • Inaccurate for detecting sleep disorders • Only provides cross-sectional data • May have missing data • May report time in bed (TIB) rather than total sleep time (TST)
Parental questionnaire	• Inexpensive • Quick to administer • Allows collection of data from large samples • Less labour intensive	• Subjective • Recall bias • Inaccurate for older children and adolescents • Parents unaware of nighttime awakenings • More likely to report TIB rather than TST • Only provides cross-sectional data • May have missing data • Variable response rates
Sleep/time diary	• Can obtain longitudinal data • Can obtain detailed information on other sleep variables (time in bed [TIB], total sleep time [TST], nighttime awakenings, naps, sleep quality) • Inexpensive • Quick to administer • Allow data collection from large samples • Less labour intensive (researcher)	• Fatigue • Recall • Failure to complete or return • May have missing data • Labour intensive (participant) • Requires participant motivation for completion

1.2 The regulation of sleep timing and duration

Sleep is regulated by two interconnected processes – called Process S and C shown in Figure 1.7. Process S is appetitive and related to sleep debt and prior wakefulness, while Process C (circadian) determines the timing of sleep and wakefulness.[8] These processes are regulated by both neuronal and humoral factors. Circadian rhythms are entrained to a 24-hour period, regulated by the hypothalamic suprachiasmatic nucleus (SCN). The SCN serves as the central circadian pacemaker and synchronizes various internal biological rhythms through both internal and external cues, which regulate the timing of sleep. External cues (zeitgebers) include light (the most powerful zeitgeber), which influence the SCN through the retinohypothalamic tract. In the absence of external cues, particularly light, the internal clock oscillates between 23.8 and 27.1 hours,[9] termed the 'free-running circadian period'. Previous studies have demonstrated that humans have a free-running circadian period of just over 24-hours.[10]

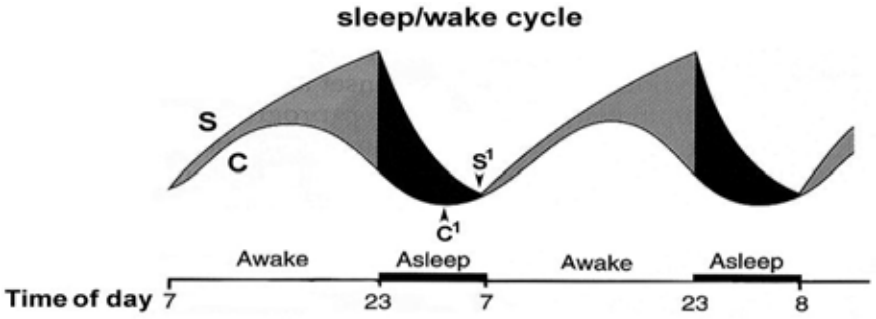

Figure 1.7: The two-process model of sleep-wake regulation.[8]

The drive from Process C ensures evening wakefulness despite accumulated Process S (sleep debt). There is increased ability to sleep when Process C is low and Process S is high. Misalignment of the two processes is responsible for jet lag and shift-work disorders.

Physiological alterations in circadian sleep timings commonly occur in adolescents and older adults (Figure 1.8). The former may experience a delay in sleep timing whereas the latter may encounter sleep advancement compared to those with 'normal sleep phase', governed by the SCN.

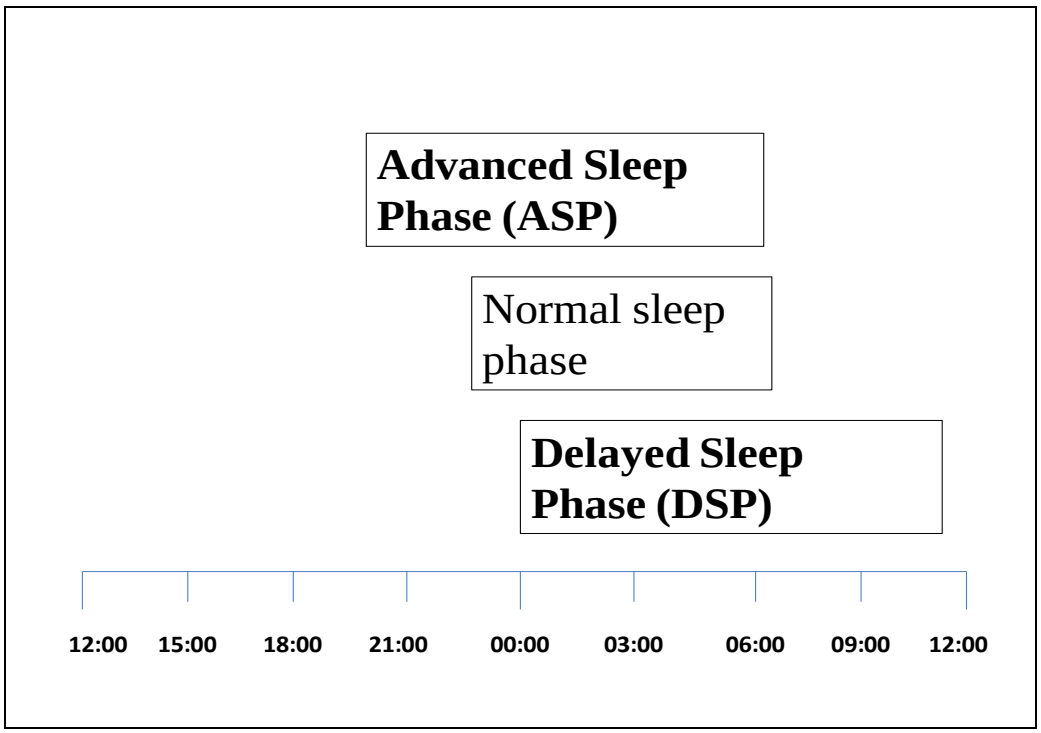

Figure 1.8: Alterations in circadian sleep timings compared to those with a 'normal sleep phase'.

Those with advanced sleep phase find it difficult to remain awake during the early evening and awake in the early hours of the morning (sometimes called "larks"). Those with delayed sleep phase, however, experience the opposite; they have difficulty falling to sleep, even late in the evening and commonly fall to sleep in the early hours of the morning and have difficulty waking in the morning, sometimes waking after 12:00 if unprompted (sometimes called "owls").

1.3 Sleep duration across the lifespan

Whilst EEG and other sleep equipment have provided important information about the characteristics and physiology of sleep, less is known about what normative and optimal sleep duration should be. This is important because of the increasingly recognised potential consequences of sleep loss which include increased daytime sleepiness,[11] reduced cognitive function,[12] mood alterations,[13] memory loss,[14] emotional insecurity,[15] and impulsive and risky decision making.[16] Most of the evidence investigating the effects of sleep deprivation, however, has been derived from subjecting individuals to acute total sleep deprivation (TSD). These findings are valuable but are not good models of normative contemporary sleep behaviour. More recent research has shifted its focus to studying the effects of chronic partial sleep deprivation, a behaviour, which is becoming increasingly common in today's modern society. To define what is optimal sleep duration, large representative population studies are necessary although it must also be noted that individuals have different needs and requirements and so there will always be exceptions to the rule. Sleep need alters with age; thus existing literature regarding sleep duration in children, adolescents, adults and older adults are discussed below.

1.3.1 Sleep in children

Sleep duration and sleep quality are both important for children's growth and healthy development.[17;18] This is partly due to the release of growth hormone (GH) which peaks shortly after sleep onset.[19] GH stimulates growth and regeneration. Early observational studies revealed that children sleep more than healthy adults (Figure 1.9) and that sleep

duration decreases across childhood. The extra sleep duration acquired consists mainly of additional REM sleep,[20] (Figure 1.10) which is believed to aid brain maturation[21] and learning through the processing of new information.[22]

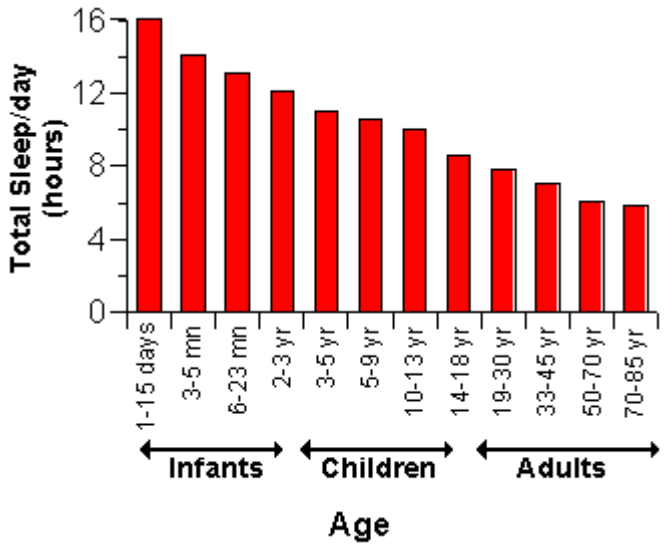

Figure 1.9: Total sleep duration according to age in humans.

Sleep need is longer at birth and gradually declines with age.

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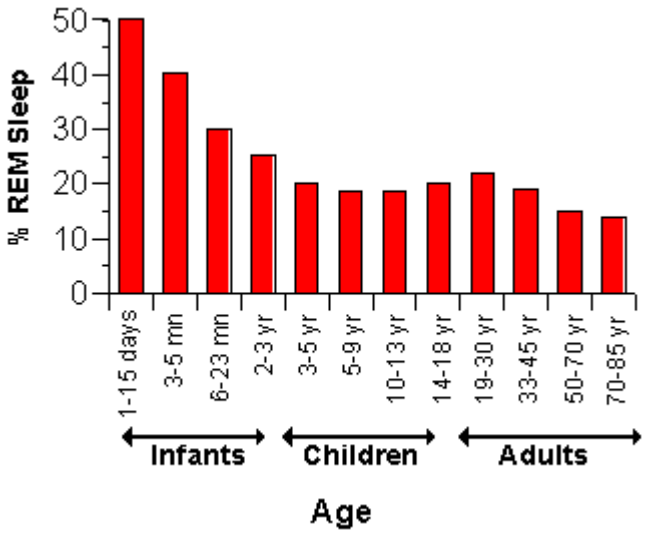

Figure 1.10: The percentage of REM sleep according to age in humans.

More REM sleep is needed in infants and gradually decreases with age but increases slightly during young adulthood.

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Despite sleep being a major determinant of healthy development in children, data suggest that sleep problems are common, occurring in up to 25% of the paediatric population.[23] The consequences of sleep disturbances and insufficient sleep duration have been explored. Short sleep duration and sleep disturbance in children have been associated with important public health problems such as obesity,[24] poorer academic achievement,[25] and emotional instability.[15] Thus, if sleep is problematic across childhood, then it may be accompanied by important negative effects on psychological wellbeing, performance, behaviour, and metabolic function. Based on large United States (US) population polls conducted by the National Sleep Foundation (NSF), data suggest optimal sleep duration for this age group is at least 10 hours a day.[26] *Chapter 2* examines the potential relationship between sleep duration and obesity in young children.

1.3.2 Sleep in adolescents

The transition from childhood to adolescence is when significant changes occur, both for physical development and sleep. In adolescence, there is a tendency to retire to bed later in the evenings and awaken later in the day compared with the younger age group or healthy adults.[27] This physiological delayed sleep phase (DSP) is shown in Figure 1.8. DSP accompanies puberty and transition to adult sleep patterns is closely related to the end of pubertal processes.[28] In modern society, adolescence becomes a period of sleep deprivation (sleep debt occurs) because waking later on weekdays is prevented by early school times. The increased amount of sleep debt is sometimes recovered during the weekend with adolescents commonly staying in bed until the late morning or early afternoon.[29] The shift in sleep pattern and insufficient sleep is a result of both intrinsic and extrinsic factors including pubertal development, social acceptance, peer pressure, increased need for independence, enhanced social activities, increased academic pressures and responsibilities, reduced parental control of bedtimes, additional extracurricular opportunities, part-time employment and self-identification,[30] all of which point to a challenging phase of life to contend.

The majority of evidence identifying sleep timing, reduced sleep duration and excessive daytime sleepiness (EDS) in adolescence stems from work performed by Professor Mary Carskadon.[27;30-34] In one publication, Carskadon concluded that adolescents did not obtain the sleep they needed and proposed circadian regulatory systems as a contributor to the DSP commonly experienced by adolescents.[30] Carskadon and colleagues further investigated longitudinal alterations in sleep architecture from early adolescence (9/10 years old) following up 1-3 years later using PSG. They found a 29% decline in N3 sleep at follow up and an increase of 17% in N2 sleep.[35] Further support for inadequate sleep and its negative

consequences in adolescence was identified in the National Sleep Foundation 2006 *Sleep in America* poll, which reported that only one in five American adolescents obtained pre-defined 'optimal' amounts of sleep. The majority reported feeling tired or sleepy during the day and 45% slept less than 8 hours on a weekday.[36] Although there is still doubt as to optimal adolescent sleep duration, evidence from the most recent US poll indicates about nine hours to be sufficient for this age group.[37]

Sleep loss is highly prevalent in adolescence[38] and subsequently, daytime sleepiness is widely reported in this age group with an array of negative consequences.[39] Adolescents are also vulnerable to other negative health behaviours and outcomes such as drug use, smoking, alcohol use, suicide, obesity and more. Inadequate sleep has been previously linked to impulsive and risky decision-making and may therefore be associated with engaging in deleterious behaviours. Furthermore, there is evidence suggesting a relationship between short sleep duration and obesity in adolescents. *Chapter 3* will investigate the link between sleep and obesity in adolescence.

1.3.3 Sleep in adulthood

The shifted sleep pattern experienced in adolescence is usually adjusted back as adulthood emerges. The need for sleep in adulthood becomes reduced compared to healthy children and adolescents. Additional responsibilities in adulthood such as work, economic, family and health and other social factors, may all have an impact on an individual's sleep. Artificial lighting along with the recent abundance of technological advances has resulted in a modern society which is operational 24-hours a day, 7 days a week. Consequently, individuals try to

include as many activities into their waking day as possible, thus resulting in increased wake time and reduced sleep opportunity. Indeed, this is supported by recent data from USA showing a higher proportion of adults to be sleeping 6 hours or less in 2004 compared to 1985 across several age groups (Figure 1.11).

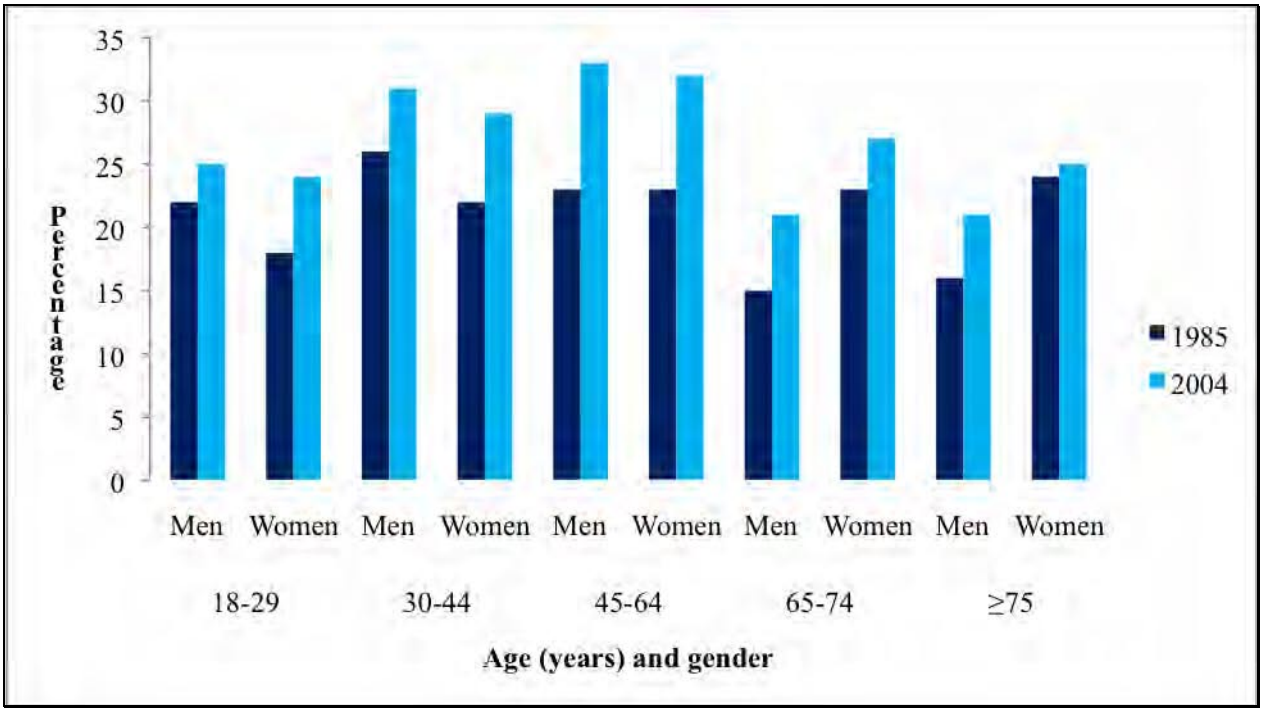

Figure 1.11: The percentage of US adults sleeping 6 hours per 24-hour period in 1984 and 2004 by age and gender.

Adapted with permission, from Taheri.[40]

Voluntary sleep curtailment is an increasingly common behaviour but few are aware of the potential adverse consequences with which it is associated. Six hours or less of sleep is currently considered to be inadequate for adults. This is based on the findings of a large population study, which surveyed 1.1 million adults about various health related behaviours

as part of a Cancer Prevention Study. The preliminary findings dating back to 1964 with follow up results published in 2002, consistently demonstrated that seven hours of sleep may be optimal in adults for mortality,[3;41] and body mass index (BMI).[3] The mortality and optimal sleep duration data are consistent with findings from other countries.[42] The results of 636,095 women in the follow up study (Cancer Prevention Study II) are shown in Figure 1.12 and demonstrate a U-shaped relationship between sleep duration and mortality as well as BMI.

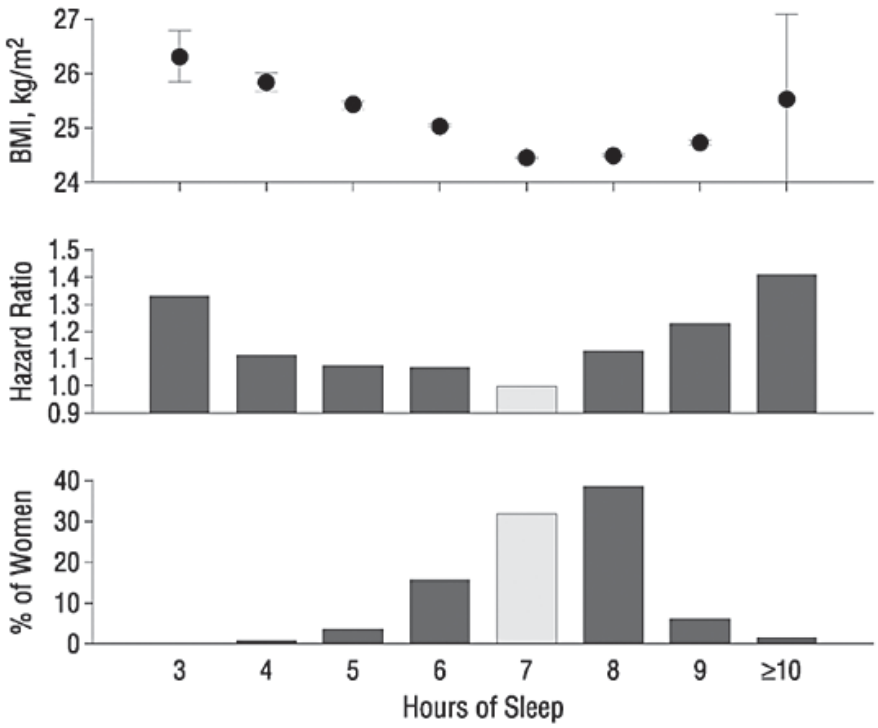

Figure 1.12: The mean BMI and hazard ratios for mortality according to reported hours of sleep in 636,095 women from the Cancer Prevention Study II.

Used with permission from Professor Daniel Kripke.[3]

Mortality is lowest in those sleeping 7 hours and highest in those sleeping 3 hours and ≥10 hours. Similarly, those sleeping 7 hours had a healthy BMI but those with the shortest and longest sleep duration had increased BMI.

1.3.4 Sleep in the older adult

Sleep duration, sleep quality and sleep patterns all change noticeably as the human adult ages. These changes are due to alterations in both Process S and C (Figure 1.7). Sleep complaints are common in older adults.[43] Indeed, a large epidemiological study demonstrated that more than 80% of older adults (>65 years) reported at least one sleep problem on a regular basis.[44] The same study followed up participants after 3 years and found that the 15% who reported no baseline sleep problems had developed disturbed sleep at follow up, suggestive of an annual incidence rate of 5%. Early evidence demonstrated that sleep need decreases with age[45] although the National Sleep Foundation do not differentiate between young, midlife and older adults but rather state that the recommended adult sleep duration is 7-9 hours. Older adults are prone to experiencing a variety of sleep disturbances, making it difficult to achieve the optimal amount. Ageing per se, does not result in disrupted sleep but the ability to fall and remain asleep declines with age. Common sleep complaints in the older adult include:

1. Inability to stay awake in the evening and early awakening (advanced sleep phase – Figure 1.8).
2. Difficulty initiating and maintaining sleep (insomnia).
3. Sleep disturbances (poor sleep quality).
4. Undiagnosed sleep disorders which individuals may attribute to the ageing process.
5. Excessive daytime sleepiness, often leading to daytime napping.
6. Not feeling rejuvenated after a night's sleep.

The reasons underlying sleep disturbances in older adults are complex. Some can be due to lifestyle while others are age-related. They include the need to urinate more frequently at night, chronic pain caused by chronic health conditions, medication use, sedentary lifestyle, use of stimulants such as caffeine and smoking, and poor diet and/or nutrition. Other explanations are, however, physiological and suggestive of disruptions to the homeostatic and circadian mechanisms, both of which regulate sleep (see above). *Chapter 4* examines the relationship between sleep duration in older adults and the metabolic syndrome.

1.4 Obesity

1.4.1 Prevalence

The World Health Organization (WHO) fact sheet 311, updated in March 2011, shows that the levels of obesity have more than doubled since 1980.[46] In 2008, 1.5 billion adults were overweight and almost 500 million were obese.[46] The problem of overweight and obesity is not limited to adults. The same report showed just less than 43 million children (<5 years) were overweight in 2010.[46] Despite obesity being potentially preventable, rates have escalated, which has attracted research attention in recent years. The rise in overweight and obesity is a major concern and has significant cost implications, not only to the individual but also for society. Obesity is a direct result of excessive energy intake and inadequate energy expenditure. While body weight has a strong genetic link, the rise in obesity is mainly driven by environmental factors. Lifestyle behaviours, such as sleep that, based on emerging data, can potentially alter the energy balance equation, have been recently implicated in the rise in obesity levels.

1.4.2 Defining childhood overweight and obesity

Currently, there is no universal consensus on a cut-off point to define overweight or obesity in children and adolescents. Usually, for clinical practice and large epidemiological studies, child overweight and obesity are assessed by indicators based on weight and height measurements, such as weight-for-height or BMI, calculated using the following equation:[47]

$$\mathrm{BMI} = \frac{\text{mass (kg)}}{(\text{height(m)})^2}$$

The World Health Organization (WHO) Child Growth Standards were developed using data collected in the WHO Multicentre Growth Reference Study.[48] These data include BMI charts for infants and young children up to age 5 years. Measuring overweight and obesity in children aged 5-14 years however, is challenging because there is no standard definition of childhood obesity, which has been applied worldwide. For children and adolescents, BMI ranges above a normal body weight ascribe different indicators of risk ("at risk of overweight", "overweight", "obese"). Furthermore, BMI ranges for children and adolescents are specified by age and gender.

The Centers for Disease Control and Prevention (CDC) defines "obese" as being ≥95th percentile of BMI for age and "overweight" as being between ≥85th and <95th percentiles of BMI for age.[49] Similarly, the European Childhood Obesity Group classifies overweight as being at or above the 85th percentile of BMI and obesity as being at or above the 95th percentile of BMI.[50]

The International Obesity Task Force (IOTF) uses a different definition to define overweight and obesity in children and adolescents based on data collected from geographically diverse surveys of six large growth studies (Brazil, Great Britain, Hong Kong, the Netherlands, Singapore, and the US). For each survey, centile curves, that passed through the widely used cut-off points of adult overweight and obesity (see defining adult overweight and obesity), were identified. The resulting curves were averaged to provide age and sex specific cut-off points from 2-18 years old.[51] These BMI cutpoints for children are reported to be more universal than other definitions making this definition widely used in research studies.

One further method to determine adiposity is by use of skinfold callipers, used to determine skinfold thickness for various body areas, such as triceps, biceps, abdominal, subscapula, thigh and suprailiac. The problem with this method is that of accuracy and standardisation. Furthermore, it only provides an estimate of body fat (BF) and there are no definitive cut-points for determination of overweight or obesity. This technique is therefore sometimes used as an additional measure alongside BMI calculation.

A further method for measuring adiposity is through bioelectrical impedance analysis (BIA). Different methodologies have been used to estimate body compositions through BIA giving values for fat mass (FM), fat free mass (FFM), distribution of adiposity, and body fat percentage (BF%) and more. The technique is highly variable depending on time of day, level of hydration, ethnicity, physical activity and caffeine consumption, prior to testing. A more useful and accurate technique is dual energy x-ray absorptiometry (DXA). This method, however, uses radiation, albeit at a small dose, and is not easy to implement in large population studies. Other measures such as computed tomography (CT) and magnetic

resonance imaging (MRI) are also accurate at measuring metabolically active visceral fat but are expensive, time consuming, and difficult to use in community settings.

The majority of obesity research studies have used BMI to determine child and adolescent overweight and obesity. BMI, however, is not always the best the measure for adiposity (see below).

1.4.3 Defining adult overweight and obesity

Adult overweight is defined as a BMI of 25-29.9kg/m² and a BMI of ≥30kg/m² is defined as obesity. As an overall index of obesity, however, BMI does not differentiate fat mass from muscle mass and does not reflect fat distribution. Because BMI may not be entirely reflective of body fat and hence health risk, others have used waist circumference (WC), and/or neck circumference.

Central adiposity is known to increase the risk of metabolic complications such as dyslipidemia, impaired glucose tolerance, hypertension and is also one of the criteria for the metabolic syndrome according to the American Heart Association and National Heart Lung and Blood Institute's definition.[52] WC is a crude but relevant index of the absolute amount of abdominal fat and has been found to correlate better with visceral fat deposits, measured by CT.[53] The problem with this measure is that there is not a universal cutpoint for gender and ethnic-group. For example, central obesity defined by waist circumference for Asia-Pacific criteria is ≥90 cm in men and ≥80 cm in women, as defined by the WHO.[54] Other ethnic groups, stratified by gender are detailed in Table 1.2.

Table 1.2: Country/ethnic-specific values for central obesity according to waist circumference.

Country/ethnic group	Gender	Waist circumference† (as measure of central obesity)
Europids*	Male	≥ 94 cm
	Female	≥ 80 cm
South Asians‡	Male	≥ 90 cm
	Female	≥ 80 cm
Chinese	Male	≥ 90 cm
	Female	≥ 80 cm
Japanese§	Male	≥ 85 cm
	Female	≥ 90 cm
Ethnic South and Central Americans		Use South Asian recommendations until more specific data are available
Sub-Saharan Africans		Use European data until more specific data are available
Eastern Mediterranean and Middle East		Use European data until more specific data are available (Arab) populations

These are pragmatic cut-points and better data are required to link them to risk. Ethnicity should be the basis for classification, not the country of residence.

*In the USA the Adult Treatment Panel III values (102 cm male; 88 cm female) are likely to continue to be used for clinical purposes.
†In future epidemiological studies of populations of Europid origin, prevalence should be given using both European and North American cut-points to allow better comparisons.
‡Based on a Chinese, Malay and Asian-Indian population.
§Subsequent data analyses suggest that Asian values (male 90 cm; female 80 cm) should be used for Japanese populations until more data are available.
Reprinted with the permission of G. Alberti.[54]

1.5 The sleep-obesity association

1.5.1 Background

Data show a decline in adult sleep duration over recent decades.[55] There are many probable reasons for this, including lifestyle choice, family or work commitments, and psychological or physical problems. Sleep curtailment, as a result of voluntary bedtime control has become increasingly common in today's modern world.[55] Technological advances may have altered leisure time behaviours with individuals spending their leisure time watching television, video gaming, using mobile telephone and Internet surfing. Use of these media may result in chronic sleep deprivation through delayed bedtime.[37;56] Physiological pathways may also be involved such as increased exposure to light which suppresses the release of melatonin.[57] Additionally, these behaviours are sedentary and may have replaced more active pursuits.

Sleep duration has declined simultaneously with the increased prevalence of obesity, thereby suggesting a potential link. Sleep could be a novel factor that impinges on both sides of the energy balance equation with data suggesting that sleep duration is associated with obesity.

1.5.1.1 Animal models

Rodent models of total sleep deprivation (TSD) have been used to identify the biological significance of sleep. Rechtschaffen and colleagues applied the "disk-over-water" method (Figure 1.13), which subjected the experimental rat to TSD.[2;58] When the TSD rat goes to sleep, the computer is activated to rotate the motor causing the rat to wake and walk/run on

the disk otherwise it will fall into water surrounding the disk, which rats dislike. The control rat is also sleep deprived to some extent but has sleep opportunity when the TSD rat is awake. The TSD rats died after 11-32 days of TSD and displayed a number of abnormalities including debilitated appearance, skin lesions, and decreased body temperature during the late stages of deprivation. Hormone alterations were also observed: increased plasma norepinephrine and decreased plasma thyroxine. Importantly, despite significant increases in food intake, weight loss occurred through increased excessive energy expenditure. Changes in energy balance also occurred in the early stages of the experiment. After just a few days the rats had increased body temperatures on awakening and thus elevated energy expenditure. To compensate, food intake increased, although body weight reduced suggesting that the rats could not compensate through hyperphagia. In later stages, before death, body temperature decreased dramatically parallel with increased energy expenditure. The results of this study were recently reconfirmed in sleep deprived rats which demonstrated a 25-35% increase in food intake accompanied by a reduction in body weight.[59] Interestingly, the provision of a high fat diet prevented the risk of mortality. Of course, although attempted (including through use of stimulants) prolonged TSD is not usually possible in humans and has ethical considerations. Experimental rodent studies indicate that food intake is an adaptive reaction to increased energy expenditure during sleep deprivation. This may, in part, explain the recent rise in obesity in parallel with voluntary sleep curtailment. A review of the literature in children and adults has been performed to examine the evidence regarding sleep and obesity in human populations.

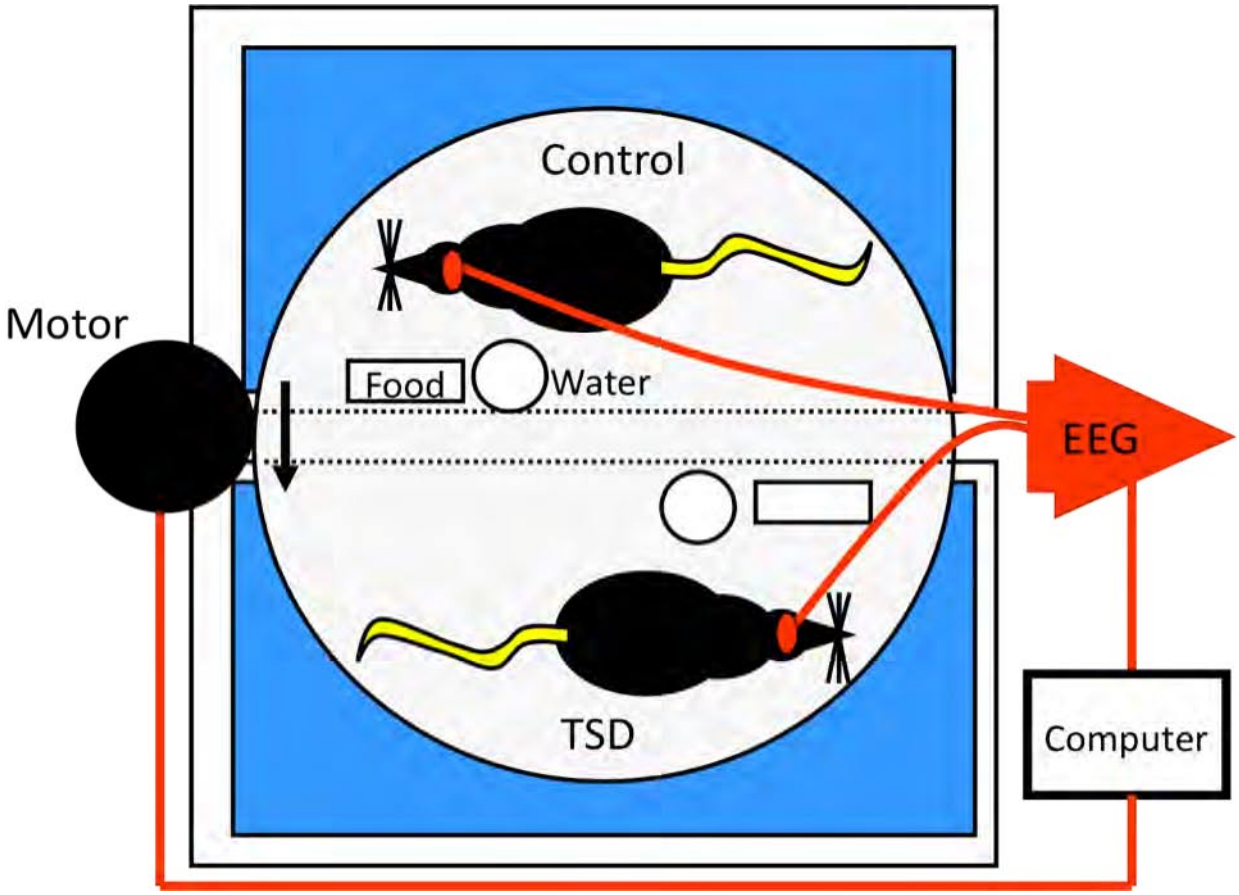

Figure 1.13: The disk-over-water method used in rodent models of total sleep deprivation.

When the totally sleep deprived (TSD) rodent enters sleep, as shown by the EEG activity, the computer is activated which, in turn, rotates the motor. If the TSD rodent does not wake, it falls into the water surrounding the disk. The control rodent is also sleep deprived but has the opportunity to sleep when the TSD is awake. Adapted, with permission, from Taheri.[40]

1.5.2 The sleep-obesity association: methods and procedures for literature search/review

Chapter 2 examines the sleep-obesity link in children and *Chapter 3* in adolescents. A search of the available literature for sleep-obesity in children and adolescents was therefore conducted using the PubMed database for manuscripts published between 1980 and September 2010. The following searches were conducted:

- Sleep AND obesity AND child
- Sleep AND overweight AND child
- Sleep AND obesity
- Sleep AND overweight
- Sleep AND adolescen* AND overweight
- Sleep AND adolescen* AND obesity
- Sleep AND teenage* ANS overweight
- Sleep AND teenage* AND obesity

Additionally, "paediatric" and "pediatric" were used as MeSH keywords. Articles were also sourced using the "related article" option in PubMed as well as through published reviews and meta-analyses. Studies were excluded if they were not published in English, or where full text was unavailable. If the same study population was assessed and published more than once, only the first study was included. A total of 37 articles were identified, of which 7 were cross-sectional studies in children (up to the age of 10 years), 11 cross-sectional studies in adolescents (10-20 years of age), 7 cross-sectional studies in children and adolescent age ranges, and 12 longitudinal studies in children and adolescents, detailed in Tables 1.3, 1.4, 1.5 and 1.6, respectively. If regression analyses were conducted the referent category of sleep is highlighted in *italics.*

Table 1.3: Cross-sectional studies examining the relationship between sleep duration and weight status in children (3-10 years of age).

First author, year	Sample size	Country	Age (yrs)	Obesity measure	Sleep measure	Relationship
von Kries, 2002 [60]	6,645	Germany	5-6	Objective BMI (90^{th}/97^{th} percentile) Fat mass (n=1676)	Parental report (*≤10,* 10.5-11, ≥11 hrs)	Negative linear for BMI and fat mass
Sekine, 2002 [24]	8,274	Japan	6-7	Objective BMI	Parental report (<8, 8-9, 9-10, *>10* hrs)	Negative linear, boys at greater risk
Hui, 2003 [61]	343	Hong Kong	6-7	Objective BMI (≥92^{nd} percentile)	Parental report (*<9*, 9-11, >11)	Negative linear trend
Padez, 2005 [62]	4,511	Portugal	7-9	Objective BMI (IOTF)	Parental report (8, 9-10, >11hrs)	Obese boys and overweight girls in a dose-dependent manner for sleep duration using chi square analysis
Chaput, 2006 [63]	422	Canada	5-10	Objective BMI & WC	Parental report (8-10, 10.5-11.5, *12-13* hrs)	Negative linear for combined sex sample.
Nixon, 2008 [64]	519	New Zealand	7	Objective BMI (IOTF) BF%	Parental report and 24hr actigraphy (<9, *≥9* hrs)	Negative association between sleep duration and overweight/obese and BF%
Bayer, 2009 [65]	7,767	Germany	3-10	Objective BMI and skin fold thickness to calculate BF%	Parental report (hrs)	Negative association

BMI=body mass index; IOTF=international obesity task force; WC=waist circumference; BF%=body fat percent.

Table 1.4: Cross-sectional studies examining the relationship between sleep duration and weight status in adolescents (10-20 years of age).

First author, year	Sample size	Country	Age (yrs)	Obesity measure	Sleep measure	Relationship
Gupta, 2002 [66]	383	USA	11-16 yrs	Objective BMI & FFM	24 hr actigraphy	Negative linear
Knutson, 2005 [67]	4,486	USA	15-18 yrs	Objective BMI ($\geq 95^{th}$ centile)	Self-report (hrs) (non-validated questionnaire)	Negative linear for boys only
Chen, 2006 [68]	656	Taiwan	13-18 yrs	BMI from school records ($>85^{th}$ percentile=overweight)	Self report (AS: 6-8hrs $\geq$4 p/w)	Negative association
Knutson, 2007 [69]	1,546	USA	10-19 yrs	BMI from records ($>95^{th}$ percentile = overweight)	Self report sleep hrs and 24 hr time diary	Self reported sleep time was associated with overweight but not linearly. Time diary was not associated with overweight
Seicean, 2007 [70]	529	USA	14-18 yrs	Self report height and weight (30% objectively measured) $>95^{th}$ percentile=obese (CDC)	Self report (<5, 5-6, 6-7, 7-8, >8hrs)	Negative linear trend
Yu, 2007 [71]	500 (twins)	China	10-20 yrs	Objective BMI, WC, HC, BF% (DXA)	Self report & parental questionnaire (PSQ & PSQI) and 7 day sleep diary (<8, *8-8.9*, $\geq$9hrs)	U-shaped association for BF%, truncal fat and WC in girls only although some have borderline significance. Increased WC and HC in boys who slept for $\geq$9hrs

BMI=body mass index; FFM=fat free mass; AS=adequate sleep; CDC=Centers for Disease Control; WC=waist circumference; HC=hip circumference; BF%=body fat percent; DXA=dual-energy X-ray absorptiometry; PSQ=Pediatric sleep questionnaire; PSQI=Pittsburgh sleep quality index.

Table 1.4 cont'd

First author, year	Sample size	Country	Age (yrs)	Obesity measure	Sleep measure	Relationship
Wells, 2008 [72]	4,452	Brazil	10-12	Objective BMI (IOTF), skin fold and BF	Self-report (<8, 8–10.9, ≥11 hrs)	Negative association between sleep duration and all measures of overweight/obesity
Sun, 2009 [73]	5,753	Japan	12-13	Objective BMI (IOTF)	Self report (<7, 7-8, *8-9*, >9hrs)	Negative association in girls only
Shaikh, 2009 [74]	489	India	16-19	Objective BMI, BF%, TBFM, WC	Self report in hrs (*>7* vs <7 hrs)	Negative association between BMI, BF%, FM, TBFM and sleep duration in both genders
Liou, 2010 [75]	8,640	Taiwan	13-16	BMI (IOTF)	Self report (PSQI)	Negative association for weekend sleep duration and obesity. Effect present in both genders but girls had higher risk
Danielsen, 2010 [76]	9,430	Norway	10-12	Parental report heights & weights – BMI (IOTF)	Self and parental reports	U-shaped association. Negative association between sleep and obesity but not overweight

BMI=body mass index; IOTF=international obesity task force; BF=body fat; BF%=body fat percent; TBFM=total body fat mass; WC=waist circumference; FM=fat mass; PSQI=Pittsburgh Sleep Quality Index.

Table 1.5: Cross-sectional studies examining the relationship between sleep duration and weight status in both children and adolescent age ranges.

First author, year	Sample size	Country	Age (yrs)	Obesity measure	Sleep measure	Relationship
Eisenmann, 2006 [77]	6,324	Australia	7-15	Objective BMI (IOTF) & WC	Self report (≤8, 8-9, 9-10, ≥10hrs)	Negative linear
Kuriyan, 2007 [78]	598	India	6-16	Objective BMI, WC, HC (IOTF)	Self-report but questionnaire not specified (≤8.5, 8.51-9.5, >*9.5* hrs)	Negative linear
Liu, 2008 [79]	335	USA	7-17	Objective BMI z score (<85th percentile=normal weight; 85th to<95th percentile=at risk for overweight; ≥95th=overweight	3 nights PSG	Negative association: overweight associated with reduced sleep duration, reduced sleep efficiency and reduced REM sleep
Wing, 2009 [29]	5,159	Hong Kong	9.25 (mean)	Parental report BMI z score (≥85th percentile)	Parent report (Hong Kong Children Sleep Questionnaire)	Negative association between sleep duration and BMI, particularly amongst those who did not compensate sleep during weekend/holidays
Hitze, 2009 [80]	414	Germany	6-19	Objective BMI SDS, WC z score, FM, FFM. >90th percentile BMI/WC = overweight/overwaist	Self (>11 yrs) or parent (<11 yrs) report (short sleep <10hrs if <10 yrs or <9hrs if >10 yrs)	Negative association with BMI and WC. Short sleep associated with overweight/overwaist in girls

BMI=body mass index; IOTF=international obesity task force; WC=waist circumference; HC=hip circumference; PSG=polysomnography; REM=rapid eye movement sleep; SDS=standard deviation score; FM=fat mass; FFM=fat free mass.

Table 1.5 cont'd

First author, year	Sample size	Country	Age (yrs)	Obesity measure	Sleep measure	Relationship
Ozturk, 2009 [81]	5,358	Turkey	6-17	Objective BMI, WC, MUAC & tricep skin fold (IOTF)	Parental report (≤8, 8-9, 9-10, ≥10hrs)	Negative linear in girls for sleep duration and BMI. Negative association in boys between sleep duration and WC, MUAC and BMI
Kleiser, 2009 [82]	13,450	Germany	3-17	Objective BMI (IOTF)	Parental report (3-10 yrs; self report in 11-17 yrs). Categorised by tertiles	Negative association in 3-10 year olds only

BMI=body mass index; WC=waist circumference; MUAC=mid upper arm circumference; IOTF=international obesity task force.

Table 1.6: Longitudinal studies examining the relationship between sleep duration and weight status in children and adolescents.

First authors name, year	Sample size	Country	Baseline age (yrs)	Follow up	Obesity measure	Sleep measure	Relationship
Agras, 2004 [83]	150	USA	0	Annually from ages 2-5 yrs for sleep duration	Objective BMI 85th – 95th percentile & ≥95th	Parent annual report from 2-5 yrs	Negative association with sleep duration and overweight
Sugimori, 2004 [84]	8,170	Japan	0	Sleep at 3 and 6 yrs	Objective BMI >90th percentile	Parental report (<10.5, 10.5-11.4, 11.5-11.9, ≥*12hrs*)	Negative association in boys
Reilly, 2005 [18]	8,234	UK	0	Sleep at 3 yrs	Objective BMI ≥95th percentile	Parental report	Negative linear
Snell, 2007 [85]	1,441	USA	3-12	5 yrs	Objective BMI (IOTF)	Parent/self report (2 time diaries: 1 weekday, 1 weekend) at BL and FU (<8, 8-8.9, *9-9.9*, 10-10.9, ≥11hrs)	Negative linear
Lumeng, 2007 [86]	785	USA	9-11	3 years	Objective overweight as BMI ≥ 95th percentile	Maternal report (CSHQ)	Negative association
Touchette, 2008 [87]	1,138	Canada	2.5	Sleep annually from 2.5-6yrs. BMI at 2.5 & 6yrs	Objective BMI (IOTF)	Maternal report	Negative association

BMI=body mass index; IOTF=international obesity task force; BL=baseline; FU=follow up; CSHQ=child sleep habits questionnaire.

Table 1.6 cont'd

First authors name, year	Sample size	Country	Baseline age (yrs)	Follow up	Obesity measure	Sleep measure	Relationship
Taveras, 2008 [88]	915	USA	0	Sleep: 6m, 1yr and 2yrs Obesity: birth, 6m, 3yrs	Objective BMI z score & skinfold thickness. Risk of overweight (85-95th centile) overweight (≥95th)	Maternal report (<12hrs vs ≥12hrs)	Sleep negatively associated with BMI z score, subscapular and tricep skinfold & risk of overweight
Landhuis, 2008 [89]	1,037	New Zealand	0	5, 7, 9 & 11 years of age for sleep duration. TIB @ 32yrs. BMI @5 & 32 yrs	Objective BMI	Parental report	Negative association for childhood sleep duration and BMI but not adult sleep
Berkey, 2008 [90]	5,036 (girls)	USA	9-14	Annually for 5 yrs	Self-report height and weight (85-95th percentile, >95th)	Self-report (≤5, 6, 7, *8*, ≥9 hrs)	Negative linear
Rutters, 2010 [91]	98	Netherlands	7	Annual objective BMI & WC 7-16 yrs; annual sleep data 12-16 yrs	Objective BMI (IOTF) & WC	Self-report (hrs)	Negative association

BMI=body mass index; TIB=time in bed; WC=waist circumference; IOTF=international obesity task force.

Table 1.6 cont'd

First authors name, year	Sample size	Country	Baseline age (yrs)	Follow up	Obesity measure	Sleep measure	Relationship
Calamaro, 2010 [92]	13,568	USA	12-18	1-2yrs	Self-report (wave 1 & 2). Objective BMI (wave 2) Obesity >95th percentile	Self-report (hrs) 1 question (<6, 6-8, >8-11, >11hrs)	No association
Bell, 2010 [93]	1,930	USA	0-13	5 yrs	Objective BMI at FU. BL BMI parental report if ≥5yrs but no data for those <5yrs @ BL. 85-95th, >95th percentile	1 x weekday,1 x weekend time diary. Short sleep <25th percentile	Negative association. Those 0-4 yrs @ BL with overweight/obesity at FU. No association in 5-13 yrs between BL sleep and weight

BMI=body mass index; FU=follow up; BL=baseline.

The many studies conducted in adults are highlighted in Table 1.7 (cross-sectional) and Table 1.8 (longitudinal). *Chapter 4* assesses sleep in relation to the metabolic syndrome of which central obesity is a major component. A full review of literature surrounding sleep duration and the metabolic syndrome is provided in *Chapter 4.*

Table 1.7: Cross-sectional studies examining the relationship between sleep duration and weight status in adults.

First author, year	Sample size	Country	Age (years)	Obesity measure	Sleep measure	Relationship
Vioque, 2000 [94]	1,772	Spain	≥15	Objective BMI	Self-report	Negative linear association
Shigeta, 2001 [95]	453	Japan	53	Objective BMI	Self-report	Negative association
Heslop, 2002 [96]	6,797	UK	35-64	Objective BMI	Self-report	Negative association
Kripke, 2002 [3]	1,116,936	USA	33-102	Self-report	Self-report	U-shaped association
Taheri, 2004 [97]	1,024	USA	30-60	Objective BMI	Sleep diaries and PSG	Negative association
Tamakoshi, 2004 [42]	104,010	Japan	40-79	Self-report	Self-report	U-shaped association
Cournot, 2004 [98]	3,127	France	32-62	Objective BMI	Self-report	Negative association in women but not men
Gangwisch, 2005 [99]	9,588	USA	32-86	Objective BMI	Self-report	Negative association
Singh, 2005 [100]	3,158	USA	18-65	Self-report	Self-report	U-shaped association
Vorona, 2005 [101]	924	USA	18-91	Objective BMI	Self-report	Negative association
Kohatsu, 2006 [102]	990	USA	48 (mean)	Objective BMI	Self-report	Negative linear association
Moreno, 2006 [103]	4,878	Brazil	40 (mean)	Objective BMI	Self-report	Negative association
Gottlieb, 2006 [104]	5,910	USA	40-100	Objective BMI	Self-report	U-shaped association
Lauderdale, 2006 [105]	669	USA	35-49	Objective BMI (3y prior to sleep measure)	72-hr actigraphy and sleep diaries	No association

BMI=body mass index.

Table 1.7 cont'd

First author, year	Sample size	Country	Age (years)	Obesity measure	Sleep measure	Relationship
Bjorvatn, 2007 [106]	8,860	Norway	40-45	Objective BMI	Self-report	Negative association
Fogelholm, 2007 [107]	7,641	Finland	30+	Objective BMI & WC	Self-report	Negative association
Ko, 2007 [108]	4,793	Hong Kong	17-83	Objective BMI & WC	Self-report	Negative linear association
Park, 2007 [109]	6,174	Korea	18-80	Objective BMI	Self-report	Negative association
Patel, 2008 [110]	6,107	USA	67-99	Objective BMI, WC & DXA	Actigraphy & PSG	<5 hours associated with increased BMI, obesity, central body fat distribution and BF%
Stamatakis, 2008 [111]	1,203	USA	20-92	Self-reported height/weight	Self-report	Negative association
van den Berg, 2008 [112]	983	The Netherlands	57-97	Objective BMI	6 nights actigraphy	U-shaped association
Vgontzas, 2008 [113]	1,300	USA	≥20	Objective BMI	1 night PSG	Negative association
Park, 2009 [114]	8,717	Korea	20-65	Objective BMI & WC	Self-report	Negative association
Watson, 2010 [115]	122 (twins)	USA	36.9 (mean)	Self-reported height/weight	Self-report	Negative association
Buxton, 2010 [116]	56,507	USA	18-85	Self-report	Self-report	U-shaped association
Chaput, 2010 [117]	537	Canada	18-64	Objective BMI	Self-report	Negative association
Magee, 2010 [118]	45,325	Australia	≥45	Self-report height/weight	Self-report	U-shaped association in 55-64yrs. No association in those ≥65yrs

BMI=body mass index; WC=waist circumference; DXA=dual energy x-ray absorptiometry; PSG=polysomnography; BF%=body fat percent.

Table 1.7 cont'd

First author, year	Sample size	Country	Age (years)	Obesity measure	Sleep measure	Relationship
Theorell-Haglow, 2010 [119]	400 women	Sweden	20-70	Objective WC	1 night PSG	Negative association
Anic, 2010 [120]	5,549 women	USA	20-75	Self-reported height/weight	Self-report	Negative association

WC=waist circumference; PSG=polysomnography.

Table 1.8: Longitudinal studies examining the relationship between sleep duration and weight status in adults.

First author, year	Sample size	Country	Age at baseline (yrs)	Follow up (yrs)	Obesity measure	Sleep measure	Relationship
Hasler, 2004 [121]	496	Switzerland	27	2, 7 & 13	Self-report BMI	Self-report	Negative linear
Gangwisch, 2005 [99]	3,208	USA	32-86	8-10	Objective height @ BL, objective weight 1982/4 & self-reported 1987/1992	Self-report	Short sleep at BL was significantly associated with higher BMI
Patel, 2006 [122]	68,183 (women)	USA	30-55	16	Self-report BMI	Self-report	Negative association

BMI=body mass index; BL=baseline.

Table 1.8 cont'd

First author, year	Sample size	Country	Age at baseline (yrs)	Follow up (yrs)	Obesity measure	Sleep measure	Relationship
Chaput, 2008 [123]	276	Canada	21-64	6	Objective BMI	Self-report	U-shaped association
Lopez-Garcia 2008 [124]	3,576	Spain	≥60	2	Objective BMI & WC	Self-reported at BL	U-shaped association in women only
Watanabe, 2010 [125]	34,852	Japan	Mean age 38 yrs (women), 40 yrs (men)	1	Objective BMI	Self-report	U-shaped in men but no association in women
Hariston, 2010 [126]	1,107	USA	18-81	5	CT scan: visceral adipose tissue and subcutaneous adipose tissue; objective BMI	Self-report	Negative association in those <40 yrs

BMI=body mass index; WC=waist circumference; BL=baseline; CT=computerised tomography.

1.5.2.1 A review of the sleep-obesity evidence in children, adolescents and adults

Evidence identifying an association between sleep duration and weight status in a paediatric population was first reported in 1992.[127] Paediatric studies are identified in Tables 1.3, 1.4, 1.5 and 1.6. A number of studies will be highlighted and discussed. There is increasing evidence suggesting a negative association between sleep duration and overweight or obesity in children. The cross-sectional data identified were from 97,200 children and were conducted between 2002-2010, spanning multiple ethnicities, a range of cultures, and geographically diverse countries including Germany, Portugal, Japan, Taiwan, Hong Kong, China, USA, Brazil, Canada, Australia, New Zealand, India, Turkey and Norway.

1.5.2.1.1 Sleep-obesity cross-sectional evidence in children

Early evidence came from a large German study, which recruited 6,862 children aged 5-6 years. The study reported a dose-dependent relationship between obesity and sleep duration categories. In those who slept ≤10 hours, 10.5-11.0 hours and ≥11.5 hours, prevalence of objectively measured obesity was 5.4%, 2.8%, and 2.1%, respectively. Logistic regression analysis was conducted comparing those with shortest sleep duration (≤10 hours) with the other sleep categories. After adjustment for parental education, parental obesity, birthweight >90th quartile, weight gain in first year, TV or video game use and snacking during media use, those with a sleep duration of 10.5-11.0 hours were less likely to be obese, odds ratio (OR) 0.52 (95% confidence interval (CI) 0.34-0.78) and those who slept ≥11.5 hours had a further reduced risk,

OR 0.46 (95% CI 0.28-0.75). Other studies have shown gender differences in sleep duration[73;75;81] but surprisingly, this study did not adjust for gender. Information on fat mass (FM) estimated from anthropometric measures in a sub-sample of 1,676 produced similar findings i.e. shorter sleep duration was associated with increased FM. The results however, are tentative due to the nature of questioning used for sleep duration. Parents were asked to choose from selected time slots to indicate what time their child went to bed and got up. The difference was calculated between the two responses. Unfortunately, this equates to time in bed (TIB) and not estimated sleep duration per se. Whilst parental sleep estimates have been shown to correlate with actigraphy in 4-7 year old children,[128] parents tend to overestimate sleep duration, potentially due to providing TIB data or as a result of bias. The study also did not obtain information on nighttime awakenings, bedtime resistance and other sleep related problems, all of which may impact on the child's total sleep time (TST). That said, the study benefits from a large sample and used other measures of adiposity besides BMI.[60]

Also in 2002, the Toyama Birth Cohort Study, which had recruited 10,400 children, reported cross-sectional data at ages 6 and 7 years from 8,274 children.[24] A large array of information was obtained through parental questionnaires. Anthropometric measures were collected to assess BMI. Overweight and obesity were defined using Cole's international cutpoints.[51] The large sample size and a comprehensive data collection allowed adjustment for a broad range of confounders including age, self-reported parental obesity, physical activity, TV viewing, frequency of taking breakfast and snacking frequency. Results were presented as total sample and gender stratified, which revealed a significant effect of obesity in those with the shortest sleep duration (<8hrs) with fully adjusted OR of 2.87 (95% CI 1.61-5.05) compared to those who

slept ≥10 hours. Other categories of sleep duration showed a dose-dependent relationship. Stratified analysis showed the effect was stronger in boys compared to girls, consistent with other findings.[67;71;84] A later study, however, in the same sample showed that the relationship became stronger in girls during adolescence,[73] consistent with other studies.[75;80] The Toyama Study relied on parental report; forcing responses of 1-hour incremental bed/wake times rather than exact timings. This method of data acquisition is common in paediatric sleep-obesity studies thus the information provided and assessed is actually based on time in bed (TIB) rather than total sleep time (TST) which may produce inaccuracies. The study used parental report for all variables, which may be subject to bias. Furthermore, a non-validated questionnaire was administered for data acquisition and although the authors report a 3-month pre-test for reliability of lifestyle factors, the Kappa coefficient range of 0.48-0.64 is not convincing. The same group, however, validated parental reported sleep with an objective sleep measure in 3 and 4 year old children.[129]

The majority of paediatric sleep-obesity evidence is based upon parental report, which can be subject to over-reporting bias either through parents reporting time in bed and not sleep duration per se, or by failing to take account of nighttime awakenings, which are common in younger children. There are no studies to date that have used objective measures to determine sleep in young children (<7 years old) alongside objectively determined overweight/obesity measures. Thus, further investigation is needed to ascertain the possibility of the short sleep-obesity relationship from early childhood to aid a better understanding and develop future strategies for educating parents and children about the importance of sleep from a young age.

1.5.2.1.2 Sleep-obesity cross-sectional evidence in adolescents

Different methods of collected sleep duration have been utilised in other studies. Knutson and Lauderdale asked 1,546 adolescents to complete two 24-hour time diaries (1 x weekday and 1 x weekend day), which included information on sleep times as well as asking "How many hours of sleep do you usually get a night?" They then compared the two sleep measures and found that sleep duration, measured through time diaries, was not associated with objective overweight measures but self-reported total sleep time was, although not linearly.[69] Although time/sleep diaries are considered to be more detailed, they may not be more accurate or reliable since additional information is needed along with more commitment and motivation for completion. Arguably, for self-report sleep measures, a number of short, brief questions may be adequate and may be more accurate for determining sleep parameters. The study demonstrates how different sleep questioning can produce inconsistent results in relation to adiposity outcomes and so the acquisition of sleep information must be considered through carefully designed studies when examining the sleep-obesity relationship.

A Chinese study of 500 twins (10-20 years old) completed a 7-day sleep diary and the Pittsburgh Sleep Quality Index (PSQI) was administered to 19-20 year old participants only. Those who were ≤18 years old completed the Pediatric Sleep Questionnaire (PSQ) with their parent(s) for determination of sleep disordered breathing, snoring, excessive daytime sleepiness (EDS) and behavioural problems. Usual sleep duration was ascertained by one question: "How many hours of sleep does this child usually get?" The study obtained BMI, waist circumference (WC), hip circumference (HC) and body fat percent (BF%) through dual energy x-ray absorptiometry

(DXA) scanning. This study revealed gender differences amongst sleep duration and anthropometric measures. The relationship was U-shaped for BF%, truncal fat and WC in girls. Boys who slept for ≥9 hours had increased WC and HC compared to those sleeping 8-8.9 hours.[71] The U-shaped association, unlike that observed in other paediatric studies,[63;68;70;77;78] has been more commonly observed in adult populations. This sample, however, spanned into early adulthood which may have contributed to the non-linear relationship observed, although gender stratification analysis was not presented making this difficult to determine. Furthermore, the array of sleep questioning may be problematic in this study. Different questionnaires were administered to different participants according to age. For example, the PSQI was administered to older participants (19-20 years) for determination of insomnia which assumes younger participants did not suffer with insomnia. The assumption that EDS is a direct consequence of insomnia may not be accurate in adolescent populations but may be a result of delayed sleep phase rather than insomnia, per se. Although the study benefits from multiple objective adiposity measures and assessed twins, which can help to tease out differences between genetics and lifestyle factors, the sleep questioning does not fully complement the study. Furthermore, the sample includes a broad age range comprised of children, adolescents and emerging adults, making conclusions difficult, particularly when parents of adolescents have contributed to the sleep data provided, which may produce bias through a lack of knowledge as their offspring develop greater autonomy during this phase of life.

1.5.2.1.3 The sleep-obesity evidence in children and adolescents using objective sleep measures

There have been just 3 cross-sectional studies that have applied objective sleep measures. Gupta and colleagues used a single 24-hour actigraphy in 383 adolescents (11-16 years) as well as BMI and fat free mass, as measured by bioelectrical impedance analysis. A negative linear relationship was found between sleep duration and objectively measured BMI after adjustment for age, gender, ethnicity and pubertal status.[66] The study is limited to just 1 day of objectively determined sleep through actigraphy, which may not reflect usual sleep habits.

Another study used 24-hour actigraphy concurrent with parental reports and collected objectively measured BMI and body fat percent (BF%) in 7-year-old children. Parental reports of time in bed were longer than actigraphy measured sleep (10.9 hours and 10.1 hours, respectively). For those who slept <9 hours the odds of overweight/obesity was 3.32 (95% CI 1.40-7.87) compared to those sleeping ≥9 hours, after adjustment for gender, physical inactivity, and maternal age, BMI and marital status. Furthermore, BF% was higher by 3.34% in those sleeping <9 hours after adjustment.[64] Again, use of 24-hour actigraphy only provides a snapshot of an individual's normal sleep behaviours and may not be fully representative. Thus, there is a need for longitudinal objective sleep measures, assessing paediatric populations in all ethnicities to ensure that the relationship is consistent whilst, at the same time, attempting to establish at what age the relationship starts to develop.

A more detailed study used three consecutive nights of PSG to determine differences in sleep architecture comparing normal weight to overweight children and adolescents (n=335). Interestingly, they found objectively measured BMI z-scores were significantly related to total sleep time (TST), sleep efficiency and REM sleep. Those who were overweight obtained less sleep (-22 minutes), had less sleep efficiency, reduced REM and a prolonged initial REM onset compared to normal weight participants. After adjustment for demographic factors, pubertal status and psychiatric problems, 1 hour less of TST was associated with almost 2-fold increased odds of overweight and 1 hour less of REM was associated with almost 3-fold increase.[79] These findings are consistent and support the short sleep obesity link in children and adolescents whilst identifying the need for more rigorous study designs that employ objective sleep measures. They also identify REM sleep as a potentially important sleep stage in the sleep-obesity relationship.

1.5.2.1.4 Differences between weekday and weekend sleep

Evidence shows that sleep duration on weekdays and weekends differ, particularly in adolescents who tend to have more sleep debt during the week due to later bedtimes and early rising for school attendance. The relationship between BMI and these two sleep parameters was examined by Wing and colleagues who identified that the relationship was negative and accentuated in those who did not compensate for weekday sleep debt during weekends/holidays.[29] It should be noted, however, that this study obtained parental sleep reports, which may be inaccurate for younger adolescents who become more independent from the family and spend more leisure time

in their bedrooms. Thus, parents may not be aware of actual sleep-wake times or total sleep time (TST). Therefore, parental estimates of adolescent TST may produce bias and inaccurate data.

1.5.2.1.5 Conclusions of cross-sectional sleep-obesity evidence in children and adolescents

The cross-sectional evidence provides extensive data regarding short sleep duration and obesity, covering almost 100,000 children and adolescents. Collectively, the relationship is mainly linear although some have reported U-shaped associations,[71;76] diminished relationships after age 10 years[82] or gender differences.[73;80;81] This may be due to differences in methodological designs, the various methods used to obtain sleep duration estimates and/or variations in adiposity measures. The many studies reporting an association between short sleep duration and obesity in children and adolescents however, do not provide unequivocal evidence as many did not obtain data on, or adjust for, major risk factors associated with obesity such as physical activity,[65;76;77;79;81] and/or dietary parameters.[64;66;71;72;76;77;79;81] Others, however, have identified specific questions relating to food intake such as frequency of fast foods, breakfast, speed of food consumption, snacking and portion sizes, all of which are important when considering overweight/obesity as an outcome measure.[73;92] Furthermore, cross-sectional evidence cannot confirm a causal relationship.

1.5.2.1.6 Prospective sleep-obesity evidence in children and adolescents

There are a number of longitudinal studies, which can potentially help to determine causal inferences and available data is promising. The first longitudinal study was a small birth cohort followed up to the age of 9.5 years. Accelerometers were used to determine activity levels each year for a 24-hour period. For sleep, the authors relied on annual parental reports from ages 2-5 years. A 24-hour period of dietary intake was monitored through delivering a fridge of chilled food to the household. Parents were instructed to only provide their child with food from the fridge during the 24-hour period. Subsequent calculations were made for 24-hour consumption of calories, carbohydrates, protein and fat. This study showed a negative association between sleep duration at ages 3-5 years and overweight at 9.5 years. Children who became overweight had 30 minutes less sleep compared to those who remained a normal weight.[83] Interestingly, this difference was due to shorter daytime sleep with only a 5 minute difference in nighttime sleep thus making daytime napping an interesting sleep parameter to further investigate. Despite data collection regarding food intake, no association between this and sleep duration was found. Physical activity, however, was negatively associated with hours of sleep.

The only UK study performed was conducted in a birth cohort based in the Southwest. The Avon Longitudinal Study of Parents and Children (ALSPAC; also known as Children of the 90s) investigated 25 putative factors at aged 2.5 years associated with obesity at age 7 years. Eight significant relationships were found in 8,234 children. One of these factors was short sleep duration (<10.5 hours) at age 3 with an increased OR of 1.45 (95% CI 1.10-1.89), after adjustment for gender, maternal education and energy intake at 3 years, compared to those who

slept for >12 hours.[18] Interestingly, dietary measures of junk food and healthy food, measured at 38 months, was not significantly related to obesity. Conversely, physical inactivity, measured by hours of TV viewing (parental report) was positively and significantly associated with obesity.

Another cohort study comprising of 1,441 US children (3-12 years) utilised 2 time diaries (1 x weekday and 1 x weekend) and obtained objectively measured BMI. Cross-sectional associations were not found but longitudinal analysis showed that those with longer sleep (≥11 hours) at baseline had a lower risk of being overweight at 5-year follow up compared to those who slept for 9-10 hours. Later bedtimes at baseline were also predictive of higher BMI at follow up.[85] In line with cross-sectional data[82] the linear relationship was significant in younger children (3-7.9 years) compared to older children (8-12.9 years) in stratified age analysis. Thus, the sleep-obesity relationship appears to be consistently stronger in younger children but this still needs to be confirmed through objectively measured sleep duration in young children from different ethnicities before generalisations and robust conclusions can be drawn.

Further prospective evidence comes from a birth cohort with a 32-year follow up. Information regarding time in bed (TIB) was reported by parents at ages 5, 7, 9 and 11 years and self-reported TIB at follow up. Objectively measured BMI was obtained at 5 years and at follow up. A negative relationship was found between childhood sleep duration and adult BMI after adjustment for BMI at 5 years, childhood socioeconomic status (SES), parental BMI's, TV viewing during adolescence and adulthood, and adult physical activity, smoking and sleep duration.[89] Despite the impressive follow up duration of this study, all measures were obtained through either parental or self-report, with the exception of participant's BMI. A further

limitation of this study is parent reported sleep duration, based on the night before the assessment as this may be unrepresentative of usual sleep time.

The only longitudinal adolescent study to report no association between sleep duration and obesity was from a large study (n=13,568) of US adolescents. The study surveyed 12-18 year olds at baseline and again after 1-2 years. Objectively measured BMI were only obtained at FU and only one question was asked concerning sleep duration: "How many hours of sleep do you usually get?" Sleep data were then categorised into <6 hours (short sleep), 6-8, >8-11 (referent) and >11 hours. These sleep categories appear to be somewhat arbitrary and the referent category relatively broad. Unadjusted analysis demonstrated that short sleep duration was significantly associated with an almost 2-fold increase in BMI at follow up. After adjustment for self-reported obesity at baseline, age, gender, ethnicity and parental income, the finding became non-significant.[92] The limitations of this study include self-reported obesity at baseline, which may have resulted in biased responses. Secondly, despite comprising a large sample and having sufficient statistical power to adjust for multiple potential confounding factors, the study only adjusted for five confounders. Also, the study did not consider any measure of physical activity, a major determinant of obesity, or media use as potential confounders. This is surprising considering the authors previous publication on sleep and technology.[130] These methodological issues and oversights may have produced an inaccurate picture of the sleep-obesity link in adolescents. It is possible, however, that the sleep-obesity relationship was not observed due to the upper age of some of the participants who would have become adults at follow up.

1.5.2.1.7 Conclusions of prospective sleep-obesity evidence in children and adolescents

The evidence discussed above suggests a reasonably consistent negative relationship between sleep duration and subsequent overweight/obesity. There is a less consistent linear association in adolescents compared to children.[82] Further support for this comes from a systematic review and meta-analysis which stated the relationship is steady up to the age of 10 years.[131] A further systematic review supported the notion that the linear relationship decreases with age.[132]

1.5.2.1.8 The adult sleep-obesity evidence

As previously stated, the largest study to identify a link between increasing BMI and short sleep duration was published in 2002.[3] Previous smaller adult cross-sectional studies reported similar findings (Table 1.7), although the relationship is less consistent than the data from children and adolescents. Adult studies have reported negative,[94;115] U-shaped,[3;123;133] gender-specific associations,[98;125;134] or no relationship at all.[118] There is, however, overwhelming evidence from adult population studies demonstrating short sleep duration could be an important but potentially modifiable risk factor for overweight/obesity.[3;94-102;108;123;135-137]

The sleep-obesity relationship has also been confirmed in prospective longitudinal studies comprising different ethnicities (see Table 1.8).[99;121-123] Accumulating evidence has been discussed in a number of reviews to date[131;132;138-143] with some more critical of the observation

than others.[140;143] These reviews, along with the published evidence, place more emphasis on short sleep duration, despite the U-shaped association more commonly observed in adults. There has been lesser focus on long sleep duration in adult samples with most acknowledging the association only briefly suggesting it is possibly due to potential underlying health conditions or the presence of obstructive sleep apnoea (OSA). Notably, the relationship between short sleep duration and obesity appears to diminish with age.[118;132] Since ageing is associated with significant changes in sleep duration, quality and timing, there is a need to study the impact of various sleep parameters on health and wellbeing in this age group.

1.5.3 Potential mechanisms for the sleep-obesity relationship

Currently it is unclear how sleep is related to metabolism. The systems that regulate body homeostasis (the nervous and endocrine systems) are likely to be involved. There are two emerging hormones that have been implicated: leptin and ghrelin. These will be discussed in turn.

1.5.3.1 Leptin

The adipocyte-derived hormone, leptin, first discovered in 1994 through the study of mutant rodents with severe obesity, plays a key role in metabolism.[144] Circulating leptin levels are directly proportional to total body fat and signal the extent of fat stores to the hypothalamus. While leptin, acting through the hypothalamus, signals satiety, obesity is associated with higher leptin levels suggesting the presence of leptin resistance.[145] The physiological role of leptin is

likely to be more important in energy deficit states where low leptin is a powerful signal for increasing appetite.

Large epidemiology studies,[97;135] and smaller sleep laboratory experimental studies[146;147] suggest that leptin levels are lower with sleep deprivation or shorter sleep durations. Data from a small experimental study subjecting young, healthy male volunteers to 4, 8 or 12 hours in bed concurrent with identical carbohydrate-rich meals showed that leptin concentrations were exceptionally responsive to sleep duration in a dose-dependent manner. Mean levels were 19% lower in volunteers when sleeping for 4 hours compared to 12 hours.[147] Conversely, a study of 561 adults using PSG measured sleep, reported a 10% increase in leptin levels for every 1 hour of total sleep time reduction, after adjustment for age, gender and ethnicity. Furthermore, leptin increased by 15% for every 1-hour decrease in REM sleep.[148] Another small 7-day experimental study in both men and women found that 1 night of total sleep deprivation (TSD) was associated with increased leptin levels but did not affect hunger. The study included four "normal" consecutive sleep nights followed by one night of TSD and two nights of sleep recovery. The authors concluded that acute TSD, in a less stressful environment, had the opposite effect on leptin levels to that of reduced sleep duration.[149] Arguably, four normal sleep nights under laboratory controlled conditions in an attempt to control for stress may have produced opposite effects through feelings of isolation. Although the study benefits from a mixed gender sample, the volunteers were still healthy and young and may not be representative of the population. Further limitations of this study are TSD, which does not represent normative sleep behaviour.

There is only one study that has examined the relationship between sleep duration and leptin levels in children and adolescents. This study of German children and adolescents, aged 6-19 years paradoxically found a negative association between leptin levels and sleep duration in girls.[80] Although this study performed stratified gender analysis, only age was adjusted for and the relationship was assessed through partial correlations, rather than more detailed statistical techniques. Pubertal status is associated with leptin levels in both boys and girls[91] and so this important unadjusted factor may have confounded the observed correlation given the age of the participants.

The relationship between leptin and sleep duration is inconsistent but this may be due to differences in study design and methodological approaches. Low leptin levels stimulate hunger and food intake. Thus alterations in leptin levels with sleep reduction could contribute to increased energy intake, which, in turn, may partially explain the development of obesity.

1.5.3.2 Ghrelin

Ghrelin is a hormone is derived from the stomach. Circulating ghrelin levels stimulate hunger via the hypothalamus. Levels are higher in the fasted state and decreased after food intake. Some of the previously discussed studies that assessed leptin also examined the association between short sleep duration (from population studies) and sleep deprivation (from laboratory studies) and ghrelin levels. These studies show that shorter sleep or the sleep-deprived state is associated with higher ghrelin levels.[97;146] One further study in lean and obese adolescent girls found an inverse

relationship between self-reported sleep duration and ghrelin in female adolescents.[150] Interestingly, the study also found increased carbohydrate intake (self-reported diet) in those sleeping <5 hours.

Data examining sleep duration and ghrelin are reasonably consistent although some have found no relationship after 2 nights of sleep restriction with ghrelin or leptin.[151] Results from this study were restricted to a small (n=15), healthy, lean, male only sample and allowed the volunteers to leave the laboratory during the day and return to free-living conditions. A previous study, however, by the same group subjected 9 healthy male volunteers to three conditions at least 2 weeks apart: 1) 7 hours of sleep; 2) 4.5 hours sleep; 3) total sleep deprivation. Volunteers subjectively rated hunger and ghrelin levels were assessed. Hunger and ghrelin exhibited a dose-dependent relationship with highest levels observed in condition 3.[152]

1.5.3.3 Explaining the link between reduced sleep duration and metabolic hormone alterations

It is believed that the association between reduced sleep duration and appetite-regulating hormones discussed above are related to increased sympathetic nervous system activity.[142] The sympathetic nervous system is core for regulating responses to environmental change and stress. A reduction in sleep duration may therefore result in over-activation of the sympathetic nervous system and the stress-related response may, in turn, produce alterations in metabolic hormones.

1.5.3.4 Sleep and energy balance

Alterations in sleep duration have been linked to disruptions in the energy balance equation. The evidence is highlighted and discussed below.

1.5.3.4.1 Sleep and appetite

Studies reporting ghrelin and leptin alterations as a consequence of altered sleep duration have also shown that these are related to increases in subjective hunger and appetite for unhealthy foods types that are dense in carbohydrates and calories[146] – both of which promote weight gain if excess energy is not expended.

A more detailed study of adolescent nutrient intake and sleep has provided further evidence. The study recruited 240 participants in a free-living environment and implemented 24-hour food recall to measure diet alongside actigraphy measures for sleep. Adolescents sleeping <8 hours consumed a significantly higher amount of calories from fats compared to those who slept for >8 hours on weekdays. After adjustment, short sleep duration remained significantly associated with a daily average increase of calorie intake consumed from fat.[153] Similar findings were reported in a small (n=11) sleep manipulation study, which calculated calories consumed from snacks and meals after 5.5 hours and 8.5 hours of sleep. Sleep restriction was associated with increased consumption of calories from snacking.[154] Furthermore, these categories of sleep are not extreme and may be representative of normative sleep behaviours.

Recent evidence shows that resting and post-prandial energy expenditure after a 24-hour period of total sleep deprivation were significantly reduced compared to when volunteers had a sleep opportunity of 8 hours. Despite ghrelin and glucose being significantly elevated, there was no difference in food intake from a free-choice lavish buffet.[155]

Based on the evidence discussed above, it is possible that small alterations in food intake, potentially triggered by sleep reduction, may promote obesity over time. Both leptin and ghrelin appear to be sensitive to alterations in sleep duration and may mediate the link between short sleep and increased appetite. Further confirmation is needed through experimental sleep studies that minimally manipulate sleep as well as over a prolonged time period. Such a model has been piloted as part of the work presented in this thesis (see *Chapter 5).*

1.5.3.4.2 Sleep and energy expenditure

Reduced energy expenditure in those obtaining insufficient sleep may be a further contributory factor for metabolic dysfunction. Acute total sleep deprivation (TSD) in healthy, lean men (n=14) showed reduced resting and postprandial energy expenditures, assessed using a ventilated-hood system (indirect calorimetry), compared to when volunteers had a usual sleep opportunity within a 24-hour period.[155] Consistent with these findings was another small study of healthy, lean men (n=15), which did not subject individuals to TSD but to sleep restriction. In a randomised crossover design volunteers were provided with 2 nights sleep opportunity of 4 hours

and 15 minutes and 2 nights of regular sleep opportunity (8 hours and 15 minutes) whilst being monitored by accelerometry. The study found physical activity levels significantly decreased during the day in free-living conditions after the first night of sleep restriction. Furthermore, physical activity was less intense and less time was spent engaging in intense activity after sleep restriction compared to usual sleep opportunity.[151] Another study used a similar crossover design applying sleep restriction. Healthy, lean male volunteers (n=12) were provided with 8-hour and 4-hour sleep opportunities. Physical activity levels were recorded through waist actigraphy and compared across the two conditions. The study reported significantly lower levels of nighttime physical activity during recovery sleep following 1 night of sleep restriction.[156]

Based on the highlighted evidence, it is possible that sleep loss may result in decreased energy expenditure and may subsequently promote obesity over time. Furthermore, combining this evidence with that surrounding sleep loss and alterations in leptin and ghrelin, food intake, food selection and reduced energy expenditure, together, these changes may influence the regulation of energy balance and ultimately promote obesity.

1.6 Type 2 diabetes mellitus

Type 2 diabetes mellitus (T2DM) is a chronic illness with a rapidly rising global prevalence.[157] It is a complex genetic condition, associated with increased cardiovascular risk. The main risk factors for developing T2DM include ageing and obesity. T2DM is a metabolic disorder characterised by increased levels of blood glucose, insufficient insulin production and cells

failing to respond to insulin (insulin resistance). Biochemically, the World Health Organization (WHO) has defined diabetes as fasting plasma glucose level of ≥7.0 mmol/l (126 mg/dl) or with an oral glucose tolerance test, two hours after the oral dose, plasma glucose of ≥11.1 mmol/l (200 mg/dl).[158] Although diabetes per se is well characterised, there is some debate about the classification of impaired fasting glucose (IFG). The WHO suggest ≥6.1 mmol/L to 7.0 mmol/L[158] whereas the American Diabetes Association (ADA) state ≥5.6 mmol/L to 7.0 mmol/L.[159]

1.6.1 Sleep as a risk factor for type 2 diabetes mellitus

Sleep curtailment has become increasingly common in today's modern society. Parallel with this is the rapid increase in interrelated chronic diseases such as obesity and type 2 diabetes mellitus (T2DM). T2DM is no longer limited to adult populations but is now increasingly diagnosed in children, although this is strongly related to family history of the disease and overweight/obesity.[160] As previously outlined, sleep duration is a strong predictor of obesity in children and adults. There is also evidence surrounding sleep duration in relation to glucose metabolism. A number of cross-sectional and longitudinal studies have linked both short and long sleep duration with T2DM.[137;161-168]

Acute total sleep deprivation has been previously associated with glucose intolerance and insulin insensitivity,[169] both precursors of T2DM. Total sleep deprivation in individuals, however, does not represent usual sleep behaviour. Although sleep is commonly curtailed in adults, acute total

sleep deprivation may produce different results compared to a few hours of sleep loss over a prolonged period of time (chronic partial sleep deprivation). The effects of chronic partial sleep deprivation have therefore been more recently investigated. A study examined 11 healthy men after 6 days of sleep restriction (4 hour sleep opportunity) followed by 7 days of sleep recovery (12-hour sleep opportunity). Volunteers also underwent a baseline study with 8-hour sleep opportunities, considered to be the 'optimal' sleep duration in adults. Subsequent to each sleep condition an intravenous glucose tolerance test was conducted followed by 24-hour blood sampling where energy expenditure was limited and food intake was restricted to identical carbohydrate-rich meals. Following sleep restriction, glucose clearance was reduced 40% compared to the sleep recovery condition. Leptin levels showed a dose-response relationship with sleep duration with the highest levels observed during 12 hours of sleep opportunity. Furthermore, homeostatic model assessment (HOMA-IR; a measure of insulin resistance) levels in response to breakfast increased by >50% after sleep restriction compared to when subjects were sleep extended.[147;170;171] Although HOMA is usually measured in a fasting state to assess insulin resistance, in this study HOMA values were measured during meal ingestion as an integrated measure of the glucose and insulin responses to the three identical carbohydrate-rich meals. It should be considered that laboratory sleep studies are not representative of normal sleep environments. Furthermore, these experimental sleep studies have been performed only in healthy men. Finally, 4 hours of sleep, although not total sleep deprivation, is still at the extreme end of the sleep duration spectrum and is unusual. These extreme sleep conditions are subjected over a short time period and do not provide full information on the long-term effects of sleep curtailment that may result in chronic disease.

1.6.1.1 Mechanisms linking sleep duration with type 2 diabetes mellitus

Short sleep duration may lead to insulin resistance and predispose to diabetes through various physiological changes including increased sympathetic nervous system activity (an important link between sleep, generally a brain activity, with peripheral organ function), alterations in GH secretion, decreased brain glucose utilisation, increased evening cortisol levels, or through alterations in the appetite hormones and energy expenditure, as previously discussed. The reasons proposed for associations between long sleep duration and increased diabetes risk are more tentative. Most studies did not collect information on the presence of OSA, of which a common characteristic is excessive daytime sleepiness. OSA has previously been identified as a potential independent risk factor for insulin resistance and diabetes and could be a major unadjusted confounder.[172]

1.7 The metabolic syndrome

The metabolic syndrome comprises a number of inter-related factors known to increase the risk of cardiovascular disease. There are variations in the definition of the metabolic syndrome. The World Health Organization (WHO) was the first establishment to provide a practical definition of the metabolic syndrome.[173] In response, the European Group for the Study of Insulin Resistance commented and provided a modification of the WHO definition.[174] In 2001, the National

Cholesterol Education Program (NCEP) released its own definition.[175] To accomplish an accepted global definition, the International Diabetes Federation (IDF) proposed a new definition in 2005.[176] Simultaneously, the American Heart Association made a minor but important alteration to the NCEP ATP III definition, which reduced the plasma glucose component from the original ≥ 6.1 mmol/L to ≥ 5.6 mmol/L.[177] This definition is now more widely accepted and reached consensus during a meeting where multiple organisations agreed on the criteria in 2009.[52]

Currently, the three main definitions applied in research are similar but have small distinct differences.

The US National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III[175] definition requires the presence of at least three of the following components:

1. Elevated waist circumference of ≥102 cm for males and ≥88 cm for females (or ethnic specific values – see Table 1.2).
2. Elevated triglyceride level of 150 mg/dL (≥1.7 mmol/L).
3. Reduced HDL-Cholesterol level of <40 mg/dL for males, <50 mg/dL for females.
4. Elevated blood pressure of ≥130/85 mmHg.
5. Elevated fasting plasma glucose level of 110 mg/dL (≥6.1 mmol/L).

The consensus definition,[52] (an update of the NCEP ATP III definition) is the most recent and requires the presence of at least three of the following components:

1. Elevated waist circumference of ≥102 cm for males and ≥88 cm for females (or ethnic specific values – see Table 1.2).

2. Elevated triglyceride level of 150 mg/dL (≥1.7 mmol/L).

3. Reduced HDL-Cholesterol level of <40 mg/dL for males, <50 mg/dL for females.

4. Elevated blood pressure of ≥130/85 mmHg.

5. Elevated fasting plasma glucose level of 100 mg/dL (≥5.6 mmol/L).

The International Diabetes Federation (IDF) can be globally applied with ethnic-specific cutpoints.[176] To qualify for the syndrome, the definition denotes that an individual must have the following:

1. Central obesity (defined by waist circumference according to ethnic specific values). If BMI is >30 kg/m², however, then central obesity is assumed and waist circumference is not measured.

Plus any <u>two</u> of the following components:

2. Raised triglycerides: >150 mg/dL (1.7 mmol/L), or specific treatment for this lipid abnormality.

3. Reduced HDL cholesterol: <40 mg/dL (1.03 mmol/L) for males and <50 mg/dL (1.29 mmol/L) for females, or specific treatment for this lipid abnormality.

4. Raised blood pressure: systolic BP > 130 or diastolic BP >85 mm Hg, or treatment of previously diagnosed hypertension.

5. Raised fasting plasma glucose: >100 mg/dL (5.6 mmol/L), or previously diagnosed type 2 diabetes.

1.7.1 Sleep as a risk factor for the metabolic syndrome

Not only has sleep duration been linked to all cause mortality in large population samples[3] including a smaller study that used objective sleep, estimated through actigraphy[178], but it has also been associated with chronic conditions such as obesity and T2DM. As previously outlined, short and/or long sleep durations have been associated with obesity, and glucose intolerance, both key components of the metabolic syndrome.[170;179;180] The relationship with sleep duration has also been reported for hypertension,[116;181] and lipid abnormalities,[182] two further components of the syndrome. It is therefore not surprising that investigations assessing sleep duration in relation to the metabolic syndrome have been conducted. A full review of the literature surrounding sleep duration and metabolic syndrome is discussed in *Chapter 4*.

1.8 Aims of thesis

Sleep has not only been linked to all cause mortality but the literature discussed suggests sleep is also important for metabolic health outcomes. Due to differences in methodological study designs, adjustment for different potential confounders, inconsistent sleep category comparisons by age groups, differences in methods used for determining sleep duration and other sleep parameters, it is difficult to draw robust conclusions. Through careful consideration of all

potential confounders and subsequent adjustment, rigorous study designs, appropriate use of sleep duration categories according to age and in-depth information concerning various sleep parameters using previously validated measures, further knowledge can be obtained and a better understanding developed for the relationship between sleep duration and metabolic function.

The aim of this thesis is to assess how sleep duration is related to a number of metabolic alterations across the lifespan including young children, adolescents and older adults spanning different ethnicities. This will expand our knowledge and understanding of this area and work towards developing future strategies to help potentially reduce the burden of common chronic metabolic diseases which are rapidly increasing in prevalence across the globe in children and adults.

Despite the large amount of evidence demonstrating a link between sleep duration and obesity, particularly in children, there are a number of aims addressed in this thesis. There is only one UK study that has examined the sleep-obesity relationship in children, which was conducted in a largely Caucasian birth cohort. The study reported on the association between parental reported sleep duration at age 3 years and obesity at age 7 years, finding a negative relationship.[18] Not only is data limited in the UK, but no study has specifically investigated objectively measured sleep duration and adiposity in a UK paediatric population. Furthermore, the sleep-obesity relationship has not yet been examined in young paediatric South Asian populations, particularly those residing in the UK. Not only does the UK have a large number of South Asian residents but this ethnic group have higher levels of metabolic disorders such as obesity[183] and type 2 diabetes mellitus.[184] The aim of *Chapter* 2 is therefore to objectively examine the sleep-obesity

relationship in a young Birmingham cohort of South Asian children. Three adiposity measures were obtained alongside objectively measured sleep and 'parent' estimates of sleep duration, which were used to examine the sleep-obesity link and make comparisons across different measures of adiposity and reports of sleep duration.

The sleep-obesity relationship in adolescents has been consistently identified in a number of countries. The majority have identified self-reported sleep duration which has been previously shown to correlate with sleep diaries and actigraphy.[185] Use of previously validated sleep questionnaires are useful tools which need to be utilised. Some studies, however, have asked just one question about sleep duration and others have forced the response in hours. Sleep questioning should seek information on a variety of sleep parameters such as time to bed, sleep onset, frequency and duration of nighttime awakenings, quality of sleep, wake time, rise time, estimated total sleep time (TST) and napping so that a clearer picture of the sleep-obesity relationship can be examined. TST should be identified rather than time in bed to provide a more accurate estimate of sleep duration. Finally, parental sleep reports should be obtained for young children but not adolescents for the reasons outlined. There are no UK data, however, for this relationship in UK adolescents thus warranting investigation in this population. TV viewing has been previously associated to increased adiposity[94] and reduced time in bed but contemporary adolescents now have ownership and access to numerous technologies which may confound the sleep-obesity relationship. *Chapter 3* obtains information from a large number of adolescents concerning sleep habits and BMI and reports on the sleep-obesity relationship in contemporary UK adolescents. The study was carefully designed to address the potential confounding of multiple technologies upon the sleep-obesity relationship. The aim was to examine singular

potential links between sleep duration and multiple technologies, BMI as well as academic performance.

The evidence directly investigating the relationship between sleep duration and the presence of the metabolic syndrome is less well researched. Data has been obtained from the US in a large majority Caucasian sample, in Europeans and Korean populations. These studies have produced conflicting results, possibly due to applying different definitions of the metabolic syndrome, inconsistent sleep duration categories, and variable adjustment of potential confounding factors. Furthermore, two studies examined the association in broad age ranges and the other in midlife adults but none have specifically investigated the association in older adults or in a Chinese population. *Chapter 4* assesses the potential relationship between sleep duration and the metabolic syndrome in a large Chinese cohort of older individuals.

Accumulating evidence suggests convincing data surrounding sleep duration and metabolic function. Since voluntary sleep curtailment has become increasingly common, a number of experimental sleep studies have provided useful insights into the effects of sleep loss and sleep extension. The studies available, however, are limited in a number of ways:

1. Volunteers are monitored in unnatural sleep settings through laboratory attendance rather than in their own natural sleep environment;
2. Volunteers are subjected to extreme sleep spectrums, which may not be representative of usual sleep behaviours where small amounts of sleep loss/extension are most likely;

3. Sleep manipulation studies have been conducted over relatively short periods of time, rather than prolonged periods making the cumulative effects of sleep loss/extension difficult to examine.

There is a need for additional sleep manipulation models that can be applied to examine the effects of sleep restriction/extension in the individual's own environment, over a prolonged time period but with small amounts of sleep manipulation. The aim of *Chapter 5* therefore, is to propose and examine the possibility of a sleep model, which could potentially address all previously discussed limitations. Through piloting this specific experimental sleep model, if successful, this will be one step closer to identifying the long-term cumulative effects of sleep loss and/or extension which can then be applied to more closely investigate the effects of sleep on physiological, behavioural, social and psychological outcomes.

2 SLEEP DURATION AND OBESITY IN CHILDREN

2.1 Background

Childhood obesity is becoming a widespread problem in today's modern world. Data from the Health Survey for England (HSE) show that 31% of boys and 29% of girls were either overweight or obese in 2008.[186] Despite increased awareness through government campaigns, obesity persists with data showing that among children aged 2-15 years, the proportion that were obese increased in the period between 1995 to 2008 from 11.1% to 16.8% in boys and from 12.2% to 15.2% in girls.[186] The National Health Service (NHS) report titled 'Statistics on obesity, physical activity and diet: England 2010' identified physical inactivity, lower household income and parental overweight and obesity as risk factors for development of childhood obesity but, despite growing evidence, did not discuss or include sleep as a potential contributor.

Parallel with the increase in obesity, Wilson states that "Average nightly sleep duration has fallen from approximately 9 hours in 1910 to 7 hours in 2002." [187] Reduced sleep duration is not only common in adults but is becoming an increasing issue in children. The Sleep in America Poll revealed that 52% of school aged children did not obtain the recommended nighttime sleep duration for this age group of 10 hours.[188] The previous chapter highlighted the importance of sufficient sleep in children for health.

Despite the link between short sleep duration and obesity being first identified in children through a case-control study in 1992,[127] this potentially modifiable risk factor for obesity, believed to potentially alter both energy intake and expenditure, is still largely ignored. Since 1992, there have been a significant number of studies spanning 21 geographic and culturally diverse countries, which have supported the association between short sleep duration and overweight or obesity in children and adolescents. Tables 1.3, 1.4 and 1.5 highlight cross-sectional sleep-obesity studies in children and adolescents whilst the longitudinal studies are summarized in Table 1.6. The studies in both tables demonstrate a consistent negative association with few exceptions, mostly gender related. Given the accumulating evidence that short sleep duration may be a risk factor for childhood obesity and is a potentially modifiable behaviour, it could become an important component of future obesity interventions.

The association between sleep duration and obesity has been shown in children from a variety of ethnic backgrounds, but no data is available from children of South Asian origin, living in the United Kingdom (UK). This is important because South Asians are at greater risk of obesity, type 2 diabetes mellitus and cardiovascular disease compared to white Caucasians. There are two studies of South Asian children available from different areas in India. One study investigated children from a broad age range of 6-16 years[78] and the other was limited to older adolescents, 16-19 years of age.[74] Both studies reported a negative association between sleep duration and BMI and both had relatively small sample size (n=598 and n=489, respectively). Interestingly, South Asian children, when compared with the general population, tend to exhibit a higher prevalence of obesity and its comorbidities[183;184] but reasons for this remain largely unknown.

2.1.1 Aims

This chapter investigates the sleep-obesity relationship in young children of South Asian descent residing in the UK. There are a large number of South Asian residents in the West Midlands. Statistics from the West Midlands Regional Observatory reveal almost half a million South Asians residents, of which 82,400 are children (0-15 years).[189] In this study, baseline recordings of sleep, and anthropometric measures were obtained as part of a three-year longitudinal study investigating obesity in South Asian children. The primary aim of the sleep study was to investigate the association between sleep duration and adiposity.

2.1.1.1 Hypotheses

In this chapter, the following hypotheses will be tested, using data from the Birmingham healthy Eating and Active lifestyle for Children Study (BEACHeS):

Sleep duration is associated with adiposity in young South Asian UK resident children.

Parental estimates of sleep duration are correlated with Actiheart (objective) sleep duration estimates in young South Asian UK resident children.

2.2 Methods

The BEACHeS is an ongoing three-year longitudinal study whose primary aim is to develop and implement a series of obesity intervention schemes in children, with a particular emphasis on South Asian children residing in the UK. Written parental/caregiver consent was obtained for all children who participated in the study. Data were collected between December 2006 and June 2007 from participants who attended one of eight primary schools in Birmingham, UK. Participating primary schools were Christ Church J & I (C.E.) and NC School, Sparkbrook; Heathfield Primary School, Handsworth; Nansen Primary School, Washwood Heath; Yew Tree Community School, Aston; Adderley Primary School, Washwood Heath; James Watt Primary School, Handsworth; Anderton Park Primary School, Sparkhill and Starbank School, Small Heath. A map of the primary school locations in Birmingham can be found in Figure 2.1. This can be compared to Figure 2.2 which details the proportions of overweight children (4-5 year olds) by location in 2008-2009.[190] The study was funded by the National Prevention Research Initiative and ethical approval was granted by Birmingham East, North and Solihull Research Ethics Committee.

Figure 2.1: A map of participating primary schools in the BEACHeS study.

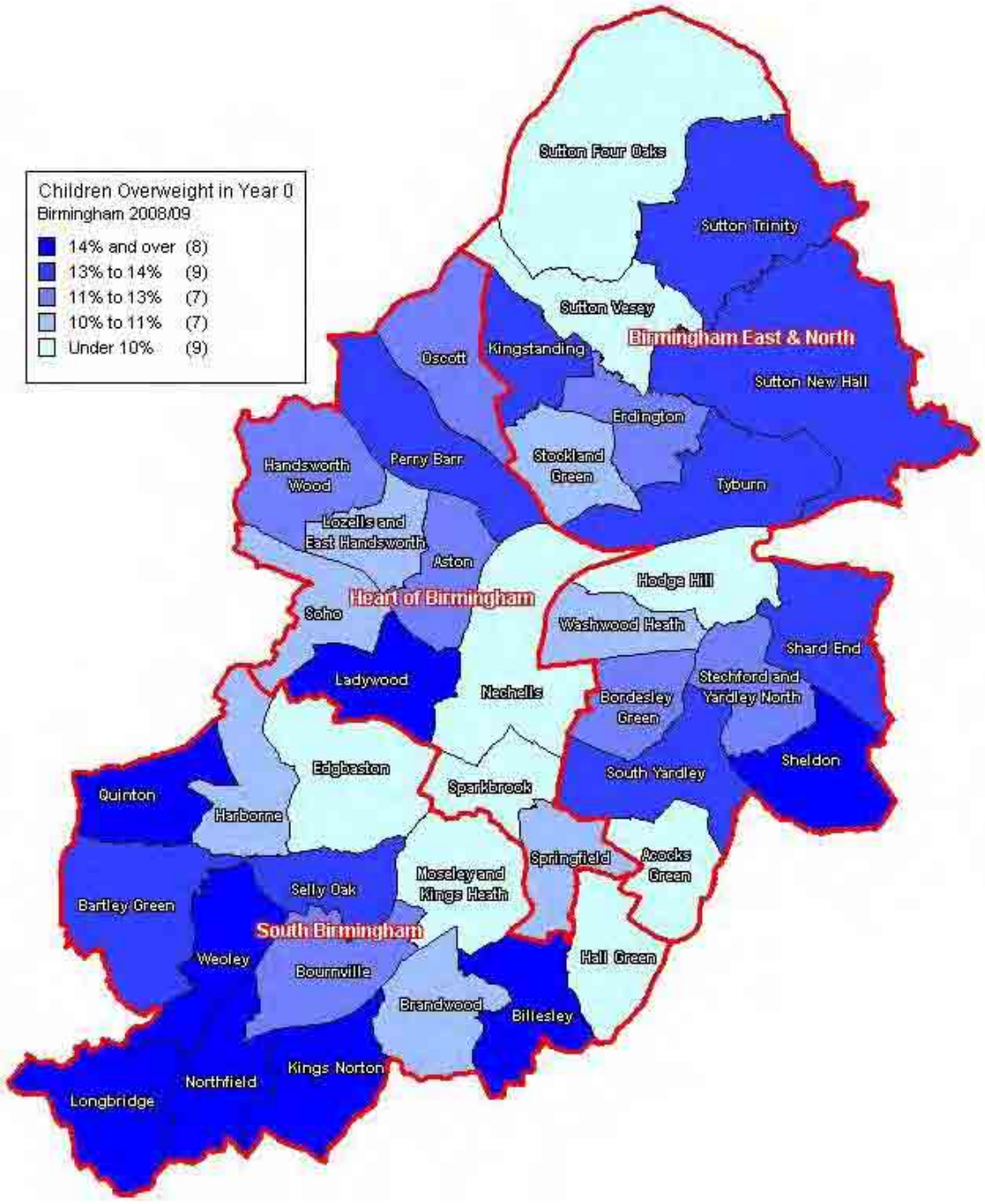

Figure 2.2: A map of the West Midlands showing the proportions of overweight 4-5 year old children by location, 2008-2009.

2.2.1 The Actiheart device

The Actiheart device (Figure 2.3) is a combined heart rate and movement sensor (accelerometer). The device is a compact, chest-worn device that records heart rate (ECG), inter-beat-interval (IBI), and physical activity. The device was configured by the BEACHeS research study team through the manufacturer's software programme for data recording. At the time of configuration, IBI, heart rate, and activity were set to record for later download. The device measures activity and heart rate and can be used for estimating energy expenditure for ambulatory activities. Using a validated system, the Actiheart uses both activity and heart rate data to calculate energy expenditure in children.[191] The combination of activity and heart rate increases the accuracy of energy expenditure measurements over systems that use accelerometry data alone. For the purposes of the analyses in this thesis, the Actiheart was used for estimating physical activity and sleep duration, according the manufacturers software default algorithms. Sleep duration was estimated by the device based mainly on detection of reduced movement.

The Actiheart is designed for use over a number of days. It is water resistant and is compatible with daily activities. Placement of the device to record accurate data is confirmed by a flashing heart rate signal LED. The device weighs less than 8 grams making it easy to wear, particularly in paediatric populations.

Figure 2.3: A picture of an Actiheart device worn by participants in the BEACHeS study.

The Actiheart was attached to the child's chest via ECG gel electrodes. The first ECG electrode was applied in the anterior axillary line (level to the base of the sternum) and the second ECG electrode was applied to the middle of the chest, and the monitor was then attached onto the ECG electrodes.

2.2.2 Sleep and physical activity measures

Sleep duration was estimated using the Actiheart (Cambridge Neurotechnology, UK). Information on sleep duration was also collected through 'parental' report by asking "How long does your child usually sleep each day (hours and minutes)?" The question was asked for weekdays as well as weekends and average sleep duration was calculated using the following equation ([school day sleep duration x 5] + [weekend sleep duration x 2] /7).

Trained members of the research team from the University of Birmingham fitted the device to each child participant according to manufacturer instructions. Participants were provided with an emergency pack which included additional ECG pads to re-fit the device if it became detached. Children were instructed to wear the Actiheart continuously for 5 consecutive days, two days of which covered a weekend period. Data from the Actiheart were downloaded and analysed using

the manufacturer's software. Data regarding the earliest and latest times the child could have gone to sleep and woken the following morning were obtained and the average between these times were calculated for sleep onset and wake onset for each of the nights/days the device was worn by the child. Average sleep duration was then determined for each of the days/nights the device was worn by calculating the difference between the average estimates of sleep onset and wake onset. The majority of the participants wore the device for the first 2 days of recording (84.8%). The average sleep duration across these 2 days was therefore calculated and used for subsequent statistical analyses. Actiheart and 'parent' reported average sleep duration were categorised into <10 hours (short sleep duration) and ≥10 hours ("recommended" sleep duration). The sleep duration categories were decided for this study based on the US National Sleep Foundation's recommendations for sleep duration of at least 10 hours for this age group which are based on expert consensus.[26]

Specific sleep questions from the PedsQL[192] questionnaire were used to determined sleep quality, assessed by asking participants if they had trouble sleeping (not at all, sometimes, a lot). Information on daytime sleepiness was also determined by asking the child if they ever felt too tired to play (not at all, sometimes, a lot).

The Actiheart, previously validated in a paediatric sample for activity and energy expenditure, also provided information regarding physical activity.[191] Activity levels were calculated for each day the device was worn and the manufacturer software derived an average 'counts per minute' of activity.

2.2.3 Adiposity measures

All consenting participants had objective measurements of height and weight obtained and recorded by trained research staff. Height was measured to the nearest 0.1cm using a Leicester portable stadiometer. Body weight was obtained (to the nearest 0.1kg) using regularly calibrated Tanita T6360 scales. Measurements were obtained whilst individuals wore light indoor clothing and were asked to remove shoes and socks or tights. Heights and weights were then used to calculate BMI (kg/m^2). The prevalence of underweight, healthy weight and overweight/obese were calculated using the International Obesity Task Force (IOTF) cutpoints specific to age and gender.[51] IOTF categories were dichotomised so that underweight and healthy weight represented 'non-overweight/obese' and overweight and obese individuals were classified as 'overweight/obese'.

Additional measures of adiposity were also collected. Bioelectrical impedance analysis (BIA) using Tanita T6360 scales was used to estimate body fat percentage (BF%), although this model has not yet been validated against objective measures of BF% such as DXA scanning. Prior to BIA assessment, children were instructed to empty their bladder and removed shoes and socks or tights. Information on the child's age, gender and height (cm) were entered into the device. Children were instructed to stand on the scales and remain still until an estimate of BF% was shown.

Waist circumference (WC) was measured twice using a standard tape measure, which was placed at the half way point between the 10th rib and iliac crest. Both readings were recorded to the nearest 0.5cm. The average of the two values was used for analysis.

2.2.4 Other measures

Information regarding age and gender were obtained from school records for all consented children. Trained staff sat with each child to administer the PedsQL questionnaire by reading out each question, offering all outcome options and then recording the participant's response. Symptoms of depression were obtained by a question from the PedsQL[193] which asked if the child felt sad (not at all, sometimes, a lot). The children were also asked "Do other kids tease you?" (not at all, sometimes, a lot).

A parent questionnaire, developed specifically for the study, was used to determine socio-economic status (SES) and dietary habits of the child. Response rate for the parent questionnaire was 59.2% thus any analysis conducted that used parental reported information reduced the sample size. A proxy for SES was obtained by identifying any wage earner(s) in the household (yes, no). Dietary measures were also collected by 'parental' report, which asked about frequency of eating fruit and vegetables. Response options were at least once a day, 5-6 times per week, 2-4 times per week, once a week or less and responses were then dichotomised combining the first two responses as 'adequate' and the latter two as 'inadequate'. Similarly, frequency of eating crisps and chocolate were obtained and dichotomised ([at least once a day

and 5-6 times per week were classified as 'overconsumption'] and [2-4 times per week and once a week or less were classified as 'acceptable']).

Perception of 'parental' obesity was determined by an adapted figure rating scale for body image,[194] originally developed by Collins.[195] Perception of 'parental' obesity was obtained using a 9 scale visual image (1=extremely thin through to 9=very fat). A median split was obtained and the variable was dichotomised (1-5 = non-obese, 6-9 = overweight/obese).

Full details of the parental questionnaire can be found in Appendix 1. Data collected through this questionnaire were not necessarily completed by a parent. Only 20.7% of the questionnaires were completed by a parent. Others completing the questionnaire included other family members e.g. grandparents (72.1%), aunts or uncles (5.4%), older siblings (0.9%), or cousins (0.9%). For this reason, data collected from the parental questionnaire are in quotes ('parental').

2.2.5 Statistical analysis

All data analyses were performed using the Statistical Package for the Social Sciences (SPSS, version 15.0 Chicago, IL, USA) with the exception of the Bland-Altman plot, which was performed in the statistical software package MedCalc, version 11.6.1.0.

2.2.5.1 The relationship between Actiheart sleep duration and IOTF overweight/obesity

Potential confounders were selected *a priori* according to available scientific evidence (Table 2.1). Logistic regression models were constructed to assess the relationship between sleep duration and overweight/obesity according to international standard cutpoints. Complete data was available for 410 children. The odds ratios (ORs) together with their 95% confidence intervals (CIs) of two models are presented in Table 2.2. In Model 1, age and gender were adjusted. Model 2 further adjusted for daytime sleepiness, symptoms of depression, being teased, physical activity and sleep quality in addition to age and gender (see Table 2.3 for full model). The logistic regression analysis was then repeated further controlling for 'parental' report variables adjusting for SES, 'parental' obesity and consumption of crisps, chocolate, fruit and vegetables, in addition to the variables adjusted for in Model 2. Full information from 'parental' reported variables and Actiheart sleep duration was available for 223 children and details of the logistic regression analyses after further adjustment for 'parental' reported variables are presented in Table 2.4 and Table 2.5 provides ORs and 95% CIs for all potential confounders entered into the models. A linear regression model was also constructed to assess the relationship between Actiheart sleep duration and BMI z-score whilst adjusting for age, gender, being teased, symptoms of depression, trouble sleeping, daytime sleepiness and physical activity.

2.2.5.2 The relationship between 'parental' reported child sleep duration and IOTF overweight/obesity

The analyses described above were repeated replacing Actiheart sleep duration with 'parental' reported sleep duration. Full information on all 'parental' variables of interest was obtained for 215 children (96.4%). Table 2.6 shows the ORs and 95% CIs for univariate, Model 1 (age and gender adjusted) and Model 2 (adjusted for age, gender, daytime sleepiness, symptoms of depression, being teased, physical activity, sleep quality, SES, 'parental' obesity and consumption of crisps, chocolate, fruit and vegetables). Full details of the models including ORs and 95% CIs are shown in Table 2.7.

2.2.5.3 The relationship between Actiheart sleep duration and body fat percentage

Full information was obtained for Actiheart sleep duration and body fat percentage (BF%) in 410 children. Linear regression models were constructed to assess the relationship between sleep duration and BF%. Standardized beta values of two models are presented in Table 2.8. In Model 1, age and gender were adjusted. Model 2 further adjusted for daytime sleepiness, symptoms of depression, being teased, physical activity and sleep quality. Full details of the models including standardized beta coefficients and 95% CIs are shown in Table 2.9. As there was no significant association between Actiheart sleep duration and BF%, the analysis was not further adjusted for 'parental' report variables (SES, 'parental' obesity and consumption of crisps, chocolate, fruit and vegetables).

2.2.5.4 The relationship between Actiheart sleep duration and waist circumference

Full information was obtained for Actiheart sleep duration and waist circumference (WC) in 410 children. Linear regression models were constructed to assess the relationship between sleep duration and WC. Standardized beta coefficient values of two models are presented in Table 2.10. In Model 1, age and gender were adjusted. Model 2 further adjusted for daytime sleepiness, symptoms of depression, being teased, physical activity and sleep quality. Full details of the models including standardized beta coefficients and 95% CIs are shown in Table 2.11. As there was no significant association between Actiheart estimated sleep duration and WC, the analysis was not further adjusted for parental report variables (SES, 'parental' obesity and consumption of crisps, chocolate, fruit and vegetables).

2.2.5.5 The relationship between Actiheart sleep duration and 'parental' reported child sleep duration

Descriptive statistics were used to calculate the mean difference between Actiheart sleep duration and 'parental' reported child sleep duration. The distribution of the data was checked for normality before conducting a Pearson's correlation test to assess the strength of the relationship between Actiheart sleep duration and 'parental' reported child sleep duration. Given that correlation techniques only assess the strength of the linear relationship between the two sleep duration measures but do not indicate agreement, a Bland-Altman plot[196;197] was also conducted

to compare the two sleep measurements showing differences between the two techniques, plotted against the averages of the two measures.

2.3 Results

A total of 493 South Asian children were recruited into the study. Full information on 410 (83.2%) was obtained. Descriptive statistics of the sample by sleep duration category are shown in Table 2.1. Gender and physical activity were significantly related to Actiheart sleep duration categories. Girls were more likely to obtain the recommended sleep duration compared to boys ($p<0.0001$). Short sleepers had significantly higher levels of physical activity compared to those gaining recommended sleep duration ($p=0.003$). Interestingly, there was no significant difference between the two sleep duration categories and IOTF status, BF% or WC. Only 26.6% of the sample obtained the recommended sleep duration and 20.7% were classified as overweight/obese.

Table 2.1: Sample characteristics according to Actiheart sleep duration categories among 410 South Asian children.

Characteristics	Sleep duration		p value
	< 10 hours (n=301)	≥ 10 hours (n=109)	
Gender			<0.001
Male %	58.5	37.6	
Female %	41.5	62.4	
Age (year); mean ± SD	6.49 ± 0.57	6.52 ± 0.60	>0.05
IOTF			>0.05
Non-Obese %	79.7	78.0	
Overweight/Obese %	20.3	22.0	
BF%; mean ± SD	18.2 ± 6.4	19.6 ± 8.3	>0.05
WC (cm); mean ± SD	54.9 ± 7.0	56.1 ± 8.3	>0.05
Physical Activity (counts per minute); mean ± SD	81.8 ± 22.7	74.4 ± 18.8	0.003
Symptoms of depression			>0.05
Not at all %	62.5	55.0	
Sometimes %	28.2	34.9	
A lot %	9.3	10.1	
Being teased			
Not at all %	47.8	52.3	
Sometimes %	30.9	24.8	
A lot %	21.3	22.9	
Daytime sleepiness			>0.05
Not at all %	42.2	45.0	
Sometimes %	40.2	43.1	
A lot %	17.6	11.9	
Trouble sleeping			>0.05
Not at all %	56.8	57.8	
Sometimes %	24.9	28.4	
A lot %	18.3	13.8	

All data are reported as % or mean ± SD, where indicated.
p values were calculated using either chi square analysis or an independent t-test for categorical and continuous variables, respectively.

2.3.1 The relationship between Actiheart sleep duration and IOTF overweight/obesity

Results of the logistic regression analyses are shown in Table 2.2 and details of potential confounders adjusted for can be found in Table 2.3. In the total sample, the fully adjusted model indicated no significant difference of overweight/obesity in short sleepers before or after adjustment.

Table 2.2: The prevalence and odds of IOTF overweight/obesity, according to Actiheart sleep duration in 410 South Asian children.

	Overweight/obesity			
Sleep Duration	**n (%)**	**Univariate**	**Model 1**	**Model 2**
<10 hours	61 (20.3)	0.90 (0.53-1.53)	0.92 (0.53-1.59)	0.99 (0.56-1.72)
≥10 hours	24 (22.0)	1.00	1.00	1.00

Data are odds ratio (95% confidence interval) unless otherwise stated.
Model 1 adjusted for age and gender.
Model 2 additionally adjusted for daytime sleepiness, symptoms of depression, being teased, physical activity and sleep quality.

Table 2.3: The odds ratios and 95% confidence intervals for all potential confounders in each of the models assessed for the relationship between Actiheart sleep duration and overweight/obesity.

Confounder	**Odds ratio (95% CI) Model 1**	**Odds ratio (95% CI) Model 2**
Sleep duration <10 hours	0.92 (0.53-1.59)	0.99 (0.56-1.72)
Age	0.75 (0.49-1.13)	0.69 (0.45-1.07)
Male gender	0.86 (0.53-1.40)	0.86 (0.52-1.42)
Daytime sleepiness (sometimes)	-	0.68 (0.39-1.19)
Daytime sleepiness (a lot)	-	0.70 (0.33-1.48)
Depression (sometimes)	-	1.16 (0.65-2.05)
Depression (a lot)	-	1.61 (0.70-3.73)
Teased (sometimes)	-	0.67 (0.36-1.22)
Teased (a lot)	-	0.99 (0.52-1.89)
Physical activity	-	1.00 (0.99-1.01)
Trouble sleeping (sometimes)	-	1.25 (0.71-2.22)
Trouble sleeping (a lot)	-	0.49 (0.22-1.10)

The Cox and Snell R^2 value for Model 2 (final model) was 0.03.

The main logistic regression analysis was repeated with further adjustment for all 'parental' report variables (n=223), additionally controlling for SES, 'parental' obesity and consumption of crisps, chocolate, fruit and vegetables (Table 2.4). The odds ratios and 95% CIs for all of the potential confounders adjusted for can be found in Table 2.5. The fully adjusted model showed no significant alterations in the risk for IOTF overweight/obesity and short sleep duration.

Table 2.4: The prevalence and odds of IOTF overweight/obesity, according to Actiheart sleep duration in 223 South Asian children with full adjustment of 'parental' reported potential confounders.

		Overweight/obesity		
Sleep Duration	**n (%)**	**Univariate**	**Model 1**	**Model 2**
<10 hours	14 (24.1)	0.70 (0.34-1.44)	0.61 (0.29-1.28)	0.62 (0.28-1.40)
≥10 hours	30 (18.2)	1.00	1.00	1.00

Data are odds ratio (95% confidence interval) unless otherwise stated.
Model 1 adjusted for age and gender.
Model 2 additionally adjusted for daytime sleepiness, symptoms of depression, being teased, physical activity, sleep quality, 'parental' obesity, SES and consumption of crisps, chocolate, fruit and vegetables.

Table 2.5: The odds ratios and 95% confidence intervals for all potential confounders in each of the models assessed for the relationship between Actiheart sleep duration and overweight/obesity including 'parental' reported variables.

Confounder	**Odds ratio (95% CI) Model 1**	**Odds ratio (95% CI) Model 2**
Sleep duration <10 hours	0.61 (0.29-1.28)	0.62 (0.28-1.40)
Age	0.53* (0.29-0.94)	0.47* (0.25-0.89)
Male gender	1.08 (0.55-2.12)	0.99 (0.47-2.09)
Daytime sleepiness (sometimes)	-	0.53 (0.22-1.25)
Daytime sleepiness (a lot)	-	0.73 (0.26-2.01)
Depression (sometimes)	-	0.93 (0.39-2.24)
Depression (a lot)	-	1.29 (0.35-4.74)
Teased (sometimes)	-	0.71 (0.30-1.71)
Teased (a lot)	-	1.28 (0.49-3.33)
Physical activity	-	1.00 (0.98-1.02)
Trouble sleeping (sometimes)	-	1.46 (0.62-3.41)
Trouble sleeping (a lot)	-	0.35 (0.09-1.38)
Parental obesity	-	0.64 (0.27-1.52)
SES (no wage earner)	-	1.40 (0.63-3.13)
Crisps intake (over-consumption)	-	0.45 (0.20-1.05)
Chocolate intake (over-consumption)	-	1.97 (0.84-4.60)
Vegetable intake (inadequate)	-	1.77 (0.81-3.87)
Fruit intake (inadequate)	-	1.41 (0.57-3.45)

The Cox and Snell R^2 value for Model 2 (final model) was 0.10.
*****$p<0.05$.

When BMI-z score and Actiheart estimates of sleep duration (minutes) were entered into a linear regression model, after adjustment for age, sex, trouble sleeping, symptoms of depression, daytime sleepiness, being teased and physical activity, no significant relationship was found $\beta=0.025$, $p>0.05$.

2.3.2 The relationship between 'parental' reported child sleep duration and IOTF overweight/obesity

The relationship between average (weekday and weekend) 'parental' reported sleep duration and IOTF defined overweight/obesity was also examined to determine potential differences between sleep duration estimates and IOTF overweight/obesity. OR's and 95% CI's are shown in Table 2.6. The odds ratios and 95% CIs for all of the potential confounders adjusted for are shown in Table 2.7. 'Parental' reported child sleep duration of <10 hours was not identified as an independent predictor for IOTF overweight/obesity.

Table 2.6: The prevalence and odds of IOTF overweight/obesity, according to 'parental' reported sleep duration in 215 South Asian children.

		Overweight/obesity		
Sleep Duration	**n (%)**	**Univariate**	**Model 1**	**Model 2**
<10 hours	14 (14.1)	0.59 (0.28-1.25)	0.60 (0.28-1.29)	0.63 (0.28-1.41)
≥10 hours	30 (21.9)	1.00	1.00	1.00

Data are odds ratio (95% confidence interval) unless otherwise stated.
Model 1 adjusted for age and gender.
Model 2 additionally adjusted for daytime sleepiness, symptoms of depression, being teased, physical activity, sleep quality, 'parental' obesity, SES and consumption of crisps, chocolate, fruit and vegetables.

Table 2.7: The odds ratios and 95% confidence intervals for all potential confounders in each of the models assessed for the relationship between 'parental' reported sleep duration and IOTF overweight/obesity.

Confounder	Odds ratio (95% CI) Model 1	Odds ratio (95% CI) Model 2
Sleep duration <10 hours	0.60 (0.28-1.29)	0.63 (0.28-1.41)
Age	0.60 (0.34-1.07)	0.56 (0.29-1.05)
Male gender	1.02 (0.51-2.06)	0.97 (0.46-2.07)
Daytime sleepiness (sometimes)	-	0.61 (0.25-1.50)
Daytime sleepiness (a lot)	-	0.73 (0.25-2.15)
Depression (sometimes)	-	1.09 (0.45-2.67)
Depression (a lot)	-	0.99 (0.26-3.87)
Teased (sometimes)	-	0.69 (0.28-1.70)
Teased (a lot)	-	0.98 (0.37-2.61)
Physical activity	-	1.00 (0.98-1.02)
Trouble sleeping (sometimes)	-	1.27 (0.52-3.07)
Trouble sleeping (a lot)	-	0.48 (0.12-1.94)
Parental obesity	-	0.55 (0.22-1.37)
SES (no wage earner)	-	1.44 (0.63-3.29)
Crisps intake (over-consumption)	-	0.48 (0.21-1.11)
Chocolate intake (over-consumption)	-	2.05 (0.86-4.87)
Vegetable intake (inadequate)	-	1.66 (0.76-3.63)
Fruit intake (inadequate)	-	1.47 (0.58-3.74)

The Cox and Snell R^2 value for Model 2 (final model) was 0.08.

2.3.3 The relationship between Actiheart sleep duration and body fat percentage

Results of the linear regression analysis, which examined the association between Actiheart sleep duration and body fat percent (BF%), are reported in Table 2.8. The odds ratios and 95% CIs for all of the potential confounders adjusted for are shown in Table 2.9. No significant relationship was found between BF% and Actiheart sleep duration before or after adjustment.

Table 2.8: Linear regression analyses to assess the relationship between Actiheart sleep duration and body fat percentage, as determined by bioelectrical impedance analysis, in 410 South Asian children.

	Standardized beta coefficient	**t value**	**p value**	**95% lower bound CI**	**95% upper bound CI**
Univariate	0.07	1.29	0.20	-0.26	1.24
Model 1	0.09	1.62	0.11	-0.13	1.37
Model 2	0.08	1.42	0.16	-0.22	1.33

Model 1 adjusted for age and gender.
Model 2 additionally adjusted for daytime sleepiness, symptoms of depression, being teased, physical activity and sleep quality.

Sleep duration was entered into the models as a continuous variable (hours).

Table 2.9: The standardized beta coefficients and 95% confidence intervals for all potential confounders in each of the models assessed for the relationship between Actiheart sleep duration and BF%.

Confounder	**Beta coefficient (95% CI) Model 1**	**Beta coefficient (95% CI) Model 2**
Age	0.08 (-0.24-2.25)	0.09 (-0.17-2.38)
Male gender	0.09 (-0.18-2.73)	0.09 (-0.19-2.77)
Daytime sleepiness	-	0.02 (-0.41-0.62)
Depression	-	-0.13* (-1.25- -0.11)
Teased	-	0.02 (-0.38-0.56)
Physical activity	-	-0.06 (-0.05-0.02)
Trouble sleeping	-	0.04 (-0.31-0.68)

The R^2 value for Model 2 (final model) was 0.04.
* $p<0.05$.

2.3.4 The relationship between Actiheart sleep duration and waist circumference

Results of the linear regression analysis, which examined the association between Actiheart sleep duration and waist circumference (WC) are reported in Table 2.10. The odds ratios and 95% CIs for all of the potential confounders adjusted for are shown in Table 2.11. No significant relationship was found between Actiheart sleep duration and WC before or after adjustment.

Table 2.10: Linear regression analyses to assess the relationship between Actiheart sleep duration and waist circumference in 410 South Asian children.

	Standardized beta coefficient	**t value**	**p value**	**95% lower bound CI**	**95% upper bound CI**
Univariate	0.05	0.94	0.35	-0.40	1.12
Model 1	0.05	0.92	0.36	-0.41	1.13
Model 2	0.03	0.66	0.51	-0.52	1.05

Model 1 adjusted for age and gender.
Model 2 additionally adjusted for daytime sleepiness, symptoms of depression, being teased, physical activity and sleep quality.

Sleep duration was entered into the models as a continuous variable (hours).

Table 2.11: The standardized beta coefficients and 95% confidence intervals for all potential confounders in each of the models assessed for the relationship between Actiheart sleep duration and WC.

Confounder	Beta coefficient (95% CI) Model 1	Beta coefficient (95% CI) Model 2
Age	0.09 (-0.14-2.38)	0.10 (-0.07-2.50)
Male gender	-0.00 (-1.50-1.44)	0.00 (-1.49-1.50)
Daytime sleepiness	-	0.02 (-0.41-0.63)
Depression	-	-0.12* (-1.21- -0.07)
Teased	-	0.03 (-0.33-0.62)
Physical activity	-	-0.07 (-0.06-0.01)
Trouble sleeping	-	0.05 (-0.26-0.73)

The R^2 value for Model 2 (final model) was 0.03.
* $p<0.05$.

2.3.5 Comparisons between Actiheart sleep duration and parental report

The mean Actiheart sleep duration (minutes) for the first two days the device was worn was 569.98 ± 56.98 compared to the mean 'parental' report time (minutes) of 626.88 ± 65.73. Parental reports were over-estimates by an average of 63 minutes. Pearson's correlation revealed a significant positive relationship between objective sleep duration and parental report r=0.17, p=0.012.

The Bland-Altman plot (Figure 2.4) compares the two measures of sleep duration (Actiheart and 'parental' report) when the true values are unknown. The mean of the two measures are plotted on the X axis and the differences between the two measures are plotted on the Y axis. The upper and lower confidence intervals of the difference are calculated to ±1.96 standard deviations from

the mean of the difference and are highlighted in the Figure. Bias in the data is calculated according to the mean of the difference of the two measurements, Y axis (-56.0), demonstrating bias between the two measures of sleep duration. The region of agreement between the two measures ranged from 108.5 to -220.4, as shown in the Figure. The intervals are wide, reflecting great variation of the differences. This is also indicative of an unacceptable level of agreement with a number of data points falling outside of the upper and lower bound limits.

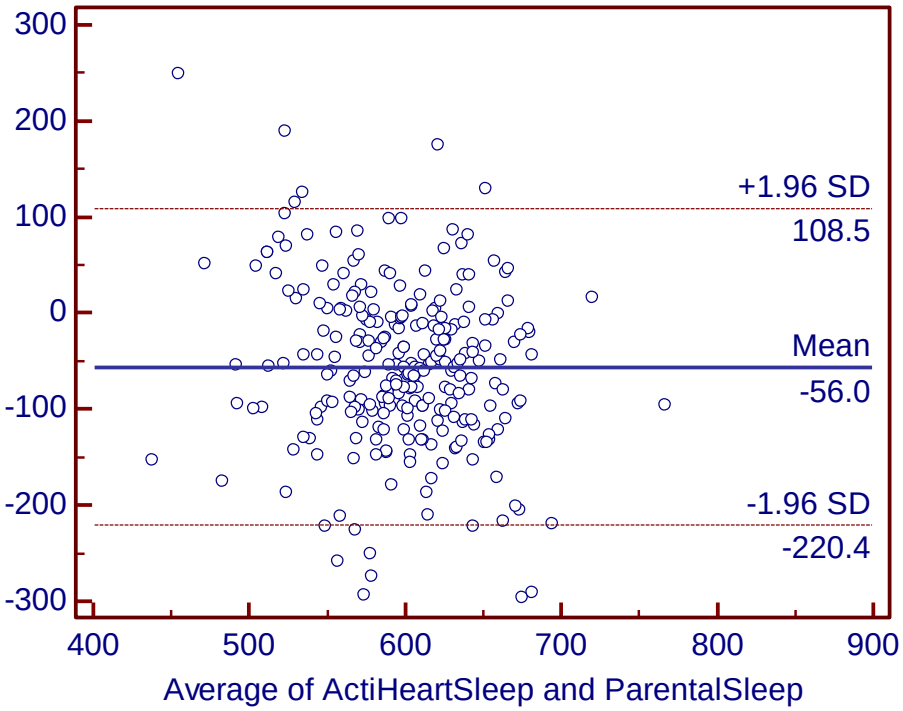

Figure 2.4: A Bland-Altman plot showing the mean values and differences between the two sleep duration measures.

2.4 Discussion

The primary aim of this study was to investigate the association between sleep duration and obesity as well as compare Actiheart sleep duration with 'parent' reported child sleep duration in young South Asian children, residing in the UK. Currently, there are no published data that have examined the sleep-obesity relationship in South Asian children or adolescents residing in the UK. The BEACHeS is the first study to assess the relationship between sleep duration and adiposity in this study population. The data indicate no significant associations between Actiheart sleep duration and three adiposity measures in a large sample of young South Asian UK resident children. Replacement of Actiheart sleep duration with 'parent' reported child sleep duration also showed no significant relationship. The two measures of sleep duration were positively correlated although 'parents' overestimated sleep duration by 63 minutes.

2.4.1 Sleep-obesity studies in South Asian children/adolescents

Currently, the sleep-obesity literature available in South Asian children is restricted to two small studies from India.[74;78] Findings from BEACHeS are opposite to the two studies reported in South Asian children/adolescents, both of which found a negative association between sleep duration and obesity. It should be noted that one study was conducted in a much broader age range (6-16 years old) to the BEACHeS study sample presented.[78] The diverse age range in the

study, which includes children and adolescents, did not provide information on age distribution, making it difficult to compare the younger children in this sample to those recruited into BEACHeS. Kuriyan and colleagues did not use previously validated questionnaires and information collected on sleep duration was not fully specified although sleep information was self-reported. Adolescent sleep duration estimates may be more accurate than parental reports. Self-reported sleep duration for younger children, however, may not be as reliable as parental reports, as acknowledged by the authors.

The sleep categories identified in Kuriyan and colleagues study were divided into ≤8.5, 8.51-9.5 and >9.5 hours and applied across the total sample but as highlighted in *Chapter 1*, children and adolescents have different sleep requirements. Unfortunately, age stratification analysis and application of different sleep duration categories by different age groups were not identified in the study, which would have enabled a clearer comparison of the data with findings from the BEACHeS.

As previously stated, obesity is a direct result of excessive energy intake (food/diet) and reduced energy expenditure (exercise). Studies examining the sleep-obesity association should therefore try to include accurate measures of these two variables. The study by Kuriyan and colleagues obtained self-reported data for these two major factors. The BEACHeS benefitted from Actiheart determined physical activity and attempted to obtain accurate information regarding diet from parents for adjustment of these factors in analysis. Despite objective measures of BMI being determined in Kuriyan's study, just 6.4% of the sample were classified as overweight/obese, using the same age and gender cutpoints as the BEACHeS. Given the authors report a 30%

prevalence rate of overweight in other Indian cities, representativeness of this sample is questionable considering the small number of overweight/obese participants contained in the sample.

Although in a much older age group than the BEACHeS study, the other study from India deserves a brief discussion. This most recent study examining sleep duration and obesity reported a negative association in much older adolescent girls (aged 16-19 years).[74] This study also used self-report information on all variables of interest, except for a number of adiposity measures, objectively obtained. Only one sleep duration question was asked in this study. Participants were asked to calculate sleep duration from time going to bed to the time they woke in the morning. This information only provides information about time in bed and does not take into account activities that may be undertaken whilst in bed. Data from adolescent sleep studies and findings in the next chapter, demonstrate that the time this age group go to bed is not usually the time they go to sleep, with many reporting use of electronic devices in bed before sleeping.[37;198-200] Furthermore, sleep categories used in this study were not justified and seem more suitable for adult comparison rather than adolescents. The study reported <7 hours as inadequate sleep duration and >7 hours the optimal amount. The general consensus for optimal sleep duration in adolescents is around 9 hours.[26,30]

The BEACHeS population sample, although of South Asian descent, were UK residents. The population is more heterogeneous than the population from India. Unfortunately, no data was available regarding the precise South Asian ethnic origin of the children; given the areas where the schools were selected from, it is likely that the there was a mixture of South Asian ethnic

backgrounds. Unfortunately, no sleep-obesity studies in Pakistani/Bangladeshi/other South Asian children were identified for comparison purposes.

2.4.2 Parental sleep reports and its association with obesity

The two studies of South Asians in India and many others that have assessed the sleep-obesity relationship have used self-reported sleep duration. Objective measures are, of course preferable, particularly in children where subjective sleep reports may be inaccurate. Despite Actiheart sleep duration estimates, the BEACHeS findings were not consistent with the majority of paediatric sleep-obesity evidence. In addition to Actiheart sleep estimates, the study also benefitted from parental reports of sleep duration. Previous evidence has shown parental estimates of sleep in young children are highly correlated with objectively determined sleep.[128;129] When the Actiheart sleep data were replaced with parental sleep estimates, results were consistent across the two sleep estimates showing no significant sleep-obesity relationship. Parental sleep estimates, as expected, were overestimated by 63 minutes compared to the Actiheart sleep data, in line with other evidence.[201] Although the two sleep duration measures were significantly correlated, the strength of the association was weak. Furthermore, the Bland-Altman plot showed limited agreement between the two sleep duration measures. Although the Actiheart is a more objective measure of sleep duration compared to parental reports, these measures are not comparable and should not be used interchangeably but should both be validated against polysomnography in future studies. Sleep duration was not an independent risk factor for adiposity, whichever way it was measured in the BEACHeS.

2.4.3 Sleep duration in South Asian children

Short sleep duration in this study was highly prevalent with 74.1% of children sleeping ≤10 hours. Kuriyan and colleagues did not explicitly identify sleep duration by age making age group comparisons difficult. Shaikh and colleagues investigated older South Asian adolescents who have different sleep needs to young children. It is therefore not possible to compare the sleep of South Asian children residing in the UK to those residing in India or other areas as data is limited. Data from other countries, however, can be compared to assess if South Asian children recruited to the BEACHeS are in line with other cultures and ethnicities. A German study of 5 and 6 year old children which classified inadequate sleep duration as ≤10 hours, was present in just 14.5% of the sample.[60] Conversely, a large cohort of 6 and 7 year old Japanese children showed inadequate sleep duration (<10 hours) was prevalent in 94.3% of the sample.[24] Similar prevalence rates for insufficient sleep come from a study in Hong Kong in 6 and 7 year old school children which categorised sleep duration into <9 hours, 9-11 hours and >11 hours. Ninety-one percent reported sleep duration of <11 hours. Other data in 7 year old Australian children showed negatively skewed actigraphy determined sleep duration data.[64] Aside the German study, the data is suggestive of a sleep deprivation problem in paediatric populations but confirmation is needed in other paediatric ethnic groups. The long-term health effects of sleep deprivation in childhood are still being unravelled but in the meantime, good sleep hygiene and consistent bedtime routines for young children may help to minimise short and long term adverse consequences.

2.4.4 Explanation of the findings

The association between Actiheart sleep duration and three adiposity measures (BMI, WC, BF%) was not observed in South Asian UK children. There are a number of potential reasons for this. Firstly, the sample size was relatively small compared to other studies that have examined sleep-obesity in paediatric populations.[24;60;65] Secondly, it is possible that there are ethnic differences for the sleep-obesity association. Potentially, South Asians, who are a high-risk population for obesity and its co-morbidities, may have shorter sleep duration due to a variety of reasons, making it difficult to determine the sleep-obesity association. To assess this in more detail, a comparison of sleep duration with White European children and South Asian children could provide evidence regarding this possibility. Thirdly, absence of the sleep-obesity association in this sample may also, in part, be explained by significantly higher levels of physical activity amongst those with shorter sleep, although this factor was adjusted for in the statistical analyses. This group of young and active but short sleeping South Asian children do not exhibit a cross-sectional sleep-obesity link. Prospective follow up data in these children, however, will help to clarify if persistent short sleep results in later obesity in this ethnic group. Such data may reveal the sleep-obesity link to develop at a later stage in South Asian children. Indeed, this group may be susceptible to the negative effects of reduced sleep duration at different ages or may need greater reductions in sleep duration to exhibit the sleep-obesity relationship.

Culture, tradition, religion and moral values may all be contributory factors for short sleep duration in South Asian children. The majority of the sample (74.1%) did not achieve the recommended amount of sleep for this age group. There are a number of potential explanations

as to why South Asian children may be sleep deprived. Research shows that cultural and religious commitments can result in reduced sleep duration,[202] possibly due to later bed times and early morning wake times. For some South Asian children, daily mosque/temple attendance after school is expected. There may also be early Morning Prayer commitments but there is no scientific evidence to show if these children retire back to bed or remain awake. Sleep may therefore be shortened at both ends of the spectrum (night and morning). South Asians families may also place emphasis on family evening meals. Sitting down for dinner may be delayed until later in the evening when all family members arrive home which may delay the child's bedtime. Academic homework also needs to be completed and bedtime routine may be less structured, particularly if more than two generations reside in the same household, which is common in South Asian families. It is possible that a combination of cultural values, traditional moral and religious aspects may explain shorter sleep duration observed in this sample of young South Asian children. It is possible that sleep needs are different in South Asians or that they become accustomed to the cultural and religious command and adapt to sleep deprivation better than other ethnicities but further investigation is required for confirmation. It is also possible that reduced sleep duration in South Asian children may be a result of environmental change and/or stress if recently immigrated to the UK. Although we did not obtain this data, it is likely that the studied sample were born in the UK due to the growing South Asian communities in the West Midlands over previous decades. Future research should, however, examine longitudinal sleep parameter alterations in immigrants. It is possible that no association was found between short sleep duration and overweight/obesity in this sample due to the ethnic background of the children.

The cutpoints of sleep duration applied in the BEACHeS were based on a large US National Sleep Foundation where the recommended sleep duration, based on consensus, was proposed to be at least 10 hours for this age group.[26] It is unknown if this sleep consensus is biologically or culturally driven. It is, of course, possible that cultural demands challenge the biological needs of sleep, which may in turn adapt to cultural and lifestyle choices in specific ethnic groups but further investigation is needed for confirmation.

Interestingly, of all potential confounders considered in the analysis, based on prior scientific evidence, none were significantly related to the relationship examined. The parent questionnaire was produced in English, which may have created language barriers, misinterpretation of questions and inaccurate and unreliable responses. Furthermore, the majority of parental questionnaires were completed by grandparents where English is unlikely to be their main/first language. Responses from the third generation may also be subject to increased inaccuracies compared to parental reports. Future work in these populations where the parent's first language may not be English should produce questionnaires in alternative languages, which may encourage higher return rates and more reliable responses.

2.4.5 Strengths and limitations

The BEACHeS benefits from a unique and less-studied sample and has provided useful insights into ethnic differences in relation to the sleep-obesity link. Unlike previous studies, the

BEACHeS also benefits from Actiheart sleep duration and objective measures of physical activity, which is a major factor for obesity, one which data has not been obtained or adjusted for in previous sleep-obesity paediatric studies. There are, however, several potential limitations to the BEACHeS. The mean sleep duration was calculated from the first two days of recording because the majority complied with the device for this time period enabling optimal sample size for analysis. The Actihearts, however, were issued to children on different weekdays (Tuesday, Thursday or Friday) and so it is difficult to determine if the two days of Actiheart data correspond with two weekdays, weekends or a combination of both. Sleep duration has been shown to differ during weekdays compared to weekends,[29;203] which may, in part, explain the lack of sleep-obesity association in the studied sample. Actigraphy is often used as an objective estimate of sleep duration since this method has been validated against polysomnography (PSG).[204] Although Actihearts have been validated for physical activity and energy expenditure, the device has not yet been validated against polysomnography for sleep. This may explain the absence of association between short sleep duration and overweight or obesity in this sample, although 'parental' sleep estimates were not related to adiposity either. Examination of the raw Actiheart sleep data showed that some children were awake as early as 03:00. It is possible that if a child woke and got out of bed, perhaps to use the toilet or due to sleep disturbance, that the device then reported this as the wake time without reporting any further sleep durations if the child then went back to sleep. Although these extreme data were excluded in the analysis, it is possible that some participants may have obtained more sleep than the device actually recorded which would affect the relationship examined.

Technology use in young children is becoming more prevalent and access to media devices may be easily accessible to this age group. Research shows that screen time is an independent predictor for obesity development and can also have major impacts on sleep.[73] Unfortunately, the BEACHeS study did not obtain screen time data and so this factor was not adjusted for in the analyses. Finally, the only data in the sleep-obesity field originates from children residing in India and not other South Asian countries such as Pakistan, Bangladesh, Bhutan, Nepal or Sri Lanka. Limited data makes it is difficult to draw representative sleep-obesity conclusions in South Asian populations.

2.5 Conclusions

In summary, the data suggest no association between short sleep duration and three adiposity measures in South Asian UK resident children. The BEACHeS is the first study to examine the sleep-obesity association in this ethnic-specific population. The observation, however, is inconsistent with other paediatric sleep-obesity studies. Although the majority of the sample did not obtain recommended sleep amounts, South Asian UK resident children may exhibit the short sleep-obesity association at a later stage or not at all but prospective data is needed to determine this relationship. Short sleep duration in young South Asian children may be due to different lifestyle behaviours, culture, traditional values or religious commitments. The present findings highlight potential ethnic differences in the relation between sleep and adiposity in a group that has not been previously examined. Future studies should make longitudinal sleep-obesity assessments in various ethnic groups and immigrant populations through use of objective sleep, adiposity, physical activity and dietary measures.

3 SLEEP DURATION AND OBESITY IN ADOLESCENTS

3.1 Background

The importance of sleep for healthy development is increasingly appreciated, but sleep loss and daytime sleepiness appears to be a widespread problem in adolescents.[39;205] As identified in *Chapter 1*, at least nine hours of sleep is recommended for this age group[33] but evidence consistently reveals that many adolescents are not obtaining optimal amounts.[27] Sleep loss in adolescents has been linked with a number of adverse consequences including reduced cognitive function,[206] depression,[207] and suicidal behaviour.[208] It has been also been suggested that sleep deprived adolescents are more likely to engage in risky behaviours.[209] It is therefore essential to better understand why sleep is compromised in adolescence.

A number of reasons for reduced sleep duration in adolescence are postulated. The transition from junior to secondary school places additional academic demands, potentially resulting in increased stress levels. Adolescence is commonly associated with a delayed circadian phase, resulting in a biological need for later bedtimes and waketimes,[210] in conflict with early school start times. The disparity between biological delayed phase and early school attendance has been previously related to sleep deprivation.[27] Delays in circadian phase enhances evening leisure time. There are numerous opportunities to utilise this time including: television (TV) viewing, digital video disc (DVD) viewing, mobile telephone use, Internet surfing, social networking, and video gaming, along with other social activities.[211] Furthermore, parents are less likely to enforce bedtimes as their child develops,[30] allowing greater independence.

Research in this age group has demonstrated not only consistent links between short sleep duration and obesity, but also with lower academic performance, and increased media device use. A review of the data surrounding sleep and obesity in children and adolescents is detailed in *Chapter 1*. A search of the literature has been performed for the purposes of the present chapter to identify and review studies, which have examined the association between:

1. Sleep and technology use;

2. Sleep and academic performance.

3.1.1 The associations between sleep and technology use and academic performance: methods and procedures for literature search/review

A search of the literature was conducted using the PubMed database using related keywords for manuscripts published in the area of sleep and technology use up to and including September 2010. The following searches were conducted for sleep and technology use:

- Sleep AND technology
- Sleep AND Internet
- Sleep AND mobile telephone*
- Sleep AND video gam*
- Sleep AND computer
- Sleep AND television

Articles were also sourced using the "related article" option in PubMed as well as through one published existing literature review.[212] Articles were included if they were written in English, the study population was aged between 10-19 years, and full access to the manuscript was obtained. A total of 30 articles were identified of which 23 were cross-sectional, 4 longitudinal and 3 experimental (see Tables 3.1, 3.2 and 3.3, respectively). Negative associations between sleep measures and at least one type of technology were reported in 28 of the 30 articles.

A further search of the available literature was conducted using the PubMed database using related keywords for manuscripts published in the area of sleep and academic performance up to and including September 2010. The following searches were conducted for sleep and school performance in adolescents:

- Sleep duration AND school performance
- Sleep duration AND school achievement
- Sleep duration AND school attainment
- Sleep duration AND academic performance
- Sleep duration AND academic achievement
- Sleep duration AND academic attainment

Articles were also sourced using the "related article" option in PubMed as well as through existing reviews. Articles were included if they were written in English, and full access to the manuscript was obtained. A total of 10 articles were identified, of which 8 were cross-sectional and 2 longitudinal, detailed in Tables 3.4 and 3.5, respectively.

3.1.2 Sleep and obesity in adolescents

Many large population studies have reported associations between short sleep duration and obesity in children and adults as highlighted in *Chapter 1*. Data in adolescents, however, is much more limited and inconsistent, with some exploring the association in relatively small samples[66;68;70;74;213] and others reporting no association.[92] Notably, some studies include a combination of children and adolescents.[78-80] This is problematic when making assessments by sleep categories given the inverse relationship between sleep duration and age, meaning different age groups have different sleep needs.[214;215] There are some larger sleep-obesity studies, specific to the adolescent age range.[67;69;72;73;75;76;216] Geographically, these data cover North and South America, Japan, Spain, Taiwan and Norway but there are no published data in the UK, where rates of overweight and obesity are rising.[217] The data available are reasonably consistent with most reporting negative associations. There are however, some who note gender differences;[67;216] the Norwegian study reported a U-shaped association, more commonly observed in adults;[76] and no association was found between short sleep duration and obesity in Calamaro's large (n=13,568) prospective study.[92] A review stated that the negative linear relationship consistently found in children was only constant until the age of 10 years.[132] Thus, more detailed investigations are necessary in adolescents, particularly contemporary UK adolescents who frequently use electronic devices, a behaviour which could exacerbate the sleep-obesity relationship.

3.1.3 Sleep and technology use in adolescents

Most sleep-obesity adolescent studies have collected limited data on the use of technology, which is surprising given that technology use is highly prevalent and readily accessible to the majority of contemporary adolescents. It is well documented that media devices are not only independent risk factors for obesity[218-220] but also have profound effects on sleep parameters.[212;221] Recent statistics published by OfCom, an independent regulator for the UK communications industries, revealed that individuals spend half of their waking day using a combination of technologies.[222] In line with this, data from the US National Sleep Foundation's 2006 'Sleep in America Poll', reported that 97% of American adolescents had at least one media device in their bedroom.[36] The 2011 poll suggested that technology use before bedtime may be associated with prolonged sleep onset latency and sleep disturbance.[37] The survey also found that adolescents with four or more devices in their bedroom obtained significantly less sleep on weekdays as well as weekends compared to those with less than four devices. Data of this type is, however, lacking in the UK, warranting further study. As adolescents face the circadian phase delay and their biological clock demands greater evening waking time, device use may serve as an attractive diversion and compromise sleep onset with subsequent sleep loss.[211] It is vital to better understand the potential effects of multiple technologies upon adolescent sleep. Furthermore, specific technologies may impact differently on sleep duration but data in this area is sparse. Table 3.1 provides cross-sectional evidence concerning sleep and media use. Table 3.2 provides longitudinal evidence and Table 3.3 highlights the experimental data.

Table 3.1: Cross-sectional studies examining the relationship between sleep and technology use.

First authors name, year	Sample size	Country	Age (years)	Technology	Sleep measure	Relationship
Tynjala, 1993 [223]	40,202	Europe (11 countries)	11-16	Self-report TV	Self-report	Excessive TV/DVD was associated with going to bed later and more difficulty falling to sleep
Nalwa, 2003 [224]	100	India	16-18	Self-report Internet	Self-report	Prolonged Internet use was associated with sleep loss
Van den Bulck, 2003 [225]	2,546	Belgium	13.16 (mean)	Self-report MT use	Self-report	Mobiles attributed to increased sleep disturbances
Van den Bulck, 2004 [226]	2,546	Belgium	12-17	Self-report TV, VG, Internet	Self-report	Presence of TV, Internet and video console associated with later bed times (weekday and weekend) and later rise times (weekends). Less TIB with TV and gaming console in bedroom
Gaina, 2005 [227]	643	Japan	12-15	Self-report TV, MT and VG	Self-report questionnaire	No significant differences found between SOL and media use
Alexandru, 2006 [228]	9,199	Japan	12.8 (mean)	Self-report TV and VG	Self-report	Long durations of TV and video gaming play were associated with prolonged SOL
Eggermont, 2006 [229]	2,546	Belgium	12-17	Self-report TV, VG	Self-report	Negative association between sleeping hours, tiredness, time to bed and TV, VGs and music
Olds, 2006 [230]	1,039	Australia	10-13	24-hr recall of TV, VG, PC and cinema	Self-report	Boys used media more than girls. Screen time was negatively associated with sleep duration
Chen, 2006 [68]	656	Taiwan	13-18	Self-report TV and PC	Self-report	No association between TV or PC use and sleep duration

TV=television; PC=personal computer; MT=mobile telephone; VG=video games; TIB=time in bed; SOL=sleep onset latency.

Table 3.1 cont'd

First authors name, year	Sample size	Country	Age (years)	Technology	Sleep measure	Relationship
Mesquita, 2007 [231]	160	Brazil	15-18	Self-report PC	Self-report (PSQI)	Nocturnal PC use impaired sleep quality
Gaina, 2007 [232]	9,261	Japan	12.8 (mean)	Self-report TV and VG	Self-report	Dose-response between sleepiness and media use time
Punamaki, 2007 [233]	7,292	Finland	12-18	Self-report Internet, MT	Self-report	Video gaming in boys and mobile use in girls were associated with reduced sleep and increased tiredness
Yen, 2008 [234]	8,004	Taiwan	12-18	Self-report Internet and MT	Self-report	Internet use was associated with reduced sleep duration
Soderqvist, 2008 [235]	1,269	Sweden	15-19	Self-report MT, TV.	Self-report	Increased mobile telephone use was associated with increased levels of tiredness. No significant association between MT use and sleep disturbance
Calamaro, 2009 [130]	100	USA	12-18	Self-report TV, MT, PC	Self-report	Negative association
Knutson, 2009 [236]	3,108	USA	15-17	Time diary for PC (self-report)	Time diary (self-report)	PC use was predictive of later bed time
Choi, 2009 [237]	2,336	Korea	16.7 (mean)	Self-report Internet	Self-report	Negative association between Internet use and sleep duration
Yang, 2010 [238]	11,111	Taiwan	15 (median)	Self-report MT	Self-report	Younger girls (<15 yrs) and all boys with problematic CPU was associated with shorter sleep duration
Rehbein, 2010 [239]	10,060	Germany	15.3 (mean)	Self-report VG	Self-report at interview	VGD associated with reduced sleep duration and increased sleep disturbance

TV=television; PC=personal computer; MT=mobile telephone; VG=video games; CPU=cellular phone use; VGD=video game dependency; PSQI=Pittsburgh sleep quality index.

Table 3.1 cont'd

First authors name, year	Sample size	Country	Age (years)	Technology	Sleep measure	Relationship
Qidwai, 2010 [200]	401	Pakistan	12-18	Self-report TV	Self-report	TV and music were related to shorter sleeping hours
Ortega, 2010 [240]	2,179	Spain	13-18	Self-report TV	Self-report	Short sleep associated with excessive TV viewing in boys. Excessive TV viewing associated with morning tiredness in males and females
Shochat, 2010 [241]	470	Israel	14 (mean)	Self-report TV, PC	Self-report	Those with TV in bedroom had later bed times, longer SOL and shorter sleep duration

TV=television; PC=personal computer; SOL=sleep onset latency.

Table 3.2: Longitudinal studies examining the relationship between sleep and technology use.

First authors name, year	Sample size	Country	Age (years) at BL	Age (years) at FU	Technology	Sleep measure	Relationship
Johnson, 2004 [242]	759	USA	13-17	16 & 22	TV by interview. Separate interview with mother and then with child	Self-report by interview	Longer duration of TV viewing in adolescence had increased sleep problems in early adulthood
Fuligni, 2006 [243]	750	USA	14-15	14-15 (2 week FU)	Self-report TV, PC	Self-report diary	PC use was negatively associated with sleep duration
Van den Bulck, 2007 [244]	1,656	Belgium	13.7 and 16.9 (mean)	1 year	Self-report MT use	Self-report tiredness	Negative association between frequency of MT use and tiredness
Wells, 2008 [72]	4,452	Brazil	Birth (no TV data collected at birth)	10-12	Self-report TV	Self-report	Negative association

TV=television; PC=personal computer; MT=mobile telephone.

Table 3.3: Experimental studies examining the relationship between sleep and technology use.

First authors name, year	Sample size	Country	Age (years)	Technology	Sleep measure	Relationship
Dworak, 2007 [245]	10 (males)	Germany	13.45 (mean)	Objective TV/DVD and VG	PSG	Sleep efficiency decreased after TV viewing. Increased SOL after video gaming
Ivarsson, 2009 [246]	19 (males)	Sweden	12-15	TV/VG by instruction – violent vs non-violent vs no play	Self-report via questionnaire	Later bed times in experimental vs control. Non-violent game participants reported falling to sleep easier and had earlier out of bed times the following morning
Weaver, 2010 [198]	13	Australia	14-18	Observation of stimulating VG vs calm DVD for 50 minutes	PSG	Video game playing was associated with increased sleep onset latency and reduced subjective sleepiness.

TV=television; VG=video games; DVD=digital video disc; SOL=sleep onset latency; PSG=polysomnography.

3.1.3.1 Sleep and television viewing

Television (TV) broadcast became available in the UK during the 1930's.[247] Since then, TV sets have progressed from black and white images to colour; from small screens to large cinema-like screens; from box-shaped to flat screens; from a few hours of daily broadcast to 24-hour availability; from 2 dimensions to 3 dimensions; and from a limited number of channels to hundreds, now in high definition. Today, large wide-screen TVs are increasingly prevalent and affordable with many homes now possessing multiple sets.[248] Research into the impact of TV on paediatric sleep emerged almost three decades ago.

Early research reported no association between TV viewing and sleep duration in children.[249] More recently, adolescent studies directly examining the relationship between sleep duration and TV viewing have produced conflicting results although evidence weighs towards a negative relationship between TV viewing and sleep duration. A 2-week longitudinal study utilising a daily checklist reported no relationship between sleep duration and TV viewing although the study only examined the self-reported data through correlation analyses rather than more sophisticated statistical techniques.[243] Similarly, a Taiwanese study reported no association between TV viewing and inadequate sleep duration, which was defined as 6-8 hours per night for four or more nights per week.[68] Conversely, a study of Belgian adolescents reported that those who watched TV to serve as a sleep aid, actually had later bedtimes and thus fewer sleeping hours compared to those who did not.[229] A study of young Australian adolescents found an inverse relationship between sleep duration and screen time, of which TV was included.[230] Data from Pakistan, Spain, USA and Israel has also provided consistent evidence for a negative

association between TV viewing and sleep duration.[200;202;240;241] A further Belgian study, conducted in a large sample of adolescents (n=2,546), found TV viewing was associated with less time in bed (TIB) on weekdays and delayed weekday and weekend bedtimes,[226] later wake up or out of bed times, increased sleep onset latency (SOL) and reduced sleep duration, all of which are consistent with other evidence.[130;200;223;228-230;232;240;241;250] Despite early studies purporting no link between sleep duration and TV viewing, recent research has provided further insight and consistently suggests a link between TV and numerous sleep parameters.

Some studies have not directly examined the relationship between TV viewing and sleep duration but have investigated a number of other sleep parameters including time in bed (TIB),[226] sleep onset latency (SOL),[227;242] wake after sleep onset (WASO),[242] sleep disturbance/quality,[242] daytime sleepiness,[226;232] morning sleepiness,[240] bedtimes and/or wake times.[241] All of these sleep parameters are directly linked to and influence overall sleep duration. These studies are therefore important for determining more detailed information about the impact TV has upon sleep. It is still unclear, however, which aspects of TV relate to sleep. For example, the frequency, duration, content, light brightness, volume, and timing of viewing may all be important considerations when examining the impact of TV on sleep. Experimental evidence is lacking but the limited available literature has provided some useful insight. One small study (n=10) subjected male adolescents to a stimulating film 2-3 hours before bedtime and monitored sleep parameters by polysomnography. During the control evening, volunteers did not watch any TV at all. The results revealed participants had significantly reduced sleep efficiency on the experimental night compared to the control. The authors, however, noted no effects on other sleep variables including TST (the actual amount of time spent asleep), WASO (the time spent

awake from sleep onset to final awakening) and SOL (the amount of time it takes to fall to sleep).[245] A longitudinal study found that more frequent TV viewing during adolescence preceded sleep problems in early adulthood. Interestingly, if TV viewing was reduced to less than an hour a day during adolescence then the risk of sleep problems were significantly reduced.[242] It should, however, be noted that this was based on subjective reports which may produce bias.

3.1.3.2 Sleep and video gaming

In today's world, TVs have multiple uses from viewing broadcasted programmes, films from DVD player and box office (Sky/cable/Freeview), viewing photographs and playing video games (VG) through connected consoles. VG were first released in the 1970s and their popularity has since rapidly grown and is now a multi-billion pound industry.

Surprisingly, there is limited data concerning the relationship between sleep duration and VG, despite the recent rise in popularity, numerous consoles (Xbox, Playstation, Nintendo Wii) and portable devices (Playstation Portable, Nintendo DS range) to choose from. The literature search identified 10 studies: 7 cross-sectional, and 3 experimental. Two large (n=2,546) Belgian studies of adolescents found a negative link between VG and various sleep parameters. One found VG to be associated with less time in bed, later bed times (weekdays and weekends), later rise times (weekend) as well as increased tiredness.[226] The other Belgian study found similar results with VG being linked with later bed times and shorter weekday sleep duration. A large national German survey showed video game dependency (VGD) to be more prevalent in boys than girls,

3% and 0.3%, respectively. The study found that boys classified as 'video game-dependent', determined by one question on a 6-point likert scale, experienced increased levels of sleep disturbance compared to those who were non-dependent.[239] In line with these gender differences, Gaina *et al* also found that increased duration of VG was related to increased sleepiness in adolescent boys but not girls.[232] Another Japanese study reported similar findings identifying a dose-dependent relationship between increased VG and prolonged sleep onset latency.[228] Similarly, an Australian study found an inverse relationship between sleep duration and screen-time, of which VG was included.[230]

Detailed experimental evidence is sparse and data available, thus far, are inconsistent. In the first study, sleep architecture was studied using polysomnography in 10 adolescent boys subjected to 3 randomised conditions: 1-hour of VG, an exciting film, a control evening with no screen time. The VG condition resulted in significantly reduced slow wave sleep (SWS), prolonged sleep onset latency (SOL) and increased N2 sleep, compared to the control evening.[245] Weaver and colleagues also reported prolonged SOL in 13 adolescent boys, using a similar study design but found no significant differences in sleep architecture.[198] A further, less detailed study, made assessments on VG and heart rate variability (HRV) in 19 boys who engaged in violent, non-violent and no gaming conditions. The study investigated differences between the 3 conditions and a number of self-reported sleep variables. Although significant differences were found between conditions for HRV, no significant differences were reported between conditions for subjective sleep difficulties.[246]

3.1.3.3 Sleep and mobile telephone use

The first handheld mobile telephone (MT) was developed in 1973. The Japanese then launched the first commercially automated cellular network in 1979. Subsequently, the technology then rapidly cascaded into many countries. When MTs were first introduced, they were originally used to make and receive calls. Now, devices have multiple purposes, used to send and receive text messages; access the Internet; play games; store and listen to music; take, store and view photographs; set alarms, reminders and/or diary dates; download a diverse range of applications; and navigate street maps. With the rapid advance of MT technology during the last three decades, national statistics on MT ownership have paralleled this rise. Growth in MT ownership increased from 65% in 2001/2 to 81% in 2009.[251] In 2006, it was reported that 4 in every 5 children own a mobile telephone by age 11.[252] Consistent with these data are the findings of Calamaro *et al* which revealed 90% MT ownership in 12-18 year olds.[130] Not only are MTs accessible, prevalent and highly utilised by adolescents, technology within them is now multi-faceted making investigation of this device essential, particularly in adolescents.

A review of the data surrounding sleep specific to MT identified 6 cross-sectional studies and 1 longitudinal. Of the 6 cross-sectional studies, the Japanese and Taiwanese studies showed no significant associations between MT and sleep onset latency (SOL)[227] or sleep duration,[234] respectively. A larger Taiwanese study of 11,111 adolescents identified short sleep duration as <6 hours through a previously validated insomnia questionnaire. A further questionnaire was administered to determine problematic MT use, which included items to identify tolerance, withdrawal and excessive use of MTs ('problematic' MT use). They found that girls were more

likely to have problematic MT use, particularly girls younger than 15 years, compared to boys. Problematic MT use was significantly associated with insomnia scores in younger and older adolescents in both boys and girls.[238] Findings from a large sample of Finnish 12-18 year olds (n=7,292) also showed that girls with regular MT use had lower sleeping hours and increased tiredness.[233] Further support came from a Swedish study which also reported MT use was more prevalent in girls (15-19 years) and that frequent use was significantly associated with tiredness.[235]

MT use is not limited to making and receiving calls but has other facilities. The first to specifically examine MT use and the effect of text messaging after lights out upon sleep disturbance produced interesting findings. Adolescents who experienced more frequent awakenings by text messages reported being significantly more tired compared to those never woken.[225] A 1-year follow up showed increased MT use was dose-dependently associated with increased tiredness. The study also showed that those using their MT between the hours of 00:00-03:00 experienced the highest levels of tiredness.[244]

3.1.3.4 Sleep and computer/Internet use

Personal computers (PC) were first introduced to the public domain in the 1970s and in subsequent years, laptops and the Internet became available. Internet surfing is now a worldwide phenomenon and popularity has surged in recent years. Accessing the Internet on a daily basis has almost doubled from 2006 to 2010 (Figure 3.1).[253]

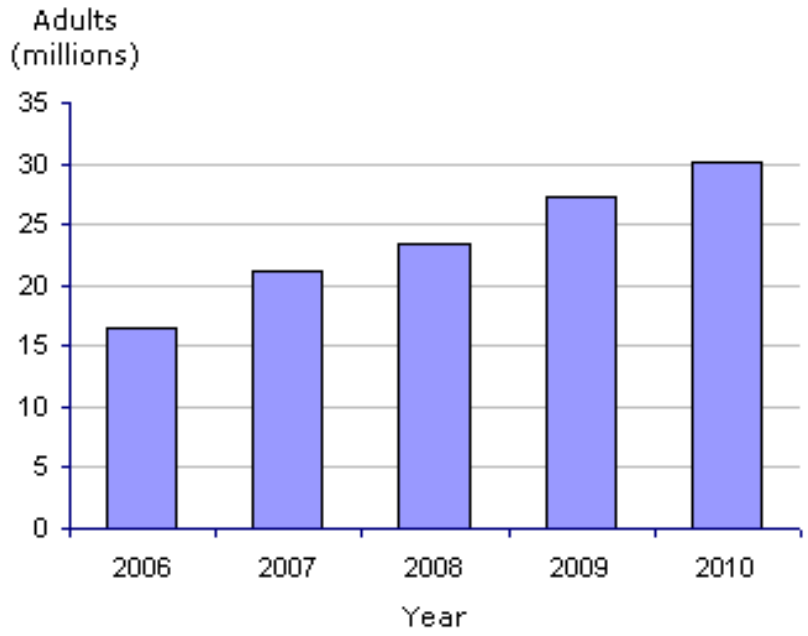

Figure 3.1: The number of UK adults accessing the Internet on a daily basis.[253]

Data from the Office for National Statistics (UK) shows that Internet usage has increased year on year between the period 2006-2010.

The UK's Office for National Statistics showed that Internet use was linked to various socio-economic and demographic factors such as age, location, marital status and education.[253] The same survey also reported 60% of individuals aged ≥65 years had never accessed the Internet, compared with just 1% of 16-24 year olds.[253] Furthermore, 97% of adults educated to degree level had accessed the Internet compared to just 45% without any formal qualifications.[253] Social networking became popular in 2010, with 43% of Internet users posting messages to social networking sites, chat sites or blogs.[253] Social networking activities were more popular among the 16-24 years age range with 75% posting messages.[253] In 2010, 73% of UK households had Internet connection.[253] Internet use is highly prevalent in adolescents and is now part of daily

life. The effect of PCs and/or Internet on adolescent sleep has been previously studied but not extensively. The literature search identified 10 cross-sectional studies and 1 longitudinal study.

The only study to find no association between PC use and sleep duration came from Taiwan.[68] The sample was relatively small (n=656) and defined adequate sleep duration as 6-8 hours in 13-18 year olds, a sleep category that is more widely applied to adult populations. Conversely, findings from large population studies in Australia,[230] Finland,[233] Taiwan,[234] and Israel[221] have produced consistent findings linking frequent PC/Internet use to sleep loss in adolescents. Associations between PC/Internet use and other sleep parameters have also been reported. For example, Van den Bulck found that adolescents who spent more time using the Internet had significantly later bedtimes on weekday and weekends. She also revealed later wake times at weekends, less time in bed during the week and increased tiredness.[226] Data from two US national probability samples compared data from one sample in 1981 to data from another adolescent sample in 2003-2006 produced similar findings. PC use was strongly associated with bedtimes which were delayed by 15 minutes for every additional hour spent using the PC.[236]

The effect of excessive Internet/PC use has also been studied in relation to sleep. A study in India administered a semi-structured interview to obtain qualitative data concerning Internet addiction and dependency. The findings demonstrated Internet dependent users experienced more sleep loss due to late night use compared to non-dependent users.[224] Similarly, a large Korean study reported a higher prevalence of sleep problems including insomnia related parameters, snoring, apnoea, bruxism and nightmares in Internet addicts compared to non-

addicts, determined by questionnaire. Furthermore, addicts reported significantly increased levels of excessive daytime sleepiness.[237]

The only longitudinal study to examine the impact of PC use upon sleep duration was conducted in the US. Seven hundred and fifty 14-15 year olds were provided with a daily checklist to complete over a 14-day period. Surprisingly, the authors found duration of TV viewing to be unrelated to sleep duration but PC use was significantly associated with reduced sleep time.[243]

3.1.4 Sleep and academic performance in adolescents

Sleep is vital for healthy development, learning and memory and has therefore been linked to academic performance.[254;255] Preference for 'eveningness' commonly results in shortened sleep duration for adolescents who typically have later bedtimes and forced to wake early for school attendance.[27] Subsequently, a typical adolescent has reduced time in bed which, in turn, decreases sleep duration.

Many extrinsic factors are believed to be associated with reduced sleep duration in adolescents. These include increased academic workload, greater autonomy, social and peer pressure, part-time employment, extra-curricular activities, increased use of technology and less parental control. These, combined with intrinsic factors, such as puberty and the substantial body of evidence suggestive of physiological delayed sleep phase,[256-258] may all contribute to reduced sleep duration during adolescence, which may, in turn, impact on academic performance.

Table 3.4: Cross-sectional studies assessing the relationship between sleep and academic performance.

First author, year	Sample size	Country	Age (years)	Performance measure	Sleep measure	Relationship
Wolfson, 1998 [207]	3,120	USA	13-19	Self-report	Self-report	More TST and earlier bed times associated with higher grades
Eliasson, 2002 [259]	1,200	USA	14.5 (mean)	Self-report GPA	Self-report	No correlation between sleep time and academic performance
Drake, 2003 [260]	450	USA	11-15	Self-report	Self-report PDSS	Low school achievement and low TST reported significantly higher levels of daytime sleepiness compared to children with better school related outcomes
Meijer, 2004 [261]	153	Netherlands	10-13	Self-report	Self-report	Less chronic sleep reduction was associated with better school performance
Lazaratou, 2005 [262]	658	Greece	16.5 (mean)	Self-report	Self-report AIS	Students with lower academic performance were more likely to have higher insomnia scores
Chung, 2008 [203]	1,629	Hong Kong	12-19	Self-report	Self-report	Students with marginal academic performance reported later bedtimes and shorter sleep during school nights, greater weekend delays in bedtime, and more daytime sleepiness than those with better grades
Ng, 2009 [263]	59	Hong Kong	Year 11	Self-report SSHS	Self-report SSHS	Maths performance positively correlated with sleep duration. Excessive sleepiness on rising identified as significant risk factor for poor performance in English and Maths. Sleepiness during the 3rd and 4th lessons identified as significant risk factor for poor performance in Maths
Noland, 2009 [264]	384	USA	9-12th	Self-report	Self-report	60.8% reported not gaining enough sleep which was associated with lower school grades

TST=total sleep time; GPA=grade point average; SSHS=schools sleep habits survey; AIS=Athens Insomnia Scale.

Table 3.5: Longitudinal studies assessing the relationship between sleep duration and academic performance.

First author, year	Sample size	Country	Age at baseline	Follow up	Sleep measure	Performance measure	Findings
Fredriksen, 2004 [265]	2,259	USA	11-14 years	Annually for 3 years	Self-report	Self-report	Positive correlation between 8th grade sleep and school attainment. Less sleep in 6th grade was associated with lower grades
Warner, 2008 [266]	310	Australia	15-18 years	Holiday versus term time	Self-report SSHS & retrospective sleep log for 2 weeks	Self-report 8 point scale	Sleep factors impacted negatively on mood and ability to function at school during the day, which predicted poorer academic achievement

SSHS=schools sleep habits survey.

Of the 8 cross-sectional studies examining sleep duration and school performance, only 1 reported no association (Table 3.4). In this early study, a questionnaire was developed to examine the association between sleep duration and academic performance. It was stated that the questionnaire took 3-5 minutes to complete but the authors provide no detail concerning reliability or validity testing for the questionnaire.[259] The findings should therefore be considered cautiously, particularly as they oppose the results of all other studies. A more recent study examined associations between specific subject performance and sleep duration. Mathematics performance was positively correlated with sleep duration and excessive morning sleepiness was identified as a significant risk factor for poor performance in both English and Mathematics.[263] Both longitudinal studies reported reduced school performance according to sleep measures although the study designs and follow up time points differed.[265;266] Further to the studies directly examining the relationship between sleep duration and academic performance, there are others which have assessed other sleep parameters in relation to academic performance, including sleep quality[203] and daytime sleepiness.[203;261]

The majority of evidence points to a positive association between sleep and academic performance. Reasons for this, based on available evidence, suggest that sleep is associated with cognitive consolidation, in particular, executive functioning.[254] Neurological processes that occur during sleep may influence daytime cognition as well as physical and mental performance.[38] Complex cognitive tasks requiring higher order functioning have been linked to the prefrontal cortex area of the brain, also associated with sleep.[267] It is therefore believed that sleep loss may impair cognitive functioning in the prefrontal cortex and result in lower academic attainment through reduced learning capacity.

3.1.5 Aims

The relationships among short sleep duration and obesity, various technologies and academic attainment are relatively consistent but are not homogeneous, possibly due to variations in study design. The relationships between all of these variables in combination have not been rigorously explored or previously reported but determination of these inter-related associations are vital for a better understanding of the sleep-obesity relationship.

No study has examined the relationships among sleep, obesity, technology use, and school performance among contemporary UK adolescents. Also, no study has examined these factors together in a large sample. A study (Midlands Adolescent Schools Sleep Education Study; MASSES) was commenced in the Midlands region of the UK to address these knowledge gaps and test a number of hypotheses.

3.1.5.1 Hypotheses

1. Technology use (TV, Internet use, video games, mobile telephones) before bedtime on weekdays will alter sleep duration;
2. Short sleep duration is an independent predictor of BMI;
3. Short sleep duration is an independent predictor of academic performance.

3.2 Methods

3.2.1 Study population

The MASSES was first conducted as a pilot during 2008-2009. The primary aim was to examine adolescent sleep and its associations with media use, academic performance and overweight/obesity. Six schools across the Midlands region of the UK were recruited. The purpose of recruiting six schools was to ensure a number of schools were included with students from a variety of socioeconomic groups and teaching standards. Data were collected from participants who attended one of six secondary schools in the East (Derbyshire and Leicestershire) or West Midlands (Birmingham), UK (Figure 3.2). Participating secondary schools were Ashby School, Ashby-de-la-Zouch, Leicestershire; Bishop Vesey's Grammar School for Boys, Sutton Coldfield, Birmingham; Hamstead Hall Community Learning Centre, Handsworth Wood, Birmingham; Highclare School, Sutton Coldfield, Birmingham; Repton School, Repton, Derbyshire; Sutton Coldfield Grammar School for Girls, Sutton Coldfield, Birmingham.

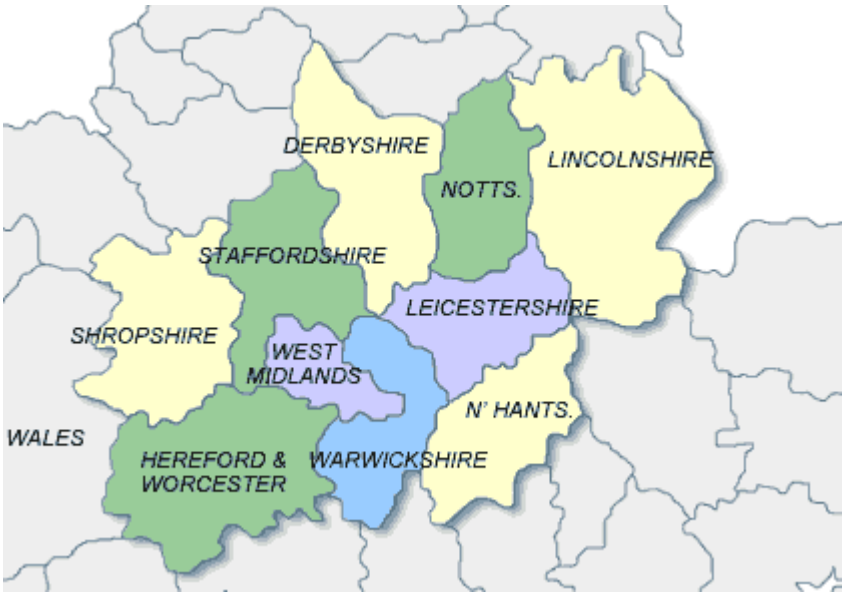

Figure 3.2: A map of the Midlands showing the different regions where MASSES was conducted.

An innovative approach was used by training sixth form students (16-18 years), interested in conducting the research project, to work with the author of this thesis throughout the research process. Sixth form students worked voluntarily on the project and helped to supervise data collection from other students within their individual school. The 6th form students were involved in the project and received a number of educational sessions with the author of this thesis, including:

1. Researching and reviewing existing literature in the specified area;

2. Understanding ethical guidelines and compliance;

3. Development of participant information sheet, parental consent letter, debriefing, promoting research to teachers, students and parents;

4. Assisting with data collection – BMI measures, providing instructions on how to access survey, clarifying questions to participants, debriefing volunteers;

5. Statistical analysis: correlation testing between all variables of concern;

6. Producing a scientific abstract based on the results of the study.

Parents of registered students within each school received a letter regarding study participation, either via the student or through the postal service. Opt in and opt out procedures operated, according to the Head Teacher's preference. Parents were provided 2 weeks from the date on the letter to respond and indicate consent or non-consent for their offspring. Student participants were included if they had parental consent, provided personal written consent, did not have a physician diagnosed sleep disorder, were not taking sleep medication or had not travelled to a different time zone 4 weeks prior to data collection. Ethical approval was granted by the University of Birmingham Ethics Committee (Ref: ERN_08-437).

The total number of students across the six schools was 5,596. The overall parental response rate was 26.7% with 18.6% (n=1,043) providing positive parental consent for study participation. Comparisons between respondents and non-responding parents were not possible due to data protection laws within schools. Of those eligible, a sample of 759 (72.8%) volunteers took part in the study and provided data, which was used for subsequent analyses. Of those consented who did not provide data, there were more boys (62.8%) than girls (37.2%). Main reasons for not providing data were either related to inclusion/exclusion criteria, or appeared to be related to absenteeism, extracurricular activities and/or sporting/musical group commitments since most

sessions were held during lunchtimes. All participants were aged between 11-18 years and were registered students in Years 7-13 of secondary education.

3.2.2 Exposure and outcome measures

Participants completed a secure online survey (www.surveymonkey.com) using the validated School Sleep Habits Survey (SSHS).[185] A Technology Use Questionnaire, previously developed for a cohort study[268] was used to assess technology use before bedtime followed by the Cleveland Adolescent Sleepiness Questionnaire (CASQ),[269] and the Pubertal Development Scale.[270] All questionnaires were age-appropriate and previously validated. Details of the survey can be found in Appendix 2. All measures were self-reported; information gained on weekday sleep duration (minutes) through the SSHS was categorised into 3 groups (<8 hours, 8-9 hours, >9 hours). Recommended sleep duration for adolescents is 9 hours and 15 minutes,[37] therefore >9 hours served as the reference in logistic regression analyses for assessment of potential dose-dependent relationships. Use of technology (TV viewing, video games, Internet/laptop, mobile telephone use) after going to bed but before attempting to go to sleep was acquired (never, sometimes, usually, always) and responses were dichotomised into yes (sometimes, usually, always) or no (never). We further calculated the amount and types of technology the volunteers used before bedtime on weekdays (non-user, any 1 type, any combinations of 2 types, any combinations of 3 types, and all 4 types of technology). Overall academic achievement was also acquired from the SSHS by asking the question: "Are your grades in school mostly..." allowing volunteers to respond with: 'A's, B's, C's, D's or E's". Grades A, B were categorised as high performance and

grades C, D or E were categorised as low performance. Stadiometers and scales, calibrated regularly, were used for measures of height (to the nearest 0.5cm) and weight (to the nearest 0.1kg), which were then used for BMI calculation, using the standard equation. The prevalence of underweight, normal/healthy weight and overweight/obese were calculated using the International Obesity Task Force (IOTF) cutpoints.[51]

3.2.3 Other measures

The type of school (secondary, independent, mixed gender and same gender)[271] at which the participants were registered was used as a proxy for socioeconomic status (SES), as well as for the adjustment of potential variation in teaching standards. Of the total sample, 55.1% were from secondary schools, the main type of school in England, 17.1% were from an all girl's school, 6.9% from an all boy's school and 20.9% from independent schools. Information was also obtained to identify whether the volunteer was a day or boarding student. This information was considered to be important as the enforced policy of 'lights out' in a boarding school may impact on sleep behaviours.

Other demographic information was acquired on age, gender, ethnicity and year of study (Years 7-13). In addition to obtaining data concerning mobile telephone use before bedtime, participants were asked if they took their mobile to bed and left it switched on during the night (never, sometimes, usually, always), responses were dichotomised into yes (sometimes, usually, always) or no (never). Similarly, we asked if text messages were received during the night, which woke

the participant from sleep (never, sometimes, usually, always) and responses were dichotomised in the same way (yes, no).

Method of travel to school was obtained and categorised to determine activity levels (inactive [public transport or car], active [walk, cycle]) while assessment of snacking before bedtime was obtained for dietary measures (yes, no).

The SSHS identified symptoms of depression by asking volunteers "in the past 2 weeks, how often were you bothered by feeling unhappy, sad or depressed?" Participants were asked if they felt they usually obtained enough, too much or too little sleep. Daytime sleepiness was determined by asking if volunteers felt tired or worn out in the day during the 2 previous weeks (yes, no). Information on snoring was obtained (yes, no) while stopping breathing/gasping for air whilst asleep (yes, no) was used to identify participants with potential obstructive sleep apnoea (OSA). Finally, ease of getting up on a weekday was obtained and dichotomised (yes [easy or very easy], no [not easy, hard or very hard]).

3.2.4 Statistical Analysis

Data analyses were performed using the Statistical Package for the Social Sciences (SPSS, version 15.0, Chicago, IL, USA). Linear regression analysis was performed to examine the effect on sleep duration by the number of technology activities individuals engaged in before bed time on weekdays. Potential confounders were selected *a priori* according to scientific evidence. For

binary variables with a 'yes/no' response, 'no' was taken as the reference. An independent samples t-test was used to assess differences in total sleep time and sleep onset latency between users and non-users of technology before bedtime on weekdays. Linear regression analysis was also performed to examine the individual effects of specific technologies before bedtime on weekdays upon sleep duration. Logistic regression models were then constructed to assess the relationship between sleep duration and BMI (underweight and normal weight participants were combined and used as a reference group to compare with overweight/obese participants). Odds ratios (ORs) with 95% confidence intervals (95% CIs) of two models are presented. Model 1, adjusted for age, gender and ethnicity, while Model 2 fully adjusted for technology use before bedtime, diet, activity, school type, day/boarding student, symptoms of depression, potential OSA, snoring, daytime sleepiness and academic achievement, in addition to the aforementioned factors. Logistic regression models were also built to assess the relationship between sleep duration and academic achievement and two models are presented. Again, Model 1 adjusted for age, gender and ethnicity and Model 2 fully adjusted for technology use before bedtime, school type, day/boarding student, symptoms of depression, potential OSA, snoring, daytime sleepiness and BMI, in addition to the aforementioned factors.

3.3 Results

3.3.1 Sample characteristics

Of the 759 volunteers who participated in the study, 135 (17.8%) were excluded due to incomplete data, leaving a total of 624 (82.2%) available for subsequent analysis. The mean age of the sample was 13.9 ± 2.0 years. Those obtaining >9 hours of sleep were younger (12.8 years) compared to those obtaining either 8-9 hours or <8 hours (14.1 and 14.8 years, respectively) (Table 3.6). Of those who were overweight/obese, the majority reported a sleep duration of <8 hours (51.3%). Overweight/obesity was more prevalent in 11-year-olds (43.3%) but lowest in 18-year-olds (11.1%). Of those sleeping <8 hours, 40.5% engaged in the use of all 4 technologies before bedtime on weekdays, compared to 28.3% who slept 8-9 hours and 24.7% who slept >9 hours ($p=0.003$). Also, of those reporting lower academic performance, 52.5% were short sleepers (<8 hours) compared to 27.2% who reported high academic achievement ($p<0.001$).

Table 3.6: MASSES sample characteristics of 624 UK adolescents, according to sleep duration.

Characteristics	Sleep duration <8 hours (n=215)	8-9 hours (n=223)	>9 hours (n=186)	p value
Gender n (%)				0.070
Boys	78 (35.6)	66 (30.2)	75 (34.2)	
Girls	137 (33.8)	157 (38.8)	111 (27.4)	
Age (year); mean±SD	14.8±1.9	14.1±1.9	12.8±1.7	<0.001
Ethnicity n (%)				0.004
White	80 (35.7)	94 (42.0)	50 (22.3)	
South Asian	93 (32.2)	95 (32.9)	101 (34.9)	
Black	17 (27.4)	21 (33.9)	24 (38.7)	
Other	25 (51.1)	13 (26.5)	11 (22.4)	
BMI n (%)				
	135 (28.8)	183 (39.1)	150 (32.1)	<0.001
Underweight/Healthy Weight				
Overweight/Obese	80 (51.3)	40 (25.6)	36 (23.1)	
Technology Use n (%)				0.003
Non-User	19 (20.0)	38 (40.0)	38 (40.0)	
1 Technology	24 (27.3)	31 (35.2)	33 (37.5)	
2 Technologies	44 (31.9)	53 (38.4)	41 (29.7)	
3 Technologies	41 (38.3)	38 (35.5)	28 (26.2)	
4 Technologies	87 (44.4)	63 (32.1)	46 (23.5)	
Academic				<0.001
Performance n (%)				
Low	94 (52.5)	53 (29.6)	32 (17.9)	
High	121 (27.2)	170 (38.2)	154 (34.6)	

All data are reported as % or mean ± SD, where indicated.
p values for continuous and categorical variables were calculated using ANOVA and chi square analysis, respectively.

3.3.2 Sleep characteristics

Chi square analysis showed that sleep duration was not significantly related to gender $\chi^2=5.05$, $p=0.08$ but was significantly related to ethnicity $\chi^2=20.96$, $p=0.02$. Spearman's rho bivariate correlation showed a significant negative relationship between sleep duration and age $r=-0.42$, $p<0.001$. The majority of the sample reported feeling tired in the day (83.3%), found it difficult to get up on weekday mornings (58.8%) and reported feeling depressed (53.2%). Obtaining too little sleep was reported by 43.3%. Importantly, 74% of our sample reported taking their mobile telephone to bed with them and leaving it switched on. Of these participants, 53% stated they were woken from sleep by receiving text messages in the night.

3.3.3 Sleep and technology use before bedtime on weekdays

Use of technology before bedtime on weekdays was highly prevalent with 84.8% of the sample engaging in this behaviour. Results in Table 3.7 suggest that use of four technologies before bedtime on weekdays had a reduced and significant association on sleep duration ($\beta=-33.37$, $p<0.0001$) compared to non-users. Other variables that were significantly associated with sleep duration were BMI, age, 'other' ethnicity, attending an independent (mixed gender) school, girls' school, day and boarding students, potential OSA and low academic performance. Users of 1, 2 or 3 technologies gender, diet, physical activity, depression, snoring and daytime sleepiness had no significant association on weekday sleep duration.

Table 3.7: Linear regression analysis determined variables that are associated with weekday sleep duration.

		Estimate β	Std. Error	t value	p value
BMI		-24.93	2.87	-8.68	<0.0001
Age		-13.85	1.77	-7.85	<0.0001
Ethnicity	Asian	-5.30	7.67	-0.69	0.490
	Black	0.59	10.99	0.05	0.957
	Other	-28.08	11.13	-2.52	0.012
Technology	Use of 1	-4.59	9.50	-0.48	0.629
	Use of 2	-3.33	8.64	-0.39	0.670
	Use of 3	-8.54	9.12	-0.97	0.334
	Use of 4	-33.37	8.38	-3.98	<0.0001
School	Boys	-19.59	15.88	-1.23	0.218
	Secondary (mixed)	7.90	15.07	0.52	0.600
	Independent (girls)	-10.56	17.27	-0.61	0.541
	Independent (mixed)	-49.71	15.22	-3.27	0.001
	Girls	-27.86	13.60	-2.05	0.041
Student type	Boarder	41.52	15.45	2.69	0.007
	Day student	67.07	21.69	3.09	0.002
Potential OSA	Yes	-16.45	7.66	-2.15	0.032
Grades	C or below	-19.15	6.41	-2.99	0.003

Inadequate sleep duration (≤9 hours) was reported by 70.2% of our sample. The mean (±SD) sleep duration in minutes for non-users, 1, 2, 3, and 4 technology users were 528.51 ± 83.48, 516.14 ± 65.59, 508.89 ± 76.96, 494.53 ± 74.05, and 484.55 ± 86.71 ($p<0.05$), respectively.

Descriptive statistics showed that non-users of technology before bedtime on weekdays obtained mean sleep duration of 528.51 ± 83.48 compared to users who reported a mean sleep duration of 498.18 ± 79.23 (Figure 3.3). The independent t-test used to examine the relationship between sleep duration by users and non-users of technology revealed a significant effect t=3.41, p=0.001.

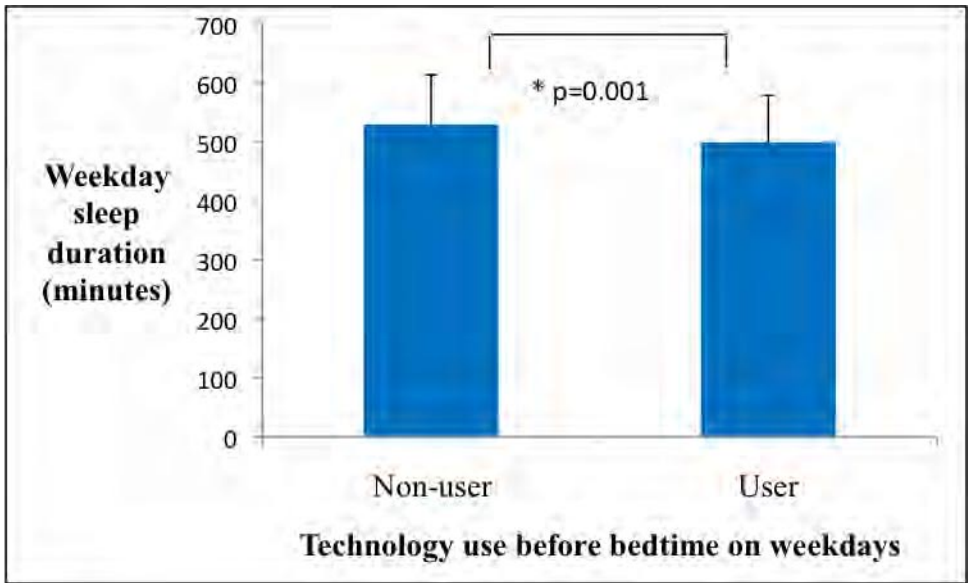

Figure 3.3: The mean differences and standard deviations in weekday sleep duration between users (1-4 technologies) and non-users (no technology) of technology before bedtime on weekdays.

Descriptive statistics also revealed that non-users of technology before bedtime on weekdays had mean sleep onset latency (SOL) of 25.87 ± 24.79 minutes compared to users of technology 26.59 ± 23.36 minutes (Figure 3.4). Despite users of technology reporting longer SOLs to non-users, the independent t-test showed no significant differences t=-0.30, p=0.76.

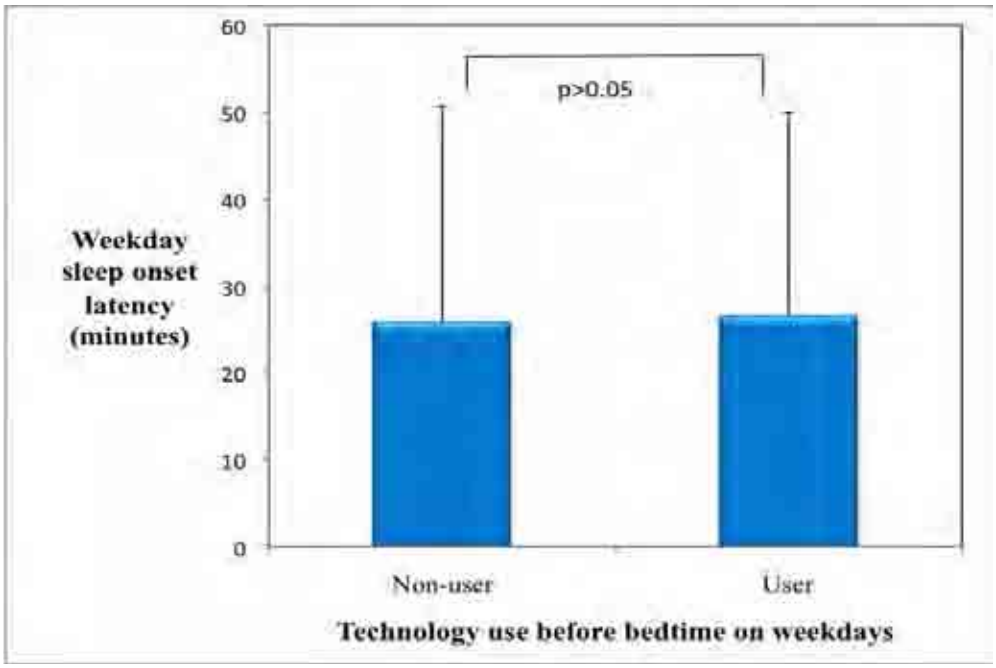

Figure 3.4: The mean differences and standard deviations in sleep onset latency between users (1-4 technologies) and non-users (no technology) of technology before bedtime on weekdays.

Results of the linear regression analysis used to examine the relationship between sleep duration and specific technology types, after adjustment for age and gender, are shown in Table 3.8. To summarise, there were significant negative effects on sleep duration when engaging in the use of all technologies: video games β=-0.23, $p<0.001$; TV viewing β=-0.19, $p<0.001$; mobile telephones β=-0.13, $p=0.001$; and laptop/Internet use β=-0.18, $p<0.001$ before bedtime on weekdays.

Table 3.8: Specific types of technology associated with weekday sleep duration.

		Standardised β coefficient	Std. Error	t value	p value
Technology*	Video games	-0.23	0.10	-6.13	<0.001
	TV viewing	-0.19	0.10	-5.08	<0.001
	Mobile telephones	-0.13	0.11	-3.49	0.001
	Laptop/Internet	-0.18	0.10	-5.04	<0.001

*Adjusted for age and gender.

Sleep duration (minutes) was entered as a continuous variable.

3.3.4 Sleep and obesity

One hundred and fifty six volunteers (25.0%) were classified as overweight or obese. The linear relationship between sleep duration (continuous) and the raw BMI data (continuous) is shown in Figure 3.5. Multivariate logistic regression analysis suggested a significant association between overweight/obesity and <8 hours sleep duration (OR = 2.72 [1.44-5.12]) compared to those sleeping >9 hours (Table 3.9). The analysis showed no effect of gender or ethnicity with sleep duration. The *p* values for trend indicate a dose-dependent relationship between sleep duration and overweight/obesity in the sample. Odds ratios and 95% CI's for all potential confounders entered into the fully adjusted model are displayed in Table 3.10.

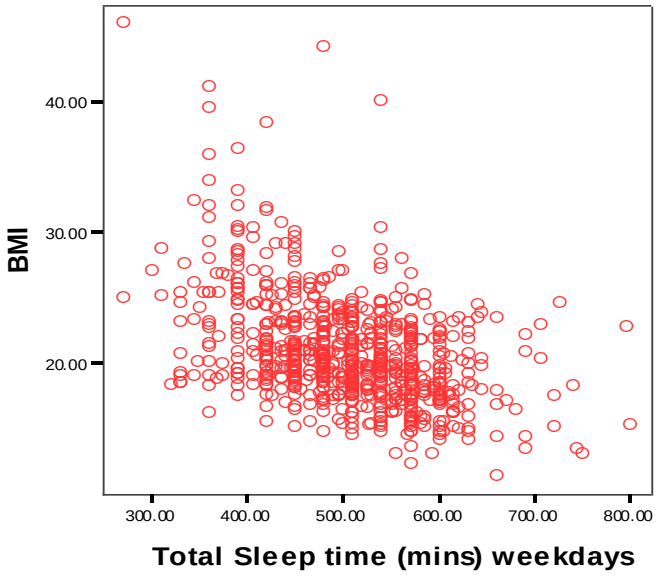

Figure 3.5: A scatterplot showing the relationship between weekday sleep duration and BMI from 624 adolescents recruited to the MASSES.

Table 3.9: The prevalence and odds of overweight/obesity according to sleep duration.

		Overweight/obesity	
Sleep duration (n)	**n (%)**	**Univariate**	**Fully adjusted**
<8 hours (215)	80 (37.2)	2.47** (1.56-3.90)	2.72* (1.44-5.12)
8-9 hours (223)	40 (17.9)	0.91 (0.55-1.50)	1.16 (0.65-2.09)
>9 hours (186)	36 (19.4)	1.00	1.00
p value for trend		<0.001	0.001

* p<0.01, ** p<0.001
Data are odds ratio (95% confidence interval) unless otherwise stated.
† Fully adjusted model adjusted for age, gender, ethnicity, technology use, diet, activity, school type, day/boarding student, symptoms of depression, potential OSA, snoring, daytime sleepiness, and academic performance.
The Cox & Snell R^2 value for the fully adjusted model was 0.31.

Table 3.10: A table showing the odds ratios and 95% confidence intervals for all potential confounders entered into the model assessing the sleep-obesity relationship in a sample of 624 UK adolescents

Confounder	**Odds ratio (95% CI)** **Fully adjusted model**
Sleep duration <8 hours	2.72* (1.44-5.12)
Sleep duration 8-9 hours	1.16 (0.65-2.09)
Age	0.81* (0.69-0.95)
Male gender	1.56 (0.97-2.53)
Bishop Veseys (Boys Grammar)	2.00 (0.41-9.74)
Hamstead Hall (Secondary)	1.38 (0.31-6.21)
Highclare (Independent)	0.95 (0.16-5.77)
Repton (Independent)	1.78 (0.37-8.64)
Sutton Girls (Girls Grammar)	1.83 (0.43-7.74)
1 technology	0.56 (0.22-1.41)
2 technologies	0.58 (0.27-1.27)
3 technologies	1.20 (0.56-2.57)
4 technologies	1.02 (0.50-2.11)
White ethnicity	0.54 (0.22-1.30)
Asian ethnicity	0.84 (0.40-1.75)
Black ethnicity	1.14 (0.46-2.83)
Boarding student	1.81 (0.43-7.59)
Day student	2.27 (0.39-13.32)
Snack after bedtime (yes)	1.42 (0.85-2.37)
Physical inactivity	1.05 (0.64-1.71)
Snoring (yes)	1.08 (0.68-1.73)
Academic achievement (low)	4.31* (2.73-6.79)
Daytime sleepiness (no)	1.41 (0.79-2.50)
Depression (no)	1.21 (0.76-1.92)
Potential OSA (yes)	1.50 (0.82-2.73)

* $p<0.05$

3.3.5 Sleep and academic performance

Short sleep duration (<8 hours) was reported by 34.5% of the sample and lower academic achievement by 28.7%. Multivariate logistic regression analysis revealed a dose-dependent relationship between sleep duration and academic performance. There was a significant

association between poor academic performance and <8 hours sleep duration (OR = 3.99 [95% CI 2.16-7.38]) compared to those sleeping >9 hours (Table 3.11). No effect was found for age, gender or ethnicity. Full details of the fully adjusted model can be found in Table 3.12 including the odds ratios and 95% confidence intervals of all potential confounders entered into the model.

Table 3.11: The prevalence and odds of lowered academic performance according to sleep duration.

	Lower academic achievement		
Sleep duration (n)	**n (%)**	**Univariate**	**Fully adjusted†**
<8 hours (215)	94 (43.7)	3.74** (2.35-5.96)	3.99** (2.16-7.38)
8-9 hours (223)	53 (23.8)	1.50 (0.92-2.45)	1.77 (0.99-3.17)
>9 hours (186)	32 (17.2)	1.00	1.00
p value for trend		<0.001	<0.001

* p<0.05, ** p<0.001

Data are odds ratio (95% confidence interval) unless otherwise stated.
† Fully adjusted model adjusted for gender, age and ethnicity, technology use, school type, day/boarding student, symptoms of depression, potential OSA, snoring, daytime sleepiness and overweight/obesity.
The Cox & Snell R^2 value for the fully adjusted model was 0.34.

Table 3.12: A table showing the odds ratios and 95% confidence intervals for all potential confounders entered into the model assessing the sleep-obesity relationship in a sample of 624 UK adolescents.

Confounder	**Odds ratio (95% CI)** **Fully adjusted model**
Sleep duration <8 hours	3.99* (2.16-7.38)
Sleep duration 8-9 hours	1.77 (0.99-3.17)
Age	1.09 (0.93-1.26)
Male gender	0.89 (0.56-1.42)
Bishop Veseys (Boys Grammar)	0.36 (0.10-1.33)
Hamstead Hall (Secondary)	0.74 (0.23-2.42)
Highclare (Independent)	0.68 (0.18-2.61)
Repton (Independent)	0.12* (0.03-0.48)
Sutton Girls (Girls Grammar)	0.22 (0.07-0.65)
1 technology	0.89 (0.33-2.42)
2 technologies	2.37* (1.08-5.21)
3 technologies	2.08 (0.93-4.64)
4 technologies	3.43* (1.66-7.09)
White ethnicity	1.38 (0.55-3.46)
Asian ethnicity	2.03 (0.94-4.41)
Black ethnicity	1.24 (0.48-3.18)
Boarding student	2.73 (0.61-12.29)
Day student	4.76 (0.74-30.67)
Snoring (yes)	1.33 (0.84-2.10)
Overweight/obese	4.57* (2.91-7.19)
Daytime sleepiness (no)	1.18 (0.65-2.13)
Depression (no)	0.86 (0.55-1.35)
Potential OSA (yes)	0.91 (0.50-1.67)

* $p<0.05$.

3.4 Discussion

3.4.1 Sleep and technology use

The negative impact of media device usage through increased screen time on the health and wellbeing of adolescents has been previously highlighted.[230] In contrast to a structured leisure

activity with a defined beginning and end, unstructured activities, such as technology use, may defer bedtimes and result in less time spent in bed.[250] Evidence suggests that TV viewing,[229] Internet use,[234] video gaming,[239] and mobile telephones,[233] are all associated with a reduction in adolescent sleep. These studies, however, did not directly assess the potential effects of engaging in the use of multiple technologies, particularly before bedtime on weekday nights. The majority of previous studies have focused on just one[231;237] or two[241;243] types of technology rather than collective use of all technologies available to adolescents. With the rapid development of technology and the increased prevalence and accessibility of media devices, combined technology use should be considered in future research.

Data from the MASSES, using a more comprehensive assessment of technology use in contemporary adolescents, showed that those engaging in 1, 2 or 3 technologies before bedtime had a negative association on sleep duration compared to non-users. Adolescents using 4 technologies before bedtime on weekdays had a statistically significant negative effect on weekday sleep duration. A recent study by Calamaro and colleagues reported increased multi-tasking of media (TV, MT, PC and MP3 player) was associated with reduced sleep duration.[130] The study also identified media use to be related to increased caffeine consumption which may, in part, explain sleep loss through stimulant use.[130] The only study to assess combination of technologies identified a significant negative correlation between screen time (TV, VG, cinema and PC use) and sleep duration in young adolescents.[230] The results of both these studies are in line with findings from the MASSES study although neither of the studies examined the specific combination of technologies assessed in the MASSES (TV, VG, MT and PC).

The majority of other studies examining individual technologies and various sleep parameters are in line with results of the MASSES study although findings are not completely homogeneous. Interestingly, the two studies reporting no association between technology and sleep originate from similar geographic areas.[68;227] Taiwan and Japan are technologically advanced countries and so it could be argued that the negative effects of technology devices may have upon sleep parameters diminish over time and our bodies adapt to the physiological stimulation. This warrants future prospective studies, which should attempt to examine this possibility more thoroughly. As technology has advanced over the past few decades, it is important that future research conducted in this area examines more than one or two types of technology. Simply assessing the effects of TV upon sleep is no longer sufficient, particularly as ownership of mobile telephones, video gaming consoles and laptops have increased in recent years, particularly in adolescents, according to national statistics. Indeed, use of multiple devices immediately before bedtime on schooldays had a negative association on sleep duration in this sample of UK adolescents.

The sample of UK adolescents in the MASSES also demonstrated that using technology on weekdays before bedtime was associated with a significant reduction of weekday sleep duration compared to non-users of technology. All of the cross-sectional studies reviewed in this chapter identified either duration or frequency of adolescent technology use. Surprisingly, other studies have not made direct comparisons concerning sleep parameters between users and non-users of technology. The only study to draw comparisons was a Swedish experimental study (n=19, all males). The study examined the impact of playing a violent or non-violent video game and comparing that with a control evening of no video gaming.[246] The findings provided evidence of

later bed times for the experimental groups compared to the control group but no differences were reported for sleep duration. All measures of video gaming and sleep parameters, however, were subjective and based on one night for each condition. Although this is the only study which compared the effects of non-users and users of technology, it is not known if the subjects were pre-existing regular users of technology before bedtime and had to simply withhold from gaming during the control evening. This is an important consideration because pre-existing users may have developed an adaptation or, conversely, an accumulation of stimulation/stress, which may have affected sleep parameters, compared to non-users. Such variations, which were not determined at the start of the experiment, may produce inaccurate results.

Future studies should try to draw comparisons between present users and non-users of technology as there may be important differences between these two groups, particularly in adolescents. It is necessary to explore and determine the impact of different types of technology upon sleep duration as specific types of technology may alter sleep parameters more radically than others, an area which the MASSES study did examine. It is possible that non-users may read before bedtime, which one study found was related to increased sleep time,[229] or non-users may undertake other non-technology related activities or they may simply go straight to bed without engaging in any activity. Results from the MASSES study has revealed that non-users acquire more sleep on weekdays compared to users. This has made a start on uncovering important comparisons for sleep duration between these two groups. Future research should aim to deeply explore these relationships in depth and attempt to identify what activities, if any, non-users undertake before bedtime and determine why their sleep duration is different to users of technology through objective measures of both sleep and technology.

Potential explanations as to why non-users of technology have an increased sleep duration compared to users are lifestyle and biological. Firstly, it could be argued that individuals engaging in the use of technology may encounter more mental stimulation/stress compared to those undertaking no activities or other non-technology related activities before bedtime. Potential effects of mental stimulation from video games (VG), Internet, TV or mobile telephones (MT) may result in a delayed sleep onset latency (SOL) and subsequently reduced sleep duration, although two studies reported no significant effects of prolonged SOL following media use.[227;246] Interactive technologies such as Internet, VG and MT may result in increased psychological distress thus potentially resulting in higher stress levels. The consequences of this could possibly delay SOL and increase sleep disturbance and future research should focus on this aspect as data is limited. Secondly, the artificial light radiating from the device may be postponing the release of melatonin, which, in turn, may hinder sleep onset. Available evidence shows TV viewing to be associated with lowered urinary melatonin concentrations in pubertal children.[272] Findings in relation to MT use, however, have shown no difference between exposure and non-exposure during the evening.[273] Data is not only limited but also heterogeneous so future studies should further explore this idea through experimental design. Thirdly, technology is fundamental to adolescent populations who commonly experience delayed sleep phase. Arguably, teenagers who are unable to fall to sleep due to a shift in circadian timing and a lack of physiological drive, may be using technology devices to avoid boredom and pass time during the evening and so use of technology may be related to an individual's pubertal development stage and ultimately, sleep loss. Indeed, dependency and addiction to different types of technology have been explored and associated with later bed times and less total sleep time.[224;237;239] Excessive use, whether it be to

pass time or not, may result in reduced awareness of clock time. Continued use alongside being unaware of the time and captured in the technology mode often with determination to complete the next level of a VG, finish watching a film so the ending can been seen, following the next link on a webpage of interest or online chatting with friends can all lead to later bedtimes, coupled with the early school start times will ultimately result in sleep loss.

Unfortunately, the majority of the cross-sectional studies reviewed only identified duration of technology use, perhaps to explore dose-response relationships. These study designs, however, do not identify the time of day/night technology is being used and so findings may differ between day time and night time usage. It must also be considered that some types of technology are used within the school curriculum (PC, Internet) and so if it is not specified at what time of day or night usage occurs then all adolescents will be considered as users thus not allowing for comparisons to be made between users and non-users. Arguably, use of devices during the day may not have such a significant impact on sleep parameters compared to use immediately before bedtime. Indeed, experimental evidence has shown that using specific technologies during the evening can stimulate the brain and alter sleep architecture as well as other sleep parameters.[198;245;246] There is no experimental evidence, however, that has examined the effects of daytime technology use in relation to sleep parameters and so this remains undetermined. For example, nighttime technology use may have more profound negative effects upon sleep parameters compared to daytime technology use but this has not been previously explored. The MASSES study is the only study able to make direct comparisons between users and non-users relating to a specific time of day - before bedtime on weekdays. The large sample of mixed gender contemporary adolescents is the first to be reported in the UK. The findings demonstrate

that users of technology have a significantly reduced sleep duration compared to non-users of technology before bedtime on weekdays.

Based on the idea surrounding mental stimulation of technology devices and the subsequent impact on sleep, the carefully designed MASSES made assessments on individual types of technology and sleep duration. The findings demonstrated that all types of technology assessed in the MASSES study had a statistically significant and negative association on sleep duration. Interestingly, the use of mobile telephones (MT) had the least effect on sleep duration. Although it is not known what video games (VG) were played, what TV programmes/films were viewed, and what activities the participants performed on the PC/Internet, these technologies, arguably, provide more mental stimulation/excitation compared to MT use. Considering the size of the devices (VG, TV and PC), the light radiated from these may be more intense compared to that of a MT. Evidence examining melatonin concentrations following exposure of TV and MT support this argument. The two studied showed levels to be reduced subsequent to TV exposure[272] but no alterations were found after MT use.[273] These arguments support the potential explanations for reduced sleep duration amongst technology users before bedtime. Future studies should aim to explore these ideas through objective measures of sleep, technology use, brain imaging, and hormone concentration levels whilst deploying rigorous study designs.

3.4.2 Sleep duration and obesity

The relationship between sleeping hours and obesity in adult population samples is U-shaped.[3;97] In children, short sleeping hours and obesity show a negative linear association.[63] The alteration in this association from childhood to adulthood lies in adolescence. Evidence in adolescents, however, has been sometimes limited to smaller samples[66;213] and has not always produced consistent findings.[92] The primary aim of the MASSES was to determine if a relationship exists in UK adolescents for sleep duration and obesity. The findings demonstrated a dose-response association between sleeping hours and the prevalence of overweight/obesity. Those with the shortest sleep duration (<8 hours) were almost 3 times (OR 2.72, 95% CI 1.44-5.12) more likely to be overweight or obese compared to those who obtained the recommended duration of sleep for adolescents (>9 hours), even after adjustment for potential confounders.

These findings are parallel with other adolescent studies in this area[66;68;70;72-75;213]. Some have previously reported negative associations with gender differences[67;71;216], whilst others report either U-shaped associations[71;76] or no association at all.[92] Inconsistent findings are likely to be the result of different study designs, methods of statistical analysis or failure to adjust for confounding factors. For example, some study designs ask just one[92] or two[76] questions concerning sleep duration. A recent longitudinal study asked one question during home interview in relation to sleep duration 'How many hours of sleep do you usually get?'[92] Similarly, another large population study asked "How many hours of sleep do you usually get a

night?" and compared this with two 24-hour time diaries.[69] The large Norwegian study determined sleep duration by calculating the time difference between responses to two sleep questions, answered by both the adolescent and their parent: 1) 'When do you usually go to bed on school days?' and 2) 'When do you usually get up on school days?'[76] Not only did these three studies report three different types of associations but all produced different findings in relation to sleep duration and obesity compared to the MASSES. Clearly, the first study outlined asks a question which is limited and restricts the individual to respond with whole hours rather than hours and minutes.[92] Participants are likely to either round up or round down their responses, which will unequivocally produce inaccurate answers. Not only will this produce imprecise results, but this type of questioning fails to account for more detailed sleep measures, such as total sleep time, sleep onset and sleep quality. When utilising two sleep measures, as described in the second study,[69] this produced conflicting results. Self-reported sleep time was associated with overweight albeit non-linearly. Whereas the time diary, thought to be a more detailed method, was not associated with overweight. In the third study,[76] asking the time to bed and the time of getting up does not necessarily equate to accurate sleep duration either. Time to bed does not account for any activities performed in bed before attempting sleep. Equally, rise time does not account for time that may be spent in bed awake before rising. Arguably, asking parents of adolescents to estimate their child's time to bed and rise may be poorly correlated with adolescent reports. The MASSES study utilised a previously validated and reliable sleep questionnaire, which was also age-appropriate and was carefully designed to address the flawed designs of some sleep questionnaires. The schools sleep habits survey (SSHS) collects detailed information concerning sleep across a number of parameters such as sleep quality, sleep duration, nighttime awakenings, daytime sleepiness. The questionnaire also identifies responses for information on

potential confounders of sleep such as depression, worrying, possible sleep disorders, sleeping with lights on, bed sharing, room sharing and more. Such detailed information ensures that the data can be fully explored for confounders whilst at the same time examining specific sleep parameters and their associations with other factors.

Differences in study designs and thus findings may also be a result of differing sleep duration categories. For example, inadequate sleep duration was defined as <6 hours in one adolescent study. [92] A cutpoint of <6 hours is more widely applied to adult population studies.[123] Indeed, some adult studies have even classified inadequate sleep duration as <7 hours.[99;116] It is therefore clear, based on early experimental evidence,[274;275] large US sleep polls,[26] and comprehensive reviews,[30;38;39] that adolescents require at least 9 hours of sleep per night and so categorising >6 hours as adequate sleep is not a standardised grouping. Similarly, another difficulty when trying to draw comparisons between adolescent studies lies with inconsistencies of obesity measures. There are a variety of methods used to determine different categories of body weight, as discussed in *Chapter 1*. BMI is the most widely used measure for obesity and MASSES benefitted from obtaining anthropometric measures to calculate BMI and then define overweight/obesity according to a standardised worldwide definition,[51] originally developed from six geographically diverse international surveys of large growth studies, of which the UK was included. Future studies in this area should attempt to homogenise both sleep duration and obesity categories to allow for more stringent comparisons to be drawn without potential bias.

The observed association in the MASSES between sleep duration and obesity may be linked to physiological and lifestyle factors. Not only is obesity development linked to reduced energy

expenditure and increased energy intake but sleep could be linked to both sides of the energy equation. Figure 3.6 highlights the potential causal pathways for obesity development in relation to sleep. Large population[97] and smaller experimental studies[146] suggest that short sleep duration is associated with alterations in the metabolic hormones, leptin and ghrelin.[97;146;148] Leptin and ghrelin are two key opposing hormones in the regulation of appetite. A detailed discussion relating these two hormones to sleep and obesity was discussed in *Chapter 1*. It is important to note, however, that metabolic hormone studies according to sleep duration, whether experimental or observational, have been mainly conducted in adults[97] with some specifically limiting samples to healthy lean males.[146;156] The first adolescent study was published in 2010 and compared lean girls to obese girls, aged 14-18 years. The self-reported total number of hours in the day slept was obtained to create sleep duration categories of <5 hours, 5-7 hours and >7 hours. A 24-hour food recall was performed and overnight fasting blood samples were drawn to determine hormone levels. There was a significant negative relationship between ghrelin and sleep duration, when treated as a continuous variable but no significant relationship was identified between sleeping hours and leptin.[150] The results of this study differ to that of adult studies but there are a number of important considerations. Firstly, the sample only included adolescent girls and failed to take account of pubertal status. It was not identified what proportion of the sample had begun to menstruate. For studies including females, particularly when determining hormone levels, it is recommended that bloods are taken between days 1-10 of the menstrual cycle to avoid any fluctuation or confound that may alter the actual measurements. The study does not state if this criteria was followed and so results of this study are tentative. Secondly, the sleep duration categories are unrepresentative of adolescent sleep needs, a point raised in the previous paragraph concerning other studies in the area. Thirdly, the subjective measure of sleep and diet may not

provide accurate information about the adolescent girls' sleep duration, sleep quality or calorie intake. Future studies should utilise objective sleep measures, standardise sleep duration categories, assess metabolic hormone alterations in short, normal and long sleepers within four arms: underweight, lean, overweight and obese girls and boys. Finally, investigators should identify and aim to minimise potential confounding factors.

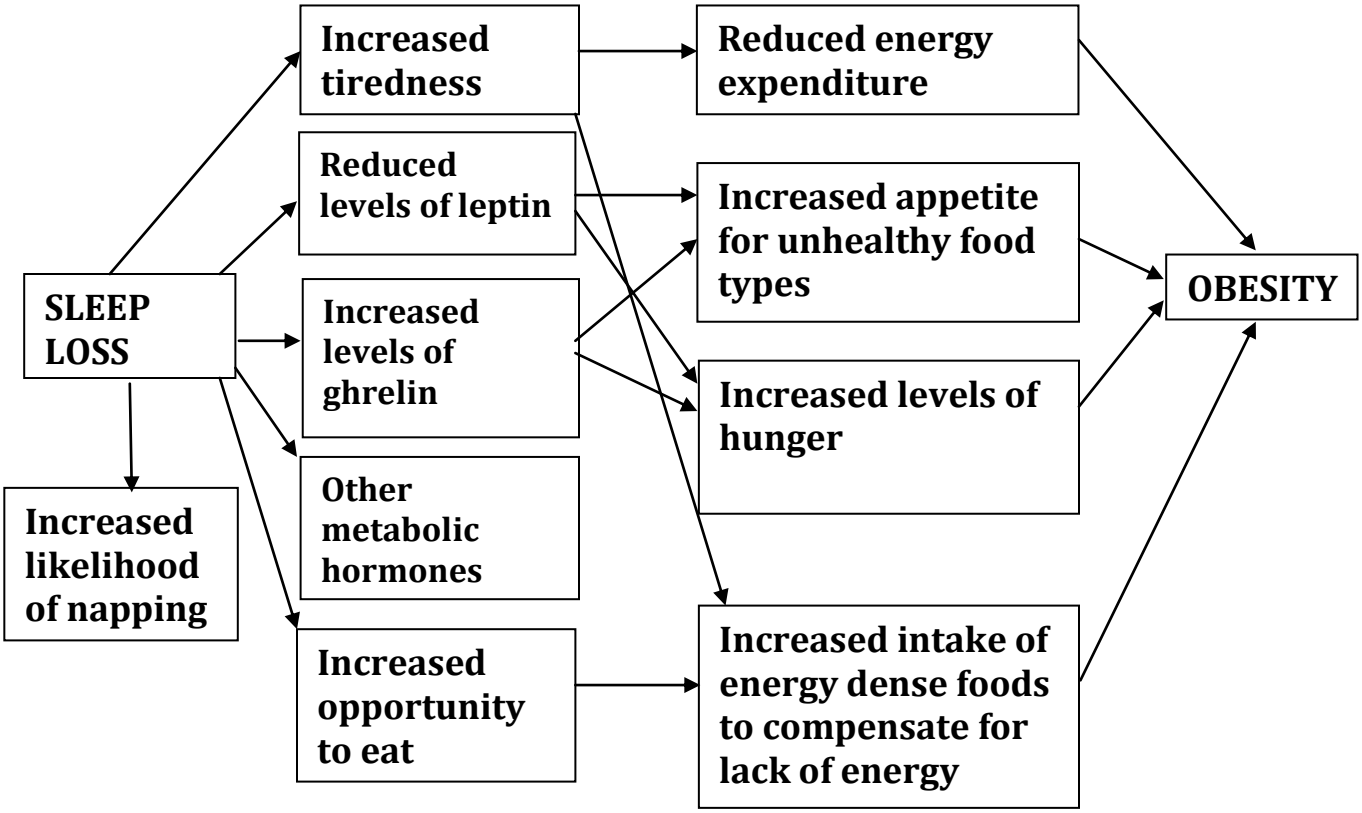

Figure 3.6: A diagram to show how sleep loss may promote obesity.

Sleep loss increases the propensity to nap which may promote poorer nocturnal sleep quality and a reduction in total sleep time (TST). Sleep loss is also related to increased tiredness which may result in less motivation to engage in physical activity and promote obesity. Experimental sleep loss has also been associated with decreases in leptin levels and increases in ghrelin and other metabolic hormones are likely to be involved. Alterations in these hormones have been linked to increases in subjective hunger and appetite for unhealthy food types which may promote obesity. A reduction in TST also results in increased time awake and thus an increased opportunity to eat. Tiredness, as a result of sleep loss, may also result in eating quick, processed and/or high energy dense foods to compensate for the lack of energy which may, in turn, result in obesity.

3.4.3 Sleep and academic performance

In this large sample of UK adolescents, short sleep duration was identified as an independent risk factor for poor school performance. Short sleep duration and poor quality sleep have been previously linked to lower academic performance and reduced daytime functioning.[255;276] It is well documented that daytime sleepiness has profound negative effects on cognitive function[277] and behaviour.[278] Furthermore, students who report daytime sleepiness state they are unable to work to their maximum academic potential.[264] Delayed sleep phase is experienced across the adolescent phase of life resulting in later bedtimes.[30] Constraints of early morning school commitments result in adolescents losing out on sleep in the morning. It is therefore plausible that poor academic achievers may be in a state of sleep debt as a potential consequence of technology use, which has become detrimental to their ability to perform academically.

A dose-dependent relationship between reduced sleep duration and cognitive performance is well established.[12] Associations have been previously documented between sleep loss and poorer problem-solving,[279] risky decision-making,[16] slower psychomotor reaction times,[280] and reduced memory consolidation.[281] Although these different types of cognition are undoubtedly important for an individual's performance, there are a limited amount of studies that have specifically assessed the association between academic achievement in adolescents and sleep duration. Despite different methodologies and academic measures applied in these studies, taken together, the findings from these studies are relatively consistent, as previously discussed. There are a number of potential explanations for the link between short sleep duration and reduced academic

achievement. Firstly, it is already known that REM sleep increases with each progressive cycle of sleep and so a healthy individual will encounter more REM sleep at the end of the last cycle of sleep compared to the first. In adolescents, however, who need to wake in time for school attendance, it is possible that this bout of REM sleep is either cut short or not even encountered at all. A number of literature reviews have suggested that REM sleep is associated with memory consolidation[282] as well as the processing of information.[283] Furthermore, experimental evidence of REM sleep suppression has shown that depression of REM sleep can result in higher levels of forgetfulness and poorer consolidation of episodic memories.[284] It is therefore possible, that loss of REM sleep at the end of the last sleep cycle may have a subsequent impact on an adolescent's ability to learn, process information, and consolidate memories. This, in turn, may produce adverse effects on performance at school. Secondly, sleep loss inevitably results in increased levels of daytime sleepiness, a condition, which is common in adolescents. Not surprisingly, sleep loss and daytime sleepiness have also been linked to more frequent daytime napping.[285] Other data indicate falling asleep during school classes is a common problem in teenagers.[130] Falling asleep during taught classes at school is arguably as a result of inadequate sleep duration and this will almost unequivocally produce adverse effects upon an adolescent's performance at school. Thirdly, there is not enough longitudinal evidence to determine causality between the relationship of sleep duration and school performance. Arguably, reduced school performance may not be a direct result of sleep loss but another factor and could consequently lead to sleep loss through stress mechanisms. It is therefore important to consider stress as a potential confounder in future sleep and academic performance research studies.

Other potential confounders should also be considered in future research studies when assessing the link between sleep duration and academic attainment. For example, pubertal status should be considered as a confounder as this is linked to a delayed sleep phase in pubertal adolescents and with subsequent sleep loss. Furthermore, obesity per se has been associated with reduced school performance[286] and since obesity is also related to sleep duration then this may be an important confounder that past studies have failed to adjust for. Statistical analysis performed for MASSES when assessing the relationship between sleep duration and school performance did control for BMI but the association was still present. Future studies should always adjust for obesity so that results are not confounded. The MASSES also benefitted from adjustment of technology use since it could be argued that some types of technology may enhance learning and school performance. For example, Internet use and TV documentaries may aid an adolescents learning and understanding through providing information. Other studies examining the relationship between sleep and academic performance have not taken this important factor into account during performance of statistical analysis.

In conclusion, evidence from the MASSES as well as other studies consistently shows that inadequate sleep duration in adolescents is associated with reduced academic performance, although longitudinal assessment is required. Future research should conduct more detailed studies of adolescents including sleep architecture and subsequently assess academic performance. This will help to determine if specific sleep stages are related to school performance. These types of studies would ideally need to be performed longitudinally so that comparisons could be drawn between short, adequate and long sleep durations in adolescents. Objective measures of sleep as well as academic performance should be standard for future

studies in this area. Data should also be obtained on other potential confounders, where evidence is pre-existing, and should be subsequently adjusted for in all statistical analyses. Finally, behavioural interventions aimed at improving sleep should be potentially integrated into the curriculum in an attempt to enhance school performance.

3.4.4 Strengths and limitations

The MASSES has a number of strengths and potential limitations. Data collected were all self-reported, with the exception of BMI where objective measures of height and weight were obtained. Although it can be argued that self-reported sleep data is unreliable, the SSHS has been previously validated and is comparable with more objective measures of sleep such as actigraphy.[185] The findings revealed that inadequate sleep was common in the studied sample but this is unlikely to be a consequence of either a diagnosed or undiagnosed sleep disorder(s) since those with diagnosed sleep disorder(s) were excluded and symptoms of OSA were identified and adjusted for in our analyses. The data does not, however, determine causality. It is therefore possible those having more difficulty with sleep may be more inclined to use technology, serving as a distraction and possibly a time-filler before attempting sleep.

Previous adolescent sleep-obesity studies [66;67;70;213;287] did not adjust for engaging in technology as a confounding factor, with the exception of one which controlled for TV viewing only.[68] The results have demonstrated a strong association between technology and sleep and other studies

have related technology use to obesity.[94] Technology use in this age group is easily accessible and highly prevalent so it is essential for future sleep-obesity studies to control for this inter-related factor. It is no longer sufficient to adjust for TV and future research in this area should either adjust for individual or combination technologies. Failure to adjust for multiple technologies or obtain full data concerning different types of device will unequivocally produce an inaccurate and confounded picture of the sleep-obesity relationship. The study benefitted from this information and therefore benefitted from adjustment for combined technology use.

Limitations of the study also include data collected on physical activity and diet that provide only a snapshot of participant lifestyles and may not account for full details on these important variables. Future studies should utilise objective measures of physical activity as well as sleep although this would be difficult from a logistical and financial perspective for large epidemiological studies like MASSES. Objective measures of academic performance should also be identified from school records to ensure subjective schools grades are not biased in any way but this could potentially reduce parental consent rates and result in a smaller sample. The study did not obtain duration of technology use before bedtime; this should be collected in future studies to determine potential dose-dependent relationships. It does, however, seem plausible to assume use of multiple devices would result in longer overall use.

Although MASSES online survey was comprised of validated questionnaires in order, full information was not obtained from these due to a number of technical errors and/or time restraints encountered. On occasions the screen on the survey would freeze during completion, which resulted in incomplete data. Due to school curriculum time restraints students only receive

one attempt at the survey and so these technical errors resulted in incomplete data for some students. Only the first 2 questionnaires were completed by the majority of students. Response rates for the CASQ, which would have allowed more rigorous assessment of daytime sleepiness was just 29.1% and would have therefore reduced the sample size considerably if this data were considered in the analysis. Daytime sleepiness was therefore adjusted for from a question asked in the SSHS. The PDS appeared at the end of the survey and response rate for this was just 28.7% although the majority of those who did answer this questionnaire responded with the "I don't know" option, which is coded as missing values in analysis. Reasons for these responses are likely due to the sensitive nature of the questions relating to puberty. Objective measures of pubertal development by Tanner staging were not possible or ethically applied/approved as this would have considerably reduced the sample. Pubertal development has been previously related to obesity and so this should have been adjusted for in the analysis. However, considering only those with PDS data along with full data on all other variables of interest would reduce the sample size drastically. Subsequently, this reduces the statistical power and may not have allowed for the numerous confounders to be controlled for in the main analyses. Another problem with the online survey was that some answers were 'forced' and thus did not allow the participant to work past these until they were answered. This resulted in some participants skipping unforced questions and answering the forced options only. Subsequently, full data were not available for these individuals. Future questionnaire based studies which are administered online should perhaps force all questions asked to avoid recurrence of this issue.

The 6th form students were all trained in ethical procedures and did not divulge hypotheses to the volunteers and did not influence development or delivery of the project. Use of 6th form students

to assist with data collection, however, may have affected responses from the participants. Volunteers may have been less likely to respond accurately for fear that other students may access their data, despite being advised that data collected would remain confidential. On the other hand, utilising sixth form students may also have had a beneficial effect in terms of student recruitment. The 6th form students were responsible for promoting the research project via posters, delivery of oral presentations about the project during assemblies and registration time as well as managing stands and providing information to parents at school events. These types of promotion would not have been possible across all participating schools by the author of this thesis alone. Arguably, without this marketing from the 6th form students, the volunteers would not have been as motivated to take part in the project and provide their data. Similarly, parents may have been less likely to consent their child to take part without the presence of the project being promoted to raise student and parental awareness at school events. Effectiveness of using students to assist with research has many advantages and disadvantages. Future studies should perhaps aim to examine the effectiveness of utilising students to assist with projects of this kind. Assessment of both positive and negative effects of student involvement should be made to determine how useful it is from a volunteer's as well as a researcher's viewpoint.

Parental consent response rates varied according to the individual school procedure (opt in/out). Schools which operated an opt out method had increased samples of eligible students to participate. The overall parental response rate was 26.7%, which is reasonably low. This could be potentially improved in future studies by raising parental awareness of the research at school events which parents attend such as parents evenings, theatrical shows and more. The response rate of the students was relatively high (72.8%) but the main reasons for not providing data were

absenteeism, attendance at curriculum lessons, musical or sporting activities. Students who did not give consent were not required to provide a reason, thus this remains unexplained. Response rate of students providing data in similar studies could attempt to heighten awareness of the research by placing posters around the school and providing more information through presentations, rather than simply providing the students with an information sheet, which they may not read.

Finally, due to the cross-sectional nature of the study causality remains undetermined, thus prospective studies are needed to verify the findings and external validity of the MASSES. It would be particularly useful to establish at what point of the adolescent time phase sleep patterns change. This, coupled with experimental studies, would help to identify why and when these sleep changes occur and if these alterations are related to other variables such as academic performance, obesity, pubertal development and specific technologies.

3.5 Conclusions

The present findings could have significant public health implications. Constant advances in technology promote media use that is easily accessible and available at any time of the day for all age groups, displacing activities such as consistent sleep patterns and regular exercise. An increasing number of technology devices are being used in the home before bedtime, which may result in shortened sleep durations and increasing levels of obesity. Should these results be confirmed through prospective studies, then technology use may need to be better managed in

adolescents and perhaps engaged in during the day rather than directly before bed. This may then enhance sleep duration, with potential improvement in academic performance, health and wellbeing of the next generation.

4 SLEEP DURATION AND THE METABOLIC SYNDROME IN OLDER ADULTS

4.1 Background

The metabolic syndrome is a cluster of several inter-related risk factors, which includes central adiposity, hyperglycaemia, dyslipidemia, and hypertension. *Chapter 1* provides details of different definitions applied for the metabolic syndrome. The individual components, as well as the syndrome itself, have been associated with increased cardiovascular disease risk. Individuals who have the metabolic syndrome are five times more likely to develop type 2 diabetes mellitus and it is estimated that 80% of the 200 million people with diabetes globally will die of cardiovascular disease.[176] As previous chapters have highlighted, obesity (a component of the metabolic syndrome) is a global problem, which continues to rise. The current picture is concerning with the International Diabetes Federation estimating around 25% of the world's adult population to have the metabolic syndrome.[176] It is therefore essential to develop a better understanding of the syndrome so that future attempts can be made to minimise incidence rates.

4.1.1 Aetiology

The risks associated with the syndrome are well characterised but factors contributing to the pathogenesis of the syndrome are less well understood. The precise mechanisms of the complex

pathways related to the metabolic syndrome have not yet been fully identified. What is known is that the majority of individuals with the syndrome have increased body weight, a sedentary lifestyle, are older and have insulin resistance. Although obesity and insulin resistance appear to be the two main factors driving the development of the syndrome but there is current debate surrounding the cause and consequence of obesity and insulin resistance in relation to the metabolic syndrome. Other underlying causes remain unclear although genetics, ageing, hormone alterations and lifestyle behaviours are all thought to play a causal role with development of the metabolic syndrome.

4.1.2 Sleep as a risk factor for the metabolic syndrome

It is well established that lifestyle behaviours play a major role in the development of type 2 diabetes mellitus and obesity. Physical inactivity, poor diet and excessive food intake are unequivocally associated with the two diseases. More recently, it has emerged that sleep is closely linked with all cause mortality as well as disease. Currently, the largest population study to identify a relationship between sleep duration and mortality sampled 1.1 million American adults aged 30-102 years.[3] The study reported lowest mortality rates in individuals with a nocturnal sleep duration of 7-8 hours. Those who slept for less than 6 hours or more than 8.5 hours were found to be at higher risk for all cause mortality. This relationship was recently re-confirmed by the same group in a smaller sample but utilising objective sleep measures.[178] Furthermore, the original study found a U-shaped association between sleep duration and BMI. The association between sleep duration and obesity has been previously identified and discussed

in *Chapter 1*. Since obesity is an important component of the metabolic syndrome, believed to drive the development of the syndrome, this is an important consideration.

4.1.3 Sleep and its association with components of the metabolic syndrome

There is an abundance of research studies identifying a relationship between sleep duration and the individual features of the metabolic syndrome, the evidence will be presented and discussed for each component in turn.

4.1.3.1 Obesity

Epidemiological and experimental studies have provided strong evidence to suggest a link between short sleep duration and various obesity measures in children,[60] adolescents,[81] and adults.[97] It is believed that sleep loss is associated with obesity through over-activation of the sympathetic nervous system along with metabolic hormone alterations. Long sleep duration has also been linked with an increased BMI but is more widely reported in adults[3] and so it is believed that this may be a consequence of other adverse health conditions rather than a direct cause. Obesity is considered to be a major component of the metabolic syndrome, which may be responsible for driving the development of the other features.

4.1.3.2 Impaired fasting glucose

There is substantial evidence suggesting short sleep and poor quality sleep are linked with insulin resistance, glucose intolerance and the subsequent development of type 2 diabetes.[170] There is a wide range of experimental, cross-sectional epidemiology and prospective cohort studies that have shown either short sleep, long sleep or both are associated with type 2 diabetes and/or insulin resistance.[116;137;154;162;164-166;168;170;180;288-292] A systematic review and meta-analysis of the available data also showed a significant relative risk (RR) of diabetes of 1.28 in short sleepers (≤5-6hrs) and 1.48 in long sleepers (>8-9hrs).[293] Aside obesity, impaired fasting glucose is considered to be a further major component associated with onset of the metabolic syndrome.

4.1.3.3 Elevated blood pressure

It is believed that obesity and impaired fasting glucose are the driving forces behind development of the metabolic syndrome and evidence linking sleep duration with these two components is well established. Hypertension has also been reasonably well investigated in relation to sleep duration. Epidemiological evidence has revealed hypertension is associated with both short and long sleep duration across all age groups.[72;104;116;181;294;295] The Sleep Heart Health Study recruited 5,910 volunteers aged 40-100 years to investigate the relationship between self-reported sleep duration and hypertension. The results showed that those who slept for <6 hours were 66% more likely to have hypertension after adjustment, compared to those who slept 7-<8 hours. Long sleepers (≥9 hours) also had a significantly increased risk with odds ratio of 1.30 (95% CI 1.04-1.62).[104] It is believed that sleep loss stimulates the sympathetic nervous system which may

cause hypertension. Sleep restriction has also been associated with alterations in cortisol secretion which may be linked to hypertension.[296] The mechanisms responsible for the association between long sleep duration and hypertension are less clear but may be associated with depression and/or physical inactivity.

4.1.3.4 Lipid abnormalities

There is a small but limited amount of evidence relating sleep duration with lipid abnormalities such as high cholesterol and raised triglycerides. Emerging evidence has suggested persistent short sleep duration is associated with an increased risk of high cholesterol in adolescents.[182] Both long and short sleep duration have been linked to raised triglyceride levels and lower levels of HDL-cholesterol in adults.[297] Further investigation into the mechanisms which link lipid abnormalities with sleep duration are needed.

Based on the accumulating evidence surrounding sleep duration and its relationship with the individual components of the metabolic syndrome, it is therefore possible that sleep duration may be a potential risk factor for the metabolic syndrome per se, as well as some, or all of the individual components.

4.1.4 Sleep duration and the metabolic syndrome: methods and procedures for literature search/review

A search of the available literature was conducted using the PubMed database using related keywords for manuscripts published in the area of sleep and metabolic syndrome up to and including February 2010. The following searches were conducted for sleep and metabolic syndrome in adult samples:

- Sleep AND metabolic syndrome
- Sleep AND Syndrome X
- Sleep duration AND metabolic syndrome
- Sleep duration AND Syndrome X

Articles were also sourced using the "related article" option in PubMed. Articles were included if they were written in English and the study population was aged ≥18 years. A total of 3 articles were identified, all of which were cross-sectional and are discussed.

4.1.4.1 Sleep duration and the metabolic syndrome

The relationship was between sleep duration and the metabolic syndrome was first hypothesized by Scheen in 1999.[298] Since then, a small number of geographically diverse cross-sectional studies have examined and supported the association between sleep duration and the metabolic syndrome. The literature search performed identified three studies that have directly examined the relationship between the metabolic syndrome and sleep duration. Table 4.1 provides a summary of the studies in this area and details comparisons between designs.

The first study was published in 2007 and was conducted in Portugal.[299] The authors recruited a total sample of 2,164 adults, aged 18-92 years. A structured interview was conducted to obtain self-reported social, demographic, personal and family disease history as well as lifestyle characteristics (physical activity, sedentary leisure activity, resting, work activity, household chores, alcohol intake and smoking status). Sleep was measured by simply asking the participant to indicate the average amount of time spent sleeping. Anthropometric measures and blood samples were obtained following a 12-hour fast to determine the metabolic syndrome, based on the original NCEP ATP III definition.[300] The sleep category of ≥9 hours was used as the reference and compared with ≤6 hours, 7 hours and 8 hours of sleep. After adjustment for age, education, smoking and alcohol consumption in stratified gender analysis, the findings suggested that women obtaining ≤6 hours, 7 hours and 8 hours of sleep had less likelihood of the metabolic syndrome compared to women sleeping ≥9 hours. The corresponding odds ratios (OR) and 95% confidence intervals (CI) were 0.46 (0.28-0.75), 0.50 (0.33-0.76) and 0.58 (0.41-0.84), respectively. Although the authors report a similar relationship in men, the results were not statistically significant following adjustment. The data suggest short sleep is protective against the presence of the metabolic syndrome and that long sleeping hours (≥ 9 hours) is associated with an increased likelihood of the metabolic syndrome in women only. Although this was the first study to directly examine sleep duration and the presence of the metabolic syndrome, the study did not identify specific components of the syndrome or the number of features that long sleep duration was associated with.

The largest studied sample to date comes from the Korean National Health and Nutrition Survey, conducted in 2001.[301] The study examined 4,222 adults aged ≥20 years and compared those who

slept for 7 hours to those sleeping ≤5 hours, 6 hours, 8 hours and ≥9 hours. Despite this study specifically examining the relationship between sleep duration and the metabolic syndrome, the exact methods of ascertaining sleep duration was not detailed within the paper. Objective measures of the metabolic syndrome, defined using the AHA modified NCEP ATP III criteria,[177] were identified. The findings showed that individuals with long sleep duration (8 hours and ≥ 9 hours) had a significantly higher likelihood of the syndrome compared to those sleeping 7 hours, after adjustment for age, gender, family history of diabetes and/or hypertension, residential area, education, income, alcohol, smoking, physical activity and BMI. Although shorter sleeping hours (≤ 5hours and 6 hours) were associated with an increased likelihood of the metabolic syndrome in the base model, after adjustment the relationship became statistically non-significant. Also, the study identified prevalence rates of individual components as well as frequency of components according to sleep duration categories. Those who had ≥2 or ≥3 features demonstrated a statistically significant U-shaped relationship with sleep duration i.e. both the shortest and longest sleep duration participant groups displayed higher prevalence rates. Stratified age analysis revealed that younger participants (<60 years) were driving the association between sleep duration and the presence of the metabolic syndrome. In particular, the hypertension and raised triglycerides components were significantly related to sleep duration in the younger sample group.

The third study from the USA was conducted in a large majority Caucasian sample and is the only published study to assess if sleep duration was an independent potential risk factor for the metabolic syndrome as well as its individual features.[302] The total sample size was comprised of 1,214 participants with a specific focus on mid-life adults, aged 30-54 years. The American

Heart Association definition[177] was applied for determination of the metabolic syndrome as well as its individual features, following a 12-hour overnight fast. Sleep duration was ascertained by asking the participant about the number of hours slept each night in the preceding 7 nights and were asked separately about weekdays and weekends. As previously discussed, however, asking participants about sleep duration in whole hours can distort the data and findings. A referent sleep category of 7-8 hours was applied allowing comparisons to be drawn between those sleeping <6 hours, 6-<7 hours, and >8 hours ('long sleep'). Initial logistic regression analysis demonstrated that 'very short' sleepers (<6 hours), 'short' sleepers (6-<7 hours) and 'long' sleepers (>8 hours) all had an increased likelihood for the presence of the metabolic syndrome, after adjustment, compared to those who slept 7-8 hours. Furthermore, the study identified sleep duration categories that were associated with individual features of the syndrome. In brief, 'long' sleepers had a significantly increased prevalence of the glucose component whilst 'very short' sleep was independently associated with both central adiposity and glucose criteria. The authors then performed sensitivity analysis in a sub-sample (n=1,173) of participants who were not taking anti-hypertensive medication to adjust for the potential confounding factor that these medications are believed to increase glucose concentration. Findings from the sensitivity analysis altered the original results. 'Long' sleep was no longer significantly associated with an increased risk of the metabolic syndrome although the high-density lipoprotein cholesterol (HDL-C) component was. The findings in 'very short' (<6 hours) and 'short' sleepers (6-<7 hours) remained consistent for potential risk of the metabolic syndrome, although slightly attenuated. Furthermore, the central adiposity and glucose components remained as an increased potential risk for 'very short' sleepers.

Table 4.1: The cross-sectional studies directly examining the relationship between sleep duration and the metabolic syndrome.

Sleep measure	Metabolic syndrome measure	Age (yrs)	Sample size	Country	Confounders	Definition
Self-report ≤6hrs, 7hrs, 8hrs, ***≥9hrs***	Objective	18-92	2,164	Portugal	Age, education, smoking, alcohol	NCEP-ATP III
Self-report <5hrs, 6hrs, **7hrs**, *8hrs ≥9hrs*	Objective	≥20	4,222	Korea	Age, gender, family history, SES, education, income, alcohol, smoking, physical activity, BMI	AHA
Self-report *<6hrs*, *6-<7hrs* >8hrs, **7-8hrs**	Objective	30-54	1,214	USA	Age, gender, education, ethnicity, smoking, physical activity, depression, LDL-C	AHA

Sleep categories marked in *italics* indicate significant increased risks for the metabolic syndrome.
Sleep categories marked in **bold** indicate the referent category.
AHA=American Heart Association; NCEP ATP III=National Cholesterol Education Programme Adult Treatment Panel 3rd Report.

4.1.4.2 Rationale for the assessment of sleep duration and the metabolic syndrome

The few studies that have examined the relationship between sleep duration and the metabolic syndrome have produced conflicting results, possibly due to a variation of sleep duration categories, application of different syndrome criteria or adjustment for different confounding factors. The smallest study showed that short and long sleep duration were associated with an increased likelihood of the metabolic syndrome but after exclusion of those taking anti-hypertensive medication, the relationship only remained significant and elevated in 'very short' (<6 hours) and 'short' sleepers (6-<7 hours). The other two larger studies reported long sleep duration to be an independent risk factor for the metabolic syndrome. Notably, these two studies sampled a diverse adult age range comprising of emerging adults, young adults, midlife adults as well as older adults. The US study specifically examined midlife adults but did not obtain or adjust for information relating to stress. Stress is common in this age group and has recently been attributed to increased nocturnal sleep problems and daytime sleepiness.[303] Aside from the stratified age analysis in the Korean study, none of the studies exclusively examined older individuals or considered total sleep duration combining daytime and nocturnal sleep. This group is not only at increased risk of disease but also experience higher levels of sleep fragmentation, as identified in *Chapter 1*. Sleep disruption in older adults is accompanied by increased daytime sleepiness and a higher frequency of napping.[304] Sleep fragmentation and daytime napping become increasingly common with chronological age advancement and so it is therefore essential consider these factors when examining the association between sleep duration and the metabolic syndrome, particularly in older adults.

4.1.5 Aims

The aim of the current chapter is to examine the association between total self-reported sleep duration and prevalence of the metabolic syndrome and its components in a large, well-characterized older Chinese population.

4.1.5.1 Hypotheses

In this chapter, the following hypotheses will be tested, using data from the Guangzhou Biobank Cohort Study (GBCS):

1. Total sleep duration is a potential risk factor for the metabolic syndrome in older Chinese.
2. Total sleep duration is a potential risk factor for the individual features of the metabolic syndrome in older Chinese.

4.2 Methods

The work presented in this chapter is derived from data gathered from the Guangzhou Biobank Cohort Study (GBCS). Background of the study relevant to this chapter is described below.

4.2.1 Overview of the Guangzhou Biobank Cohort Study

The GBCS[305] is a prospective study which aims to recognise health determinants in an older Chinese population who have experienced social transition from pre-industrial to modern economic development.

The study, jointly instigated by the Universities of Birmingham and Hong Kong, as well as the Guangzhou Number 12 People's Hospital, commenced in 2003. The GBCS focuses on individuals aged ≥50 years in a city of Southern China, Guangzhou. After baseline assessment, all participants have been followed up to date for health service use and cause-specific mortality. Participants have been contacted periodically for examination and collection of morbidity information. In participants with specific diseases of interest, more intensive follow-up is in progress.

4.2.1.1 Study area

Guangzhou is the provincial capital of Guangdong Province, in subtropical southern China, covering an area of 7,434.4 km^2 (Figure 4.1). Guangzhou has a population of approximately 10 million. It is southern China's largest city and the third largest city in China.

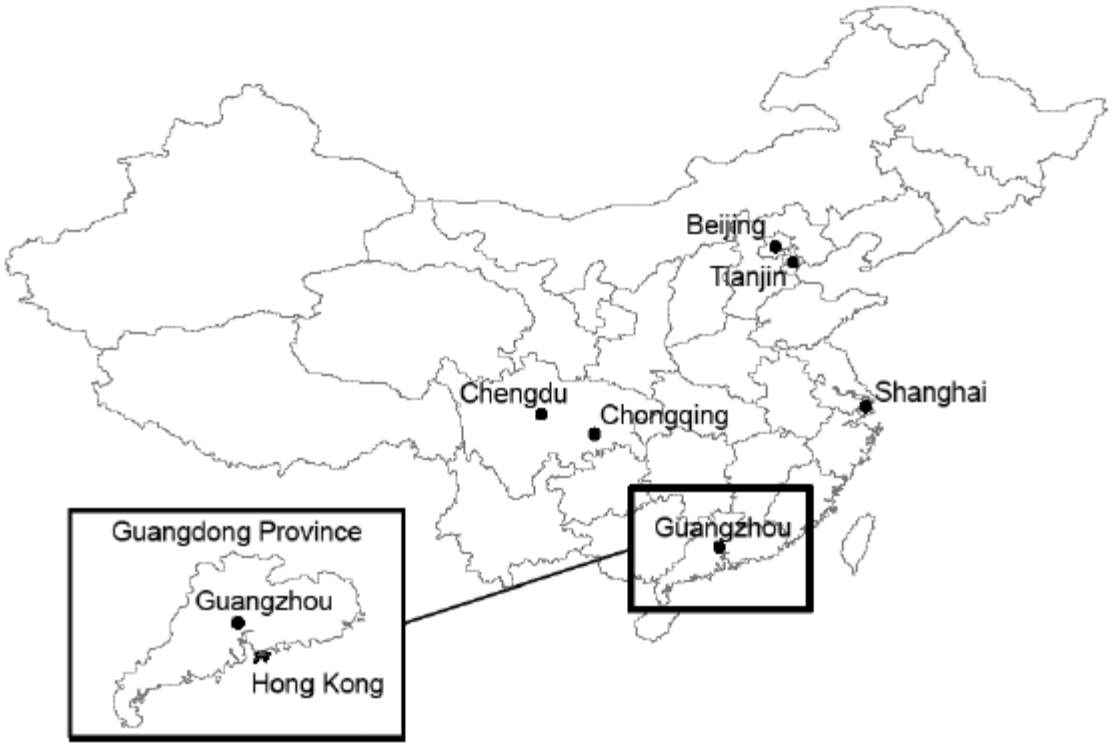

Figure 4.1: Location of major urban areas in China, with populations of more than 10 million in 2000.

4.2.1.2 Study population

As in many developing countries, Chinese patients are not registered with primary care providers, so an alternative sampling frame based on a local community social and welfare association "Guangzhou Zunlao Kangle Xiehui", or "the Guangzhou Health and Happiness Association for the Respectable Elders (GHHARE)" was chosen for this study. The GHHARE, being aligned with the municipal government, has branches throughout the ten districts of Guangzhou, and its membership is open to anyone aged ≥50 years for a nominal monthly fee of 4 Yuan (US$1 = 8

Yuan). Of the 1.4 million permanent Guangzhou residents in this particular age group, approximately 7% are members of GHHARE.

Participant recruitment was performed in three phases (phase I: September 2003 to November 2004; phase II: April 2005 to May 2006; and phase III: September 2007 to February 2008), in each of which 10,000 men and women (or 11% of the membership population) were randomly selected and invited to participate. Participants were included if they were: (1) permanent Guangzhou residents; (2) capable of consenting and agreed to participate; (3) ambulatory; and (4) not receiving treatment for life threatening diseases. Approximately 5% of the eligible subjects refused to participate in each of the recruitment phases. The target of 30,000 participants was reached in 2008, which marked the end of recruitment. The study protocol was approved by the Medical Ethics Committee of the Guangzhou Medical Association. Written, informed consent was obtained prior to participation.

4.2.1.3 Baseline assessment

A total of 30,519 participants attended a dedicated centre at the Guangzhou Number 12 People's Hospital for a half-day examination and interview. Every day, 40-50 participants were enrolled and attended the centre. After fasting blood and urine samples were collected, the participants were given breakfast, and circulated through a series of stations for interviews, examinations and measurements, including anthropometric indices, and blood pressure.

Due to the complexity of the questionnaire and relatively high illiteracy rate, face-to-face interviews were conducted. Trained interviewers administered the interviews collecting information on a broad range of topics, including SES, family and disease histories, cognitive function, smoking history, alcohol and tea use, diet (in the form of a semi-quantitative food frequency questionnaire), and physical activity. Data were directly entered into a computerised structured questionnaire system.

The reliability of the questionnaire responses was examined. Two hundred participants from phase I was re-interviewed after 1 month. Kappa statistics for categorical variables and intra-class correlation coefficient for continuous variables were calculated, and the results suggested good reproducibility of the study data collected.[305] A further random sample of 224 participants reassured validity of self-reported physical activity.[306]

4.2.1.4 Biochemical markers

Blood samples were taken in the GBCS survey following a 12-hour overnight fast. Samples were drawn using a vacutainer tube. Lipids (triglycerides, high-density lipoprotein [HDL]-cholesterol, low-density lipoprotein [LDL]-cholesterol, and total cholesterol) and glucose were determined automatically by a clinical chemistry analyser (Shimadzu CL-8000, Kyoto, Japan) in the central laboratory in the Guangzhou Number 12 People's Hospital.

4.2.1.5 Anthropometric indices

Body weight (to the nearest 0.5 kg), standing height, sitting height, waist circumference, and hip circumference (all to the nearest 0.5 cm) were measured in light indoor clothing and without shoes using a standard protocol.[305]

4.2.1.6 Blood pressure

Blood pressure was measured in a sitting position after a 5-minute rest period. Three measurements were taken at 1-minute intervals using a digital sphygmomanometer (GBCS: Omron 705CP, Japan; HSE: Critikon Dinamap 8100, USA). All three readings of systolic blood pressure, diastolic blood pressure, and heart rate were recorded, but only the last two measurements were used to calculate the respective mean values.

4.2.1.7 Sleep habits

The nurse-led interview included questions on total sleep duration (including daytime naps) in a 24-hour period. Total sleep duration was categorized into <6 hours, 6-<7 hours, 7-<8 hours, 8-<9 hours and ≥9 hours. Data were collected on snoring (yes, no, don't know), current use of hypnotics (yes, no), the presence of insomnia (taking >30 minutes to initiate sleep (yes, no)), and daytime sleepiness (yes, no).

4.2.1.8 The metabolic syndrome and associated components

The metabolic syndrome was defined using the consensus statement,[52] requiring the presence of three or more of the following: (i) elevated waist circumference for Asians (≥90 cm in men or ≥80 cm in women); (ii) elevated triglyceride level: ≥150 mg/dL (1.7 mmol/L), or specific treatment for this lipid abnormality; (iii) reduced HDL-cholesterol: <40 mg/dL (1.03 mmol/L) in males and <50 mg/dL (1.29 mmol/L) in females, or specific treatment for this lipid abnormality; (iv) elevated blood pressure: systolic blood pressure ≥130 or diastolic blood pressure ≥85 mmHg, or treatment of previously diagnosed hypertension; (iv) elevated fasting plasma glucose (FPG) ≥100 mg/dL (≥5.6 mmol/L), or use of medication for elevated glucose.

4.2.1.9 Other measures

Self-reported information on age, gender, smoking history (never, ever) and alcohol consumption (never, ever) was obtained and considered as potential confounders of the relationship between sleep duration and the metabolic syndrome and its individual components. Physical activity was assessed using the short version of the International Physical Activity Questionnaire (IPAQ) validated in the Chinese population (inactive, minimally active, active).[306] Reported educational level (primary or below, secondary, tertiary or above) was collected as a proxy for socioeconomic status (SES).

Evidence suggests mental health conditions, such as depression and anxiety, are significantly associated with both sleep duration[307] and cardiometabolic risk,[308] therefore details on self-reported physician-diagnosed mental illness (yes, no) obtained were used in analyses. Health status was assessed by an objective measure (hospital admission in the previous six months) and a subjective 4-scale rating (very good, good, poor or very poor), which was dichotomized into good or poor. Participants were asked to report if they had ever been diagnosed with any type of cancer (yes, no) and past or present physician-diagnosed cardiovascular disease including coronary heart disease, stroke, myocardial infarction, angina, or peripheral artery disease (yes, no).

4.2.2 Statistical Analysis

Data were analysed using the Statistical Package for the Social Sciences (SPSS, version 15.0 Chicago, IL, USA). The percentages of various study characteristics were calculated according to sleep duration category. ANOVA and chi squared analyses were conducted to determine significant differences between each study characteristic by sleep duration category for continuous and categorical variables, respectively (see Tables 4.2 and 4.3). Logistic regression modelling was used to assess the risk of metabolic syndrome according to sleep duration. The odds ratios (ORs) together with their 95% confidence intervals (CIs) of the three models are presented. The crude model (Model 1) was identified; age and gender were then adjusted for (Model 2). The final model (Model 3) included education level, smoking status, alcohol consumption, physical activity level, self-reported physician-diagnosed mental illness, insomnia,

use of hypnotics, daytime sleepiness, and snoring, in addition to age and gender. Furthermore, when assessing the risk for the individual components, the other features of the metabolic syndrome were adjusted for in Model 3. The only exception was central obesity, which was not adjusted for when assessing the individual components since it is in the direct aetiological pathway for the development of these components and is a significant risk factor for cardiovascular disease.[309]

In an attempt to address the potential issue of reverse causality, participants who perceived themselves as having poor health, who had been admitted to a hospital 6 months prior to participation as well as those who had past or present physician-diagnosed cardiovascular disease and/or cancer were excluded. This sub-sample was classified as 'healthy' (n=21,789) and the logistic regression analysis was repeated.

The total sample was then stratified by age, using a median split, to assess the risk of metabolic syndrome and its components in middle-aged (50-61 years) and older (≥62 years) participants by sleep duration. The fully adjusted odds ratios (OR) together with their 95% confidence intervals (CI) are presented. Further, the total sample was also stratified by gender to assess the risk of metabolic syndrome and its individual features in males and females according to the sleep duration categories.

4.3 Results

Of the total sample, 29,333 had complete information on all variables of interest and were included for subsequent analyses. There were more women (n=21,239) than men (n=8,094) because of the predominance of women in the membership (due to the population age structure), and a combination of job engagements and a cultural reluctance to give blood among men. Participant age ranged from 50 to 96 years; the men were slightly older (mean ± SD: 63.9 ± 6.7 years) than the women (60.6 ± 7.1 years).

Of the total sample, 13.5% reported a total sleep duration of <6 hours ("short" sleepers) whilst 8.8% reported a total sleep duration of ≥9 hours ("long" sleepers). The characteristics of the study population according to sleep duration are summarized in Table 4.2. In men, long total sleep duration (≥9 hours) was more common (35.8%) compared to 21.1% who reported short total sleep duration (<6 hours). The use of hypnotics decreased as total sleep duration increased, with short sleepers being more likely to use hypnotics (7.4%) compared to long sleepers (1.5%). Similarly, reports of daytime sleepiness were more prevalent in short sleepers (5.7%) compared to long sleepers (2.3%). Differences in metabolic markers according to different total sleep duration categories are detailed in Table 4.3.

Logistic regression models for the metabolic syndrome and its various components are shown in Table 4.4. Briefly, the data show a statistically significant likelihood of the metabolic syndrome in those with longer total sleep durations (8-<9 and ≥9 hours) after adjustment for potential confounders. The corresponding odds ratios were 1.16 (1.08-1.25) and 1.21 (95% CI 1.10-1.34),

respectively. The likelihood for raised triglycerides and central obesity were significantly increased with corresponding odds ratios 1.13 (95% CI 1.02-1.24) and 1.12 (95% CI 1.01-1.23), respectively. Associations between the other components and longest total sleep duration (≥9 hours) were small and did not reach statistical significance.

Table 4.5 shows that in the 'healthy' sub-sample, the increased likelihood of the metabolic syndrome remained in long sleepers although the fully adjusted OR was slightly attenuated 1.19 (1.06-1.34). ORs across all components of the metabolic syndrome remained similar by sleep duration although most were slightly attenuated.

Total sample stratified age analysis, using a median split, was performed and the fully adjusted logistic regression model for the metabolic syndrome and its various components by total sleep duration are shown in Table 4.6. In summary, 'middle-aged' participants (50-61 years) with the longest total sleep duration (≥9 hours) had an increased likelihood of impaired fasting glucose (IFG) and central obesity with OR of 1.17 (95% CI 1.03-1.32) and 1.25 (95% CI 1.09-1.42), respectively. 'Older' participants (>61 years) with the longest total sleep duration had an increased likelihood of raised triglycerides, OR 1.18 (95% CI 1.02-1.37). Collectively, 'middle-aged' participants with the longest total sleep duration had a stronger likelihood of the metabolic syndrome, OR 1.33 (95% CI 1.16-1.52), compared to the total sample.

Total sample stratified gender analysis was performed and the fully adjusted logistic regression model for the metabolic syndrome and its various components by sleep duration are shown in Table 4.7. In summary, men who had a total sleep duration of 8-<9 hours had a significantly

increased odds of the metabolic syndrome 1.18 (95% CI 1.02-1.36) and reduced HDL-Cholesterol 1.24 (95% CI 1.03-1.48). Similarly, women with long total sleep durations of 8-<9 hours and ≥9 hours had significantly increased odds of the metabolic syndrome 1.12 (95% CI 1.03-1.22) and 1.19 (95% CI 1.05-1.34), respectively. Furthermore, women with long total sleep duration (≥9 hours) had an increased likelihood of hypertension and raised triglycerides, OR 1.16 (95% CI 1.03-1.30) and 1.14 (95% CI 1.02-1.29). Women who slept 8-<9 hours also had a significantly increased likelihood of IFG, OR 1.10 (95% CI 1.01-1.19) compared to those sleeping 7-<8 hours.

Table 4.2: The characteristics of 29,333 Chinese adults aged ≥50 years according to total sleep duration, Guangzhou Biobank Cohort Study, 2003-2008.

Characteristics	Total sleep duration					p value
	<6 hrs (n=3,961)	6-<7 hrs (n=7,146)	7-<8 hrs (n=8,754)	8-<9 hrs (n=6,905)	≥9 hrs (n=2,567)	
Gender						<0.001
Male	21.1	24.8	27.7	31.0	35.8	
Female	78.9	75.2	72.3	69.0	64.2	
Age in years	63.3 (7.3)	62.2 (7.2)	60.8 (7.0)	60.9 (6.9)	61.2 (7.1)	<0.001
Education						<0.001
Primary or below	54.6	47.4	38.2	37.9	40.7	
Secondary	24.1	25.2	28.3	27.1	27.4	
Tertiary or above	21.3	27.4	33.5	35.0	31.9	
Physical activity†						0.083
Inactive	8.2	7.8	8.7	7.8	8.3	
Minimally active	39.6	40.1	41.2	41.3	40.1	
Active	52.2	52.1	50.1	50.9	51.6	
Smoking status						<0.001
Never	79.0	77.3	75.6	73.8	69.9	
Ever	21.0	22.7	24.4	26.2	30.1	
Alcohol use						0.013
Never	88.1	88.2	87.4	87.3	85.7	
Ever	11.9	11.8	12.6	12.7	14.3	
Snoring						<0.001
No	39.2	38.3	37.4	37.3	39.4	
Yes	37.5	42.3	43.2	44.6	45.5	
Don’t know	23.3	19.4	19.4	18.1	15.1	
Hypnotics						<0.001
No	92.6	96.9	98.0	98.8	98.5	
Yes	7.4	3.1	2.0	1.2	1.5	
Daytime sleepiness						<0.001
No	94.3	95.7	97.0	97.5	97.7	
Yes	5.7	4.3	3.0	2.5	2.3	

Data are means (SD) or percentages.
†Physical activity was quantified using the short version of the International Physical Activity Questionnaire (IPAQ).

Table 4.3: The differences in metabolic markers among 29,333 Chinese adults aged ≥50 years according to total sleep duration, Guangzhou Biobank Cohort Study, 2003-2008.

	Total sleep duration					
Metabolic features	<6 hrs (n=3,961)	6-<7 hrs (n=7,146)	7-<8 hrs (n=8,754)	8-<9 hrs (n=6,905)	≥9 hrs (n=2,567)	p value
Total cholesterol mmol/L	5.95 (1.15)	5.92 (1.15)	5.93 (1.12)	5.93 (1.14)	5.89 (1.14)	0.301
Triglycerides mmol/L*	0.16 (0.23)	0.15 (0.23)	0.15 (0.23)	0.16 (0.23)	0.18 (0.23)	0.009
Systolic blood pressure mmHg	131.42 (22.62)	131.10 (22.36)	129.14 (21.45)	130.36 (22.35)	131.44 (21.89)	<0.001
Fasting glucose mmol/L	5.82 (1.73)	5.76 (1.65)	5.67 (1.59)	5.77 (1.69)	5.82 (1.78)	<0.001
Waist circumference cm	78.66 (9.05)	78.91 (9.09)	78.53 (8.95)	78.95 (8.85)	79.65 (9.09)	<0.001
HDL-Cholesterol mmol/L	1.69 (0.40)	1.68 (0.40)	1.66 (0.40)	1.63 (0.40)	1.62 (0.39)	<0.001
LDL-Cholesterol mmol/L	3.26 (0.71)	3.24 (0.71)	3.27 (0.70)	3.27 (0.71)	3.26 (0.71)	0.048
Body mass index Kg/m²	23.64 (3.43)	23.80 (3.30)	23.78 (3.29)	23.81 (3.25)	23.86 (3.44)	0.061

Data are presented as mean (standard deviation).
*Triglycerides were log transformed due a non-normal distribution.

Table 4.4: The prevalence and odds ratios for the presence of the metabolic syndrome and its associated components among 29,333 Chinese adults aged ≥50 years according to total sleep duration, Guangzhou Biobank Cohort Study, 2003-2008.

	Metabolic syndrome				**Reduced HDL-cholesterol**			
Total sleep duration	**n (%)**	**Model 1**	**Model 2**	**Model 3**	**n (%)**	**Model 1**	**Model 2**	**Model 3**
<6 hrs	1,142 (28.8)	1.14* (1.05-1.24)	0.98 (0.90-1.06)	0.97 (0.88-1.06)	634 (16.0)	0.95 (0.86-1.05)	0.90 (0.82-1.00)	0.88* (0.79-0.99)
6-<7 hrs	2,020 (28.2)	1.10* (1.03-1.18)	1.02 (0.95-1.09)	1.00 (0.93-1.08)	1,152 (16.1)	0.96 (0.88-1.04)	0.93 (0.86-1.01)	0.93 (0.85-1.01)
7-<8 hrs	2,303 (26.2)	1.00	1.00	1.00	1,467 (16.7)	1.00	1.00	1.00
8-<9 hrs	1,995 (28.8)	1.14* (1.06-1.22)	1.16* (1.08-1.25)	1.16* (1.08-1.25)	1,233 (17.8)	1.08 (0.99-1.17)	1.09* (1.01-1.19)	1.07 (0.98-1.17)
≥ 9hrs	762 (29.6)	1.18* (1.07-1.30)	1.22* (1.11-1.35)	1.21* (1.10-1.34)	454 (17.7)	1.07 (0.95-1.20)	1.10 (0.98-1.23)	1.05 (0.93-1.18)
	Elevated blood pressure				**Impaired fasting glucose**			
	n (%)	**Model 1**	**Model 2**	**Model 3**	**n (%)**	**Model 1**	**Model 2**	**Model 3**
<6 hrs	2,216 (55.9)	1.15* (1.06-1.24)	0.96 (0.89-1.04)	0.93 (0.85-1.01)	1,623 (41.0)	1.18* (1.09-1.27)	1.07 (0.99-1.16)	1.06 (0.99-1.16)
6-<7 hrs	3,969 (55.4)	1.12* (1.06-1.20)	1.02 (0.96-1.09)	1.00 (0.93-1.07)	2,808 (39.2)	1.10* (1.03-1.17)	1.04 (0.97-1.11)	1.01 (0.95-1.08)
7-<8 hrs	4,609 (52.5)	1.00	1.00	1.00	3,253 (37.1)	1.00	1.00	1.00
8-<9 hrs	3,720 (53.8)	1.05 (0.99-1.12)	1.04 (0.98-1.11)	1.02 (0.95-1.09)	2,737 (39.6)	1.11* (1.04-1.19)	1.11* (1.04-1.19)	1.08* (1.01-1.16)
≥ 9 hrs	1,448 (56.3)	1.16* (1.07-1.27)	1.14* (1.04-1.25)	1.08 (0.98-1.19)	1,042 (40.5)	1.16* (1.06-1.27)	1.14* (1.05-1.25)	1.08 (0.98-1.19)
	Elevated triglycerides				**Elevated waist circumference**			
	n (%)	**Model 1**	**Model 2**	**Model 3**	**n (%)**	**Model 1**	**Model 2**	**Model 3**
<6 hrs	1,331 (33.6)	0.99 (0.92-1.07)	0.97 (0.90-1.05)	0.92 (0.84-1.00)	1,479 (37.3)	1.20* (1.11-1.30)	1.01 (0.93-1.10)	1.02 (0.94-1.11)
6-<7 hrs	2,337 (32.6)	0.95 (0.89-1.01)	0.94 (0.88-1.00)	0.90* (0.84-0.97)	2,599 (36.3)	1.15* (1.08-1.23)	1.06 (0.99-1.13)	1.04 (0.98-1.12)
7-<8 hrs	2,966 (33.8)	1.00	1.00	1.00	2,905 (33.1)	1.00	1.00	1.00
8-<9 hrs	2,499 (36.1)	1.11* (1.04-1.18)	1.11* (1.04-1.19)	1.08* (1.01-1.16)	2,309 (33.4)	1.01(0.95-1.08)	1.05 (0.98-1.12)	1.04 (0.97-1.12)
≥ 9 hrs	960 (37.3)	1.17* (1.06-1.28)	1.18* (1.08-1.29)	1.13* (1.02-1.24)	888 (34.5)	1.07 (0.97-1.17)	1.15* (1.05-1.27)	1.12* (1.01-1.23)

Data are odds ratio (95% confidence interval) unless otherwise stated.
* $p < 0.05$.
Model 1: unadjusted; Model 2: adjusted for age, gender.
Model 3: additionally adjusted for education, smoking, physical activity, diagnosed mental illness, insomnia, use of hypnotics, daytime sleepiness, alcohol consumption, snoring, and as appropriate, mean systolic blood pressure, glucose, total cholesterol, and triglycerides.

Table 4.5: The prevalence and adjusted odds ratios for the presence of the metabolic syndrome and its associated components among 21,789 'healthy' Chinese adults aged ≥50 years according to total sleep duration, Guangzhou Biobank Cohort Study, 2003-2008.

Total sleep duration	Metabolic syndrome (n=5,790)	Reduced HDL-cholesterol (n=3,379)	Elevated blood pressure (n=11,476)	Impaired fasting glucose (n=8,213)	Elevated triglycerides (n=7,343)	Elevated waist circumference (n=7,351)
<6 hrs	0.93 (0.84-1.04)	0.80* (0.70-0.92)	0.92 (0.83-1.02)	1.01 (0.91-1.12)	0.90 (0.81-1.00)	1.03 (0.93-1.14)
6-<7 hrs	0.98 (0.90-1.07)	0.87* (0.79-0.97)	0.96 (0.89-1.04)	1.01 (0.94-1.10)	0.90* (0.83-0.98)	1.05 (0.97-1.14)
7-<8 hrs	1.00	1.00	1.00	1.00	1.00	1.00
8-<9 hrs	1.14* (1.05-1.23)	1.06 (0.96-1.17)	0.99 (0.92-1.07)	1.10* (1.02-1.19)	1.07 (0.98-1.16)	1.02 (0.94-1.10)
≥ 9 hrs	1.19* (1.06-1.34)	0.96 (0.83-1.11)	1.07 (0.96-1.19)	1.11 (0.99-1.24)	1.09 (0.97-1.22)	1.14* (1.02-1.28)

Data are odds ratio (95% confidence interval) unless otherwise stated.
* p <0.05
ORs were adjusted for age, gender, education, smoking, physical activity, insomnia, use of hypnotics, daytime sleepiness, diagnosed mental illness, alcohol consumption, snoring, and as appropriate, mean systolic blood pressure, glucose, total cholesterol, and triglycerides.

Table 4.6: The prevalence and adjusted odds ratios for the presence of the metabolic syndrome and its associated among 15,574 'middle-aged' and 13,814 'older' Chinese according to total sleep duration, Guangzhou Biobank Cohort Study, 2003-2008.

Total sleep duration	Metabolic Syndrome	Reduced HDL-cholesterol	Elevated blood pressure	Impaired Fasting Glucose	Elevated triglycerides	Elevated waist circumference
Middle-aged (n)	3,629	2,564	6,916	5,229	5,350	4,827
<6 hrs	1.05 (0.91-1.20)	0.79* (0.66-0.93)	0.91 (0.80-1.02)	1.08 (0.95-1.23)	1.01 (0.89-1.15)	1.00 (0.88-1.14)
6-<7 hrs	1.03 (0.92-1.14)	0.87* (0.77-0.99)	0.95 (0.87-1.04)	1.04 (0.94-1.14)	0.88* (0.80-0.98)	1.08 (0.98-1.18)
7-<8 hrs	1.00	1.00	1.00	1.00	1.00	1.00
8-<9 hrs	1.14* (1.03-1.26)	1.08 (0.96-1.21)	1.00 (0.92-1.09)	1.05 (0.96-1.15)	1.09 (0.99-1.20)	1.02 (0.93-1.13)
≥ 9 hrs	1.33* (1.16-1.52)	1.04 (0.88-1.22)	1.07 (0.95-1.21)	1.17* (1.03-1.32)	1.08 (0.94-1.23)	1.25* (1.09-1.42)
Older (n)	4,593	2,376	9,046	6,234	4,743	5,353
<6 hrs	0.93 (0.83-1.05)	0.97 (0.83-1.12)	1.00 (0.89-1.13)	1.05 (0.94-1.18)	0.84* (0.74-0.95)	1.04 (0.93-1.17)
6-<7 hrs	0.98 (0.89-1.09)	0.99 (0.87-1.12)	1.09 (0.98-1.20)	0.99 (0.90-1.09)	0.91 (0.83-1.01)	1.01 (0.91-1.11)
7-<8 hrs	1.00	1.00	1.00	1.00	1.00	1.00
8-<9 hrs	1.18* (1.07-1.31)	1.06 (0.93-1.21)	1.05 (0.94-1.17)	1.11* (1.00-1.22)	1.06 (0.96-1.19)	1.07 (0.96-1.18)
≥ 9 hrs	1.10 (0.95-1.27)	1.06 (0.88-1.27)	1.09 (0.94-1.26)	0.99 (0.86-1.14)	1.18* (1.02-1.37)	1.00 (0.87-1.16)

Data are odds ratio (95% confidence interval) unless otherwise stated.
* $p < 0.05$.
ORs were adjusted for age, gender, education, smoking, physical activity, insomnia, use of hypnotics, daytime sleepiness, diagnosed mental illness, alcohol consumption, snoring, and as appropriate, mean systolic blood pressure, glucose, total cholesterol, and triglycerides.

Table 4.7: The prevalence and adjusted odds ratios for the presence of the metabolic syndrome and its associated components among 21,239 women and 8,094 men according to total sleep duration, Guangzhou Biobank Cohort Study, 2003-2008.

Total sleep duration	Metabolic Syndrome	Reduced HDL-cholesterol	Elevated blood pressure	Impaired Fasting Glucose	Elevated triglycerides	Elevated waist circumference
Males n(%)	1788 (22.1)	1079 (13.3)	4778 (59.0)	3269 (40.4)	2619 (32.4)	1549 (19.1)
<6 hrs	1.06 (0.87-1.30)	1.04 (0.80-1.36)	0.88 (0.74-1.05)	1.09 (0.92-1.30)	0.89 (0.74-1.07)	0.95 (0.77-1.19)
6-<7 hrs	1.13 (0.97-1.31)	1.08 (0.89-1.31)	0.96 (0.84-1.09)	1.09 (0.96-1.24)	0.91 (0.79-1.05)	1.00 (0.85-1.18)
7-<8 hrs	1.00	1.00	1.00	1.00	1.00	1.00
8-<9 hrs	1.18* (1.02-1.36)	1.24* (1.03-1.48)	0.93 (0.82-1.05)	1.01 (0.89-1.14)	1.10 (0.97-1.26)	0.91 (0.78-1.07)
≥ 9 hrs	1.15 (0.96-1.39)	1.18 (0.93-1.49)	0.91 (0.77-1.06)	1.03 (0.88-1.21)	1.07 (0.90-1.26)	0.94 (0.77-1.15)
Females						
n(%)	6424 (30.2)	3858 (18.2)	11155 (52.5)	8171 (38.5)	7459 (35.1)	8617 (40.6)
<6 hrs	0.96 (0.86-1.06)	0.85* (0.75-0.96)	0.96 (0.88-1.06)	1.08 (0.98-1.19)	0.95 (0.86-1.04)	1.04 (0.95-1.15)
6-<7 hrs	0.98 (0.90-1.06)	0.90* (0.82-1.00)	1.03 (0.95-1.11)	1.01 (0.93-1.09)	0.93 (0.86-1.00)	1.04 (0.96-1.13)
7-<8 hrs	1.00	1.00	1.00	1.00	1.00	1.00
8-<9 hrs	1.12* (1.03-1.22)	1.02 (0.92-1.12)	1.04 (0.96-1.12)	1.10* (1.01-1.19)	1.05 (0.97-1.14)	1.03 (0.95-1.12)
≥ 9 hrs	1.19* (1.05-1.34)	1.02 (0.88-1.18)	1.16* (1.03-1.30)	1.09 (0.97-1.22)	1.14* (1.02-1.29)	1.12 (1.00-1.26)

Data are odds ratio (95% confidence interval) unless otherwise stated.
* $p < 0.05$.
ORs were adjusted for age, gender, education, smoking, physical activity, insomnia, use of hypnotics, daytime sleepiness, diagnosed mental illness, alcohol consumption, snoring, and as appropriate, mean systolic blood pressure, glucose, total cholesterol, and triglycerides.

4.4 Discussion

The results of this chapter demonstrate that long total sleep duration is independently associated with an increased likelihood of the metabolic syndrome. Adjusted stratified age analysis revealed middle-aged participants with long total sleep duration (≥9 hours) had an increased likelihood of impaired fasting glucose (IFG) and central obesity whilst older participants were at increased risk of having raised triglycerides. Gender stratification showed that females with longer than recommended total sleep durations (8-<9 hours or (≥9 hours) had an increased risk of hypertension, IFG and raised triglycerides as well as for the presence of the metabolic syndrome per se. Males with long total sleep duration had increased odds of the metabolic syndrome as well as reduced HDL-C. In the total sample, although odd ratios generally increased, there were no statistically significant associations between the various components and long total sleep after full adjustment, except for raised triglycerides and central obesity. After full adjustment, short total sleep duration was not related to the presence of the metabolic syndrome or any of its features in this sample of older Chinese.

Despite early hypotheses that sleep duration could predispose individuals to the metabolic syndrome,[298] this relationship has only recently been explored cross-sectionally. In a study of middle-aged American Caucasians previously discussed, short and long sleep duration was associated with a higher risk of the metabolic syndrome after adjustment for potential confounders. The relationship, however, remained only in short sleepers following sensitivity analysis where the statistical tests were re-performed in a sub-sample of participants who were not taking anti-hypertensive medications.[302] This type of sensitivity analysis was not appropriate

in our study given that the consensus statement applied states treatment for hypertension classifies individuals as having the presence of that particular feature. In the Korean National Health and Nutrition Survey,[301] only long sleep duration was significantly associated with an increased prevalence of the metabolic syndrome. Furthermore, this study also reported more components of the metabolic syndrome associated with sleep duration in younger subjects (<60 years) compared to older counterparts, both aspects being consistent with the findings in this chapter. A study from Portugal also demonstrated that increasing sleep hours was associated with an elevated risk of the metabolic syndrome,[299] again in line with the GBCS study. It should, however, be noted that this study combined reports of time lying awake as well as time spent sleeping to determine a period of rest rather than sleep per se. Furthermore, the Portuguese study, despite obtaining information about participant's level of physical activity, this was not adjusted for, which could confound the results, particularly as it is well established that physical activity is associated with positive health outcomes.

Although the consensus definition (introduced in 2009) is considered to have worldwide application, the three studies discussed predated this. The Portuguese study was the only one that applied the NCEP ATP III criteria, as identified in *Chapter 1*. Both the US and Korean studies used a version of the NCEP ATP III, revised by the American Heart Association (AHA), which identified the fasting glucose criterion as 5.6 mmol/L rather than 6.1 mmol/L, the same as the one applied in the GBCS. Findings from the studies are similar but control for different potential confounders, which could explain the heterogeneous findings. Despite the overwhelming evidence demonstrating that short sleep duration is associated with diabetes and obesity,[97;139;146;170;310;311] the evidence for the metabolic syndrome per se, arguably indicates that

long sleep duration is a significant and independent risk factor, especially in the older age group. It should, however, be noted that the three studies examining the link, as well as the GBCS were all cross-sectional. To date, there is no longitudinal evidence to confirm a causal link. Still, the possibility remains that long sleep is a consequence, rather than a cause of the metabolic syndrome. The GBCS, however, did attempt to address this issue in the best way possible with the data available repeating the analysis in a 'healthy' sub-sample of participants. The relationship remained significant for long sleepers and the metabolic syndrome although the odds were slightly attenuated.

Obesity and type 2 diabetes mellitus are not only rising at an irrepressible global rate but are also believed to be the two main components driving the development of the metabolic syndrome. Each will now be discussed in relation to sleep duration.

4.4.1 Sleep duration and obesity

The results of this study do not show an association between short total sleep duration and obesity in the older Chinese sample, after adjustment for age and gender. This study, however, did find a significant association between long total sleep and obesity after full adjustment. This is consistent with other large cross-sectional population studies[3;116] as well as longitudinal evidence.[123] Furthermore, this relationship remained and strengthened slightly after adjustment of ill health in the sub-sample of 'healthy' individuals. Stratified analyses also showed the association between long total sleep duration and central obesity in middle-aged but not older Chinese, consistent with other large scale evidence.[118] Also, gender stratification analysis almost

reached statistical significance in long sleeping women with central obesity, OR 1.12 (95% CI 1.00-1.26). It appears that short sleep duration and its association with obesity diminishes with age progression, as suggested in a systematic review[132] and confirmed by a more recent large Australian study.[118] Conversely, a large study of older individuals measured sleep by actigraphy showed a strong association between short but not long sleep duration with obesity, BMI, BF% and central body fat distribution.[110] Another large study conducted in older adults in the Netherlands, utilising actigraphy, showed a U-shaped association between sleep duration with BMI and obesity. Interestingly, after adjustment for sleep fragmentation, short sleep did not remain significantly associated with obesity.[112] The possibility therefore still remains that obstructive sleep apnea may confound the short sleep-obesity relationship, through the effects of sleep fragmentation.

The mechanisms underpinning the observed associations between sleep and obesity are believed to relate to hormone alterations. Experimental studies have demonstrated that shortening sleep duration can disrupt the normal functionality of metabolic and endocrine action.[146;170;310] Experimental studies that have manipulated sleep to both reduced and extended durations have shown that short sleep duration increases levels of ghrelin, a hormone signalling of hunger; and decreases leptin, which is linked to satiety.[146] Alterations in these two appetite-regulating hormones can, in part, help to explain and better understand the development of obesity, particularly as US polls have indicated a 1-2 hour reduction in sleeping hours in recent decades.[26] The explanation for long sleep and its association with obesity may be more simplistic. Longer sleep duration provides less time for the individual to engage in physical activity and can therefore directly contribute to lower energy expenditure, which can lead to subsequent weight

gain. It is also possible that chronic inflammation associated with central obesity may, in turn, increase sleep duration due to metabolic and sleep-inducing effects of some pro-inflammatory cytokines.[312]

4.4.2 Sleep duration and diabetes

The results of this study only found a significant association between impaired fasting glucose (IFG) and short total sleep duration in the univariate model but after adjustment, this association diminished. Conversely, long total sleep was associated with IFG after adjustment for age and gender but not after full adjustment for other potential confounders. Interestingly, in the 'healthy' sub-sample, those who slept for 8-<9 hours had a significantly increased risk of IFG. Stratified analyses showed middle-aged and older individuals as well as women with longer total sleep duration had a significant and increased risk of IFG. The association between sleep duration and type 2 diabetes is again heterogeneous with some reporting increased risks in short sleepers only,[170;313] both long and short sleep duration,[164-166;180;291;314] and others just in women.[292] Notably, the large US cohort of men demonstrated a causal association between short and long sleep duration and the development of type 2 diabetes after a 15-17 year follow up period. The relative risk in long sleepers (>8 hours), however, were much higher (3.12) compared to those who were self-reported short sleepers (≤5 hours and 6 hours) who had a relative risk of 1.95 for diabetes onset.[165] These findings are parallel with that of the First National Health and Nutrition Examination Survey (NHANES), suggesting a heightened risk in long sleepers compared to short sleepers.[180] Further support for a stronger association between long sleep and diabetes development comes from a recently published systematic review and

meta-analysis which reported a relative risk of 1.28 in short sleepers compared to an increased relative risk of 1.48 in long sleepers.[293]

In relation to the development of type 2 diabetes, it is believed that short sleep duration is contributory to insulin resistance through a number of potential mechanisms including elevated sympathetic activity, a reduction in brain glucose utilization, increased growth hormone secretion and elevated evening cortisol. There is a less clear explanation of potential mechanisms mediating the effect of long sleep duration as a direct potential cause of type 2 diabetes. Depressive symptoms, SES, reduced physical activity, undiagnosed health conditions, and ill health have all been shown to be associated with long sleep which will undoubtedly confound the relationship with mortality and morbidity. The GBCS, however, did adjust for diagnosed mental illnesses, education and physical activity level as well as ill health in the 'healthy' sub-sample. A recent review suggested a link between diabetes mellitus and obstructive sleep apnoea (OSA).[315] Snoring and daytime sleepiness, however, both common features of OSA, were adjusted for in the analyses but the relationship remained between long total sleep and IFG. The sample did not display any relationship between sleep duration and hypertension except for in the gender-stratified analysis where long sleeping women had an increased risk. Hypertension is a common co-morbidity of OSA,[316] further suggesting OSA may not be responsible for the observed association. Future studies should make more detailed assessments of the sleep parameters and diabetes such as daytime napping. Although the evidence highlighted is reasonably consistent surrounding sleep duration and type 2 diabetes mellitus, the association is more commonly found with short sleep duration, however defined. Despite some reporting a U-shaped association, most have highlighted short sleep duration with

less emphasis or explanation of long sleep duration. One feature that has not been considered so far in the relationship between sleep duration and T2DM, includes daytime napping. The effect of napping on diabetes should be investigated, particularly in older individuals who have an increased propensity of napping and who are at increased risk of T2DM development.

4.4.3 Sleep duration and other components of the metabolic syndrome

An independent relationship was found between long total sleep duration and elevated triglycerides in the total sample with the association in the older participants driving this observation. An increasing number of experimental studies have focused on identifying mechanisms between short sleep duration and raised triglycerides but data is lacking in long sleepers. One recent study reported an increased odds of 1.45 (95% CI 1.00-2.11) for long sleepers and elevated triglycerides.[317] Raised triglycerides are linked to an increased risk of cardiovascular disease[318] which is also associated with long sleep duration, diabetes, obesity and reduced physical activity, all of which were controlled for in the present study. Future studies should attempt to identify independent mechanisms in both long and short sleepers. Some data, however, suggest that long sleep may be a stronger predictor of adverse outcomes than short sleep duration[319] but further investigation and confirmation is needed.

4.4.4 Causality

It is well documented that sleep duration and quality declines with age.[320] Conversely, disease increases with age but which occurs first is difficult to determine. To address the possibility of

long sleep duration as a consequence of ill health, the same analyses were conducted in a sub-sample of 'healthy' participants. The relationships between the metabolic syndrome and most components were slightly attenuated after adjustment compared to the total sample analysis, suggesting long total sleep duration is a determinant of an increased risk of the metabolic syndrome in this large sample of 'healthy' older Chinese. Of course, this data is cross-sectional and causality cannot be determined but collection of the GBCS follow up data will provide opportunity to identify causal inferences, which no other study has done in this area to date. It should, however, be acknowledged that the issue of reverse causality was addressed to the best possible extent with the data available.

4.4.5 Strengths and limitations

The study benefits from a large sample size, which is sufficiently powered statistically to address a wide variety of potential confounders, more than most studies. While attempts were made to control for a wide range of potential confounders, it is acknowledged that the observed association could have been confounded by factors that were not measured. That said, the GBCS was conducted in a setting with unique social and cultural characteristics, which enables the investigation of issues that might not be possible in many Western populations. The GBCS is also the first study to assess the relationship between sleep duration and the metabolic syndrome in older adults who are at increased risk of disease. It is also the only study which has specifically assessed total sleep duration rather than nocturnal sleep duration. Future studies should, however, make assessments of daytime sleep duration and frequency as well as nocturnal

sleep duration as well as investigating shift workers in an attempt to identify if the timings of sleep are important in relation to the metabolic syndrome and other diseases.

There are several potential limitations to the GBCS. Due to the cross-sectional design, the temporal sequence of the association between total sleep duration and the metabolic syndrome and its components was unable to be established. Prospective studies are needed to further examine the relationship. Although recruited from an association whose membership is open to anyone for a nominal fee, our sample is unlikely to be totally representative of the older population in China. Nevertheless, bias would only be introduced if we had systematically missed those who had a specific relation between total sleep duration and the metabolic syndrome, which is unlikely. The lack of objective sleep measures and its associated variables might also limit the interpretation of the finding, but actigraphy and polysomnography are not practical in a large scale study, and the inaccuracy should most likely have weakened any association, which might account for the lack of significant association between short sleep duration and hyperglycaemia, central obesity and hypertension.

4.5 Conclusions

The findings suggest an association between long total sleep duration and higher prevalence of the metabolic syndrome in older Chinese. The present finding highlights the need for further prospective and mechanistic studies to assess the nature of these associations, particularly in naturally long sleepers. Mechanistic studies have to date concentrated on the metabolic consequences of sleep deprivation which is also an easier experimental paradigm to study. Other potential mechanisms requiring exploration is the impact of sleep duration on circadian

regulation including secretion of metabolic hormones. If long sleep duration is shown to increase the risk of metabolic syndrome and some or all of its components, this would have important public health implications where there is an emerging diabetes, obesity and metabolic syndrome epidemic in the face of rapid socioeconomic transition.

5 THE DEVELOPMENT OF AN EXPERIMENTAL SLEEP MODEL

5.1 Background

The recent global rise in obesity and type 2 diabetes mellitus and other metabolic disorders has instigated much research interest. Although physical activity and a healthy diet are important lifestyle factors for healthy metabolic function, other lifestyle behaviours may also be crucial and help us to better understand the rapid rise in metabolic disorders. Sleep is a behaviour practised by all known species and may be related to energy imbalance through its potential effects on food selection, food quantity and energy expenditure. Sleep is not only essential for survival but has recently been implicated and investigated in relation to various health outcomes, including obesity, type 2 diabetes and the metabolic syndrome. The rise in these metabolic disorders parallels a steady decline in sleep duration over the past century.[187]

The decrease in sleep duration over recent decades may be due to a number of reasons including the 24/7 modern day world in which we live, powered by artificial lighting, access to the array of technology that is now available, simultaneous with family, work and social commitments and household chores. Attempting to fit everything into our waking day is challenging. Daily time limitations may have altered human behaviour over time; for example, increased use of quickly prepared ready meals. Time may also be occupied by other tasks and prioritised over physical

activity. Furthermore, some have argued that sleep may be curtailed to prolong wakefulness in order to achieve the daily demands of lifestyle choices. The challenge of completing daily activities may be rewarding but the consequence of sleep loss may prove to be detrimental on health.

Although mortality rates and metabolic hormone alterations amongst those with short sleep duration have been investigated in large population studies,[3;97;135] the effects of manipulating sleep experimentally is still in its early stages. If voluntary sleep curtailment is, in part, responsible for the rising metabolic disorder epidemics, then manipulation of sleep through experimental study is needed to provide a better understanding of the mechanisms underpinning the relationships. Sleep manipulation has been investigated in both animal and human studies and has provided a number of useful insights into how sleep loss can affect metabolic and cognitive function, energy expenditure and energy intake.

5.1.1 The effects of sleep restriction

Early experimental sleep studies focused on acute total sleep deprivation in both humans and animals. Rodent models of total sleep deprivation (TSD) served as an indicator of the health and metabolic effects produced (see Figure 1.13). The rodents exposed to prolonged TSD developed a number of symptoms and signs including hyperphagia, a paradoxical reduction in body weight and temperature, increased energy expenditure, skin lesions and various hormone alterations. The rodents subsequently died but the precise cause of death is unknown.

Although the early rodent study found increased energy expenditure and energy intake, available human research contests this. A recent TSD human study produced conflicting results to the early rodent studies in relation to energy expenditure.[155] Fourteen healthy, young men were recruited into a crossover design study. The participants received 1 night of normal sleep whilst being monitored by polysomnography (PSG) and 1 night of continuous wakefulness. Resting and postprandial energy expenditure was assessed after each condition and a buffet offered during the afternoon. The results showed that resting and postprandial energy expenditure was reduced by 5% and 20%, respectively, after TSD. No significant differences were found for food intake by sleep condition. Differences between rodent and human findings may be due to incomparable study designs or differences across species. For example, the effect of increased energy expenditure may have only been observed in rodents after a number of days/nights continuous wakefulness whereas this was examined in the human study after just 1 day/night where the effects may not have begun to fully occur. The rodent experiment was performed over a prolonged period of time until the animals died but prolonged total sleep deprivation, without use of psycho-stimulants is difficult and unethical in humans. The human study outlined only included male participants who were relatively young and healthy, questioning if the findings can be generalised to others in the population such as women, those who are obese, underweight or who have type 2 diabetes mellitus. Potentially, the differences observed in energy expenditure and intake between humans and rodents may simply be because they are unique and independent species.

Other human experimental sleep studies investigated brain activity alterations surrounding TSD. Six healthy young men were recruited to remain awake for a period of 64 hours. EEG output

showed that sleep architecture was altered during 2 nights of subsequent sleep recovery compared to EEG activity recorded during 2 nights of baseline sleep.[321] In particular, REM and SWS increased. Although this study provides useful insights into sleep architecture alterations after a short period of TSD, it is also restricted to young and healthy males, which are not fully reflective of the general population.

The focus of assessing human responses to TSD shifted to examining the effects of continuous sleep disruption on functionality and performance. Bonnet found that waking participants after 1 minute of EEG determined sleep across 2 nights/days resulted in reduced functionality and increased sleepiness during sleep fragmentation and similar sleep architecture alterations to those previously reported during 2 nights of sleep recovery.[322] It seems therefore, that sleep disturbances may produce similar negative outcomes as TSD, although this has not yet been fully established.

The studies discussed above provide useful insights into the effects of TSD and severely disturbed sleep. Both of these sleep conditions, however, are extreme and not commonly or consistently experienced by the general population. This has led to other work that has investigated and compared the effects of TSD with various durations of sleep opportunity.

A pioneering study that revealed dose-dependent effects of cumulative sleep loss was published in 2003.[12] Healthy participants (n=48), aged 21-38 years old were randomised to one of four conditions: 14 consecutive nights of either 4, 6 or 8 hours of sleep opportunity or 3 consecutive nights of total sleep deprivation (TSD). All participants had 3 nights of baseline sleep and 3

nights of recovery sleep and were monitored by EEG throughout. The findings revealed that those with a 4 or 6 hour sleep opportunity had significant and dose-dependent decreased cognitive performance. The authors concluded that prolonged sleep restriction of 6 hours or less per night produced similar cognitive deficits to 2 nights of TSD and that moderate sleep restriction can impair waking neurocognitive functionality in otherwise healthy, young adults. A further finding revealed that cumulative wakefulness of more than 15.8 hours was associated with reduced performance in all four conditions suggesting that sleep loss may have neurobiological consequences that accumulate over a period of time. This study provided the foundation for further investigation into small amounts of sleep loss and its potential effects on metabolic function over a period of time. Similar studies have also suggested that the neurocognitive responses to sleep deprivation may vary between individuals. More recent research has investigated the metabolic consequences of chronic partial sleep deprivation.

The problem with the studies described above is that total sleep deprivation and severely disrupted sleep are not natural or realistic of societal sleep behaviours. Extreme acute sleep manipulation studies have highlighted the importance of sleep on human performance but provide no information concerning the effects of sleep loss in relation to metabolic function, which is important so that a better understanding of how sleep loss may be related to the recent rise in metabolic disorders such as type 2 diabetes mellitus and obesity.

5.1.2 An overview of the chronic partial sleep deprivation experimental studies

Although there are some recent studies examining the effects of total sleep deprivation (TSD) in humans,[155] sleep research is now more focused on the impact of chronic partial sleep deprivation. This type of sleep manipulation is believed to be more representative of societal sleep behaviours, which have steadily declined over the past century. There are a number of experimental studies that have examined the effects of chronic partial sleep restriction on metabolic function to aid a better understanding of how sleep loss may be linked to the rise in metabolic disorders. A number of studies are discussed below.

The first detailed laboratory study which examined the effects of chronic partial sleep restriction on metabolic hormones in humans was published by Spiegel and colleagues in 1999.[171] Eleven healthy, young (18-27 years old) male volunteers had 3 nights of 8 hour sleep opportunity (baseline) and were then subjected to 6 consecutive nights of 4 hours (01:00-05:00) sleep opportunity (sleep restriction) followed by 7 nights of 12 hours (21:00-09:00) sleep opportunity (sleep recovery). At the end of the sleep debt and sleep recovery phases, carbohydrate metabolism and various hormonal profiles were assessed; sleepiness, sympathovagal balance and salivary cortisol were compared between the 3 sleep conditions. Sleep was recorded using polysomnography on the last 2 nights of baseline and sleep debt and on the first 2 nights of sleep recovery. The findings showed that, compared to sleep recovery, glucose clearance was impaired by almost 40%, following an intravenous glucose tolerance test during the sleep debt phase. Glucose effectiveness (the ability to dispose of glucose, independent of insulin; measured following intravenous glucose tolerance test) was reduced by 30% following sleep debt

compared to the sleep recovery phase. Estimates of sympathovagal balance were derived from recordings of heart-rate variability and were significantly increased in the sleep debt condition compared to sleep recovery. Afternoon and early evening cortisol levels increased significantly during the sleep debt phase compared to sleep recovery. The authors concluded that sleep debt produces negative effects on carbohydrate metabolism and endocrine function, similar to those that occur during the ageing process and thus argue that sleep debt may increase the severity of age-related chronic disorders.[171]

This initial detailed laboratory study provided useful insights into how sleep restriction over a short period of time can alter human physiology. The same group then went on to conduct a further experimental sleep study applying a different methodological approach for sleep manipulation. The first study only examined recovery sleep following sleep debt thus sleep extension following sleep restriction is easier to achieve but does not reveal if sleep can actually be extended when sleep debt has been repaid. The same group conducted a further study, which recruited twelve healthy, young men to take part in a randomised crossover study, spaced 6 weeks apart. Two nights of 4 hours (01:00-05:00) of sleep opportunity and 2 nights of 10 hours (22:00-08:00) of sleep opportunity were permitted.[146] The mean (standard deviation) age of the male participants was 22 years (±2 years) and the mean BMI was 23.6 Kg/m^2 (±2.0). The participants were non-smokers and did not take any medication. Anyone travelling across time zones 4 weeks prior to the study was excluded to avoid changes in sleep patterns as a direct result of time zone alterations. Participants were included if they had a regular nocturnal time in bed (TIB) and were recruited if their TIB ranged between 7-9 hours. This was assessed the week preceding participation by asking participants not to deviate from a fixed TIB (23:00-07:00) by

more than 30 minutes. Napping was prohibited for the duration of the study. After the 2 nights of sleep restriction and sleep extension, from 08:00, participant's caloric intake remained constant to avoid fluctuations of hunger and satiety. This was achieved by an intravenous glucose infusion at a constant rate of 5 g/kg of body weight every 24-hours. No other calories were allowed and 20-minute blood sampling was performed between 08:00-21:00 for levels of the two appetite regulating hormones, leptin and ghrelin. From 09:00-21:00, the participants completed visual analogue scales (0-10 cm) for hunger and appetite for various food types including categories such as sweets; salty foods; starchy foods; fruits; vegetables; meat, poultry, fish and eggs; and dairy products.

This landmark study showed that an average total sleep time of 9 hours and 8 minutes and 3 hours and 53 minutes was acquired during the sleep extension and sleep restriction phases, respectively. Leptin levels were 18% lower and ghrelin levels 28% higher following sleep restriction compared to sleep extension. Subjective hunger ratings were 24% higher following sleep restriction compared to sleep extension and a 23% increase in appetite ratings for all food categories combined were observed. Appetite was greater, specifically for food types, which were higher in calories and carbohydrates (sweets, salty and starchy food groups). Protein-rich foods such as meat, poultry, fish and dairy were not significantly altered by sleep duration condition.

Despite this study providing interesting and useful insights into the sleep and metabolic dysfunction relationship, it is not without its flaws. Firstly, the study was conducted in a small sample which may not be generalisable to the population, particularly as the participants were all

male, young, and healthy. Secondly, the participants' nocturnal sleep behaviours were not assessed through natural sleeping behaviours but by instructing them not to deviate by more than 30 minutes from a pre-defined bedtime set by the investigators. Although the financial incentive is not detailed for the young men recruited to the study, asking them to alter their sleep to assess eligibility for study participation may have resulted in compliance in order to remain recruited to the study but this may not representative of their natural sleep behaviours. Thirdly, the authors did not identify the method used to validate the participant's nocturnal sleeping and so it is not known if this technique was self-reported or objectively measured, an important yet unknown factor. Finally, although the measures of appetite and hunger are valuable in this study, subjective ratings are not indicative of actual food type consumption, a point, which has been addressed through a number of other studies.

A more recent experimental trial, registered at www.clinicaltrials.gov (NCT00986492), has provided further support and a better understanding for the sleep-obesity relationship in relation to the effects of acute partial sleep restriction on energy intake and physical activity.[156] Twelve healthy, young, male students were recruited to a 2-condition randomized crossover study. Inclusion criteria were general healthiness, absence of regular medication, 7.5-8 hours of nocturnal sleep duration, healthy BMI, stable weight for 6 months prior to study participation and moderate physical activity. Smokers (n=4) were included if they smoked ≤5 cigarettes per day and were allowed to smoke during the experimental conditions. Exclusion criteria were shift work, substance use, sleeping medication, eating disorders, excessive caffeine and/or alcohol consumption, food restriction, excessive snacking and dislike of foods offered during the experimental conditions.

Immediately before the initial randomized experimental sleep condition, participants completed a sleep diary for 2 consecutive days/nights to assess sleep duration and quality. Physical activity and food intake (measured to the nearest gram) was recorded by the participants concurrent with the sleep diary. During the experimental conditions, participants were permitted either 1 night of 8 hours (00:00-08:00) sleep opportunity or 1 night of 4 hours (02:00-06:00) sleep opportunity, spaced at least 5 days apart. Food intake was consumed ad libitum for breakfast (jam on buttered toast), lunch (buffet) and dinner (free menu). Physical activity was monitored through an accelerometer (Actimeter) during each experimental sleep condition. On the first experimental day, between 08:00-19:00, the participants were left in free-living conditions whilst recording food intake. Between 19:00-14:00 the following day, the participant was restricted to a laboratory setting. Participants completed a questionnaire at various time points to assess preprandial hunger (H), pleasantness of food (P) and sensation of sleepiness (S), determined through use of a 10 cm visual analogue scale. After 20:30, the participants joined the experimenter for discussions, games and movies until their allocated sleep opportunity. Upon waking, participants were asked to indicate what time they thought they fell to sleep as well as sleep quality. Breakfast (16-32 pieces of buttered toast with jam) was provided (08:00-08:30). Following breakfast, the participants walked outside with the researcher. Further questioning concerning motivation to exercise (M) was assessed. From 12:30-13:15, a buffet lunch (20 food items) was provided. From 14:00-08:00 the next morning, participants returned to free-living conditions where they were left free to consume, but record, whatever they wanted during the afternoon and dinner (except for caffeine-based drinks) and engage in any activities which were recorded by the Actimeter. Dinner (unrestricted) was provided and from 20:00 onwards,

participants could go to sleep at whatever time they wished and wake at whatever time they chose. These times were recorded by the participant upon awakening.

The mean sleep duration (determined by the Actimeter) during the sleep restriction and 8 hour sleep condition was 3 hours and 46 minutes and 7 hours and 14 minutes, respectively. The self-reported sleep duration for these sleep conditions was 3 hours and 44 minutes and 7 hours and 14 minutes, respectively. The day after sleep restriction, participants consumed 22% more energy compared to the 8 hour sleep opportunity. Despite significantly higher levels of sleepiness, physical activity was higher between 12:15-20:15 after sleep restriction, compared to when participants had the 8 hour sleep opportunity. No significant differences were reported for pleasantness of food by sleep condition.

Although this study extends knowledge surrounding the sleep-obesity link, the methodology is flawed in several ways. Firstly, the results of this study may not be generalisable to the rest of the population, particularly women, those with disease and older adults. Secondly, the inclusion of smokers may have potentially minimised the observation of increased energy intake by sleep restriction since smoking has been shown to have anorexic effects.[323] Furthermore, although the study shows increased food intake subsequent to sleep restriction, feeding ad libitum in a laboratory setting may further minimize food intake, possibly due to the psychological effects of being observed. Thus feeding behaviour may not be representative of natural feeding behaviour in the individual's own environment. Thirdly, although the trial was conducted in a laboratory setting, polysomnography was not used for determining sleep parameters.

Despite not determining metabolic hormone alterations by sleep condition, the trial provides further useful information concerning the potential link between sleep restriction and obesity development through actual increased energy intake. Surprisingly, sleep restriction in this study, was also associated with increased energy expenditure during a certain time period (12:15-20:15). One possible explanation for this increase in physical activity during this time may be psychological whereby the participants were aware that the study was almost drawing to an end and therefore decide to engage in more physical activity to overcome potential boredom and use some of the time remaining before the study end. Of course, it is possible that those who are sleep deprived are more active but this needs to be confirmed through further investigation.

A similar, improved study recruited 11 healthy volunteers (45% female, mean age 39.0 ± 5.0 years, mean BMI 26.5 ± 1.5) to a randomised crossover design with two 14-day stays, one allowing 5.5 hours of sleep opportunity and the other 8.5 hours, spaced at least 3 months apart.[324] Prior and subsequent to the 14-day visits, participants remained at bed rest for 48 hours with identical caloric intake including oral and intravenous doses of glucose at 09:00 and identical carbohydrate-rich meals at 14:00 and 19:00. In the final 24-hours, 30 minute blood sampling was conducted, commencing at 20:00 for the assessment of ghrelin and leptin levels. Participants were asked to obtain 7 hours of sleep before each of the 14-day visits. A dietitian interviewed each participant to exclude potential eating disorders as well as ascertain any disliked foods and work out a nutritionally balanced meal plan with a selection of palatable snacks and soft drinks. During each bedtime condition the same customised 3 meals per day were provided. All meals were served in excess to allow ad libitum energy intake, which were weighed before and after consumption. Participants also had unlimited access to a snack bar

within their laboratory room which included soft drinks and 10 customised snacks during each study period. Items consumed from the snack bar were recorded twice (07:00-19:00 and 19:00-07:00) every 24-hours. The calorie content and macronutrient composition of all meals and snacks consumed between 07:00 of day 1 and 07:00 on day 14 of each sleep condition, using polysomnography.

Sleep duration was decreased by 122 ± 25 minutes per night in the 5.5 hour sleep condition compared to the 8.5 hour sleep condition. No significant differences were found between any of the 3 meals for energy intake or macronutrient by sleep condition. There were, however, significant differences in energy intake and macronutrients according to sleep condition. During the 5.5 hour sleep opportunity, energy intake increased and comprised of significantly higher carbohydrate content, compared to 8.5 hours of sleep opportunity. Interestingly, the increased consumption of snacks was significantly higher during the period from 19:00-07:00 in the sleep restriction condition (371 ± 272) compared to the 8.5 hour sleep condition (236 ± 227). Although energy expenditure was assessed in this study along with leptin and ghrelin levels, no significant differences were found by sleep condition.

This study addressed some of the previous methodological concerns by the inclusion of females, older adults (34-49 years), overweight (BMI range 24-29) and the sleep restriction condition was conducted over a longer period, offering further information about the prolonged effects of sleep loss on metabolic function, energy intake and expenditure. The findings are interesting since they are suggestive of increased energy intake from snacking during the evening. It is possible that sleep restriction directly causes an increased desire to consume carbohydrate-dense foods,

essential for neural function, to provide the body with energy and is a natural survival mechanism. Other potential explanations are that snacking during the evening may be a consequence of media advertising through TV viewing, a common evening leisure activity, permitted during the study. Alternatively, snacking may have occurred simply through the availability of an appealing snack and/or boredom. Although the authors did not report on the potential dose-dependent effects of nighttime snacking with accumulating sleep loss, this is beneficial information to better understand the effects of consecutive nighttime sleep restriction.

In spite of the above studies outlined above which have investigated the effects of chronic partial sleep deprivation on metabolic function, energy intake and/or energy expenditure, there are a number of methodological issues and restrictions, making robust conclusions tentative. Firstly, allowing sleep opportunities of 4 hours, 5.5 hours or 10 hours are somewhat unrealistic and unrepresentative of normative sleep behaviours. They are at the extreme end of the sleep duration spectrum and only a very small minority of individuals will actually acquire this amount of sleep. Sleep opportunity must also be considered cautiously since this is actual time in bed and not total sleep time. The psychological effects of allowing individuals a specific sleep 'window' should also be scrutinised. For example, does this sleep 'window' effect sleep efficiency, sleep quality, sleep onset latency and/or wake after sleep onset and ultimately total sleep time. This is currently unknown and the problem appears to be that such sleep parameters can only be ascertained through polysomnography techniques, usually in a sleep laboratory. Secondly, just 1 or 2 nights of sleep restriction/extension undoubtedly only provide a snapshot of the metabolic effects, energy expenditure and energy intake. If sleep duration does play a role in the development of metabolic dysfunction, then this is likely to occur over a prolonged period of

time. Thirdly, sleep research has shifted from acute total sleep deprivation to examining the effects of partial sleep loss. Arguably, the studies outlined are acute partial sleep restriction and do not examine the effects of chronic partial sleep restriction. Most have used polysomnography to examine sleep parameters to ensure sleep manipulation compliance and although this technique is considered to be the gold-standard for sleep architecture, it is not practical for examining natural sleep behaviours either due to a change in the participants sleep environment or being unfamiliar/uncomfortable with the equipment which is connected to various parts of the body. Studies in laboratory settings where behaviours (sleep, feeding, and energy expenditure) are monitored may not be representative of natural human behaviour. Accumulation of small amounts of sleep debt over a prolonged period of time, particularly in an individual's own environment, is yet to be investigated but will provide further information concerning the effects of sleep restriction on energy balance. The possibility that small amounts of sleep reduction, accumulated over time, are associated with slow but steady increases in metabolic dysfunction is plausible, based on the evidence discussed. Rigorous investigation in this area is therefore timely.

5.1.3 Aims

A pilot study was carried out to examine the possibility of prolonged experimental sleep manipulation.

The primary aim of this experimental sleep pilot study was to establish if sleep can be restricted and extended in small amounts (30/60 minutes) over a prolonged period of time (28 days) compared to an individual's mean sleep duration.

The secondary aim was to assess if food intake was altered according to sleep manipulation over a prolonged period of time (28 days).

5.1.3.1 Hypotheses

Based on the evidence discussed and the need for a sleep manipulation model comprising of small amounts of sleep restriction over a prolonged period of time in an individual's own environment, the following hypotheses were tested:

1. Reducing sleep duration by 30/60 minutes can be achieved over 28 consecutive days/nights.
2. Extending sleep duration by 30/60 minutes can be achieved over 28 consecutive days/nights.
3. Food consumption will be altered with sleep manipulation.

5.2 Methods

The study was approved by the NHS Birmingham East, North and Solihull Research Ethics Committee (Reference: 08/H1206/116). A visual protocol for the study is shown in Figure 5.1. Volunteers were recruited through an online advertisement placed on the University of Birmingham website for staff and students to access. Potential participants were directed to an

online screening survey, which acquired information on the following inclusion and exclusion criteria:

5.2.1 Inclusion criteria

1. Healthy

2. Volunteers

3. Male and Female

4. Aged 18-50 years

5. Non-smokers

6. BMI 18.5 – 24.9 kg/m²

7. Consistent sleep schedules

5.2.2 Exclusion criteria

1. Current illicit substance use

2. Sufferers of febrile illnesses within the week prior to the study, or those who have chronic illnesses involving regular medication or steroids

3. Volunteers on medication (excluding contraceptive medication)

4. Extreme 'owls' or 'larks', determined by the Horne-Ostberg questionnaire[325]

5. Sleep modifying medications (prescription or over the counter)

6. Travelled to a different time zone 4 weeks prior to study participation or during the study

7. Current shift worker or shift worker in the previous year

8. Diagnosed sleeping disorder(s)

9. Diagnosed eating disorder(s)

10. Diagnosed psychiatric disorder(s)

11. Pregnant

12. Menopausal

13. Excessive alcohol consumption, determined by NHS guidelines

(http://units.nhs.uk/howMany.html)

14. Napping

15. Donated blood up to 4 months prior to commencement of the study

Potential volunteers who fulfilled all study criteria were then sent a participant information sheet with details of the study. They were given 72-hours to decide if they wanted to participate. A total of 19 volunteers were recruited. Of the 19 recruits, 8 were eliminated due to not fulfilling all inclusion/exclusion criteria, 1 was eliminated due to missing actigraphy data, and 6 withdrew, leaving a total of 4 volunteers (50% male) who completed the study. Detailed information concerning the study protocol is described for each visit below.

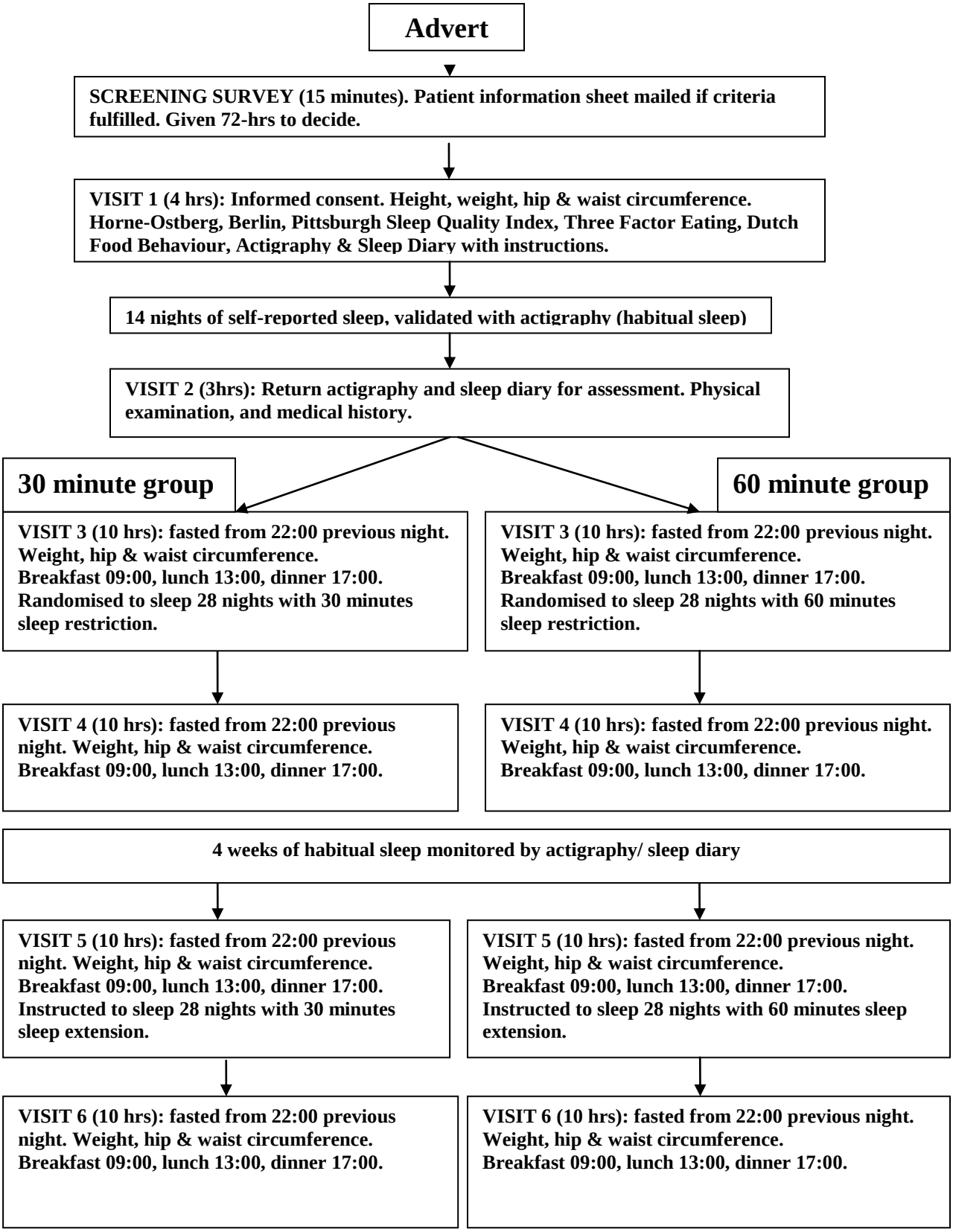

Figure 5.1: The visual protocol for the sleep manipulation pilot study.

5.2.3 Visit 1

Volunteers provided written consent during this visit and completed a series of questionnaires. These included the following:

1. Horne-Ostberg questionnaire[325] was administered and used to exclude individuals with extreme circadian sleep timings.

2. Berlin questionnaire[326] was administered and used to exclude individuals with potential undiagnosed obstructive sleep apnoea.

3. Pittsburgh Sleep Quality Index questionnaire[327] was administered and used to exclude individuals with sleep problems.

4. Three Factor Eating questionnaire[328] was administered and used to exclude individuals with potential undiagnosed eating disorder(s).

5. Dutch Eating Behaviour questionnaire[329] was administered and used to exclude individuals with potential undiagnosed eating disorder(s).

All questionnaires were scored according to standard guidelines prior to visit 2. After completion of the questionnaires, the volunteer was provided with an accelerometer (Actiwatch 2, Philips Respironics, The Netherlands), worn on the non-dominant wrist. The volunteer was instructed to wear the device for 2 weeks alongside completing a sleep diary. The 2 week actigraphy and sleep diary data were used to validate a consistent sleep pattern as well as identifying napping habits. Sleep patterns were considered to be consistent if sleep and wake times did not deviate more/less than 60 minutes for each sleep/wake time across weekdays and

separately for weekends, since these two sleep parameters are known to differ,[29] particularly in adolescents and young adults.

5.2.3.1 The Actiwatch 2 device

The Actiwatch 2 is a device worn on the non-dominant wrist. It has a motion sensor (accelerometer), which is used to record sleep-wake activity. The Actiwatch 2 is able to record sleep-wake activity up to a period of 30 days and has a large 1MB storage capacity, a rechargeable battery and a waterproof casing. Communication to the device is achieved via a USB connection to the docking station where the Actiwatch can be programmed, charged and information can be downloaded to the computer. For the purposes of this study, epochs were set to record every 1 minute. Sleep estimates of sleep duration were achieved according to the manufacturers default algorithms. A picture of the device is shown in Figure 5.2.

Figure 5.2: A picture of the Actiwatch 2 worn by volunteers in the sleep manipulation pilot study.

The device is worn like a watch, on the non-dominant wrist. It records sleep-wake activity through the in-built accelerometer. The Actiwatch 2 is able to record sleep-wake activity up to a period of 30 days and has a large 1MB storage capacity, a rechargeable battery and a waterproof casing allowing it to be worn in water for up to 30 minutes.

5.2.4 Visit 2

During the second visit, the actigraphy data were downloaded according to the manufacturer's software and was used to validate this data against the sleep diary information. A physical examination was performed by a clinician and a blood sample was drawn for assessment of potential blood abnormalities. Height was measured to the nearest 0.5cm using a stadiometer. Weight was recorded to the nearest 0.1kg using regularly calibrated scales. Blood pressure was also measured and recorded with the participant sitting at rest for at least 5 minutes. Measures of hip and waist circumference to the nearest 0.5cm were obtained. Volunteers were instructed not to deviate by more or less than 30 minutes from their mean sleep duration (calculated by actigraphy at visit 2) the night before attendance at visit 3 which took place the following morning.

5.2.5 Visit 3 (baseline)

Actigraphy data were downloaded on attendance to the research centre to ensure that volunteers had slept +/-60 minutes of their mean sleep duration as determined by actigraphy at visit 2. This criterion was used to ensure that volunteers sleep duration was similar to their mean sleep duration (determined at visit 2) and that they were not sleep extended or sleep deprived to +/- 60 minutes from their usual sleep duration. Volunteers were weighed to the nearest 0.1kg, one measure of blood pressure was recorded following at least 5 minutes of rest in a seated position without talking, hip and waist circumference was measured to the 0.5cm. Volunteers were

provided with an isocaloric nutritious shake at 09:00 for breakfast and 13:00 for lunch followed by a large buffest-style dinner at 17:00. The dinner was selected by the volunteer from a hospital menu. Three portions of the meal were provided on one plate along with 3 pieces of cake and 1 piece of fruit. The same meal was provided to the volunteer for each of the subsequent visits. Unknown to the volunteer, all food items were weighed before and after dinner. These measures were used to calculate the total weight (ounces) of food the volunteer consumed during each visit. At the end of visit 3, volunteers were randomised into one of two sleep conditions by selecting a folded piece of paper from a bag containing equal numbers of each sleep condition:

1. Thirty minute sleep manipulation.
2. Sixty minute sleep manipulation.

According to the sleep condition that each volunteer was randomised to, they were then instructed to reduce their mean sleep duration by at least 30/60 minutes every night for the next 28 days whilst being monitored by actigraphy and completing corresponding sleep diaries.

5.2.6 Visit 4 (sleep deprivation)

After the 28 days/nights of 30/60 minutes sleep deprivation in their own environment, the volunteer returned for visit 4. The protocol previously described in visit 3 (except for randomisation) was repeated and actigraphy/sleep diary data were validated to establish protocol compliance according to sleep instruction. At the end of visit 4, volunteers were instructed to sleep as they normally would with no restrictions and returned to their own environment for a

further 28 days. This served as a 'wash-out' period. The intention was that any sleep debt would be repaid during this time whilst still being monitored by actigraphy and corresponding sleep diaries.

5.2.7 Visit 5 ('wash-out')

After the 28 days of unrestricted sleep, the volunteer returned for visit 5. The protocol previously described in visit 3 (except for randomisation) was repeated and actigraphy data were downloaded and sleep diary data were inputted to validate the sleep habits of the volunteer. At the end of visit 5 the volunteers, according to which sleep condition group they had been randomised, were instructed to extend their baseline mean sleep duration (calculated by actigraphy at visit 2) by 30/60 minutes for the next 28 days whilst being monitored by actigraphy and completing corresponding sleep diaries. The volunteer then returned for visit 6.

5.2.8 Visit 6 (sleep extension)

After the 28 days/nights of 30/60 minutes sleep extension, the volunteer returned for visit 6. The protocol previously described in visit 3 (except for randomisation) was repeated and actigraphy/sleep diary data were validated to establish protocol compliance according to sleep instruction. Unlimited water was permitted during all visits and drinks containing caffeine/alcohol were prohibited.

5.3 Results

5.3.1 Sleep manipulation models

Four volunteers completed the pilot study. Two were female and both were randomised into the 30 minute sleep manipulation group. All participants were Caucasian and the age range was 20-22 years. The means and standard deviations for all baseline anthropometric measurements obtained during visit 3 are detailed in Table 5.1. An independent samples t-test showed no significant gender differences for any anthropometric and physical measurements or mean sleep duration (hours) at baseline (visit 2). The individual breakdown of each volunteer for actigraphy determined mean sleep duration (minutes) at visit 2 and then the night before visit 3 as well as the difference between the two is detailed in Table 5.2.

Table 5.1: The means and standard deviations for the anthropometric/physical measurements obtained at baseline, sleep restriction and sleep extension.

Anthropometric/Physical measurement	**Baseline (visit 3)**	**Sleep restriction (visit 4)**	**Wash-out (visit 5)**	**Sleep extension (visit 6)**
Body mass index (Kg/m^2)	22.38 ± 1.82	22.09 ± 1.93	22.10 ± 2.00	22.08 ± 2.31
Systolic blood pressure (mmHg)	122.50 ± 14.18	125.75 ± 20.04	115.25 ± 6.40	121.50 ± 10.66
Diastolic blood pressure (mmHg)	68.75 ± 7.93	70.00 ± 12.52	62.75 ± 4.43	67.50 ± 0.58
Hip circumference (cm)	98.50 ± 7.14	96.50 ± 8.85	96.88 ± 7.26	96.63 ± 8.62
Waist circumference (cm)	76.38 ± 6.65	77.50 ± 7.90	74.88 ± 9.02	77.70 ± 8.60

Data are presented as mean ± standard deviation.

Table 5.2: The mean total sleep duration (minutes) determined by actigraphy at visit 2 and the night before visit 3 along with the difference (minutes), according to each volunteer.

Volunteer	Mean sleep duration* (minutes) at visit 2	Sleep duration* (minutes) obtained the night prior to visit 3	Difference (minutes)
1001	465	420	-45
1002	495	435	-60
1005	450	420	-30
1006	465	510	+45

*Actigraphy determined sleep duration (minutes) was rounded up or down to the nearest 15 minutes for ease of interpretation.

The details of individual volunteer's mean actigraphy determined sleep duration according to each sleep manipulation phase (30 minutes and 60 minutes) are shown in Tables 5.3 and 5.4, respectively.

Table 5.3: The 30 minute sleep randomisation volunteers mean actigraphy determined sleep duration (minutes) according to sleep manipulation phase.

Volunteer	Mean sleep duration, determined by actigraphy* at visit 2 (baseline)	Mean sleep duration, determined by actigraphy* at visit 4 (sleep restriction)	Mean sleep duration, determined by actigraphy* at visit 6 (sleep extension)
1002	495	**405**	495
1005	450	**375**	**495**

*Actigraphy determined sleep duration (minutes) was rounded up or down to the nearest 15 minutes for ease of interpretation.

Sleep duration marked in **bold** indicates that the volunteer met the required threshold, according to the sleep manipulation phase.

Table 5.4: The 60 minute sleep randomisation volunteers mean actigraphy determined sleep duration (minutes) according to sleep manipulation phase.

Volunteer	Mean sleep duration, determined by actigraphy* at visit 2 (baseline)	Mean sleep duration, determined by actigraphy* at visit 4 (sleep restriction)	Mean sleep duration, determined by actigraphy* at visit 6 (sleep extension)
1001	465	420	**525**
1006	465	**360**	**525**

*Actigraphy determined sleep duration (minutes) was rounded up or down to the nearest 15 minutes for ease of interpretation.

Sleep duration marked in **bold** indicates that the volunteer met the required threshold, according to the sleep manipulation phase.

Figures 5.3 to 5.10 provide full details, by volunteer, for the breakdown of each of the 28 nights of sleep restriction and sleep extension. The proportion of nights where sleep manipulation was complied with, according to randomisation group, is detailed below each Figure.

Volunteer 1002 under 28 nights of 30 minute sleep randomisation: sleep restriction

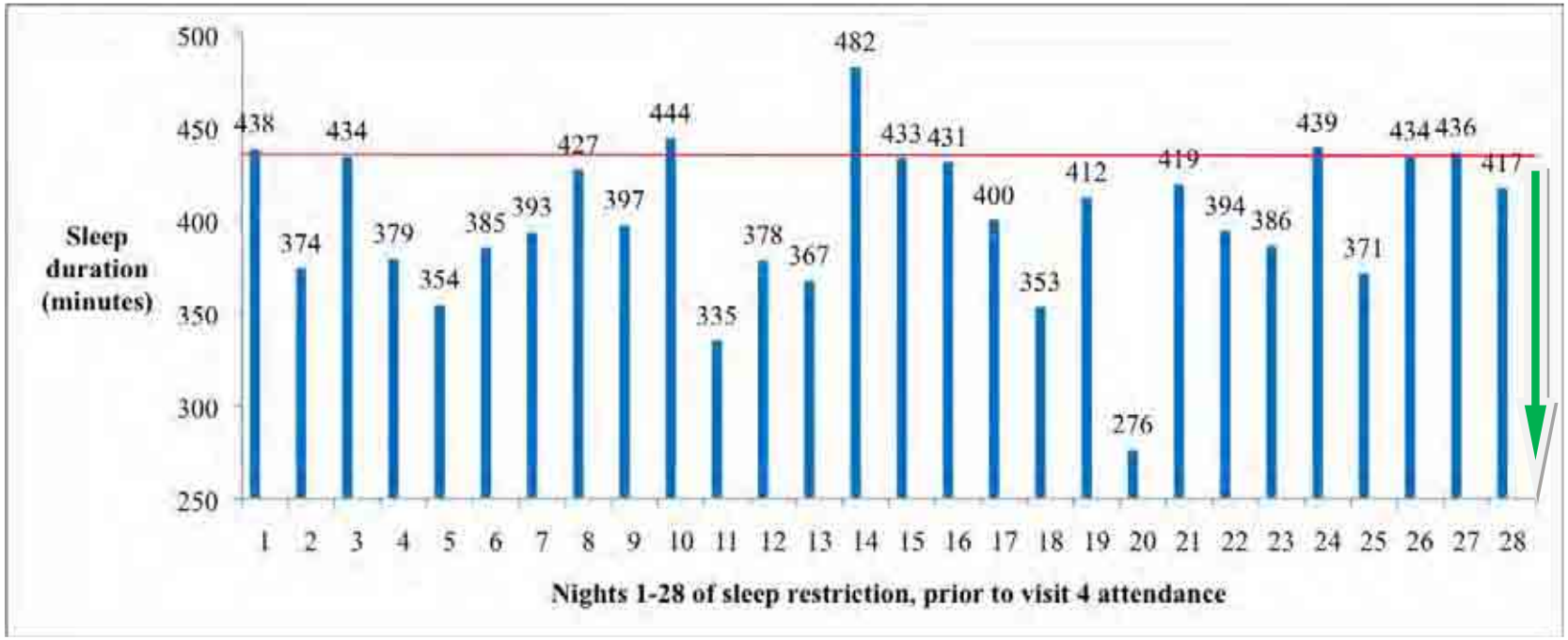

Figure 5.3: A bar chart demonstrating actigraphy determined sleep duration for volunteer 1002 during 28 nights of sleep restriction.

The threshold for this volunteer was to obtain ≤435 minutes of sleep across the 28 nights, as shown by the line in red. The compliance rate was 82% (23/28 nights).

Volunteer 1002 under 28 nights of 30 minute sleep randomisation: sleep extension

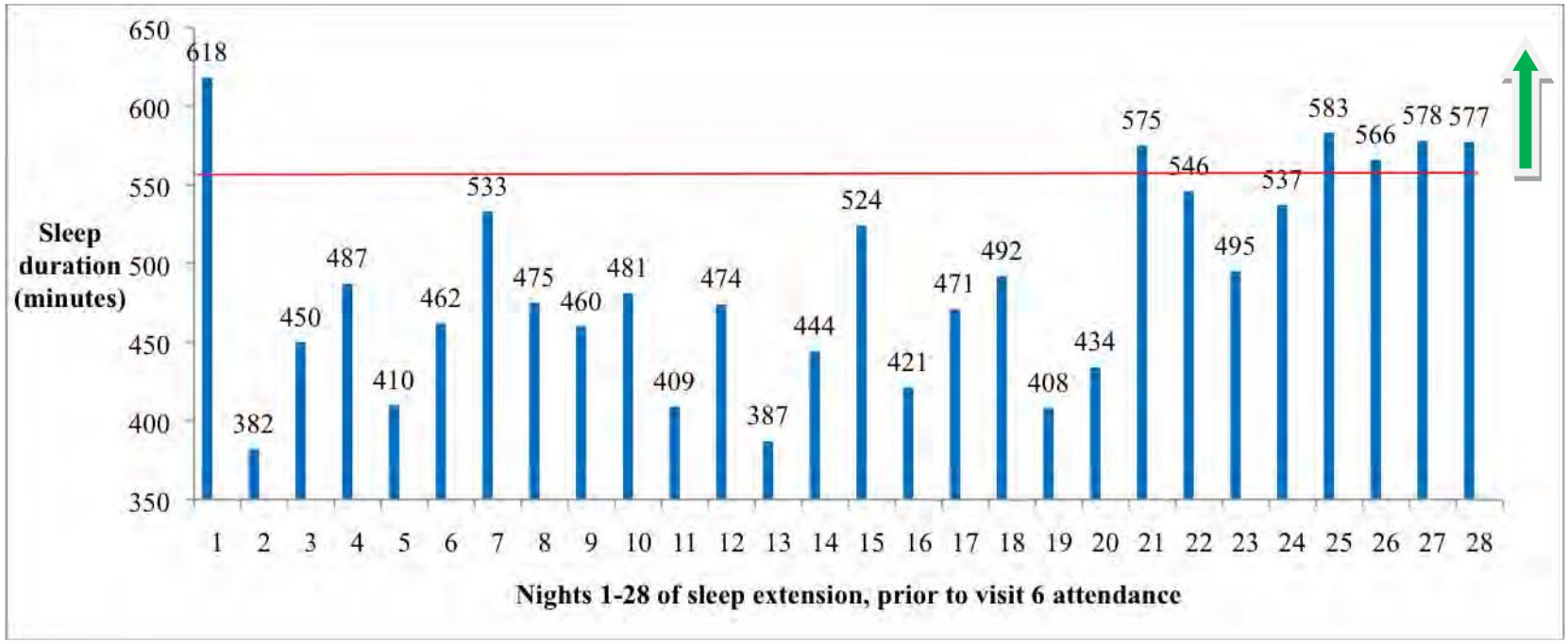

Figure 5.4: A bar chart demonstrating actigraphy determined sleep duration for volunteer 1002 during 28 nights of sleep restriction.

The threshold for this volunteer was to obtain ≥555 minutes of sleep across the 28 nights, as shown by the line in red. The compliance rate was 21% (6/28 nights).

Volunteer 1005 under 28 nights of 30 minute sleep randomisation: sleep restriction

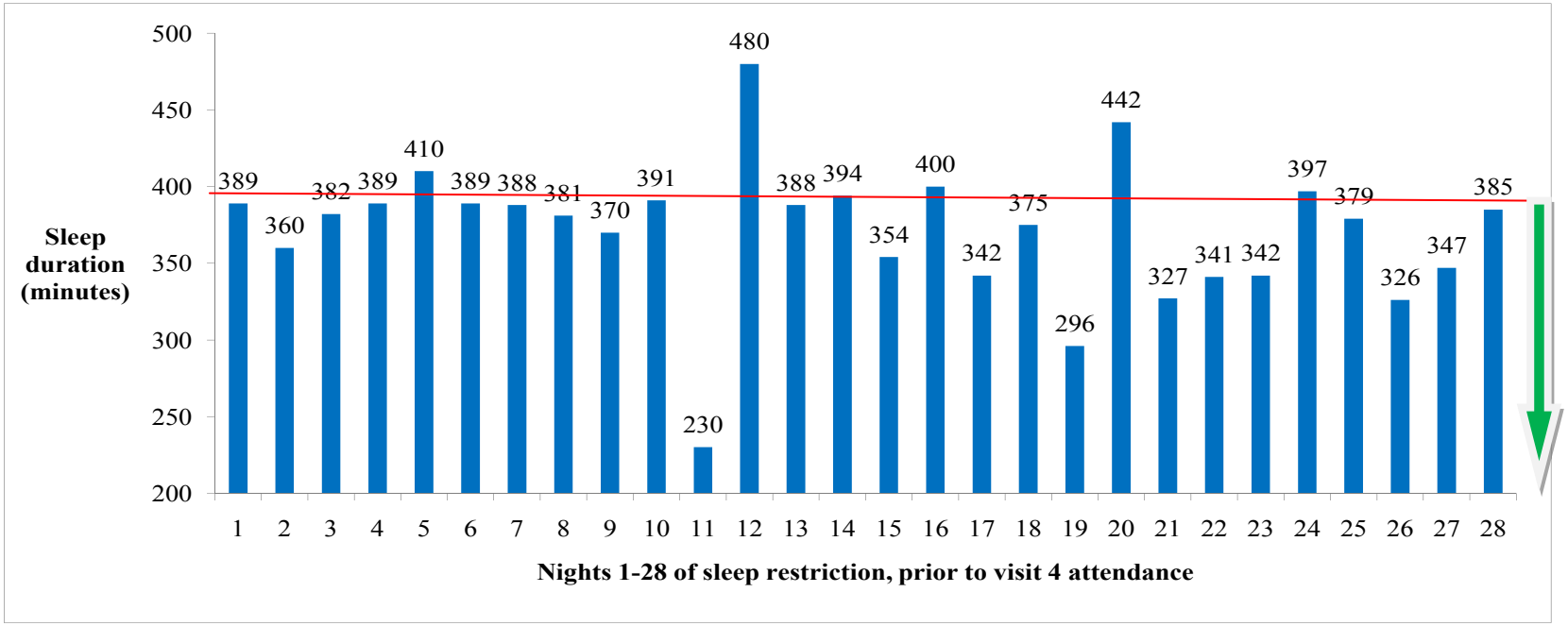

Figure 5.5: A bar chart demonstrating actigraphy determined sleep duration for volunteer 1005 during 28 nights of sleep restriction.

The threshold for this volunteer was to obtain ≤390 minutes of sleep across the 28 nights, as shown by the line in red. The compliance rate was 79% (22/28 nights).

Volunteer 1005 under 28 nights of 30 minute sleep randomisation: sleep extension

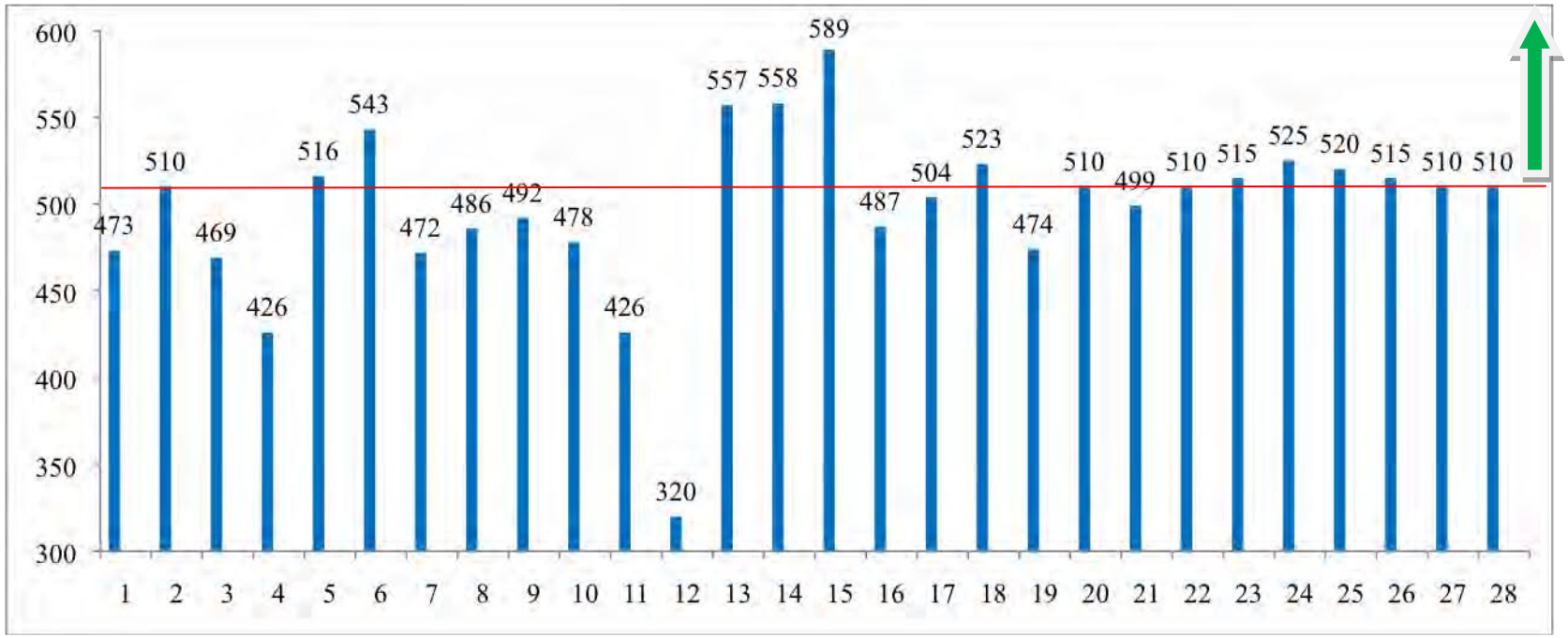

Figure 5.6: A bar chart demonstrating actigraphy determined sleep duration for volunteer 1005 during 28 nights of sleep restriction.

The threshold for this volunteer was to obtain ≥510 minutes of sleep across the 28 nights, as shown by the line in red. The compliance rate was 54% (15/28 nights).

Volunteer 1001 under 28 nights of 60 minute sleep randomisation: sleep restriction

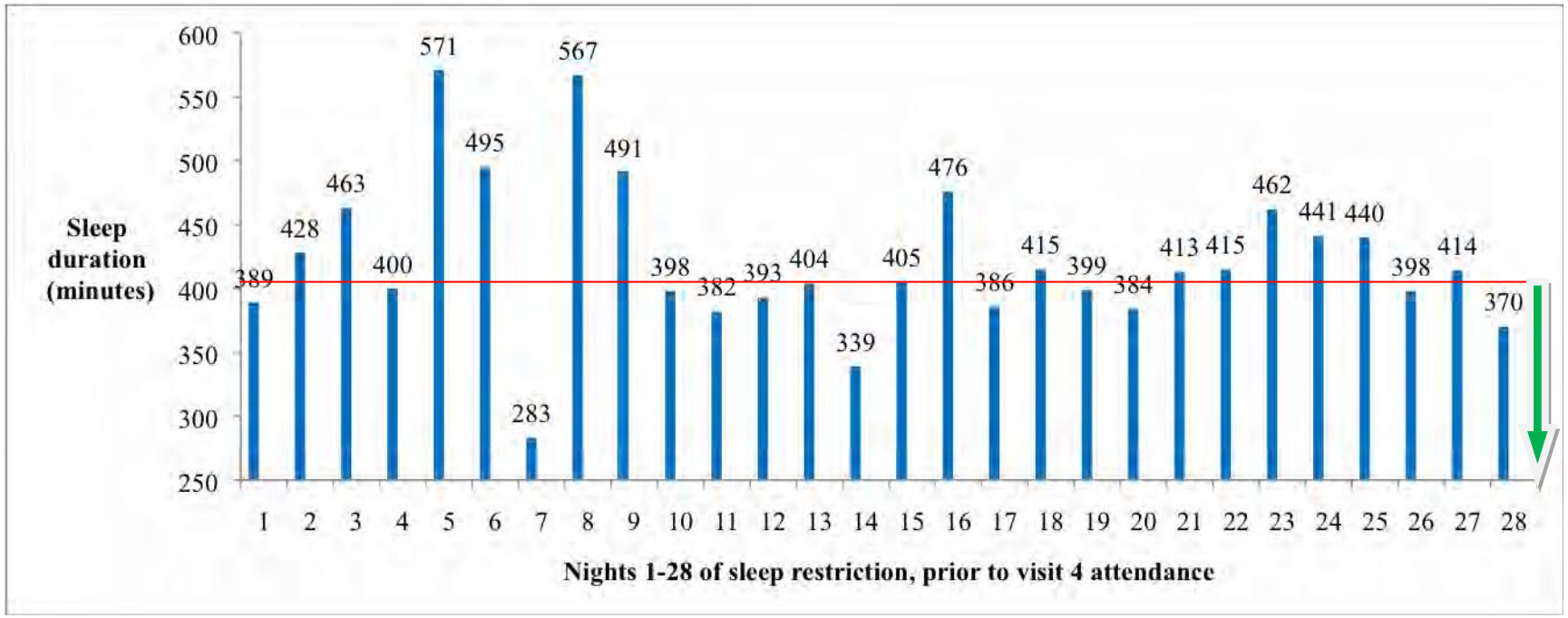

Figure 5.7: A bar chart demonstrating actigraphy determined sleep duration for volunteer 1001 during 28 nights of sleep restriction.

The threshold for this volunteer was to obtain ≤405 minutes of sleep across the 28 nights, as shown by the line in red. The compliance rate was 50% (14/28 nights).

Volunteer 1001 under 28 nights of 60 minute sleep randomisation: sleep extension

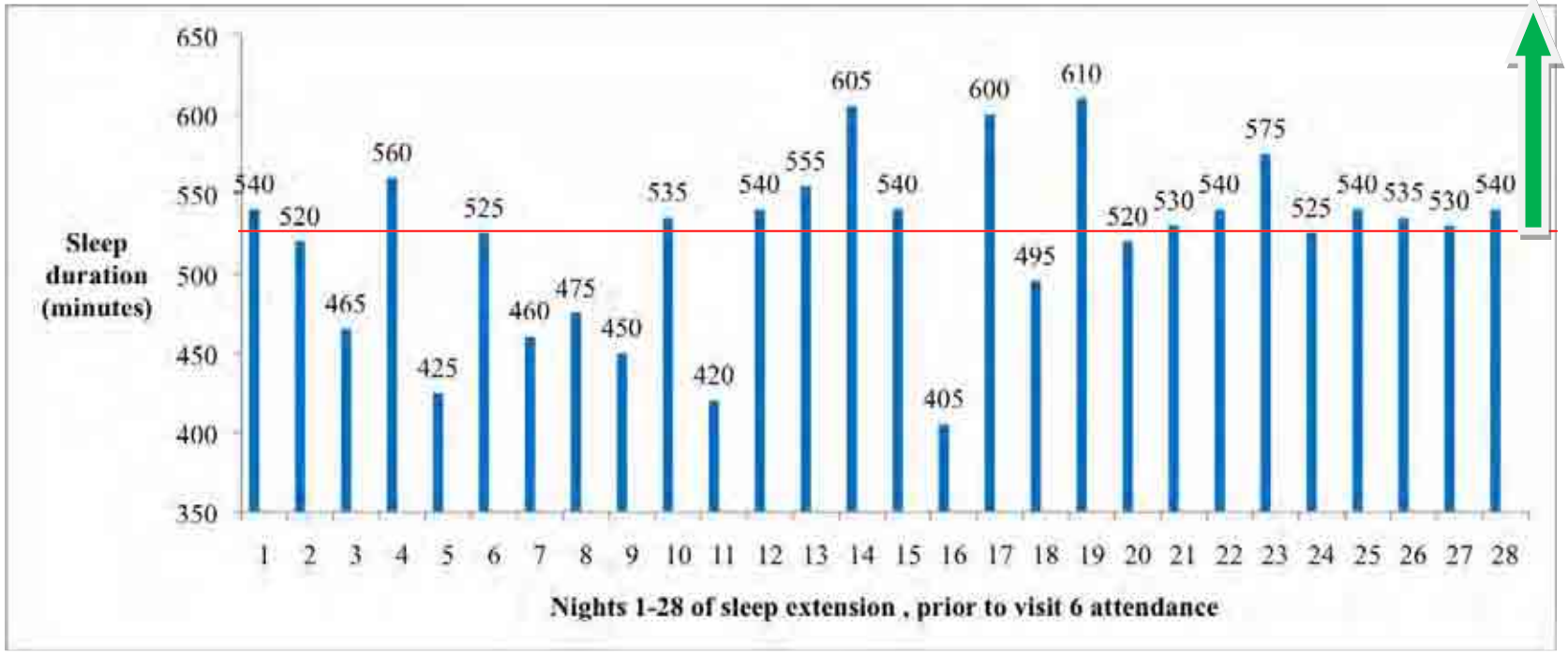

Figure 5.8: A bar chart demonstrating actigraphy determined sleep duration for volunteer 1001 during 28 nights of sleep extension.

The threshold for this volunteer was to obtain ≥525 minutes of sleep across the 28 nights, as shown by the line in red. The compliance rate was 64% (18/28 nights).

Volunteer 1006 under 28 nights of 60 minute sleep randomisation: sleep restriction

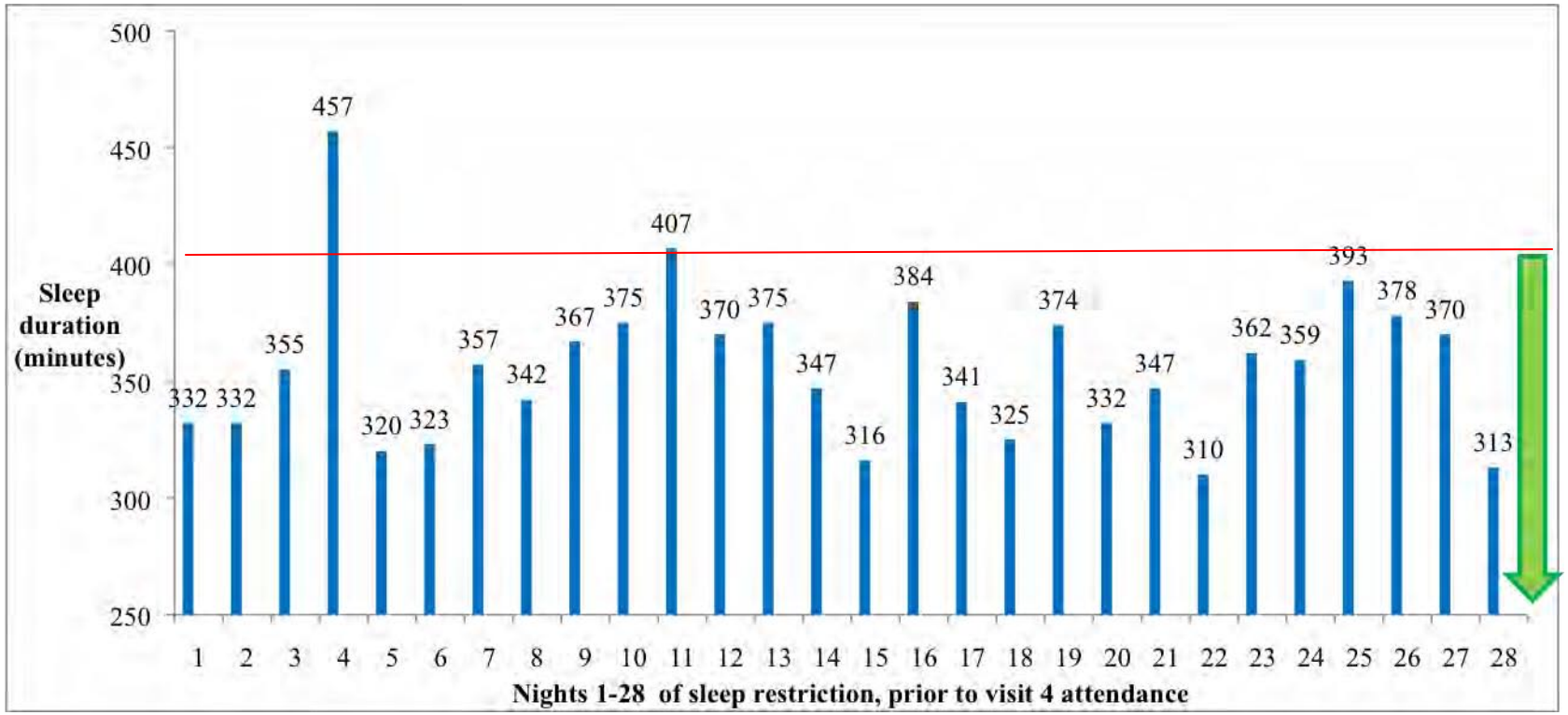

Figure 5.9: A bar chart demonstrating actigraphy determined sleep duration for volunteer 1006 during 28 nights of sleep restriction.

The threshold for this volunteer was to obtain ≤405 minutes of sleep across the 28 nights, as shown by the line in red. The compliance rate was 93% (26/28 nights).

Volunteer 1006 under 28 nights of 60 minute sleep randomisation: sleep extension

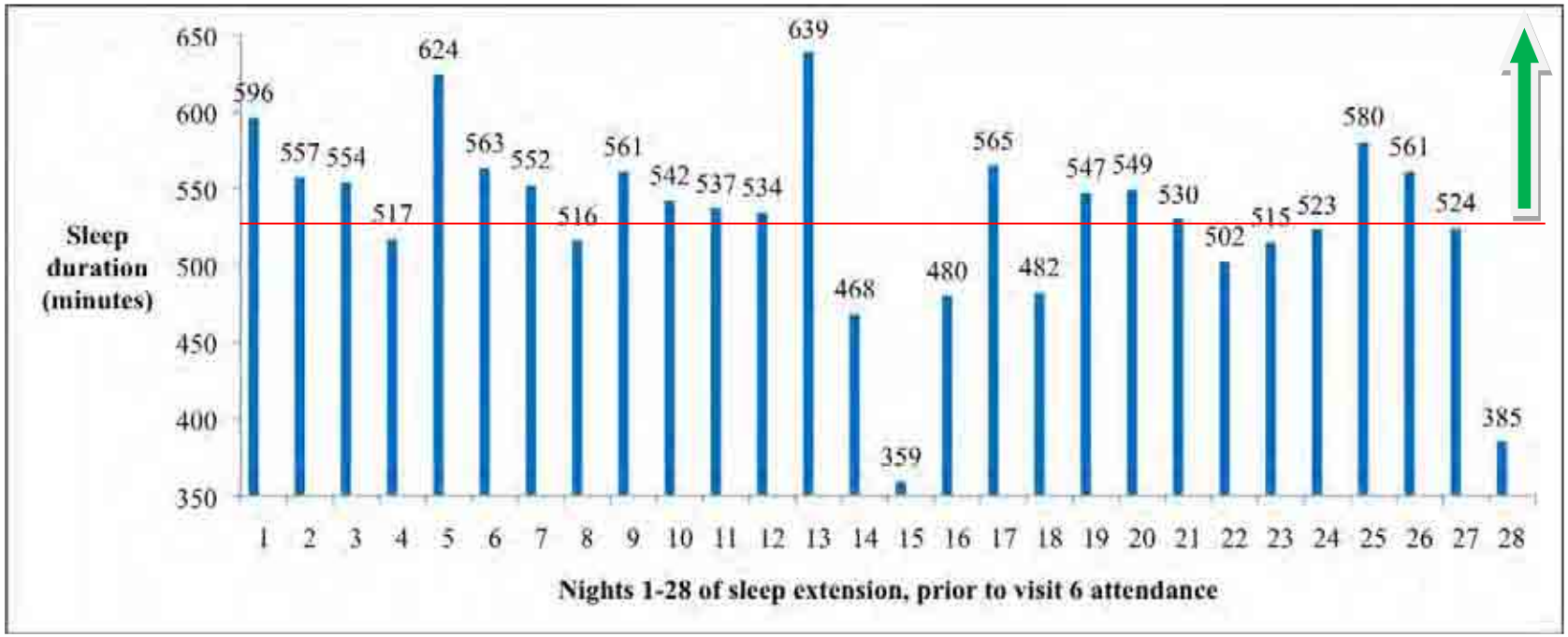

Figure 5.10: A bar chart demonstrating actigraphy determined sleep duration for volunteer 1006 during 28 nights of sleep extension.

The threshold for this volunteer was to obtain ≥525 minutes of sleep across the 28 nights, as shown by the line in red. The compliance rate was 61% (17/28 nights).

5.3.2 Food intake according to sleep manipulation

The main meal, cake and fruit consumption (ounces) by volunteer and sleep condition, are detailed in Figures 5.11, 5.12 and 5.13, respectively. Formal statistical techniques were not used to examine significant differences in food intake by sleep manipulation phase due to the small sample size.

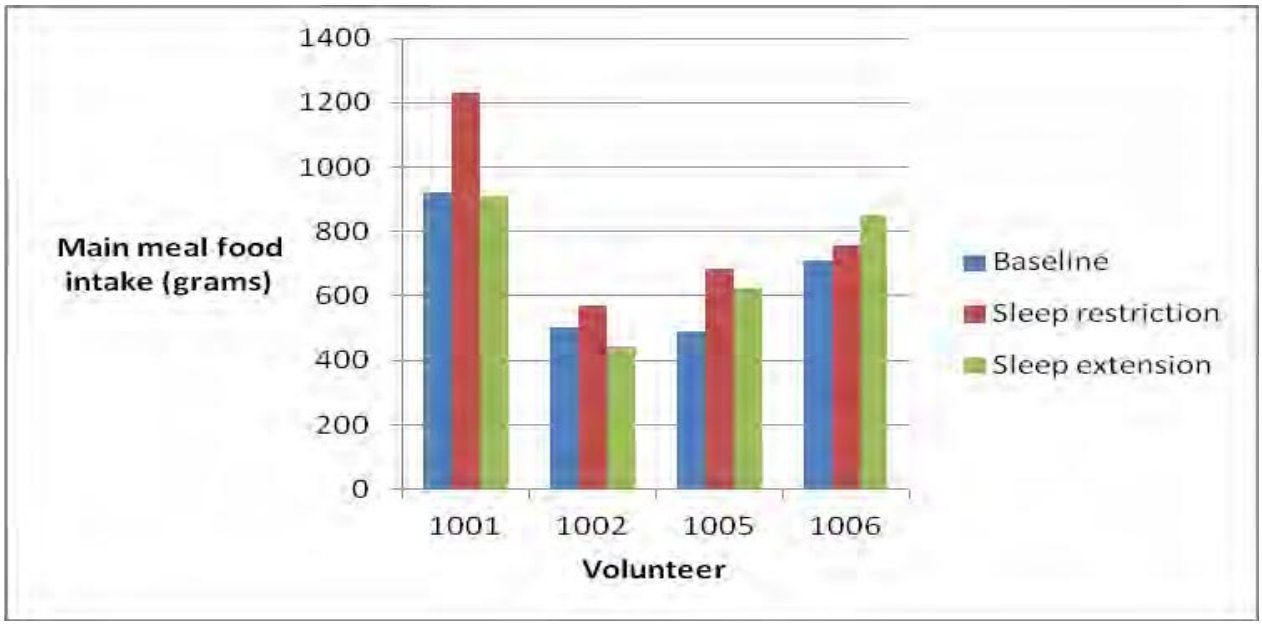

Figure 5.11: Main meal food consumption (grams) according to sleep conditions and volunteer. Volunteers 1002 and 1005 were randomised to the 30 minute sleep conditions. Volunteers 1001 and 1006 were randomised to the 60 minute sleep conditions.

When comparing main meal food consumption at baseline with 28 nights of sleep restriction, all volunteers consumed more, irrespective of the sleep randomisation category (30/60 minutes). When comparing baseline to 28 nights of sleep extension, the findings are less consistent. Two

(50% male) of the four volunteers consumed less following sleep extension compared to baseline. The remaining two volunteers consumed more main meal when sleep extended compared to baseline. Comparisons by sleep manipulation show that 3 of the 4 volunteers consumed more main meal when in a prolonged sleep deprived state compared to a prolonged sleep extended state.

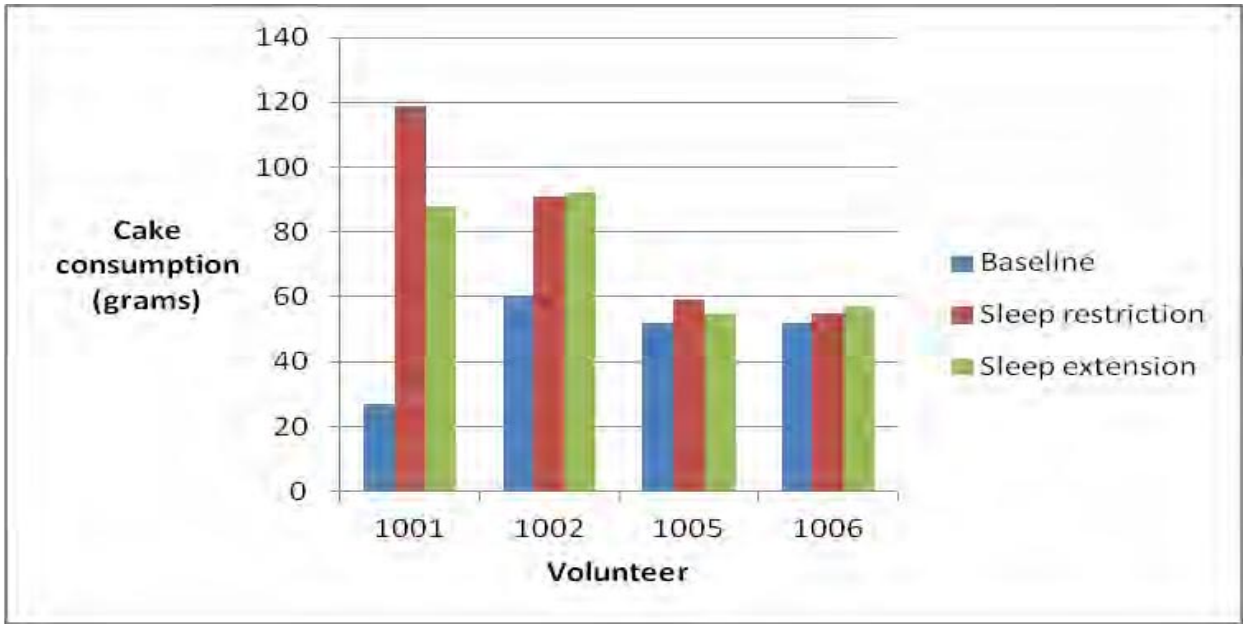

Figure 5.12: Cake consumption (grams) according to sleep conditions and volunteer.

Volunteers 1002 and 1005 were randomised to the 30 minute sleep conditions. Volunteers 1001 and 1006 were randomised to the 60 minute sleep conditions.

When comparing cake consumption at baseline with 28 nights of sleep restriction, all volunteers consumed more, regardless of which sleep category they were randomised to. Comparisons between baseline and the sleep extended phase also showed that all volunteers consumed higher quantities when in a sleep extended state. Comparisons by sleep manipulation are less

consistent. Two of the four volunteers consumed more cake under the prolonged sleep restriction condition compared to under the prolonged sleep extended condition. The remaining two volunteers consumed just slightly less in the prolonged sleep restriction condition compared to the prolonged sleep extended condition.

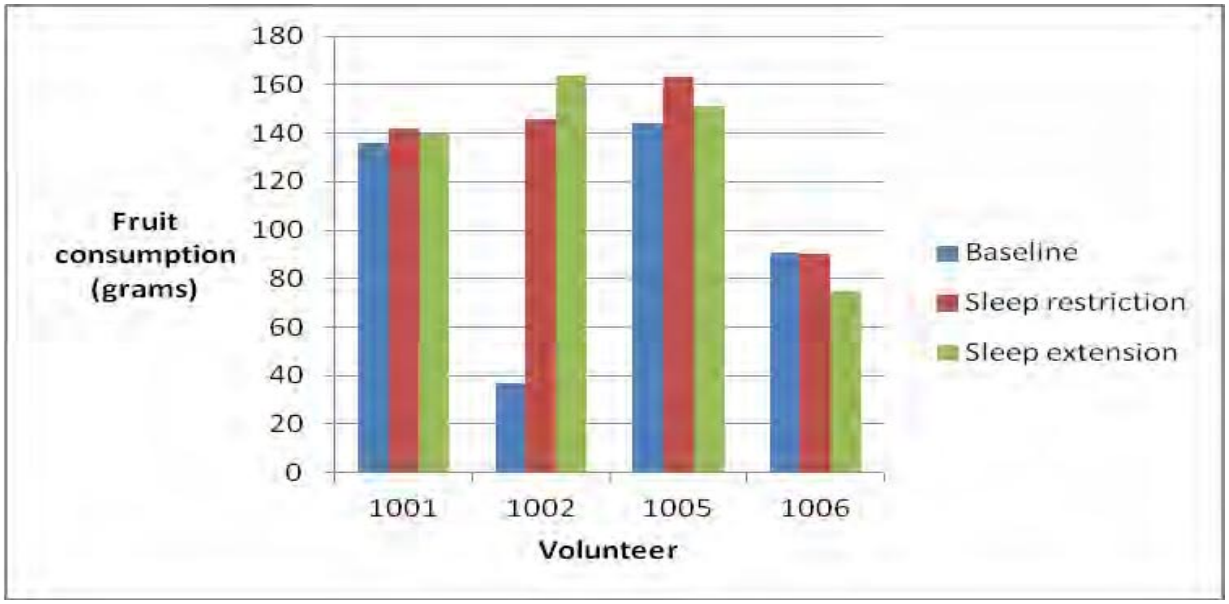

Figure 5.13: Fruit consumption (grams) according to sleep conditions and volunteer.

Volunteers 1002 and 1005 were randomised to the 30 minute sleep conditions. Volunteers 1001 and 1006 were randomised to the 60 minute sleep conditions.

Comparisons of fruit consumption at baseline with 28 nights of sleep restriction showed that three of the four volunteers consumed more, regardless of which sleep category they were randomised to. Comparisons between baseline and the sleep extended phase show three of the four volunteers consumed higher quantities when in the sleep extended state. Comparisons by sleep manipulation are also reasonably consistent. Three of the four volunteers consumed more

fruit under the prolonged sleep restriction condition compared to under the prolonged sleep extended condition. The remaining volunteer consumed less fruit in the prolonged sleep restriction condition compared to the prolonged sleep extended condition.

5.4 Discussion

The main findings from this experimental pilot sleep study have revealed useful and unique results. Firstly, it has been shown that a small amount of sleep loss and sleep extension (30 minutes and 60 minutes) can be achieved, in part, in an individual's own environment over a prolonged period of time (28 nights). Furthermore, food intake (main meal and cake) was consistently higher following 28 nights of sleep restriction compared to baseline in all volunteers. Although the study needs to be repeated in a larger sample, this novel pilot data supports the notion that sleep loss, over a prolonged time period, may, in part, contribute to weight gain through increased food consumption, which may translate to weight gain over time.

5.4.1 Explanation of the findings

5.4.1.1 Sleep manipulation

From the data obtained, the compliance rate for sleep restriction was good, ranging from 50-93%. With the exception of one volunteer who only achieved 21% compliance rate for sleep extension, the other three volunteer's compliance range was 54-61%. This indicates that voluntary sleep restriction is less problematic than attempting to extend sleep duration. Only one

volunteer did not meet the threshold for the mean sleep restriction duration. This volunteer was randomised to the 60 minute condition and despite not achieving a mean reduction of 60 minutes of sleep over 28 night's, the volunteer did achieve a 45 minute reduction. This still shows that small amounts of sleep restriction are possible over a period of time.

Curtailing sleep has become increasingly common and this study shows that individuals can readily restrict sleep by small amounts over a prolonged period of time, thus allowing more time for other activities. Conversely, extending sleep duration may be more physiologically challenging, particularly if sleep debt has been repaid. In this study, any sleep debt acquired following 28 nights of sleep restriction would have been repaid during the wash-out period (visit 5) giving volunteers a chance to extend sleep duration in the absence of sleep debt. It is possible that volunteers found sleep extension more challenging due to personal, work or social commitments and lifestyle choices. Alternatively, sleep extension may have been more difficult due to internal physiological restrictions or the presence of external cues (zeitgebers) such as light, which may have delayed sleep onset and triggered wakefulness in the morning. All volunteers were recruited during Spring/Summer and attended the final visit during Autumn/Winter. More daylight occurs during Spring/Summer and sleep restriction occurred during these seasons, this should have made sleep restriction easier to achieve. The same could be argued about sleep extension, which would have occurred during Autumn/Winter when there is less daylight, making sleep extension easier to achieve. Zeitgebers alone cannot therefore explain the lower compliance rate for sleep extension and so internal physiological functions must play a stronger role in the regulation of extending sleep.

5.4.1.2 Food intake

Food intake, following 28 nights of sleep restriction, increased in all volunteers compared to consumption at baseline. This was consistent across volunteers for the main meal as well as for cake consumption. Fruit intake was also increased in all but one volunteer, where the difference was marginal, when comparing baseline consumption with the prolonged sleep restriction phase. Interestingly, a dose-dependent relationship was not observed according to sleep randomisation. If sleep loss is related to weight gain then it could be assumed that increased amounts of sleep loss would be associated with increased food intake and although this was not observed in this study, the sample is very small, making dose-dependent relationships difficult to detect. Thus, the same study would need to be repeated with greater number of participants to potentially determine such relationships where statistical analysis of the data could be performed. Given the findings, it may be that the threshold for increased food intake is minimal. For example, it may be that just 30 minutes of sleep loss over a prolonged period is all that is required to increase appetite and subsequent food consumption but this requires further investigation.

5.4.1.2.1 Main meal consumption

All volunteers consumed more when sleep restricted compared to baseline. Two volunteers consumed less following 28 nights of sleep extension compared to baseline. The remaining two volunteers consumed more main meal after sleep extension, compared to baseline. The effect of sleep loss appears therefore to have a more powerful effect on main meal consumption compared to sleep extension. Short sleep duration has been linked to alterations in appetite regulating

hormones, ghrelin and leptin,[97] increased hunger as well as an increased appetite for carbohydrate and calorie dense food types.[146] Alterations in metabolic hormones may therefore result in increased appetite and hunger and subsequently, excessive food intake. Although levels of ghrelin and leptin were not measured, potential alterations in these metabolic hormones with sleep reduction may have contributed to the increased food intake observed. When volunteers were in a prolonged sleep extended state, the results were less consistent. There is a substantial amount of evidence suggesting that both short and long sleep duration is associated with increased body weight,[3;123;133;330] although the data is inconsistent with others reporting only an association between short sleep duration and increased body weight.[99;114;121] Indeed, the findings from this study show less consistency for food intake when in a sleep extended state where some consumed more whilst others consumed less. The mechanisms underpinning this relationship have not yet been determined and further work examining hormone alterations in naturally long sleepers is needed.

The direct comparisons between food intakes whilst sleep restricted versus sleep extended are interesting. The majority (3/4) of volunteers consumed more food subsequent to sleep restriction compared to sleep extension. This provides further support for the relationship between short sleep and obesity in adults. The relationship between long sleep and obesity is less consistent where long sleep may be a result of underlying health condition(s). Alternatively, long sleep may be associated with reduced energy expenditure, a major risk factor for obesity.

5.4.1.2.2 Cake consumption

Cake consumption was increased following sleep restriction compared to baseline in all volunteers, consistent with the findings of others.[324] A similar pattern was observed when volunteers were sleep extended compared to baseline consumption. This, if replicated may help explain the U-shaped sleep-obesity association commonly observed.[3] When making direct comparisons between the sleep restriction and sleep extension phases, the results were less consistent. Half of the volunteers increased cake consumption when sleep restricted compared to when sleep extended. The other half had a small but minimal reduction in cake consumption when sleep restricted compared to when they were sleep extended. Overall, the evidence suggests a stronger effect of cake consumption following prolonged sleep restriction.

5.4.1.2.3 Fruit consumption

The majority (3/4) of volunteers consumed more fruit subsequent to sleep restriction and sleep extension compared to baseline. The direct comparisons by sleep condition showed that three of the four volunteers consumed more fruit under the prolonged sleep restriction condition compared to under the prolonged sleep extended condition. Again, the effect of sleep loss appears to be stronger for this food type compared to when in a sleep extended state. This opposes other previous evidence, which found sleep loss was not associated with an increased appetite for fruits or vegetables.[146] It should, however, be noted that the present study examined actual consumption rather than subjective appetite for the fruit provided. If sleep loss and/or

sleep extension is associated with increased food intake of all food types then this will undoubtedly contribute to metabolic disorders, particularly as sleep curtailment is increasingly common.

5.4.2 How the findings relate to previous studies

Previous sleep manipulation studies have shown that sleep alteration is possible over a short period of time when enforced through human intervention. The findings reported by Spiegel and colleagues showed that 2 nights of 4-hour sleep opportunity was associated with a 24% higher subjective hunger rating compared to when volunteers were subjected to 2 nights of 10-hour sleep opportunity.[146] This finding is consistent with the pilot study presented. Volunteers increased food consumption following prolonged sleep restriction compared to baseline measures. Furthermore, the majority of volunteers consumed more food subsequent to sleep restriction compared to sleep extension. Spiegel and colleagues also reported an increased subjective appetite for sweets, a further finding supported by the current study where objective cake consumption increased following prolonged sleep restriction.

Nedeltcheva and colleagues allowed volunteers 14 nights of 5.5 hours and 8.5 hours sleep opportunity in a randomised order whilst measuring food intake.[324] This group showed that meal intake was unaltered by sleep condition but an increase in calories from snacks was observed during sleep restriction, particularly during the period 19:00-07:00. The results from the current

study are similar but not all are consistent. Food consumed as part of the main meal increased following prolonged sleep restriction and sleep extension compared to baseline measures. Given that Nedeltcheva and colleagues did not ascertain baseline measures of food consumption, comparisons are difficult and can only be made according to the sleep manipulation conditions. Interestingly, snacking increased following sleep restriction, in line with the findings of the increased cake consumption subsequent to sleep restriction in the current study.

A further study subjecting a small number of male volunteers to 1 night of 4-hour sleep opportunity showed an increase in energy intake on the subsequent day.[156] Although the pilot study presented in this thesis did not measure calorie intake, additional food consumed will inevitably result in increased calories. The findings of the current study therefore support the argument that energy intake is increased following sleep restriction which may promote weight gain over extended time periods and exacerbate the current metabolic disorder epidemic.

5.4.3 Strengths and limitations

Previous sleep manipulation studies have been conducted in laboratory settings where researchers have enforced sleep duration timings. There are a number of problems with this approach. Firstly, enforcing and ensuring compliance to sleep timings only demonstrates that sleep durations are attainable through researcher intervention, not through voluntary efforts, particularly for sleep restriction. The current study benefitted from voluntary sleep restriction and extension demonstrating that sleep can be voluntarily altered over an extended period of

time. Secondly, some studies enforce extreme sleep opportunities such as 4 and 10 hours, which are not normative sleep behaviours. The current study benefitted from ascertaining individual's baseline sleep duration for a 2 week period using an objective measure of sleep whilst in their own environment. This allowed for a small manipulation of sleep, according to the individual's baseline sleep duration. This approach has never been previously attempted and arguably small proportions of sleep loss and extension may be more representative of sleep behaviours so that the effects of these can, in turn, be examined. Thirdly, sleep manipulation in a laboratory may not be representative of the individual sleeping in their own environment due to differences in various stimuli (comfort of the bed, bedtime routine, sounds, room temperature) and/or being wired up to polysomnography (PSG) equipment which may require adaptation before adjusting back to normal sleeping habits. Thus use of PSG in a laboratory may not be truly representative of an individual's normal sleep behaviours. The current study benefitted from an objective sleep measure (actigraphy), which was accompanied by a corresponding sleep diary for validation purposes. This method overcomes the potential problems of a changed environment and equipment, which may alter natural sleep behaviour. Finally, sleep studies conducted in a laboratory are restricted to a small number of nights due to the inconvenience to the volunteer and high financial implications. Whilst the study described in this chapter did not use PSG, sleep was objectively measured through the use of actigraphy, which the volunteers wore in their own environment, allowing for measures of sleep to be determined over a prolonged period of time. This approach is unique and has not been previously attempted. The results are promising and this model of sleep restriction/extension may be the foundation for future sleep manipulation studies. Most experimental sleep studies have only investigated the effects in males, largely due to hormone alterations in females due to the menstrual cycle. The current study recruited both

males and females, controlling for effects of the menstrual cycle by only recruiting female volunteers during days 1-10 of their cycle for visits 3-6.

Limitations of the study include the small sample size, which may not be generalisable at a population level although this is in line with other experimental sleep studies. The problem with small samples is that there is insufficient statistical power to examine significant differences. Instead, the raw data from this initial sleep model has been explored and has produced interesting findings. A further limitation is that all of the volunteers recruited to the study were students and Caucasian. Some may have had work/study commitments, which prevented them from fully extending their sleep. Clearly, the model could be repeated in a more varied sample. Although an increase in food intake was observed after sleep restriction, the study did not obtain measures of the metabolic hormones previously associated with increased hunger and appetite,[146] thus it is difficult to determine what the mechanisms are that link increased energy intake and sleep alteration. Furthermore, food intake was only measured during visit 3-6 and not over the 28 days periods, which separated them.

5.5 Conclusions

A successful model of small amounts of sleep restriction/extension over a prolonged period, specific to the individual, has been piloted in this study in the absence of a laboratory setting. This model will serve as the foundation for other sleep research into the effects of sleep on various outcomes. There is a substantial amount of evidence suggesting a relationship between

sleep duration and increased body weight, as previously discussed, but further work is needed. This sleep model could be applied to a larger sample comprising of different ethnicities, age, health, workforce and socio-economic backgrounds to ascertain if small amounts of sleep alteration are sustainable. Once this has been established, the effects of minimal sleep loss/extension can be thoroughly investigated. In particular, activity levels could be recorded under experimental sleep conditions to determine if physical activity is altered according to sleep duration. This will help us to better understand if/how sleep is related to obesity.

The sleep model could also be applied to establish alterations in the previously established appetite regulating hormones, ghrelin and leptin since these data are inconsistent. Other metabolic hormones should also be investigated including peptide tyrosine tyrosine (PYY), glucagon-like peptide-1 (GLP-1), insulin, cortisol, and glucose to provide a clearer picture of the mechanisms underpinning the relationship between sleep duration changes and hormone alterations. Alongside determining other hormones, which may be associated with hunger and appetite, food intake could also be monitored through use of food diaries or cameras.

In summary, the experimental sleep model developed, piloted and presented, provides an opportunity for more rigorous investigation into the effects of sleep alterations on various outcomes. Although the focus of this thesis surrounds metabolic function, the proposed sleep model can be applied to examine the effects of other outcomes of interest including cognitive, behavioural and social.

6 CONCLUSIONS AND FUTURE WORK

6.1 Summary of the BEACHES

The BEACHeS was the first ever sleep-obesity investigation to be conducted in young South Asian UK resident children. The findings showed no association between sleep duration and adiposity. The study benefited from two measures of sleep duration (Actiheart and parental report) and three objective adiposity measures whilst considering a panel of potential confounders. The majority of paediatric sleep-obesity studies report a negative linear association but data obtained in the BEACHeS found no relationship. Despite short sleep being highly prevalent in the sample, obesity, however measured, was not associated with objectively determined or self-reported sleep duration. The findings have provided unique evidence within the South Asian paediatric population. It is possible that the sleep-obesity relationship was not observed due to culture, traditions and/or religious commitments.

6.1.1 Future work

The majority of paediatric sleep-obesity studies have been cross-sectional and have used parental or self-reported sleep. It is therefore essential for future work to make longitudinal assessments of sleep in young children to establish more robust conclusions. Furthermore, detailed metabolic hormone assessments are urgently needed in children to assess if the adult determined metabolic

hormones, leptin and ghrelin, which are altered by sleep duration, exhibit similar patterns in paediatric populations and to assess if the relationships are consistent by age and ethnicity. Data of this type will provide the foundation for developing a better understanding of the sleep-obesity relationship to help address the obesity epidemic, which has huge financial and public health implications. By determining if sleep duration and/or quality are contributing factors to future development of obesity, particularly in ethnic minorities who have elevated risks for obesity and diabetes, future strategies and education programmes can be developed and trialled in an attempt to tackle the growing obesity epidemic.

Interactions between genetic, cultural and environmental factors need to be fully explored to determine the role of ethnicity. Additional research needs to be conducted in immigrant children, which examines various sleep parameters and these children need to be followed longitudinally to determine if sleep changes according to an environment change. It is possible that emigration may alter sleep due to changes in temperature, environment, stress and other external stimuli. Although there are data in Indian children and adolescents residing in their country of origin, there are no available sleep-obesity data in children who immigrate to the UK. Further work needs to be conducted in these populations who are at greater risk of metabolic disease.

Finally, standardized sleep categories and adiposity measures, which are age and gender appropriate should be determined, applied and obtained objectively to enable direct comparisons between studies. Age-specific sleep needs should be determined through rigorous scientific

study to investigate if sleep is driven by biological processes and to ascertain if these differ according to ethnicity and culture.

6.2 Summary of the MASSES

The MASSES is the only study to provide information in contemporary UK adolescents concerning sleep habits and associations with use of multiple technologies, obesity and academic performance. The data obtained has specifically identified technology use before bedtime on weekdays rather than collectively across the day. Results showed that increasing media use frequency was associated with less sleep time and that all types of technology (TV, video games, mobiles and Internet/PC) were associated with sleep loss. Media users had a significantly reduced sleep duration and prolonged sleep onset latencies compared to non-users. Insufficient sleep duration was an independent predictor of overweight/obesity as well as poorer academic performance, after adjustment for a range of potential confounders.

6.2.1 Future work

Longitudinal data concerning adolescent sleep and adiposity measures should be obtained through objective sleep measures. Future research could retain the MASSES methodology whilst using actigraphy on all volunteers for one week period. The use of actigraphy would ascertain objective sleep and physical activity levels. Data could be obtained across the academic year, avoiding holidays, providing the season was adjusted for in subsequent analysis. It is planned for the MASSES to be conducted as a cohort study where objective sleep and

physical activity measures are determined at the beginning of adolescence (11 years) and collected each year until students are at least 16 years of age. This would allow for changes in adolescent sleep patterns to be identified so future determination of sleep need could be fully recognised in this age group.

Future work in this area should also include physiological measures such as hormone profiles and cardiovascular risk factors such as pulse wave velocity and arterial stiffness. Profiles of ghrelin and leptin should be obtained and variations in other metabolic hormones thoroughly investigated. These investigations should be performed in all possible adolescent groups determined by weight and sleep duration. Comparisons by these groups would allow us to determine which groups have an increased risk for cardiovascular disease and metabolic dysfunction. These types of investigations, if conducted longitudinally across different groups, will help to provide a better understanding of temporal sequences and 'at risk' individuals so that treatment strategies and education programmes can be developed and delivered to future generations.

6.3 Summary of GBCS

A relationship between long total sleep duration and the metabolic syndrome was found in this large sample of older Chinese, after adjustment for a range of potential confounders. Although the data were cross-sectional, analysis was re-performed in a subsample of 'healthy' individuals in an attempt to address reverse causality and the relationship remained. Age and gender stratified analysis showed that females and younger individuals were more likely to drive the

association. Individual components of the syndrome were also analysed which revealed long total sleep duration was significantly associated with central obesity, impaired fasting glucose and elevated triglycerides.

6.3.1 Future work

The GBCS study presented in *Chapter 4* has provided the foundation for future studies to be conducted in this under-researched area. Data is limited for the relationship between the metabolic syndrome and sleep duration. In particular, causal relationships should be examined in large samples, spanning different ethnicities, through prospective longitudinal studies. Follow up data from the GBCS, once complete, will offer a unique insight into the cause-effect relationship and will help to rule out the possibility that OSA is partly responsible for the relationship observed in the presented study.

Although objective sleep measures would be difficult in such a large sample, it would be feasible to obtain actigraphy measured sleep in a smaller sub-sample of the cohort. This would not only help to validate self-reported sleep duration and other sleep parameters but it would also provide a clearer and more accurate picture surrounding the relationship between sleep and the metabolic syndrome.

Future work should also focus on assessing sleep parameters in relation to endocrine and immune function as well as metabolic hormones in older individuals. Metabolic hormone

assessment would also help us to better understand why the short sleep-obesity relationship diminishes during older age.

6.4 Summary of the experimental sleep model

The unique experimental sleep manipulation model that was piloted has provided some useful insights into how sleep can be voluntarily altered. Previous experimental evidence has subjected individuals to extreme spectrums of sleep duration over just a short period of time but there are no data surrounding prolonged sleep restriction/extension. The model was shown to be more successful for sleep restriction compared to sleep extension. Sleep extension may not be possible due to biological and/or social factors. Sleep restriction, on the other hand, was shown to be achievable by all of the recruited volunteers. This is in line with the steadily decrease in sleep duration observed in the general population. The study suggested that prolonged sleep restriction is associated with increased food intake of all types measured (main meal, cake and fruit) intimating that cumulative sleep loss may promote obesity over time.

6.4.1 Future work

The effects of long term sleep loss have not been previously examined but the piloted sleep manipulation model can now be applied to future research. The experimental sleep model can be used to examine the metabolic hormone alterations with sleep manipulation. The model should be applied to determine the potential alterations of ghrelin and leptin as well as assess other hormones such as GLP-1, insulin, glucose, PYY and cortisol. Rigorous scientific study of these

hormones will help us to better understand the processes and mechanisms that link sleep with metabolic function.

The sleep model could also be applied alongside objectively determining physical activity levels and food intake, through accelerometry and food diaries, respectively. This would provide additional explanation of how sleep is linked to potential weight gain and subsequent obesity.

6.5 Final conclusions

Despite accumulating evidence linking sleep duration to various metabolic dysfunction, it should be considered that sleep is not stable across the lifespan and different stressors will occur throughout the course of life with subsequent effects upon sleep. Although the sleep experimental evidence identified for the development of type 2 diabetes and obesity demonstrate connections, it is unlikely that extreme sleep durations can acutely promote these chronic diseases. Subjecting individuals to 4 or 10 hours of sleep is not representative of normative sleep habits and it should be considered that sleep duration has gradually declined in parallel with an increase in obesity prevalence over a number of decades. The relationship between sleep duration and chronic disease needs to apply more thoroughly designed studies of a prospective nature where data collection is closely monitored and data on all potential confounders are obtained. Observational study is urgently needed to ascertain age-specific biological sleep needs so that a worldwide consensus can be reached and applied to sleep research to ensure consistent comparisons are made.

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Appendix 1

Birmingham healthy Eating
& Active lifestyle for Children

UNIVERSITY OF BIRMINGHAM

QUESTIONNAIRE FOR PARENTS

Completing the questionnaire

This questionnaire will take about 15 minutes to complete

All information about you and your child will remain **confidential**

Please answer the questions in relation to the child named below

Please answer all the questions by ticking the boxes or writing in the spaces provided

If you have any queries or require more information relating to this questionnaire or the BEACHeS project, please contact a member of the BEACHeS project team on **0121 414 8694**

Please remember to complete and return the questionnaire by [insert date] in order to be entered into the **free prize draw**!

Child's name……..

Your relationship to this child

- ❑ Mother
- ❑ Father
- ❑ Guardian
- ❑ Other (please state)…….

In this first section, we would like to know a bit more about your household and where you live

1. ***How many other children under the age of 16 are there (including brothers or sisters) in the same household?***

☐ 0 ☐ 1 ☐ 2
☐ 3 ☐ 4
☐ More than 4 (please write how many)……

2. ***How many of the following adults over the age of 16 (including yourself) live in the same household with your child? (please write a number for each row)***

Relationship of adult with your child	Number of such adults in your household
Mother	
Father	
Guardian	
Grandparent	
Sister	
Brother	
Other relative (please state relationship to child) ……... ……	
Other adult (please state relationship to child/family) ……. …….	

3. ***Please now indicate to what extent you agree or disagree with each of the following statements:***

	Strongly agree	Agree	Neither	Disagree	Strongly disagree	Don't know
There is heavy traffic in our local streets						
I am concerned about strangers when my child goes to play in the neighbourhood						
Road safety is a concern in our area						
There are no lights/ crossings in the neighbourhood streets						
My child would need to cross several roads to get to play areas						
There are few sporting venues within our local area						
Public transport is limited in our area						

4. Now please tell us about your family's eating habits. In general, how often does your family:

	Less than once a year	1-4 times a year	5-11 times a year	1-3 times a month	1-2 times a week	More than 2 times a week
Go out for a meal (breakfast, lunch or dinner)?						
Have take away food from a fast food shop?						
Have ready made meals?						
Cook food from fresh ingredients?						

5. To what extent does each of the following influence the foods which you buy, prepare and eat as a family?

	Very important	Important	Neither	Not important	Not at all important
Price					
Palatability (taste)					
Satiety (being filling)					
Family preference					
Nutritional value					
Availability					
Food safety					
Advertising					
Religious restrictions					
Health of family members(e.g. diabetes, heart disease)					
Shelf-life/storage					

We would now like to know a little bit more about your child and his/ her usual habits

6. For an average <u>school day (24 hours)</u> and <u>weekend day (24 hours</u> – i.e. a Saturday or a Sunday, not both) please estimate the time (in hours/minutes) that your child spent doing the following activities:

This is an EXAMPLE of how to fill in the boxes in the question below

ACTIVITY	***TOTAL HOURS/MINUTES in <u>SCHOOLDAY</u>***	***<u>TOTAL HOURS/MINUTES in WEEKEND DAY</u>***
Sleeping *(including night time and day time)*	*11 hours 30 minutes*	*10 hours 0 minutes*

ACTIVITY	***TOTAL HOURS/MINUTES in <u>SCHOOLDAY</u>***	***TOTAL HOURS/MINUTES in <u>WEEKEND DAY</u>***
Sleeping (including night time and day time)		
Sitting activities for example: classroom work, homework, reading, watching TV, playing computer, sewing, eating, sitting in car or bus		
Light activities for example: getting dressed or undressed, tidying a room, feeding or playing with pets, imaginary play, playing a musical instrument, cooking		
Mildly energetic activities for example: playing in the garden, playground games, walking, bicycling (slow/moderate speeds), swimming for fun, dancing, gymnastics		
Energetic activities for example: running, bicycling (fast speeds), football, tennis, rugby, roller-skating, length swimming		

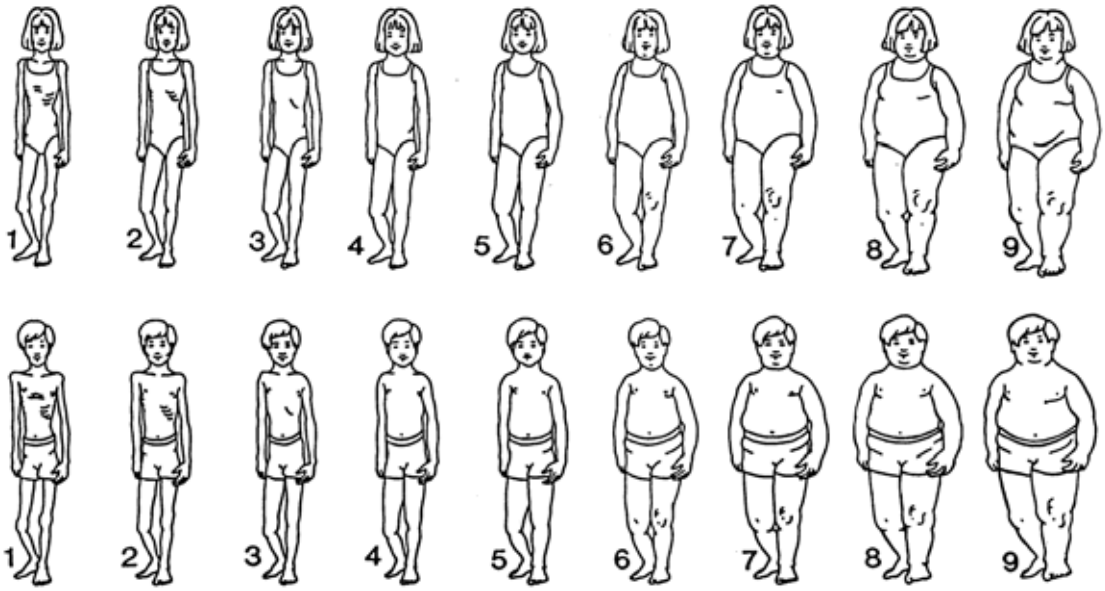
7. Now think about a <u>typical weekday</u> and a <u>typical weekend day</u> for your child in the last year.

	Weekday		Weekend day	
	Hours	**Minutes**	**Hours**	**Minutes**
How much time would you say your child spends playing outdoors on a warmer day, such as spring and summer?				
How much time would you say your child spends playing outdoors on a colder day such as in autumn and winter?				

8. Which of the following places are within walking distance (no more than half hour walk) from your home? How often does your child walk or cycle to each of these places?

	Within walking distance		If yes, how often does your child walk/ cycle there?			
	No	**Yes**	**Never**	**Less than 1 time a week**	**1-3 times a week**	**More than 3 times a week**
School						
Playground/ park						
Leisure centre						
Train/ bus station						
Shops selling fresh fruit and vegetables						
Fast food/ take-away shops						
Other food shops						
Child's friends' home						
Place of worship						

9. Please look at the following drawings of children and for each of the questions below, write a number representing the drawing closest to your choice.



	1	2	3	4	5	6	7	8	9
Which picture looks the most like your child?									
Which picture shows the way you want your child to look?									
Which picture shows the way you think is best for boys to look?									
Which picture shows the way you think is best for girls to look?									

10. On average, how often does your child choose to eat each of the following types of foods?

	At least once a day	5-6 times a week	2-4 times a week	Once a week or less	Don't know
Piece of fruit					
Vegetables					
Chocolate bar					
Packet of crisps					

11. What is your child's date of birth?.....

12. Is your child:

☐ Male ☐ Female

13. Which of the following would you say best describes your child's ethnic group?

☐ British
☐ Irish
☐ Other white……
☐ White and black Caribbean
☐ White and black African
☐ White and Asian
☐ Other mixed……
☐ Indian
☐ Pakistani
☐ Bangladeshi
☐ Other Asian……
☐ Black African
☐ Black Caribbean
☐ Other black……
☐ Chinese
☐ Other .....

Finally we would like to know a little bit more about you and your family

14. What is your age (please tick the box that applies to you)

☐ Younger than 20
☐ 20 - 24
☐ 25 - 29
☐ 30 - 34
☐ 35 - 39
☐ 40 - 44
☐ 45 - 49
☐ 50 - 54
☐ 55 - 59
☐ 60 and over

15. Are you:

☐ Male
☐ Female

16. In a typical week (7 days) how many times on average do you do the following kinds of exercise for <u>more than 15 minutes</u> during your <u>free time</u>? Write the appropriate number in each box below.

Times per week

a) **Strenuous exercise** (heart beat rapidly)
(e.g. jogging, vigorous swimming, netball, aerobics, circuits) ☐

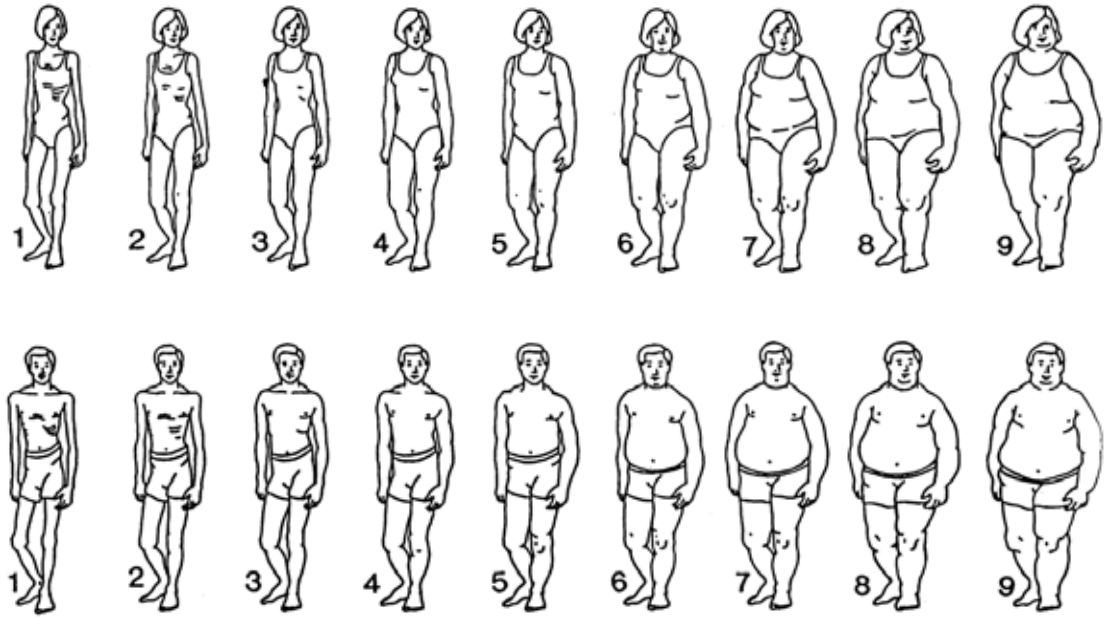
b) **Moderate exercise** (not exhausting, but tiring)
(e.g. fast walking, tennis, cycling, easy swimming, dancing) ☐

c) **Mild exercise** (minimal effort)
(e.g. yoga, archery, bowling, golf, easy walking) ☐

17. In a typical week (7 days), during your leisure time, how often do you engage in any regular activity long enough to work up a sweat (heart beats rapidly)?

Often	Sometimes	Never/Rarely
☐	☐	☐

18. Please look at the following drawings of adults and answer the questions below



	1	2	3	4	5	6	7	8	9
Which picture looks the most like you?									
Which picture shows the way you want to look?									
Which picture shows the way you think is best for a man to look?									
Which picture shows the way you think is best for a woman to look?									

19. Has anyone in your family (including yourself) been diagnosed with diabetes?

☐ No

☐ Yes Please state the relationship of the family member(s) with diabetes to your child

……

20. Has anyone in your family (including yourself) been diagnosed with heart disease?

☐ No

☐ Yes Please state the relationship of the family member(s) who have heart disease to your child

……

21. What is the main language spoken in your home?

☐ English

☐ Other (please state)…….....

22. Is anyone in your household currently earning wages?

☐ Yes - Please state the occupation of the main wage earner in your household……

☐ No - is this because you/ other adults in the house are:

- ☐ Students
- ☐ Retired – what was the previous occupation?.....
- ☐ Unemployed – what was the previous occupation?.....
- ☐ Never worked

That is the end of the questionnaire.
Thank you very much for taking the time to complete this.

Please now return the questionnaire in the envelope provided, to be entered in the free prize draw!

Appendix 2

The MASSES online survey

1. Introduction

Thank you for taking the time to complete this survey, your responses should be honest and accurate.

PLEASE DO NOT COMPLETE THIS SURVEY IF YOU HAVE:

1. A DIAGNOSED SLEEP DISORDER
2. ARE TAKING SLEEP ALTERING MEDICATIONS
3. HAVE TRAVELLED TO A DIFFERENT TIME ZONE IN THE LAST 4 WEEKS
4. HAVE NOT GAINED YOUR PARENTS CONSENT

The survey will take around 20 minutes to complete and all responses will remain confidential and anonymous.

You will be asked questions relating to times of the day, please use the 24 hour clock at all times.

You will be asked about your height and weight - if you DO NOT know your height and/or weight, ask the researcher where the facilities are located to measure this.

If you have any questions before, during or after this survey please consult the researcher.

You have the right to withdraw from the survey at any time.

2. Demographics & School Information

This section will request general demographic information. Please provide accurate responses.

* 1. Please enter your personal ID number which has been provided to you in the box below.

* 2. What is your age in years?

* 3. If you are completing this survey you should be a registered student at Repton. Please indicate if you are a boarder or day student.

- ◯ Boarder
- ◯ Day Student

* 4. What year are you currently in at school?

- ◯ Year 7
- ◯ Year 8
- ◯ Year 9
- ◯ Year 10
- ◯ Year 11
- ◯ Year 12
- ◯ Year 13

* 5. What are your grades in school mostly?

- ◯ A*'s
- ◯ A*'s and A's
- ◯ A's
- ◯ A's and B's
- ◯ B's
- ◯ B's and C's
- ◯ C's
- ◯ C's and D's
- ◯ D's
- ◯ D's and E's

6. What is the highest level of education you expect to complete?

- ◯ GCSE's
- ◯ A-Level
- ◯ Degree (BSc or BA)
- ◯ Postgraduate (Masters or PhD)
- ◯ Not sure yet

7. What is your ethnicity?

- ◯ White (British)
- ◯ White (non-British)
- ◯ European
- ◯ Indian
- ◯ Pakistani
- ◯ Chinese
- ◯ Japanese
- ◯ Mixed Race
- ◯ Black (Jamaican)
- ◯ Black (African)
- ◯ Other

Please specify

8. What is your height in cm?
(If you know your height in feet and inches but not in cms, please ask the researcher to convert this for you)

9. What is your weight in kg?

(If you are unsure of your weight in KG but know your weight in stones and pounds, please minimise your screen and copy and paste the following link to convert your weight http://www.hintsandthings.co.uk/bathroom/weights.htm)

3. Sleep Habits on Weekdays:

These questions are about your usual schedule, when you have to go to school the next day.

There are no right or wrong answers.

Please choose the the answer that best describes the way your sleep has been for the last 2 school weeks.

1. With whom do you usually share a bedroom? (Tick all that apply)

- [ ] Mother/step-mother
- [ ] Father/step-father
- [ ] Brother(s)/sister(s)
- [ ] Other family member(s)
- [ ] With a friend(s)
- [ ] I don't share a bedroom with anyone

2. What time do you USUALLY get into bed on school days?

3. What time do you USUALLY start trying to go to sleep?

4. How long does it USUALLY take you to fall asleep? (In minutes)

5. There are many reasons for doing things at one time or another. What is the main reason you USUALLY go to bed at this time on school days? (Choose one)

- ◯ I have decided this is the best time to go to bed
- ◯ My parents/school have set my bedtime
- ◯ I feel sleepy
- ◯ I finish my homework
- ◯ The TV programmes I watch have finished
- ◯ My brothers/sisters go to bed
- ◯ I have finished talking to my friends/family
- ◯ I get home after going out for the evening
- ◯ I get home from my job
- ◯ Other

Please specify

6. Do you have a light on in your room at night?

- ◯ Yes
- ◯ No

7. AFTER you go to bed on a school night:
(select one response for each scenario)

	Never	Sometimes	Usually	Always
Do you watch TV/DVD?	◯	◯	◯	◯
Drink tea/coffee/fizzy drinks?	◯	◯	◯	◯
Do you listen to music/radio?	◯	◯	◯	◯
Do you read?	◯	◯	◯	◯
Do you worry?	◯	◯	◯	◯
Do you play video games (Wii, XBox, PS etc.)	◯	◯	◯	◯
Do you eat a snack?	◯	◯	◯	◯
Do you use the internet/PC/laptop?	◯	◯	◯	◯
Do you use your mobile phone to call/text?	◯	◯	◯	◯
Do you take your mobile phone to bed and leave it switched on whilst sleeping?	◯	◯	◯	◯
Do you receive texts/calls that wake you up?	◯	◯	◯	◯

If so, how long does it usually take to get back to sleep? (In minutes)

8. What time do you USUALLY wake up on school days

9. What time do you USUALLY get up on school days?

10. What is the main reason you usually wake up at this time on school days? (Choose one)

- ◯ Noises or my pets wake me up
- ◯ My alarm clock/clock radio wakes me up
- ◯ My parents/other family members wake me up
- ◯ I need to go to the toilet
- ◯ Because I'm hot/cold
- ◯ I don't know, I just wake up
- ◯ Other

Please specify

11. How easy do you find it to get up on school days?

- ◯ Very easy
- ◯ Easy
- ◯ Not easy
- ◯ Hard

12. If you could choose, what time would you get up?

13. Work out how long you USUALLY sleep on a normal school night and fill it in here. Do not include time you spend awake in bed. (Remember to mark hours AND minutes even if the minutes are zero)

Hours

Minutes

14. What time do you USUALLY leave home on school days?

15. How do you USUALLY travel to school?

- ◯ Walk
- ◯ Bus
- ◯ Get a lift with parents
- ◯ Get a lift with friends
- ◯ Bike
- ◯ Other

Please specify

16. What time do you need to arrive at school?

4. Sleep Habits at Weekends

These questions are about your usual sleep schedule, when you do not have to go to school the next day (e.g weekends or school holidays).

There are no right or wrong answers.

Please choose the answer that best describes the way your sleep has been over the last two weeks.

1. What time do you USUALLY get to bed on weekend days?

2. What time do you USUALLY start trying to go to sleep?

3. How long does it USUALLY take for you to fall asleep?

4. There are many reasons for doing things at one time or another. What is the main reason you USUALLY go to bed at this time on weekend days? (Choose one)

- ◯ My parents/school have set my bedtime
- ◯ I feel sleepy
- ◯ I finish my homework
- ◯ The TV programmes I watched have finished
- ◯ My brothers/sisters go to bed
- ◯ I have finished talking to my friends/family
- ◯ I get home after going out for the evening
- ◯ I get home from my job
- ◯ Other

Please specify

5. After you go to bed on a weekend day:
(Choose one from each scenario)

	Never	Sometimes	Usually	Always
Do you watch TV/DVD?	◯	◯	◯	◯
Drink coffee/tea/fizzy drinks?	◯	◯	◯	◯
Do you listen to music/radio?	◯	◯	◯	◯
Do you read?	◯	◯	◯	◯
Do you worry?	◯	◯	◯	◯
Do you play video games (Wii, XBox, PS etc.)	◯	◯	◯	◯
Do you eat a snack?	◯	◯	◯	◯
Do you use the internet/PC/laptop?	◯	◯	◯	◯
Do you use your mobile phone to call/text?	◯	◯	◯	◯
Do you take your mobile phone to bed and leave it switched on whilst sleeping?	◯	◯	◯	◯
Do you receive texts/calls that wake you up?	◯	◯	◯	◯

If so, how long does it usually take to get back to sleep? (In minutes)

6. What time do you USUALLY wake up on a weekend?

7. What time do you USUALLY get up on a weekend?

8. What is the main reason you usually wake up at this time on weekend days?
(Choose one)

- ◯ Noises or my pet wakes me up
- ◯ My alarm clock/clock radio wakes me up
- ◯ My parents/other family members wake me up
- ◯ Because I'm hot/cold
- ◯ I need to go to the toilet
- ◯ I don't know, I just wake up
- ◯ Other

Please specify

9. How easy do you find it to get up on weekend days?

- ◯ Very easy
- ◯ Easy
- ◯ Not easy
- ◯ Hard

10. If you could choose, what time would you get up?

11. Work out how long you USUALLY sleep on a normal weekend night and fill it in here.

*DO NOT include time you spend awake in bed.

Remember to to mark hours and minutes even if the minutes are zero.

Hours

Minutes

5. Your sleep pattern

1. Some people wake up in the night, others never do. How many times do you USUALLY wake up in the night? (Choose one)

- ◯ Never
- ◯ Once
- ◯ 2 or 3 times
- ◯ More than 3 times
- ◯ I don't know

2. People sometimes feel sleepy during the day. During your day time activities, how much of a problem do you have with sleepiness (feeling sleepy, struggling to stay awake)?

- ◯ No problem at all
- ◯ A little problem
- ◯ More than a little problem
- ◯ A big problem
- ◯ A very big problem

3. Some people take naps in the daytime every day, others never do. When do you nap? (Tick all that apply to you)

- ☐ I never nap
- ☐ I never nap unless I am ill
- ☐ I sometimes nap on school days
- ☐ I somtimes nap on weekends

4. During the last two weeks, have you struggled to stay awake and/or fallen asleep in the following situations? (Tick one from each scenario)

	Not struggled to stay awake at all	Struggled to stay awake	Fallen asleep	Not applicable
In face to face conversation with another person?	◯	◯	◯	◯
Travelling in a bus, train or car?	◯	◯	◯	◯
Attending a performance (film, concert, play)?	◯	◯	◯	◯
Watching TV?	◯	◯	◯	◯
During a test?	◯	◯	◯	◯
In a class at school?	◯	◯	◯	◯
Whilst working on a computer?	◯	◯	◯	◯
Playing a games console?	◯	◯	◯	◯
Riding a bicycle?	◯	◯	◯	◯
Eating a meal?	◯	◯	◯	◯

5. Can you work out how much sleep you NEED?

Fill in how much sleep you think you would need each night to feel your best every day.

Remember to mark hours and minutes even if the minutes are zero.

Hours

Minutes

6. In general, do you feel you usually get: (Choose one)

- ◯ Too much sleep?
- ◯ Enough sleep?
- ◯ Too little sleep?

7. How often do you think you get enough sleep? (Choose one)

- ◯ Always
- ◯ Usually
- ◯ Sometimes
- ◯ Rarely
- ◯ Never

8. Do you consider yourself to be a:

- ◯ Good sleeper?
- ◯ Poor sleeper?

9. When you have difficulty falling asleep or getting back to sleep, what do you do? (tick all that apply)

- ☐ Stay in bed and try to get to sleep
- ☐ Do something in bed (e.g read or watch TV)
- ☐ Get up and watch TV
- ☐ Get up and drink alcohol
- ☐ Get up and drink warm milk
- ☐ Get up and drink a carbonated drink
- ☐ Get up and drink coffee/tea
- ☐ Get up and drink water
- ☐ Get up and have a cigarette

Other (please specify)

10. Please tick a number from 0-10 to indicate how much difficulty you have in "slowing down" or "turning off" your mind while trying to sleep

*(0 = No Difficulty, 5 = Some Difficulty, 10 = Great Difficulty)

	0	1	2	3	4	5	6	7	8	9	10
Difficulty	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯	◯

6. What suits you?

1. The bad news: you have to take a two hour exam.

The good news: you can take it when you think you'll do your best.

What time is that? (Choose one)

- ◯ 08:00 - 10:00
- ◯ 11:00 - 13:00
- ◯ 15:00 - 17:00
- ◯ 19:00 - 21:00

2. When do you have the most energy doing your favourite things? (Choose one)

- ◯ Morning! I am tired in the evening
- ◯ Morning more than evening
- ◯ Evening more than morning
- ◯ Evening! I am tired in the morning

3. One hears about "morning" and "evening" types of people. Which ONE of these types to you consider yourself to be?

- ◯ Definitely a morning type
- ◯ More a morning than evening type
- ◯ More an evening than morning type
- ◯ Definitely an evening type

4. If you could choose your bedtime regardless of commitments, what time would that be? (Choose one)

- ◯ 20:00 - 21:00
- ◯ 21:00 - 22:15
- ◯ 22.15 - 00.30
- ◯ 00.30 - 01.30
- ◯ 01.45 - 03:00

5. When does your body start to tell you it's time for bed? (even if you ignore it)

- ◯ 20:00 - 21:00
- ◯ 21:00 - 22:15
- ◯ 22.15 - 00.30
- ◯ 00.30 - 01.30
- ◯ 01.45 - 03:00
- ◯ Not sure

6. How alert are you in the first half hour after you get up? (Choose one)

- ◯ Out of it
- ◯ A little dazed
- ◯ Okay
- ◯ Ready to take on the world

7. Imagine you had to get up at 06:00 every day. What would that be like?

- ◯ Awful!
- ◯ Not so great
- ◯ Okay (if I have to)
- ◯ Fine, no problem

8. When you wake up in the morning, how long does it take for you to feel fully awake?

- ◯ Less than 10 minutes
- ◯ 11-20 minutes
- ◯ 21-40 minutes
- ◯ More than 40 minutes

7. Health Habits

1. IN THE PAST MONTH...

How much coffee / tea did you drink?

- ◯ More than 3 cups per day
- ◯ Between 1-3 cups per day
- ◯ Less than 1 cup per day
- ◯ None

2. IN THE PAST MONTH...

How many caffeinated / energy soft drinks did you drink (Pepsi, Dr Pepper, Coke, Red Bull etc.)?

- ◯ More than 3 glasses/cans per day
- ◯ Between 1-3 glasses/cans per day
- ◯ Less than 1 glass/can per day
- ◯ None

3. IN THE PAST TWO WEEKS...

	More than twice a day	Once or twice a day	1-5 times per week	Never
Did you drink a fizzy drink with caffeine/energy?	◯	◯	◯	◯
Did you drink coffee/tea?	◯	◯	◯	◯

4. IN THE PAST TWO WEEKS...

	Never	Once	Twice	Several times	Every day/night
Have you arrived at school late because you overslept?	◯	◯	◯	◯	◯
Have you stayed up until 3am?	◯	◯	◯	◯	◯
Have you stayed up all night?	◯	◯	◯	◯	◯
Have you slept until after 12 noon?	◯	◯	◯	◯	◯
Have you felt tired or worn out during the day?	◯	◯	◯	◯	◯
Have you needed more than one reminder to get up in the morning?	◯	◯	◯	◯	◯
Have you had fearful thoughts or images whilst falling asleep?	◯	◯	◯	◯	◯
Have you had bad dreams/nightmares during the night?	◯	◯	◯	◯	◯
Have you walked in your sleep?	◯	◯	◯	◯	◯
Have you wet your bed?	◯	◯	◯	◯	◯
Have you snored?	◯	◯	◯	◯	◯
Have you stopped breathing while you sleep or woke up gasping for breath?	◯	◯	◯	◯	◯
Have you gone to bed because you couldn't stay awake any longer?	◯	◯	◯	◯	◯
Have you done dangerous things without thinking?	◯	◯	◯	◯	◯
Have you had a good night's sleep?	◯	◯	◯	◯	◯

5. IN THE PAST TWO WEEKS...

How often were you bothered by the following?

	A lot	Somewhat	Not at all
Feeling too tired to do things	◯	◯	◯
Having trouble going to sleep or staying asleep	◯	◯	◯
Feeling unhappy, sad or depressed	◯	◯	◯
Feeling hopeless about the future	◯	◯	◯
Feeling nervous or tense	◯	◯	◯
Worrying too much about things	◯	◯	◯

8. Sleep Beliefs

In order to better understand your sense of the average teenager's sleep, please answer the following questions based on your beliefs for an average teenager who does not have sleep problems:

1. How many hours of sleep does the average teenager get?

2. How long does it take the average teenager to get to sleep? (minutes)

3. How many times does the average teenager wake up in the night?

4. How long does the average teenager spend awake in bed during the night?

(Hours)

(Minutes)

5. Do you think most teenagers get enough sleep?

- ◯ Yes
- ◯ No
- ◯ Don't Know

9. Cleveland Adolescent Sleepiness Questionnaire

We would like to know about when you might feel sleepy during the usual week. For each statement, tick the answer that best fits with how often it applies to you.

It's important to answer them yourself - don't have people help you.

There are no right or wrong answers.

1. Select one response for each scenario:

	Never	Rarely (less than 3 times per month)	Sometimes (1-2 times per week)	Often (3-4 times per week)	Almost everyday (5+ times per week)
In the morning when I am at school, I fall asleep	◯	◯	◯	◯	◯
I fall asleep during my morning classes	◯	◯	◯	◯	◯
During the school day, there are times when I realise that I have just fallen asleep	◯	◯	◯	◯	◯
I fall asleep in my afternoon classes	◯	◯	◯	◯	◯
I fall asleep during the last class of the day	◯	◯	◯	◯	◯
I fall asleep when I do schoolwork at home in the evening	◯	◯	◯	◯	◯
I fall asleep when I ride in a bus, car or train	◯	◯	◯	◯	◯
I feel sleepy when I ride in a bus to a school event like a trip or sports game	◯	◯	◯	◯	◯
I feel drowsy if I ride in a car for longer than 5 minutes	◯	◯	◯	◯	◯
I feel sleepy in the evening after school	◯	◯	◯	◯	◯
I feel sleepy when I do my homework in the evening after school	◯	◯	◯	◯	◯
I go throughout the whole school day without feeling tired	◯	◯	◯	◯	◯
I feel wide awake the whole day	◯	◯	◯	◯	◯
I feel alert during my classes	◯	◯	◯	◯	◯
When I am in class, I feel wide awake	◯	◯	◯	◯	◯
I feel wide awake the last class of the day	◯	◯	◯	◯	◯

10. Rating scale for Pubertal Development

The next questions are about changes that may be happening to your body. These changes normally happen to young people at different ages. They may have something to do with your sleep patterns so do your best to provide accurate answers.

If you do not understand a question or do not know the answer, just mark "I don't know".

1. Would you say that your growth in height:

- ◯ Has not yet begun to spurt
- ◯ Has barely started
- ◯ Is definitely underway
- ◯ Seems completed
- ◯ I don't know

2. Would you say that your body hair growth:

- ◯ Has not yet begun to grow
- ◯ Has barely started to grow
- ◯ Is definitely underway
- ◯ Seems completed
- ◯ I don't know

3. Have you noticed any skin changes, especially spots?

- ◯ Skin has not yet started changing
- ◯ Skin has barely started changing
- ◯ Skin changes are definitely underway
- ◯ Skin changes seem complete
- ◯ I don't know

4. This page has been divided into two separate sections: One for males and one for females.

Please state whether you are male or female to be re-directed to the appropriate section.

- ◯ Male
- ◯ Female

11. Section for Boys

1. Have you noticed a deepening in your voice?

- ◯ Voice has not yet started changing
- ◯ Voice has barely started changing
- ◯ Voice changes are definitely underway
- ◯ Voice changes seem complete
- ◯ I don't know

* 2. Have you begun to grow hair on your face?

- ◯ Facial hair has not yet started growing
- ◯ Facial hair has barely started growing
- ◯ Facial hair growth has definitely started
- ◯ Facial hair growth seems complete
- ◯ I don't know

12. Section for Girls

1. Have you noticed your breasts have begun to grow?

- ◯ Have not yet started growing
- ◯ Have barely started growing
- ◯ Breast growth is definitely underway
- ◯ Breast growth seems complete
- ◯ I don't know

2. Have you begun to menstruate (started your periods)?

- ◯ Yes
- ◯ No

If yes, how old were you when you started to menstruate?

13. Debriefing

Thank you for completing this online survey.

You will now be entered into a prize drawer to win a voucher.

This project was supported by the Heart of England Foundation Trust, University of Birmingham and Aim Higher.

This research aims to examine the role of modern technology, sleeping habits, school performance and body mass index amongst adolescents.

Should you have any questions about this research or feel that you have been affected in any way, please contact a member of the research team. Alternatively, you can contact the Chief Investigator, Teresa Arora on [redacted]

Appendix 3

MANUSCRIPT PUBLICATIONS

Lam KB, Jiang CQ, Thomas GN, **Arora T**, Zhang WS, Taheri S, Adab P, Lam TH, Chang KK. Napping is associated with increased risk of type 2 Diabetes: the Guangzhou Biobank Cohort Study. *Sleep* 2010;33:402-407.

Arora T, Jiang CQ, Zhang WS, Lam KB, Cheng KK, Lam TH, Thomas GN, Taheri S. Self-reported long total sleep duration is associated with increased risk of the metabolic syndrome: The Guangzhou Biobank Cohort Study. *Diabetes Care*. In Press.

Arora T, Yao LG, Bishop J, o'Hartaigh B, Campbell M, Lam KB, Thomas GN, Taheri S. A cross-sectional study of sleep, technology use, obesity and academic performance in contemporary UK adolescents. Submitted to Sleep Medicine.

BOOK PUBLICATIONS

Hampson P, Rossi A, **Arora T**, Lord JM, Taheri S. Sleep and immunity in older age. In Psychoneuroimmunology of Aging (Eds JA Bosch, AC Phillips and JM Lord), Springer Publishing. In Press.

Arora T, Taheri S. Sleep and the metabolic syndrome. In Encyclopedia of Sleep and Dreams, ABC-CLIO. In Press.

ABSTRACT PUBLICATIONS

Arora T, Yao L, Hussain S, Thomas G Neil, Taheri S. A population study examining the role of sleep duration as a mediator of the interactions between technology use and obesity in adolescence. *Sixth Annual Conference on Pediatric Sleep Medicine* 27-30 October, 2011, Florida, USA.

Arora T, Broglia E, Hampson P, Lord J, Taheri S. Sleep duration and quality in elders and its relationship with health status. *Aging and Sleep meeting* 25-26 June, 2010, Lyon, France.

Arora T, KB Lam, Jiang CQ, Zhang WS, Cheng KK, Lam TH, Taheri S, Thomas GN. Long sleep duration is associated with the metabolic syndrome: The Guangzhou Biobank Cohort Study. *Sleep* 2010;33. Abstract 0305.

Arora T, Lam KH, o'Hartaigh B, Broglia EL, Wheeler G, Campbell M, Thomas GN, Taheri S. Relationships between sleep and technology use, body mass index and academic performance in a cohort of UK adolescents. *Sleep* 2010; 33. Abstract 0285.

Broglia EL, **Arora T**, Hampson P, Lord JM, Taheri S. Sleep duration and quality in elders and its relationship with health status. *Sleep* 2010; 33. Abstract 1045.

Arora T, Lam KH, Jiang CQ, Zhang WS, Cheng KK, Thomas GN, Lam TH, Taheri S. Adverse cardiometabolic risk and napping: The Guangzhou Biobank Cohort Study. Abstract 0982. *International Sleep Meeting, 2009.* Seattle, USA.

Arora T, Lam KH, Jiang CQ, Thomas GN, Zhang WS, Taheri S, Adab P, Lam TH, Cheng KK. Napping is associated with an increased risk of the metabolic syndrome. Abstract P128. *British Endocrine Society Annual Meeting, 2009.* Harrogate, UK.

AWARDS

Student Researcher of the Year 2010, Association for the Study of Obesity
Travel merit award based on scientific merit 2010; Sleep Research Society
Travel merit award based on scientific merit 2009; Sleep Research Society
Travel and attendance award at the British Endocrinology Society Annual Meeting, 2009; British Endocrinology Society
Travel, accommodation and attendance award at the British Physiological Society Meeting, 2008; British Physiological Society