Dealing with Delirium: the Importance of Good Sleep

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Abstract

Delirium is defined as a sudden disturbance in attention, awareness, and cognition and is a common, and serious surgical complication amongst the older adult population. It is significantly correlated with adverse clinical outcomes including increased mortality and the loss of independence. The Thesis consists of 5 Chapters and includes a systematic review, a sleep deprivation and a clinical study.

The systematic review aims to bridge the gap in sleep screening methodologies by evaluating the use of subjective screening tools and providing recommendations for the use of each tool for researchers and clinicians. Following a review of 25 studies, results were summarised and the needs for researchers and clinicians were considered. For sleep disorders, researchers were recommended to use the Insomnia Severity Index, the Observational Sleep Assessment Instrument (OSAI), the Mayo Sleep Questionnaire and the Sleep Symptom Checklist (SSC), and for clinicians the Insomnia Severity Index, the Observation-based Nocturnal Sleep Inventory, the OSAI, the Mayo Sleep Questionnaire, and the Sleep Interview. The review recommends the use of the Insomnia Severity Index, the OSAI, and Mayo Sleep Questionnaire for both researchers and clinicians. When screening for sleep behaviours and disturbances both researchers and clinicians are recommended to use one of the following include the Pittsburgh Sleep Quality Index, and the Karolinska Sleepiness Scale.

This systematic review provides novel guidance and has potential to be incorporated into routine assessments. Older adults are at an increased risk of developing sleep disorders and experience poorer sleep quality, often left untreated due to lack of routine screening, and research has identified sleep disruption to be a risk factor for post-operative delirium. There is potential for patient care to be improved through addressing these underlying sleep disorders, effectively monitoring for changes to sleep quality, and identifying those at greater risk of post-operative delirium as a result.

The first study explored the interaction a 24-hour period of sleep deprivation has on the sleep/wake cycle and the effects of the increasing pressure to sleep on changes to attention, psychotic-like symptoms, sleepiness, memory, emotion and scores on a validated delirium assessment scale in healthy adults. The increasing pressure to sleep was found to induce reversible changes in a non-clinical population across the 7 assessments that took place over the 24-hour study duration. Participants become faster at completing the reaction time task, made more mistakes through incorrectly suppressing their responses, exhibited greater variability in reaction time, experienced changes in feelings of delusional thinking, anhedonia, paranoia, positive emotion, as well as presented with

fluctuating delirium scores. Our study observed similar attentional deficits previously reported in post-operative delirium, namely changes in reaction time and intra-trial variability, during periods participants should normally be awake. The study was able to detect acute changes in cognitive functioning and provides an alternative perspective on delirium assessment. We observed cognitive deficits appearing relatively quickly following several hours of disruptions to the sleep/wake cycle in our young, healthy adult sample without predisposing factors for delirium. Our findings highlight the importance of further exploring the modifiable factor of sleep disruption to reduce delirium risk, particularly in older adults who are at a greater risk of developing delirium.

In the clinical study, sleep disruption within a clinical population was explored with the aim of investigating pre- and post-operative sleep, as measured using actigraphy monitors, an objective measure of sleep, and delirium, where the pre-operative baseline for sleep is taken at home. A cohort of 45 older adults undergoing elective hip or knee replacement surgery were enrolled into the study. Assessments took place at baseline, 1-day post-surgery, 4-days post-surgery and 3-months post-surgery. The actigraphy data obtained provided an insight into the quality and quantity of sleep achieved in those awaiting and having recently undergone surgery. General comparisons were made and participants were found to have experienced changes to their normal habitual sleep, through spending less time in bed, less time asleep, and sleeping for a shorter period of time in hospital when compared to their sleep at home. Moreover, participants who experienced an increase in their activity levels and an increase in the amount of time spent awake when they were awoken, were associated with an increase in delirium at 1-day and 4-day post-surgery. The greater degree of change to activity level and average awakening length, the greater the risk of post-operative delirium.

Our findings have identified additional sleep measures which increase the risk of post-operative delirium, as well as adding to our knowledge and understanding of sleep disruption in the hospital environment. This supports the importance of sleep, particularly sleep that occurs at home prior to hospitalisation for delirium risk. This has potential implications for improving routine care. Interventions that reduce sleep disruption during periods patients normally sleep may improve sleep quality and in turn reduce delirium risk. The routine monitoring of changes to sleep is recommended to identify those who develop a greater risk of delirium during hospitalisation.

This Thesis contributes to the literature on sleep and delirium, providing recommendations for the use of screening tools, which should form a part of regular routine healthcare management. Specific types of sleep disruption that occur prior to and during hospitalisation were identified to increase the

risk of post-operative delirium and has important implications for patient care. A pre-hospitalisation routine for elective surgery should include maintaining good sleep habits to reduce delirium risk.

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Abbreviations

95%CI, 95% Confidence Interval

AD, Alzheimer disease

AD, Alzheimer's Dementia

AHI, Apnea/Hypopnea Index

ALF, Assisted Living Facilities

AR, Abigail Renick

ArL, Arousal Index

ASDA, American Sleep Disorders Association

BI, Barthel Index

BiPAP, Bi-level Positive Airway Pressure

BMI, Body Mass Index

CAI, Central apnea index

CBTI, Cognitive Behavioural Therapy for Insomnias

CDR, Clinical Dementia Rating

CESD, Center for Epidemiologic Studies Depression scale

CF, Professor Chris Farmer

CGA, Comprehensive Geriatric Assessment

CNS, Central Nervous System

CPAP, Continuous Positive Airway Pressure

CVD, Cardiovascular Disease

DEB, Dream Enactment Behaviour by History and/or PSG

DSM, Diagnostic and Statistical Manual of Mental Disorders

EDS, Excessive Daytime Sleepiness

EMA, Early morning Awakening

ES, Elizabeth Smith

FOSQ, Functional Outcomes of Sleep Questionnaire

GDS-5, Geriatric Depression Scale

HR, Heart Rate

ICD-10, 10th Edition of the International Classification of Diseases

ICD-10, International Classification for Diseases 10th Edition

ICSD-2, International Classification of sleep disorders, second edition

IMI, Intermovement Interval

Inpatient PAR, Inpatient Post-Acute Rehabilitation

iRBD, Idiopathic REM Sleep Behavior Disorder;

ISI, Insomnia Severity Index

LM, Leg movements

MCI, Mild Cognitive Impairment;

MD, Multiple Domain

MI, Movement Index

MI, Myoclonus Arousal Index

MrOS, Outcomes of Sleep Disorders in Older Men Study

MSCA, Mayo Clinic Study of Aging

MSQ, Mayo Sleep Questionnaire

NEMESIS, North East Melbourne Stroke Incidence Study

NoW, Number of Wake Bouts

NSHAP, National Social Life, Health, and Aging Project

OAGS, Older Adults with Good Sleep

OAHI, obstructive apnea-hypopnea index

OAI, obstructive apnea index

OSA, Obstructive Sleep Apnea

OSAS, Obstructive Sleep Apnea Syndrome;

PASE, Physical Activity Scale for the Elderly

PD, Parkinson Disease

PI, Pervasion Index

PLMS, Periodic Limb Movements of Sleep;

POMS, Profile of Movement States

PSG, Polysomnogram;

PSQI, Pittsburgh Sleep Quality Index;

Q_1, Q_2, Median

RB, Rowena Bicknell

RBD, Rapid Eye Movement Sleep Behaviour Disorder

RBDSQ-J, REM Sleep Behavior Disorder Screening Questionnaire Japanese Version;

RCT, Randomized Controlled Trial

RDI, Respiratory Disturbance Index

RLS, Restless Legs Syndrome

ROC AUC, Receiver Operating Characteristic Area Under Curve

RSWA, Rapid Eye Movement Sleep with Atonia

SaO_2 <90%, Percentage of Sleep Time with Oxygen Saturation below 90%

SCOPES, Stroke Care Outcomes Providing Effective Services

SD, Single Domain

SD, Standard Deviation

SDB, Sleep-Disordered Breathing

SOF, Study of Osteoporotic Fractures

SOL, Sleep Onset Latency

SRLC, Sleep Related Leg Cramps

SSD, Subsyndromal delirium

SW, Sleepwalking

TIB, Time in Bed

TSP, Total Sleep Period

VA, Veterans Administration

WASO, Wake After Sleep Onset

$\bar{x}$, Mean

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Chapter 1: What is Delirium?

1.1 Importance of delirium research

Post-operative delirium most often presents in the older adult hospitalised population (Inouye, Schlesinger, & Lydon, 1999) and is a common, yet serious complication of hospitalisation following elective surgery (Gillick, Serrell, & Gillick, 1982), with a high mortality rate, rising by 11% per every 48 hours of delirium duration (González et al., 2009). Despite this, the impact delirium has on health is frequently underestimated (Young & Inouye, 2007).

Delirium is an acute state of confusion when a 'disturbance of consciousness occurs, with reduced ability to focus, sustain, or shift attention' which can develop and fluctuate over short periods of time (American Psychiatric Association, 2013). Although delirium in the community is low (1 - 2%), this increases with age (14% in those over 85 years old) (Fong, Tulebaev, & Inouye, 2009). The incidence of delirium increases in emergency departments, rising to 10 - 30% where delirium is often indicative of an underlying medical illness (Siddiqi, House, & Holmes, 2006). Individuals presenting with delirium on hospital admission range from 14 - 24% with this increasing to 6 - 56% during hospitalisation (Inouye, 1998).

The Multifactorial Model (Inouye & Charpentier, 1996), describes an inter-relationship between predisposing and precipitating factors for delirium has been validated in the older adult population, with those with a higher baseline level of vulnerability at greater risk of delirium than those without. Predisposing factors include old age, illness severity, length of hospitalisation, low albumin visual impairment and use of a urinary catheter, all of which increase delirium risk in acute hospital care (Ahmed, Leurent, & Sampson, 2014). In the older adult population, the prevalence of delirium is estimated in 15 - 53% of post-operative individuals (Inouye, 2006) and in 70 - 87% of those in intensive care (Pisani, McNicoll, & Inouye, 2003).

Post-operative delirium is associated with numerous adverse post-operative clinical outcomes, including an increased risk of falls, disruptive behaviour, incontinence, prolonged hospital admission, increased care costs, dementia, institutionalisation and death (Rockwood et al., 1999; Marcantonio et al., 2000; Franco et al., 2001; McCusker et al., 2002; Siddiqi et al., 2006; Stenvall et al., 2006; Inouye, 2006; Leslie et al., 2008; Witlox et al., 2010).

Research has suggested that delirium can be preventable in an estimated 30 – 40% of cases, however these prevention protocols are often not embedded into routine hospital care (Inouye, Westendorp, & Saczynski, 2014). Intervention strategies involve targeting the specific risk factors and a combination of orientation (or reorientation), mobilisation, cognitive activation, and non-pharmacological sleep promotion, with these methods showing success in the prevention of delirium and cognitive decline (Rubin, Neal, Fenlon, Hassan, & Inouye, 2011). Furthermore, a systematic review of 14 studies showed multi-component non-pharmacological interventions are effective in reducing post-operative delirium and falls in older adults by up to 50% (Hshieh, Yue, Puelle, Dowal, Travison, & Inouye, 2015).

The financial cost of treating delirium is high, and creates a burden on healthcare services (Inouye, Schlesinger, Lydon et al., 1999). Several studies have estimated total healthcare costs in 2011 range from $16,303 to $64,421 per patient and in total up to $164 billion USD in the United States (Leslie, Marcantonio, Zhang, Leo-Summers, & Inouye, 2008) and $182 billion USD in European countries per year (Inouye, Westendorp, & Saczynski, 2015). The cost of delirium on the German healthcare system, including the time attributed to delirium treatment which is often not taken into account, provides a more accurate estimate of total costs. In this study, a range of settings (including the ICU) was included in the analysis with ten tasks associated with delirium care identified. Some of which included: observation, mobilisation, safety measures and medication. Each patient with delirium was estimated to cost up to 1200 euros after taking into account all costs associated with patient care including personnel, medication and hospital stay of trained hospital staff.

In 2017, the Office of National Statistics UK population overview (2018) estimated the population of the United Kingdom to be 66 million. This is projected to continue to grow to 73 million by 2041 due to the overall increasing ageing population through enhancements to health provision, the advancement of technology and lifestyle choices. This is evident in population estimates demonstrating the population of older adults (> 65 years) has continued to grow from 15.9% in 1997 to 18.2% in 2017 and is predicted to increase to 24% by 2041. Within the next 50 years, the figure is predicted to reach 8.6 million. Furthermore, statistics from the Hospital Admitted Patient Care and Adult Critical Care Activity report (National Health Service Digital, 2018) show an overall 2.8% increase in the last 20 years in Finished Consultant Episodes (FCEs). The progressively ageing population is causing an increase in patient numbers. When the data is split by age, patients in the 70 – 74 age group accounted for 7.9% of episodes and were overall the highest number.

With people living longer, and the number of older adults requiring surgery expected to increase (Raats, Steunenberg, De Lange, D.C., & Van Der Laan, 2016), it is of paramount importance to improve our understanding of preventable conditions that the older adult population are at higher risk of developing. Delirium is arguably one of the most common complications of hospitalisation in the older adult population with 90% likely to develop delirium (Pisani, McNicoll, & Inouye, 2003) and it is expensive to treat. It is imperative that risk factors are further investigated so that interventions can be developed to reduce the incidence of delirium (Inouye et al., 1999). Attempts to reduce the incidence of delirium will contribute towards alleviating the burden on health services.

This Chapter discusses the definition of delirium, including the development of the classification of delirium in current diagnostic criteria. It continues on to describe assessment tools used to diagnose delirium and how these have been developed through the advancement of the DSM criteria and its implications on the healthcare system. Furthermore, the aetiology and risk models of delirium, its phenomenology and the adverse clinical outcomes, and a discussion of the important role sleep has on delirium is outlined.

1.2 Definition

The defining features of delirium are the changes in mental states, occurring in the absence of both pre-existing neurocognitive disorders and reduced levels of consciousness (American Psychiatric Association, 2013). It is defined in both the International Classification of Diseases, Tenth Revision (ICD-10) (World Health Organisation, 1992) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (American Psychiatric Association, 2013) classification systems which provide information on the clinical characteristics of delirium, causes, preventions, treatments and outcomes (Tyrer, 2014). The ICD-10 defines delirium as 'an etiologically nonspecific organic cerebral syndrome characterised by concurrent disturbances of consciousness and attention, perception, thinking, memory, psychomotor behaviour, emotion, and the sleep-wake schedule. The duration is variable and the degree of severity ranges from mild to very severe' (World Health Organisation, 1992). These are the most recent versions and are regarded to be the diagnostic gold standard in clinical practice.

Delirium was officially acknowledged in the Diagnostic and Statistical Manual of Mental Disorders (DSM) III (American Psychiatric Association, 1980) in the 1980s and in the International Classification for Diseases 10th Edition (ICD-10) in 1992 (World Health Organisation, 1992). There have been several editions of the Diagnostic and Statistical Manual of Mental Disorders (DSM) which has been published describing delirium. In previous versions of the DSM, delirium was described as an

organic mental disorder whereas now it contains new information regarding prevalence, the course of the disturbance and prognosis. It contains more information on criteria and definitions than the ICD-10 and is therefore important in providing an accurate diagnosis. Delirium is defined as a neurocognitive disorder alongside Parkinson's disease, Alzheimer's disease and other specified and unspecified categories of delirium. A common core feature of these neurocognitive disorders is the shared feature of impaired cognition. The DSM characterises delirium as a sudden, but temporary change, in mental state. The full diagnostic criteria can be seen in Table 1.

Table 1 DSM-5 diagnostic criteria for delirium (American Psychiatric Association, 2013)

A	A disturbance in attention (i.e., reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment).
B	The disturbance develops over a short period of time (usually hours to a few days), represents a change from baseline attention and awareness, and tends to fluctuate in severity during the course of the day.
C	An additional disturbance in cognition (e.g., memory deficit, disorientation, language, visuospatial ability or perception).
D	The disturbances in Criteria A and C are not better explained by another pre-existing, established, or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal, such as coma.
E	There is evidence from the history, physical examination, or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal (i.e., due to a drug of abuse or to a medication), or exposure to a toxin, or is due to multiple aetiologies.

The DSM-5 describes specific subtypes which should be specified alongside the diagnosis of delirium, and include substance intoxication and withdrawal delirium, medication-induced delirium, delirium due to another medical condition and delirium due to multiple aetiologies. Other types of delirium outlined in the DSM-5 include Other Specified Delirium and Unspecified Delirium. These types describe instances where symptoms are observed but do not meet the full criteria for delirium or other neurocognitive disorders. Additionally, the term Subsyndromal Delirium (SSD) is sometimes used. This is used in instances where some symptoms of delirium are observed but do not meet the criteria or progress to delirium (Levkoff et al., 1996). As noted in Cole, Ciampi, Belzile, and Dubuc-Sarrasin (2013),

and Serafim et al., (2017), despite being commonly observed in hospitalised older adults, SSD is not currently included in the DSM-5 and there is no mention of these subcategories of delirious states which do not progress to delirium.

Duration and the subtype should be specified when describing delirium, either in its acute or persistent form. Subtypes for delirium include hyperactive, hypoactive or mixed level of activity. A Hyperactive type is characterised by increased activity, changes in mood and being less supportive when receiving medical care. Hypoactive involves reduced activity, and lethargy. A Mixed level of activity is where activity levels are normal when disturbances to attention and awareness are present (American Psychiatric Association, 2013). Delirium usually persists for seven days and symptoms may still present even after hospital discharge. Patients experiencing delirium may shift and exhibit symptoms from the different subtypes with the most frequently observed and recognised being hyperactive. This subtype is most commonly associated with individuals experiencing the side effects of medication and also drug withdrawal. The hypoactive subtype is observed more frequently in older adults.

The DSM-5 classifies delirium as a disturbance in attention or awareness, alongside a change in baseline cognition which is not explained by a pre-existing neurocognitive disorder (NCD). Difficulties in attention may include impairments in the ability to redirect, focus, sustain and or shift attention. The individual experiencing delirium may be difficult to communicate with, particularly when questions are being directed to them, and they may require these to be repeated due to their inability to focus. It is also common for patients to exhibit a delayed response to questions. An individual experiencing delirium may respond to a previous question they were asked rather than the current question due to their inability to shift attention appropriately. They may also be easily distracted and show a reduction in their ability to orientate with the environment and or themselves. These symptoms fluctuate and manifest over a short period of time, with disturbances worsening in the evenings. This is suggested to be because it is more difficult to find clues to the environment later in the day when it is dark (e.g., sunlight to tell the time). The individual may also show changes in memory (in particular short-term memory), learning, disorientation (especially the ability to identify the date and time), use of language and or perceptual distortions (e.g., visual hallucinations). Visual hallucinations can range from simple to complex.

It is also important to note that the DSM delirium diagnosis is dependent on the level of cognition of the individual. For example, delirium cannot be diagnosed if the individual is comatose (despite having a reduced level of arousal and therefore meeting some of the criteria for the diagnostic

definition for delirium), as they are unable to respond to verbal stimulation and are therefore unable to engage with the current standard of assessment for delirium.

Delirium has historical references ranging back to the first century AD, where the term *L. delirare* (out of the furrow) was first used to describe mental conditions often observed alongside fever (Caraceni & Grassi, 2011). A variety of descriptive terms have been used over time to describe the changes in mental state associated with delirium. More recently, in acute care, terms including Intensive Care Unit (ICU) psychosis, sundowning, acute confusional state and acute brain failure have been used (Maldonado, 2008). The variation of terminology used over time has complicated the ability to differentiate between delirium and other conditions described in-text, as well as our ability to interpret them Hall, Meagher & Maclullich, 2012). This has created some challenges in being able to accurately map the development of the understanding of delirium in the literature. However, it is important to note that over the last 30 years significant advances have been made which are observed in the various revisions of the definition of delirium in the DSM in 1987, 1994 and 2013.

1.3 Assessment and diagnosis of delirium

It was not until the 1980s that delirium was recognised by the DSM as a neurocognitive disorder and a standardised diagnostic criterion developed. Prior to this, a range of terms were used to describe the condition, resulting in subsequent inconsistencies in the literature. There have been significant improvements in our understanding of the condition which has been reflected in the revisions to the DSM delirium criteria. Developments to our understanding of delirium have helped shape the use of a range of assessment tools used to detect delirium.

Tools used in delirium research and clinical assessments vary considerably. The includes variations in the version of the DSM criteria classification system used in diagnosis (some do not use a criteria) (Trzepacz, 1994), time taken to administer the assessment, type of rater, and whether the tool uses screening scales or symptom severity. Some assessments feature a dichotomous approach whereas others use a more quantitative one in determining *severity* through observational data. A systematic review was carried out on delirium scales (Adamis, Sharma, Whelan, & MacDonald, 2010), which focused on measures used in delirium research, specifically within the older adult population. The review identified 24 scales that had been used in research and highlights the numerous delirium assessments which have been used in the literature. Although it is important to note that the review emphasises the importance of conducting additional research on certain assessments to further establish and replicate their reliability and validity. The review recommends the use of scales with a

greater number of items to provide greater accuracy, inter-rater reliability, reduced variability, and higher sensitivity and specificity (Adamis et al., 2010).

In this Thesis, only the two most commonly utilised delirium assessment tools will be discussed as they focus on the most up-to-date DSM criteria. This includes the Confusion Assessment Method (CAM) and the Delirium Rating Scale Revised-98 (DRS R-98). In accordance with the suggestions made by Adamis et al. (2010), these two tools are recommended for use in delirium assessment for their reliability and validity when compared against other tools.

The CAM is the most common method of assessing delirium and consists of a brief series of yes/no questions covering four key features: acute onset and fluctuating course, inattention, disorganised thinking and altered levels of consciousness (Inouye et al., 1990). Diagnosis requires that individuals are identified to exhibit symptoms of the first two features and either of the last two features. The test can be completed in five to ten minutes and can be conducted by non-psychiatrists; consequently, it is useful for a research context. Responses to the CAM are based on observations made by the researcher during the course of an interview with the individual where delirium is either scored as present or absent. Diagnostic accuracy is improved when it is completed alongside a cognitive assessment such as the Mini Mental State Examination (MMSE) (Adamis et al., 2010). The CAM has good psychometric properties with a specificity of between .92 and .97 and sensitivity ranging from .46 and .68.

The DRS R-98 is a 16-item scale that measures delirium severity, and can also be used for diagnosis and to differentiate from other disorders such as dementia, schizophrenia and depression (Trzepacz, Baker, & Greenhouse, 1988; Trzepacz et al., 2001). It consists of individual items rated on a scale of 0 to 3 which specifically, sensitively, and reliably measures delirium symptoms. These items include aspects on temporal onset of symptoms, perceptual disturbances, hallucination type, delusions, psychomotor behaviour and cognitive status. Depending on the cut-off point chosen the DRS R-98 has excellent psychometric properties, including high sensitivity ranging from .91 to 1.00. It is also highly correlated with other related assessments such as the original DRS, Cognitive Test for Delirium (CTD) and Global Clinical Impression Scale Scores (CGI) as well as exhibiting high inter-rater reliability and internal consistency (Trzepacz et al., 2001).

1.4 Aetiology, risk models and epidemiological data

As previously discussed, the DSM-5 defines delirium as a disorder of cognition, arousal and attention. Based on this, multiple theories have been proposed to explain the manifestation of delirium, many of which are homogeneous and multifactorial as multiple biological changes occur. A review by Maldonado (2013) identified seven current aetiological theories. These include: the Neuroinflammatory (NIH), Neuronal Aging (NAH), Oxidative Stress (OSH), Neurotransmitter (NTH), Neuroendocrine, Diurnal Dysregulation (or Melatonin Dysregulation) and the Network Disconnectivity (NDH) Hypotheses.

The Neuroinflammatory Hypothesis (NIH) suggests that delirium is a result of chemical imbalances in the brain. These imbalances occur when the brain experiences certain stressors, otherwise referred to as inflammation, which may come about through infection, surgery or other trauma to the body. This additional stimulation to the hypothalamus has a ripple effect in the signalling of the central nervous system, resulting in neuronal and synaptic dysfunction through changes in cell secretion. The NIH suggests the subsequent neurobehavioural and cognitive symptoms exhibited are those associated with delirium. This theory is supported through the observation of protein levels in the body, namely the C-reactive protein (C-RP). C-RP rises in response to inflammation and can subsequently cross the Blood Brain Barrier (BBB). The BBB is a protective, selectively permeable feature of the neuroimmune system, which keeps the passage of blood from the brain separate from the movement of fluids involved in the Central Nervous System. Disruption to the permeability of this barrier results in the diffusion of CNS fluids into the blood stream. Research has shown evidence to support high levels of C-RP are associated with delirium, with it being both a predictor and an indicator in delirium recovery (Macdonald, Adamis, Treloar, & Martin, 2006).

The Neurotransmitter Hypothesis (NTH), proposes that delirium is a result of neurotransmitter dysfunction and or availability. Research has provided support to this theory, with certain neurotransmitters known to be involved in key neuronal processes. These include acetylcholine, serotonin, dopamine, gamma-aminobutyric acid and glutamate. A reduced level of acetylcholine, increases in dopamine, norepinephrine and glutamate, and altered levels of histamine, serotonin and gamma-aminobutyric acid are known to play a role in delirium, again owing to the BBB permeability changes.

Acetylcholine (ACh), one of the key cholinergic pathways, is known to contribute towards wakefulness and cognition (Robbins & Everitt, 1995); particularly contributing towards attention, memory, disorganised thinking and perceptual distortions (Gunther, Morandi, & Ely, 2008; Maldonado,

2008). There is evidence to suggest the use of anticholinergic drugs independently increases delirium risk in hospitalised older adults (Han et al., 2001) as well as those in the post-operative period (Tune, Carr, Cooper, Klug, & Golinger, 1993). Anticholinergic processes can be monitored via Serum Anticholinergic Activity (SAA), with research strongly suggesting it to be a predictor for delirium (Flacker et al., 1998); high levels were associated with delirium (Hshieh, Fong, Marcantonio, & Inouye, 2008). This is reinforced by Mussi, Ferrari, Ascari, & Salvioli (1999), where all participants with SAA levels higher than 20 pM were found to be delirious when assessed using the Confusion Assessment Method (CAM).

Serotonin, another common neurotransmitter responsible for physiological processes, is derived from Tryptophan (TRP). Changes in TRP levels impacts the body's ability to synthesise serotonin, with reduced levels of TRP resulting in a reduction of serotonin levels in the brain. The role of serotonin in delirium has been demonstrated by Robinson, Raeburn, Angles, and Moss (2008) where a link between reduced levels of TRP and a higher incidence of postoperative delirium was found. Similar links between other neurotransmitters have been found to be associated with delirium incidence as discussed above, namely dopamine, gamma-aminobutyric acid (GABA) and glutamate. Impairments to oxidative processes involved in metabolic pathways result in higher than normal dopamine levels. Theories have proposed this to be a contributing factor in the frequent hallucinations and delusions observed in the hyperactive type of delirium due to the psychotic effects which dopamine toxicity can produce (Maldonado, 2008).

The Oxidative Stress Hypothesis (OSH) highlights the implications of changes to physiological processes that alter the availability and consumption of oxygen in the body. Originally proposed by Engel and Romano (1959), this neurophysiological theory suggests that changes to oxygen levels in the body available for cellular function leads to cerebral dysfunction resulting in the manifestation of cognitive and behavioural symptoms associated with delirium. This theory is supported by the electroencephalogram (EEG) studies where changes in brain activity were found to decrease in line with delirium severity (Engel and Romano, 1959). Contrary to this, an increase in EEG frequency is observed in delirium tremens and drug withdrawal related conditions raising questions around the validity of this hypothesis.

The Neuronal Aging Hypothesis (NAH) focuses on the physiological changes to the body that come about as a result of advancing age. Individuals become more vulnerable to stress and illness as they grow older. The NTH, NAH, OSH are linked through the common theme of ageing. This contributes towards changes in hormones, a decrease in ACh production and reduced cerebral oxidative metabolism

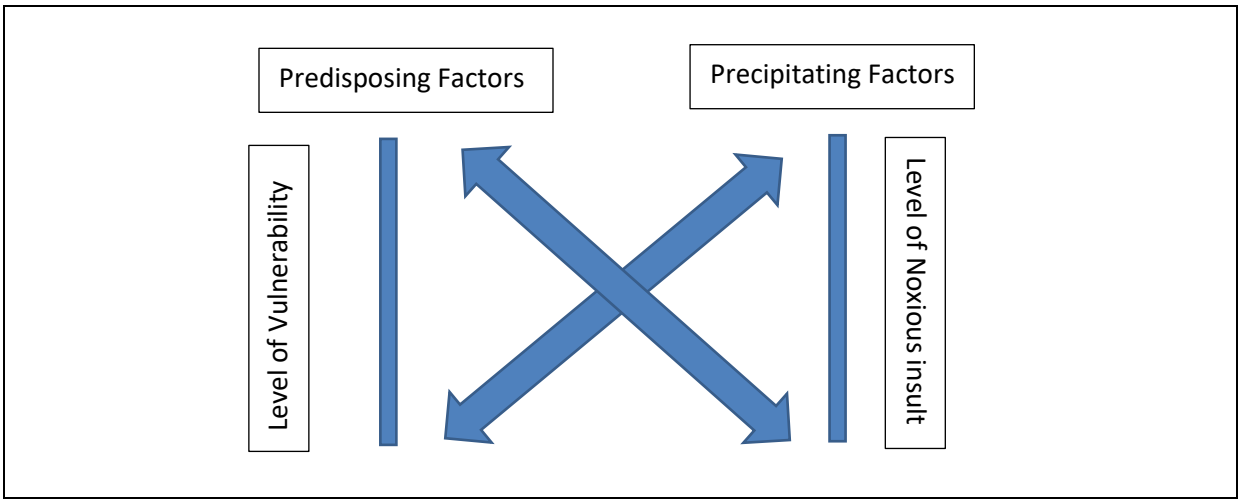
levels. The NAH is the basis of risk models for delirium, namely the Inouye et al (1996) Multifactorial Model which is discussed later in this Chapter.

The Diurnal Dysregulation (or Melatonin Dysregulation) Hypothesis presents disruption to the natural internal processes that regulate the sleep-wake cycle as a contributing factor towards the onset of delirium (Maldonado, 2008). This is supported by the sleep related symptoms of delirium which include, in extreme instances, the complete reversal of the sleep-wake cycle. Melatonin is secreted by the pineal gland through the breakdown of tryptophan and is a key marker of circadian rhythm (Arendt, 1994), with research suggesting a relationship between irregularities in secreted levels of this hormone and delirium. Evidence has shown low melatonin levels to be associated with ICU Psychosis (Miyazaki et al., 2003), as mentioned in Chapter 1.2, is a term used to describe psychotic signs and symptoms, otherwise referred to as delirium. The administration of melatonin has been demonstrated to be effective in resetting the sleep/wake cycle in patients experiencing post-operative delirium. In three case studies by Hanania and Kitain (2002), melatonin was used on each occasion. These included an instance where antipsychotics and benzodiazepines were not effective, where a medical history of post-operative delirium was present and where melatonin was used preventatively following multiple surgeries.

As mentioned above, the NAH theory is a key element of the Inouye et al (1996) Multifactorial Model (see Figure 1), which suggests an inter-relationship between the presence of predisposing and precipitating factors that contribute to the development of delirium. Individuals with a higher baseline level of vulnerability are at a greater risk as they are more susceptible to triggers in comparison to those at lower risk. Five precipitating factors which were identified here include the use of physical restraints, malnutrition, the addition of more than three medications, use of catheters and medical complications. For example, someone who is already severely ill and cognitively impaired experiences a relatively minor illness (e.g., a Urinary Tract Infection (UTI)) alongside their pre-existing condition is at a higher risk of developing delirium compared to their healthy counterparts.

The Multifactorial Model is validated in the older adult patient population. It predicts patients who experience at least one of these five precipitating factors during hospitalisation to be at a 17.5-fold increased risk of developing delirium compared to patients who did not identify with any (Inouye & Charpentier, 1996).

Figure 1 The Multifactorial Model (Inouye et al., 1996)



This model is supported by a systematic review on the incidence of delirium in the acute hospital care setting which identified the following predisposing factors associated with an increased risk of developing delirium. These included: old age, illness severity, length of hospitalization, low albumin visual impairment and use of a urinary catheter (Ahmed, Leurent, & Sampson, 2014). Some of these were included in the Inouye model above (Inouye et al., 1996). Additionally, delirium incidence in the included studies in this review ranged from 5% to 38% (Inouye, & Charpentier, 1996; Franco et al., 2010; Bo et al., 2009; Ranhoff et al., 2006; Wilson, Broadhurst, Diver, Jackson, Mottram, 2005; Villalpando-Berumen et al, 2003; Wakefield, 2002; Foy et al., 1995; Inouye, Viscoli, Horwitz, Hurst, & Tinetti, 1993; Foreman, 1989). However, it is important to note that the criteria for inclusion in this review specifically examined studies involving the older adult population (≥ 55 years old). Studies with ICU patient samples were excluded and time-points for delirium assessment varied across publications. With this in mind, it is possible that the incidence of delirium is much higher if studies on ICU patients were included as these individuals are likely to more ill and therefore have more precipitating factors.

A more recent theory for delirium is the neuroplasticity theory. This suggests individual differences in neuroplasticity plays a role in developing delirium (Shafi et al., 2017). Neuroplasticity is the brain's ability to adapt following injury or disease by creating new neural connections over time (Pascual-Leone, Amedi, Fregni, & Merabet, 2005). The theory suggests that delirium is a result of stressors that break down neural networks in the brain. Individuals who have a lower baseline level of neuroplasticity are at greater risk of developing delirium with more severe symptoms as they are less able to compensate for these changes. Stressors that may affect the brain include major surgery,

general anaesthesia, systematic inflammation, infections, and psychotropic drugs. It is also suggested that those with pre-existing health conditions are also at a greater risk. Conditions such as Mild Cognitive Impairment (MCI), Alzheimer's Disease (AD) (Di Lorenzo et al., 2016), diabetes (Fried et al., 2017) and renal impairment are also suggested to impair neuroplasticity. This theory suggests that these stressors trigger changes in brain connectivity and these disruptions can result in symptoms associated with inattention, a key marker of delirium. Symptoms would be greatest in individuals who have pre-existing conditions which have impaired their brain connectivity. These impairments are not sufficiently accommodating for these changes due to the reduced baseline level of neuroplasticity and this is where symptoms associated with delirium will arise.

1.5 Phenomenology

The experience of delirium is frightening. It can include auditory and visual hallucinations as well as feelings of paranoia and a sense of loss of control (McCurren & Cronin, 2003). It is common for verbal communication to be complicated due to these perceptual distortions. Individuals experiencing a delirious episode may have difficulty focusing and maintaining their attention to the conversation, and questions may have to be repeated for them to respond appropriately. They are often easily distracted and may also find it difficult to respond in a timely manner. It is common for individuals to provide a response to a previous question, rather than the current one, due to the difficulty in shifting attention appropriately. It is typical for symptoms to increase in severity in the evening where there are fewer external stimuli in the environment for the individual to orientate themselves to.

Disturbances to the sleep-wake cycle are common in individuals with delirium. Symptoms include: daytime sleepiness (including excessive daytime sleepiness), agitation in the night, difficulty falling asleep, and or wakefulness during the night. In more severe instances, there can be a complete reversal in the sleep-wake cycle. This is where night becomes as day and the patient sleeps during the day rather than at night. There may also be changes in emotion as delirious individuals can become anxious, fearful, depressed, irritable, angry, euphoric and or apathetic. These emotional and mood changes can occur rapidly and in an unpredictable manner with some calling out, screaming, cursing, muttering, moaning or making other sounds. Again, this is most common during the night where external environmental cues are limited.

Delirium can result in changes to emotion where feelings associated with anxiety, fear, depression, irritability, anger, euphoria and apathy are heightened and can be exhibited verbally through speech or other sounds. This has many implications to both the patient, their family, and their

care team. The patient may become distressed through experiencing these frightening changes, as well as for their family, who witnesses their out of character shifts in cognition and behaviour. It also complicates the delivery of care and clinical interventions if the patient is no longer cooperative and ultimately experiences the loss of capacity to make informed decisions for themselves. Other factors which have been identified to be likely risk factors include sleep disturbances and sleep deprivation (Weinhouse et al., 2009).

1.6 Sleep and delirium

Sleep patterns are regulated by the body's circadian rhythm, which are maintained by cues called zeitgebers. Zeitgebers can be endogenous (internal) or exogenous (external). The most important zeitgeber is light (Sander, Markvart, Kessel, Argyraki, & Johnsen, 2015) and problems may arise as a direct result of this. Too much, or too little light at the wrong time of day can induce changes in mood and health; contributing to hypertension and diabetes (Sander et al., 2015). The importance of good sleep is further affirmed by links between poor sleep quality and a higher mortality rate. Additionally, higher incidences of cardiovascular disease, strokes, and suicide, have been identified (Bernert, Turvey, Conwell, & Joiner, 2014; Ensrud et al., 2012; Li et al., 2014; Pan, De Silva, Yuan, & Koh, 2014). Sleep disruption is a common feature of delirium and is of vital importance to our health and wellbeing; its imperative role is often underestimated.

Disturbed sleep has been suggested to play a role in delirium due to the poor sleep quality patients experience within the hospital environment (Watson, Ceriana, & Fanfulla, 2012). Over half of inpatients reported experiencing insomnia, excessive daytime sleepiness and or both (Meissner et al., 1998), with ICU patients reporting difficulties in sleep onset, the presence of fragmented sleep, early awakenings and reduced total sleep time (Watson et al., 2012). A study on ICU patients (Trompeo et al., 2011) identified an association between < 6% total sleep time and delirium. This decreased amount of Slow Wave Sleep (SWS) and Rapid Eye Movement (REM) sleep, also referred to as sleep deprivation, has been hypothesised to be a contributing factor to delirium. However, a cause-and-effect relationship has yet to be established. Total sleep deprivation can lead to deleterious physiological outcomes, and eventually death (Rechtschaffen, Bergmann, Everson, Kushida, & Gilliland, 1989). Altered states of consciousness, confusion and psychosis are extremely distressing psychological consequences of Total Sleep Deprivation. Disturbances of sleep can have a profound impact on cognitive functioning and are associated with increased risk of falls, accidents, illness and death (Vitiello & Borson, 2001; Tractenberg, Singer, & Kaye, 2005; Sinforiani et al., 2007; Moe, Vitiello, Larsen, & Prinz, 1995; Christos, 1993;

Bombois, Derambure, Pasquier, & Monaca, 2010; Nilsson, Nilsson, Hedblad, & Berglund, 2001; Stone, Ensrud, & Ancoli-Israel, 2008) with an increasing amount of data suggesting an important relationship between the development and progression of dementia (Potvin et al., 2012, Lim, Kowgier, Yu, Buchman, & Bennett, 2013; Yaffe et al., 2011; Guarnieri et al., 2012). Similarities have also been drawn between sleep deprivation and key characteristics of delirium, specifically attentional deficits, cognitive dysfunction and changes to mental state including emotion (Dinges and Kribbs, 1991; Harrison and Horne, 2000; Weinhouse et al 2009). Problems with sleep are costly, precipitating the need for greater levels of health and social care interventions, including institutionalisation (O'Donnell et al., 1992).

Sleep deprivation has been shown to have the capacity to induce reversible psychosis-like symptoms in healthy adults. These symptoms have been shown to be similar to those associated with delirium, notably fluctuating mental status and cognitive dysfunction that follow sleep loss (Dinges & Kribbs, 1991; Harrison & Horne, 2000). Psychotic behaviour, alongside paranoia, have also been reported following 112 hours of sleep deprivation, with this also showing a pattern of fluctuation throughout the day (Tyler, 1955). Evidence suggests that performance in cognitive tasks involving attention, working memory and cognitive processes (Lim & Dinges, 2010) are most affected by sleep deprivation. Impairments in attentional functioning are also observed in partial sleep deprivation paradigms (Alhola & Polo-Kantola, 2007). These domains appear to be particularly vulnerable to sleep disruptions, with its negative consequences well documented (Durmer & Dinges, 2005).

Research on sleep deprivation involves using a study protocol where participants are kept continuously awake for a period of time, which can range from 24 to 72 hours to investigate the effects, often with a focus on measures on attentional functioning and memory. For longer periods, a partial sleep deprivation paradigm is used to restrict total sleep time over consecutive nights.

There are many causes of sleep disorders and poor sleep quality, with older populations particularly vulnerable to insomnia, sleep-related movement, and sleep-disordered breathing disorders (Young et al., 2002). For example, it is likely that at least one in five older people experience sleep-disordered breathing, and perhaps as many as eight in 10 older people with co-morbid vascular disease are affected (Gehrman, Martin, Shochat, Nolan, Corey-Bloom, & Ancoli-Israel, 2003; Herrscher, Akre, Øverland, Sandvik, & Westheim, 2011). Despite this, most sleep problems are often undiagnosed and are left untreated due to lack of routine screening and under-reporting of symptoms (Mold et al., 2011).

Sleep disturbances are common in the intensive care unit and patients with delirium experience more fragmented sleep, a reduction in deep sleep and a reduction of slow wave sleep and rapid eye

movement sleep. Additionally, these ICU patients often present with either hypoactive or mixed types of delirium (Figueroa-Ramos, Arroyo-Novoa, Lee, Padilla, & Puntillo, 2009).

The gold standard measure of assessing sleep is polysomnography (PSG). PSG is used in sleep medicine as a diagnostic tool, where assessments are conducted in specialised sleep laboratories. The individual's sleep is summarised in a polysomnogram, which reports information on bodily functions including; brain function, eye movements, skeletal muscle activation and heart rhythm. This method is however impractical to collect without specialised equipment and is burdensome on the individual being assessed as it requires a prolonged stay in a sleep laboratory.

A more pragmatic and practical method of assessing sleep is actigraphy, which has been deemed an adequate comparison to polysomnography by the American Academy of Sleep Medicine (Littner et al., 2003). Actigraphy monitors have been validated and recommended for use in assessing sleep behaviour for research purposes in the older adult population in the community (Ancoli-Israel, Clopton, Klauber, Fell, & Mason, 1997; Morgenthaler et al., 2007) and are a valid and reliable measure of sleep in healthy adult populations (Littner et al., 2003). Data from these monitors are highly correlated with polysomnography in measuring total sleep time (91%). Actigraphy monitors have features which make them durable and able to be worn in day-to-day life with minimum burden on the individual. Examples of this include basic water resistance and Velcro straps which make them easy to wear, removable and adjustable where necessary. These devices are to be worn on the wrist of the non-dominant hand and are similar in appearance to a small watch. It records movement of the limb which are then reinterpreted following algorithms to provide a measurement of sleep behaviour which can be used as a proxy of sleep behaviour including: sleep latency, total sleep time, number and frequency of awakenings and sleep efficiency. These devices have also been validated for the assessment of sleep patterns in patients suspected of having a primary sleep disorder, including: insomnia, restless limb syndrome, advanced sleep phase syndrome, delayed sleep phase syndrome, shift work sleep behaviour and circadian rhythm disorders (Morgenthaler et al., 2007).

The parallel use of self-reported sleep diaries alongside actigraphy is proposed to be a valid method to monitor sleeping patterns as well as time spent asleep (Levenson et al., 2013). Its use as a supplement is supported by the American Academy of Sleep Medicine. A more accurate and comprehensive view of sleep can be obtained when the two are used in conjunction as more specific information can be included (e.g., bed time) (Littner et al., 2003). Sleep diaries are easy to use. Individuals are asked to report details of their sleep, this commonly includes subjective waketime,

bedtime and the presence and duration of any naps (if taken). Individuals are encouraged to provide additional notes on events which may have occurred during the assessment period that may have affected their sleep quality (e.g., woke up in the middle of the night to go to the bathroom) to support comparisons between actigraphy data, adjusting sleep/wake periods where necessary (Littner et al., 2003). This could be useful for recognising episodes that should not be interpreted as sleep, such as low activity activities e.g., quiet reading.

There are a multitude of other self-reported measures of sleep that are often used in place when it is not possible to use objective polysomnography and or actigraphy. During the development of this Chapter, it became increasingly apparent more needed to be done to help navigate around the vast number of subjective sleep measures available. There is currently a lack of clarity in being able to easily select the use of the best tool under specific conditions. This identified a need for a systematic review which is discussed in Chapter 2.

1.7 Chapter summary

Delirium is a severe condition associated with changes in consciousness, cognitive function and is common in the hospitalised older adult population. The condition is multifactorial with additional research required to further understand the mechanisms of delirium. Sleep has been identified to have a potential link with delirium, with objective measures including polysomnography and actigraphy used as the gold standard, however this is not always possible. Difficulties are present in navigating between the various subjective measures currently available to most effectively monitor sleep in instances where it is not possible to use objective measures.

This Thesis explores the importance of sleep and the implications that changes to the habitual sleep/wake cycle has on delirium. The systematic review aimed to explore the use of screening tools to assess sleep quality in the older adult population and provide recommendations for their use to aid the detection of pre-existing sleep disorders, behaviours and disturbances in both research and clinical contexts. The novel systematic review provides guidance that did not previously exist through a summary of screening tools to use to identify sleep disorder and in measuring sleep quality in older adults. The first study describes a 24-hour sleep deprivation paradigm which investigated the impact sleep propensity had on the neuropsychological profile of a cohort of healthy adults, with a particular focus on computerised assessments which measured attentional functioning. This study adds to our knowledge of sleep and delirium by exploring whether these attentional deficits, particularly the fluctuation in variability of reaction time previously observed in patients with sub-syndromal delirium

are present in a group of healthy sleep deprived adult population with high sleep propensity. The second study is an observational study which was carried out in parallel which examined sleep disruption in a clinical population. Here, the relationship between pre- and post-operative sleep and delirium, where the pre-operative baseline for sleep quality is taken at home, is investigated in a cohort of older adults scheduled for elective surgery. This study is novel as collects an objective measure of sleep prior at home prior to hospitalisation, where previously only self-report methods have been used, as well as incorporating the battery of computerised assessments on attention used in the first study to explore whether attentional deficits are present in post-operative older adults who experience disrupted sleep.

The new knowledge that may emerge has the potential to contribute towards change in clinical pathways. With sleep problems often undiagnosed and left untreated due to lack of routine screening (Mold et al., 2011) the recommendations from the systematic review may assist in improving the screening of sleep disorders, behaviours and disorders, with this information used to support patient care. Results from the sleep deprivation and clinical study contributes to our understanding of the modifiable factor of sleep disruption to reduce delirium risk, with the clinical study exploring this specifically in the context of post-operative delirium.

Chapter 2: A Systematic Review of Screening tools to detect Sleep Disorders and assess Sleep Quality in Older People

2.1.1 Introduction

This Chapter outlines a systematic review on the use of screening tools to assess sleep quality in the older adult population. The prevalence of sleep disorders is high in the general population, with at least 10% of adults experiencing a symptom associated with a chronic sleep disorder (Ram, Seirawan, Kumar, & Clark, 2010), and 50% experiencing short-term symptoms relating to sleep-wake dysfunction (Morse & Bender, 2019). Older adults are at an increased risk of developing a chronic sleep disorder due to age-related changes that occur to the sleep-wake cycle. As discussed in Chapter 1, sleep disturbances are a core feature of delirium. Daytime sleepiness, and difficulties in the night, including increased agitation, difficulties falling asleep and or wakefulness are common. It is therefore important to identify the potential presence of sleep disturbances and or issues with an individual's quality of sleep to facilitate the introduction of strategies to prevent these issues, and subsequently delirium.

This novel review, evaluating the use of subjective screening tools, will provide guidance that has not previously existed. The comprehensive nature of a systematic review allows conclusions to be drawn based on an evaluation of the evidence. This type of synthesis has not been conducted on this topic area and will address this gap in knowledge. The reference guide produced because of this review is valuable to test administration to ascertain which assessment is the most appropriate for use within the specific context it is applied in. Through the review, a summary of the most appropriate tool to use to identify a specific sleep disorder(s) and/or in measuring sleep quality, whilst considering the needs within the setting it is conducted in. This is either for clinical or research requirements for the older adult population, without excluding those with Alzheimer's Disease. In addition to this, there was an intention of utilising the findings from this Chapter to contribute to the study design for the subsequent, experimental chapters, which are discussed later in this Thesis.

2.1.2 Background/rationale

The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) classifies sleep disorders into groups to assist with the management of diagnoses. These include: insomnia, hyposomnolence disorder, narcolepsy, breathing related sleep disorders, and parasomnias. The features of the diagnostic criteria for sleep disorders involve disturbances to a patient's quality of, timing, amount of sleep, which in turn result in daytime sleepiness and in some instances distress and or impairment in day-to-day functioning

(Reynolds & O'Hara, 2013; American Psychiatric Association, 2013). Sleep quality, despite its frequent used in sleep medicine, lacks a definitive definition. It encompasses various sleep measures that share similarities to the diagnostic criteria discussed above and quantifies this into total sleep time, onset latency, fragmentation, total wake time, sleep efficiency, arousals and or apnoeas, as well as variations in individual differences in the perception of sleep experience (Krystal & Edinger, 2008). There are different methods to assess an individual's sleep. These include objective measures (e.g., polysomnography and actigraphy), and subjective, questionnaire-based tools (e.g., the Pittsburgh Sleep Quality Index, PSQI).

Older adults are at an increased risk of developing sleep disorders and experience poorer sleep quality. The main age-related change to the sleep-wake cycle is phase advance, where the sleep-wake cycle is shifted earlier. Older adults often go to bed earlier and wake up earlier in the day (Wolkove, Elkoly, Baltzan, and Palayew, 2007). This may result in experiencing more difficulties in falling asleep and maintaining sleep, with more frequent awakenings occurring during the sleep period, which in turn results in greater sleep fragmentation (Edwards et al., 2010, Wolkove et al., 2007). Older adults are also particularly vulnerable to insomnia, sleep-related movement, and sleep-disordered breathing disorders (Young et al., 2002). It is estimated that at least one in five older people experience sleep-disordered breathing, and as many as eight in 10 older people with co-morbid vascular disease are affected (Gehrman, Martin, Shochat, Nolan, Corey-Bloom, & Ancoli-Israel, 2003; Herrscher, Akre, Øverland, Sandvik, & Westheim, 2011). Despite this, most sleep problems are often undiagnosed and are left untreated due to lack of routine screening and under-reporting of symptoms (Mold et al., 2011).

Previous literature has identified a relationship between the Apolipoprotein E (APOE), a protein involved in metabolism of fats, as a genetic risk factor for Alzheimer's Disease (AD). Moreover, better sleep consolidation, as calculated using the metric $k_{RA,}$ which is the probability of having an arousal after a period of inactivity, was found to reduce the effect of APOE genotype as well as the subsequent risk of developing dementia (Lim et al., 2013). Sleep disruptions are a common complaint in AD type dementia, and with the increasingly aging population, as discussed in Chapter 1, it is important to improve our understanding of conditions older adults are at higher risk of developing. Poor sleep quality has a negative impact of cognition and health, with it being a predictor for cognitive decline and as well as increasing the associated risk factors for AD (i.e., the development of metabolic and or cardiovascular disease) (Landry & Liu-Ambrose, 2014). It was therefore imperative to ensure that studies which

included AD participants were not excluded as part of the search criteria for this systematic review to enhance the generalisability of the findings to the wider population.

As discussed in Chapter 1.7, the gold standard for the assessment of sleep, including sleep disorders, is polysomnography (PSG). This involves an overnight stay in a sleep laboratory where a battery of physiological and observational assessments are conducted. However, PSG does have its limitations which include prohibitive costs, limited availability, and disruption to the patient undergoing the assessment as it requires spending a period of time in an unfamiliar environment, away from home. In the UK, it is recommended that moderate to severe obstructive sleep apnoea/hypopnea can be diagnosed within the patients' own home using portable monitoring devices (National Institute for Health and Care Excellence, 2008). An alternative objective method of assessing sleep that can be used at home is actigraphy. These are device which are worn on the wrist and record movements and are a validated measure of sleep quality. In addition to these objective measures, subjective questionnaires can be used to identify individuals who may be experiencing problems with their sleep. When compared to objective measures, these questionnaires are quick, easy to administer, do not require specialised equipment and are more practical for use.

The aim of this review is to describe and evaluate subjective sleep assessments and scales used with older adults, including those with dementia. To explore their psychometric properties, including diagnostic accuracy, and more specifically, to evaluate the accuracy of subjective, (i.e., sleep diary, questionnaire-based assessments) compared against objective measures (i.e., polysomnography, actigraphy and or polygraphy data).

2.1.3 Research objectives and aims

The use of screening tools to detect sleep disorders and assess sleep quality has the potential to form an important first step in the patient care pathway. However, the use of these tools are not always integrated into routine practice. A survey carried out on 99 primary care providers (PCPs) in America found that despite being aware of the significance sleep disorders has on health, and having an appreciation of the importance of being aware of and diagnosing sleep disorders, reported comfort levels were low in comparison. 78% of PCPs felt comfortable having discussions about sleep disorders, with 62% in the management of and follow-up, 60% in the diagnosis of and 48% in treating their patients (Klingman, Morse, Williams, Grandner, & Perlis, 2020). PCPs identified time constraints as a barrier, with the need of a more efficient method of screening for sleep disorders beneficial if incorporated into the practice. A follow-up study found out of the 1021 PCP respondents, the

percentage of sleep disorders diagnosed ranged from 58 – 89%, with treatment ranging between 50 – 91%. An average of 2.5% of patients were both diagnosed and treated (Klingman, Morse, Williams, Grandner, & Perlis, 2020); with this low rate of detection and treatment of sleep disorders further supporting the need to bridge this gap. Additionally, an alternative view by Luyster et al (2015), suggested this inconsistency in routinely screening for sleep disorders is due to an embedded dependence on the patient requiring to first disclose sleep related difficulties they are experiencing with their healthcare provider. Many older adults may attribute these changes as part of the normal aging process, and as a result, symptoms are not investigated, and the sleep disorder goes undetected.

There is a need to identify and evaluate the use of validated subjective screening tools for the detection of sleep disorders and sleep quality in the older adult population, including those with dementia, to explore its reliability and validity when compared against an objective sleep measure. The outcome of this novel review is to compile guidance for the most appropriate subjective assessment tools to use for both the context of the needs of a clinician and a researcher, whilst also providing an indication of reliability and validity of scales currently used in the population.

2.2 Methods

This systematic review was carried out using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure clarity and transparency of the report. The full review process is summarised in Figure 2.

2.2.1 Search strategy

This search strategy included the following types of studies: meta-analyses, systematic reviews, randomised controlled trials, prospective observational studies, case-control studies, cross-sectional studies, and case reports.

The Ovid online platform was used. These included (but were not limited to) the following electronic databases: EMBASE, MEDLINE (OVID Medline and EBSCO Medline), CINHAL and PubMed. CNHAl was searched via the EBSCO online platform, where we excluded records listed on Medline and not published in English. The PubMed.gov platform was used to search PubMed electronic database including the National Library of Medicine's Electronic database. This search was conducted up to and including the 14th of December 2017. We identified constituent concepts that would reflect the topic area we are investigating.

This resulting combination of keywords was then incorporated into the following search string: ((‘screen*’ OR ‘diagnose*’ OR ‘assessment’ OR ‘case finding’ OR ‘index’ OR ‘reference’ OR ‘questionnaire’ [tiab]) AND (‘polysomnograph*’ OR ‘actigraph*’ OR ‘polygraphy’) AND (‘sleep’ OR ‘circadian’ OR ‘night’ OR ‘somnolence’ OR ‘insomnia’ OR ‘apnoea’ OR ‘apnea’ OR ‘hypopnea’ OR ‘hypopnoea’ OR ‘parasomnia’ OR ‘restless leg’ OR ‘periodic limb’ OR ‘REM’ OR ‘rapid eye movement’ [tiab]) AND (‘valid*’ OR ‘reliab*’ OR ‘psychometric’ OR ‘internal’ OR ‘consistency’ OR ‘test-retest’ OR ‘repeatability’ OR ‘accuracy’ OR ‘sensitivity’ OR ‘specificity’ OR ‘quality’ [tiab]) AND (‘geriatric’ OR ‘old*’ OR ‘elder*’ OR ‘veteran’ OR ‘senior’ OR ‘dement*’ OR ‘Alzheimer*’ OR ‘aged’ [tiab])).

2.2.2 Inclusion criteria

The articles generated from the search were screened for inclusion by two authors, RB and DL. DL was the PhD project supervisor at the time and their involvement was solely for this stage of the systematic review. Article screening was done independently through evaluating each article’s title and corresponding abstract. This information was compiled into two separate documents to ensure its independence. Any discrepancies in decisions on the inclusion of specific articles between authors were discussed and a consensus reached. The following inclusion criteria was used:

- Primary research comparing subjective screening tools for sleep quality, sleep behaviour or sleep disorder to objective measures of sleep. Objective measures being polysomnography, actigraphy, polygraphy data, or wearables (including accelerometers and telemetric monitoring methods). In this context, subjective screening tools includes methods that incorporate an element of self-report. Participants contribute their own experiences of how they perceived their sleep to be which may include self-completed instruments, taking part in interview and or observer-completed questionnaires.
- Present data from adult participants (≥55 years) with or without a co-morbid neurocognitive disorder
    - Selection criteria specifically exclude those <55 years old
    - Sample is predominantly ≥55 years, i.e., mean age minus one standard deviation is not less than 55 years
    - Performed a subgroup analysis on those ≥55 years
- Report concurrent validity or diagnostic accuracy

Articles were excluded if the abstract was in a language other than English, a duplication of an article had already been identified and included, and or if the full text was not retrievable following attempts made by both authors. These attempts made included accessing the article online (via the University of Kent LibrarySearch, Google Scholar, and a general web search), and discussions with the faculty librarian team.

2.2.3 Data extraction

Data was extracted by one of the authors where information on recruitment source, selection criteria, description of reference standard and index measure, was recorded in a table. Where available, the following participant clinical, and demographic data, was also extracted: age, gender, education and mini-mental state examination, number diagnosed with sleep or co-morbid condition (including stroke, dementia, depression and others).

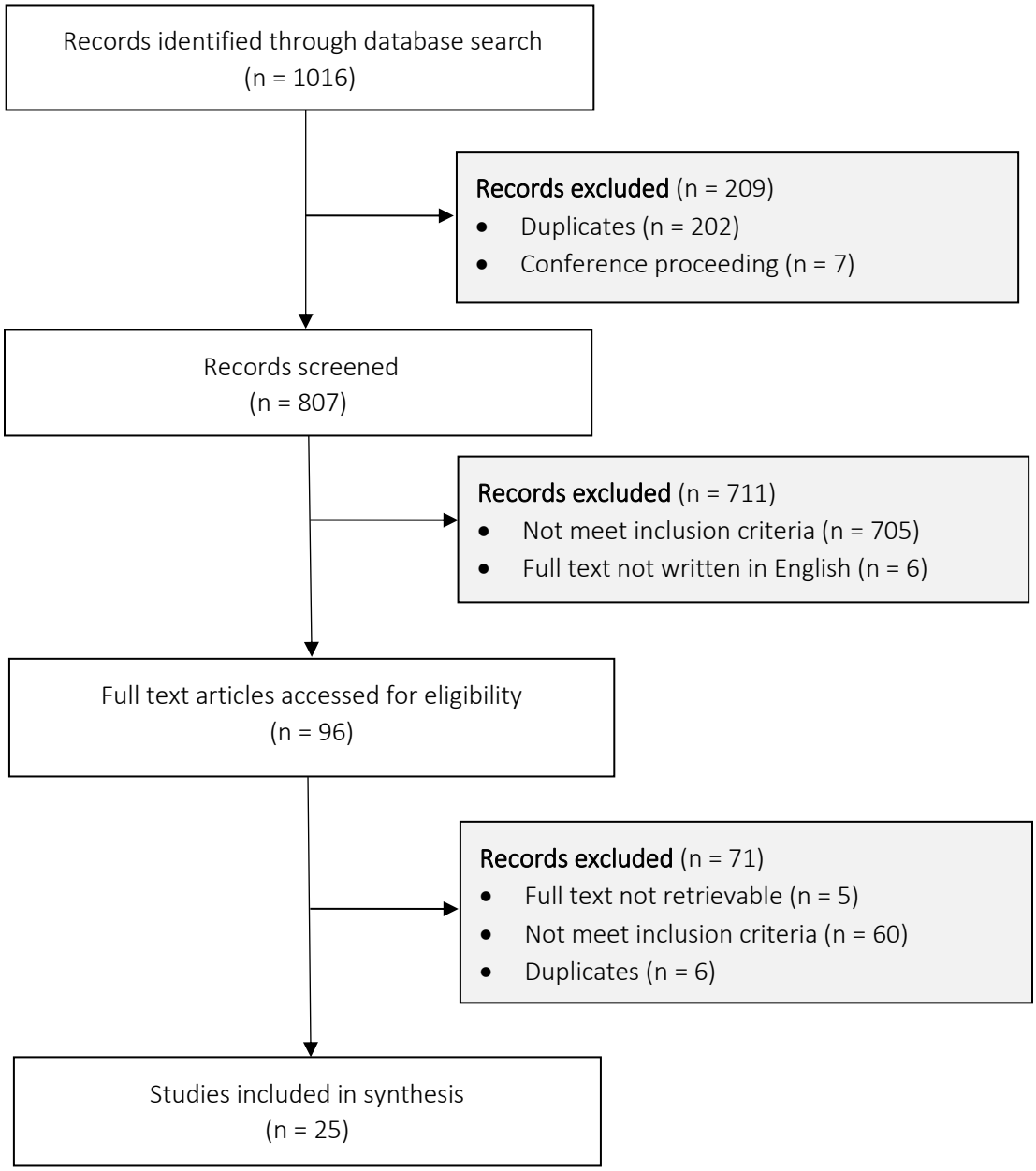
Each screening tool's diagnostic accuracy, sensitivity, specificity, positive predictive value, negative predictive value, receiver operator characteristics (including area under the curve) was included. Where diagnostic accuracy was unavailable, the concurrent criterion validity, internal consistency and internal reliability were collated. Any discrepancies at this stage were again resolved through discussion between the two authors.

2.3 Results

The systematic review process is outlined in the flow chart below (See Figure 2).

Figure 2

Systematic review flowchart



2.3.1 Selection of articles

The initial search strategy resulted in the identification of 1016 publications. Following the screening the title and abstracts of 807 articles, 96 studies met the inclusion criteria. These were subsequently accessed for review of the full-text, of which, 25 eligible studies were included in the review. Full text studies were excluded for the following reasons: not using a wearable sensor, unclear

age requirement, and absence of the use of a screening tool, an intervention study, not a primary study and not evaluating diagnostic accuracy or validity.

2.3.2 Description of included studies

Twenty-five papers were included in the qualitative synthesis. Of which, 10 provided data related to a screening tool with a primary aim of screening for a sleep disorder (Insomnia Severity Index n = 2; Observation-based Nocturnal Sleep Inventory n = 1; Observational Sleep Assessment Instrument n = 1; Mayo Sleep Questionnaire n = 2; REM Sleep Behaviour Disorder Screening Questionnaire – Japanese version n = 2; Sleep interview n = 1; Sleep Symptom Checklist n = 1). Eighteen related to the assessment of sleep behaviour and disturbances (Pittsburgh Sleep Quality Index n = 10; Dutch Sleep Disorders Questionnaire n = 1; Self-rated Sleep Scale n = 1; Sleep Disorders Inventory n = 1; Comprehensive Geriatric Assessment n = 1; Sleep Diary / EMA n = 1; Epworth Sleepiness Scale n = 2; Karolinska Sleepiness Scale n = 1). Settings included both clinical (n = 8) and community-based (n = 16), with one study taking place in both (when taking into account recruitment). Three articles provided data for more than one assessment tool, hence the perceived discrepancy.

The screening tools included in this systematic review are summarised in Table 2 and the Systematic Review extraction forms can be found in Appendix A.1. Further information on the scale name, participant recruitment and selection, reference measure, the disorder and or construction, demographic data (including information on participants) as well as diagnostic accuracy and or psychometric properties are illustrated in these Appendices.

Table 2 – Summary of Assessment Tools included in the Systematic Review

Scale name	Disorder or Disturbance type	Authors
Insomnia Severity Index (ISI)	Insomnia	Bastien, Vallieres, & Morin (2001); Postuma, Gagnon, Pelletier, & Montplaisir (2017)
Observation-based Nocturnal Sleep Inventory (ONSI)	Sleep Apnoea	Onen et al. (2008)
Observational Sleep Assessment Instrument (OSAI)	Sleep Apnoea	Martin, Mory, & Alessi (2005)
Mayo Sleep Questionnaire (MSQ)	Sleep Apnoea and RBD	Boeve et al. (2011); Boeve et al. (2013)

REM Sleep Behaviour Disorder Screening Questionnaire – Japanese version (RBDSQ-J)	RBD	Miyamoto et al. (2009); Nomura, Inoue, Kagimura, Uemura, & Nakashima (2011);
Sleep Interview	RBD	Eisensehr, Lindeiner, Jäger, & Noachtar (2001)
Sleep Symptom Checklist	General tool for sleep disorder detection	Bailes et al. (2008)
Pittsburgh Sleep Quality Index (PSQI)	Sleep quality	Beaudreau et al. (2012); Buysse et al. (1991); Curcio et al. (2013); Chen, (2013); Dew et al. (1994); Fung et al. (2012); Landry, Best, & Liu-Ambrose (2015); Most, Aboudan, Scheltens, & Van Someren, (2012), Postuma et al. (2017); Van Den Berg et al. (2008);
Dutch Sleep Disorders Questionnaire (SDQ)	Sleep quality	Most, Aboudan, Scheltens, & Van Someren, (2012)
Self-rated Sleep Scale (SSA)	Sleep quality	Happe et al. (2005)
Sleep Disorders Inventory (SDI)	Sleep behaviour and habits	Tractenberg, Singer, Cummings, & Thal (2003)
Comprehensive Geriatric Assessment (CGA)	Sleep behaviour and habits	Dos Santos Silva et al. (2015)
Sleep Diary / EMA	Sleep time	Baillet et al. (2016)
Epworth Sleepiness Scale (ESS)	Daytime sleepiness	Beaudreau et al. (2012); Postuma, Gagnon, Pelletier, & Montplaisir (2017)
Karolinska Sleepiness Scale (KSS)	Daytime sleepiness	Paavilainen et al. (2005)

2.3.3 Data Synthesis and analysis

The quality of each article included was assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) checklist. QUADAS-2 is recommended for use to evaluate the risk of bias and applicability of diagnostic accuracy in studies. It is also the only validated tool for assessing the quality of studies. The QUADAS-2 is a follow-on from the previous Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool which has since been refined to include additional information evidence, clinical experience and anecdotal reports and feedback from researchers (Whiting, Rutjes, Reitsma, Bossuyt, & Kleijnen, 2003).

QUADAS-2 consists of four domains and includes: patient selection, index test, reference standard and flow and timing. Each domain assesses for the risk of bias and applicability. Signalling questions are used to help in categorising risk as either low, high or unclear to determine the rating for each study. Studies which have a low level of risk are indicative of high-quality validation of diagnostic scales.

2.3.3.1 Insomnia Severity Index (ISI)

Two studies were included that used the Insomnia Severity Index (ISI) (Bastien, Vallieres, & Morin, 2001; Postuma, Gagnon, Pelletier, & Montplaisir, 2017). The ISI consists of a 7-item questionnaire with self-ratings ranging from zero to four on questions on severity of sleep onset, sleep maintenance, early morning awakening problems, satisfaction with sleep pattern, interference with daily functioning, noticeability of impairment and level of distress. A clinical threshold is provided, with scores range from 0 – 28, and a cut-off score of 10 indicating insomnia.

The aim of the Bastien et al (2001) paper was to report on the clinical validation of the ISI as a screening tool for insomnia and as an outcome measure in research. In this study, 78 participants were enrolled in a trial of Cognitive Behavioural Trial for primary insomnia. Participants met the DSM-111-R (American Psychiatric Association, 1987) and International Classification of Sleep Disorders (ICSD) (American Sleep Disorders Association, 1980) criteria for primary insomnia and were free from comorbid major psychiatric disorders, any medical disorders known to affect sleep, did not use medications known to affect sleep, and did not have significant cognitive impairment. Polysomnography (PSG) data totalling a period of 3-nights on three occasions over three months was obtained, and this measured Sleep Onset Latency (SOL), Wake after Sleep Onset (WASO), Early morning awakenings, and Sleep Efficiency (SE). ISI scores were correlated against sleep diary data and PSG at pre- and post-treatment. Cronbach's alpha ranged from .32 to .90, and concurrent validity comparing participant

completed ISI and clinician completed ISI also reported. Correlations between the following measures were as follows: sleep onset and initial insomnia (r = .39, p < .05, and r = - .45, p < .05); WASO and middle insomnia (r = .16, p = n.s, and r = .45, p < .05), early morning awakening and terminal insomnia (r = .07, p = n.s, and r = - .23, p = n.s) and sleep efficiency and total ISI score (r = -.09, p = n.s., and r = -.35, p < .05). This suggests a weak relationship between the use of the ISI and PSG with the absolute value of the Pearson correlation coefficients reported at r < .50.

The second study is Postuma et al. (2017), which uses data from a longitudinal study on idiopathic rapid eye movement (REM) sleep behaviour disorder (RBD) patients collected between 2004 and 2015. Here, 158 participants were evaluated to assess whether insomnia and daytime sleepiness was a predictor for the development of RBD, as well as monitoring changes over the course of the disorder development. As part of the clinical aspect of the study, participants completed sleep scales in the follow-up period. Those included in the RBD group were confirmed with idiopathic RBD by PSG, and the control group confirmed to not have idiopathic RBD by PSG. Patients with Parkinson's Disease or Dementia were excluded from the study. One-night of PSG was obtained, measuring SOL, TST, SE, Stage 1%, Stage 2%, SWS %, REM %, Phasic REM density %, and Tonic REM %. Out of the sample of 158, 151 participants were included in the analysis which required at least one baseline measure of sleep. In the RBD group, mean age was 66.4 years, with RBD symptoms persisting from symptom onset for 8.7 ± 9.3 years. In the control group, mean age was 68.9 ± 8.5 years. Mean ISI scores were found to be statistically different between RBD patients compared to controls (p < .001) with RBD patients reporting more abnormal ISI scores (p < .001). Differences between the two groups were greatest for items relating to general sleep disturbances, worry and its impact than for questions directly relating to insomnia.

2.3.3.2 Observation-based Nocturnal Sleep Inventory (ONSI)

The ONSI is a tool tailored for the screening of sleep apnoea, this behavioural assessment consists of five, five-minute observations by a nurse to monitor for interrupted breathing, gasping or choking, snoring and/or awakening. Onen et al., (2008), aimed to measure the effectiveness of the ONSI in detecting for Sleep Apnoea Syndrome (SAS) in the older adult population. Participants were recruited from consecutive referrals to a geriatric sleep centre in France from five geriatric hospitals for a potential diagnosis of sleep apnoea. These participants were identified to be at risk of apnoea following complaints of snoring, excessive daytime sleepiness and or overweight/obesity. Participants over the age of 70 of 'Caucasian race' were included, with those with a previous history of heart failure, nocturnal oxygen supplementation, severe dementia (MMSE < 10), major psychiatric disorder, were too sick to be

evaluated, had a condition that prevents the use of polysomnography, had previously undergone sleep study, and or received care for SA excluded.

One-night of PSG was compared against ONSI observations (n = 121) and inter-observer reliability was reported as a k = 0.89^. The ONSI was found to have provided optimal diagnostic accuracy within a sample of neurologically healthy individuals with sensitivity at 89.7% and specificity at 81.4% This suggests that the ONSI is an effective tool which can be used in the screening of SAS when observations are made by a nurse.

2.3.3.3 Observational Sleep Assessment Instrument (OSAI) - SDB

The Observational Sleep Assessment Instrument (OSAI) is a tool used to screen for sleep disordered breathing (SDB). It consists of hourly 3-minute observations, with the nature of these observations similar to the ONSI; instead consisting of recording versions of snoring, breathing rate, loudness, continuity and chest movements; Oxygen Desaturation Index (ODI) was derived from estimated Total Sleep Time (TST) from actigraphy.

In Martin, Mory, & Alessi, (2005), the use of the OSAI was evaluated in a cohort of older adults in nursing homes with daytime sleepiness and night-time sleep disturbances. These individuals were enrolled in a Randomised Control Trial (RCT) of nonpharmacological interventions to improve sleep. To be included, participants had to meet the criteria for observed daytime sleepiness, and score asleep < 80% of the time between 22:00 hours and 06:00 hours. Individuals who were bed bound, were in contact isolation or had left the nursing home prior to screening were excluded. In total, 109 participants were included, with a mean age of 86.2 ± 9.2. Actigraphy was collected over 2-nights and compared against the OSAI.

Only observed loud breathing was found to show a statistically significant relationship with ODI (r = .28, p = .003). No statistically significant relationships were found for the number of observations per night (r = .04, p = .71), discontinuity of breathing (r = -.007, p = .94), discontinuity of chest movement (r = .14, p = .15), percentage of observations with snoring (r = .13, p = .12) or for breathing rate (per minute) (r = -.01, p = .91). It was noted that only participants with acceptable actigraphy recordings were included in this analysis. This group were found to be more neurologically impaired (lower MMSE score) but more medically healthy (fewer medical conditions and on less medication) compared to those with unacceptable actigraphy recordings. The authors commented that this may have impacted the accuracy of the measure. The ODI is an indirect method of measuring SDB, highlighting another limitation to this

study. The ONSI was conducted within an inpatient setting, but could easily be conducted by video observations like the OSAI.

2.3.3.4 Mayo Sleep Questionnaire (MSQ)

The MSQ is an informant-based questionnaire consisting of 16-items include responses from bed partners who were asked if particular behaviours have been observed at least three times in the past. Responses were yes/no with yes responses followed by further sub-questions. The full questionnaire includes items on REM Behaviour Disorder, Periodic Limb Movement (PLM) during sleep, Restless Leg Syndrome (RLS), Sleepwalking, Obstructive Sleep Apnoea (OSA), Sleep Related Leg Cramps, and Insomnia. In this systematic review, the MSQ was found to have been used to screen for both Sleep Apnoea (SA) and REM Sleep Behaviour Disorder (SBD) (the latter which it is a validated measure for). The MSQ consists of items related to SA, but it is not a tool designed specifically to screen for SA.

Its use in screening for SA and REM SBD was explored in Boeve et al (2011). Here, the aim was to validate the use of the MSQ in older adults with dementia. Participants were recruited from patients enrolled in the Mayo Alzheimer's Disease Research Centre, Clinic at Rochester or Jacksonville. No inclusion or exclusion criteria was specified in the study design. Participants underwent one night of PSG, a comprehensive sleep interview, and a physical examination (using The International Classification of Sleep Disorders (ICSD), second edition criteria). 176 participants were included, with a mean age of 71 years, and 15% were women. Cognitive functioning within this sample was as follows: no dementia, n = 8; mild cognitive impairment, n = 44; Alzheimer's disease, n = 23; dementia with Lewy bodies, n = 74; other dementias and/or parkinsonian syndromes, n = 27. The sensitivity and specificity for the MSQ questions with regards to sleep-disordered breathing ranged from 38 – 41% and 29 – 41% respectively. This is too low to recommend its use in identifying those at risk. For REM SBD, sensitivity was 98% and specificity was 74%.

In Boeve et al (2013), the aim was to validate the MSQ in a community-based population for REM SBD. Participants were enrolled in the Mayo Clinic Study of Aging (MSCA) and their bed partner had completed the MSQ between October 2004 and December 2008. This cohort was aged 70-89 years at baseline. Only data for 97 subjects was included as some did not achieve REM sleep or had EMG tone. Demographics for the 97 participants but instead for the full 128 enrolled. PSG data was collected between January 2003 and December 2008. The mean age of participants ranged from 60 – 90 (60 – 69, *n* = 7; 70 – 79, *n* = 68; 80 – 89, *n* = 52; < 90, *n* = 1). The median age was 77 years and 104 males were

included. Out of the 128 enrolled, 126 had a bed partner to report MSQ scores for. In this study, only 1-item out of the 16-item questionnaire was used:

- Have you ever seen the patient appear to "act out his/her dreams" whilst sleeping? (Punched or flailed arms in the air, shouted or screamed).

The sensitivity of 'yes' responses were found to be 100% (95% CI: .63 – 1.0) and for 'no' responses 95% (95% CI: .88 – .98) for PSG confirmed RBD. The MSQ appears to show high sensitivity (> 98%) and good to high specificity (> 74%) for identify those at risk in those with dementia and in neurologically healthy populations.

2.3.3.5 REM Sleep Behaviour Disorder Screening Questionnaire – Japanese version (RBDSQ-J)

The REM Sleep Behaviour Disorder Screening Questionnaire-Japanese version (RBDSQ-J) screens for REM Sleep Behaviour Disorder (RBD) symptoms and is a validated version of the original RBD questionnaire (RBDSQ) that has been translated into Japanese. It consists of a series of yes/no questions on sleep behaviours relating to the frequency and content of dreams, nocturnal movements and behaviour, self-injuries and injuries to their bed partner, nocturnal motor behaviour, nocturnal awakenings, disturbed sleep in general and the presence of neurological disorders.

In Miyamoto et al. (2009), the validity and reliability of a 10-item version of the RBDSQ-J was explored in a sample of 52 participants with a mean age of 66.4 ± 6.9. Patients with PSG-confirmed idiopathic RBD (iRBD) were randomly recruited from a University Hospital and Somnology Center. PSG was conducted to define the presence of iRBD using the ICSD-2 criteria. PSG data was compared against RBDSQ-J responses, and Cronbach's alpha was 0.87. Test–retest reliability was reported at 0.84 (95% CI = .60–.94). There was very good AUC for ROC (> .918) was reported with sensitivity (> 88.5%) and specificity (> 88.6%) across healthy and Obstructive Sleep Apnoea Syndrome (OSAS) participants. However, it was unclear how participants were randomly selected in both studies, with a lack of or vague inclusion and exclusion criteria specified.

In Nomura, Inoue, Kagimura, Uemura, & Nakashima (2011), the utility of the RBDSQ-J questionnaire was explored in a group of 76 patients with Parkinson's disease (PD). Consecutive patients admitted to a University Hospital in Japan were recruited. The mean age was 72.9 $\pm$ 9.1 years. The reference measure used was overnight PSG alongside a clinical interview as per the scoring criteria of the American Sleep Disorders Association. PSG scores were compared against responses to responses to the full, 13-item version of the RBDSQ-J. A Cronbach's alpha of .73 was reported. For detecting any RBD

symptoms, an optimal cut-off score of 6-points was reported. This was alongside a very good Area Under the Curve (AUC) for Receiver Operator Characteristics (ROC) (> .953), a sensitivity of 84.2% and a specificity of 95.3%. For violent RBD symptoms only, the RBDSQ-J had an optimal cut-off of 6-points, and a sensitivity of 100% and a specificity of 87.5%.

2.3.3.6 Sleep Interview - REM Sleep Behaviour Disorder

In Eisensehr et al. (2001), a review of all PSGs performed at the University of Munich Sleep Lab over a 3-year period was conducted to evaluate the sensitivity and specificity of rapid eye movement behaviour disorder (iRBD) using the diagnosis criteria of PSG. Participants included had been scheduled for a PSG following complains of non-restorative sleep, difficulties in maintaining sleep, excessive daytime sleepiness and or complex nocturnal behaviour. PSG was collected for a minimum of 2-nights, between 22:00 hours and 06:00 hours. A neurologist specialising in sleep medicine conducted the Sleep Interview. The neurologist asks a series of questions to the individual, and where possible their bed partner, their history of self-injuries or injuries of the patient's bed partners and the presence of violent dreaming, and or aggressive behaviour during sleep.

A sample of 292 participant were included, consisting of non-PD patients (n = 273). In PD-patients, sensitivity was 33% and specificity was 90%, and in non-Parkinson's patients, sensitivity was 100% and specificity was 99.6%.

2.3.3.7 Sleep Symptom Checklist (SSC)

The Sleep Symptom Checklist (SSC) has been used as a more general tool to detect the presence of sleep disorders. The SSC included a 21-item self-reported questionnaire consisting of signs and symptoms of sleep disorder. It includes items on snoring, breathing interruption in sleep, insomnia, daytime fatigue, sleepiness, and psychological maladjustment. Responses were three-fold, requiring participants to mark next to each item its severity (0 - 3), whether it has been previously discussed with their physician and whether it was experienced within the last year. In addition to this, if recommendations had been made by a doctor (either referral or treatment), respondents were asked to include details of this in an open-ended format.

In Bailes et al. (2008), the aim of the study was to explore sleep disorder related symptoms in a cohort of older adults in primary care and to assess for any patterns in self-reported symptoms which can identify participants who would benefit from further examination in a sleep clinic. Participants were recruited from the waiting areas of three family practice centres, and the inclusion criteria meant they

all had to be > 50 years and over, a community resident, have volunteered to participate and did not have any cognitive impairment or language difficulties to prevent them from being able to complete assessments in either English or French. Results from one-night of PSG taken between 22:00 hours to 07:00 hours was compared against SSC scores. 196 participants were included in the study, 71 were male (mean age was 69.93 $\pm$ 9.1) and 125 women (mean age was 69.96 $\pm$ 10.8). Out of the sample of 196, data for 21 participants was available to explore temporal stability of scores for a 3-week test re-test period (14 women, 7 male, with a mean age of 46.1 years $\pm$ 12.1). The SSC was reported it have acceptable temporal stability for total scores (r = .79, p < .01), and good internal consistency (α = .68 – .88). The temporal stability of individual items including insomnia, day-time aspects, sleep disorder and psychological maladjustment was r > .77.

2.3.3.8 Pittsburgh Sleep Quality Index (PSQI)

The Pittsburgh Sleep Quality Index (PSQI) was the most frequently used screening tool amongst the articles included in this systematic review. The PSQI provides a global measure of sleep quality in the preceding month. It consists of 19-items which generate 7 component scores, including subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction. Originally, a seven-factor scale was validated, and later a three-factor scale was validated.

In Beaudreau et al. (2012), the PSQI and ESS were validated for their use in women from diverse racial backgrounds. Participants were recruited from the Study of Osteoporotic Fractures (SOF), which consists of 9,704 community dwelling women who were aged ≥ 65 years between 1986 and 1988 in America. Evaluations were conducted in a series of follow-up visits involving a clinic interview, anthropometry, performance measures, and actigraphy. Participants who were unable to walk without assistance, or had a bilateral hip replacement were excluded. Home PSG and or 3-days of consecutive actigraphy was obtained as a reference measure. 2,968 participants with a mean age of 83.4 $\pm$ 3.7 years were included. Out of this sample, 2,968 were older white women (89.7%), and 306 were older black women (10.3%). 17-items of the PSQI were found to have good internal consistency, with a Cronbach's α for the total sample of .78, and when broken down α, .78 in white women, and α, .80 in older black women and item-total correlation ranged between .12 – .69. When PSQI sub-scales were merged, Cronbach's α was .72 in the total sample, α =.72 in older white women and α = .74 in older black women. Statistically significant correlations were reported for PSQI and daytime inactivity (r_s, *0.05; p* <

.05), total sleep time (r_s, -0.02; p = .34), and Wake After Sleep Onset (WASO) (r_s, 0.14; p < .001). Total Sleep Time was not statistically significant (p = .34).

Buysse et al. (1991) investigated how aging affected subjective sleep quality. Participants were identified using presentations to senior citizens' groups, newspaper and poster advertisements and word of mouth. Those included were of good health (through medical and psychological evaluation) and were excluded if they had any serious medical illnesses (with chronic medical conditions exempt from this if it is stable and controlled without medication or with medication that did not affect sleep), and free from psychiatric disorders. For the purpose of our systematic review, only data from the 'elderly' subgroup was included in the analysis, which included 44 participants aged < 80 who underwent 2-nights of PSG. No significant differences between PSQI and PSG for sleep latency or for sleep efficiency were observed. Participants were found to score higher on the PSQI for sleep duration and Sleep Efficiency (SE) when compared to PSG (sleep duration: t = -3.18, p = .002; SE: t = - 2.04, p = .04). PSQI global scores were not found to be statistically significantly correlated with PSG sleep variables.

Studies where versions of the PSQI in languages other than English were also included in this review. Curcio et al. (2013) aimed to validate an Italian version of the PSQI in five subgroups of participants including: healthy young, older adults, SAS patients, patients with depression, and dementia patients. 50 participants were included, with 10 in each subgroup. Mean age for healthy older adults was 68.6 years $\pm$ 6.98 and PD-patients had a mean age of 75 years $\pm$ 6.52. One-night of PSG was compared against PSQI scores. Cronbach's α was reported as .835 and statistically significant correlations between global PSQI and stage 2 (p = .04), and slow wave sleep latencies (p < .001); and stage 1 (p = .02) and stage 2 sleep efficiency (p = .01) were reported.

In Chen, (2013), a PhD Thesis examining quality of sleep in Osteoarthritis (OA) patients in Taiwan, 30 participants were recruited with a mean age of 65.6 years ± 10.6 from two musculoskeletal clinics in Taiwan between October 2010 and March 2011. This cohort agreed to take part in this follow-on study. Participants were included if they had a diagnosis of OA, were < 40 years of age, able to respond to questions in Mandarin or Taiwanese and were community residents based in Taiwan. Individuals who had a cognitive impairment or were unable to understand the instructions were excluded. 3-days of actigraphy was obtained and correlated against PSQI scores. There were no statistically significant correlations between subjective and objective measures of sleep for sleep latency, Total Sleep Time (TST) and or Sleep Efficiency (SE). A Wilcoxon matched pairs signed-ranks test did show statistically significant variability for all three sleep measures (sleep latency p = .04, TST p <.

001, and SE p = .002). When actigraphically measured sleep was compared against dichotomised global PSQI scores ('good', n = 8 vs 'poor' sleepers, n = 22), a Mann-Whitney U test showed statistically significant differences for SE, Wake After Sleep Onset (WASO) and number of awakenings after sleep onset (p = .049 - .009). No statistically significant differences were observed for sleep latency or TST. SE as measured by actigraphy was poorer in subjectively poorer sleepers when compared against good sleepers. WASO was longer, and the number of awakenings after sleep was greater in subjectively measured poorer sleepers.

Dew et al. (1994) explored sleep in older adults using longitudinal data collected over a period of 12-months from 57 healthy older adults with a mean age of 74.3 years ± 7.96. Participants were recruited from a prior study on sleep intensity and propensity in later life. Those who had sleep complaints, a previous or current history of psychiatric disorders, had serious or uncontrolled health problems or took medication that affected their sleep or mood were excluded. 3-nights of PSG was collected. When PSQI scores were compared against PSG, no statistically significant associations were identified at baseline or for 1-year follow-up. When all three groups (good sleepers, inefficient sleepers and poorer sleepers) were collated, PSQI scores was found to be significant at the p = .10 level.

In Fung et al. (2012), the PSQI and actigraphy were used to evaluate whether sleep disturbances detected with these measures presented in assisted living facilities (ALFs) and to identify predicting factors of disturbances in AFLs. This was a prospective, observational cohort study which included 18 ALFs in California, USA. Participants were recruited following a 30-minute presentation about sleep research during which the Principle Investigator described the research study. Recruitment took place between April 2006 and March 2008 and participants had control over their sleep schedules. The inclusion criteria was ≥ 65 years and those who were not able to communicate with staff, or were unable to provide consent were excluded from the study. 3-days and nights of actigraphy data was collected and compared against PSQI score. 121 participants were included in the analysis with a mean age of 85.3 years ± 6.5. Paired t-tests showed no statistically significant relationships between Total Sleep Time (TST), night-time percent sleep and or total PSQI score. Bivariate testing found no statistically significant relationships between subjectively and objectively measured sleep disturbances and participant characteristics and no statistically significant relationships between objectively measured sleep and total PSQI scores were detected.

Landry, Best, & Liu-Ambrose (2015), explored the predictive ability of the PSQI when compared against actigraphy in a sample of 78 participants with a mean age of 71.6 years ± 6.6. Participants were

recruited through advertisements distributed at community centres and through word of mouth. Individuals over the age of 55, with an MMSE score of ≥ 24 who were able to read write and speak English were included. Those with dementia or any other neurodegenerative or neurological condition which affected cognition and or sleep were excluded, including those enrolled in other clinical trials and those unable to communicate to the research team via telephone. PSQI scores were correlated against actigraphy. No statistically significant relationships were reported for sleep efficiency or sleep latency. Sleep duration and sleep time was statistically significantly correlated ($r = 0.29$; $p < .01$).

In Most, Aboudan, Scheltens, & Van Someren (2012), the discrepancy between subjective and objective sleep disturbances in Alzheimer's Disease (AD) was investigated using both the PSQI and the Dutch Sleep Disorders Questionnaire (SDQ) (See Section 2.3.2.9). Older adults clinically diagnosed by a neurologist or geriatrician, with probable AD were recruited. The diagnoses made were 1.07 ± 1.11 years prior to participation. Individuals were excluded if they had been diagnosed with another neurological or psychiatric disorder, Sleep Apnoea (SA) or Restless Leg Syndrome (RLS). 2-weeks of actigraphy data was collected and compared against the PSQI. 55 participants with AD were included in the analysis with a mean age of 70.4 ± 3.2, alongside 26 participants who formed part of a normal comparison group (mean age 73.0 ± 4.4. The control group consisted of six partners of the AD participants, and 20 volunteers from the local community. Question 4 of the PSQI was found to accurately predict actigraphically estimated Total Sleep Time (TST) ($df = 50$, $t = 2.57$, $\beta = .35$, $p = .01$), for AD patients, and ($df = 24$, $t = 2.10$, $\beta = .40$, $p = .05$), for the normal comparison group. Question 2 of the PSQI was found to statistically significantly predict actigraphically estimated Sleep Onset Latency (SOL) in the normal comparison group only ($df=24$, $t=3.29$, $\beta = .57$, $p = .003$). Here, the PSQI was found to be a good predictor for TST in both neurologically healthy and AD patients, and a good predictor for SOL in a neurologically healthy sample.

Postuma et al. (2017), which was included and outlined previously in the Insomnia Severity Index Section, 2.3.2.1, is a longitudinal study on idiopathic rapid eye movement (REM) sleep behaviour disorder (RBD) patients. As well as using the ISI to assess sleep in their cohort, the PSQI was also used here to measure sleep quality. PSQI mean scores were found to be statistically significantly higher in patients with RBD confirmed through PSG when compared to controls (7.2 ± 3.8 vs. 4.9 ± 3.4, $p = .004$). A greater difference in the proportion of abnormal PSQI scores were observed in RBD patients than the control group (68.5% vs. 44.9%, $p = .029$), with these differences accounted for by the 'sleep

disturbance' item (1.49 ± .65 vs 1.21 ± .56, p = .035) and the 'sleep medications' item (1.51 ± 1.43 vs .28 ± .80).

In Van Den Berg et al. (2008), the discrepancies between subjective and objectively measured sleep duration in older adults was explored. The source of the data was part of the Rotterdam Study, which is a prospective population-based cohort study started in 1990 which investigated the incidence of and risk factors for chronic and disabling diseases. In December 2004, participants were invited to participant in the actigraphy aspect of the study. To be included at least 3-nights of valid actigraphy data was required. Actigraphy was collected for 5-7 consecutive days and participants were asked to press an event marker button each night when they were trying to fall asleep and when they got out of bed each morning. 969 participants were included in the analysis with a mean age of 68.5 years ± 6.9. A 'direction of disagreement' measure was used in the study. This was defined as the average of the normal differences and signals whether an individual has a tendency to over- or underestimate their Total Sleep Time (TST) in their sleep diary when compared with the actigraphically measured TST. Positive differences indicate that diary estimates are higher than actigraphic parameters, whereas negative differences reflect lower subjective than actigraphic values. Participants with poorer sleep quality as defined by the PSQI had shorter diary estimates of TST than their actigraphic measures β = -7.12, (-8.12 – -6.13), p < .001. Additionally, 'level of disagreement' was used which is defined as the average of the absolute differences between night-by-night diary estimates of TST and actigraphically measured TST. Poorer PSQI score was found to increase the level of disagreement β = .72, (.02 – 1.42), p = .04.

2.3.3.9 Dutch Sleep Disorders Questionnaire (SDQ)

The Dutch Sleep Disorders Questionnaire (SDQ) measures sleep quality and consists of 75 questions on a Likert scale ranging from "never" to "very often or always". It includes six types of complaints, including insomnia, periodic limb movement, excessive daytime sleepiness, narcolepsy, psychiatric diseases, and sleep apnoea. Each item is rated (1 – 5), with a cut-off score of 3 for a likely presence of the specific sleep complaint.

The SDQ was used in Most et al (2012), which has been summarised previously in 2.3.2.10. The study included both the Pittsburgh Sleep Quality Index and the SDQ questionnaire. Here, when SDQ excessive daytime sleepiness scores for Alzheimer's Disease (AD) patients were regressed they were able to predict actigraphically measured estimated daytime activity levels (df = 49, t = −3.19, β = −.42, p = .002).

2.3.3.10 Self-rated Sleep Scale (SSA)

The Self-rated Sleep Scale (SSA) is a self-rated questionnaire which contains items on subjective sleep, quality of time awake and somatic disturbances during awakenings. Scores are summed to form a total score. Its use was explored in Happe et al. (2005), where the aim of the study was to investigate subjective sleep perceptions in PD patients and compare this against a sample of healthy adults. PD patients from Vienna were recruited and control group data was obtained from a previous study, "SIESTA". PD patients were investigated using the same study protocol. For inclusion purposes, the control group were age matched with PD-patients, had fully completed sleep logs, and a Pittsburgh Sleep Quality Index (PSQI) score of ≤ 5. Participants in the PD group required a clinical assessment by an experienced neurologist and classified according to Hoehn and Yahr. Participants were excluded from participation in either group if they used sleep medication, and in the control group the presence of any relevant somatic and or psychiatric disorders. 79 participants were recruited (PD patients n = 17, mean age 64.1 ± 6.2, in the control group n = 62, with a mean age of 64.4 ± 8.4) and following 2-nights of PSG, scores was compared against SSA responses. There was a statistically significant correlation between SSA and PSG measures of sleep period time (r > .280, p < .04) and sleep efficiency (r > .381, p < .004).

2.3.3.11 Sleep Disorders Inventory (SDI)

The Sleep Disorders Inventory (SDI) is an informant-based questionnaire on sleep behaviour and habits, containing seven items rated on frequency (1 - 4), severity (1 - 3). These are summed to provide an item-level score. Items include difficulty initiating, maintaining sleep, excessive sleep and other night-time behaviours that bother the informant. Total SDI score is determined by the sum of the item level scores with higher scores indicating greater frequency and severity (0 - 96). Caregivers are also asked to rate their distress for each item (1 - 5).

In Tractenberg, Singer, Cummings, & Thal (2003), the use of the SDI was explored in post-hoc analysis in people with Alzheimer's Disease (AD) taking part in a trial for melatonin as a therapy for sleep disturbances. Participants were included if they had probable or possible AD and had an average Total Sleep Time (TST) of < 7 hours in the previous 2-3 weeks, and experienced at least two episodes of night-time awakenings in this same period. Actigraphy was used as an objective measure to estimate night-time TST (NTST) between 20:00 hours and 08:00 hours over a 2-3 week period. 104 participants with a mean age of 75.5 ± 8.6 completed actigraphy and the SDI. It was reported to have good concurrent validity for night sleep time (*rho*, -.244; p < .01), sleep efficiency (*rho*, -.283; p < .05), WASO (*rho*, .243; p

< .01) and night and day sleep time (*rho*, .215; $p < .01$). There were no statistically significant relationships for day sleep time or 24-hour sleep time.

2.3.3.12 Comprehensive Geriatric Assessment (CGA)

Within the Comprehensive Geriatric Assessment (CGA), there are a series of yes/no questions which explore an individual's perceived sleep. These include: difficulty sleeping, waking up during the night, difficulty to get back to sleep and walking up too early in the morning.

Dos Santos Silva et al. (2015), explored the relationship between subjective sleep and PSG in older adults. Older adults (≤ 60 years) living in Sao Paulo, Brazil who underwent a medical assessment were recruited. Participants were included in the study if they responded to the questionnaire and agreed to undergo a PSG. Those who refused PSG, or had issues that meant they were unable to have the medical assessment were excluded (illness). 1-night of PSG was compared against responses to the CGA. 40 participants were included with a mean age of 73.68 years. The CGA was positively correlated with PSG on a number of measures. These include difficulty sleeping, waking up at night and sleep onset latency ($p = .02$), sleepiness and TST ($p = .005$) and sleep efficiency ($p = .004$), snoring and TST ($p = .03$), sleep efficiency ($p = .03$), stage 2 sleep ($p = .075$), awakenings ($p = .01$), pause in breathing and sleep efficiency ($p = .02$) and sleep apnoea/hypopnea index ($p = .001$). No statistically significant relationships were reported between PSG and CGA measures on difficultly sleeping, waking up at night and leg movements.

2.3.3.13 Ecological Momentary Assessment (EMA)

The Ecological Momentary Assessment (EMA) is an electronic version of a sleep diary which uses a Samsung Galaxy S. It measures current context, psychological phenomena and interactions in daily life. This is completed five times a day over a period of 1-week and each entry takes approximately 5-minutes to complete.

In Baillet et al., (2016), the role of mood plays in the discrepancies between subjective and objective measures of sleep duration were explored in older adults. Participants from the AMImage2 research programme were recruited. These individuals were ≤ 65 years, retired, having previously worked in agriculture for ≤ 20 years, had been affiliated to the MSA under their own name and were living in a rural area. Those who used sleep medications, had a diagnosed sleep disorder, or depression (CESD < 16) were excluded. 7-days and 8-nights of actigraphy was collected measuring Total Sleep Time (TST) and Sleep Efficiency (SE). Actigraphy data was compared against responses to the following

question in the EMA: “how many hours did you sleep last night?”. 45 participants were included in the analysis, with a mean age of 75.39 $\pm$ 0.62, consisting of a total of 175-nights worth of EMA data. Paired t-tests found statistically significant differences between actigraphically measured TST 08:09 ± 00:05 (p < .001) and self-reported TST 06:40 ± 00:06 (p < .001). The average discrepancy between objective and subjective TST measures was 1-hour and 29 minutes (p < .001). This suggests there is limited support for the use of the EMA as accurate measure for TST.

2.3.3.14 Epworth Sleepiness Scale (ESS)

The ESS consists of eight items on daily situations and respondents are asked their likelihood of falling asleep in each. Items are rated on a Likert scale ranging from one to three, which is summed to generate a total score ranging between 0 - 24. Higher total scores suggest greater excessive daytime sleepiness.

The ESS was used In Beaudreau et al. (2012), a study which has been previously discussed in this review in Section 2.3.2.10, having been included for using the Pittsburgh Sleep Quality Index (PSQI). In this sample of 2,968 participants, Cronbach’s α was .76, ranging between .31 and .54. Statistically significant correlations were reported between ESS scores and daytime inactivity (r_s, *.15; p* < .001), Total Sleep Time (TST) (r_s, *-.19; p* < .001*)* and for Wake After Sleep Onset (WASO) (r_s, *.05; p* < .01).

In Postuma et al. (2017), which has been previously included twice in this systematic review for the Insomnia Severity Index (Section, 2.3.2.1), and in the Pittsburgh Sleep Quality Index (PSQI) (Section 2.3.2.10) is a longitudinal study on idiopathic rapid eye movement (REM) sleep behaviour disorder (RBD) patients. In addition to using the ISI and PSQI, the ESS was used to measure daytime sleepiness. For mean ESS scores, no significant differences between idiopathic RBD patients and controls was reported (7.0 ± 4.6 vs 7.2 ± 4.7, n=57, p = .77), nor any significant difference in the proportion of abnormal ESS (28.7% vs. 28.1%, p = 1.0).

2.3.3.15 Karolinska Sleepiness Scale (KSS)

The KSS is a 9-item questionnaire on day and evening alertness. Responses range from one to nine (1 = *very alert*, 9 = *very sleepy, fighting sleep, an effort to keep awake*).

The use of the KSS was explored in Paavilainen et al. (2005), a study exploring the use of telemetric monitoring as a non-invasive method of measuring sleep/wake cycles in older adults in both nursing homes and at home. Participants were recruited from nursing homes in Finland who had previous experience of using the IST Vivago 3001 devices. Participants were screened for dementia with

the Clinical Dementia Rating Scale (CDR) and the Mini-Mental State Examination (MMSE). Those who refused to use the telemetric devices for a continuous period of 24-hours and or had a chronic condition which resulted in impaired wrist mobility were excluded om the study. The devices consist of a write unit, a base station and an alarm (to call for help). The wrist unit has a sensor which monitors activity and usage. 16 participants were included in the study (women n = 15) over a period of 113 days. Positive correlations were found for the KSS and the wrist worn unit for both daytime alertness ($p < .001$) and evening alertness ($p < .001$).

2.3.4 QUADAS-2 Assessment

A number of issues were identified from the studies included in this systematic review. A majority of these involved not being consistent in adhering to the original inclusion and or exclusion criteria, not providing explanation for this criteria, not providing a full description of the source of the data obtained, using terms synonymously (dementia and Alzheimer's), unclear timeframe between index and reference measures, inconsistencies in the number of items of the subjective assessment measure used, inconsistencies in the statistics reported (resulting in multiple assumptions being made to understand the results) and general vagueness in the terms used. This evaluation of risk of bias and applicability of diagnostic accuracy in the included studies is illustrated in Table 3.

Table 3 QUADAS-2 assessment

Study	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Insomnia Severity Index (ISI)							
Bastien et al. (2001)	☺	☺	☺	☺	☺	☺	☺
Postuma et al. (2017) *	☺	?	?	☹	☺	?	?
Observation-based Nocturnal Sleep Inventory (ONSI)							
Onen et al. (2008)	?	☺	☺	☺	☺	☺	☺
Observational Sleep Assessment Instrument (OSAI)							
Martin et al. (2005)	☺	☺	☺	☺	☺	☺	☺
Mayo Sleep Questionnaire (MSQ)							
Boeve et al. (2011)	☺	?	☺	☺	☺	?	☺
Boeve et al. (2013)	☺	☺	☺	☹	☺	☺	☺

REM Sleep Behaviour Disorder Screening Questionnaire – Japanese version (RBDSQ-J)							
Miyamoto et al. (2009)	☹	☺	☺	☺	☹	☺	☺
Nomura et al (2011)	?	☺	☺	☺	☺	☺	☺
Sleep Interview							
Eisensehr et al. (2001)	☺	☺	☺	☺	☺	☺	☺
Sleep Symptom Checklist							
Bailes et al. (2008)	☺	☺	☺	☺	☺	☺	☺
Pittsburgh Sleep Quality Index (PSQI)							
Beaudreau et al. (2012) *	☺	☺	☺	☺	☺	☺	☺
Buysse et al. (1991)	☹	☺	☺	?	☺	☺	☺
Curcio et al. (2013)	☹	☺	☺	☺	☹	☺	☺
Chen (2013)	☺	☺	☺	☺	☺	☺	☺
Dew et al. (1994)	☺	☺	☺	☺	☺	☺	☺
Fung et al. (2012)	☺	☺	☺	☺	☺	☺	☺
Landry et al. (2015)	☺	☺	☺	☺	☺	☺	☺

Most et al. (2012)*	☹	☺	☺	☺	☺	☺	☺
Postuma et al. (2017)*	☺	?	?	☹	☺	?	?
Van Den Berg et al. (2008)	☺	☺	☺	☺	☺	☺	☺
Dutch Sleep Disorders Questionnaire (SDQ)							
Most et al. (2012)*	☹	☺	☺	☺	☺	☺	☺
Self-rated Sleep Scale (SSA)							
Happe et al. (2005)	☺	☺	☺	☺	☺	☺	☺
Sleep Disorders Inventory (SDI)							
Tractenberg et al. (2003)	☹	☺	☺	☺	☹	☺	☺
Comprehensive Geriatric Assessment (CGA)							
Dos Santos Silva et al. (2015)	☺	☺	☺	☺	☺	☺	☺
Sleep Diary / EMA							
Baillet et al. (2016)	☺	☺	☺	☺	☺	☺	☺
Epworth Sleepiness Scale (ESS)							
Beaudreau et al. (2012) *	☺	☺	☺	☺	☺	☺	☺

Postuma et al. (2017)*	☺	?	?	☹	☺	?	?
Karolinska Sleepiness Scale (KSS)							
Paavilainen et al. (2005)	☺	☺	☺	?	☺	☺	☺

* Article examined more than one screening tool

☺Low Risk ☹High Risk ? Unclear Risk

2.4 Discussion

The aim of this systematic review is to examine the literature on sleep complaints through collating, describing and comparing subjective tools used in the older adult population where concurrent validity or diagnostic accuracy is reported. This review consisted of articles where the use of screening tools for sleep disorders, behaviours and habits used in both a community and clinical setting.

Selected articles included studies of patient pools enrolled in clinical trials, sleep laboratories, sleep centres and musculoskeletal referrals, research centres for Alzheimer's Disease, university hospitals, community dwelling projects as well as more generally recruiting from centre waiting areas. Many of participants formed part of a larger cohort study. In accordance to best practices, a QUADAS-2 Assessment (Table 3) was conducted assessing the risk for bias and applicability concerns for each of the included studies. Each article was assessed on their patient selection criteria, use of index test, reference standard and its flow and timing which is incorporated into the recommendations discussed later in this section and are summarised in Table 4 and 5.

2.4.1 Insomnia

The Insomnia Severity Index (ISI) is quick and easy to complete, consisting of a series of questions on sleep where respondents are asked to provide responses to the 7-items. The ISI appears to be a broad measure of sleep related problems. However, the it appears to have mixed, limited support in its use for screening for sleep disorders. Validity of the ISI appears to lack consistency, with Cronbach's alpha ranging across the board from unacceptable to excellent. However, this may be due to the differences in concurrent validity between the ISI's ability to reliability assess for different features associated with insomnia. The ISI appears to be a good measure for some insomniac symptoms; however, it is less suited in measuring terminal insomnia (when compared against early morning awakening scores from PSG), with total ISI scores not appearing to be an effective measure of sleep efficiency. It appears to be a good measure of initial and middle insomnia when compared against sleep onset and WASO polysomnography data, with an additional study supporting its use in measuring changes in WASO discrepancies and variability.

Out of the two studies which explored the use of the ISI included in this review, one was identified to have issues surrounding and unclear risk of bias and applicability concerns for both the index test used and reference standard as well as the flow and timing. This was in Postuma et al. (2017). It was noted that not all participants had completed the scales, as this data was only routinely collected in 2013 onwards. The article also did not specify the timing between in which the PSG and the

questionnaire data was collected, with only a range of 2.6+ / -2.1 years provided for the ISI. Comparisons made between PSQ and assessment scales in this article were since 2003, which raises further questions in the interpretation of these results in regards to our systematic review needs.

It is therefore recommended that the ISI is to be used by both clinicians and researchers to measure initial and middle sleep and data relating to Wake After Sleep Onset (WASO).

2.4.2 Sleep Apnoea

The Observation-based Nocturnal Sleep Inventory (ONSI) and Observational Sleep Assessment Instrument (OSAI) appear to be valid and reliable measures. This was as expected as both measures are tailored for sleep apnoea. Both assessments involve short behavioural observations, one in person and the other through recordings.

However, the QUADAS-2 assessment did identify a risk of bias in the ONSI. In Onen et al (2008), the patient selection criteria lacked clarity in the study design. It was not made clear the reasons as to why some participants were excluded from the final analysis (those who had previously undergone sleep studies and or received care of any type for proven or suspected Sleep Apnoea Syndrome). Additionally, four participants reportedly could not be assessed by the ONSI, which was not explained, with their data was subsequently excluded. No other risks were identified in the study.

In the OSAI, no risks of bias or issues surrounding applicability were identified. A suggestion for future research would be exploring the potential digitalisation of this screening tool inspired by the methodology of the ONSI. This would remove the requirement for a nurse to be present, with all three recordings edited into one 15-minute recording; reducing the amount of time required to observe the individual, and allowing a more efficient use of staff resources.

The validity and diagnostic properties of the Mayo Sleep Questionnaire (MSQ) varies greatly and is therefore not recommended for the screening of sleep apnoea. In Boeve et al (2011), sensitivity and specificity ranged from 29 – 41% which is too low to recommend its use. Additionally, potential issues with flow and timing in the QUADAS-2 assessment were identified in both studies (Boeve et al., 2011; Boeve et al., 2011). The time interval between the administration of the MSQ and the PSG was not specified and varied. The author notes that in some instances weeks or months may have passed between the completion of the MSQ after PSG data had already been collected at a much earlier date.

2.4.3 REM Sleep Behaviour Disorder

For REM Sleep Behaviour Disorder, both the Mayo Sleep Questionnaire (MSQ) and REM Sleep Behaviour Disorder Screening Questionnaire – Japanese version (RBDSQ-J) are highly sensitive and specific measure for both neurologically healthy populations as well as those at risk of dementia. Findings suggests the RBDSQ-J is a sensitive, specific and reliable measure for screening REM SBD in both Parkinson's patients and is also appropriate for use in the older adult Japanese population. For the purpose of this systematic review however, the MSQ is favoured as the RBDSQ-J is in Japanese. It is assumed that the recommendations provided in this review are aimed at English-speaking countries considering articles not in English were excluded. A bias representation of non-English questionnaires may be present as those that did not benefit from cross translation were omitted.

Some ambiguities are also reported in the QUADAS-2 assessment for the RBDSQ-J. In Miyamoto et al. (2009), participants were described vaguely as having been randomly selected. A inclusion and exclusion criteria was also absent in Nomura et al. (2011).

In Boeve et al. (2013), a risk for flow and timing was also identified. Demographic data for solely those participants who were included in the final analysis were not reported. Instead, the presentation of this data was grouped amongst those who had been excluded for reasons including: not having valid PSG data for comparison against the MSQ (n = 20), and increased electromyogram (EMG) tone rates (n = 11). Demographics for a total of 126 participants was reported, which included data for 31 participants which had less relevance which may have been beneficial to omit, or provide the option of presenting two summaries.

The Sleep Interview requires the use of a neurologist which limits its use from a researcher's perspective as this may not be a resource available. However, it does appear to be suitable for use in the neurologically healthy population, but not for those with PD. No issues surrounding risk of bias or applicability were identified in the QUADAS-2 assessment.

The MSQ is therefore recommended for use in screening for REM Sleep Behaviour Disorder for clinicians and researchers as it is validated in English-speaking populations. Clinicians are also recommended to use the Sleep Interview if they have the resources available to recruit a neurologist to assist in patient interviews.

2.4.4 General screening tools

For a more general tool the Sleep Symptom Checklist (SSC) has good internal consistency and validity, and appears to be suitable for use in a neurologically healthy population based on the reported values for its diagnostic accuracy. It also performed very well in the QUADAS-2 assessment with no risks associated with bias and or applicability of diagnostic accuracy. The SSC appears to be an acceptable screening tool, one perhaps more suited towards researchers and used as part of a broad screening tool. It would be less suitable to clinicians who would value a more precise measure. Recommendations are summarised in Table 4.

Table 4 Summary of subjective sleep assessment tools for sleep disorders and its recommended use for clinicians and researchers

	Clinician	**Researcher**
Insomnia		
Insomnia Severity Index (ISI)	Yes	Yes
Sleep apnoea		
Observation-based Nocturnal Sleep Inventory (ONSI)	Yes	No
Observational Sleep Assessment Instrument (OSAI)	Yes	Yes
Mayo Sleep Questionnaire (MSQ)	No	No
REM sleep behaviour disorder		
Mayo Sleep Questionnaire (MSQ)	Yes	Yes
REM Sleep Behaviour Disorder Screening Questionnaire – Japanese version (RBDSQ-J)	No	No
Sleep Interview	Yes	No
General screening tools		
Sleep Symptom Checklist (SSC)	No	Yes

2.4.5 Sleep Behaviour and Disturbances

For the screening of sleep quality, the Pittsburgh Sleep Quality Index (PSQI) was the most frequently used assessment. However, it appears to have mixed results for its use. Greatest support for its use was found for included studies using actigraphy data, when compared to studies that compared its performance against polysomnography. It has acceptable internal consistency and is an effective tool

in measuring Total Sleep Time (TST) with some evidence to also support its use in Alzheimer's populations. Across the various studies, there also appears to be a relationship between nocturnal frequency, sleep quality, Wake After Sleep Onset (WASO), TST and Time in Bed (TIB). There is however limited support for its use in measuring sleep latency and efficiency. The PSQI is versatile, having been translated into languages other than English, namely Dutch and Italian, with the Italian version featuring a high internal consistency and can effectively differentiate between participants with and without sleep complaints. However, the applicability of these versions are limited as it is not in English.

Issues were identified in the QUADAS-2 assessment for the studies included for the PSQI. In Buysse et al, (1991), only a broad outline detailing participant recruitment was described. Information on specifically where this took place were not provided and it is not clear how many places recruitment took place at, despite several methods of advertisement being described. There was also an unclear bias for flow and timing, with information on the timeframe between participants undergoing PSG and completing the PSQI not included. In Curcio et al., (2013) a risk of bias and applicability concerns was identified in participant selection as little information was provided for the participants who took part in screening. Only participant demographics for gender, age and mean age was provided. Additionally, it was not specified what cut-off score was used in the Hamilton Depression Rating Scale in the depression subgroup. For Most et al. (2012), which included both the PSQI and the Dutch version of the PSQI, participant recruitment lacked detail and it was not clear where these participants were sourced from. The unclear risk of bias and applicability concerns for both the index test used and reference standard as well as the flow and timing for Postuma et al. (2017) has previously been discussed in 2.4.1. No issues of risk or bias were identified in Beaudreau et al. (2012), Chen et al. (2013), Dew et al. (1994), Fung et al. (2012), Laudry et al. (2015) and Van Den Berg et al. (2008).

The Self-rated Sleep Scale (SSA) overestimated sleep latency, efficiency and sleep period time. Only one study using this tool was included in this review, with limited data on its use in other groups other than healthy controls, and may therefore not be suitable for use. No issues of risk or bias were identified.

2.4.6 Sleep behaviour and habits

For sleep behaviour and habits, three studies in total were included which examined the Sleep Disorders Inventory (SDI), the Comprehensive Geriatric Assessment (CGA) and the Ecological Momentary Assessment (EMA).

Although the SDI was found to be appropriate for use for some sleep measures, included night sleep time, sleep efficiency, Wake After Sleep Onset (WASO), and night and day sleep time. It was not for other measures of sleep time (including day and 24-hour periods) (Tractenberg et al., 2003). In the QUADAS-2 assessment, issues were identified in patient selection as this study did not adhere to its original inclusion criteria. This lack of consistency in adherence raises questions on the quality of the research in the SDI as participants were included despite meeting the initially described exclusion criteria.

The CGA effective in identifying participants with difficulty sleeping, waking up at night and sleep onset latency, sleepiness and TST and sleep efficiency, snoring and TST, sleep efficiency, stage 2 sleep, awakenings, pause in breathing and sleep efficiency and sleep apnoea/hypopnea index. It was however not for difficultly sleeping, waking up at night and leg movements. No issues surrounding risk of bias or applicability were identified.

It appears that both the SDI and CGA can identify some elements of sleep time, sleep efficiency and WASO, but neither tool is able to encompass all elements of sleep behaviour and habits. This is a very broad area, covering many aspects of sleep and only two studies were included here. To thoroughly screen for problems in sleep behaviours it is arguably more effective to use an alternative assessment to capture a more accurate and reliable picture of the presence of a specific sleep disturbance.

For sleep time, the Ecological Momentary Assessment (EMA) was included. Limited support was provided for the use of this electronic sleep diary as a statistically significant discrepancy between objective and subjective TST measures was observed. Its use is therefore not recommended for the purpose of this systematic review.

2.4.7 Daytime Sleepiness

For daytime sleepiness, three articles in total were included, exploring the use of the Epworth Sleepiness Scale (ESS), and the Karolinska Sleepiness Scale (KSS). Both tools share similarities where responses consist of selecting a corresponding number from a scale multi-point scale.

Two studies examined the ESS which showed acceptable internal consistency, appearing to be a good measure of daytime inactivity, TST and WASO. Internal consistency was good, although this ranged greatly between .31 and .54 (Beaudreau et al., 2012). However, in Postuma et al (2017) found limited support for its use as it was not found to be able to detect significant differences in abnormal ESS compared to controls. A strength of the Beaudreau et al study is its large sample size. The risks identified

as part of the QUADAS-2 assessment have been described previously in 2.4.6. No issues were identified in Beaudreau et al. (2012).

As there are more studies included which have used the Epworth Sleepiness Scale (ESS), there is comparatively less information on the use of the Karolinska Sleepiness Scale (KSS). In Paavilainen et al. (2015), the KSS is suggested to be effective in measuring alertness in both the day and evening. However, the QUADAS-2 assessment identified an unclear risk of bias for flow and timing as it was not clear at what time-points the KSS was used in the duration of the study.

It is more challenging to draw a conclusion here as both tools appear to measure different aspects of areas of sleep that encompass daytime sleepiness (level of inactivity, TST, WASO versus alertness). Other measures described in this review are more effective measures of TST and WASO. Daytime sleepiness is defined as the difficulty in maintaining the desired level of wakefulness (Young, 2004). With this in mind, level of alertness was determined to be a more appropriate measure of daytime sleepiness than inactivity. Recommendations are summarised in Table 5

Table 5 Summary of subjective sleep assessment tools for sleep behaviour and disturbances and its recommended use for clinicians and researchers

	Clinician	**Researcher**
Sleep quality		
Pittsburgh Sleep Quality Index (PSQI)	Yes	Yes
Self-rated Sleep Scale (SSA)	No	No
Sleep behaviour and habits		
Sleep Disorders Inventory (SDI)	No	No
Comprehensive Geriatric Assessment (CGA)	No	No
Sleep time		
Sleep Diary / EMA	No	No
Daytime sleepiness		
Epworth Sleepiness Scale (ESS)	No	No
Karolinska Sleepiness Scale (KSS)	Yes	Yes

2.5 Chapter summary

This Chapter outlines a systematic review carried out to examine the literature on common sleep complaints. Based on this review, subjective assessment tools were collated, described and compared against its ability in screening for sleep disorders and or sleep behaviour and habits. It appears that not all tools are most suited for its described use in the literature, with some commonly used assessments reporting surprising results in their concurrent validity or diagnostic accuracy. Screening tools, when used appropriately, can provide significantly valuable information to support patient care.

When screening for sleep disorders, the review recommends researchers to use the Insomnia Severity Index, the Observational Sleep Assessment Instrument (OSAI), the Mayo Sleep Questionnaire and the Sleep Symptom Checklist (SSC). For clinicians, the following tools are recommended: the Insomnia Severity Index, the Observation-based Nocturnal Sleep Inventory, the OSAI, the Mayo Sleep Questionnaire, and the Sleep Interview. The review recommends the use of the Insomnia Severity Index, the OSAI, and Mayo Sleep Questionnaire for both researchers and clinicians.

When screening for sleep behaviours and disturbances both researchers and clinicians are recommended to use one of the following include the Pittsburgh Sleep Quality Index, and the Karolinska Sleepiness Scale.

The results of this review were intended to inform the design of subsequent experimental chapters described in this Thesis. Unfortunately, due to the timeline, the systematic review and the results were collated after the experimental chapters had drawn to a close. On reflection, with the results to hand, it appears that the Sleep Symptom Checklist (SSC), would have been beneficial to incorporate as a general screening tool for sleep disorders to ensure the inclusion and exclusion criteria were met. I would have also used the Karolinska Sleepiness Scale (KSS) as an accurate and reliable measure for subjective sleepiness and the Pittsburgh Sleep Quality Index (PSQI) to assess sleep quality.

Chapter 3: Investigating the effect circadian rhythm and sleep deprivation has on neuropsychological and neuropsychiatric functioning

3.1 Introduction

This Chapter describes a sleep deprivation paradigm to investigate the impact on attentional functioning, which in turn may affect delirium risk. This study focused on a particular element of the sleep/wake cycle - sleep propensity. Sleep propensity refers to the increasing pressure for sleep and plays a key role in regulating sleep. This increase in sleep propensity can occur through sleep deprivation. As the length of time spent awake increases, there is an insufficient amount of sleep to balance this additional period of wakefulness. Sleep deprivation has been associated with reversible, fluctuating mental states in healthy adults. This fluctuation in cognition draws similarities with the DSM-5 definition for delirium, as discussed in Chapter 1.

This study examines the impact a 24-hour period of sleep deprivation has on sleep propensity and the symptoms associated with delirium, as well as its effects on neuropsychological and neuropsychiatric functioning through a range of assessments. The presence of subtle attentional deficits, previously observed in patients with Sub-Syndromal Delirium (SSD) was explored using computerised assessments to explore whether participants who were sleep deprived would share a similar neuropsychological profile to those with SSD.

3.1.1 Background/rationale

The sleep/wake rhythm is regulated by the endogenous circadian clock. This internal clock responds to the environment to regulate metabolic and physiological functions in the body. The area in the brain responsible for this regulation is the suprachiasmatic nucleus (SCN) which responds to the strongest exogenous pacemaker, light. Sleep is also regulated by homeostatic processes otherwise known as sleep propensity. This is the body's response to the amount of prior wakefulness following a period of high-quality sleep (Borbély, 1980). Sleep propensity is highest when the period of time that has passed since a period of good sleep is longest and lowest when a shorter amount of time has passed since good sleep has occurred (Borbély & Achermann, 1999). This pressure for sleep appears to be driven by two forces: a linear sleep propensity that increases with the amount of time spent awake; and a homeostatic circadian force that putatively synchronises sleep with the terrestrial day.

Disruptions to the sleep/wake cycle have negative effects on the body. This includes, and are not limited to, a higher mortality rate, a greater incidence of cardiovascular disease, stroke, suicide and

an impaired immune system (Bryant, Trinder, & Curtis, 2004; Bernert, Turvey, Conwell, & Joiner, 2014; Ensrud et al., 2012; Li et al., 2014; Pan, De Silva, Yuan, & Koh, 2014), as well as being linked to circadian rhythm disruption (SCRD) and psychiatric disorders. The relationship between SCRDs and psychiatric disorders is well documented and a known feature of neuropsychiatric diseases such as schizophrenia, bipolar disorder and depression. It is thought that the association between SCRDs and neuropsychiatric diseases are related to disruptions to the sleep/wake cycle (Jagannath, Peirson & Foster, 2013). It is therefore important to further our understanding of this complex relationship to be able to develop interventions to mitigate the detrimental effects of sleep disruption.

Furthermore, a review by Weinhouse et al (2009) explored the role of sleep deprivation as a modifiable factor to reduce delirium risk in ICU patients. Sleep complaints are a common complaint in critically ill patients, with typical sleep characterised by wakefulness and light stages of sleep, and a reduction in rapid eye moment (REM) and deep sleep. In the article, similarities were drawn between sleep deprivation and the key characteristics of delirium, namely attentional deficits, changes to mental state and cognitive dysfunction (Dinges and Kribbs, 1991; Harrison and Horne, 2000). The neurocognitive consequences of sleep deprivation are associated with a negative effect on mood, cognition, increased sleepiness, and reduced motor function (Durmer and Dinges, 2005). Studies involving total sleep deprivation have also identified specific impairments to recognition memory through event-related potentials (ERPs) and deficits to attentional control in task switching (Mograss, Guillem, Brazzini-Poisson, & Godbout, 2009; Fisher, 1980).

The use of computerised assessments has been used to quantify attentional deficits observed in patients with delirium. In Lowery, Wesnes, Brewster, & Ballard (2008), a battery of validated assessments for attention were used alongside the Mini-Mental State Examination (Folstein et al., 1975), a measure of global cognitive function, in a cohort of older adults undergoing elective orthopaedic surgery. The attentional tasks provided a measure of sustained attention, mean reaction time, and intra-trial variability of reaction time. When comparing performance in the post-operative period between those without delirium to those with delirium, patients with delirium had a greater variability of reaction time, lower accuracy, slower reaction time, and lower MMSE scores. This study also reported excellent discriminative utility in Receiver Operator Characteristics (ROC) for each of the neuropsychological measures in identifying post-operative delirium. Future research suggested additional research to validate these measures, and in exploring whether those who demonstrate a greater rate of cognitive decline are at a higher risk of the negative outcomes associated with delirium.

A secondary analysis of the data collected from the Lowery et al (2008) was conducted by (Lowery, Wesnes, Brewster, & Ballard, 2010) which focused on the neuropsychological profile of delirium. In this follow-on study, > 27% of participants presented with sub-syndrome delirium (SSD), characterised by a change in cognition, which had not been previously detected using the Confusion Assessment Method (CAM). The authors suggested that these computerised assessments which measure attentional deficits, particularly the lengthening of, and a greater variability of reaction time (as well as lower accuracy) has the potential to detect subtle changes which differentiate between those sub-syndrome delirium (SSD) and those without. It was recommended that further research is necessary to explore the utility of using these computerised attentional measures in delirium for both the clinical and research contexts.

When reviewing the literature, a gap in the research was identified. There is an absence of a systematic explanation of how circadian drivers and sleep deprivation may potentially further interact to modify cognitive functioning. Studies have yet to further examine relationships between change in attentional functioning (i.e., reaction time and variability of reaction time) in individuals who exhibit psychosis-like symptoms, similar to delirium, whilst sleep deprived.

This study will further our understanding of how endogenous drivers for sleep affect cognitive functioning. Based on previous literature a linear trend in deterioration of cognitive functioning over time, as sleep propensity accumulates, is expected. As there is a greater pressure to sleep, an individual would feel sleepier and their performance in cognitive tasks is expected to worsen the longer this sleep deprived state is maintained. Alongside this, the presence of psychosis-like symptoms, changes to mood, and the presence of variability of reaction time, which are core symptoms associated with the disturbances to consciousness found in delirium, will be explored.

3.2 Research aims and objectives

The aim of this study is to investigate the effect of one driver of sleep propensity, circadian rhythm, on the subtle deficits (and anticipated deterioration) of cognitive functions that arise following sleep deprivation such as attention and memory. It is also expected that this deterioration in performance will be most rapid during periods participants would normally be asleep. Furthermore, it was of interest to assess whether any changes, if present, during the 24-hour period relate to times where individuals should normally be asleep when compared to when they should normally be awake.

To measure this, a combination of paper and computerised assessments was used to obtain valid and reliable measurements on sleep, cognitive functioning, and psychotic-like symptoms across multiple time-points during a 24-hour period of sleep deprivation.

3.2.2 Hypotheses

It was hypothesised that:

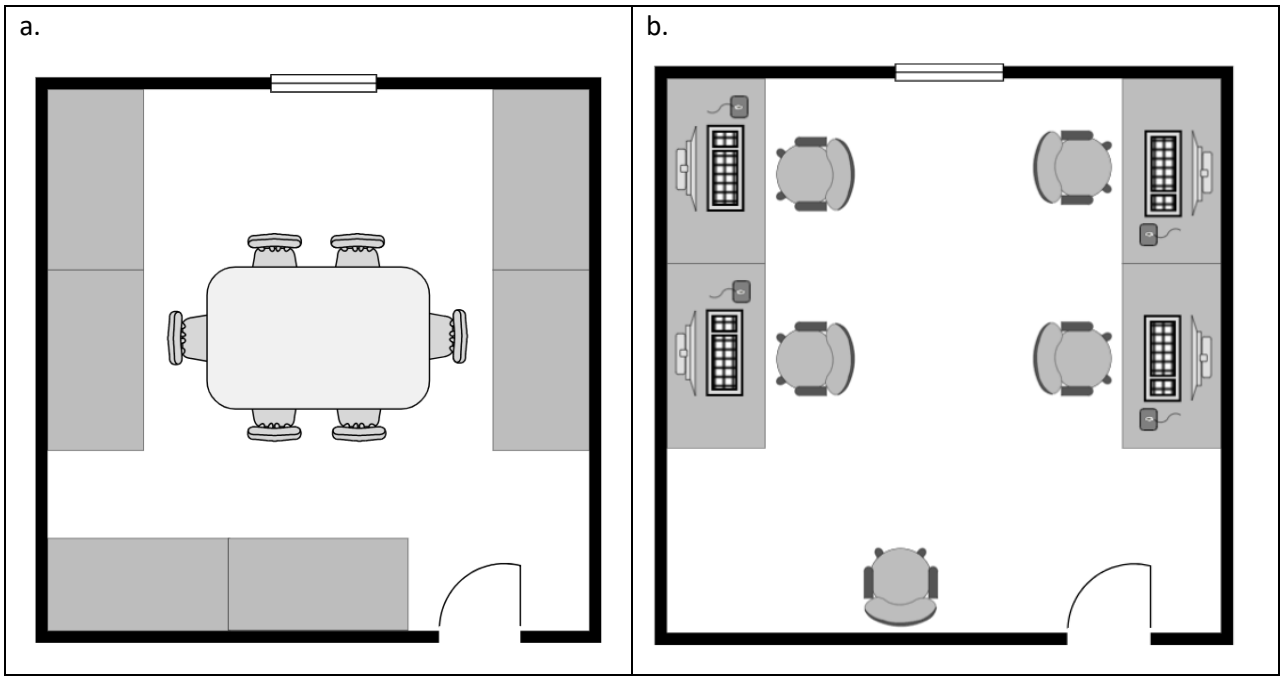
1. The increasing pressure to sleep that develops over time from sleep deprivation will affect cognitive functioning, psychotic-like symptoms and measures of sleep.
    a) Length of time elapsed will affect reaction time and intra-trial variability of reaction time
    b) Length of time elapsed will affect psychotic-like symptoms
    c) Length of time elapsed will affect subjective sleepiness
    d) Length of time elapsed will affect short-term memory
    e) Length of time elapsed will affect emotion
2. Both subjective and objective measures will be impacted as a result of sleep propensity
    a) Reaction time and intra-trial variability of reaction time will be affected by sleep propensity
    b) Psychotic-like symptoms will be affected by sleep propensity
    c) Subjective sleepiness will be affected by sleep propensity

3.3 Method

3.3.1 Study design and setting

This laboratory study was based in the Psychology Department at the University of Kent in two meeting rooms. It consisted of three parts: screening, baseline and a controlled laboratory observation phase. Participants were deprived of one night of habitual sleep and asked to stay awake for the 24-hour duration from 21:00 on Friday night to 21:00 on Saturday. Assessments took place in a separate room (assessment room) and participants were in the lounge room when not completing assessments (with access to the corridor exclusively for the bathroom). The room layouts are illustrated in Figure 3 (a – b). In total there were six sessions that took place between June and August 2017.

Figures 3 (a – b) Room layouts (a) participant lounge and (b) assessment room as illustrated with SmartDraw (SmartDraw, 1994)



To the research team's best abilities, light levels in the laboratory phase were manipulated to minimise disruption to the endogenous circadian rhythm by monitoring it using a digital light meter (see Chapter 3.4.4.4). Light was limited to 300 - 500 lux within the participant lounge and testing room and 600 lux in the corridor. This was kept in line with that of the external environment by observing sun graphs on local weather reports to determine sunrise and sunset times for each session. Natural light was allowed to enter the room during daylight hours by rolling the window blinds up. During hours of darkness, light was reduced by having the window blinds down. Room temperature was also monitored and regulated to remain between 18 to 22 degrees Celsius.

The sessions were facilitated by a team of nine Research Assistants (two at each time point) who were recruited to support the study as it was not feasible for the Principal Investigator to supervise a group of participants for the full 24-hour period alone. They were recruited through social media advertisements and or word of mouth and had a background in social sciences or where possible, specifically psychology. The Researchers were all trained prior to the study in both the administration of assessments and the study protocol with the opportunity to ask questions. Scoring consistency and inter-rater reliability was included in the training to ensure validity and reliability of data obtained. Research assistant shifts consisted of four, six-hour timeslots and are as follows:

- 21:00 – 03:00

- 03:00 – 09:00
- 09:00 – 15:00
- 15:00 – 21:00

3.3.2 Participants and recruitment

The study was advertised online via the School and University-wide Research Participation System (RPS) at the University of Kent to both students and staff. Participants were recruited through opportunity sampling. Posters were also distributed around the University campus and on social media. Participants were reimbursed £40 for their time (either in Amazon.co.uk Gift Cards or in cash). This was equivalent to four hours of continuous testing and 20-hours free time[1]. This rate equates to £10 per hour which is above the National Minimum Wage ("National Minimum Wage and National Living Wage rates", 2019).

Interested individuals were provided with a copy of the Participant Information Sheet (PIS) by the Researcher which contained a brief outline of the eligibility criteria. Those who self-identified as meeting the criteria were then invited to come to the laboratory in person to discuss the study further. The opportunity to ask questions was provided and informed consent was obtained. Each participant was assigned a unique identifier code at this point which was then subsequently used for the duration of the study.

Participants were screened using the following:

- A close-ended interview (described below)
- Presence of psychiatric disorders (Mini International Neuropsychiatric Interview (MINI))
- Sleep, including sleep quality (Pittsburgh Sleep Quality Index (PSQI)), the presence of sleep disorders (Sleep Disorder Questionnaire (SDQ)) and chronobiology (Horne-Ostberg Morningness-Eveningness Questionnaire (MEQ))
- Depression (Beck Depression Inventory (BDI))

Participants were excluded if they met any of the below criteria:

[1] For the purpose of obtaining favourable ethical approval, the remaining 20 hours participants spent in the laboratory when not completing assessments was defined as free time

- Consume ≥ 300mg of caffeine per day (> 1 ½ cups) – to only include those who consume low to moderate amounts as there is a known association between sleep disturbances and daytime sleepiness (Roehrs, & Roth, 2008)
- Consume ≥ 14 units of alcohol per week – in line with UK government recommendations (Department of Health and Social Care, 2016), to exclude those who consume high dosages of alcohol, which is associated with sleep disruption (Ebrahim, Shapiro, Williams, & Fenwick, 2013)
- Smokers (including e-cigarettes) – for practical reasons participants needed to remain indoors, inside laboratory for the full duration of the study and smoke breaks were therefore not possible to accommodate
- Experienced trans-meridian travel in the preceding two months – to account for those with pre-existing disruptions to their sleep from jetlag
- Are current shift workers – as above, but for disruptions related to reversed sleep/wake cycle
- Current consumption of drugs or medication including oral contraceptives (other than vitamins) – to exclude side effects (including potential fatigue and drowsiness) resulting from their use
- A medical history for hearing impairments – to ensure participants could respond to assessments and verbal questions
- A medical history of visual impairments other than glasses or contact lenses, corrected to normal vision - to ensure participants could respond to visual assessments (both pen and paper as well as computerised tasks)
- Presence of sleep disorders (score > 5 on the PSQI)
- Regular time of going to bed later than 12:00 (midday)
- Irregular sleep-wake rhythm (observed in actigraphy and or sleep diary data)
- Screened positive for a psychiatric disorder (using the MINI, Lecrubier et al 1997)
- Presence of depression (score > 18 on the BDI score)
- Morningness-Eveningness Questionnaire (non 'intermediate' or 'moderate' types) – for pragmatic reasons explained below

Efforts were made to mitigate confounding factors that impact cognition. To generalise the findings of this study to predict outcomes in healthy populations, it was necessary to exclude these individuals. It was therefore necessary to exclude individuals who were not neurologically healthy (e.g., Alzheimer's disease, epilepsy and brain tumours) prior to participation. This was adhered to by using the delirium measures and MINI where individuals who scored positive on the delirium scales or positive for

a psychiatric disorder were excluded. Other conditions which were identified as confounds to impacting cognition, relevant to the context of this study and were excluded included depression. Depression is known to have an effect on cognitive functioning and sleep, particularly in slower response times. It has also been identified as a core somatic symptom of delirium (American Psychiatric Association, 2013; World Health Organisation, 2000; Beck, 1970; Huibers, Leone, van Amelsvoort, Kant, & Knottnerus, 2007; Skapinakis, Lewis, & Mavreas, 2004). By excluding those who score positive for depression it helped optimise the internal validity of the findings from this study by reducing the likelihood that confounds are present.

Participants whose anatomy, condition, or other required monitoring (including allergies to polycarbonate and impaired senses) precludes the use of the wearable sleep monitoring equipment and or their ability to complete the assessments, were excluded. It is important to note that allergic reactions are rare (Bruze et al., 1988). This was identified at screening when there was the opportunity to discuss the study further with the researcher.

Non-English speakers were excluded to ensure that neuropsychological and behavioural tests were standardised. As this was a PhD study there were limited resources available to pay for a suitably qualified translator to administer behavioural and neuropsychological tests validated in other languages.

For pragmatic purposes, participants with irregular sleep/wake cycles were excluded, and in addition to this, it was decided that those who did not fit within 'intermediate' or 'moderate' types in the MEQ would be defined as outliers and excluded from the analyses. This was to ensure potential variations in circadian rhythms were minimised. This is reflected by the questions within the MEQ where those of definite type's wake and sleep patterns were significantly different to those of the other types. For example, a 'definite morning' type would wake between 5:00 AM – 6:30 AM whereas a 'moderate morning' would be 6:30 AM – 7:45 AM and an 'intermediate morning' 7:45 AM - 9:45 AM and an 'moderate evening' 9:45 AM – 11:00 AM (see Table 6). This reduces the wake period window to 4 ½ hours as opposed to 7 hours (5:00 AM – 12 noon). A similar pattern can be seen for sleep times with 'definite mornings' sleeping 8:00 PM – 9:00 PM, 'moderate mornings' 9:00 PM – 10:15 PM and 'moderate evenings' 12:30 AM – 1:45 AM. The sleep onset period was likewise reduced to 4 ½ hours from 7 hours.

Table 6 Morningness-Eveningness Questionnaire (MEQ) wake and bedtimes

	Wake time	Bed time
Definite morning	5:00AM – 6:30 AM	8:00 PM – 9:00 PM
Moderate morning	6:30 AM – 7:45 AM	9:00 PM – 10:15 PM
Intermediate	7:45 AM - 9:45 AM	10:15 – 12:30 PM
Moderate evening	9:45 AM – 11:00 AM	12:30 AM – 1:45 AM
Definite evening	11:00 AM – 12 noon	1:45 AM – 3:00 AM

NB: Rows in grey were excluded from the analysis

Participants who completed the screening process and were subsequently eligible for the study were invited to attend the other parts of the study. Based on availability, of both the participant and numbers already enrolled in each session, participants were allocated a session in the laboratory. This did not occur later than 3 weeks after the screening process due to potential changes in the sleep-wake cycle which can come about beyond this period of time.

3.3.3 Ethical approval

An application for ethical approval was submitted to the University of Kent Psychology Ethics committee. Study approval was obtained on the 24th May 2017 (ID: 201714956340944038).

Risks identified during the study's design were deemed to be of low due to the observational nature of the study. Key study information was contained in the Participant Information Sheet which allowed participants sufficient time to make appropriate arrangements.

Issues identified included:

- Tiredness - Participants were reminded not to drive or cycle home following the study. They were offered a complimentary taxi journey home. Participants who declined were reminded that it was their own responsibility to make appropriate arrangements prior to the laboratory phase to get home safety afterwards. Laboratory session were always held on a Friday evening with the study ending on a Saturday evening to ensure participants are able to return to a normal rhythm ahead of the working week (Monday). Participants were supervised at all times, reminded not to operate vehicles or heavy machinery until after a good rest at home.
- Bathroom use – Leading on from the issue of tiredness, to account for the risk of something happening to the participant whilst they were being sleep deprived and in a locked bathroom

cubicle, a standard operating procedure was devised. A member of the research team accompanied participants to the entrance of the unisex bathrooms opposite the laboratory which was no more than five meters away from the laboratory. If the participant did not emerge from the bathroom within 10-minutes the researcher was requested to knock on the door and call out to see if the participant was OK. If after repeated knocking there was no reply, the assumption was made that the participant had fallen asleep. Contact details for the University of Kent Security team was accessible to the research team in instances where they had to be contacted to ensure participant safety (e.g., if a participant was unresponsive in a locked bathroom cubicle).

- Initiation or worsening of other behavioural and psychological symptoms, e.g., agitation/aggression, which was monitored by the research team.
- Accidents – the Principal Investigator assessed the laboratory and surrounding area to assess for potential hazards and eliminate these to reduce the risk of slips, trips and falls.

For incidental findings that emerged following screening, participants were advised verbally by the Researcher to speak to their General Practitioner regarding their results. A summary that contained the relevant result was made available to the participant on request.

3.3.4 Materials

The materials used in this study included pen and paper questionnaires, observations by the research team as well as computerised tasks and measurements of the internal environment of the laboratory. As is standard for participating in a psychology experiment, both electronic and hard copies of the Participant Information Sheet were provided during, and prior to, screening and explained the purpose of the study. Informed consent was obtained at screening using hard copies and a Debrief sheet was provided.

Three meals were provided throughout the experiment to reflect breakfast, lunch and dinner. Calorific intake was monitored and kept best in line with the government recommended daily allowance for men and women accordingly. No restrictions were placed on water intake to ensure adequate hydration. Breakfast and dinner food items were purchased from local supermarkets (Sainsbury's, Kingsmead Road, Canterbury CT1) and lunch items purchased from the Students' Union shop (Essentials, on Canterbury Campus, University of Kent, Canterbury CT2).

An ILM 1335 Digital Light Meter (Iso-Tech) was used to measure light levels within the room and a Braun non-touch+ forehead thermometer NFT 3000 was used to measure body temperature. This specific brand of thermometer is a non-invasive method of recording body temperature from the forehead and therefore appropriate for the context of this experiment. The assessments conducted in the study are listed below and copies can be found in Appendix B.2.

3.3.4.1 Sustained attention

This was measured using the Sustained Attention to Response Task (SART) which is a variation of the GO/NO GO task and is a free, reliable and valid measure of sustained attention and mind-wandering (Robertson, Manly, Andrade, Baddeley, & Yiend, 1997). Poor performance on this computer-based task can be used to identify self-reported everyday attention failures, cognitive failures and attention-related cognitive errors (Allan Cheyne, Solman, Carriere, & Smilek, 2009). It involves the continuous presentation of a single digit (ranging from 1 to 9) immediately proceeded by a mask (circle with an X). Participants are required to respond by pressing a key on the computer (the spacebar in this instance) if any digit other than the number three is presented and to withhold the response if three is presented. The task takes four minutes to complete. To account for any learning effects, this task was completed three times consecutively on each occasion it is administered. Unknown to the participants, only the third trial of each time-point was used in the analysis, and consequently approximately 12-minutes to complete. Following completion of the task, a summary file is computed for each participant which includes date and time, subject and group ID number. For the purpose of this thesis, the following measures of sustained attention used are illustrated in Table 7.

Table 7 Summary of Sustained Attention measures

	Measurement scale	Definition
Script Elapsed Time	Milliseconds (ms)	Time taken to run the script. Higher values imply it took longer to complete the task.
Correct suppressions	Percentage (%)	Percentage of correct suppressions made. Responses to the digit three were successfully made. Higher values indicate greater accuracy.
Incorrect suppressions	Percentage (%)	Percentage of incorrect suppressions made. The suppression of the digit three was not made correctly. Higher values indicate lower accuracy.
Successful trials	Milliseconds (ms)	Response time of the mean latency of four consecutive trials before the **correct** suppression of response to the digit three.
Unsuccessful trials	Milliseconds (ms)	Response time of the mean latency of four consecutive trials before the **incorrect** suppression of response to the digit three.
Correct trials	Milliseconds (ms)	Mean reaction time of valid and correct trials.
Estimated standard deviation	Estimated standard deviation (std)	Estimated standard deviation of correct trials
Coefficient of Variability	Coefficient Variability (CV)	Variability independent of mean differences and is calculated as follows: CV = std/Mean.

3.3.4.2 Visual attention and task switching

The Trail Making Test (TMT) is a two part pen and paper assessment examining a participant's visual attention, including search, scanning, speed of processing, mental flexibility, and executive functioning abilities (Tombaugh, 2004). The task comprises of 25 circles presented on a piece of paper.

In Part A, these circles are numbered (1 – 25) and participants are asked to draw lines to connect the numbers in an ascending order. In Part B, circles include both numbers (1 – 13) and letters (A – L); participants are required to again draw lines between the circles but this time alternating between numbers and letters. Performance is measured in seconds as participants are timed; with a longer duration on either part of the task implying greater impairment. Participants are advised to complete the task as fast and as accurately as possible without removing their pen from the paper. A study examined its reliability by conducting alternate forms of the task to a sample of Major Depressive Disorder (MDD) patients. Test-retest reliability for Parts A and B was found to be between .76 and .89 and between .86 and .94. and therefore concluded to be highly reliable (Wagner, Helmreich, Dahmen, Lieb, & Tadić, 2011). Within the context of this thesis, and to minimise practice effects, the assessments were flipped to create horizontal and vertical versions to create a total of 8 versions of the task (4 for Part A, and 4 for Part B). The order in which these were used were counterbalanced.

3.3.4.3 Visuospatial short-term memory

The Corsi Block Tapping Test (CBTT) is a computerised task used to measure visuospatial short-term memory span (Kessels, van Zandvoort, Postma, Kappelle, & de Haan, 2000). Nine boxes are displayed on a screen and light up in sequential order. The participant is required to repeat this sequence correctly by clicking on the boxes in the same order they saw them light up. The task begins at a two-box sequence and increases to a maximum of a nine-box sequence where participants are allowed two attempts to complete each sequence length. The task increase in difficulty as the length of the sequence is increased following correct recall. This memory task has been validated for use in both brain damaged and healthy participants. In healthy controls, a normative block span score of 6.2 ± 1.3 and a total score of 55.70 ± 20.3 was reported (Kessels, Van Zandvoort, Postma, Kappelle, & De Haan, 2000).

Table 8 Summary of visuospatial short-term memory measures

	Definition
Block span	Length of the last correctly repeated sequence
Total score	Product of Block Span and the number of correct trials

3.3.4.4 Mood

Two measures for mood were used. This included the Beck Depression Inventory (BDI) for depression and the Positive and Negative Affect Schedule (PANAS) scale for emotion.

The BDI assesses depression in the 14 days preceding the assessment. This 21-item self-report questionnaire is a well-established and widely used psychometric test and is rated on a four-point Likert Scale (with the exception of sleep and appetite to distinguish between categories). The assessment contains six score bands ranging from normal (0 - 10), mild mood disturbance (11 - 16), borderline clinical depression (17 - 20), moderate depression (21 - 30) to severe depression (31 - 40) and extreme depression (≥ 40). Individuals with scores indicating borderline clinical depression or higher are recommended to seek medical treatment (Beck, Steer, & Brown, 1996). Depression is known to affect sleep and cognitive functioning, particularly in slowing response time. It has also been identified as a core somatic symptom of delirium (American Psychiatric Association, 2013; World Health Organisation, 2000; Beck, 1970; Huibers, Leone, van Amelsvoort, Kant, & Knottnerus, 2007; Skapinakis, Lewis, & Mavreas, 2004). To reduce confounding effects, individuals who scored above borderline clinical depression were considered to not be suitable and individuals who scored > 18 were excluded from participation. Within the context of this thesis, this short questionnaire was used to screen participants.

The PANAS scale is a 20-item self-report measure of an individual's perceived emotion (Watson, Clark, & Tellegen, 1988). Positive Affect (PA) is the extent an individual feels 'enthusiastic, active and alert'. Higher PA indicates a state of 'high energy, full concentration and pleasurable engagement' whilst low PA reflects 'sadness and lethargy'. Negative Affect (NA) describes 'subjective distress and unpleasurable engagements consisting of aversive mood states' (Watson et al., 1988). It is a valid and reliable (internal consistency ranged from 0.86 - 0.90 for PA and from 0.84 - 0.87 for NA) method of measuring mood and scores have been demonstrated to be stable across a 2-month timeframe and NA subscales have been demonstrated to be correlated with scores obtained from other measures assessing depression namely the BDI. It consists of two 10-item mood scales to accommodate for both positive and negative affect. Participants are asked to respond using a 5-point Likert Scale (1 = *Not at all*, 2 = *A Little*, 3 = *Moderately*, 4 = *Quite a Bit*, 5 = *Extremely*). This scale was used to measure changes in mood. This is in line with delirium assessments as liability of affect (and onset and fluctuation) is an item within the DRS R-98.

3.3.4.5 Sleep parameters

In this study, data for chronobiology, the presence of sleep disorders, sleep quality, subjective sleepiness was collected.

The Horne-Ostberg Morningness-Eveningness Questionnaire (MEQ) is a widely used 19-item self-report questionnaire to measure for individual differences in chronobiology (Horne & Östberg, 1976). Questions cover wake and bedtimes, feelings of alertness and preferences towards specific times in the day to complete tasks. Through responding to each five or four-point scale items, the summed scores identify whether the respondent has a preference towards more of a morningness or eveningness internal body clock. MEQ scores range from 19 to 86 with the following scores corresponding to specific types: Definite Evening (16 - 30), Moderate Evening (31 - 41), Intermediate (42 - 58), Moderate Morning (59 - 69), and Definite Morning (70 - 86). A review of circadian typology measures reports the reliability coefficient for the MEQ ranging from .77 to .86 and reliable in different countries (Di Milia, Adan, Natale, & Randler, 2013). For the purpose of this study, the MEQ was used as a screening tool to account for individual differences in circadian rhythm behaviour to form subgroups of participants corresponding to each type to assist data analysis.

To complement the MEQ, actigraphy monitors were used as a method of measuring sleep objectively prior to the experiment. As previous discussed in Chapter 1.7, the gold standard measure of assessing sleep is polysomnography. There are certain challenges with collecting data using this methodology; namely its impracticality and burden on the participant. For the purpose of this present study, actigraphy was a more practical method (this is described further in Chapter 1).

The Sleep Disorder Questionnaire (SDQ) (Douglass et al., 1994) identifies problems with sleeping and waking over the last six months more specifically the presence of Sleep Apnoea (SA), Narcolepsy (NAR), Periodic Limb Movement (PLM) and Psychiatric Sleep Disorders (PSY). The 175-item self-report questionnaire consists of two rating systems; a five-point Likert Scale in the first 152 items (1 = *Never*, 2 = *Rarely*, 3 = *Sometimes*, 4 = *Usually*, 5 = *Always*) and a five-point scale with one being the least and five the most for the remaining 22 items (Douglass et al., 1994). It takes approximately 20 minutes to complete and has a high test-retest reliability (Spearman rho: SA .842, NAR .753, PSY .848 and PLM .817). The role of the SDQ was to screen for participants who scored positively for a sleep disorder and to exclude them from the analysis. In the context of the clinical study (which is described in Chapter 4), the SDQ was used as both a screening tool and as a baseline benchmark for sleep problems which was later used to compare against scores obtained at 3-months follow-up.

The Pittsburgh Sleep Quality Index (PSQI) is a self-report questionnaire which measures an individual's sleep habits over the past one month and takes up to ten minutes to complete. It contains 19-items and scores within seven components are summed to create a global score. The seven components include: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction (Buysse, Reynolds, Monk, Berman & Kupfer, 1989). This sleep quality questionnaire has been found to correlate highly with subjective measures of sleep, specifically sleep diaries, in measuring sleep efficiency, total sleep time, wake-after sleep onset and sleep latency, and depression scales (Spearman's rho $p < .01$). Overall, it was found to have good internal homogeneity (Grandner, Kripke, Yoon, & Youngstedt, 2006).

To measure sleepiness, the Stanford Sleepiness Scale (SSS) (Hoddes, Dement, & Zarcone, 1972) is a simple 7-point Likert scale used to assess for alertness at a given moment in time was used. Participants are asked to respond to the question 'How alert are you feeling right now?' with a scale rating (1 = *Feeling active, vital, alert or wide awake*, 2 = *Functioning at high levels but not at peak; able to concentrate*, 3 = *Awake but relaxed; responsive but not fully alert*, 4 = *Somewhat foggy, let down*, 5 = *Foggy; losing interest in remaining awake; slowed down*, 6 = *Sleep, woozy, fighting sleep; prefer to lie down*, 7 = *No longer fighting sleep, sleep onset soon; having dream-like thoughts*, and or, X = *Asleep*). Here it was used to measure subjective sleepiness at each of the seven time points.

3.3.4.6 Psychiatric disorders

The Mini International Neuropsychiatric Interview (MINI) (Lecrubier et al., 1997) is a short, 15-minute interview which examines for the presence of psychiatric disorders described in the DSM-4 and ICD-10. Here, it was used as a method to screen for any psychiatric disorders to exclude these individuals from participation.

3.3.4.7 Psychotic-like symptoms

The Psychotomimetic States Inventory (PSI) (Mason, Morgan, Stefanovic, & Curran, 2008) is a 48-item self-report questionnaire used to measure experiences of drug-like states, and was originally devised specifically to assess cannabis and ketamine use. Responses to questions are rated on a scale of 0 to 3 (0 = *Not at all*, 1 = *Slightly*, 2 = *Moderately*, 3 = *Strongly*) and correspond to four sub-scales, with each individual item containing a different number of items. Four items are reverse scored. The sub-scales include: delusional thinking (8-item), perceptual distortions (10-item), cognitive disorganisation (9-item), anhedonia (7-item), mania (6-item) and paranoia (8-item). Scores are obtained as a total score of each item within each sub-scale. It takes less than 10-minutes to complete. Although specific to

measuring the effects of acute drug intoxication, the PSI was the only questionnaire available at the time which captured experiences associated with delirium in a self-report format. The PSI was used as a novel method of measuring symptoms associated with delirium, specifically around delusions and psychotic-like symptoms to answer the question set out in the hypotheses.

3.3.4.8 Delirium

The Delirium Rating Scale Revised-98 (DRS R-98) is a 16-item scale that measures delirium severity and can also be used for diagnosis and to differentiate from other disorders such as dementia, schizophrenia and depression (Trzepacz, Baker, & Greenhouse, 1988; Trzepacz et al., 2001). It consists of individual items rated on a scale of 0 to 3 which specifically, sensitively, and reliably measures delirium symptoms. These items include aspects on temporal onset of symptoms, perceptual disturbances, hallucination type, delusions, psychomotor behaviour and cognitive status. Depending on the cut-off point selected, the DRS R-98 has excellent psychometric properties, including high sensitivity ranging from 91% to 100%. For the purpose of this thesis, the cut-off score of 15.25 was selected for DRS R-98 *severity score* and 17.75 for *total score* in line with Trzepacz et al (2001). A cut-off score of 15.25 results in 92% sensitivity and 93% specificity, and 17.25 results in 92% sensitivity (the same) and 95% specificity. It is also highly correlated with other related assessments such as the original DRS, Cognitive Test for Delirium (CTD) and Global Clinical Impression Scale Scores (CGI) as well as exhibiting high inter-rater reliability and internal consistency (Trzepacz et al., 2001).

For the purpose of this thesis, the DRS R-98 was used as a method of measuring severity and the presence of symptoms associated with delirium. Due to the observational nature of this study, it was not anticipated any participants would become clinically delirious. The DRS R-98 was favoured over the Confused Assessment Method (CAM) based on published recommendations that it is more appropriate for use in longitudinal studies (Trzepacz et al., 2001).

3.4 Procedure

This experiment consisted of three phases and summarised in Table 9, with copies of the assessments used at each time-point described in Appendix B.2.

Table 9 Summary matrix of assessments conducted

Screening	Baseline	Laboratory						
		21:00 (1)	01:00	05:00	09:00	13:00	17:00	21:00 (2)
Informed Consent								
Interview Questions								
Depression	-	-	-	-	-	-	-	-
Sleep quality	-	-	-	-	-	-	-	-
Sleep disorders	-	-	-	-	-	-	-	-
Chronobiology	-	-	-	-	-	-	-	-
Psychiatric disorders	-	-	-	-	-	-	-	-
	Participant characteristics							
-	Actigraphy	-	-	-	-	-	-	-
-	Sleep diary	-	-	-	-	-	-	-
-	Psychotic-like symptoms	Psychotic-like symptoms	Psychotic-like symptoms	Psychotic-like symptoms	Psychotic-like symptoms	Psychotic-like symptoms	Psychotic-like symptoms	Psychotic-like symptoms

-	-	Study adherence questionnaire	-	-	-	-	-	-
-	-	Body temperature	Body temperature	Body temperature	Body temperature	Body temperature	Body temperature	Body temperature
-	-	Reaction time	Reaction time	Reaction time	Reaction time	Reaction time	Reaction Time	Reaction Time
		Sustained attention	Sustained attention	Sustained attention	Sustained attention	Sustained attention	Sustained attention	Sustained attention
-	-	Visual attention	Visual attention	Visual attention	Visual attention	Visual attention	Visual attention	Visual attention
-	-	Visuospatial short-term memory	Visuospatial short-term memory	Visuospatial short-term memory	Visuospatial short-term memory	Visuospatial short-term memory	Visuospatial short-term memory	Visuospatial short-term memory
-	-	Sleepiness	Sleepiness	Sleepiness	Sleepiness	Sleepiness	Sleepiness	Sleepiness
-	-	Emotion	Emotion	Emotion	Emotion	Emotion	Emotion	Emotion
-	-	Delirium	Delirium	Delirium	Delirium	Delirium	Delirium	Delirium
-	-	-	-	-	-	-	-	Debrief

3.4.1 Screening and baseline

Participants were screened for their eligibility no more than 3 weeks before they were due to take part in the laboratory phase. Baseline assessments took place no earlier than 7 days prior to the laboratory session and participants were asked to wear and complete the following:

- Sleep including actigraphy (see Chapter 1.7) alongside a sleep diary (see Chapter 1.7)
- Psychotic-like symptoms (Psychotomimetic States Inventory (PSI) (see Chapter 3.3.4.3))

One week of actigraphy data alongside a sleep diary was collected to assess for participant's habitual sleep-wake cycle. This was used to determine circadian sleep patterns. Individuals who were unable to attend in person and therefore unable to wear the actigraphy monitor were still included in the experiment. These individuals were instead asked to complete a sleep diary as best as they could to assess natural sleep-wake cycles. They were asked not to nap, consume alcohol or drink caffeine in the 24-hours to the run up of the study to ensure their natural sleep-wake cycle was maintained, avoid any 'preparation' (i.e., pre-napping to increase their confidence in their ability to stay away) or increase in consumption of sugary foods. This night of normal sleep was cross-referenced with actigraphy data (where available), the sleep diary and responses from the study adherence questionnaire.

Participants were also asked to complete the PSI to provide a baseline measure and had their height and weight recorded to initialise the actigraphy monitors.

3.4.2 Laboratory

On arrival, participants were asked to complete a pre-study adherence questionnaire (see Appendix B.2). This was a bespoke questionnaire designed for the project for the purpose of identifying whether participants followed the pre-study guidelines on consumption of certain drinks and food as well as the presence of naps to ensure that their natural sleep-wake cycles were unaffected by any external factors. It was made clear to participants that their responses would not affect their ability to participate and that it was to facilitate the Researcher to accommodate for confounding factors.

Assessments took place every 4 hours from 21:00, with there being seven assessment time-points in total spread out equally for the duration of the study. For the computerised tasks, participants were guided to the adjacent room to their allocated computer. The room had two computers and two participants were tested at the same time. The Researcher entered the individualised participant code as well as the session number for each participant and explained the task to them. The Researcher checked that the task was complete, and the data had been saved before guiding the participant back to

the main room. These time-points were selected to collect data as regularly as possible whilst being feasible with the study constraints of the number of researchers and with minimising participant burden in mind. There were more participants than computers and researchers at any point which resulted in a tolerance of 15-minutes from the assessment time-point being taken into account to ensure all participants were tested.

All participants were asked to remain in the laboratory for the duration of the study, where they were free to spend the 20-hours of 'free time' (when assessments were not taking place) to engage in optional activities and were supervised at all times. This involved: listening to music, reading, studying, playing games and use of electronic devices such as laptops and mobile phones. Up to eight participants took part in each laboratory session. Three meals were served to the best ability to their natural mealtimes.

3.4.3 Study Endpoints

The study ended once the last assessment (conducted 24-hours after the participant's arrival at the laboratory) was completed. Participants were debriefed verbally and in writing. Payment of £40 was provided and recorded in the form of a signature as evidence of reimbursement.

3.4.4 Study Withdrawal

Participants were able to withdraw from the study either at their own request or at the discretion of the researcher; they were made aware that this would not affect them in any way. The researcher withdrew the participant if they fell asleep, if the research posed a hazard to the safety of a participant, or if the participant posed a hazard to the safety of the research team. Those who withdrew from the study were not replaced.

3.5 Analyses

Participant characteristics including age, gender, ethnicity, sleep quality and disorders, chronobiology, psychotic-like symptoms and depression scores were recorded at baseline and reported in tables and or histograms. The responses from the study adherence were also collated and participant withdrawal was described.

Data was cleaned and those who scored below the 200ms reaction time threshold were identified as outliers and removed. Following data collection, chronobiology scores were examined. Participants who defined in the 'definite' categories (either definite morning or definite evening) and therefore outliers were excluded to account for differences in circadian rhythm. Participants with

missing data on any of the measures were also excluded from the analyses. Additionally, baseline data, collected up to one week before the laboratory phase, was also omitted to standardise the analyses across all assessments used in the study. Not all of the assessments conducted were carried out at baseline, therefore providing eight data time-points (if conducted at screening) or seven (if not conducted at screening). It was agreed that omitting this screening baseline data would generalise the number of data points across assessments.

For Hypothesis 1 (a - e), a one-way repeated measures MANOVA was initially considered as a suitable statistical test as all participants took part at each seven timepoints and addresses the question on the presence of changes in performance across time as set out in the hypothesis. To analyse data using the MANOVA, a series of assumptions need to be met. In this instance, one of the assumptions was violated. Perfect multicollinearity, as well as multicollinearity in general was present in a number of dependent variables. This was expected as many of these variables measured similar aspects e.g., reaction time being measured across two assessments and through five measures. Due to this, considerations were made to use Principal Components Analysis (PCA) to present the original dependent variables through a smaller set of linear combinations. However, this was not suitable as this reduction is already a part of the MANOVA analysis. The MANOVA analysis itself similarly creates these linear combinations. This repetition would be a source of confusion and the overall test would have the same outcome. Attempts were made to conduct MANOVA on a smaller subset of dependent variables. However, VIF scores were still > 5, indicating multicollinearity. Therefore, this dataset was most suitable to be analysed through multiple, within-subjects ANOVA and not multivariate analyses. This would allow comparison of participants' performance across the seven different time points. To answer our first hypothesis, within-subjects ANOVAs was conducted on each of the dependent variables listed below, with time being the independent variable in each instance.

- Reaction time (as measured by the Trail Making Test Parts A and B, the Sustained Attention to Response Task for percentage of correct suppressions, incorrect suppressions, time taken for successful trials, unsuccessful trials, and valid and correct trials)
- Intra-trial variability of reaction time (as measured by the Sustained Attention to Response Task for estimated standard deviation and coefficient of variability)
- Psychotic-like symptoms (as measured by the psychotomimetic states inventory scores (for total score, delusional thinking, perceptual distortion, cognitive disorganisation, anhedonia, mania and paranoia) and delirium score (using the Delirium Rating Scale R-98)

- Subjective sleepiness as measured with the Stanford Sleepiness Scale
- Short-term memory (as measured with the Corsi Block Tapping Test)
- Emotion (as measured with the Positive and Negative Affect Schedule)

To address Hypothesis 2 (a – c), paired t-tests were used to compare mean performance during periods of wakefulness versus sleep for each of the following dependent variables:

- Reaction time (as measured by the Trail Making Test Parts A and B, the Sustained Attention to Response Task for percentage of correct suppressions, incorrect suppressions, time taken for successful trials, unsuccessful trials, valid and correct trials)
- Intra-trial variability of reaction time (as measured by the Sustained Attention to Response Task for estimated standard deviation and coefficient of variability)
- Psychotic-like symptoms (as measured by the psychotomimetic states inventory scores (for total score, delusional thinking, perceptual distortion, cognitive disorganisation, anhedonia, mania and paranoia)
- Subjective sleepiness as measured with the Stanford Sleepiness Scale

To examine the effect sleep propensity has on these measures, Morningness-Eveningness Questionnaire (MEQ) scores were used to identify and group time-points when participants would have normally been asleep and awake. These were different depending on MEQ type and are described in Table 10. A paired t-test was used to compare differences in scores of each measure between periods of wakefulness versus sleep. This was done by splitting the SPSS file by MEQ type (these include moderate morning, intermediate or moderate evening) and computing new variables which were the mean value of all awake and asleep scores of reaction time, psychotic-like symptoms and subjective sleepiness measures.

Table 10 Times of normal periods of wakefulness and sleep according to MEQ type

	Moderate Morning	Intermediate	Moderate Evening
Awake	09:00 13:00 17:00	21:00 (1) 09:00 13:00 17:00 21:00 (2)	21:00 (1) 01:00 13:00 17:00 21:00 (2)
Asleep	21:00 (1) 01:00 05:00 21:00 (2)	01:00 05:00	09:00 05:00

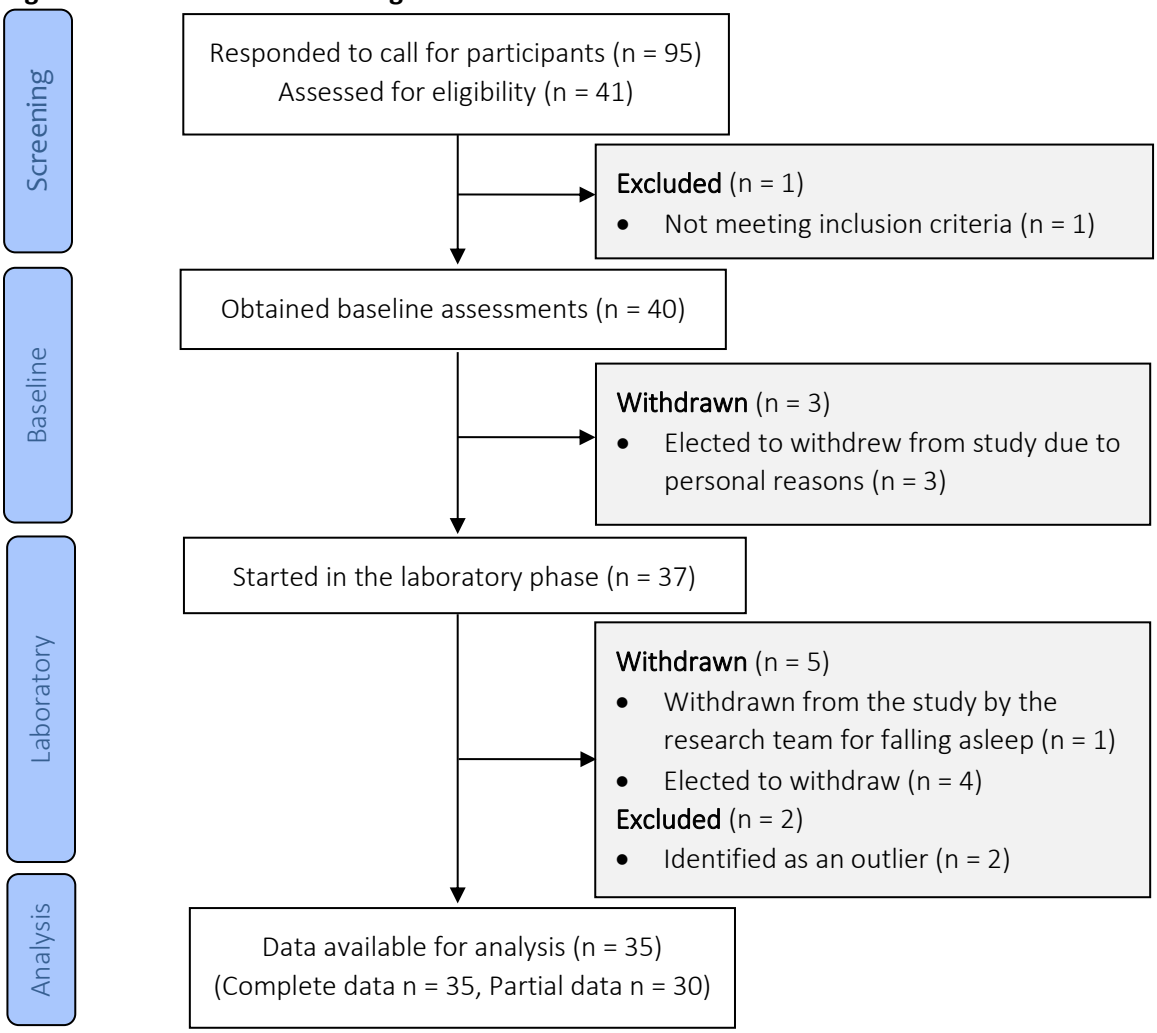
3.6 Results

3.6.1 Participants

In total, 95 participants approached the research team expressing an interest and were sent additional information on the study. This is summarised in a modified CONSORT Diagram in Figure 4.

One participant did not meet the inclusion criteria during screening for the Beck Depression Inventory and in accordance with the study protocol, was verbally advised to speak to their General Practitioner regarding their results and was provided a summary of their scores from screening. In total, eight participants were withdrawn or elected to withdraw from the study. Three participants elected to withdraw following completion of baseline assessments, citing their reasons to be due to changes in personal circumstances e.g., changing jobs, no longer able to commit to the time required to take part in the laboratory phase. Five participants in total were withdrawn during the laboratory phase, four participants elected to withdraw, and one was withdrawn by the research team due to falling asleep during the experiment. Two participants were later identified as outliers for their Morningness-Eveningness Questionnaire response and excluded from the analysis as they were 'definite morning' types. Complete data was obtained for 30 participants (35 participants with partial data).

Figure 4 Modified CONSORT diagram



3.6.2 Descriptive Data

Thirty-five participants were enrolled and took part in the laboratory phase. There was missing data on age for two female participants. All participants who provided informed consent and agreed to take part in the study were screened for their eligibility. This is summarised in Table 11.

Due to the clinical study taking place concurrently and a limited of actigraphy monitors available, a decision was made to direct resources towards the clinical study. As a result, a deviation from the initial study protocol occurred whereby actigraphy data was not collected for this study. The necessity for actigraphy in the clinical study was greater as it formed a key part of the research aims, whereas for the purpose of this study, actigraphy was for monitoring study adherence and chronobiology, which can be confirmed using the study adherence questionnaire and MEQ.

Table 11 Demographic and baseline characteristics

Characteristic	*n*	Mean (SD) or %	Range
Age	33	25.91 (8.72)	18 - 53
Gender			
Female	17		
Male	16		
Ethnicity*	35		
White/Caucasian	26	75.7%	
Black/African American	8	21.6%	
Asian/Pacific Islander	1	2.7%	
Sleep Quality	35	4.34 (2.15)	0 - 9
Chronobiology	35		
Moderate evening	6	17.1%	
Intermediate	24	68.6%	
Moderate morning	5	14.3%	
Presence of depression			
Raw score	31	4.45 (4.37)	0 - 15
Normal	27	77.1%	
Mild depression	4	11.4%	
Presence of sleep disorders	35		
Sleep apnoea		17.34 (4.67)	11 - 31
Limb movement		13.31 (3.36)	9 - 21
Psychiatric disorders		15.54 (3.62)	9 - 23
Narcolepsy		18.77 (3.14)	15 – 28
Presence of psychotic-like symptoms	34	26.29 (13.53)	4 - 51
Delusional Thinking		3.47 (2.45)	0 - 10
Perceptual distortion		2.47 (2.12)	0 - 7
Cognitive Disorganization		7.21 (4.45)	0 - 18
Anhedonia		4.94 (3.75)	0 - 15
Mania		4.68 (2.65)	0 - 11
Paranoia		3.53 (3.52)	0 - 12

* categories used in ActiLife initialisation

Clinical cut-offs: Sleep quality > 5 poor sleep quality, Depression (normal 0 – 10, mild mood disturbance 11 – 16)

Table 12 Summary of visual attention and task switching, sustained attention and visuospatial short-term memory scores

Measure	Time point													
	n	21:00 (1)	n	01:00	n	05:00	n	09:00	n	13:00	n	17:00	n	21:00 (2)
Time taken in the Visuospatial Short-term Memory task														
Part A (s)	32	29.85 ± 21.79	32	27.29 ± 17.00	28	25.47 ± 12.13	28	24.16 ± 13.54	28	20.75 ± 9.40	26	20.77 ± 10.30	27	22.02 ± 11.06
Part B (s)	32	73.63 ± 27.56	32	63.88 ± 25.89	32	59.60 ± 37.57	28	56.62 ± 25.23	28	52.06 ± 20.94	26	52.49 ± 24.09	27	52.78 ± 31.26
Time taken in the Sustained Attention task														
Correct suppressions (%)	32	42.63 ± 26.99	31	40.39 ± 24.45	32	34.38 ± 24.23	28	43.86 ± 30.95	28	38.29 ± 26.48	28	42.29 ± 22.19	27	41.33 ± 22.76
Incorrect suppressions (%)	32	1.42 ± 3.12	31	2.11 ± 4.38	32	3.70 ± 6.41	28	8.14 ± 14.80	28	7.00 ± 7.29	28	5.68 ± 7.27	27	3.98 ± 5.57
Successful Trials (ms)	31	356.35 ± 146.88	31	389.61 ± 112.68	31	395.11 ± 111.88	25	415.49 ± 137.04	27	455.07 ± 165.89	26	407.37 ±102.33	26	409.96 ± 108.31
Unsuccessful Trials (ms)	31	318.31 ± 98.70	31	333.15 ± 101.76	32	342.29 ± 95.05	27	360.43 ± 97.85	28	366.00 ± 92.66	28	342.77 ± 83.06	27	345.81 ± 93.64
Correct and valid trials (ms)	32	378.51 ± 103.58	31	390.35 ± 107.47	32	400.91 ± 97.64	28	445.82 ± 99.56	28	452.92 ± 114.86	28	420.81 ± 78.35	27	419.87 ± 94.46
Variability of reaction time in the Sustained Attention Task														
Estimated standard deviation (std)	32	102.69 ± 65.53	31	104.74 ± 49.12	32	127.08 ± 58.91	28	161.44 ± 81.71	28	169.03 ± 68.48	28	151.30 ± 71.34	27	145.94 ± 70.94
Coefficient of variability (cv)	32	.27 ± .13	31	.27 ± .10	32	.31 ± .11	28	.36 ± .15	28	.37 ± 12	28	.35 ± .15	27	.35 ± .14

Visuospatial short-term memory span														
Block span	32	6.19 ± 1.26	32	6.25 ± 1.08	32	6.28 ± 1.08	27	6.29 ± .95	28	6.25 ± 1.11	27	6.59 ± 1.01	27	6.33 ± 1.24
Total score	32	57.94 ± 21.12	32	61.41 ± 21.19	32	61.41 ± 21.19	27	61.78 ± 16.59	28	59.86 ± 21.88	27	66.41 ± 21.56	27	61.15 ± 25.50

Table 13 Summary of emotion, sleepiness, delirium scores, and body temperature

	n	21:00 (1)	n	01:00	n	05:00	n	09:00	n	13:00	n	17:00	n	21:00 (2)
Emotion														
Positive emotion	32	36.34 ± 6.7	32	29.69 ± 7.21	32	24.94 ± 8.04	28	24.82 ± 10.34	28	24.32 ± 10.16	26	23.23 ± 8.89	27	27.00 ± 9.61
Negative emotion	32	12.53 ± 3.04	32	11.84 ± 2.41	32	13.63 ± 4.52	28	13.61 ± 4.32	27	13.07 ± 5.49	27	12.44 ± 4.23	27	12.15 ± 4.13
Sleepiness	31	1.71 ± .59	31	2.74 ± 1.26	31	3.13 ± 1.18	30	3.80 ± 1.67	27	3.70 ± 1.77	26	3.96 ± 1.61	26	3.88 ± 1.93
Delirium	32	.41 ± 1.04	32	1.06 ± 1.76	32	3.38 ± 3.96	29	4.90 ± 6.24	28	1.82 ± 2.79	27	6.07 ± 5.55	27	6.15 ± 5.97
Body temperature	30	36.90 ± .84	30	37.17 ± .68	30	36.74 ± .55	29	36.85 ± .56	27	36.82 ± .46	26	36.82 ± .49	26	36.95 ± .61

Table 14 Summary of psychotic-like symptom scores

	n	Baseline	n	21:00 (1)	n	01:00	n	05:00	n	09:00	n	13:00	n	17:00	n	21:00 (2)
Total Score	34	26.29 ± 13.53	31	19.52 ± 13.78	32	19.03 ± 12.04	32	22.09 ± 14.39	30	21.73 ± 14.30	28	19.61 ± 13.20	28	18.00 ± 12.06	27	17.22 ± 10.38
Delusional thinking	34	3.47 ± 2.45	31	2.32 ± 3.29	32	1.63 ± 2.35	32	1.47 ± 2.30	30	1.23 ± 2.25	28	1.00 ± 1.92	28	.79 ± 1.39	27	1.41 ± 2.08
Perceptual distortion	34	2.47 ± 2.12	31	1.10 ± 1.79	32	1.38 ± 1.64	32	2.23 ± 2.77	30	2.30 ± 2.69	28	2.14 ± 3.16	28	1.68 ± 2.41	27	1.70 ± 2.22
Cognitive disorganisation	34	7.21 ± 4.4	31	6.26 ± 5.73	32	5.66 ± 5.37	32	6.59 ± 6.48	30	6.57 ± 5.74	28	5.25 ± 5.02	28	5.32 ± 5.38	27	5.04 ± 5.23
Anhedonia	34	4.94 ± 3.75	31	4.74 ± 2.89	32	5.44 ± 2.56	32	6.66 ± 3.45	30	6.40 ± 3.11	28	6.11 ± 3.40	28	5.61 ± 3.60	27	4.33 ± 2.62
Mania	34	4.68 ± 2.65	31	3.58 ± 2.36	32	3.88 ± 2.81	32	4.28 ± 2.75	30	4.27 ± 2.72	28	4.18 ± 2.57	28	4.04 ± 3.07	27	3.96 ± 2.77
Paranoia	34	3.53 ± 3.52	31	1.52 ± 2.72	32	1.06 ± 2.24	32	.81 ± 1.69	30	.97 ± 2.28	28	.93 ± 1.82	28	.57 ± 1.69	27	.78 ± 1.74

3.6.1.1 Adherence to the pre-study guidelines

Five out of 37 participants adhered to all aspects of the self-reported pre-study guidelines (for both parts; 7 days in advance and 24-hours in advance). The remaining 32 participants did not follow the pre-study guidelines. This is summarised in Table 15.

Table 15 A summary of responses to the pre-study adherence questionnaire

	No	Yes	Withdrew
In the last 7 days			
Did you consume alcohol (any amount)?	20	14	3
Did you take a nap? [1]	22	12	3
Was caffeine consumed?	22	12	3
Was chocolate consumed?	22	12	3
In the last 24-hours			
Did you consume alcohol?	32	2	3
Did you nap? [1]	30	4	3
Did you drink caffeine?	28	6	3

[1] 'Nap' defined as any sleeps during normal waking hours

Dietary requirements and allergies were taken into account for the meals provided, with some substitutions having to be made. This applied to instances where participants had food intolerances or allergies which they had informed the research team prior to their participation about. In some instances, the research team were only alerted to this on the day of their participation. Food substitutions were made to the best ability of the team to match the calorific intake of the standardised food item and with the limited opening hours of supermarkets on weekends in mind. Two participants brought their own food due to very specific dietary needs.

A post hoc power analysis was conducted using G*Power3 (Faul, Erdfelder, Buchner, & Lang 2009) to test the difference of within factors. Several analyses on the same set of data were carried out and the power analysis that required the highest number of participants was reported. Effect size values

were calculated using partial η^2 and were defined as small (f = .02), medium (f = .15) and large (f = .35) (Cohen, 1992). A large effect size was used (f = .35), and an alpha of .05. A post hoc power of > .99 was observed with our sample size (n = 21). This suggests that the likelihood of making a Type II error does not exceed the acceptable threshold, and the sample size was sufficiently large enough to detect any effects present at the significance level of < .05.

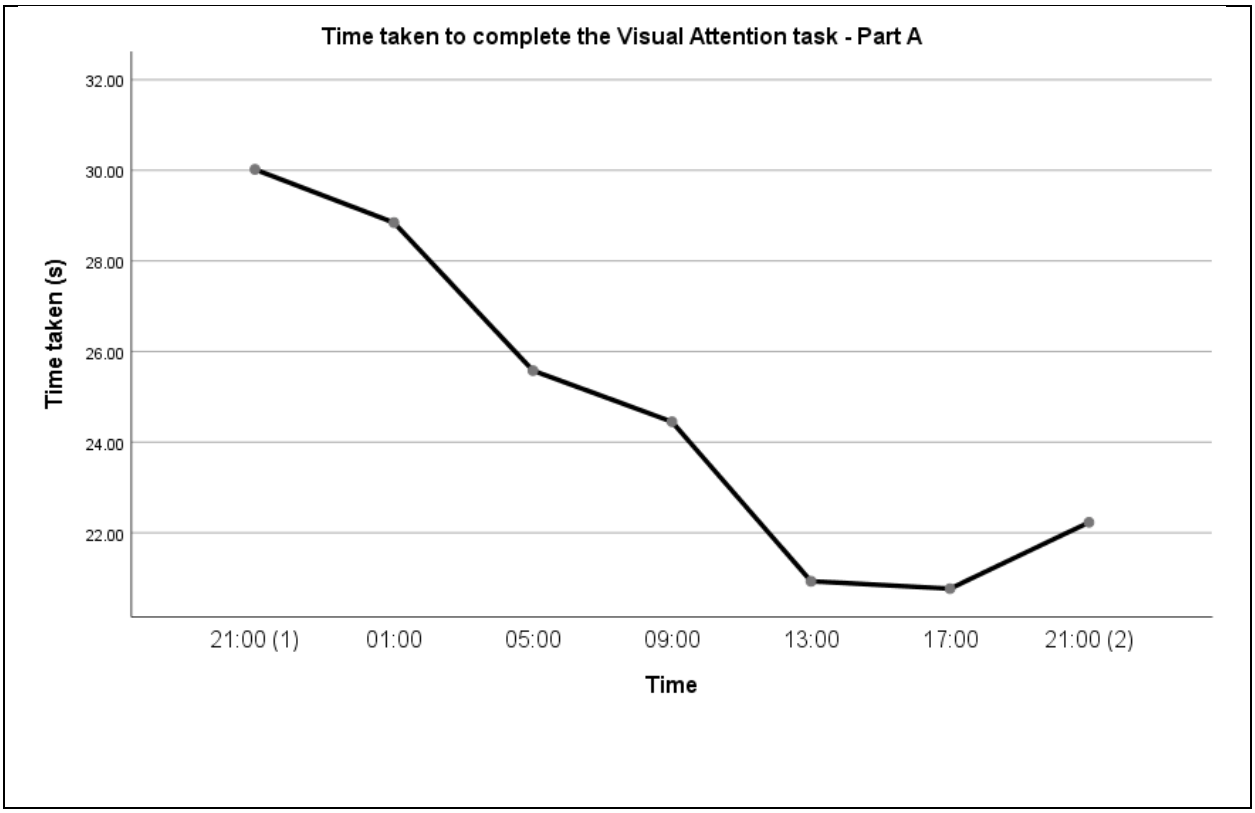
Hypothesis 1

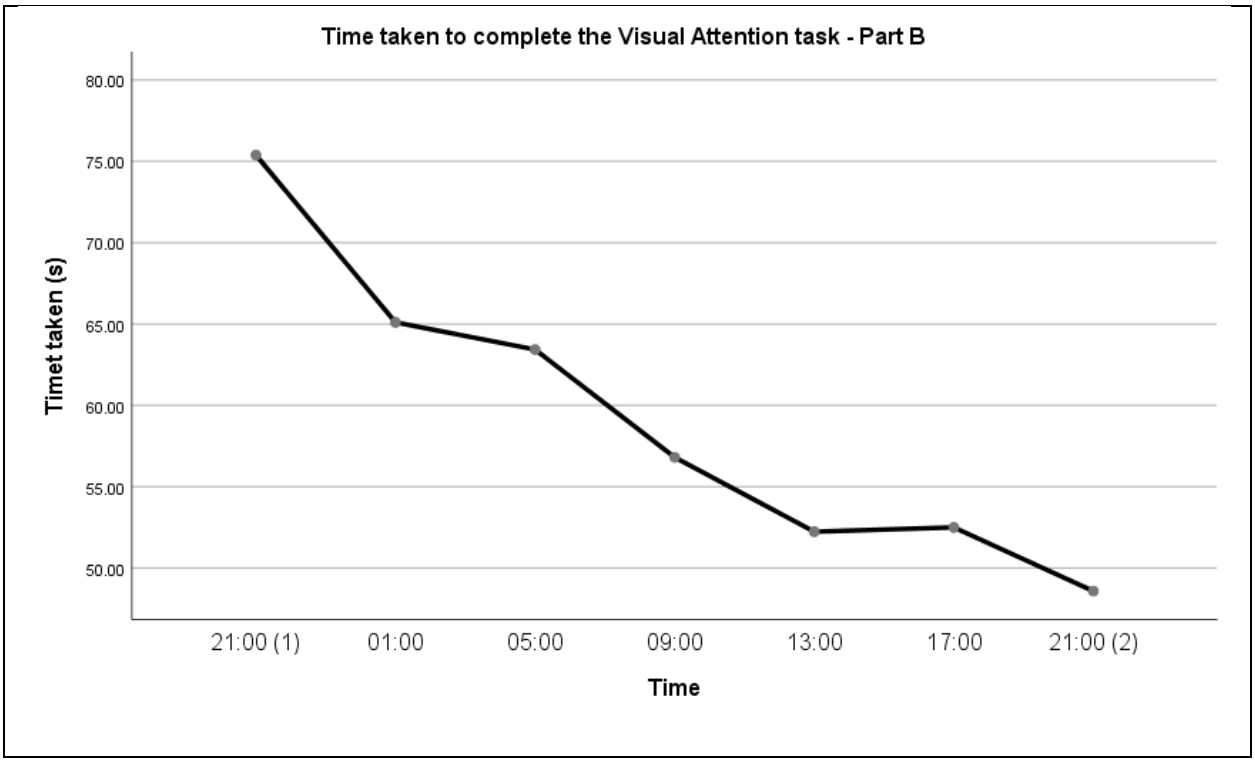
The increasing pressure to sleep that develops over time from sleep deprivation will affect cognitive functioning, psychotic-like symptoms and measures of sleep.

(a) Length of time elapsed will affect reaction time and intra-trial variability of reaction time

There was a significant main effect for length of time awake. Within-subjects contrasts demonstrated significant linear trends in both parts of the visual attention and task switching assessment (see Figure 5) suggesting reaction time is affected by sleep propensity. Specifically, as length of time awake progressed, participants became faster as completing the visual attention task.

Figure 5 Time taken to complete the Visual Attention task

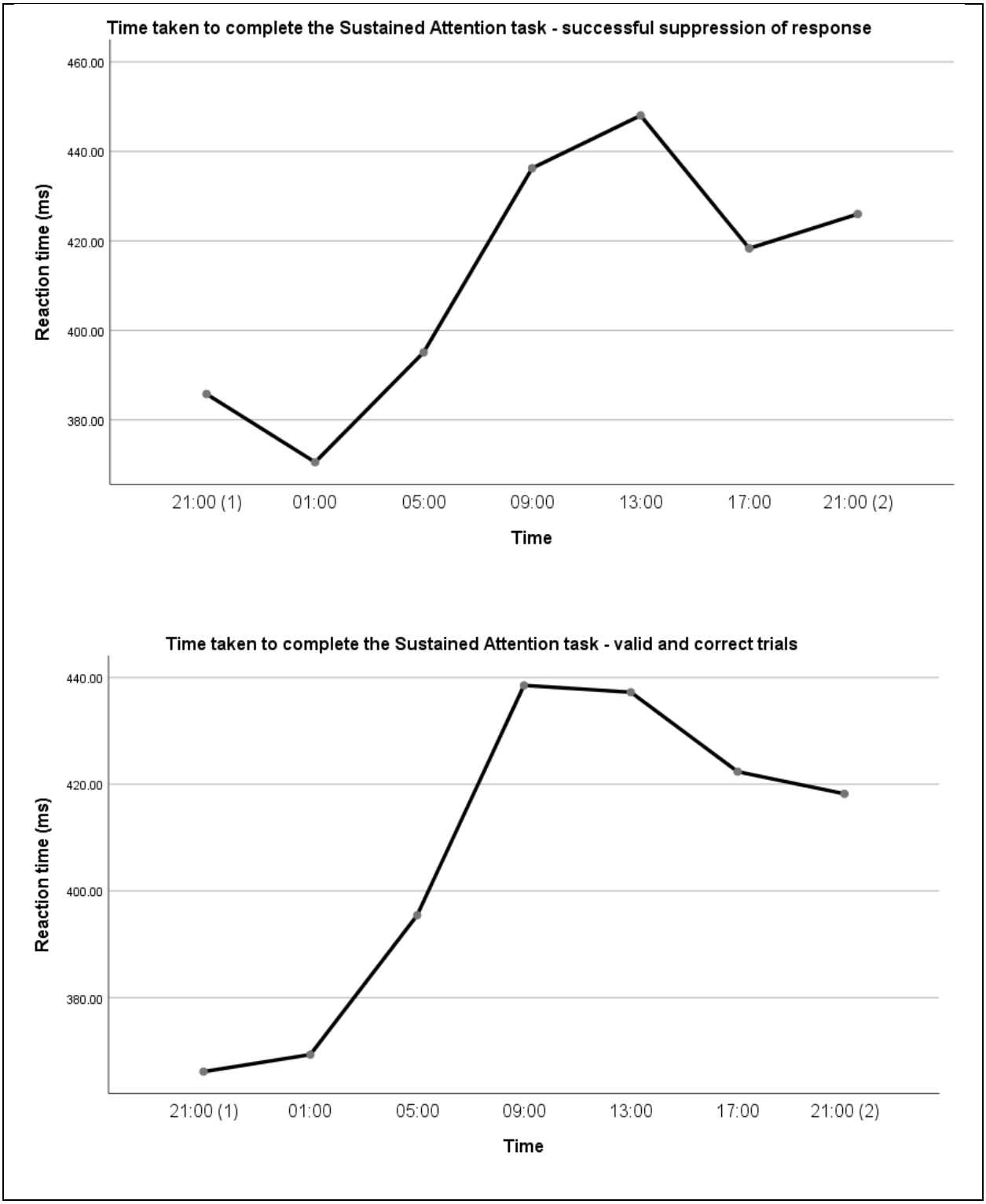


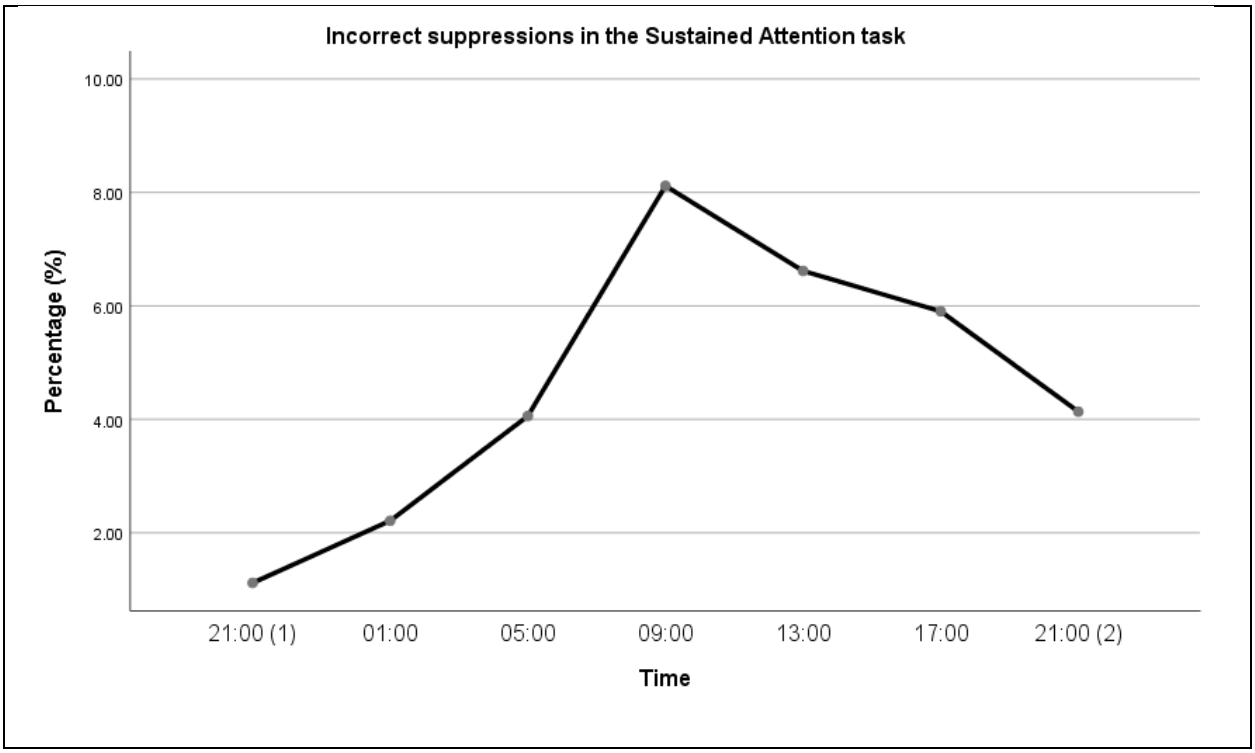


For sustained attention, there were significant main effects for reaction time in successful trials. Within-subjects contrasts demonstrated a significant linear trend in both successful suppression trials, and valid and correct trials, as well as a quadratic trend for valid and correct trials. A significant linear and quadratic trend was observed for incorrect suppressions (see Figure 6).

In addition to this, participants were slower to respond (including up to four trials prior to providing a correct response) to suppressing the digit three. They were also slower when responding correctly as the study duration progressed until 13:00 where this trend becomes quadratic. Participants made an increasing percentage of mistakes in suppressing a response which peaks at 09:00, at which point fewer mistakes were made until the end of the study. No statistically significant differences were found for reaction time in unsuccessful trials or in the percentage of correct suppressions made, suggesting no differences in reaction time were present when participants provided an incorrect response to suppressing the digit three, and no differences in accuracy when the correct suppression of the digit three was made.

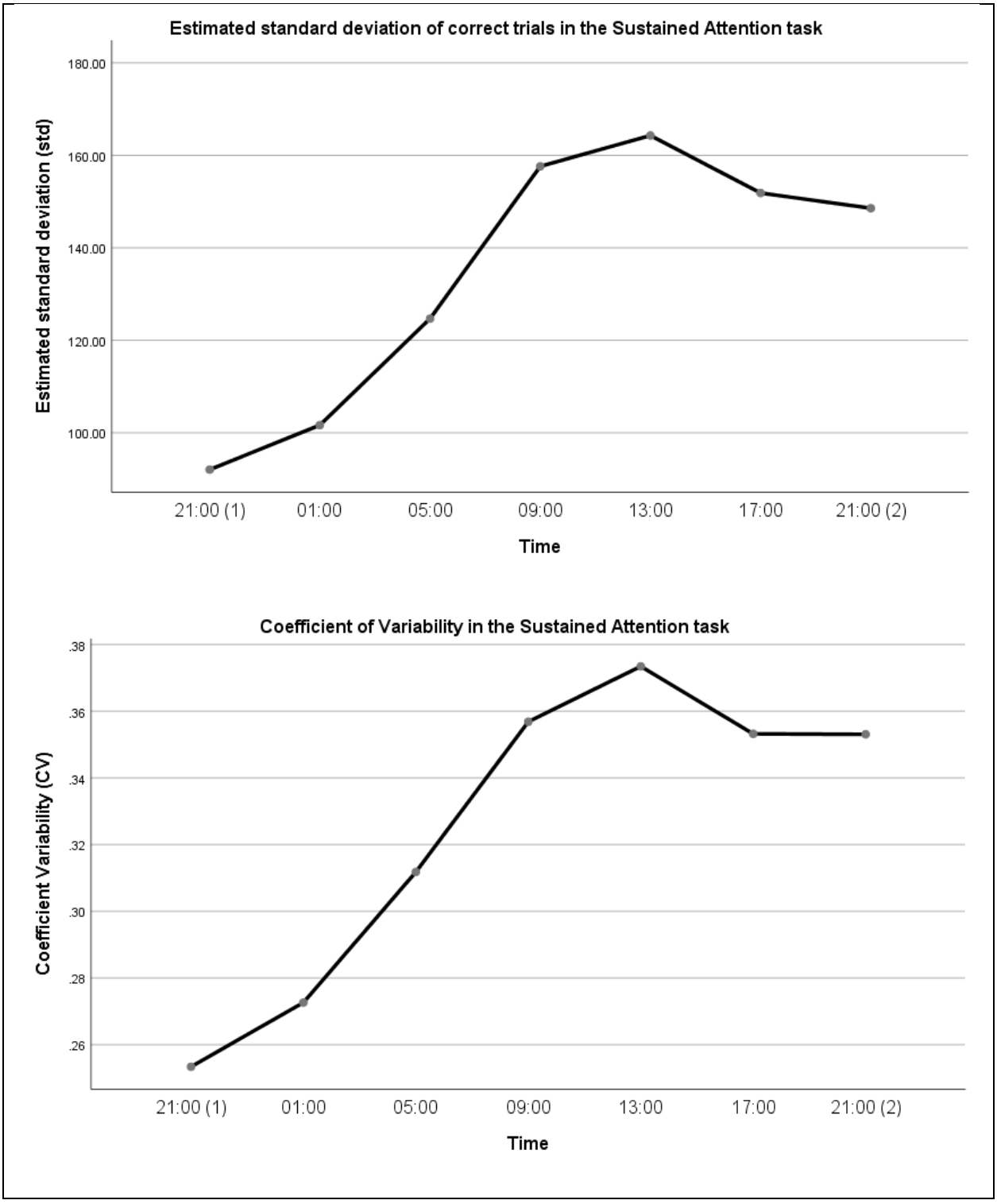
Figure 6 Reaction time in the Sustained Attention task





For variability of reaction time, there were significant main effects in estimated standard deviation and coefficient of variability, with both demonstrating significant linear and quadratic trends (see Figure 7). This suggests participants showed greater variability in their reaction time when making correct responses to each trial as study duration progressed until 09:00 (for estimated standard deviation) and 13:00 (for coefficient of variability) where this trend becomes quadratic.

Figure 7 Variability of reaction time in the Sustained Attention task



In summary, findings suggest the longer the length of time elapsed, the greater the effect on both reaction time and intra-trial variability of reaction time. Participants became faster at completing the visuospatial short term memory tasks, but slower in the sustained attention task, as the study duration progressed. This is a conflicting finding. Participants were slower to respond prior to correctly to suppressing the digit three and were slower to respond to correct trials until 09:00 where they became quicker. This is further described in Table 16.

Table 16 Summary of within subject effects from within-subjects ANOVA for H1 (a)

	n	F (df)	*p*
Time taken in the Visuospatial Short-term Memory task			
Part A (s)	26	5.44 (2.14, 53.48) #	.006*
Part B (s)	26	8.85 (3.20, 79.92) #	< .001**
Time taken in the Sustained Attention task			
Correct suppressions (%)	26	1.04 (3.42, 85.57) #	.39
Incorrect suppressions (%)	26	3.49 (1.99, 49.89) #	.003*
Successful Trials (ms)	21	2.52 (6, 120)	< .001**
Unsuccessful Trials (ms)	25	2.03 (6, 144) #	.07
Correct and valid trials (ms)	26	6.36 (3.40, 85.09) #	< .001**
Variability of reaction time in the Sustained Attention Task			
Estimated standard deviation (std)	26	10.45 (3.74, 93.41) #	< .001**
Coefficient of variability (cv)	26	6.40 (3.995, 99.87) #	< .001**

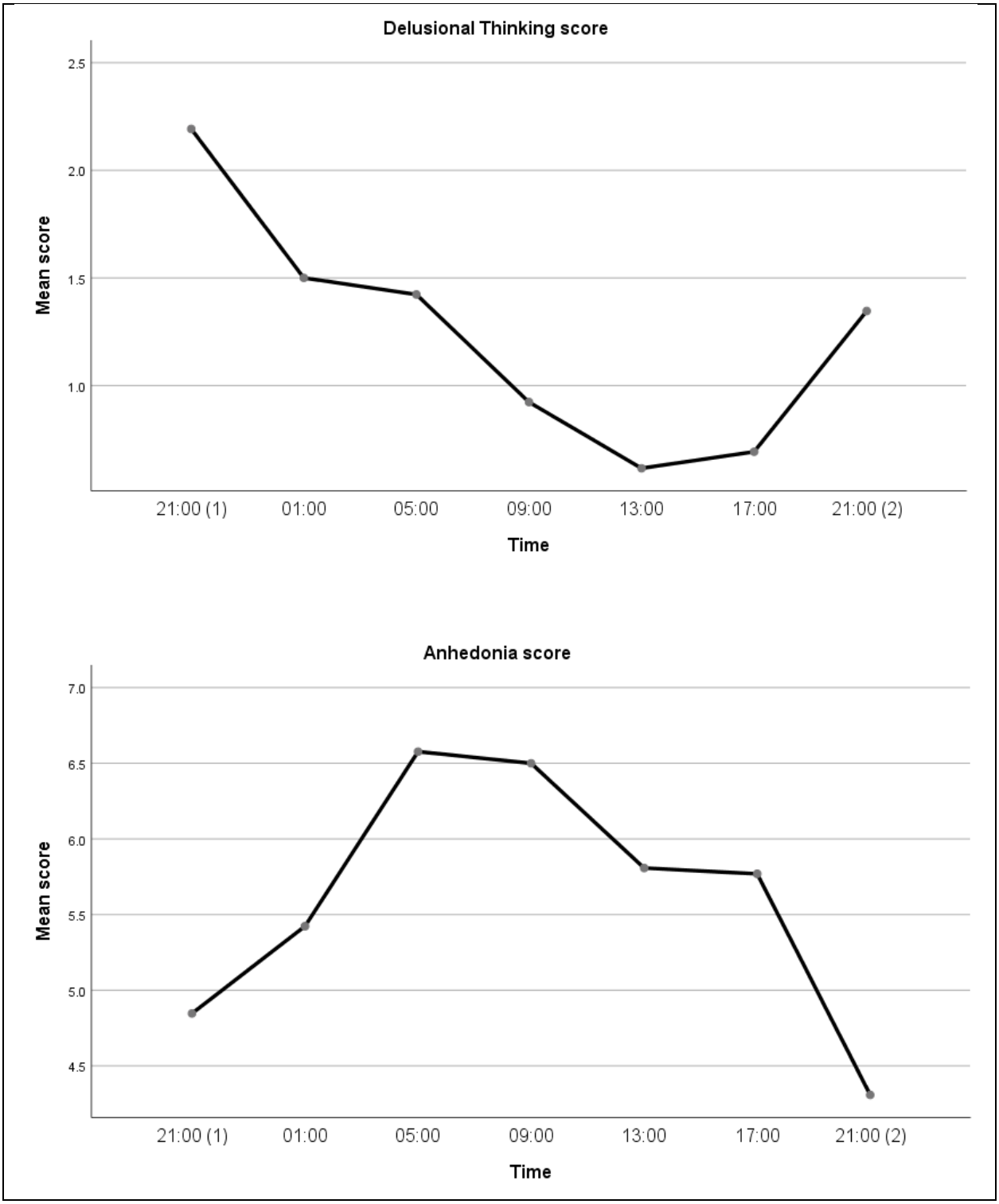
Greenhouse-Geisser correction applied, * = $p < .05$, ** = $p < .001$

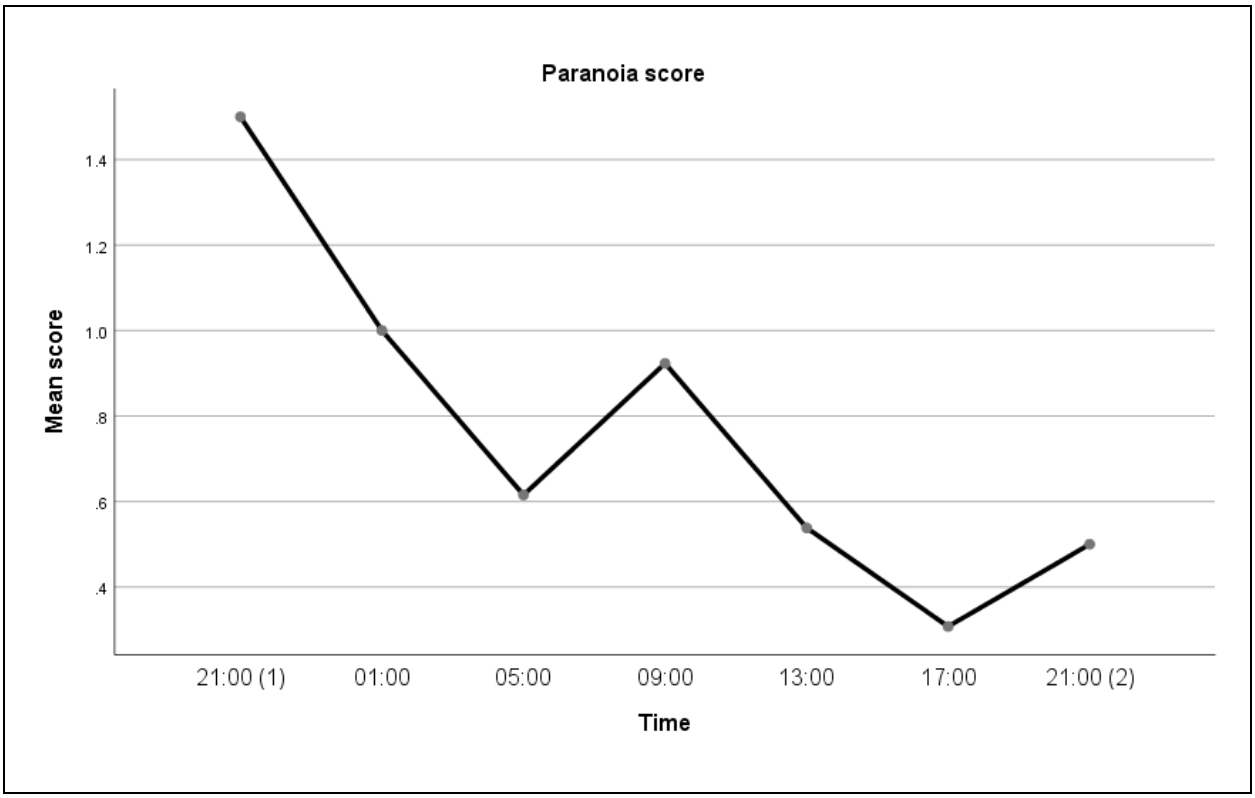
(b) Length of time elapsed will affect psychotic-like symptoms

A significant main effect and linear trend was found for paranoia, a linear and quadratic trend for delusional thinking and a quadratic trend for anhedonia. No statistically significant main effects were found for total psychotic-like symptoms score, perceptual distortion, cognitive disorganisation and

mania. Psychotic-like symptom scores increased over time, with delusional thinking and anhedonia scores fluctuating over the same period (see Figure 8).

Figure 8 Psychotic-like symptoms over time





Delirium scores showed a significant main effect, as well as a linear and cubic trend (see Figure 9). These findings suggest that delirium scores are affected by sleep propensity as demonstrated by trends across the 7 time-points. Delirium score increased steadily until 09:00, followed by over a 2-point drop at 13:00 and then spiking peaking at 17:00 where it plateaued. This is summarised in Table 17.

Figure 9 Delirium scores over time

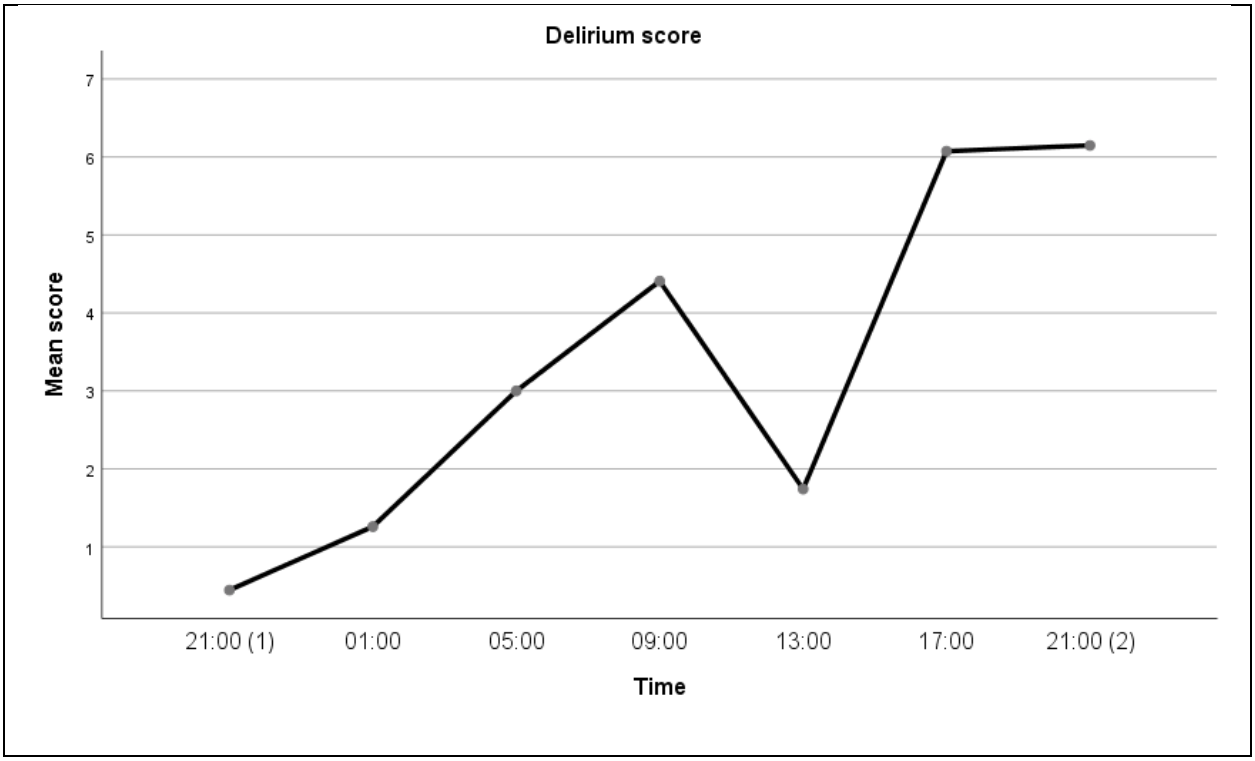


Table 17 Summary of within subject effects from within-subjects ANOVA for H1 (b)

	n	F (df)	*p*
Psychotic-like symptoms			
Total Score	26	1.93 (2.35, 58.82)	.15
Delusional thinking	26	4.98 (2.62, 65.60) #	.005*
Perceptual distortion	26	1.79 (2.77, 69.34) #	.16
Cognitive disorganisation	26	3.05 (3.56, 89.09) #	.03
Anhedonia	26	.50 (42, 110.38) #	.03*
Paranoia	26	3.01 (2.47, 61.63) #	.046*
Mania	26	.499 (2.16, 4.38)	.76
Delirium score	27	9.53 (2.41, 62.60) #	< .001**

Greenhouse-Geisser correction applied, * = $p < .05$, ** = $p < .001$

(c) Length of time elapsed will affect subjective sleepiness

A significant main effect for both a linear and quadratic trend was found for sleepiness (see Figure 10). This suggests that participants reported feeling sleepier as the study progressed and amount of time elapsed increases. A summary can be found in Table 18.

Figure 10 Subjective sleepiness over time

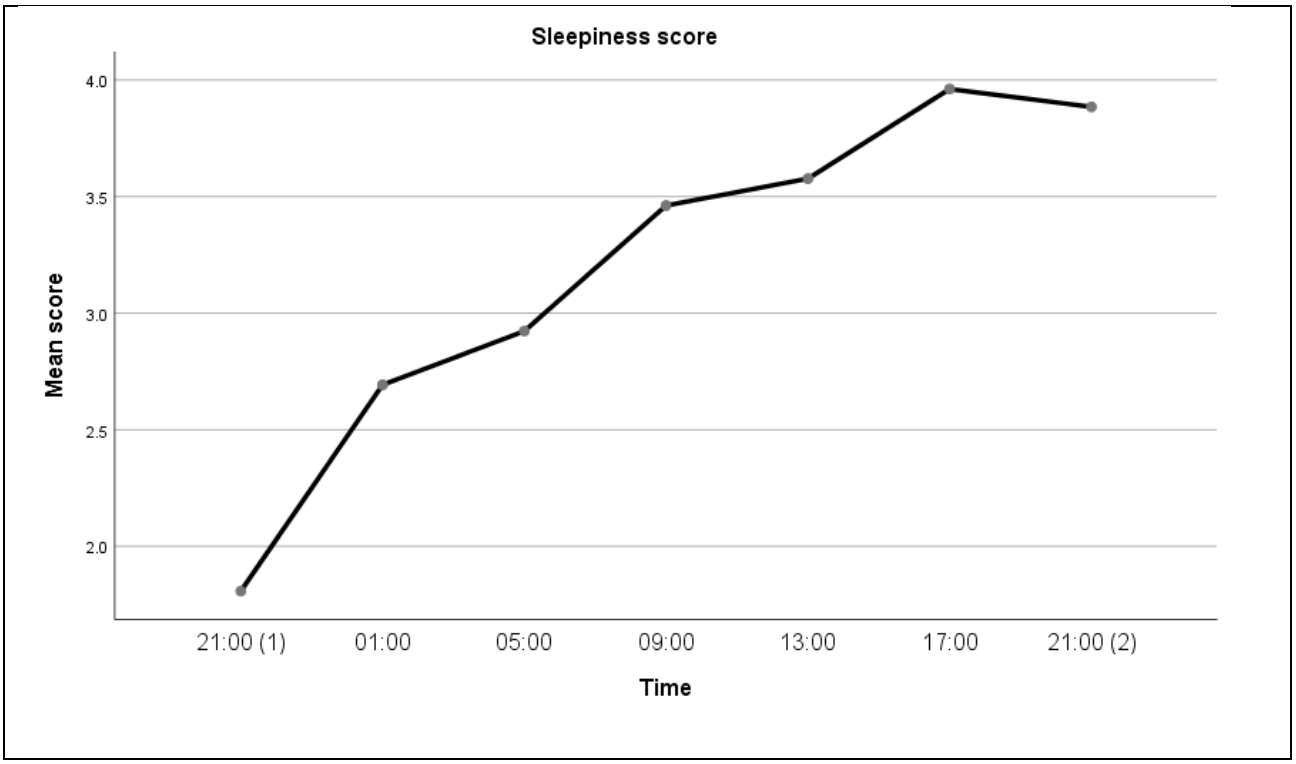


Table 18 Summary of within subject effects from within-subjects ANOVA for H1 (c)

	n	F (df)	*p*
Subjective sleepiness	26	9.88 (3.26, 81.395) [#]	< .001**

[#] Greenhouse-Geisser correction applied, * = $p < .05$, ** = $p < .001$

(d) Length of time elapsed will affect short-term memory

No statistically significant results were found for total recalled sequences, block span or total score.

Table 19 Summary of within subject effects from within-subjects ANOVA for H1 (d)

	n	F (df)	*p*
Visuospatial short-term memory span			
Total recalled sequences	26	1.62 (4.04, 101.005) [#]	.15
Block span	26	1.14 (4.24, 106.00) [#]	.36
Score	26	1.37 (6, 150)	.23

[#] Greenhouse-Geisser correction applied, * = $p < .05$, ** = $p < .001$

(e) Length of time elapsed will affect emotion

A significant main effect with both a linear and quadratic trend was found for positive emotion (see Figure 11). No statistically significant effects were found for negative emotion. These findings suggest positive emotion is affected by sleep propensity. As time elapsed, participants felt increasingly less positive. At 17:00 participants felt at their lowest, with this again increasing at 21:00 (2). These results are summarised in Table 20.

Figure 11 Positive emotion over time

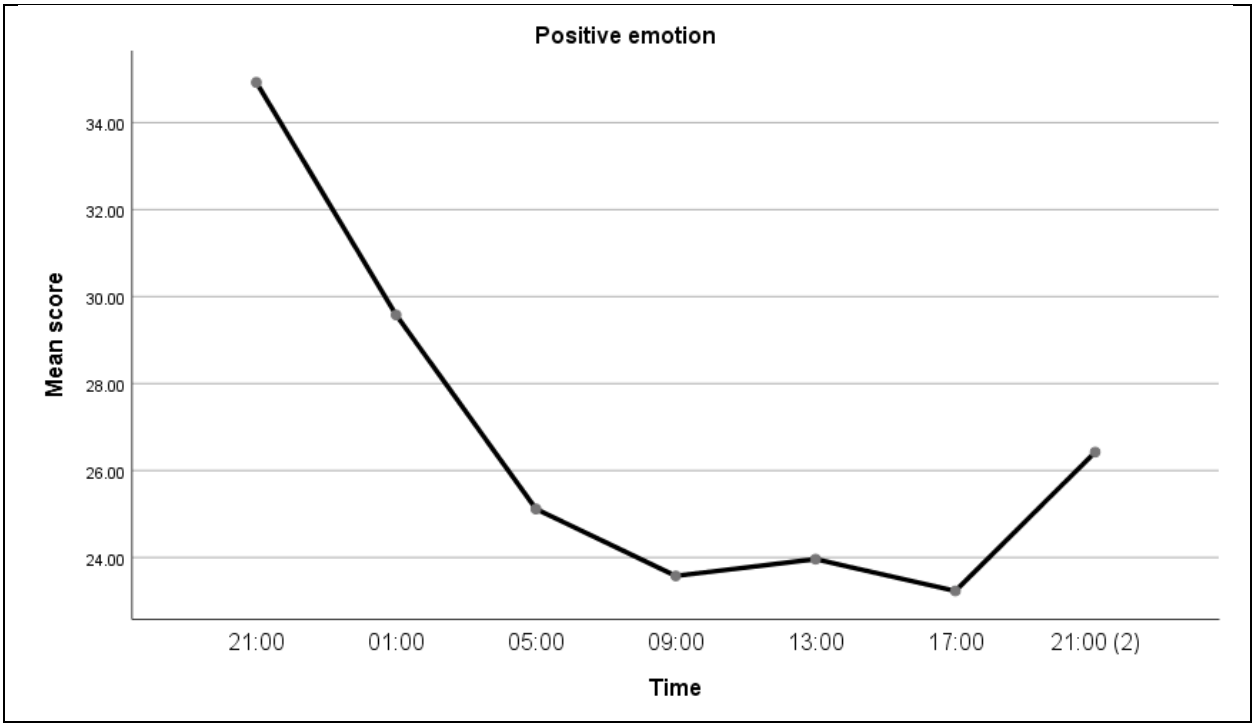


Table 20 Summary of within subject effects from within-subjects ANOVA for H1 (e)

	n	F (df)	*p*
Mood			
Negative emotion	26	1.70 (3.19, 79.71) #	.17
Positive emotion	26	14.46 (3.83, 95.76) #	< .001**

Greenhouse-Geisser correction applied, * = $p < .05$, ** = $p < .001$

Hypothesis 2

Both subjective and objective measures will be impacted as a result of sleep propensity.

(a) Reaction time and intra-trial variability of reaction time will be affected by sleep propensity

Reaction time for successful trials ($M = 25.01$, $p = .048$), valid and correct trials ($M = 27.55$, $p = .39$), estimated standard deviation ($M = 27.84$, $p = .004$) and coefficient of variability ($M = 6.44$, $p = .035$) were statistically significant between periods of sleep and wakefulness. Participants were faster in the four consecutive trials prior to a correct suppression to the digit three and had a faster response time in

correct trials during times they would normally be asleep. Standard deviation and variability in reaction time was greater during periods of wakefulness than periods of normal sleep. This suggests participants were faster at responding correctly to digits that required them to suppress a response, as well as being faster in general, and exhibiting greater variation in their response time during periods of normal wakefulness than sleep. No other statistically significant results were reported.

(b) Psychotic-like symptoms will be affected by sleep propensity

Psychotic-like symptoms were not statistically significant between periods participants should normally be awake compared to when they are asleep. This demonstrates that psychotic-like symptoms were not affected by sleep propensity.

(c) Subjective sleepiness will be affected by sleep propensity

Subjective sleepiness was not statistically significant. Participants felt no sleepier than they would expect to be when awake compared to when they should normally be asleep.

3.7 Discussion

3.7.1 Key results

These results show increasing pressure to sleep that arises from the internal sleep/wake cycle in a sleep deprived state does have an effect on subjective and objective measures of sleep, cognitive functioning and psychotic-like symptoms in healthy adults.

For Hypothesis 1 (a), length of time elapsed did have an effect on reaction time and intra-trial variability of reaction time. This was the case for both the computerised and pen and paper assessments. In the visual attention and task switching task, participants were faster at completing the task as the sleep deprivation paradigm progressed. In the sustained attention assessment, participants were found to make more mistakes through incorrectly suppressing their responses as the length of time elapsed increased. Initially, the results for the visual attention task were not in line with the literature, however, when both the visual attention and sustained attention task performance findings are presented alongside each other, the result can be explained through the speed-accuracy trade-off (SATs). The SATs phenomenon occurs when participants use attentional focusing and switch between the emphasis they place on speed and accuracy, resulting in a deterioration in performance in one over the other, which has been observed in studies involving sleep deprivation (Rinkenauer, Osman, Ulrich, Müller-Gethmann, & Mattes, 2004). Here, participants may have focused on completing the assessments quickly as opposed to correctly, as demonstrated by an increase in speed in the visual

attention and task switching task, and a greater percentage of mistakes in the sustained attention task. This again is in line with the literature as delirium is characterised by a reduced ability to focus, sustain and shift attention (American Psychiatric Association, 2013), as observed here by the impaired performance in both the increase of the number of mistakes made and also slower correct responses.

Additionally, the greater intra-trial variability of reaction time detected using the computerised assessments is in agreement with the literature and furthers our understanding of the relationship between sleep propensity and delirium. An increase in variability of reaction time has been previously observed in a cohort of older adults in the post-operative stage following elective surgery. Participants who exhibited changes to their cognition were not identified to have Sub-Syndromal Delirium (SSD) using a validated delirium assessment, but instead these subtle attentional deficits were detected through the use of computerised assessments. Differences in reaction time, namely the variability of reaction time, as well as global cognitive functioning was observed (Lowery, Wesnes, Brewster, & Ballard, 2010). Similarities can be drawn between the Lowery et al (2010) article and current study. In our study, changes to reaction time and the presence of a lengthening of reaction time are reported in a sample of healthy adults where delirium scores fluctuated across the study duration as participants became sleepier. This suggests our study findings contribute towards our understanding of sleep propensity, and how it may be a contributing factor to the similar attentional deficits observed in patients with SSD.

For Hypothesis 1 (b), psychotic-like symptoms were present and fluctuations occurred over the course of the sleep deprivation paradigm for both psychotic-like symptoms and delirium score. This trend was present for self-reported feelings of delusional thinking, anhedonia, paranoia and most importantly, scores in a validated measure for delirium severity, the Delirium Rating Scale Revised-98. This is in line with the literature, as this change in mental state supports the similarities drawn by Weinhouse et al. (2009) between changes seen in sleep deprivation and delirium. Here, these changes were observed in a sample of otherwise healthy adults, further supporting the important role sleep propensity has on cognitive fluctuations. Additionally, similarities can be drawn between the diagnostic criteria for delirium from the DSM-5 and these findings, in this instance the nature of these changes presented suddenly (across a 24-hour period) and the cognitive disturbances observed were perceptual distortion and cognitive disorganisation.

Changes to feelings of anhedonia, as defined as the inability to feel pleasure in normal pleasurable activities, also showed a fluctuating trend over the course of the study. This observation

further supports another element of delirium which is a shift in mental state, particularly emotion. The participant lounge, despite being able to bring in their own entertainment, was not an exciting environment. This was made more so by the fact participants were staying in the room for long periods of time, except for bathroom breaks and assessments. It was not unusual for participants to feel restless and bored. It is arguably unusual to see a change in the trend for anhedonia beyond the halfway point of the experiment, with participant reportedly feeling less anhedonia, and instead feeling more wanting, liking and motivated from 05:00 hours onwards. However, this change in emotional state may be explained with the feelings of elation participants may have for nearing the end of the study.

For Hypothesis 1 (c), participants reportedly felt increasingly sleepier as the study processed. This peaked at 17:00 with a score corresponding to 'somewhat foggy, let down'. This is in line with what was expected as by this point, participants have spent 20-hours awake during periods of normal sleep and sleep propensity would be high. This also provides support for our novel experimental design in inducing sleep deprivation in a teaching laboratory that has been modified for the purpose of this study. Sleep propensity is known to fluctuate over the 24-hour period, with four features during this: a significant increase at night-time, a post-noon increase, a local minimum in the morning and a local minimum in the early evening (Bes, Jobert, Schulz, 2009). Our results reflect some elements of this trend, with a noticeable increase in self-reported sleepiness during periods of normal sleep, between 21:00 (1) and 01:00, plateaus in feelings of sleepiness between 09:00 and 13:00, and between 17:00 and 21:00 (2). The four features were not more pronounced in our results, which may be a result of the self-report method used. Results from the systematic review which was carried out in parallel to the subsequent chapters of this Thesis suggest that the Karolinska Sleepiness Scale (KSS) (Paavilainen et al., 2005) may have been most appropriate for use in this study instead of the Stanford Sleepiness Scale (SSS).

For Hypothesis 1 (d), length of time elapsed was not found to affect visuospatial short-term memory span. This was an unexpected finding as deficits in performance were anticipated in memory, similar to those that were observed in the visual attention and sustained attention tasks. This was not in line with the literature (Lim & Dinges, 2010), despite the post-hoc power analysis suggesting the sample size was sufficiently large enough to detect any effects present at the $< .05$ significance level. It is not clear why statistically significant changes to short-term memory were not present.

For Hypothesis 1 (e), changes to positive emotion were observed, but not for negative emotion. Changes to mood were expected, and is in line with the literature on sleep deprivation and delirium. As

described previously, sleep deprivation is associated with negative mood (Durmer and Dinges, 2005). it is not clear as to why only positive emotion demonstrated a statistically significant change. The peak in positive emotion observed at 17:00 can potentially be explained through feelings of elation as the end of the study drew closer.

For Hypothesis 2 (a), our results are in line with the Diurnal Dysregulation Hypothesis as reaction time and intra-trial variability was affected by sleep propensity. This theory suggests delirium onset is a result of disruptions to the sleep/wake cycle. Here, changes to attention occurred during periods participants should normally been awake, and not during periods they would normally be asleep. This directional trend was not expected. For Hypothesis 2 (b) and 2 (c), no statistically significant changes in both psychotic-like symptoms and sleepiness between periods when participants should normally be awake and asleep were observed. This was not in line with what was expected as high sleep propensity, which was expected to peak during periods participants should normally be asleep, would be when greatest fluctuations in cognition was expected. These observations may be due to the use of the chronobiology questionnaire, as subjective assessments are at risk of self-report bias. This was used to compare participant responses based on periods of habitual sleep or wakefulness during the 7-study time-points, with the analysis plan categorising participants based on their individual self-reported MEQ typing. It was not difficult to ascertain what each of the multiple choice pre-determined responses to each question corresponded to in regards to how 'morning' or 'evening' someone was. Despite there being no benefit to scoring a particular way, participants may have preferred to be perceived as a certain type of person. Attempts to mitigate this effect, in all of the self-reported questionnaires, were taken into account through reminders to be truthful in responses in the Participant Information Sheet.

Despite introduction of our sleep deprivation paradigm, the circadian rhythm showed a continued profound effect in our sample of healthy adults. This has allowed us the opportunity to explore the effect of sleep propensity on cognitive function, achieving the aim of the study. With these key circadian markers present, and alongside data collected in this study, this suggests that sleep propensity may play a role that replicate those observed in delirium.

Reversible psychotic-like symptoms and emotions similar to those seen in delirium were present, and symptoms that met the DSM-5 criteria within a validated measure for delirium were observed. These fluctuations in performance present alongside changes in sleep propensity highlight the importance of sleep in delirium assessments. When using the Delirium Rating Scale Revised R-98, it can be argued that it is important to also take into consideration an individual's sleep, or lack of, as it is

shown here that sleep propensity does have an effect on delirium scores. It is important to replicate this finding to investigate this potential link further.

3.7.2 Risks and limitations

Risk and limitations which may have impacted on the reliability and validity of the results have been identified and discussed below. These included inconsistency of supervision by the research team, practice effects, retention of participants, changes to the study protocol, and trialling a new experimental design.

Whilst efforts were made for the Principal Investigator (PI) to be present at each time-point, this was not always possible. This is because the wellbeing and safety of the PI needed to be taken into account, and their ability to supervise the study would not have been as effective if they too were also sustaining a period of sleep deprivation and the risk of making human errors would have increased. To account for this, alternative arrangements were made through the recruitment of Research Assistants to support the running of the study. Due to this, there may have been some inconsistency in the way each 4-hour period was supervised. The PI attended as many of the time-points as possible to ensure the different researchers were adhering to the study protocol to a high standard, for which they had received training on. With this in mind some inconsistencies, through human error, may have been present in the administration of assessments and in participant experience across the six laboratory sessions.

An alternative explanation for the discrepancies observed in Hypothesis 1(a) between the results for the visual attention and sustained attention task findings is the presence of learning effects. There were only four versions of Parts A and B, all completed at 7 time-points in total. At one point during the study, participants would have been presented with a previous version they had already completed at an earlier time-point in the study. This explains why participants were faster at the task after the fourth time-point as this is when a previous version would be used. Participants may have remembered the location of the numbers and or letters on the page, having completed it once already at an earlier time during the study. This finding conflicts with the results for reaction time reported in the sustained attention task which found participants reactions time was instead slower as the study progressed.

Additionally, the discrepancy between the data could be due to the differing methods of test administration. The visual attention and task switching assessment was conducted as a pen and paper

assessment, whereas the sustained attention task is computerised. An advantage of the computerised task is that the presentation of the stimuli is pseudo-random, whereas the pen and paper task is not. It is also more sensitive in detecting subtle changes in performance. It is also important to note that the additional versions of the visual attention which were created through flipping the original assessments horizontally and is not a validated method, which may again explain these discrepancies. This may benefit from further research to investigate the length of this practice effect and the number of trials required to eliminate this as a confound may be of benefit.

The incentive of limited financial reimbursement for a study spanning 24 hours, despite advertised as 4 hours of testing and 20 hours of free time, was challenging. Due to the financial constraints of a PhD, the initial reimbursement amount was half of what it was. A condition of the ethics committee to obtain favourable approval was to increase this, resulting in additional funding being sought from a departmental grant. During recruitment, many potential participants expressed interest but were sometimes deterred from ultimately participating due to the lengthened time required. During both study design and meetings with the ethics committee, the concept of running this study without requiring participants to be in attendance was discussed. Ideas had included contacting participants over the phone whilst they completed the study at home with the computerised assessments on their personal computer. However, this was ultimately shelved as there would have been too many variables that would have not been possible to standardise. This includes controlling light levels, consuming set calorific intake or sugary food to stay awake and or even actually ensuring participants did stay awake for the full period of time and were equally sleep deprived. It would have been a challenge to complete the observational nature of some of the assessments in addition to the pen and paper reaction time tasks. An acknowledged risk was taken by choosing to run this study by having participants physically in attendance for the full 24-hour period.

Both the limited and financial elements of this study became a risk for participation retention. In most laboratory sessions, participants usually signed up as part of a group of friends requesting the same laboratory session and therefore knew someone else also taking part concurrently. There were instances where participants encouraged others to withdraw from the experiment to benefit from the financial gain without taking part for the full duration. This was due to the original understanding provided through the PIS that withdrawing early would not affect the amount of compensation for their time. This was identified as a risk during one of the sessions which would potentially compromise the experiment if many withdrew. In one laboratory session a participant encouraged their friend to

withdraw in their native language, unaware that a member of the research team on shift happened to also be fluent in Spanish and uncovering their scheme of financial gain irrespective of the research study. In total five participants were withdrawn with four of these under their own accord. As previously mentioned, the fifth participant fell asleep during the study, and was excluded from further participation. The reason for the four participants' withdrawals were not disclosed.

A seminar room was re-designed to simulate adequate laboratory conditions. This was a novel method to conduct this experiment and came with its challenges. Despite attempting to monitor light levels in inside the laboratory, artificial light remained much brighter than the external environment and would have been of levels that suppressed melatonin. This could explain the discrepancies as observed in subjective sleepiness between normal periods of wakefulness and sleep, particularly if melatonin secretion is being suppressed during periods of sleep due to light.

It is also important to note that the study deviated from the initial protocol. It was initially proposed that actigraphy would be used alongside the Morningness-Evening Questionnaire (MEQ) and study adherence questionnaire to more precisely characterise each participants' sleep/wake cycle, and whether they had adherence to the study guidelines in the run up to the experiment. As discussed previously, due to the limited availability of actigraphy monitors, these resources were allocated to the clinical study as data collection had commenced faster than initially anticipated. Reliance was placed on a study adherence questionnaire which was not validated for use, it is not possible to ensure that it did measure what it was intended to. It may not have effectively captured information on whether participants did or did not consume alcohol, caffeine, chocolate or nap in the 24 hour and or 7-day period prior to the laboratory phase. Responses that were not captured by our bespoke questionnaire may have implied that our data on the number of participants who did, or did not, adhere to the guidelines is not accurate. A different number of participants may have disrupted sleep/wake cycles, subsequently affecting their sleep propensity for the duration of our 24-hour experiment and the data that was collected.

There were challenges associated with the novel experimental design which was attempted. Nonetheless this experiment provides a platform for further research into the relationship between sleep propensity and its impact on cognition. This novel sleep deprivation paradigm, whilst collecting data on levels of functioning throughout a 24-hour period in a repurposed seminar room, was an effective method of investigation in a healthy adult population.

3.8 Chapter summary

This Chapter utilised a sleep deprivation paradigm to investigate the effects of sleep propensity on cognition. The increasing pressure to sleep was found to induce reversible changes in a non-clinical population to sustained attention, visual attention, psychotic-like symptoms, and most importantly, delirium, as measured using the Delirium Rating Scale Revised R-98, an extensively used validated measure for delirium.

Changes to reaction time and visual attention were present as participants experienced higher sleep propensity. There were some discrepancies in the observed results between the two measures used to assess mean reaction time. This finding is important as the computerised task detected statistically significant trends in the variability of reaction time, which supports a previous study identifying a similar trend in performance in a clinical population with sub-syndromal delirium. Additionally, the presence of and fluctuations in sustained attention, feelings of delusional thinking, anhedonia, paranoia and even delirium scores, which again draws similarities with the DSM-5 definition of delirium and also supports the Diurnal Dysregulation Hypothesis. These measures are accessible, quick and easy to administer, allowing for the detection of acute changes in cognitive functioning, and provides a novel and alternative perspective on delirium assessment.

Older adults admitted to hospital for elective surgical procedures are at a higher risk of delirium according to the Multifactorial Model for delirium (Inouye et al., 1996) due to the predisposing factors, some of which include old age and length of hospitalisation (Ahmed, Leurent, & Sampson, 2014). These individuals admitted into hospital for their post-operative care are likely to experience much greater disruption to their sleep/wake cycle over the course of multiple days, than the 24-hours participants in our study experienced. We observed cognitive deficits appearing relatively quickly following several hours of disruptions to the sleep/wake cycle in our relatively young, healthy adult sample without predisposing factors. Disruptions to sleep in the hospital environment is a common complaint, alongside a reduction in the quality of sleep that is achieved (Gellerstedt, Medin, & Karlsson, 2014). This in turn highlights the importance of further exploring the modifiable factor of sleep disruption to reduce delirium risk, particularly in a population at a greater risk of developing delirium (Weinhouse et al., 2009).

This study provided the opportunity to become more familiar with the various assessments which are used in the Clinical study described in Chapter 4. I was able to gain experience in administering, scoring and interpreting the standardised assessments in the context of an ongoing

experiment, having previously not used these assessments before in previous studies outside of this PhD. It was important to avoid unnecessary disruptions due to this as a significant proportion of time and resources was invested in the clinical study.

There is scope for a follow-on study to further investigate the effect of sleep propensity, and whether it has similar effects on cognitive functioning when reversed. The effect of this 'reversed' sleep propensity (an increased pressure to sleep during periods of normal wakefulness) is an interesting area to explore as excessive daytime sleepiness is one of the frequent complaints of ICU patients (Meissner et al., 1998). Additionally, the complete reversal of the sleep/wake cycle is a symptom of delirium, albeit one of the more extreme. It is important to find out if reversed sleep propensity would also exhibit similar patterns of cognitive deficits associated with delirium.

Chapter 4: The Role of Sleep as a Predictive and Precipitating Factor for Delirium in the Hospitalised Older Adult Population

4.1 Introduction

This observational study was designed and carried out in parallel to the systematic review and experimental study previously discussed in this thesis. This study examines sleep disruption within a clinical population to explore the relationship between pre- and post-operative sleep and delirium, where the pre-operative baseline for sleep quality is taken at home.

4.1.1 Background/rationale

Previous research has suggested a relationship between sleep disruption and post-operative delirium. Todd et al (2017) assessed sleep disruption, both at home and in the hospital, as a risk factor for the development of post-operative delirium. This research collected sleep data at specific time-points and using a variety of subjective and objective methods. Prior to hospital admission, a subjective (self-report) measure of sleep, the Pittsburgh Sleep Quality Index (PSQI), was completed by participants at home. Actigraphy monitors collected objective measure of sleep in the hospital prior to and after surgery. PSQI and actigraphy data was compared. Findings suggested that participants who experienced greater sleep disruption at home were 3.26 times more likely to experience post-operative delirium compared to those who did not. Additionally, those who experienced sleep disruption in the hospital, were 1.21 more likely to experience delirium. This is compared to those who did not experience disrupted sleep (Todd et al., 2017). Sleep disruption in this study was quantified in terms of changes in Wake After Sleep Onset (WASO, %). It was concluded that sleep disruption at home was a significant risk factor for developing post-operative delirium with disruptions experienced in the hospital further increasing this risk.

While evidence from this study is compelling, a limitation of this paper is the lack of objective sleep data at home prior to hospitalisation. In Todd et al (2017), baseline actigraphy data was obtained only for pre-surgery in the hospital. Comparisons were made between a self-report subjective method for the pre-surgical period and an objective measure for post-surgery. The absence of an objective, baseline measure, instead relying on a subjective tool alone may not be as effective in obtaining an accurate representation of an individual's average night's sleep. It is suggested that actigraphy collected at home, in a familiar environment such as a participant's home, would be a more effective measure of habitual sleep.

The aim of the present study is to provide further insight into the potential application of actigraphy devices to objectively measure sleep in clinical environments. As mentioned in the systematic review in Chapter 2, there is evidence to suggest that objective measures of sleep have greater sensitivity and specificity and are therefore advantageous over some subjective measures of sleep which are commonly used in clinical settings. This is coupled with the key features of actigraphy, being a pragmatic and practical method of objectively measuring sleep, as discussed in Chapter 1.7, may be an appropriate method to use in busy clinical environments.

A limitation of Todd et al., study is that actigraphy data was not collected at home prior to hospitalisation. To provide a more accurate representation of sleep, the present study bridges this gap in the literature by collecting actigraphy data both at home prior to hospitalisation and in hospital during hospitalisation. Comparisons can therefore be made regarding sleep quality due to the experiences of elective surgical procedures as well as changes in environment. By having a more accurate measure of the various aspects of sleep (e.g., sleep latency, total sleep time, number and frequency of awakenings and sleep efficiency), a more comprehensive understanding of the underlying factors which may contribute to delirium in sleep can be obtained.

4.2 Research Objectives

4.1.1 Research Aims

This study explored the relationship between sleep behaviour and the emergence of delirious episodes. This is with the hope to further understand the underlying mechanisms of delirium and how sleep, as well as circadian rhythms, can be incorporated into our current understanding of delirium. The study aimed to answer the following research questions:

1. Is 'poorer' sleep at home, prior to surgery associated with an increased risk of delirium?
2. Is 'poorer' sleep after surgery associated with an increased risk of delirium?
3. How does the combination of poor sleep and delirium affect clinical outcomes?

4.1.2 Hypotheses

It was hypothesised that:

1) 'Poorer sleep' at home, **prior to surgery**, will be associated with an increased risk of delirium
2) 'Poorer sleep', in the **post-surgical period** following a stay in hospital, will be associated with an increased risk of delirium

4.2 Methods

4.2.1 Study design and setting

This was an observational study utilising a prospective, longitudinal cohort design, with elements modelled on a previous study by Todd et al. (2017). Participants were recruited from one hospital in East Kent and were scheduled to receive elective total hip or knee replacement surgery (Total Knee Arthroplasty (TKA) or Total Hip Arthroplasty (THA)). Participants were admitted to one of two wards for their post-operative care. Data collection took place between February 2017 and October 2018 for a total of 20 months. Participants were followed from pre-surgery (no more than 3 weeks before) through to 12 weeks' post-surgery. The total time was 15 weeks.

The possibility of including an additional site was later explored as challenges in recruitment were encountered. Following a non-substantial amendment, a second, East Kent NHS site was included which the project supervisor, who is a clinician within the NHS, had a pre-existing working relationship with. However, due to the limited resources available of a PhD study, no participants were subsequently recruited from this second site. It was not possible for the Principal Investigator to attend the pre-admission clinics for both sites as these often ran concurrently and travel between the two sites was not feasible due to the long commute.

Potential risks and burdens were identified in the design of the study and raised in the Research Ethics Committee (REC) review, with steps to minimise these as much as possible discussed. Due to the longitudinal nature, the study can cause inconvenience and intrusions to participants' daily living as two home visits are required. Home visits are essential for the study to ensure data is collected at specific time points. To reduce burden on participants, the Principal Investigator ensured that the agreed time for both home visits was mutually convenient between both parties, with details of this included in the Participant Information Sheet. Participants were reminded that they can pause an assessment should they become tired or distressed as they are participating on a voluntary basis.

Participant's healthcare remained unaffected by the research study and there was no change of relationship with their healthcare professional. The participant was reminded of this verbally and in writing via the Participant Information Sheet. Where any incidental findings suggested participants may be experiencing important conditions that may affect their health (e.g., sleep disorders or cognitive impairments), the Principal Investigator informed the person verbally and in writing. Participants were then advised that they may benefit from further investigation by their GP and or consultant surgeon,

and that screening data can be released, with permission, to assist the appropriate medical professional in their investigation.

The risk of breaching confidentiality was low as participants were identified with a unique identifier code at the point of providing consent. Data was processed and encrypted via a password protected PC which is maintained in accordance with the Government Cyber Security Essentials guidelines. PCs and laptops used adhered to the University's security specifications with up-to-date anti-virus software. The rooms within which the PC and equipment are stored are locked and secured. The University network is regulated by its IT Security Policy and backups are taken daily and stored off site for 3 months. Additionally, the Principal Investigator's university electronic files will be deleted once they leave the university.

It was extremely unlikely that any serious adverse events occurred as a result of research procedures as it was an observational study. An adverse event (AE) was defined as any unfavourable and unintended sign, symptom, syndrome or illness that develops or worsens during the period of observation. Risks were not anticipated in this study due to the observational nature of the design; however, risk management strategies were put in place. The management and design of this research project was sponsored and indemnified by the University of Kent and covered participants in the event of negligent harm. The conduct of the study was covered by the NHS indemnity scheme as participants were recruited from an NHS site, therefore their indemnity will apply. The full protocol for managing risks and adverse events in this study can be seen in Appendix C.1.

After surgery, participants were admitted as inpatients at the hospital to one of three wards with varied layouts. Wards were either of multiple (of up to six beds per room) or single occupancy and it was not possible to control for this. Data on ward accommodation locations was recorded and reported as part of the analysis. Figures 12 (a - c) illustrates the varying layout of each of the three wards and two room types.

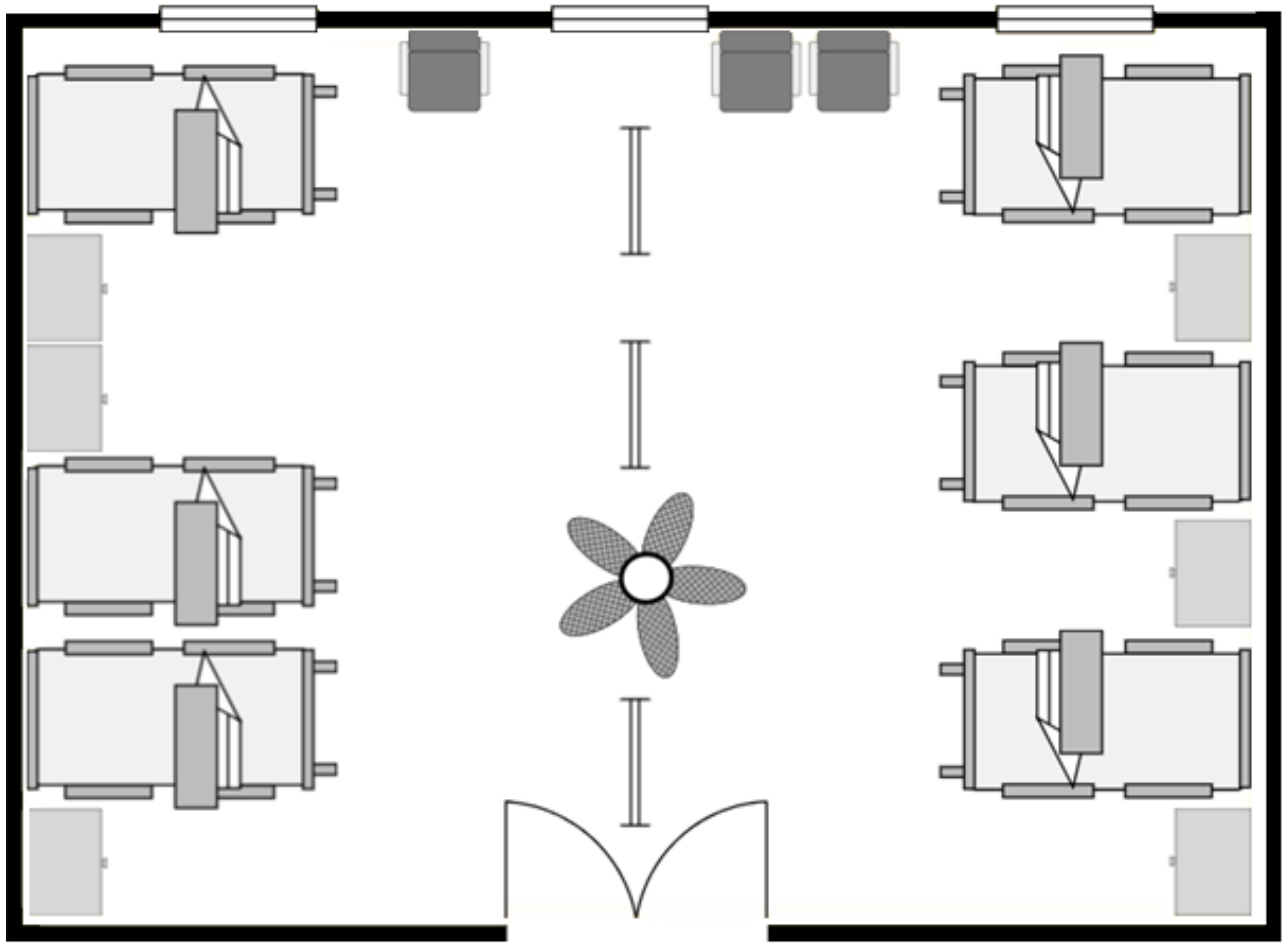
The stopping rule was put in place if, and once 104 participants, had been recruited and all home visit arrangements have been agreed upon between the participants and the research team. Participants who had expressed interest in participating following receipt of the Participant Information Sheet were sent a letter thanking them for their interest as well as notifying them that recruitment has closed for this particular study (see Appendix C.3). This letter explained there may be additional

possibilities to participate in a second, follow-up study in the future, following the outcome of this initial study.

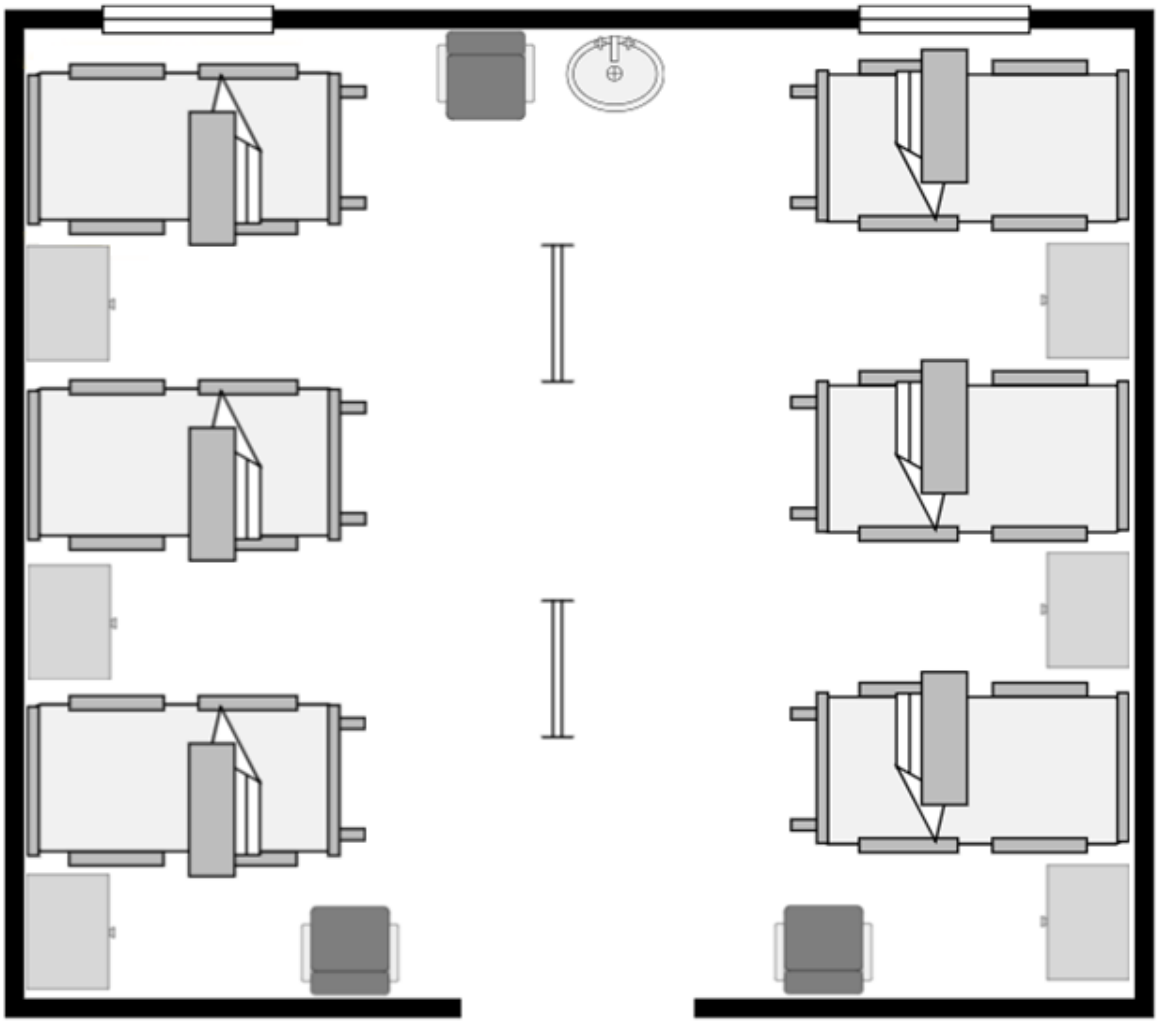
Figure 12 a-c

Floor plan of each ward type: (a) Bishopstone Ward (multiple occupancy), (b) QUEX Ward (multiple occupancy), and (c) QUEX, Bishopstone and Spencer Wing room (single occupancy)

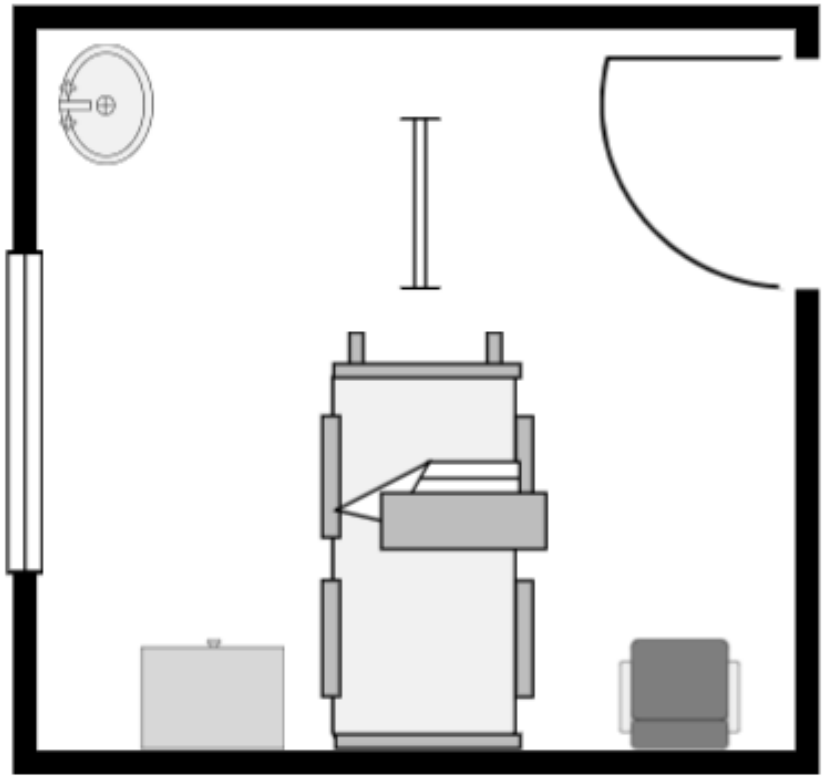
a.



b.



c.



4.2.2 Ethics approval

The study was submitted via the Integrated Research Application System (IRAS) (IRAS Project ID: 197701) on the 16th June 2016 with the subsequent study application booked for HRA approval – assessment and full REC review on 18th August 2016. A Favourable Opinion Letter was obtained on the 28th September 2016 and following clarifications of questions raised at the meeting, Health Research Authority (HRA) Approval was obtained on the 4th October 2016. The Confirmation of Capacity and Capability (R&D Reference 2016/NEURO/09) at East Kent Hospitals University NHS Foundation Trust (EKHUFT) was issued on 31st October 2016 and EKHUFT issued a Letter of Access on the 1st December 2016. Following favourable approval, four amendments (one substantial and three non-substantial) were submitted and approved. These can be found in Appendix C.4.

4.2.3 Participants and recruitment

4.2.3.1 Key considerations for research with clinical populations

The Declaration of Helsinki (World Medical Association, 2013) outlines the ethical principles for research involving human subjects. The UK Policy Framework for Health and Social Care Research outlines the principles of good practice in the management and conduct of health and social care research in the United Kingdom (Health Research Authority, 2017). These guidelines are important as they act as a series of safeguards to protect those who participate in research. The principles that apply to all research include:

1. **Safety** – where the safety and wellbeing of participants are prioritised over science and society.
2. **Competence** – those involved with the implementation of the research are qualified with relevant education, training and experience, or if they are not, are supervised by someone who is suitably qualified.
3. **Scientific and ethical conduct** – ensuring there is sufficient support for the research rationale and that it meets ethical guidelines.
4. **Patient, service user, and public involvement** - are embedded in the design, management, conduct and dissemination.
5. **Integrity, quality, and transparency** – in all aspects of the research.
6. **Protocol** – the research is described in full, with elements of the design and procedure justified.
7. **Legality** - relevant legislation is adhered to and the researchers are familiar with guidance relating to the management and conduct of research.

8. **Benefits and risks** - any potential health or care benefits to the participant directly as a result of taking part is balanced against mitigated risks or inconveniences.
9. **Approval** – obtaining favourable approval from a research ethics committee is required for the project to start.
10. **Information about the research –** is made publicly available.
11. **Accessible findings** – regardless if the results were positive or negative, ensuring they are available following study completion.
12. **Choice** – respecting participants and their capacity to understand the research, and ensuring participants are given relevant information to make an informed decision on their participation.
13. **Insurance and indemnity** – provisions are made for insurance and indemnity to cover liabilities resulting from the research.
14. **Respect for privacy** – ensuring the information collected is recorded, handled and stored appropriately, over a time period that is allows for it to be accurately reported, interpreted and verified, maintaining confidentiality.
15. **Compliance** – with sanctions for non-compliance to the above principles.

Additional principles are in place for studies involving interventions. This is where there is a change in treatment, care or other services provided to the participant as a result of the research. Principles include: justification where this change is supported by evidence, the provision of treatment is ongoing with any changes that remain following the intervention period properly explained to the participant, a record of care is kept with all information about the intervention treatment recorded, handled and stored so others who may be involved in the participant's care in the future can use these, and finally a duty of care where a relevant professional retains responsibility for the participant's treatment, care or services provided to them (and for decisions made around this).

The role of the Research Ethics Committees is to review research proposals to assess whether it meets the above ethical principles. This review process is underpinned by the Governance Arrangement for NHS Research Ethics Committees (Health Research Authority, 2020), which specifies its function and when a REC review is required. Committees are independent to the researchers submitting the application and are made up of a group of both expert and lay members, each of whom have specific knowledge to help the committee understand certain areas of the proposed research.

For this research project, a full REC review was required as it involved recruitment from a health department in the UK, here we recruited from NHS services.

As previously discussed in Chapter 1, old age is one of several predisposing factors associated with an increased risk of developing delirium. For the purpose of this study which focuses on the emergence of delirious episodes, it was pragmatic to recruit from an elective surgical population that were otherwise healthy and over the age of 70. This population is often selected in observational studies as participants are otherwise healthy. The primary purpose of their stay in hospital is to undergo an elective procedure, which they would have had to be assessed prior to admission to be fit enough to undergo surgery and therefore free from significant underlying health conditions and co-morbidities. They can be assessed prior to the occurrence of any delirious episode, whilst providing a reasonable opportunity to observe individuals experience this acute condition. As discussed, participants were required to nominate a consultee to act on their behalf if, during the course of participating in the study, they were found to have lost the capacity to consent. These participants were under secondary care following a referral from their General Practitioner and hospitalised for their surgical procedure in the care of specialist teams.

Based on local research study site NHS Trust Data, there were 747 total hip and knee operations in patients over the age of 70 between April and December 2015 in one NHS site. It was therefore anticipated there would be a sufficient pool of potential participants to recruit from. Based on a systematic review of 42 cohorts in 40 studies, the prevalence of delirium was 10 – 31% at admission, the incidence of new delirium per admission 3 – 29%, and, an occurrence rate per admission to be between 11 – 42%, where occurrence rate refers to studies which do not clearly specify between incidence or prevalence in assessments (Siddiqi, House, & Holmes, 2006). A recent systematic review by Serafim et al. (2017) that included six studies measuring subclinical delirium in ICU patients identified 2630 participants. Subsyndromal delirium (SSD) in this sample was identified in 36% of participants. Using this, it was estimated that within the proposed study sample size, 10 - 31 participants may experience delirium at admission and a further 3 - 29 may develop delirium during their hospital admission. Potentially up to 42 participants may experience delirium at any point during the study with 36 experiencing SSD.

Eligible for inclusion in the study were people:

- Over the age of 70 years or over at screening
- Scheduled to undergo total elective hip or knee replacement surgery
- Have the capacity to consent to the study at the start of their participation
- Have provided informed consent

Exclusion criteria was determined at the pre-admission clinic where there was the opportunity to discuss the study further with the researcher in the waiting room area. It is routine for patients scheduled for elective surgery to be invited to attend a pre-admission clinic. This is prior to surgery where patients meet the team of staff responsible for their care. This hospital visit often takes several hours to ensure patients have understood the procedure, are assessed for their fitness for the procedure, and that their records are up-to-date.

The exclusion criteria included:

- **Not neurologically healthy** (as defined as self-reported Parkinson's, traumatic brain injury and a positive score of > 18 on the Beck Depression Inventory) – to generalise the findings of this study to predict outcomes in healthy populations, it was necessary to exclude these individuals. Conditions included (and were not limited to): dementia, depression, Parkinson's, a history of TBI and or pre-existing delirium. Dementia is associated with pre-existing impaired cognition and could therefore independently affect cognitive functioning and sleep. Depression is known to impact cognition, sleep as well as a symptom of delirium. Those with Parkinson's syndrome often have cognitive deficits which progress over time and include fluctuations in cognition (e.g. memory, attention, executive function) due to the neurodegenerative aspect of the disorder (Alzahrani & Venneri, 2015). The above helps to optimise internal validity by reducing the likelihood that confounds are present.
- **Lacking the capacity to consent at the start of their participation** – this is in line with the 2005 Mental Capacity Act (MCA) (National Health Service, 2018). A core feature of the MCA is only to include individuals who lack capacity in research if their absence would make the research less effective. Here, their participation was not imperative to this study and therefore not recruited. Conditions include (but are not limited to) individuals who have; dementia, a learning disability, brain injury, a mental health condition, a stroke, are unconscious due to anaesthetic or accident or delirium. Capacity was also judged through interactions with the individual. The Researcher observed for any indicators for impairments affecting their ability to think and if this affects their ability in understanding the nature and timing of the decision.
- **Anatomy, condition or other required monitoring (including allergies to polycarbonate and impaired senses) precludes the use of wearable sleep monitoring equipment and or their ability to complete the assessments** – it is important to note that these allergic reactions are rare (Bruze et al., 1988). In instances where participants were unable to wear the device on their

non-dominant wrist, alterative locations including their dominant wrist and on the ankle were suggested and adapted for their comfort.

- **Non-English speakers** – due to the limited resources associated with a PhD, it was not possible to accommodate testing in alternative languages other than English.
- **Hip or knee revision surgery** – revision procedures are often more complex than a replacement as the artificial joint would need to be removed first. It is also not uncommon for some of the bone to require reconstruction. These additional steps would significantly add to surgery duration making revision and replacement procedures unsuitable to group together.
- **Considered inappropriate to approach by the clinical care team** – this was verbally communicated to the research team privately on the day by the pre-assessment team.

The study aimed to recruit a sample of 100 participants and complete final follow-up within 12-months. To aid in recruitment, two additional Research Assistants (Abigail Renick (AR) and Elizabeth Smith (ES)), were recruited to support the study and facilitated participant screening between May 2018 – July 2018. AR and ES were fully trained prior to attending pre-assessment clinics. Due to equipment and personnel resource constraints, no more than 24 participants were able to be recruited concurrently.

4.2.4 Informed consent

The research team liaised with the Booking Team who were responsible for the patient appointment process. The Booking Team were responsible for posting the pre-study information (Participant Information Sheet and Accompanying Letter) alongside the patient's written correspondence, ahead of the patient's scheduled pre-assessment appointment. To identify potential participants, an initial sift using the inclusion and exclusion criteria provided by the Principal Investigator, was carried out by the Booking Team. It was agreed this material would be sent prior to the appointment (up to 2 weeks in advance) to allow prospective participants sufficient time to consider taking part in the study. As not all patients who utilised the services in the clinic were eligible for the study, it was not appropriate for the Principal Investigator to distribute the relevant pre-study information personally. This is in line with the NHS Confidentiality Policy whereby confidential personal data should only be disclosed to appropriate individuals (Corporate Information Governance, 2019). No one outside of the direct clinical care team were involved in the reviewing or screening of identifiable personal information.

Interested individuals were identified by the pre-admission team who, on arrival, were asked verbally if they had received the pre-study information and if they were interested in participating. Where there was a deviation to the protocol and patients stated they did not receive the pre-study information and were interested in participating, they were directed to a member of the Research team in the waiting area who provided the interested individual with a hard copy of the pre-study information. The project was explained verbally and if interested, it was agreed with the individual that the Research team would contact them at a later date. This was to allow for a sufficient opportunity to read through the pre-study materials and to collate any questions they have from themselves and or their family members before providing a decision regarding their participation. Contact was made by phone and one attempt was made.

It is not known why some patients did not receive the study information by post and this should have been enclosed alongside their pre-assessment appointment clinic letter. Only patients who stated they were interested were approached by the research team regardless of whether the individual stated they had received the pre-study information or not.

All participants were aware of why they were invited to take part as well as the purpose of the study and had adequate time to ask any questions. Those who expressed an interest but requested for additional time to consider participating were also granted this. Prior to obtaining informed consent, the capacity to consent was assessed by a member of the research team alongside the opinion of (where available) a member of the clinical team. Those who were found not to have the capacity were not screened or recruited into the study.

This study focused on a condition, which has a core clinical feature of a sudden change in mental state and cognitive functioning. Participants may lose the capacity to provide ongoing consent whilst enrolled in the study. This is likely to be a temporary period lasting minutes, and sometimes hours. Research of equal effectiveness could not be carried out if confined to participants with capacity. It is highly unlikely that participants will experience episodes of diminished capacity after their discharge from hospital. Mitigation of this risk was discussed in depth at the REC review, with the introduction of a nominated consultee proposed, which is in line with the Mental Capacity Act (2005).

At the point of providing consent, the participant was requested to nominate someone to act as a consultee in the event that they lost the capacity to consent. This nominated individual could be their spouse, a relative or a friend. If the nominated consultee was found to be required to act on behalf of

the participant, they were contacted and provided with a separate Consultee Information Sheet (CIS) and a Record of Consultation Form (RoC) (see Appendix C.3) to complete. This form required the nominee to confirm that they had read and understood the CIS and had the opportunity to consider the information, ask questions (as well as have these answered satisfactorily) and to give their advice on behalf of the participant. Space was provided on the form to express the Consultee's views on the participant continuing their participation of the study (in that point in time) and what they viewed the participant's wishes and feelings about the research would likely be. Consultee views were actioned on for that specific occasion either as continuing to attempt to obtain data or as ceasing data collection at that time-point. This is in line with the recommendations provided by the HRA full REC review.

Three signed copies of informed consent forms were completed; one to be kept by the participant, one to be placed in the participant's medical notes and the original to be kept in a locked room with other researchers. Only named researchers had access. The original was kept securely and separate from other data to ensure anonymity is preserved.

4.2.5 Materials

When the Thesis timeline was mapped out, it was clear that this clinical study needed to be prioritised over other Chapters to ensure it would be completed within the set timeframe of a PhD. It was anticipated that obtaining NHS ethical approval, and, once the study recruitment had started, data collection would require a considerable period of time to complete. This study was therefore the first of the three studies described in this Thesis that was conducted. Due to these timeline constraints, it was not possible to apply the findings from the systematic review described in Chapter 2 into the design of this study. The limitations of this are discussed later in this Chapter.

4.2.5.1 Recruitment and screening

- **Accompanying letter** - provided alongside the Participant Information Sheet, inviting prospective participants to take part in the study. It thanked the reader for their initial interest and briefly outlined the purpose of the study and provided contact information for additional enquiries.
- **Participant Information Sheet –** contained a detailed explanation of what taking part in the study would involve in lay language and images of the actigraphy device to illustrate its use. There was also an explanation of the use of consultees (where required) to reassure participants this had been taken into consideration.
- **Informed Consent Form**

4.2.5.2 Researcher record keeping aids

- **Clinical Record form** – to keep a record of participant study involvement. Each phase of the study protocol was dated and signed by a member of the research team on completion. Explanations were provided for any omissions (e.g., assessment declined by participant).
- **Case notes template** – a standardised data extraction form to collect relevant medical information. The project supervisor, Professor Chris Farmer holds both a clinical role within the NHS, as well as an academic role at the University of Kent, assisted in completing this by accessing data via the Opera Theatre Management System and pathology reports as per ethical approval. This included psychotropic medical use, changes of medication, initiation of new medication, discontinuation of current prescriptions alongside reasons to why this was done as well as adherence to prescribed medication and use of 'as required' medication will be recorded. This attempted to control for possible confounds in cognitive and behavioural tests due to medications.

4.2.5.3 Resources for nominated consultees in instances of a participant losing the capacity to consent

- **Consultee Information Sheet (CIS)** – Provided to the participant's nominated Consultee only in instances where it was judged that the participant had lost the capacity to consent. The Consultee may not have been previously aware of the study and their participation. This information contains an overview of their role and the purpose of the study.
- **Record of Consultation Form (RoC)** – for the nominated Consultee to sign confirming they had read and understood the CIS, and to record the advice they provide on behalf of the participant.

4.2.5.4 Cognitive function

This was measured using the Mini Mental State Examination (MMSE). Orientation, registration, attention and calculation, recall and language is assessed (Folstein, Folstein, & McHugh, 1975) using this quick to administer (5 – 10 minutes) 30-point questionnaire. The maximum score is 30, with scores between 21 to 24 suggesting mild impairment, 10 – 20 indicate moderate impairment and < 10 as severe. A recent systematic review and meta-analysis estimated the MMSE to have a sensitivity of 84.1% (95% CI= 75.8 – 90.9%) and a specificity of 73.0% (95% CI= 59.6 – 84.5%) (Mitchell, Shukla, Ajumal, Stubbs, & Tahir, 2014). In the context of this Thesis, the MMSE was used as a screening tool and as a benchmark for global cognitive function.

4.2.5.5 Objective sleep measures

- **Actigraphy monitors** – are validated and recommended for use in assessing sleep behaviour for research purposes in the older adult population in the community (Ancoli-Israel, Clopton, Klauber, Fell, & Mason, 1997; Morgenthaler et al., 2007). Actigraphy is a reliable measure of sleep in healthy adult populations (Littner et al., 2003). In this project, 13 wGT3X-BT devices were used. They are water resistant and can be immersed in up to 1 meter of water for a maximum of 30 minutes. These devices were worn on the wrist of the non-dominant hand where possible. There were some instances of this not being the case in due to pre-existing medical conditions such as arthritis and was worn on an alternate limb. Variations in worn location were reported. Actigraphy monitors were used over a 3-day period on two occasions and supplemented with sleep diaries. Actigraphy measures used are summarised in Table 21.

Table 21 Summary of Actigraphy measures

	Measurement scale	Definition
Sleep latency	Minutes (m)	Time taken for sleep onset[1]
Total counts	Count	Level of activity[1]
Sleep efficiency (SE)	Percentage (%)	Total sleep time divided by the total number of minutes in bed[1]
Total minutes in bed	Minutes (m)	Total amount of time spent in bed[1]
Total Sleep Time (TST)	Minutes (m)	Total amount of time spent asleep[1]
Wake After Sleep Onset (WASO)	Minutes (m)	Total amount of time spent awake after sleep onset[1]
Number of Awakenings (NOA)	Count	The number of different awakening episodes[1]

Average Awakening Length	Minutes (m)	Average time spent awake of all episodes[1]
Movement index (MI)	Events/hr	Total number of limb motions (the non-dominant wrist) divided by total time spent in bed[1]
Fragmentation index (FI)	Events/hr	Amount of interruption due to physical movement[1]
Sleep fragmentation index (SFI)	Events/hr	Amount of interruption to sleep due to physical movement[1]

[1] (as defined by the Cole-Kripke algorithm)

- **Sleep diary** - Actigraphy was supplemented with a sleep diary completed by the participant. The diary was on a double-sided landscape A4 page consisting of a table outlining the requested information for the study. There was one row filled in grey completed with example data to help the participant complete the relevant fields. This was used to compare, complete and correct sleep/wake periods recorded by the actigraphy devices. This was used to identify episodes that were either interpreted or not interpreted as sleep, including afternoon naps or sitting still in a chair reading (see Chapter 1.7).

4.2.5.6 Level of functional ability

Was measured using the Functional Independence Measure (FIM) and Functional Assessment Measure (FAM), a global disability outcome used frequently in clinical settings. It includes elements of physical disability as well as cognitive and psychosocial issues (Turner-Stokes, Nyein, Turner-Stokes, & Gtehouse, 1999). The individual is observed and is given a score for each of the 30-items, on a 7-point Likert scale (1 = *total dependence,* 7 = *total independence*). Lower scores on the FIM + FAM suggest impaired functioning. It takes 30 minutes to score. Test re-test reliability was found to be excellent, ranging from 0.92 to 1.00 in individual rehabilitation professionals and 0.89 to 0.99 in multidisciplinary teams (Law, Fielding, Jackson, & Turner-Stokes, 2008).

4.2.5.7 Fitness and Frailty level

The Clinical Frailty Scale (CFS) is a measure of clinical global level of fitness and frailty in older adults (Rockwood et al., 2005). Scoring is on a 7-point scale (1 = *Very fit*, 7 = *Severely frail*). The CFS is

highly correlated with other validated measures of frailty such as the Frailty index (r = 0.80, $p < .001$) and demonstrates high construct validity (Rockwood et al., 2005). It is quick and easy to administer and only takes 5-minutes to score.

Measures listed below were also used in this study and are briefly summarised, having been previously discussed in Chapter 3.3.4.

- Sustained attention
- Visual attention and task switching
- Depression
- Sleep disorders
- Delirium

4.3 Study Endpoints and Participant Withdrawal

The study endpoint for participants includes those who had continued their participation through to the last assessments 3-months post-surgery. Once the study and data analysis were complete, a summary of results was sent to participants. This summary included information on the findings of the study.

Participants were removed from the study either at their own request or at the discretion of the research team. Those removed were made aware that this did not affect their future care. Withdrawal from the study was advised if the research study poses a hazard to the safety of a participant, or if the participant poses a hazard to the safety of their clinical care team or research team. Those who withdrew from the study or follow-up will not be replaced. Participants were not accepted as lost to follow-up unless two phone calls, letters or visits to the participant proved unsuccessful.

The criteria for withdrawal of participants included:

- Those who elected to withdraw
- Participants who died
- Participants who experienced a life-threatening Adverse Event (AE)
- Participants who experienced inpatient hospitalisation for non-elective procedures
- Participants who experienced a sudden or rapidly progressive major disablement
- Participants who experienced an event that caused the participant to seek non-routine medical treatment.

4.4 Procedure

Participants were seen, and or assessed, by a member of the research team for a total of six times. These visits included: screening, baseline, collecting the actigraphy monitor after the baseline period, 1-day post-surgery, 4-days post-surgery, and 3-months post-surgery.

As described in Informed Consent (4.2.4), it was necessary for the research team to liaise with the Booking Team to recruit participants the ensure the NHS Confidentiality Policy was adhered to. Following successful participant recruitment and study enrolment, baseline assessments were completed at the participant's home. Participants were reminded of the role of the actigraphy monitor and how it operates. This was attached to the participant's non-dominate arm and they were asked to wear the device for 3-days and complete a supplementary sleep diary alongside this. This took place no later than 3-weeks prior to their surgery date, as circadian rhythms, including sleep, can be significantly altered over a 3-week period. Consequently, where a participant's planned admission to hospital was delayed in excess of 3-weeks, the researcher arranged to obtain a new, pre-surgical, baseline assessment. Once the 3-day period was complete, the researcher returned to visit the participant to collect the actigraphy device and the completed sleep diary.

The researcher visited the participant 1-day post-surgery in the hospital to conduct assessments and to fit the actigraphy monitor for a second time. The assessment time-points outlined in the protocol best reflected and were the best fit to the estimated ward stay, which is currently 4-days after surgery. It was not suitable to test on day 0, as the residual effects of anaesthesia would still be present. Following discussions with the clinical care team, it was concluded that 1-day post-surgery was the most realistic to allow sufficient time for residual anaesthetic side effects to wear off. The side effects of anaesthesia can affect performance in assessment methods used in this study. This helped to ensure confounding factors were minimised.

At 4-days post-surgery the researcher visited the participant to retrieve the actigraphy monitor, the completed sleep diary as well as conducted assessments. Locations of the participant varied as some had been discharged early and returned home, whereas others were still in the hospital. A final, medium-term assessment was conducted at 3-months post-surgery at the participant's home. The researcher liaised with the project supervisor to complete the case notes template. This is summarised in Table 22.

Table 22 Summary matrix of study procedure

Screening	Baseline	Post-baseline	1-day post-surgery	4-days post-surgery	3-months post-surgery
Informed consent	-	-	-	-	-
	Actigraphy monitor	Actigraphy monitor collection	Actigraphy monitor	Actigraphy monitor collection	-
	Sleep diary		Sleep diary	Sleep diary collection	-
Delirium	Delirium	-	Delirium	Delirium	Delirium
-	Sleep disorders	-	-	-	Sleep disorders
Cognitive function	Cognitive function	-	Cognitive function	Cognitive function	Cognitive function
-	Level of functional ability	-	-	-	Level of functional ability
Depression	-	-	-	-	-
Fitness and Frailty	Fitness and Frailty	-	Fitness and Frailty	Fitness and Frailty	Fitness and Frailty
-	Visual attention	-	Visual attention	Visual attention	Visual attention
-	Sustained Attention	-	Sustained Attention	Sustained Attention	Sustained Attention

4.5 Analysis

All data was analysed using the SPSS statistical package v. 25.0 (SPSS Inc., Armonk, NY: IBM Corp). Data was cleaned and outliers identified through boxplots and participants with missing data were removed from the analyses. None of the statistically non-normal data was transformed. New variables were computed to determine the presence of delirium from the DRS R-98 scores.

Descriptive statistics were reported as counts, percentages, means, standard deviations, and range. Clinical characteristics were extracted and interpreted by Professor Chris Farmer (CF). Data on past medical history, past psychiatric history and use of medications was not included in the analysis due

to difficulties in obtaining the information and inconsistencies in patient self-reports and medical records. Assessment scores were compared against published normative cut-offs, and computer-based tasks were calculated using Version 4 of Inquisit Lab (Millisecond, 2015).

Actigraphy data was computed by ActiLife (Actigraph, 2019) and imported into SPSS for analysis. Scores were averaged across the days the device was worn, and a summary of baseline and post-surgical data was tabulated. In accordance to actigraphy best practices, the Cole-Kripke algorithm was used as the method of analysis (Morgenthaler et al., 2007). Technical issues with actigraphy recording were not anticipated. In instances where devices malfunctions occurred, this was recorded alongside the time-point it corresponded to.

To examine for differences between sleep at baseline, prior to surgery, and post-surgery, a within-subjects ANOVA was used. The dependent variable were the sleep measures and the independent variable was time. This was as conducted on the following matched actigraphy variables at baseline and between 1 and 4-days post-surgery:

- Sleep latency
- Total counts
- Sleep efficiency (SE)
- Total minutes in bed
- Total Sleep Time (TST)
- Wake After Sleep Onset (WASO)
- Number of Awakenings (NOA)
- Average Awakening Length
- Movement index (MI)
- Fragmentation index (FI)
- Sleep fragmentation index (SFI)

The same within-subjects ANOVA was then repeated to include age as a covariate to explore whether any changes between the two time-points relate to age. Poorer sleep was defined as lower values in sleep efficiency, total minutes in bed, TST, and increased values in sleep latency, total counts, WASO, NOAs, average awakening length, MI, FI, and SFI.

To examine for differences between cognitive function at baseline, 1-day, 4-day and 3-months post-surgery, a within-subjects ANOVA was used. The dependent variable were the cognitive measures,

the independent variable was time, and age was included as a covariate. It is known that age-related changes result in cognitive decline, the influence of this strongest for attention and memory (Glisky, 2007). It was therefore imperative that age is again included as a covariate in these analyses.

Initially, a Generalised Estimating Equations (GEE) (Hubbard et al., 2010) were considered for use to answer Hypothesis 1 and 2, to examine the predictive value of poor actigraphy measured sleep pre- and post-surgery on delirium. The GEE method had been used in previous research involving repeated measurements of DRS R-98 where the data has been clustered for comparison. This included studies investigating the relationship between motor sub-types in delirium and etiologies, medication exposure, and outcomes (Meagher et al., 2011) and between the sleep-wake cycle item, demographic, and clinical characteristics (Fitzgerald et al., 2017). However, due to the lower than anticipated number of participants who scored positive for delirium, this method of analysis was not deemed to be the most effective method of examining this dataset. Instead, a Pearson's correlation, as described below was used.

As not all measures were collected on the same number of occasions (as illustrated in Table 22), data had to be re-structured into the long format. Additionally, each sleep measure was computed into new variables. These new variables represented the difference between sleep at baseline and the period 1-4 days after surgery. For clarity, these new variables are referred to generally as 'differences in sleep' variables throughout this Chapter. These differences in sleep are defined as the degree of change to habitual sleep, and were calculated by deducting the sleep data value obtained at post-surgery from sleep at baseline. The new variable created continuous scores which allows for the appropriate use of the Pearson's correlation as it does not violate the assumptions. These 'differences in sleep' variables were computed for all sleep measures including: sleep latency, sleep total counts, sleep efficiency, total minutes in bed, TST, WASO, NOAs, average awakening length, MI, FI, and SFI.

For Hypothesis 1 and 2, to explore the potential association of 'poorer sleep' pre- and post-surgery and increased risk of delirium, a Pearson product-moment correlation was used. The newly computed 'differences in sleep' variables were correlated against delirium at 1-day and 4-days post-surgery to explore the strength and direction of potential associations between these variables.

4.6 Results

4.6.1 Participants

In total, 50 eligible participants were enroled into the study, with 45 participants included in the final analysis. The number of study invitation letters sent out was not recorded by the Booking Team. This is summarised in the Modified CONSORT Diagram in Figure 13.

At screening, two participants were excluded for neurological dysfunction. This included a history of traumatic brain injury, dementia and depression which was not disclosed to the researcher at the pre-admission clinic and for scoring above the threshold for depression. Following study enrolment, two participants were excluded due to surgery postponement as result of clinical staff shortages and illness. Due to cancellations, the participant was offered a new surgery date with very short notice which they accepted. This rescheduled date was earlier than initially anticipated and the research team were not informed in time and subsequently missed the key time-points for data collection. After baseline assessments, two participants decided to withdraw as they no longer wanted to participate as it was too time consuming and 'not for them'. One participant was unwell at the 4-days post-surgery visit and their consultee decided to withdraw the participant due to ill health. Consequently, 45 out of the 50 participants initially enroled were included in the final analysis.

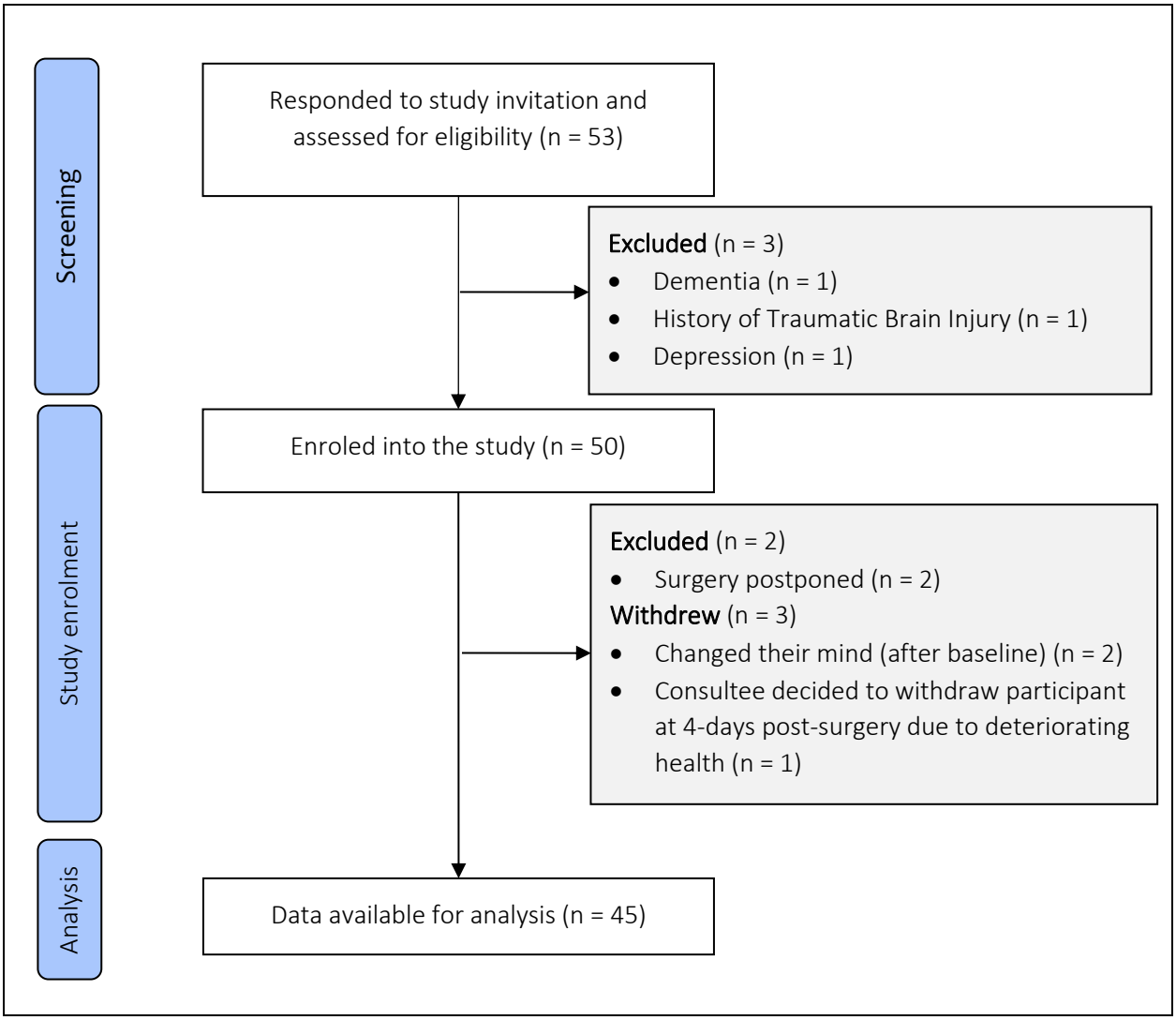
Missing data were identified. Nine participants declined to complete assessments at a specific time-point through either sickness, prior commitments (and therefore time constrained), withdrawal from the study or visual impairment from misplacement of visual aids. Participants who attempted (but did not successfully complete without errors) the visual attention task were assigned a value 2 standard deviations to the mean. This was to account for an incomplete attempt and for this to be outside of the 95% of a normally distributed data set. There were 61 instances of this.

Data was cleaned and outliers were removed from the final analysis. Nine sets of sustained attention scores were omitted for either scoring below the 200ms reaction time threshold or for being an outlier. The actigraphy monitor malfunctioned on one occasion where it failed to record data. Actigraphy data for four participants were removed due to inconsistencies against the supplementary sleep diary. Following comparisons with the theatre data, one participant's date of birth was amended. This was contributed to human error in reporting.

A post-hoc power analysis was conducted using G*Power3 (Faul, Erdfelder, Buchner, & Lang 2009) to test the difference of within factors using a medium effect size (f = .45), and an alpha of .05. A

post hoc power of .56 was observed with our sample size (n = 41). This suggests that the likelihood of making a Type II error does not exceed the acceptable threshold and the sample size was sufficient to detect effects present at the < .05 significance level.

Figure 13 Modified CONSORT Diagram



4.6.2 Descriptive statistics

For the 45 participants included in the analysis, data for five participants on ward admission was missing. Due to inconsistencies in how pyrexia is classified in the literature, both the cut-off points of ≥ 38 and ≥ 37.5 degrees Celsius (n = 44) were used. However, this data was not available for all participants as it is not routinely collected. Descriptive data is summarised in Tables 23 – 28.

Table 23 Summary of Demographic Data

Characteristics	*n*	Mean (SD) or %	Range
Age	45	78.21 ± 5.23	71 – 90
Gender			
Female	28	62.2%	
Male	17	37.8%	
Ethnicity*			
White (English Welsh/Scottish/ Northern Irish British)	45	100%	
Marital Status			
Married (including those in civil partnership)	29	64.4%	
Divorced (including formerly in a civil partnership with is now legally dissolved)	3	6.7%	
Widowed (including surviving partner from a civil partnership)	13	28.9%	
Highest level of education	44		
Primary	9	20.0%	
Secondary	17	37.8%	
Further education	2	4.4%	
Vocational qualification	7	15.6%	
Higher education	7	15.6%	
Postgraduate qualification	1	2.2%	
Total years of education	43	12.93 ± 4.295	9 – 32

* as defined by the UK Government list of ethnic groups (GOV.UK, 2018)

Table 24 Summary of Opera Theatre Management System and pathology reports

	n	Mean (SD) or %
Operation type		
Primary total prosthetic replacement of knee joint	25	55.6%
Primary total prosthetic replacement of hip joint	18	40%
Right knee replacement vanguard cr + patella resurfacing	1	2.2%
Left total hip replacement (exceed / taperloc)	1	2.2%
Ward		
QUEX Main	31	68.9%
QUEX Main and Side Ward	2	4.4%
Bishopstone Main	5	11.1%
Bishopstone Side Ward	1	2.2%
Spencer Wing (private)	1	2.2%
Max CR-P Score	31	128.61 ± 94.00
Max EWS score	44	2.02 ± 1.07
Pyrexia		
≥ 37.5 degrees Celsius	44	35.6%
≥ 38 degrees Celsius	44	8.9%
Surgery status		
Unchanged	37	82.2%
Rescheduled – staff shortage	7	15.6%
Rescheduled – illness	1	2.2%

Table 25 Summary of delirium presence over time

	Delirium Presence		
Time-point	No Delirium	Subclinical	Delirium
At any time-point	8	35	2
1-day post-surgery	6	33	2
4-days post-surgery	7	28	0
3-months post-surgery	14	10	0

Table 26 Summary of cognitive, fitness and frailty, level of functional ability, and sleep questionnaire measures across all time-points

	Baseline		**1-day post-surgery**		**4-days post-surgery**		**3-months post-surgery**	
	n	Mean (SD)	*n*	Mean (SD)	*n*	Mean (SD)	*n*	Mean (SD)
Delirium	45	1.40 ± 1.32	41	5.29 ± 4.93	36	3.06 ± 3.31	24	.63 ± .88
Cognitive function	44	28.66 ± 1.40	37	27.86 ± 3.10	33	28.67 ± 1.95	25	29.28 ± .74
Fitness and Frailty	41	4.10 ± 1.08	39	5.82 ± .99	38	4.95 ± .93	27	3.00 ± 1.41
Level of functional ability*	38	206.18 ± 4.21	-	-	-	-	25	208.20 ± 1.87
Sleep disorders*								
Sleep Apnoea	43	25.84 ± 5.12	-	-	-	-	26	25.88 ± 7.39
Periodic Limb Movement	43	19.91 ± 5.05	-	-	-	-	26	19.08 ± 5.47
Psychiatric Sleep	43	14.33 ± 4.14		-	-	-	26	14.85 ± 7.04
Narcolepsy	43	17.40 ± 2.27	-	-	-	-	26	20.31 ± 10.42

* Sleep disorders and level of functional ability data collected only at baseline and 3-months post-surgery to capture a benchmark for comparison against longitudinal, follow-up data.

Table 27 Summary of actigraphy measures, including pre- and post-surgical periods and an average of all sleep data collected

	Pre-surgery		**Post-surgery**		**All**	
	n	Mean (SD) or %	*n*	Mean (SD) or %	*n*	Mean (SD) or %
Sleep latency	40	2.27 ± 2.71	41	2.36 ± 2.55	81	2.32 ± 2.61
Wake After Sleep Onset (WASO)	45	41.42 ± 25.50	38	58.28 ± 39.68	83	49.14 ± 33.63
Total Counts	44	31835.41 ± 25567.35	45	34141.08 ± 24908.29	89	33001.20 ± 25119.15
Sleep efficiency	40	81.71 ± 14.63	42	83.13 ± 11.02	82	82.44 ± 12.86
Total minutes in bed	41	372.12 ± 104.99	42	386.57 ± 118.16	83	379.43 ± 111.41
Total Sleep Time (TST)	41	318.86 ± 110.36	42	336.46 ± 118.38	83	327.77 ± 114.14
Number of Awakenings (NOA)	41	9.37 ± 5.75	42	8.95 ± 5.29	83	9.16 ± 5.50
Average Awakening Length	39	4.93 ± 2.08	42	5.08 ± 11.14	81	5.01 ± 1.95
Movement Index (MI)	41	21.17 ± 14.20	42	21.53 ± 11.14	83	21.35 ± 12.67
Fragmentation Index (FI)	41	12.48 ± 9.93	42	9.89 ± 5.85	83	11.17 ± 8.18
Sleep Fragmentation Index (SFI)	41	33.86 ± 21.63	42	31.60 ± 13.82	83	32.72 ± 18.03

Table 28 Summary of visual attention and sustained attention scores

	Baseline		1-day post-surgery		4-days post-surgery		3-months post-surgery	
	n	Mean (SD) or %	*n*	Mean (SD) or %	*n*	Mean (SD) or %	*n*	Mean (SD) or %
Time taken in the Visuospatial Short-term Memory task								
Part A (s)	44	49.54 ± 17.04	37	70.97 ± 33.11	34	53.38 ± 21.78	18	43.29 ± 12.74
Part B (s)	44	150.27 ± 63.42	37	173.28 ± 54.27	32	180.28 ± 73.78	17	118.40 ± 57.65
Time taken in the Sustained Attention task								
Correct suppressions (%)	40	58.10 ± 25.72	29	61.38 ± 21.79	26	62.77 ± 26.93	25	60.16 ± 28.15
Incorrect suppressions (%)	40	6.40 ± 6.56	29	12.05 ± 14.22	26	6.37 ± 8.04	25	5.56 ± 6.81
Successful Trials (ms)	39	508.17 ± 128.17	28	537.54 ± 104.68	25	510.96 ± 105.08	25	491.21 ± 102.78
Unsuccessful Trials (ms)	40	429.11 ± 89.48	22	449.90 ± 89.83	22	427.11 ± 89.10	23	420.56 ± 84.32
Correct and valid trials (ms)	40	488.99 ± 101.92	29	538.47 ± 114.77	26	497.89 ± 103.68	25	477.25 ± 94.04
Variability of reaction time in the Sustained Attention Task								
Estimated standard deviation (std)	40	132.57 ± 51.39	29	143.59 ± 52.78	26	128.55 ± 46.15	25	129.88 ± 72.84
Coefficient of variability (cv)	40	.27 ± .09	29	.27 ± .08	26	.26 ± .08	25	.27 ± .12

4.6.3 Actigraphy data

A statistically significant difference between actigraphy at baseline and 1-day and 4-days post-surgery was reported for the following sleep measures with a Greenhouse-Geissier correction: sleep latency ($F(1, 35) = 4.59$, $p = .039$), sleep efficiency ($F(1, 36) = 18.52$, $p > .005$), total minutes in bed ($F(1, 37) = 5.94$, $p = .02$), Total Sleep Time (TST) ($F(1, 37) = 10.53$, $p = .002$), Wake After Sleep Onset (WASO) ($F(1, 37) = 5.14$, $p = .029$), Movement Index (MI) ($F(1, 37) = 19.90$, $p > .001$), Fragmentation Index (FI) ($F(1, 37) = 9.10$, $p > .005$), and Sleep Fragmentation Index (SFI) ($F(1, 37) = 20.07$, $p > .001$). There were no statistically significant differences in sleep total counts, number of awakenings (NOA), and average awakening length.

After controlling for age as a covariate, only changes in total minutes in bed and TST were statistically significant. Statistically significant differences with a Greenhouse-Geissier correction were observed for total minutes in bed ($F(1, 36) = 11.16$, $p = .002$), as well as TST ($F(1, 36) = 9.81$, $p = .003$). This suggests participants spent longer in bed and slept for longer at baseline when compared to post-surgery. This is illustrated in Figure 14.

Post-hoc analysis with a Bonferroni adjustment showed the following statistically significant differences at post-surgery when compared to baseline:

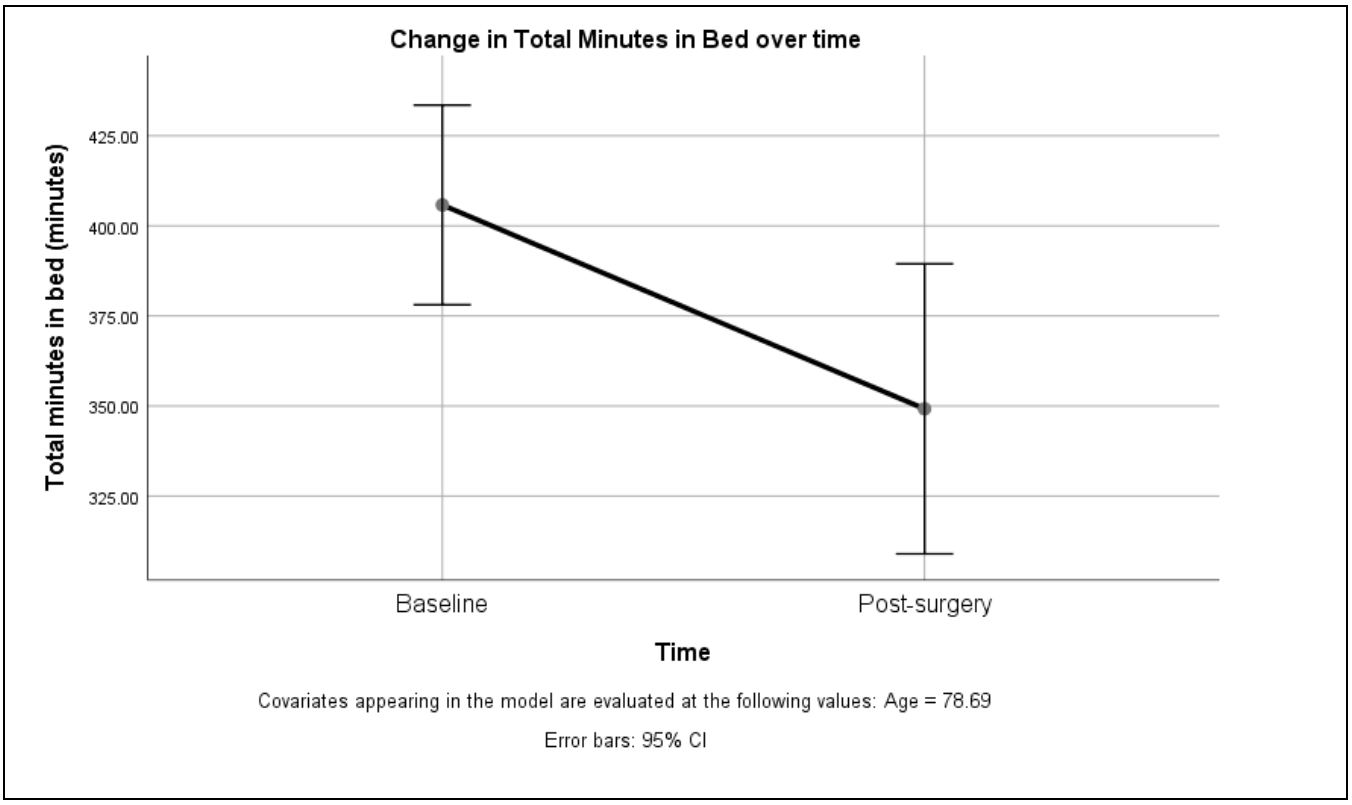
- **Increase** in sleep latency
- **Decrease** in sleep efficiency
- **Decrease** in total minutes in bed
- **Decrease** in TST
- **Increase** in WASO
- **Increase** in MI
- **Increase** in FI
- **Increase** in SFI

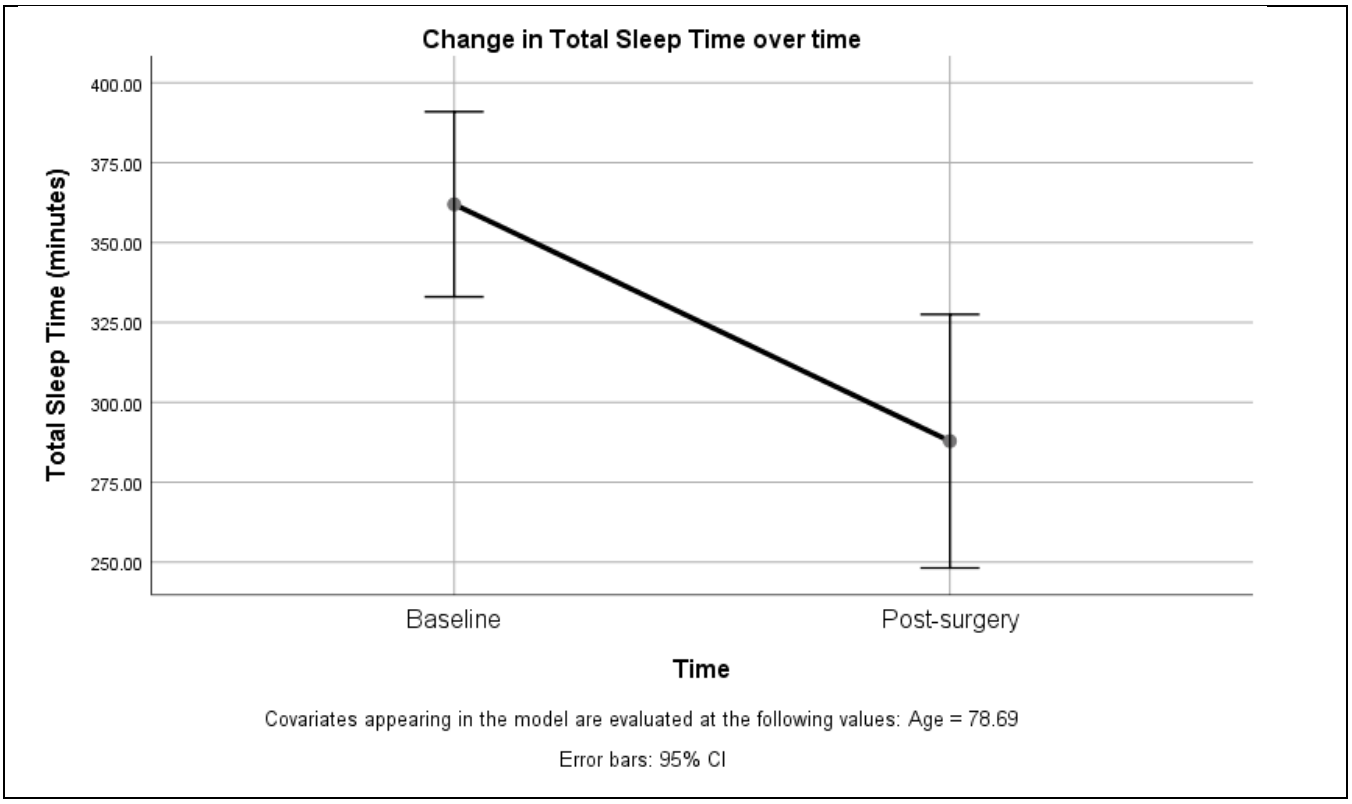
At baseline, participants took less time to fall asleep, spent longer in bed and asleep, had greater sleep efficiency, took less time to return to sleep after waking up, experienced less movement and sleep fragmentation

Due to missing data, not all 41 participants were included in each of the within-subjects ANOVAs described, a second post-hoc power analysis was conducted using G*Power3 (Faul, Erdfelder, Buchner, & Lang 2009), with the same parameters, to test the difference of within factors using a medium effect

size (f = .45), and an alpha of .05. Here, a post-hoc power of 0.73 was observed in the analysis with the smallest sample size (n = 36), suggesting the likelihood of making a Type II error does not exceed the acceptable threshold and that this sample size was sufficient to detect effects present at the < .05 significance level.

Figure 14 Statistically significant changes in actigraphy measures between baseline and post-surgery when controlling for age




Change in Total Sleep Time over time
Total Sleep Time (minutes)
400.00
375.00
350.00
325.00
300.00
275.00
250.00
Baseline
Post-surgery
Time
Covariates appearing in the model are evaluated at the following values: Age = 78.69
Error bars: 95% CI

As described in 4.4, new variables were computed using the sleep measures. The values for these new 'differences in sleep' variables are summarised in Table 29.

Table 29 Summary of 'differences in sleep' variables

	n	Mean (SD) or %
Sleep Latency*	36	1.35 ± 3.78
Total Counts*	37	-5071.09 ± 33010.83
Sleep Efficiency*	37	10.05 ± 14.21
Total minutes in bed*	38	56.61 ± 144.97
Total Sleep Time*	38	74.13 ± 140.80
Wake After Sleep Onset*	38	-16.64 ± 45.24
Number of awakenings*	38	-.56 ± 6.91
Average awakening length*	38	-.64 ± 2.65
Movement Index*	36	-9.58 ± 13.25
Fragmentation Index*	38	-5.43 ± 11.09
Sleep Fragmentation Index*	38	-15.27 ± 21.02

* Newly computed differences in sleep variables

4.6.4 Cognition, sustained attention, task switching, delirium, fitness and frailty and functional ability, and sleep disorder data

There were no statistically significant differences for measures at baseline and 1-day, 4-days, and 3-months post-surgery, nor were there statistically significant differences for measures collected at baseline and 3-months post-surgery with age as a covariate. Despite an absence of statistically significant results, fluctuations in scores were observed over time. These changes are illustrated below, in Figure 15 - 20.

Figure 15 Changes in cognition function over time

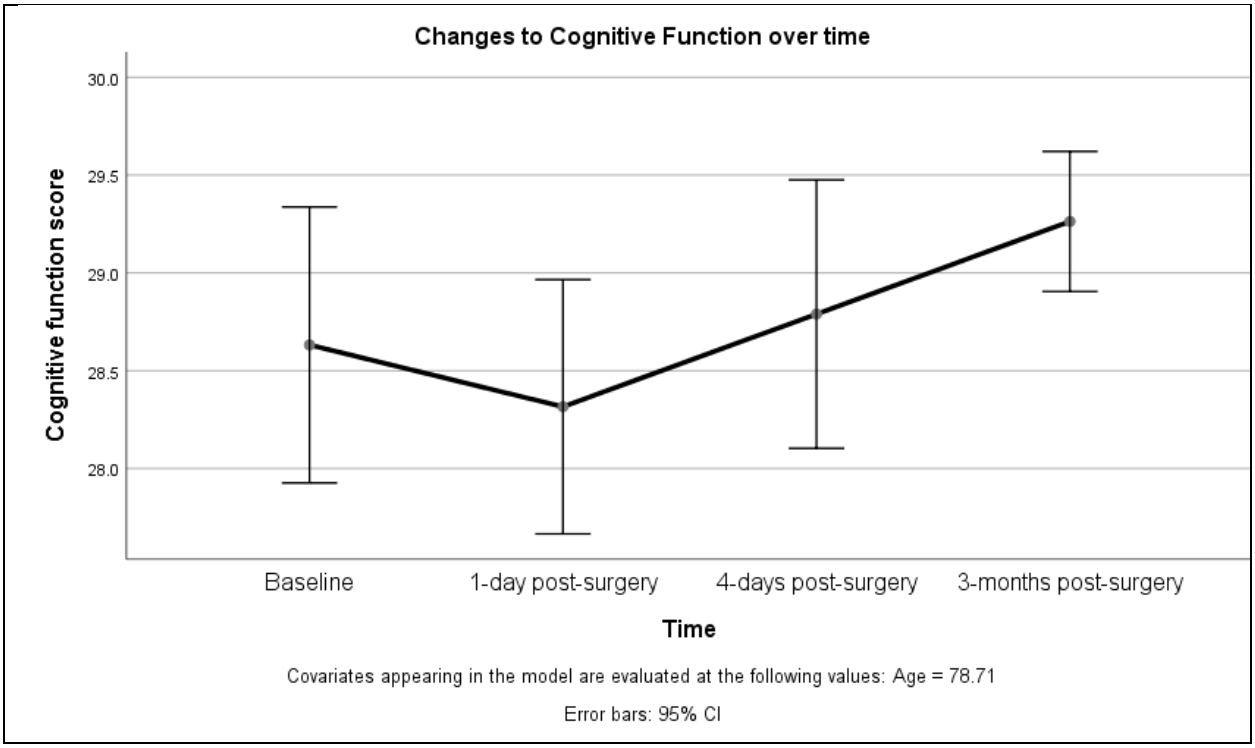
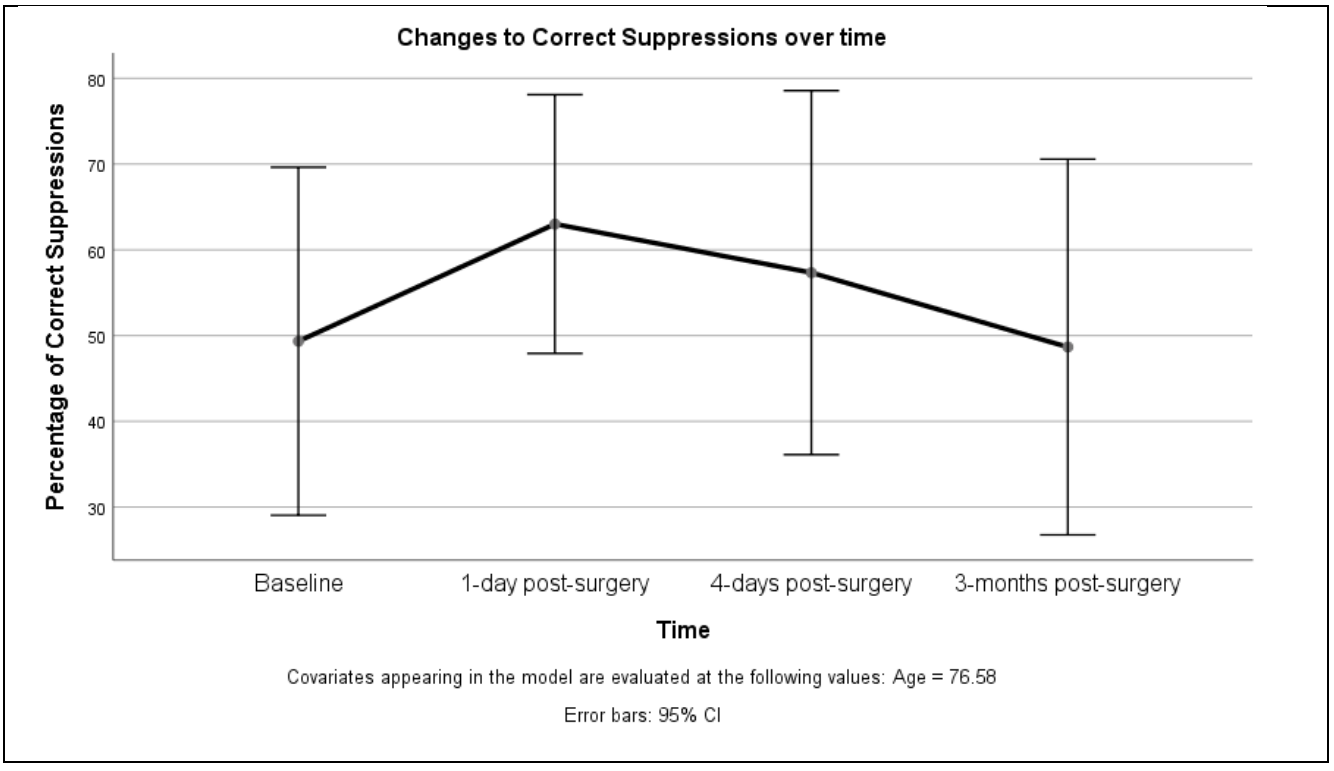
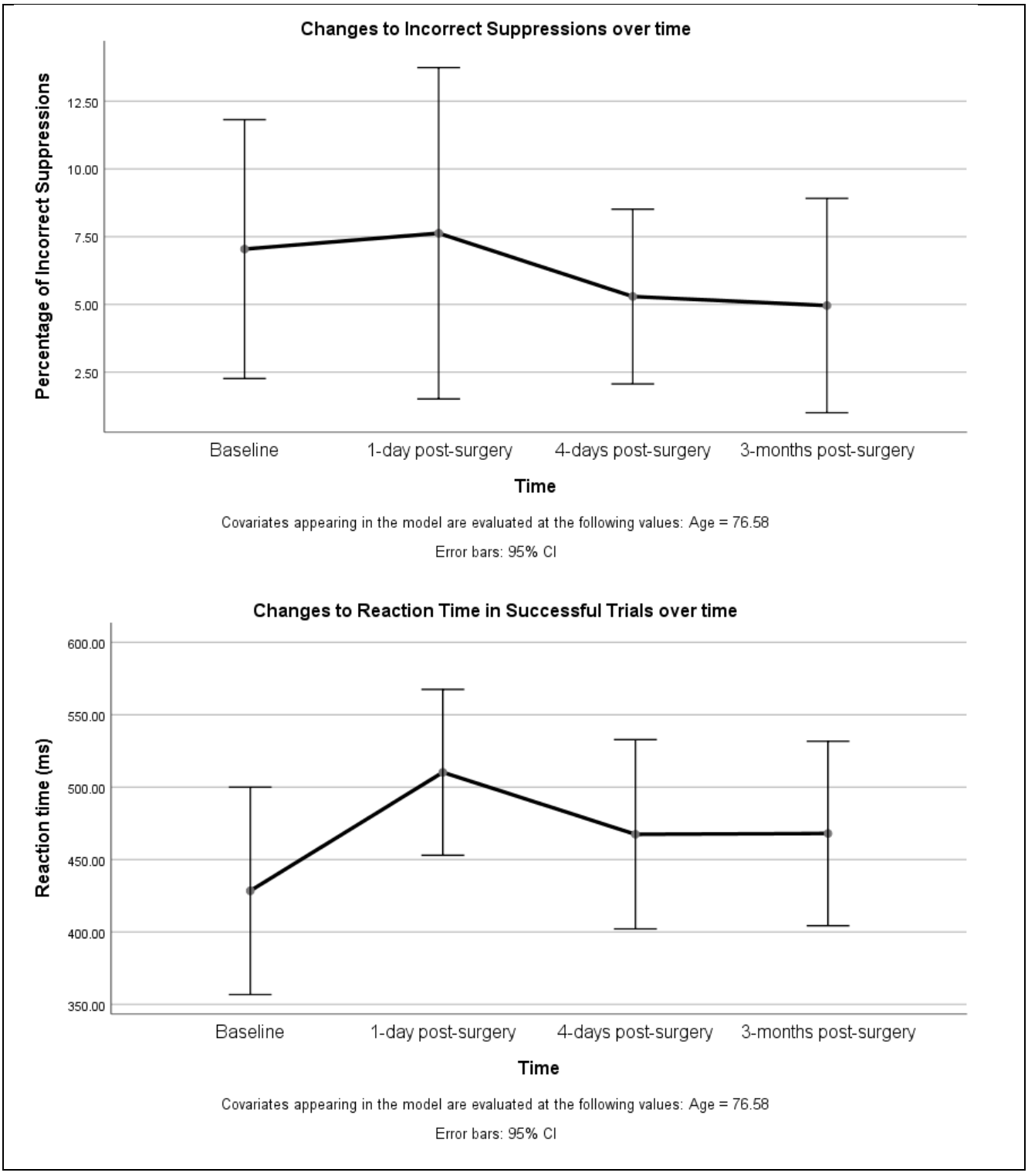
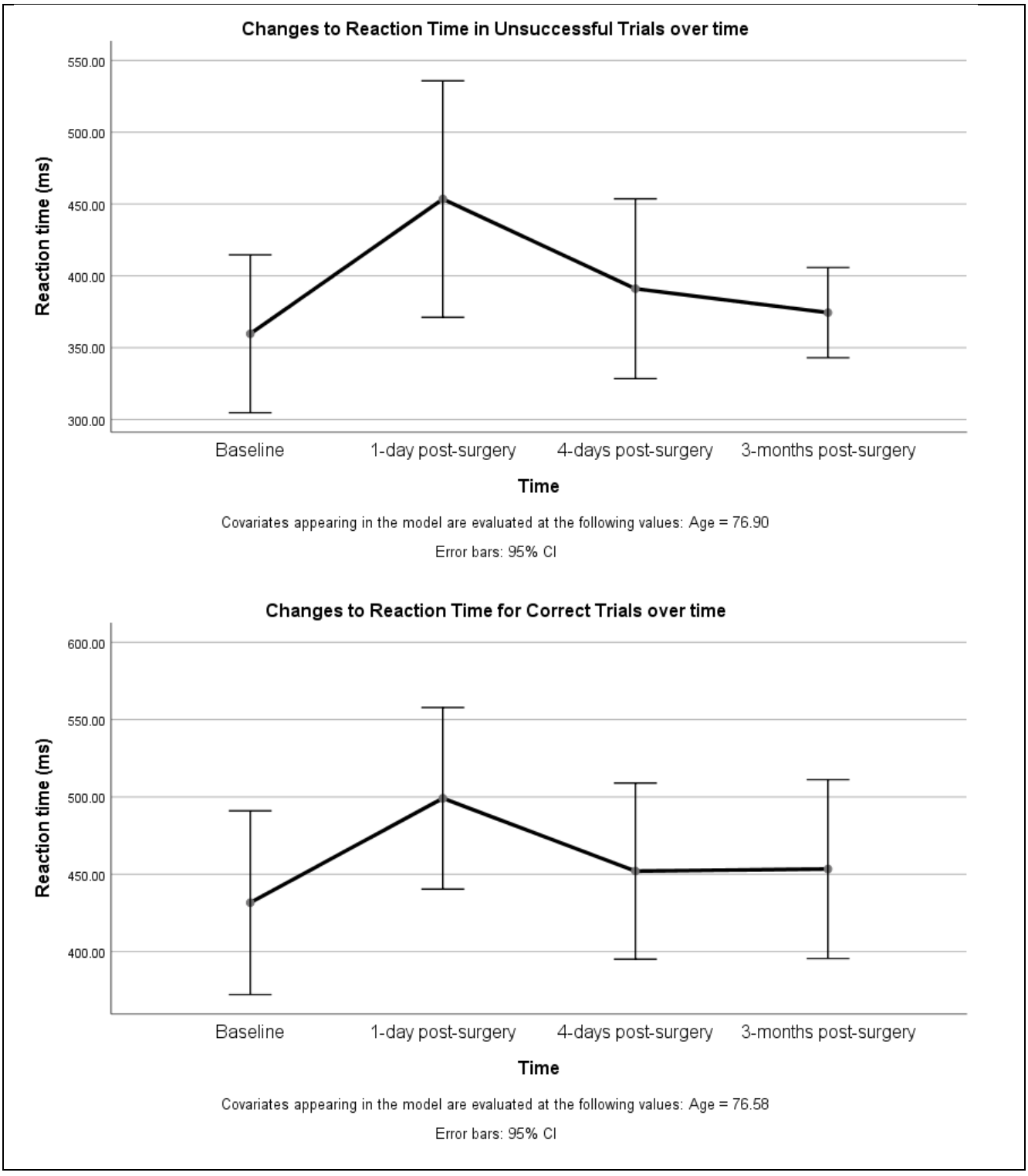


Figure 16 Changes in performance in sustained attention over time




Changes to Incorrect Suppressions over time
Percentage of Incorrect Suppressions
12.50
10.00
7.50
5.00
2.50
Baseline
1-day post-surgery
4-days post-surgery
3-months post-surgery
Time
Covariates appearing in the model are evaluated at the following values: Age = 76.58
Error bars: 95% CI
Changes to Reaction Time in Successful Trials over time
Reaction time (ms)
600.00
550.00
500.00
450.00
400.00
350.00
Baseline
1-day post-surgery
4-days post-surgery
3-months post-surgery
Time
Covariates appearing in the model are evaluated at the following values: Age = 76.58
Error bars: 95% CI


Changes to Reaction Time in Unsuccessful Trials over time
Reaction time (ms)
550.00
500.00
450.00
400.00
350.00
300.00
Baseline
1-day post-surgery
4-days post-surgery
3-months post-surgery
Time
Covariates appearing in the model are evaluated at the following values: Age = 76.90
Error bars: 95% CI
Changes to Reaction Time for Correct Trials over time
Reaction time (ms)
600.00
550.00
500.00
450.00
400.00
Baseline
1-day post-surgery
4-days post-surgery
3-months post-surgery
Time
Covariates appearing in the model are evaluated at the following values: Age = 76.58
Error bars: 95% CI

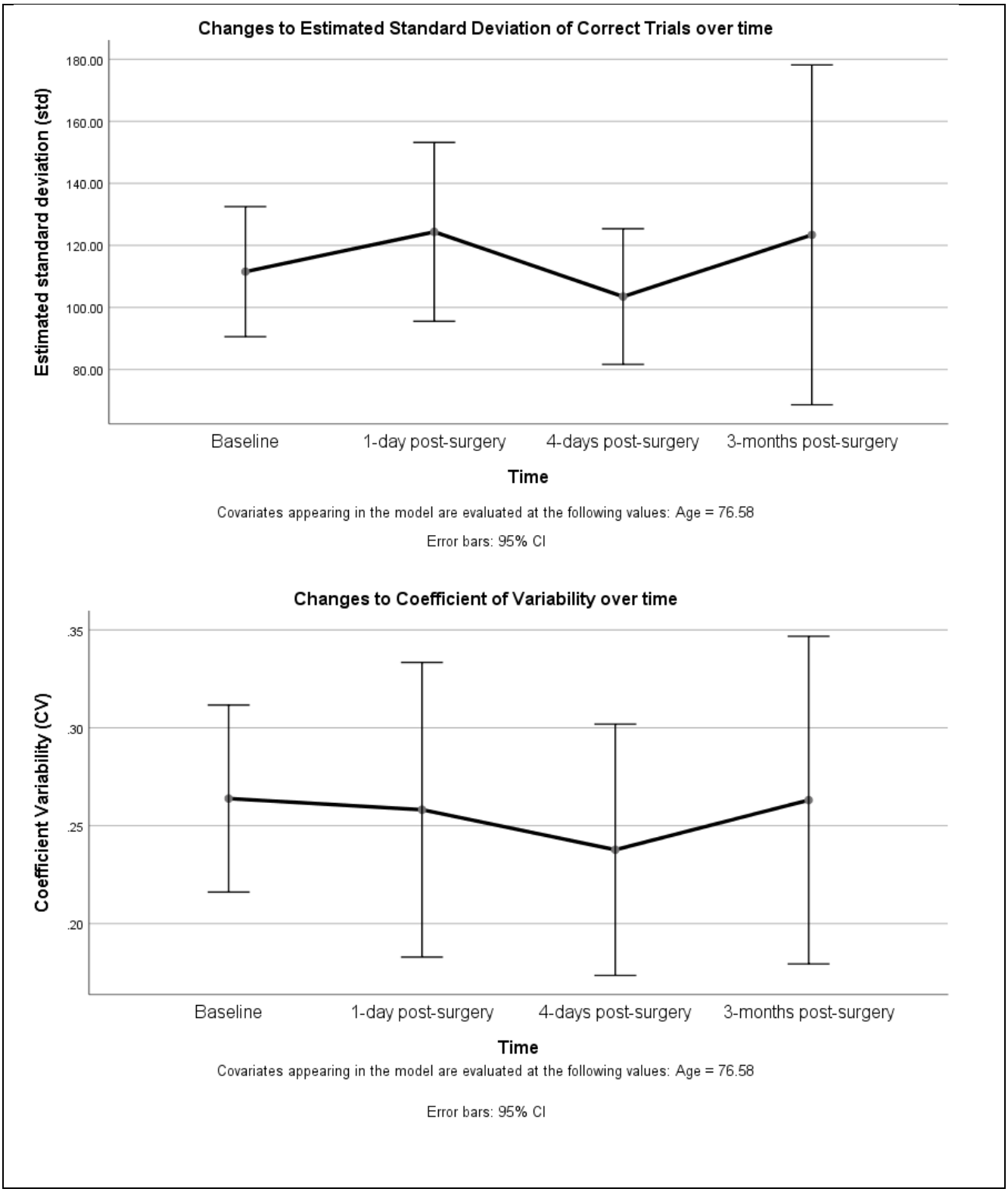

Changes to Estimated Standard Deviation of Correct Trials over time
Estimated standard deviation (std)
180.00
160.00
140.00
120.00
100.00
80.00
Baseline
1-day post-surgery
4-days post-surgery
3-months post-surgery
Time
Covariates appearing in the model are evaluated at the following values: Age = 76.58
Error bars: 95% CI
Changes to Coefficient of Variability over time
Coefficient Variability (CV)
.35
.30
.25
.20
Baseline
1-day post-surgery
4-days post-surgery
3-months post-surgery
Time
Covariates appearing in the model are evaluated at the following values: Age = 76.58
Error bars: 95% CI

Figure 17 Changes in performance in task switching over time

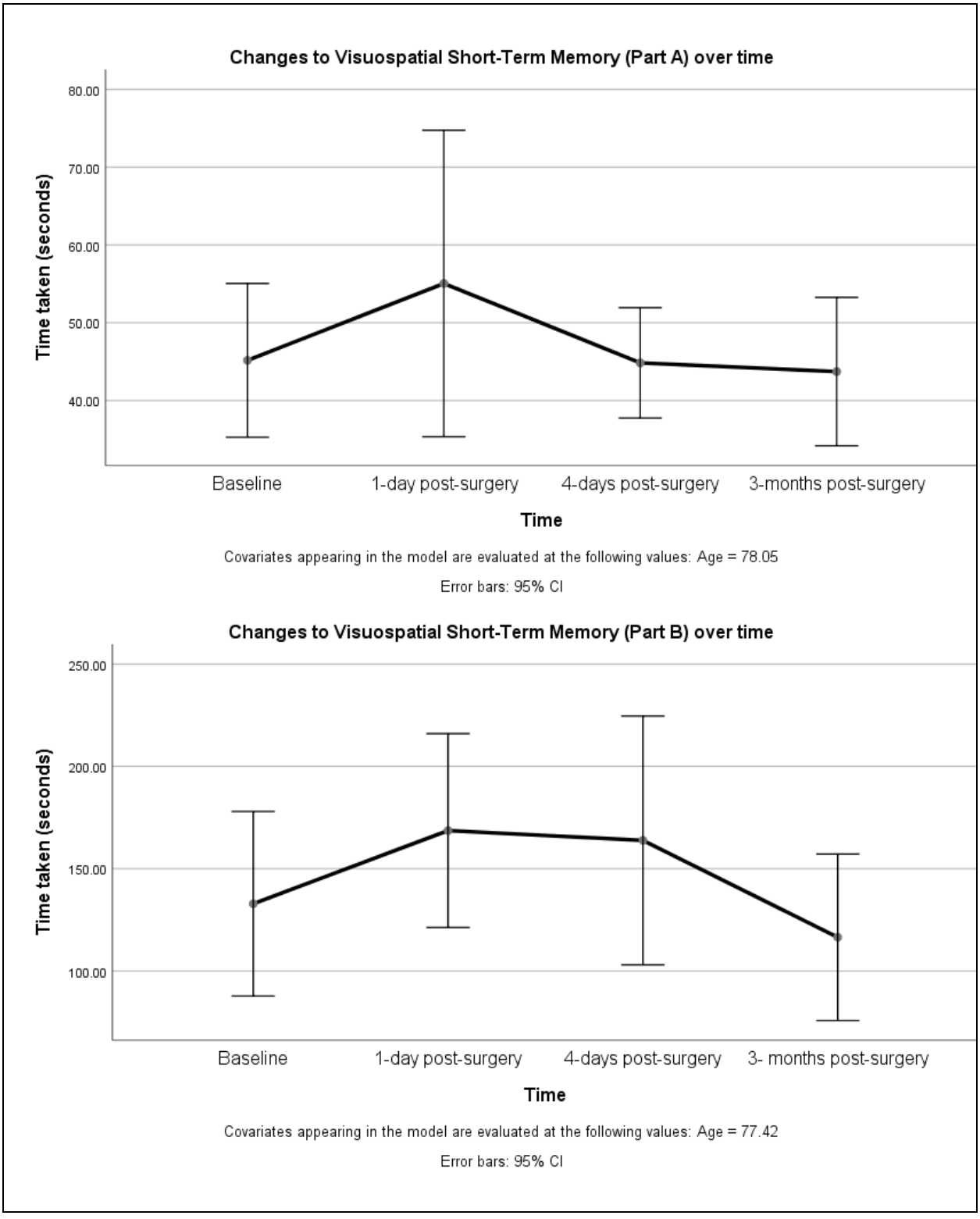


Figure 18 Changes in delirium score over time

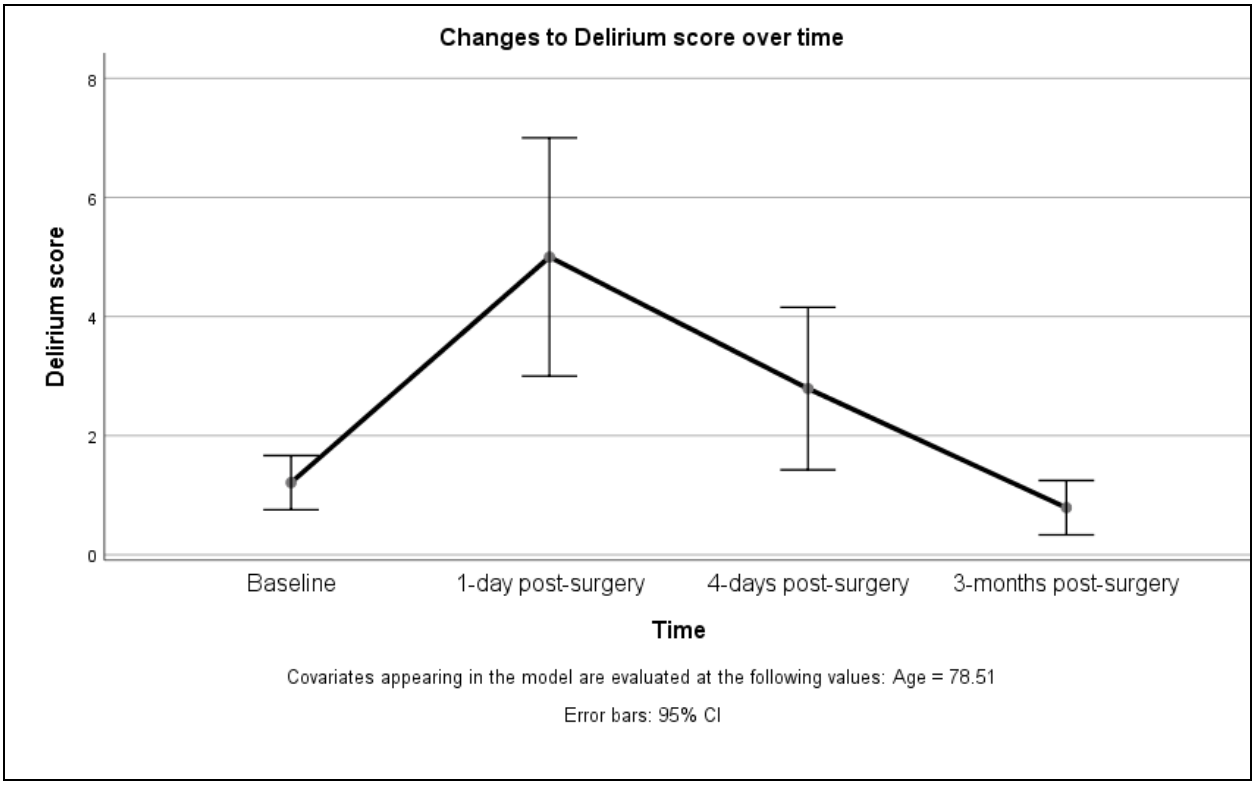


Figure 19 Changes in fitness and frailty and functional ability over time

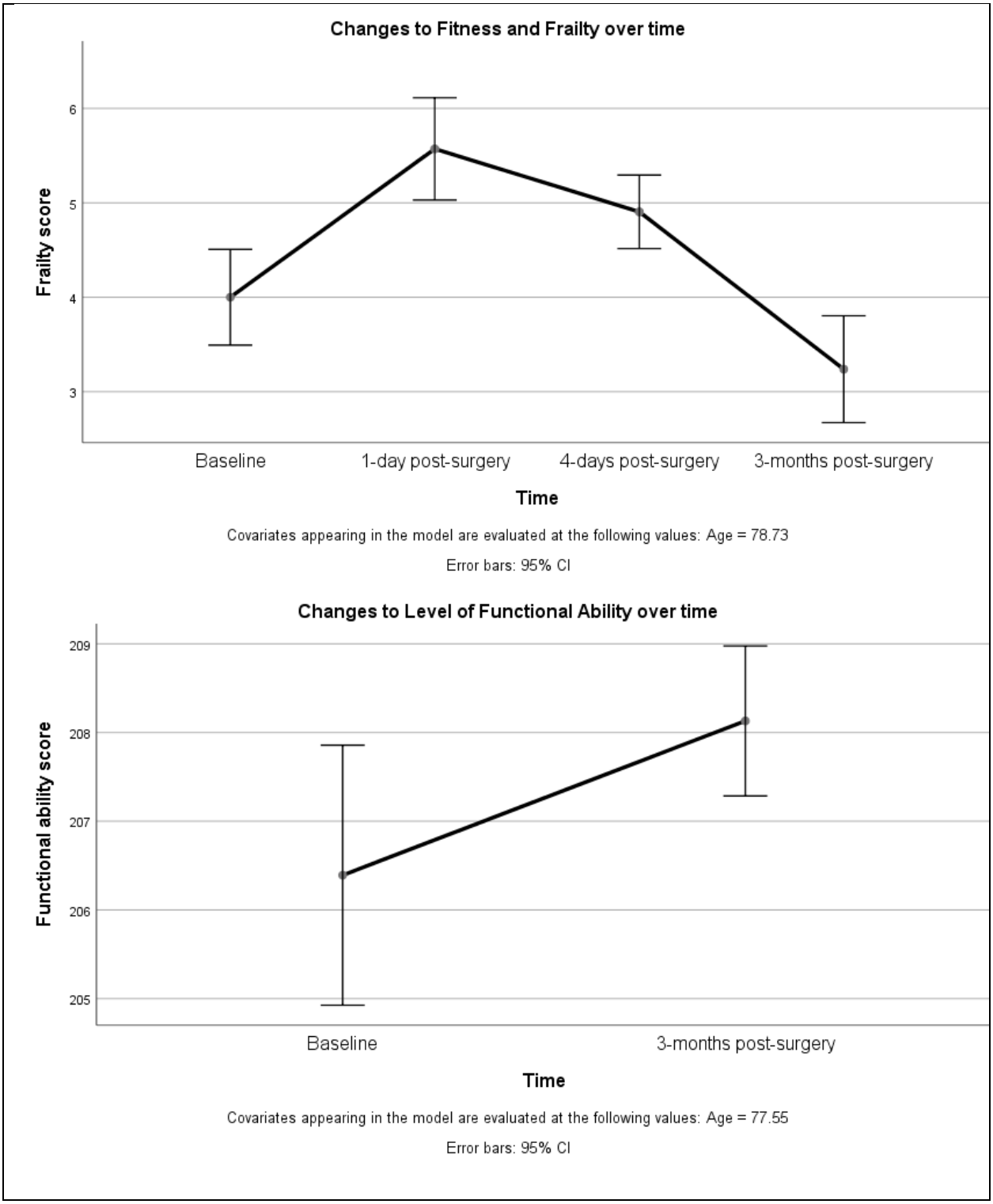
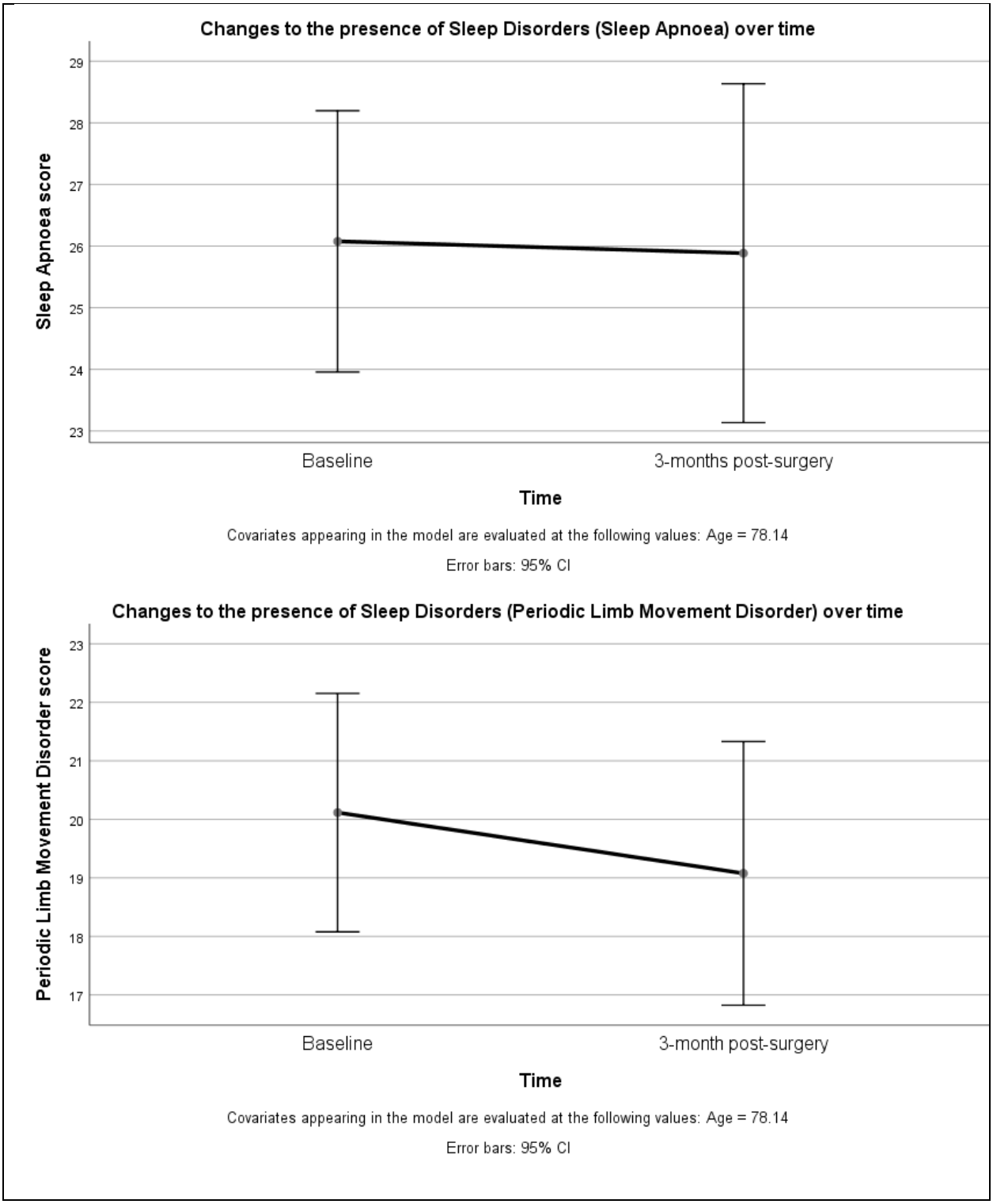
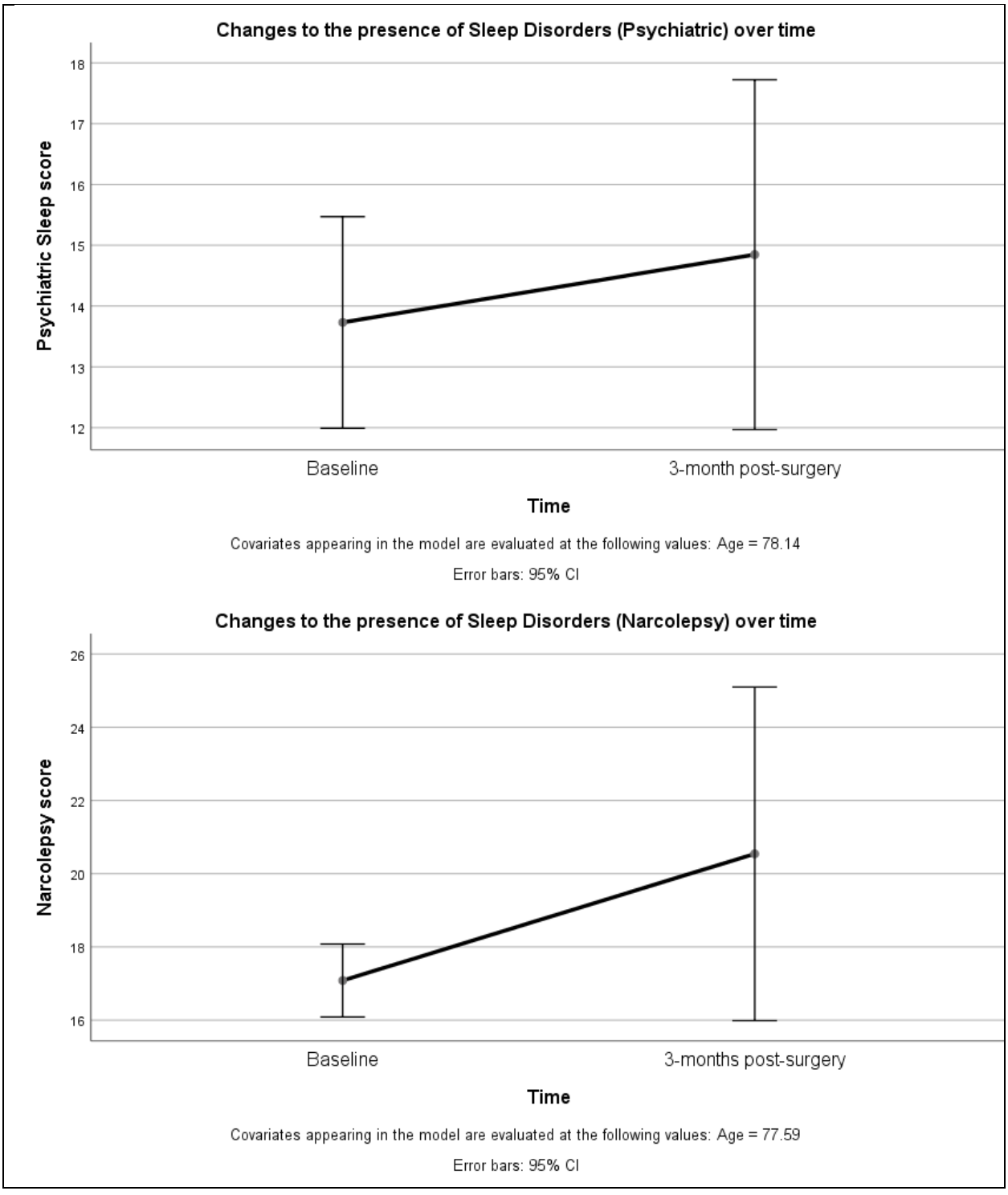


Figure 20 Changes in the presence of sleep disorders over time




Changes to the presence of Sleep Disorders (Psychiatric) over time
Psychiatric Sleep score
18
17
16
15
14
13
12
Baseline
3-month post-surgery
Time
Covariates appearing in the model are evaluated at the following values: Age = 78.14
Error bars: 95% CI
Changes to the presence of Sleep Disorders (Narcolepsy) over time
Narcolepsy score
26
24
22
20
18
16
Baseline
3-months post-surgery
Time
Covariates appearing in the model are evaluated at the following values: Age = 77.59
Error bars: 95% CI

Due to missing data, not all 41 participants were included in each of the within-subjects ANOVAs, a post-hoc power analysis was conducted using G*Power3 (Faul, Erdfelder, Buchner, & Lang 2009). This was using, again, a medium effect size (f = .45), and an alpha of .05. Results are illustrated in Table 30. This suggests that the likelihood of making a Type II error for some measures did exceed the acceptable threshold, and the sample size was not sufficiently large enough to detect effects present at the < .05 significance level.

Table 30 – Post-hoc power analysis

Measure	***n***	**Post-hoc power**
Visual attention		
Part A	11	.38
Part B	10	.16
Sustained attention		
Correct suppressions	12	.57
Incorrect suppression	19	.24
Successful trials	12	.61
Unsuccessful trials	9	.79
Correct trials	12	.82
Estimated standard deviation	12	.99
Coefficient of Variability	12	.90
Presence of Sleep Disorders		
Sleep apnoea	26	.79
Periodic limb movement disorder	26	.15
Psychiatric disorders	26	.94
Narcolepsy	24	.47
Delirium	19	.53
Cognitive function	19	.97
Functional ability	23	.22
Fitness and Frailty	21	.77

4.6.5 Hypothesis 1 and 2

A Pearson's correlation was used to explore the relationship between sleep and risk for delirium instead of a Generalised Estimating Equation (GEE), as only two participants scored above the cut-off and scored positive for delirium (as illustrate in Table 25). Both of these incidences were recorded at 1-day post-surgery. The newly computed 'differences in sleep' variables were correlated against post-surgery delirium score to explore the strength and direction of potential associations between them. Table 31 and 32 illustrate both the zero-order correlation and partial correlations.

There was a positive partial correlation between total counts (-859.11 ± 32993.91 counts) and delirium score at 1-day post-surgery (5.14 ± 4.36), whilst controlling for age (79.98 ± 5.64 years), which was statistically significant ($r(25) = .431$, $n = 28$, $p = .02$). Total counts and delirium at 4-day post-surgery (3.07 ± 3.15), again controlling for age, was statistically significant ($r(25) = .454$, $n = 28$, $p = .02$). Zero-order correlations showed there was not a statistically significant positive correlation between total counts and delirium at 1-day post-surgery ($r(26) = .364$, $n = 28$, $p = .06$), and 4-days post-surgery $r(26) = .349$, $n = 28$, $p = .07$). This suggest that age did have an influence in controlling for the relationship between total counts and delirium.

Additionally, there was a positive partial correlation between average awakening length (-.8662 ± 2.944 minutes), and delirium at 1-day post-surgery, controlling for age was statistically significant ($r(25) = .385$, $n = 28$, $p = .04$). Average awakening length and delirium at 4-days post-surgery, controlling for age, was statistically significant ($r(25) = .499$, $n = 28$, $p = .008$). Zero-order correlations showed there was not a statistically significant positive correlation between average awakening length and delirium at 1-day post-surgery ($r(26) = .344$, $n = 28$, $p = .07$). There was however a statistically significant positive correlation for delirium at 4-days post-surgery ($r(26) = .421$, $n = 28$, $p = .03$). This suggests that age does have an influence in controlling for the relationship between average awakening length and delirium, however for delirium at 4-days post-surgery, and did not have as great an influence over delirium at 1-day post-surgery.

Table 31 Summary of zero-order correlations between differences in sleep and delirium

Measure	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*13*	*14*
1. SL	-	-.361	.284	-.034	.031	-.156	.010	-.374	-.283	-.057	-.206	-.284	-.430*	-.285
2. TC	-.361	-	-.694**	.273	.005	.943**	.518*	.682	.600	.450	-.627**	.364	.349	-.148
3. SE	.284	-.694**	-	.264	.483**	-.688**	-.359	-.498**	-.872**	-.461**	-.810**	-.248	-.369	-.064
4. TMIB	-.034	.273	.264	-	.960**	.307	.325	.305	-.265	.122	-.105	-.109	-.166	-.475**
5. TST	.031	.005	.483**	.960**	-	.028	.144	.149	-.451**	-.027	-.304	-.184	-.235	-.441**
6. WASO	-.156	.943**	-.688**	.307	.028	-	.680**	.562**	.573**	.528**	.653**	.217	.177	-.219
7. NOA	.010	.518**	-.359	.325	.144	.680**	-	-.058	.295	.426*	.414*	-.132	-.163	-.174
8. AAL	-.374*	.682**	-.498**	.305	.149	.562**	-.058	-	.331	.273	.364	.344	.421*	-.080
9. MI	-.283	.600**	-.872**	-.265	-.451*	.573**	.295	.331	-	.413*	.865**	.107	.278	-.078
10. FI	-.057	.450*	-.461*	.122	-.027	.528*	.426*	.273	.413*	-	.813 **	.015	.009	-.222
11. SFI	-.206	.627**	-.810**	-.105	-.304	.653**	.414*	.364	.865**	.813**	-	.084	.184	-.165
12. Delirium 1-day	-.280	.364	-.248	-.109	-.184	.217	-.132	.344	.107	.015	.084	-	.404*	.292
13. Delirium 4-days	-.430*	.349	-.369	-.166	-.235	.177	-.163	.421*	.278	.009	.184	.404*	-	.409*
14. Age	-.285	-.148	-.064	-.475*	-.441*	-.219	-.174	-.080	-.078	-.222	-.165	.292	.409*	-

Sleep Latency (SL), Total Counts (TC), Sleep Efficiency (SE), Total Minutes in Bed (TMIB), Total Sleep Time (TST), Wake After Sleep Onset (WASO), Number of Awakenings (NOA), Average Awakening Length (AAL), Movement Index (MI), Fragmentation Index (FI), Sleep Fragmentation Index (SFI)

* = $p < .05$, ** $p < .001$

Table 32 Summary of partial correlations between differences in sleep and delirium

Measure	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*13*
1. SL	-	-.426*	.278	-.201	-.110	-.233	-.041	-.415*	-.320	-.128	-.268	-.215	-.358
2. TC	-.426*	-	-.713**	.233	-.068	.944**	.505*	.680**	.597**	.432*	.618**	.431*	.454*
3. SE	.278	-.713**	-	.265	.507*	-.721**	-.376	-.506*	-.881**	-.489*	-.833**	-.240	-.376
4. TMIB	-.201	.233	.265	-	.950**	.236	.280	.304	-.344	.019	-.211	.035	.035
5. TST	-.110	-.068	.507*	.950**	-	-.078	.076	.127	-.542*	-.143	-.426*	-.064	-.067
6. WASO	-.233	.944**	-.721**	.236	-.078	-	.668**	.559*	.571*	.504*	.641**	.301	.300
7. NOA	-.041	.505*	-.376	.280	.076	.668**	-	-.073	.287	.403*	.397*	-.086	-.103
8. AAL	-.415*	.680**	-.506*	.304	.127	.559*	-.073	-	.326	.262	.357	.385*	.499*
9. MI	-.320	.597**	-.881**	-.344	-.542*	.571*	.287	.326	-	.407*	.866**	.136	.341
10. FI	-.128	.432*	-.489*	.019	-.143	.504*	.403*	.262	.407*	-	.808**	.086	.112
11. SFI	-.268	.618**	-.833**	-.211	-.426*	.641**	.397*	.357	.866**	.808**	-	.140	.280
12. Delirium 1-day	-.215	.431**	-.240	.035	-.064	.301	-.086	.385*	.136	.086	.140	-	.326
13. Delirium 4-days	-.358	.454*	-.376	.035	-.067	.300	-.103	.499**	.341	.112	.280	.326	-

Sleep Latency (SL), Total Counts (TC), Sleep Efficiency (SE), Total Minutes in Bed (TMIB), Total Sleep Time (TST), Wake After Sleep Onset (WASO), Number of Awakenings (NOA), Average Awakening Length (AAL), Movement Index (MI), Fragmentation Index (FI), Sleep Fragmentation Index (SFI)

* = $p < .05$, ** $p < .001$

4.7 Discussion

4.7.1 Key results

This clinical study illustrates changes to sleep behaviour and how changes are associated with delirium risk. These results suggest that differences to normal, habitual sleep as measured by actigraphy were present. Participants did experience changes to their baseline sleep/wake cycle when compared to their sleep following surgery in the hospital. These changes that occurred in the hospital are interpreted as negative changes, or, in other words, 'poorer sleep'.

Due to changes to the original analysis plan, as a result of the lower-than-expected number of participants who scored positive for delirium, results for both Hypothesis 1 and 2 were generated from the same analysis. For Hypothesis 1 and 2, a relationship between sleep and risk for delirium risk was present at both pre- and post-surgery. Participants who experienced an increase in their activity levels and an increase in the amount of time spent awake when they were awoken, were associated with an increase in delirium at 1-day and 4-day post-surgery. The greater degree of change to activity level and average awakening length, the greater the risk of post-operative delirium.

Age did have an influence in controlling for these relationships (except for the relationship between average awakening length and delirium at 1-day post-surgery). Once age was included as a covariate, sleep latency, sleep efficiency, Wake After Sleep Onset (WASO), Movement Index (MI), Fragmentation Index (FI), and Sleep Fragmentation Index (SFI) were not statistically significant. By controlling for age, any age-related changes present are accounted for and our results are independent of this confounding variable.

This present study addresses one of the limitations of the Todd et al. (2017) article as here we have measured sleep objectively at home prior to surgery and in the hospital during the post-surgery time-points. Our study has identified different sleep measures which are associated with an increased risk of post-operative delirium. In Todd et al (2017), sleep disruption was defined as WASO whereas here we have found that both increases to activity levels and average awakening time were risk factors.

For the initial analysis conducted comparing baseline and post-surgery actigraphy, some general comparisons can be made. Here, only total minutes in bed and Total Sleep Time (TST) were statistically significant once age was included as a covariate. The inclusion of age as a covariate is in line with literature as older adults experience changes to their sleep (Edwards et al., 2010), and specifically for TST, a shorter sleep duration (Evans et al., 2021). In this study, our participants spent less time in bed

and less time asleep in hospital when compared to their sleep at home. It may appear unexpected to observe a decrease in time spent in bed having just undergone surgery. As part of supporting the recovery process, participants were encouraged to be active in practicing a series of tailored mobility exercises to help regain movement and flexibility in the joint. These exercises were initially introduced to participants by the pre-surgical team in preparation for surgery. Participants would be gradually regaining their independence in these crucial few days following the operation. Practicing these exercises would involve spending less time in bed, whereby participants would be increasing their mobility by getting up from bed and being more active in the ward. This would facilitate reducing the hospital discharge timeframe, with participants being able to return home sooner.

In addition to this, participants experienced a shorter sleep duration in the hospital when compared to their baseline sleep. This was not an unexpected finding, as identified in Reid (2001), there are many factors that affect the sleep of hospitalised patients. Previous research has identified patients do experience disruptions to their sleep, as well as a reduction in the quality of sleep achieved (Gellerstedt, Medin, & Karlsson, 2014). Environmental factors were found to be positively correlated with sleep disruption in hospital, which include alarms, other patients, medical observations, noise levels, room temperature (Lane & Anne East, 2008). Additionally, physiological factors may have also contributed to changes to sleep in the hospital. Pain, especially in our sample who had recently undergone surgery and likely to be experiencing a degree of discomfort following this, would have contributed to disrupted sleep (Rosenberg, 2001). This is supported by Miller, Roth, Roehrs, and Yaremchuk (2015), a study that also used actigraphy to measure sleep following total hip or knee replacement. Here, self-reported pain scores were found to be significantly correlated with decreased total sleep time. Furthermore, total hip and knee arthroplasty patients were found to have lost on average 1.5 days of sleep after surgery (Krenk, Jennum, & Kehlet, 2012). Although the exact relationship between sleep disruption and pain is not well understood, there is a known association between increased pain perception and reduced sleep quality (Redeker, 2000). Analgesic and or sedative medication is often administered to manage post-operative pain, with the interaction of these contributing to sleep disruption (Onen, Onen, Courpron, & Dubray, 2005). Considering the multitude of factors known to play a role in sleep disruption which are present in the hospital setting, it is not unsurprising that our participants also experienced disruption which resulted in spending less time asleep after surgery when compared to at home.

Two sleep measures were found to be associated with an increased risk for post-operative delirium. One of which was Differences in Total Counts. Considering it was previously highlighted earlier in this section that a potential explanation as to why participants experienced a decrease in time spent in bed was due to their engagement in mobility exercises in the post-operative period, this finding may appear to contradict this. Engaging in mobility exercises would increase the level of activity of an individual, however, the definition of total counts specifically relates to periods of sleep. Here, participants who experienced a greater change in their level of activity whilst asleep were at a higher risk of delirium, and this finding is in line with the literature. The correlation identified a strong positive linear relationship between changes to total counts and delirium score at 1 and 4-day post-surgery. This is despite the small number of participants who met the clinical cut-off threshold for delirium. Despite this being only two participants who met the cut-off for delirium, a relationship between delirium score and sleep was still present. Delirium score did not remain the same throughout the study timepoints, nor did it remain at zero, and although statistically significant changes were not identified between any specific timepoints during the study, a fluctuation in scores was present. Participants may have presented with Subsyndromal Delirium, whereby only some symptoms of delirium were observed, however not a sufficient amount to meet the threshold for delirium. As mentioned in Chapter 1, delirium can be present in different categories, with the hyperactive state is characterised by an increased level of activity (American Psychiatric Association, 2013), providing support for our findings of the association between activity level and delirium risk.

A greater Difference in Average Awakening Lengths was the second sleep measure which was found to be associated with an increased risk of post-operative delirium. This is where there was a greater change in the average amount of time participants spent awake when they were woken up from a sleep period. This result is in line with the literature as this change implies there was greater disruption, specifically to their sleep at night. Out of sleep measures associated with night-time awakenings, only Average Awakening Lengths was statistically significant. Wake After Sleep Onset (WASO) and number of awakenings were not found to be associated with delirium risk. Age-related sleep changes are known to be present, with older adults experiencing greater difficulties in falling asleep (Edwards et al., 2010). This may explain why this specific measure of night-time awakening was significant.

Variations in changes over time observed in scores for cognitive function, level of functional ability, frailty, and sleep disorders were not statistically significant. Age was included as a covariate as

age-related changes are known to have an impact on cognition. This is observed as a decline in processing speed, working memory, and executive cognitive function (Murman, 2015), features of which are included in the assessments that were selected. From the power analysis, it was noted that the data obtained from measures for visual attention, one measure of sustained attention (incorrect suppressions), sleep disorders (periodic limb movement disorder and narcolepsy), and functional ability were all underpowered. The sample size was not sufficiently large enough to ascertain whether statistically significant changes were present over time for these specific measures which may explain some of our results. It is unclear why the other measures (which did have sufficient power) for sustained attention (correct suppressions, successful, unsuccessful, correct trials, estimated standard deviation and coefficient of variability), sleep disorders (sleep apnoea, psychiatric disorders), delirium, cognitive function and fitness, and frailty were not statistically significant.

Age is an important covariate, and its inclusion is justified in this study as it did have an effect on the results, with these observations in line with the literature on sleep habits. When making comparisons between our older adult cohort and published norms, it is important to recognise that sleep needs do change across the lifespan. This is especially the case for sleep duration, where an inverse relationship is present. Older adults experience changes to their normal sleep/wake cycle, specifically phase advance. This results in experiencing greater difficulty to fall asleep, as well as maintaining this sleep (Edwards et al., 2010).

The American National Sleep Foundation provides recommendations and a systematic review of 34 studies by Kocevska (2021) has identified sleep characteristics stratified by age and sex; providing a more specific evaluation of sleep. These recommendations are interesting to draw comparisons from as the NSF is expert-opinion based whereas the systematic review is data-driven, providing a more balanced and comprehensive view of sleep requirements. When comparing actigraphy data obtained in this present study against The American National Sleep Foundation (NSF) report, participants in our present study had shorter sleep durations which did not meet the recommended threshold amount. On average, our sample size slept for 5.5 hours. The NSF recommends 7-8 hours of sleep for older adults (≥ 65 years), with the multidisciplinary expert panel identifying those with a sleep duration of 6 - 9 hours, with a greater level of cognitive functioning, fewer incidences for illnesses, and increased quality of life when compared to those who slept less than this amount. However, it is also important to note that the report specifies excessive sleep, ≥ 9 – 10 hours, were associated with negative outcomes, including an

increased risk for morbidity and mortality, and identified to be a risk marker for older adults requiring additional monitoring for their health.

Additionally, comparison can also be drawn between our data and the reference charts generated from Kocevska (2021), a systematic review consisting of 34 studies published between 2000 and 2017. In this review, sleep characteristics was stratified by age and sex, and included a reference chart for time in bed, total sleep time and sleep efficiency. When comparing our data against the age-specific recommendations outlined in the charts, participants from our study were found to experience poorer sleep than the suggested amounts. Our participants spent less time in bed, had less total sleep time, and reduced sleep efficiency when comparing actigraphy data from both baselines, at home and post-surgery to the recommended values in Kocevska (2021). Our sample are comparatively poorer sleepers than the recommended average. Participants were recruited through opportunity sampling which may have resulted in a sample population which was not truly representative of our target population. Participants who volunteered to take part may have had a personal interest in the research topic as they identify as poor sleepers.

Despite this, it is however important to also note that sleep complaints are not attributed to age alone and occur after taking into account comorbidities (Foley et al., 1996; Foley, Ancoli-Israel, Britz, Walsh, 2004; Vitiello, Moe, & Prinz, 2002). Alongside the presence of medical and psychiatric illnesses, other environmental factors can also have an effect on changes to sleep habits in older adults. This can include lifestyle changes including retirement, physical activity levels, and or moving into a long-term care facility (Neikrug, & Ancoli-Israel, 2010). With a multitude of factors in play, it is important to appreciate inter-individual differences in sleep needs are present, due to genetic and or other factors, and as well as this, these change across the lifespan. It is important to take this into consideration when using published recommendations as there is no specific amount of sleep that can be used as a generalised value across a population. Recommendations should be used as a guideline and sleep needs should aim to achieve the thresholds set in the age-appropriate sleep recommended ranges (Chaput, Dutil, & Sampasa-Kanyinga, 2018).

The actigraphy data obtained provides an insight into the quality and quantity of sleep achieved by those awaiting surgery. In this study, participants were provided with an admission date for their elective procedure, which as well as assisting the study design in being able to obtain an accurate overview of their sleep up to 3-weeks prior to surgery, allowed participants some time to prepare for

their forthcoming stay in hospital. This is a strength of this study as we were able to obtain a current, up-to-date baseline for each participant's sleep for comparison following surgery.

These findings provide support for the importance of sleep, particularly sleep that occurs at home prior to hospitalisation in predicting delirium. This is in line with the findings Todd et al (2017). As well as the predictive value of Wake After Sleep Onset, other sleep parameters observed through actigraphy were found to have a predictive value in post-operative delirium.

4.7.2 Risks and limitations

One of the main limitations of this study is the absence of data on additional factors that may have had an influence on delirium risk. As discussed, a multitude of factors contribute towards sleep quality including and not limited to: length of anaesthesia, pain, medications and environmental factors.

Medications is one of the risk factors for post-operative delirium and the use of pre-operative medication and its effect has been explored in a systematic review by Kassie et al (2017). 29 studies were included in the analysis which found the use of antidepressants, other psychoactive medicines, beta-blockers and nifedipine prior to surgery were statistically significant in their associated with post-operative delirium. The authors suggested the use of preoperative medication is a modifiable factor in reducing delirium risk. In our study data on medication use was not collected routinely and it was therefore not possible to take into account the effects these covariates may have had on our results.

Data on environmental factors was also not collected. Each participant's hospital stay was not standardised and variations in experiences would have been present due to the presence of alarms, disturbances from other patients, number of medical observations (resulting in awakenings), length of stay, noise levels and room temperature. As discussed in 4.7.1, the hospital environment is often disruptive and does not promote sleep, and to capture a more comprehensive view of the hospital sleep experience, our study protocol may have benefited from a self-report method of sleep, namely the Pittsburgh Sleep Quality Index (PSQI), identified to be an appropriate tool for use in our systematic review in Chapter 2. As outlined in the study protocol, the estimated ward stay for this cohort at the time of conducting this study was 4-days after surgery. However, data on discharge dates were not recorded during data collection. When known, this was instead used to arrange the logistics for follow-up visits between the researcher and participant.

Greater incorporation of Patient and Public Involvement (PPI) during the planning of the design of this study would have been beneficial to this study. Some of these oversights may have been

identified prior to submitting the study for ethical approval through discussing the study protocol with both those who have recently undergone elective surgery in hospital, as well as clinicians to identify the scope of what data is feasible to collect in the context of a busy hospital environment.

A case notes template was used to extract medical information for this study, however challenges were encountered with this. The template included information on psychotropic medical use, changes of medication, initiation of new medication, discontinuation of current prescriptions alongside reasons to why this was done as well as adherence to prescribed medication and use of 'as required' medication. There was some confusion when navigating around the topic of medication use. There were instances where it was not possible to ascertain whether a prescribed medication was being taken or not. Some participants explicitly requested for certain information to be omitted in instances where they stated the medication was no longer used, yet they were still being prescribed it. Instead, Max CR-P Score, Max EWS score and Pyrexia was successfully and consistently extracted from case notes and used in this study.

Additionally, the sample size resulted in some challenges in the proposed statistical analysis. With only two participants scoring positive for delirium, as it was not feasible to use the proposed Generalised Estimating Equations (GEE) in this context of this study. To ensure that the results would be applicable to the broader context of sleep and delirium, the analysis plan was amended, with a particular focus on a new variable created to represent differences in change. This did not allow for the intended statistical analysis to take place, limiting the ability to answer the research objectives in line with Todd et al., (2017).

Recruitment was a particularly challenging aspect of conducting this clinical study and the expected number of recruiting 100 participants was not achieved. The 'Winter Crisis' had a significant impact on recruitment figures for the months between December and March 2018 where all elective surgery was postponed. It was not possible to recruit participants within these three months and participants who had been recruited had their surgery cancelled. This is illustrated in Appendix C.5.

Due to the longitudinal nature of the study, multiple visits were required, often to participants' homes. Additionally, the time required to take part may be perceived as too time consuming and intrusive. This is especially true when participants are already preparing for a prolonged stay in hospital, and engaging in a rehabilitation programme to facilitate their recovery following surgery. Alongside the absence of financial incentive for participating, this study may not be viewed as appealing. Participants

were offered a personalised summary of their sleep habits but this may not be viewed as a sufficient reimbursement. The option to include an additional NHS site was explored but ultimately not included as it was not feasible to travel between both sites and be able to recruit and collect data effectively.

The retention rate for baseline assessments to 4-days post-surgery was high, however, this was not the case for the final follow-up at 3-months post-surgery. Attempts were made by the Research Team to contact participants when the final follow-up assessments were due. This was by phone, using the contact number participants provided after being recruited to the study. However, these attempts were not as successful as anticipated. 3-months is a long period of time and many changes may have occurred, and participants may no longer be interested in participating. The contact information held by the Research Team may no longer be up-to-date, as participants may have moved or changed their contact information.

There was also no financial reward for participating. Patients may instead be motivated by a vested interest in the topic area as the focus of the study was on their specific population. Findings that contribute to improvements to healthcare are of benefit to them, or their friends and family. This may not result in immediate benefits, but instead a more long-term investment for the future of research in the hospital setting. Participants were offered a personalised summary of their sleep, as recorded by actigraphy, and received additional monitoring by a member of the research team for delirium. However, this may not be viewed as a sufficient reimbursement for the 3 hour and 45-minute total assessment time across the multiple time-points having just undergone or about to undergo a surgical procedure. This could have also contributed to the low retention rate observed after 4-days post-surgery when attempts were made to contact participants for the follow up at 3-months post-surgery for a final, 55-minute assessment.

Some participants declined to complete computerised tests during a visit. This resulted in missing data. Reasons for this included inability to concentrate, feeling dizzy or sick and in some cases just a strong dislike for the sustained attention task. An inability to concentrate is one of the symptoms of delirium and may suggest that some participants experienced sub-clinical delirium but this was not detected through the computerised task.

As the systematic review in Chapter 2 was carried out in parallel to this study, it was not possible to apply the recommendations into the design this study. On reflection, it may have been more appropriate to have used either the Sleep Symptom Checklist (SSC), and or the Pittsburgh Sleep Quality

Index (PSQI), instead of the Sleep Disorders Questionnaire (SDQ). Both of these tools were recommended for use in research contexts. The SSC is a more general screening tool that would have been able to identify participants with signs and symptoms of a sleep disorder and has the potential to be incorporated as part of the baseline assessments to identify participants at baseline greater risk of delirium. The PSQI would be a useful self-report method to measure changes in sleep quality over the course of the study duration.

Ultimately the SDQ was used in this study to identify the presence of sleep disorders, and challenges were encountered with its use. Specific questions caused confusion and discomfort with some participants refusing to answer. This resulted in missing data. As discussed, an alternative questionnaire of either the SSC or PSQI may have been more appropriate, and effective, in this context. The Researcher could have also introduced the assessment more effectively by further elaborating its purpose within the context of the study. This may have helped participants understand why these questions were being asked. Examples of these included:

- Age – all participants were over the age of 70 as part of the inclusion criteria and would (and should) be ticking the category '71+'. Some participants thought this was a trick question.
- Driving – there were multiple questions on this, due to age, not all participants were still able to drive legally.
- Work – due to the age of participants, this question did not accommodate for retirement. It also caused some confusion as some participants answered the question based on their current volunteering activities which is not necessarily paid work as initially interpreted from the question.
- Sex – several participants declined to answer as they felt the nature of these questions was too personal and uncomfortable, especially in instances when they had been recently widowed (and the research team was unaware of this). Others viewed these as irrelevant due to their age.

Participants were frequently observed to have difficulty in reading the questionnaire because of the small font size. There was also the issue where participants occasionally responded using the incorrect Likert scale (one question above or below the one they should have used) because of the way the question was presented. Participation feedback stated the assessment battery was too time consuming. Following this feedback, a more concise version of the SDQ questionnaire was used. Only questions relevant to the research study were included in this condensed version. Additionally, font size was increased and the questions and Likert scales were placed in a table to reduce response errors as

participants could easily navigate to the end of the page following the box to respond in the corresponding section. This was however not a validated method of administering this assessment.

With the sustained attention task, there were inconsistencies in assessment execution due to the differences between the setting of a participant's home and in a (often) loud, busy hospital environment that also contained many distractions. The placement and positioning of the laptop (used for data collection) was not consistent as this varied from being placed on the participants lap to the foldout table on their hospital bed. On the researcher's discretion this was not actively standardised as participant comfort was prioritised. For example, it was found that it was more comfortable for participants who have had a Total Knee Replacement to place it on their lap, and for Total Hip Replacement on a desk so no pressure was being applied to the joint. This variation meant factors such as screen distance could not be controlled for which would have changed the size of the digits on the screen, potentially impacting response accuracy and time taken.

It was also the first time using a computer for many participants. To accommodate for any practice effects the task was completed three times at each time-point and the final one was used for analysis. As well as accommodating for practice effects this also helped participants familiarise themselves with the laptop and the keyboard. There was however still confusion with some participants pressing an incorrect key (near to the spacebar) when they moved their finger without realising it as they were focused on the numbers on the screen. Participants were reminded and attempts were made to encourage participants to readjust their positioning so they were pressing the correct key.

On the visual attention task, the letter 'I' and the number '1' look very similar and this was noted by many participants who made an error on part B of the visual attention task by starting at 'I' instead of '1' because they had mistaken it for the other. This was put down to poor eyesight and on noticing this error, participants were prompted to correct erroneous responses to this task.

4.8 Chapter summary

This Chapter explores the relationship between pre- and post-operative sleep and delirium, where the pre-operative baseline for sleep quality is taken at home. Initial suggestions on how this can be applied in elective surgery include greater preparation in the weeks prior to surgery. This could be done by emphasising the importance of sleep to patients so they have a greater understanding of how this may affect their recovery. The addition of validated questionnaires could be included and form part

of the pre-admission process where fitness for surgery is assessed. It may be appropriate to explore a patient's suitability for surgery if concerns are raised from sleep habits reported.

Chapter 5: Discussion

This Thesis has explored the importance of sleep and the implications that changes to the habitual sleep/wake cycle have on the manifestation of sub-syndromic delirium. It has added to the body of work on sleep screening tools, sleep propensity, objectively measured sleep and post-operative delirium.

The novel systematic review contributes by providing guidance on screening tools for sleep disorders and the assessment of sleep quality in older adults that has not previously existed. Systematic reviews are used in health research to ensure that decisions are made using the best evidence. All relevant studies on a particular topic are summarised and evaluations are made (Gopalakrishnan & Ganeshkumar, 2013). Tools used in primary research of sleep quality, behaviour and or disorder in older adults that reported concurrent validity and or diagnostic accuracy were included. This review provides recommendations for the use of each tool, tailoring this to the perceived needs of both a clinician and a researcher in instances where greater specificity would be more favourable than that of required time to complete. The implications of the systematic review were discussed, where it is highlighted that there are variations present in the literature, the inconsistent use of screening tools and risk of bias and applicability concerns around the quality of some of the studies included in the analysis. Unfortunately, as each of the chapters were carried out in parallel, it was not possible to apply the emerging recommendations into the design of each study.

Recommendations from the systematic review has implications for being integrated into routine healthcare. A significant amount of valid and reliable information can be obtained from these assessments which are quick to administer. Sleep is a known risk factor and disruptions to sleep are a common feature of delirium. Screening tools can assist in identifying individuals who are at higher risk prior to hospitalisation, improving patient outcomes through helping those with poorer baseline sleep quality prepare for their upcoming stay. It is also important to note that the systematic review was conducted in 2017 and new evidence may have emerged since that provides additional guidance on the recommendation for the use of these tools.

The first study, a 24-hour sleep deprivation paradigm investigated the effect sleep propensity had on the neuropsychological profile of healthy adults. The increased pressure to sleep following the sleep loss, induced reversible changes to sustained attention, visual attention, and psychotic-like symptoms. It was of particular interest to observe scores for a validated measure of delirium, the

Delirium Rating Scale R-98, fluctuate over the course of the study duration. Attentional deficits were observed in the variability of reaction time, which would otherwise not have been detected without the introduction of computerised assessments.

Future research should address whether the deficits in attentional functioning observed were due to biological changes during periods of normal sleep as opposed to wakefulness, or whether sleep propensity was high due to sleep loss from the deprivation paradigm. The use of an objective method to measure circadian rhythm should be explored. One alternative would be to measure melatonin levels. Melatonin is a hormone released by the pineal gland and its production is a known marker for the circadian rhythm (Lerner, Case, Takahashi, Lee, Mori, 1958). However, this is a more intrusive method involving saliva sampling every 30-minute. A more practical method would be to measure body temperature at more regular intervals than the seven time-points used.

Additionally, a greater control over environmental factors is important to improve this study protocol. Challenges were encountered when attempting to limit light levels in the laboratory. Light has a strong exogenous influence over the sleep/wake cycle and would have had an effect on inhibiting sleep propensity. Additional considerations should be made about the spaces used for such studies alongside a pilot study to ensure the environment is suitable prior to undergoing full recruitment.

The clinical study investigated the emergence of post-operative delirium within the hospital environment in a group of older adults scheduled for elective hip or knee replacement surgery. This was prioritised due to its clinical nature and the additional stages required prior to being able to start data collection and ran concurrently alongside the systematic review and laboratory study. This study was novel as it included collecting actigraphy data at baseline, in a familiar environment (the participant's home), which was compared against actigraphy data collected during the post-surgical period. Results suggested a relationship between sleep and risk for delirium risk was present for both pre- and post-surgery sleep.

Participants who experienced an increase to their activity levels and an increase in the amount of time spent awake when they were awoken, were associated with an increase in delirium at 1-day and 4-days post-surgery. The greater degree of change to activity level and average awakening length, the greater the risk of post-operative delirium. More general comparisons were also made between sleep at home and in the hospital. Participants experienced changes to their normal habitual sleep, with

participants spending less time in bed, less time asleep, and sleeping for a shorter period of time in hospital when compared to their sleep at home.

These findings are important as additional risk factors for post-operative delirium have been identified. Our study builds on the findings from Todd et al., (2017) where Wake After Sleep Onset (WASO) was found to be a risk factor for post-operative delirium. Here, we have identified additional sleep measures which increase the risk of post-operative delirium, as well as adding to our knowledge and understanding of sleep disruption in the hospital environment in the older adult population.

We report participants who spent more time awaken when awoken were at greater risk of post-operative delirium. Reducing the likelihood of these disruptions occurring during periods participants normally sleep may see improvements to their sleep quality in hospital. Individualised timetables, tailored to each patient's sleep/wake cycle may assist in reducing disruption during routine care (although the feasibility of this is questionable in hospital environments). The routine monitoring of changes to sleep is recommended to identify those who develop a greater risk of delirium during hospitalisation.

Further research is required to address the methodological limitations of the study. As discussed in Chapter 4, more data, particularly on the length of anaesthesia, pain, medications and environmental factors, all of which are contributing factors to the development of delirium, need to be collected. Self-report measures for sleep quality, such as the Pittsburgh Sleep Quality Index (PSQI), and devices to measure noise levels and temperature changes could also be incorporated into the study protocol to better capture the more individualised experiences of sleep disruption alongside actigraphy. Greater Patient Public Involvement (PPI) will also be beneficial in adapting the study protocol to ensure it is fit for purpose, not too intrusive, and or burdensome for participants undergoing a major surgical procedure. Challenges with participant recruitment were encountered and certain aspects of the clinical design may have been problematic for participants. It required visits to their homes, as well as monitoring them before, and very shortly after surgery. Alternatives to these visits taking place elsewhere was not made available to participants. This can be viewed as intrusive as the Researcher would be entering their private homes. Individuals may also not want to have to arrange these additional visits as it requires organising a mutually convenient time, adding to the burden of participation.

Other methodological limitations of this Thesis include the inconsistencies between the use of screening tools used and the recommendations that emerged from the systematic review. This includes the Sleep Disorders Questionnaire (SDQ) which was used in screening for sleep disorders and formed an integral part of the screening process in both the laboratory and clinical study. The SDQ was not included in the systematic review. This implied it did not meet the inclusion criteria whereby there were no articles comparing its validity and accuracy against objective sleep measures within the older adult population. None of the participants across any of the three studies were excluded from the study for scoring positive for a sleep disorder using the SDQ. As the SDQ was not included in the review, it is not possible the assess whether this tool was able to effectively exclude participants who had a sleep disorder. Participants with pre-existing sleep disorders, would have otherwise been excluded if instead the Sleep Symptom Checklist (SSC) (Bailes et al., 2008), one of the recommendations that emerged from the review, was used. The final sample may therefore include participants with a sleep disorder, limiting the generalisability of the study.

The Stanford Sleepiness Scale (Hoddes, Dement, & Zarcone, 1972) was used in the laboratory study, and was again not included as part of the systematic review. As with the SDQ this raises issues around the validity of the subjective sleepiness data that was obtained which has significant implications on our results. To assess daytime sleepiness, the systematic review recommended the Karolinska Sleepiness Scale (KSS) (Paavilainen et al., 2005). The KSS would be appropriate for use as it is able to measure daytime sleepiness at a particular time during the day; even able to accommodate for the multiple time-points across a 24-hour period. The sleep diary that accompanied the actigraphy monitoring used was an adapted version of the Pittsburgh Sleep Diary. This, despite containing the same information, is again not a validated measure. The sleep diary was supplementary to the actigraphy measures obtained and was not used as the primary method of assessing sleep. It was used to identify episodes that were incorrectly interpreted as sleep or wakefulness. As this was used alongside the actigraphy and not used to screen participants, the risk of using this unvalidated measure is comparatively low (when compared against the use of the SDQ and SSS). The original Pittsburgh Sleep Diary supplementing actigraphy should be used.

This Thesis was unable to methodologically build on each Chapter based on the findings of the previous Chapter. There was a lack of consistency in the measures that were used in each study (i.e. subjective sleepiness and actigraphy). On reflection, it may have been more appropriate to prioritise on the systematic review first, ensuring the recommendations that emerge form as part of the study

protocols. Although this decision may require further consideration as the clinical study did take a significant amount of preparation time prior to recruiting the first participant. Regardless, a re-ordering of the Thesis timeline would have helped to ensure the quality of the data obtained is not compromised.

This Thesis has contributed to the ongoing literature on sleep and delirium. A lack of appreciation of the importance of good sleep is present across multiple domains. It has provided recommendations on sleep screening tools, which are optimised for use in a population at an increased risk of developing delirium. These tools are effective in identifying those with pre-existing sleep disruptions using subjective methods that are quick and easy to administer, and should be included as part of regular, routine medical management. The clinical study has also contributed to identifying specific types of sleep disruption which occur between pre and post-surgery which increases the risk for post-operative delirium. The pre-hospitalisation routine for elective surgery should include maintaining good sleep habits.

As a researcher, this PhD journey has allowed me to have a greater understanding and appreciation of conducting clinical research. The primary purpose of health research is to increase our understanding of a specific element of human health, but it is important that this goal does not take precedence over the best interests of the research participants. This Thesis has provided me the opportunity to apply this to multiple research designs across a range of settings, allowing me to apply this knowledge in a range of settings, aiding my growth and development as a researcher.

References

Actigraph. Actilife [Computer Software]. Retrieved from www.actigraphcorp.com/

Adamis, D., Sharma, N., Whelan, P. J., & Macdonald, A. J. (2010). Delirium scales: a review of current evidence. *Aging & mental health*, *14*(5), 543-555.

Ahmed, S., Leurent, B., & Sampson, E. L. (2014). Risk factors for incident delirium among older people in acute hospital medical units: a systematic review and meta-analysis. *Age and ageing*, *43*(3), 326-333.

Alhola, P., & Polo-Kantola, P. (2007). Sleep deprivation: Impact on cognitive performance. *Neuropsychiatric disease and treatment*.

Alzahrani, H., & Venneri, A. (2015). Cognitive and neuroanatomical correlates of neuropsychiatric symptoms in Parkinson's disease: A systematic review. *Journal of the Neurological Sciences*, *356*(1–2), 32–44. http://doi.org/10.1016/j.jns.2015.06.037

American Psychiatric Association. (1980). *Diagnostic and Statistical Manual of Mental Disorders* (3rd ed.). Washington, DC: Author.

American Psychiatric Association. (1987). *Diagnostic and statistical manual of mental disorders* (3rd ed., rev.).

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Washington, DC: Author.

American Sleep Disorders Association. *International classification of sleep disorders (ICSD): diagnostic and coding manual.* Rochester, MN: American Sleep Disorders Association, 1990.

Ancoli-Israel, S., Clopton, P., Klauber, M. R., Fell, R., & Mason, W. (1997). Use of wrist activity for monitoring sleep/wake in demented nursing-home patients. *Sleep*, *20*(1), 24-27.

Arendt, J. (1994). *Melatonin and the mammalian pineal gland*. Springer Science & Business Media.

Bailes, S., Baltzan, M., Rizzo, D., Fichten, C. S., Amsel, R., & Libman, E. (2008). A diagnostic symptom profile for sleep disorder in primary care patients. *Journal of Psychosomatic Research, 64*(4), 427-433. doi:10.1016/j.jpsychores.2007.10.011 [doi]

Baillet, M., Cosin, C., Schweitzer, P., Peres, K., Catheline, G., Swendsen, J., & Mayo, W. (2016). Mood influences the concordance of subjective and objective measures of sleep duration in older adults. *Frontiers in Aging Neuroscience, 8*, 181. doi:10.3389/fnagi.2016.00181 [doi]

Bastien, C. H., Vallieres, A., & Morin, C. M. (2001). Validation of the insomnia severity index as an outcome measure for insomnia research. *Sleep Medicine, 2*(4), 297-307. doi:S1389945700000654 [pii]

Beaudreau, S. A., Spira, A. P., Stewart, A., Kezirian, E. J., Lui, L. Y., Ensrud, K., . . . Study of Osteoporotic Fractures. (2012). Validation of the pittsburgh sleep quality index and the epworth sleepiness scale in older black and white women. *Sleep Medicine, 13*(1), 36-42. doi:10.1016/j.sleep.2011.04.005 [doi]

Beck, A. T. (1970). *Depression: Causes and Treatment*. Philadelphia: University of Pennsylvania Press.

Beck, A. T., Steer, R. A., & Brown, G. K. (1996). Beck depression inventory-II. *San Antonio*, *78*(2), 490-498.

Bernert, R. A., Turvey, C. L., Conwell, Y., & Joiner, T. E. (2014). Association of poor subjective sleep quality with risk for death by suicide during a 10-year period: a longitudinal, population-based study of late life. *JAMA psychiatry*, *71*(10), 1129-1137.

Bes F, Jobert M, Schulz H. Modeling napping, post-lunch dip, and other variations in human sleep propensity. *Sleep*. 2009, 32(3): 392-398.

Bo, M., Martini, B., Ruatta, C., Massaia, M., Ricauda, N. A., Varetto, A., ... & Torta, R. (2009). Geriatric ward hospitalization reduced incidence delirium among older medical inpatients. *The American Journal of Geriatric Psychiatry*, *17*(9), 760-768.

Boeve, B. F., Molano, J. R., Ferman, T. J., Lin, S. C., Bieniek, K., Tippmann-Peikert, M., . . . Silber, M. H. (2013). Validation of the mayo sleep questionnaire to screen for REM sleep behavior disorder in a community-based sample. *Journal of Clinical Sleep Medicine : JCSM : Official Publication of the American Academy of Sleep Medicine, 9*(5), 475-480. doi:10.5664/jcsm.2670 [doi]

Boeve, B. F., Molano, J. R., Ferman, T. J., Smith, G. E., Lin, S. C., Bieniek, K., . . . Silber, M. H. (2011). Validation of the mayo sleep questionnaire to screen for REM sleep behavior disorder in an aging and dementia cohort. *Sleep Medicine, 12*(5), 445-453. doi:10.1016/j.sleep.2010.12.009 [doi]

Bombois, S., Derambure, P., Pasquier, F., & Monaca, C. (2010). Sleep disorders in aging and dementia. *The journal of nutrition, health & aging*, *14*(3), 212-217.

Borbély, A. A. (1980). Sleep: circadian rhythm versus recovery process. *Functional states of the brain: Their determinants*, 151-161.

Borbély, A. A., & Achermann, P. (1999). Sleep homeostasis and models of sleep regulation. *Journal of biological rhythms*, *14*(6), 559-570.

Bruze, M., Boman, A., Bergqvist-Karlsson, A., Björkner, B., Wahlberg, J. E., & Voog, E. (1988). Contact allergy to a cyclohexanone resin in humans and guinea pigs. *Contact Dermatisis, 18*(1), 46–49. http://doi.org/doi:10.1111/j.1600-0536.1988.tb05489.x

Bryant, P. A., Trinder, J., & Curtis, N. (2004). Sick and tired: does sleep have a vital role in the immune system?. *Nature Reviews Immunology*, *4*(6), 457.

Buysse, D. J., Reynolds III, C. F., Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry research*, *28*(2), 193-213.

Buysse, D. J., Reynolds, C. F.,3rd, Monk, T. H., Hoch, C. C., Yeager, A. L., & Kupfer, D. J. (1991). Quantification of subjective sleep quality in healthy elderly men and women using the pittsburgh sleep quality index (PSQI). *Sleep, 14*(4), 331-338.

Caraceni, A., & Grassi, L. (2011). *Delirium: acute confusional states in palliative medicine*. Oxford University Press.

Chaput, J. P., Dutil, C., & Sampasa-Kanyinga, H. (2018). Sleeping hours: what is the ideal number and how does age impact this?. *Nature and science of sleep*, *10*, 421.

Chen, C. J. (2013). *The Investigation and Measurement of Quality of Sleep in Individuals with Osteoarthritis in Taiwan: A cross-sectional survey* (Doctoral dissertation, The University of Manchester (United Kingdom)).

Cheyne, J. A., Solman, G. J., Carriere, J. S., & Smilek, D. (2009). Anatomy of an error: A bidirectional state model of task engagement/disengagement and attention-related errors. *Cognition*, *111*(1), 98-113.

Christos, G. A. (1993). Is Alzheimer's disease related to a deficit or malfunction of rapid eye movement (REM) sleep?. *Medical hypotheses*, *41*(5), 435-439.

Cohen, J. (1992). A power primer. *Psychological bulletin*, *112*(1), 155.

Cole, M. G., Ciampi, A., Belzile, E., & Dubuc-Sarrasin, M. (2013). Subsyndromal delirium in older people: a systematic review of frequency, risk factors, course and outcomes. *FOCUS*, *11*(4), 534-543.

Corporate Information Governance (2019). *Confidentiality Policy.* Retrieved from https://www.england.nhs.uk/publication/confidentiality-policy/

Curcio, G., Tempesta, D., Scarlata, S., Marzano, C., Moroni, F., Rossini, P. M., . . . De Gennaro, L. (2013). Validity of the italian version of the pittsburgh sleep quality index (PSQI). *Neurological Sciences : Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology, 34*(4), 511-519. doi:10.1007/s10072-012-1085-y [doi]

Czeisler, C. A., & Gooley, J. J. (2007, January). Sleep and circadian rhythms in humans. In *Cold Spring Harbor symposia on quantitative biology* (Vol. 72, pp. 579-597). Cold Spring Harbor Laboratory Press.

Czeisler, C. A., & Buxton, O. M. (2010). The human circadian timing system and sleep-wake regulation. In *Principles and Practice of Sleep Medicine: Fifth Edition* (pp. 402-419). Elsevier Inc..

De, J., & Wand, A. P. (2015). Delirium screening: a systematic review of delirium screening tools in hospitalized patients. *The Gerontologist*, *55*(6), 1079-1099.

Department of Health and Social Care (2016, August). *UK Chief Medical Officers' Low Risk Drinking Guidelines*. Retrieved from www.gov.uk/government/publications/alcohol-consumption-advice-on-low-risk-drinking

Dew, M. A., Reynolds, C. F.,3rd, Monk, T. H., Buysse, D. J., Hoch, C. C., Jennings, R., & Kupfer, D. J. (1994). Psychosocial correlates and sequelae of electroencephalographic sleep in healthy elders. *Journal of Gerontology, 49*(1), P8-18.

Di Lorenzo, F., Ponzo, V., Bonnì, S., Motta, C., Negrão Serra, P. C., Bozzali, M., … Koch, G. (2016). Long-term potentiation–like cortical plasticity is disrupted in Alzheimer's disease patients independently from age of onset. *Annals of Neurology, 80*(2), 202–210. http://doi.org/10.1002/ana.24695

Di Milia, L., Adan, A., Natale, V., & Randler, C. (2013). Reviewing the psychometric properties of contemporary circadian typology measures. *Chronobiology International*, *30*(10), 1261-1271.

Dinges, D. F., & Kribbs, N. B. (1991). Performing while sleepy: effects of experimentally-induced sleepiness.

Dos Santos Silva, M., Bazzana, C. M., de Souza, A. L., Ramos, L. R., Tufik, S., Lucchesi, L. M., & Lopes, G. S. (2015). Relationship between perceived sleep and polysomnography in older adult patients. *Sleep Science (Sao Paulo, Brazil), 8*(2), 75-81. doi:10.1016/j.slsci.2015.04.002 [doi]

Douglass, A. B., Bomstein, R., Nino-Murcia, G., Keenan, S., Miles, L., Zarcone Jr, V. P., ... & Dement, W. C. (1994). The sleep disorders questionnaire I: creation and multivariate structure of SDQ. *Sleep*, *17*(2), 160-167.

Driver, H. S., & Taylor, S. R. (2000). Exercise and sleep. *Sleep medicine reviews*, *4*(4), 387-402.

Durmer, J. S., & Dinges, D. F. (2005, March). Neurocognitive consequences of sleep deprivation. In *Seminars in neurology* (Vol. 25, No. 01, pp. 117-129). Copyright© 2005 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA..

Ebrahim, I. O., Shapiro, C. M., Williams, A. J., & Fenwick, P. B. (2013). Alcohol and sleep I: effects on normal sleep. *Alcoholism: Clinical and Experimental Research*, *37*(4), 539-549.

Edwards, B. A., O'Driscoll, D. M., Ali, A., Jordan, A. S., Trinder, J., & Malhotra, A. (2010, October). Aging and sleep: physiology and pathophysiology. In *Seminars in respiratory and critical care medicine* (Vol. 31, No. 05, pp. 618-633). © Thieme Medical Publishers.

Eisensehr, I., v Lindeiner, H., Jäger, M., & Noachtar, S. (2001). REM sleep behavior disorder in sleep-disordered patients with versus without Parkinson's disease: is there a need for polysomnography?. *Journal of the neurological sciences*, *186*(1-2), 7-11.

Engel, G. L., & Romano, J. (1959). Delirium, a syndrome of cerebral insufficiency. *Journal of chronic diseases*, *9*(2-3), 260-277.

Ensrud, K. E., Blackwell, T. L., Ancoli-Israel, S., Redline, S., Cawthon, P. M., Paudel, M. L., … Stone, K. L. (2012). Sleep disturbances and risk of frailty and mortality in older men. *Sleep Medicine, 13*(10), 1217–1225. http://doi.org/10.1016/j.sleep.2012.04.010

Evans, M. A., Buysse, D. J., Marsland, A. L., Wright, A. G., Foust, J., Carroll, L. W., ... & Hall, M. H. (2021). Meta-analysis of age and actigraphy-assessed sleep characteristics across the lifespan. *Sleep*, *44*(9).

f.lux [Computer Software]. Retrieved from https://justgetflux.com/

Faul, F., Erdfelder, E., Buchner, A., & Lang, A.-G. (2009). Statistical power analyses using G*Power 3.1: Tests for correlation and regression analyses. *Behavior Research Methods*, *41*, 1149-1160.

Figueroa-Ramos, M. I., Arroyo-Novoa, C. M., Lee, K. A., Padilla, G., & Puntillo, K. A. (2009). Sleep and delirium in ICU patients: a review of mechanisms and manifestations. *Intensive care medicine*, *35*(5), 781-795.

Fisher, S. (1980). The microstructure of dual-task interaction. 4. Sleep deprivation and the control of attention. *Perception*, *9*(3), 327-337.

FitzGerald, J. M., O'Regan, N., Adamis, D., Timmons, S., Dunne, C. P., Trzepacz, P. T., & Meagher, D. J. (2017). Sleep-wake cycle disturbances in elderly acute general medical inpatients: Longitudinal relationship to delirium and dementia*. Alzheimer's and Dementia: Diagnosis, Assessment and Disease Monitoring, 7*, 61–68. http://doi.org/10.1016/j.dadm.2016.12.013

Flacker, J. M., Cummings, V., Mach Jr, J. R., Bettin, K., Kiely, D. K., & Wei, J. (1998). The association of serum anticholinergic activity with delirium in elderly medical patients. *The American Journal of Geriatric Psychiatry*, *6*(1), 31-41.

Foley, D. J., Monjan, A. A., Brown, S. L., Simonsick, E. M., Wallace, R. B., & Blazer, D. G. (1995). Sleep complaints among elderly persons: an epidemiologic study of three communities. *Sleep*, *18*(6), 425-432.

Foley, D., Ancoli-Israel, S., Britz, P., & Walsh, J. (2004). Sleep disturbances and chronic disease in older adults: results of the 2003 National Sleep Foundation Sleep in America Survey. *Journal of psychosomatic research*, *56*(5), 497-502.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. *Journal of psychiatric research*, *12*(3), 189-198.

Foreman, M. D. (1989). Confusion in the hospitalized elderly: incidence, onset, and associated factors. *Research in Nursing & Health*, *12*(1), 21-29.

Foy, A., O'Connell, D., Henry, D., Kelly, J., Cocking, S., & Halliday, J. (1995). Benzodiazepine use as a cause of cognitive impairment in elderly hospital inpatients. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, *50*(2), M99-M106.

Fong, T. G., Tulebaev, S. R., & Inouye, S. K. (2009). Delirium in elderly adults: diagnosis, prevention and treatment. *Nature reviews neurology*, *5*(4), 210.

Franco, J. G., Valencia, C., Bernal, C., Ocampo, M. V., Trzepacz, P. T., Pablo, J. D., & Mejía, M. A. (2010). Relationship between cognitive status at admission and incident delirium in older medical inpatients. *The Journal of neuropsychiatry and clinical neurosciences*, *22*(3), 329-337.

Fried, P. J., Schilberg, L., Brem, A.-K., Saxena, S., Wong, B., Cypess, A. M., … Pascual-Leone, A. (2017). Humans with Type-2 Diabetes Show Abnormal Long-Term Potentiation-Like Cortical Plasticity Associated with Verbal Learning Deficits HHS Public Access. *J Alzheimers Dis, 55*(1), 89–100. http://doi.org/10.3233/JAD-160505

Fung, C. H., Martin, J. L., Chung, C., Fiorentino, L., Mitchell, M., Josephson, K. R., . . . Alessi, C. (2012). Sleep disturbance among older adults in assisted living facilities. *The American Journal of Geriatric Psychiatry : Official Journal of the American Association for Geriatric Psychiatry, 20*(6), 485-493. doi:10.1097/JGP.0b013e318252e3e0 [doi]

Fung, C. H., Vaughan, C. P., Markland, A. D., Huang, A. J., Mitchell, M. N., Bliwise, D. L., . . . Stone, K. (2017). Nocturia is associated with poor sleep quality among older women in the study of osteoporotic fractures. *Journal of the American Geriatrics Society, 65*(11), 2502-2509. doi:10.1111/jgs.15027 [doi]

Gehrman, P. R., Martin, J. L., Shochat, T., Nolan, S., Corey-Bloom, J., & Ancoli-Israel, S. (2003). Sleep-disordered breathing and agitation in institutionalized adults with Alzheimer disease. *The American journal of geriatric psychiatry*, *11*(4), 426-433.

Gellerstedt, L., Medin, J., & Karlsson, M. R. (2014). Patients' experiences of sleep in hospital: a qualitative interview study. *Journal of Research in Nursing*, *19*(3), 176-188.

Gillick, M. R., Serrell, N. A., & Gillick, L. S. (1982). Adverse consequences of hospitalization in the elderly. *Social science & medicine*, *16*(10), 1033-1038.

Glisky, E. L. (2007). Changes in cognitive function in human aging. *Brain aging*, 3-20.

Gopalakrishnan, S., & Ganeshkumar, P. (2013). Systematic reviews and meta-analysis: understanding the best evidence in primary healthcare. *Journal of family medicine and primary care*, *2*(1), 9.

GOV.UK (2018). *Writing about ethnicity.* Retrieved from https://www.ethnicity-facts-figures.service.gov.uk/style-guide/writing-about-ethnicity

González, M., Martínez, G., Calderón, J., Villarroel, L., Yuri, F., Rojas, C., ... & Carrasco, M. (2009). Impact of delirium on short-term mortality in elderly inpatients: a prospective cohort study. *Psychosomatics*, *50*(3), 234-238.

Grandner, M. A., Kripke, D. F., YOON, I. Y., & Youngstedt, S. D. (2006). Criterion validity of the Pittsburgh Sleep Quality Index: Investigation in a non-clinical sample. *Sleep and biological rhythms*, *4*(2), 129-136.

Guarnieri, B., Adorni, F., Musicco, M., Appollonio, I., Bonanni, E., Caffarra, P., ... & Ferrara, S. (2012). Prevalence of sleep disturbances in mild cognitive impairment and dementing disorders: a multicenter Italian clinical cross-sectional study on 431 patients. *Dementia and geriatric cognitive disorders*, *33*(1), 50-58.

Gunther, M. L., Morandi, A., & Ely, E. W. (2008). Pathophysiology of delirium in the intensive care unit. *Critical care clinics*, *24*(1), 45-65.

Han, L., McCusker, J., Cole, M., Abrahamowicz, M., Primeau, F., & Elie, M. (2001). Use of medications with anticholinergic effect predicts clinical severity of delirium symptoms in older medical inpatients. *Archives of internal medicine*, *161*(8), 1099-1105.

Hanania, M., & Kitain, E. (2002). Melatonin for treatment and prevention of postoperative delirium. *Anesthesia & Analgesia*, *94*(2), 338-339.

Happe, S., Klösch, G., Lorenzo, J., Kunz, D., Penzel, T., Röschke, J., ... & Zeitlhofer, J. (2005). Perception of sleep: Subjective versus objective sleep parameters in patients with Parkinson's disease in comparison with healthy elderly controls. *Journal of neurology*, *252*(8), 936-943.

Harrison, Y., & Horne, J. A. (2000). The impact of sleep deprivation on decision making: a review. *Journal of experimental psychology: Applied*, *6*(3), 236.

Health Research Authority (2017). *UK Policy Framework for Health and Social Care Research.* Retrieved from https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/uk-policy-framework-health-and-social-care-research/

Health Research Authority (2020). *Governance Arrangements for Research Ethics Committees.* Retrieved from https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/governance-arrangement-research-ethics-committees/

Heffler, S., Levit, K., Smith, S., Smith, C., Cowan, C., Lazenby, H., & Freeland, M. (2001). Health spending growth up in 1999; Faster growth expected in the future. *Health Affairs, 20*(2), 193–203. http://doi.org/10.1377/hlthaff.20.2.193

Herrscher, T. E., Akre, H., Øverland, B., Sandvik, L., & Westheim, A. S. (2011). High prevalence of sleep apnea in heart failure outpatients: even in patients with preserved systolic function. *Journal of cardiac failure*, *17*(5), 420-425.

Hirshkowitz, M., Whiton, K., Albert, S. M., Alessi, C., Bruni, O., DonCarlos, L., ... & Ware, J. C. (2015). National Sleep Foundation's updated sleep duration recommendations. *Sleep health*, *1*(4), 233-243.

Hoddes E., Dement W.C., Zarcone V. (1972). The development and use of the Stanford Sleepiness Scale (SSS). *Psychophysiology, 150*(9).

Horne, J. A., & Östberg, O. (1976). A self-assessment questionnaire to determine morningness-eveningness in human circadian rhythms. *International journal of chronobiology*.

Hshieh, T. T., Fong, T. G., Marcantonio, E. R., & Inouye, S. K. (2008). Cholinergic deficiency hypothesis in delirium: a synthesis of current evidence. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, *63*(7), 764-772.

Hshieh, T. T., Yue, J., Oh, E., Puelle, M., Dowal, S., Travison, T., & Inouye, S. K. (2015). Effectiveness of multicomponent nonpharmacological delirium interventions: a meta-analysis. *JAMA internal medicine*, *175*(4), 512–520. https://doi.org/10.1001/jamainternmed.2014.7779

Hubbard, A. E., Ahern, J., Fleischer, N. L., Van der Laan, M., Satariano, S. A., Jewell, N., ... & Satariano, W. A. (2010). To GEE or not to GEE: comparing population average and mixed models for estimating the associations between neighborhood risk factors and health. *Epidemiology*, 467-474.

Huibers, M. J. H., Leone, S. S., van Amelsvoort, L. G. P. M., Kant, I., & Knottnerus, J. A. (2007). Associations of fatigue and depression among fatigued employees over time: a 4-year follow-up study. *Journal of Psychosomatic Research, 63*(2), 137–42. http://doi.org/10.1016/j.jpsychores.2007.02.014

IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.

Inouye, S. K. (2006). Delirium in older persons. *New England journal of medicine*, *354*(11), 1157-1165.

Inouye, S. K., & Charpentier, P. A. (1996). Precipitating factors for delirium in hospitalized elderly persons. Predictive model and interrelationship with baseline vulnerability. *JAMA : The Journal of the American Medical Association, 275*(11), 852–857. http://doi.org/10.1001/jama.275.11.852

Inouye, S. K. (1998). Delirium in hospitalized older patients. *Clinics in Geriatric Medicine*, *14*(4), 745-764.

Inouye, S. K., Schlesinger, M. J., & Lydon, T. J. (1999). Delirium: a symptom of how hospital care is failing older persons and a window to improve quality of hospital care. *The American journal of medicine*, *106*(5), 565-573.

Inouye, S. K., van Dyck, C. H., Alessi, C. A., Balkin, S., Siegal, A. P., & Horwitz, R. I. (1990). Clarifying confusion: the confusion assessment method: a new method for detection of delirium. *Annals of internal medicine*, *113*(12), 941-948.

Inouye, S. K., Viscoli, C. M., Horwitz, R. I., Hurst, L. D., & Tinetti, M. E. (1993). A predictive model for delirium in hospitalized elderly medical patients based on admission characteristics. *Annals of internal medicine*, *119*(6), 474-481.

Inouye, S. K., Westendorp, R. G., & Saczynski, J. S. (2014). Delirium in elderly people. *The Lancet*, *383*(9920), 911-922.

Jagannath, A., Peirson, S. N., & Foster, R. G. (2013). Sleep and circadian rhythm disruption in neuropsychiatric illness. *Current opinion in neurobiology*, *23*(5), 888-894.

Judd, D. B., MacAdam, D. L., Wyszecki, G., Budde, H. W., Condit, H. R., Henderson, S. T., & Simonds, J. L. (1964). Spectral distribution of typical daylight as a function of correlated color temperature. *Josa*, *54*(8), 1031-1040.

Kassie, G. M., Nguyen, T. A., Kalisch Ellett, L. M., Pratt, N. L., & Roughead, E. E. (2017). Preoperative medication use and postoperative delirium: a systematic review. *BMC geriatrics*, *17*(1), 1-10.

Kessels, R., van Zandvoort, M., Postma, A., Kappelle, L., & de Haan, E. (2000). The Corsi Block-Tapping Task: Standardization and Normative Data. *Applied Neuropsychology, 7*(4), 252-258. doi: 10.1207/s15324826an0704_8

Kline, C. E., Durstine, J. L., Davis, J. M., Moore, T. A., Devlin, T. M., & Youngstedt, S. D. (2010). Circadian rhythms of psychomotor vigilance, mood, and sleepiness in the ultra-short sleep/wake protocol. *Chronobiology international*, *27*(1), 161-180.

Klingman, K. J., Morse, A., Williams, N., Grandner, M. A., & Perlis, M. L. (2020). 1174 assessing sleep disorders in primary care: A provider survey about the importance of sleep health. *Sleep*, *43*(Supplement_1), A448-A448.

Klingman, K. J., Morse, A., Williams, N., Grandner, M., & Perlis, M. L. (2020). 1175 Sleep Disorders Screening in Primary Care: Prevalence of Diagnosis and Treatment in the EMR. *Sleep*, *43*, A448-A449.

Kocevska, D., Lysen, T. S., Dotinga, A., Koopman-Verhoeff, M. E., Luijk, M. P., Antypa, N., ... & Tiemeier, H. (2021). Sleep characteristics across the lifespan in 1.1 million people from the Netherlands, United Kingdom and United States: a systematic review and meta-analysis. *Nature human behaviour*, *5*(1), 113-122.

Krenk, L., Jennum, P., & Kehlet, H. (2012). Sleep disturbances after fast-track hip and knee arthroplasty. *British journal of anaesthesia*, *109*(5), 769-775.

Krystal, A. D., & Edinger, J. D. (2008). Measuring sleep quality. *Sleep medicine*, *9*, S10-S17.

Landry, G. J., & Liu-Ambrose, T. (2014). Buying time: a rationale for examining the use of circadian rhythm and sleep interventions to delay progression of mild cognitive impairment to Alzheimer's disease. *Frontiers in aging neuroscience*, *6*, 325.

Landry, G. J., Best, J. R., & Liu-Ambrose, T. (2015). Measuring sleep quality in older adults: A comparison using subjective and objective methods. *Frontiers in Aging Neuroscience, 7*, 166. doi:10.3389/fnagi.2015.00166 [doi]

Lane, T., & Anne East, L. (2008). Sleep disruption experienced by surgical patients in an acute hospital. *British journal of Nursing*, *17*(12), 766-771.

Law, J., Fielding, B., Jackson, D., & Turner-Stokes, L. (2009). The UK FIM+ FAM Extended Activities of Daily Living module: evaluation of scoring accuracy and reliability. *Disability and rehabilitation*, *31*(10), 825-830.

Lecrubier, Y., Sheehan, D. V., Weiller, E., Amorim, P., Bonora, I., Sheehan, K. H., ... & Dunbar, G. C. (1997). The Mini International Neuropsychiatric Interview (MINI). A short diagnostic structured interview: reliability and validity according to the CIDI. *European psychiatry*, *12*(5), 224-231.

Lerner, A. B., Case, J. D., Takahashi, Y., Lee, T. H., & Mori, W. (1958). Isolation of melatonin, the pineal gland factor that lightens melanocyteS1. *Journal of the american chemical society*, *80*(10), 2587-2587.

Leslie, D. L., Marcantonio, E. R., Zhang, Y., Leo-Summers, L., & Inouye, S. K. (2008). One-year health care costs associated with delirium in the elderly population. *Archives of internal medicine*, *168*(1), 27-32.

Levkoff, S. E., Liptzin, B., Cleary, P. D., Wetle, T., Evans, D. A., Rowe, J. W., & Lipsitz, L. A. (1996). Subsyndromal delirium. *The American Journal of Geriatric Psychiatry*, *4*(4), 320-329.

Lewy, A. J., Wehr, T. A., Goodwin, F. K., Newsome, D. A., & Markey, S. P. (1980). Light suppresses melatonin secretion in humans. *Science*, *210*(4475), 1267-1269.

Li, Y., Zhang, X., Winkelman, J. W., Redline, S., Hu, F. B., Stampfer, M., ... & Gao, X. (2014). Association between insomnia symptoms and mortality: a prospective study of US men. *Circulation*, *129*(7), 737-746.

Lim, A. S., Kowgier, M., Yu, L., Buchman, A. S., & Bennett, D. A. (2013). Sleep fragmentation and the risk of incident Alzheimer's disease and cognitive decline in older persons. *Sleep*, *36*(7), 1027-1032.

Lim, J., & Dinges, D. F. (2010). A meta-analysis of the impact of short-term sleep deprivation on cognitive variables. *Psychological bulletin*, *136*(3), 375.

Lim, A. S., Yu, L., Kowgier, M., Schneider, J. A., Buchman, A. S., & Bennett, D. A. (2013). Modification of the relationship of the apolipoprotein E ε4 allele to the risk of Alzheimer disease and neurofibrillary tangle density by sleep. *JAMA neurology*, *70*(12), 1544-1551.

Lin, J. W., & Mai, L. J. (2018). Impact of mindfulness meditation intervention on academic performance. *Innovations in Education and Teaching International*, *55*(3), 366-375.

Lin, J., Ding, X., Hong, C., Pang, Y., Chen, L., Liu, Q., ... & Wang, X. (2019). Several biological benefits of the low color temperature light-emitting diodes based normal indoor lighting source. *Scientific reports*, *9*(1), 1-8.

Littner, M., Kushida, C. A., Anderson, W. M., Bailey, D., Berry, R. B., Davila, D. G., ... & Wise, M. (2003). Practice parameters for the role of actigraphy in the study of sleep and circadian rhythms: an update for 2002. *Sleep*, *26*(3), 337-341.

Lowery, D. P., Wesnes, K., Brewster, N., & Ballard, C. (2008). Quantifying the association between computerised measures of attention and confusion assessment method defined delirium: a prospective study of older orthopaedic surgical patients, free of dementia. *International Journal of Geriatric Psychiatry: A journal of the psychiatry of late life and allied sciences*, *23*(12), 1253-1260.

Lowery, D. P., Wesnes, K., Brewster, N., & Ballard, C. (2010). Subtle deficits of attention after surgery: quantifying indicators of sub syndrome delirium. *International journal of geriatric psychiatry*, *25*(10), 945-952.

Luyster, F. S., Choi, J., Yeh, C. H., Imes, C. C., Johansson, A. E., & Chasens, E. R. (2015). Screening and evaluation tools for sleep disorders in older adults. *Applied Nursing Research*, *28*(4), 334-340.

Macdonald, A., Adamis, D., Treloar, A., & Martin, F. (2006). C-reactive protein levels predict the incidence of delirium and recovery from it. *Age and ageing*, *36*(2), 222-225.

Maldonado, J. R. (2008). Delirium in the acute care setting: characteristics, diagnosis and treatment. Critical care clinics, 24(4), 657-722.

Maldonado, J. R. (2008). Pathoetiological model of delirium: a comprehensive understanding of the neurobiology of delirium and an evidence-based approach to prevention and treatment. *Critical care clinics*, *24*(4), 789-856.

Maldonado, J. R. (2013). Neuropathogenesis of delirium: review of current etiologic theories and common pathways. *The American Journal of Geriatric Psychiatry*, *21*(12), 1190-1222.

Marcantonio, E. R., Flacker, J. M., Michaels, M., & Resnick, N. M. (2000). Delirium is independently associated with poor functional recovery after hip fracture. *Journal of the American Geriatrics Society*, *48*(6), 618-624.

Martin, J. L., Mory, A. K., & Alessi, C. A. (2005). Nighttime oxygen desaturation and symptoms of sleep-disordered breathing in long-stay nursing home residents. *The Journals of Gerontology.Series A, Biological Sciences and Medical Sciences, 60*(1), 104-108. doi:60/1/104 [pii]

Mason, O. J., Morgan, C. J., Stefanovic, A., & Curran, H. V. (2008). The psychotomimetic states inventory (PSI): measuring psychotic-type experiences from ketamine and cannabis. *Schizophrenia research*, *103*(1-3), 138-142.

Meagher, D. J., Leonard, M., Donnelly, S., Conroy, M., Adamis, D., & Trzepacz, P. T. (2011). A longitudinal study of motor subtypes in delirium: relationship with other phenomenology, etiology, medication exposure and prognosis. *Journal of psychosomatic research*, *71*(6), 395-403.

Mental Capacity Act, 2005. (c.9). London: The Stationery Office. Retrieved from https://www.legislation.gov.uk/ukpga/2005/9/contents

McCurren, C., & Cronin, S. N. (2003). Delirium: elders tell their stories and guide nursing practice. *Medsurg Nursing*, *12*(5), 318.

McCusker, J., Cole, M., Abrahamowicz, M., Primeau, F., & Belzile, E. (2002). Delirium predicts 12-month mortality. *Archives of internal medicine*, *162*(4), 457-463.

Murray, D. M., Varnell, S. P., & Blitstein, J. L. (2004). Design and analysis of group-randomized trials: a review of recent methodological developments. *American journal of public health*, *94*(3), 423-432.

Meissner, H. H., Riemer, a, Santiago, S. M., Stein, M., Goldman, M. D., & Williams, a J. (1998). Failure of physician documentation of sleep complaints in hospitalized patients. *The Western Journal of Medicine, 169*(3), 146–149.

Miller, A., Roth, T., Roehrs, T., & Yaremchuk, K. (2015). Correlation between sleep disruption on postoperative pain. *Otolaryngology--Head and Neck Surgery*, *152*(5), 964-968.

Millisecond. Inquisit 4 Lab [Computer Software]. Retrieved from www.millisecond.com/

Mitchell, A. J., Shukla, D., Ajumal, H. A., Stubbs, B., & Tahir, T. A. (2014). The Mini-Mental State Examination as a diagnostic and screening test for delirium: systematic review and meta-analysis. *General hospital psychiatry*, *36*(6), 627-633.

Miyamoto, T., Miyamoto, M., Iwanami, M., Kobayashi, M., Nakamura, M., Inoue, Y., . . . Hirata, K. (2009). The REM sleep behavior disorder screening questionnaire: Validation study of a japanese version. *Sleep Medicine, 10*(10), 1151-1154. doi:10.1016/j.sleep.2009.05.007 [doi]

Miyazaki, T., Kuwano, H., Kato, H., Ando, H., Kimura, H., Inose, T., ... & Fukuchi, M. (2003). Correlation between serum melatonin circadian rhythm and intensive care unit psychosis after thoracic esophagectomy. *Surgery*, *133*(6), 662-668.

Moe, K. E., Vitiello, M. V., Larsen, L. H., & Prinz, P. N. (1995). Sleep/wake patterns in Alzheimer's disease: relationships with cognition and function. *Journal of sleep research*, *4*(1), 15-20.

Mograss, M. A., Guillem, F., Brazzini-Poisson, V., & Godbout, R. (2009). The effects of total sleep deprivation on recognition memory processes: a study of event-related potential. *Neurobiology of learning and memory*, *91*(4), 343-352.

Mold, J. W., Quattlebaum, C., Schinnerer, E., Boeckman, L., Orr, W., & Hollabaugh, K. (2011). Identification by primary care clinicians of patients with obstructive sleep apnea: a practice-based research network (PBRN) study. *J Am Board Fam Med*, *24*(2), 138-145.

Morgenthaler, T., Alessi, C., Friedman, L., Owens, J., Kapur, V., Boehlecke, B., … Swick, T. J. (2007). Practice parameters for the use of actigraphy in the assessment of sleep and sleep disorders: an update for 2007. *Sleep, 30*(4), 519–529.

Morone, N. E., Lynch, C. S., Greco, C. M., Tindle, H. A., & Weiner, D. K. (2008). “I felt like a new person.” The effects of mindfulness meditation on older adults with chronic pain: qualitative narrative analysis of diary entries. *The Journal of pain*, *9*(9), 841-848.

Morse, A. M., & Bender, E. (2019). Sleep in hospitalized patients. *Clocks & Sleep*, *1*(1), 151-165.

Most, E. I., Aboudan, S., Scheltens, P., & Van Someren, E. J. (2012). Discrepancy between subjective and objective sleep disturbances in early- and moderate-stage alzheimer disease. *The American*

Journal of Geriatric Psychiatry : Official Journal of the American Association for Geriatric Psychiatry, 20(6), 460-467. doi:10.1097/JGP.0b013e318252e3ff [doi]

Murman, D. L. (2015, August). The impact of age on cognition. In *Seminars in hearing* (Vol. 36, No. 03, pp. 111-121). Thieme Medical Publishers.

Mussi, C., Ferrari, R., Ascari, S., & Salvioli, G. (1999). Importance of serum anticholinergic activity in the assessment of elderly patients with delirium. *Journal of geriatric psychiatry and neurology*, *12*(2), 82-86.

National Health Service (2018, January). *Mental Capacity Act*. Retrieved from www.nhs.uk/Conditions/social-care-and-support-guide/Pages/mental-capacity.aspx

National Health Service Digital (2018, September) *Hospital Admitted Patient Care and Adult Critical Care Activity 2017-2018.* Retrieved from https://digital.nhs.uk/news-and-events/latest-news/hospital-admission-statistics-published

National Institute for Health and Care Excellence (NICE). Continuous positive airway pressure for the treatment of obstructive sleep apnoea/hypopnoea syndrome. technology appraisal guidance [TA139]. . 2008.

National Minimum Wage and National Living Wage rates. (2019). Retrieved 1 October 2019, from http://www.gov.uk/national-minimum-wage-rates

Neikrug, A. B., & Ancoli-Israel, S. (2010). Sleep disorders in the older adult–a mini-review. *Gerontology*, *56*(2), 181-189.

Nilsson, P. M., Nilsson, J. Å., Hedblad, B., & Berglund, G. (2001). Sleep disturbance in association with elevated pulse rate for prediction of mortality–consequences of mental strain?. *Journal of internal medicine*, *250*(6), 521-529.

Nomura, T., Inoue, Y., Kagimura, T., Uemura, Y., & Nakashima, K. (2011). Utility of the REM sleep behavior disorder screening questionnaire (RBDSQ) in parkinson's disease patients. *Sleep Medicine, 12*(7), 711-713. doi:10.1016/j.sleep.2011.01.015 [doi]

O'Donnell, B. F., Drachman, D. A., Barnes, H. J., Peterson, K. E., Swearer, J. M., & Lew, R. A. (1992). Incontinence and troublesome behaviors predict institutionalization in dementia. *Topics in geriatrics*, *5*(1), 45-52.

Office for National Statistics (2018, November) *Overview of the UK population: November 2018.* Retrieved from www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/articles/overviewoftheukpopulation/november2018

Onen, S. H., Onen, F., Courpron, P., & Dubray, C. (2005). How pain and analgesics disturb sleep. *The Clinical journal of pain*, *21*(5), 422-431.

Onen, S. H., Dubray, C., Decullier, E., Moreau, T., Chapuis, F., & Onen, F. (2008). Observation-based nocturnal sleep inventory: Screening tool for sleep apnea in elderly people. *Journal of the American Geriatrics Society, 56*(10), 1920-1925. doi:10.1111/j.1532-5415.2008.01862.x [doi]

Paavilainen, P., Korhonen, I., Lotjonen, J., Cluitmans, L., Jylha, M., Sarela, A., & Partinen, M. (2005). Circadian activity rhythm in demented and non-demented nursing-home residents measured by telemetric actigraphy. *Journal of Sleep Research, 14*(1), 61-68. doi:JSR433 [pii]

Pan, A., De Silva, D. A., Yuan, J. M., & Koh, W. P. (2014). Sleep duration and risk of stroke mortality among Chinese adults: Singapore Chinese health study. *Stroke*, *45*(6), 1620-1625.

Panageas, K. S., Schrag, D., Riedel, E., Bach, P. B., & Begg, C. B. (2003). The effect of clustering of outcomes on the association of procedure volume and surgical outcomes. *Annals of internal medicine*, *139*(8), 658-665.

Pascual-Leone, A., Amedi, A., Fregni, F., & Merabet, L. B. (2005). The plastic human brain cortex. *Annu. Rev. Neurosci.*, *28*, 377-401.

Pisani, M. A., McNicoll, L., & Inouye, S. K. (2003). Cognitive impairment in the intensive care unit. *Clinics in Chest Medicine,* (24), 727–737. http://doi.org/10.1007/s13398-014-0173-7.2

Postuma, R. B., Gagnon, J. F., Pelletier, A., & Montplaisir, J. Y. (2017). Insomnia and somnolence in idiopathic RBD: A prospective cohort study. *NPJ Parkinson's Disease, 3*, 9-017-0011-7. eCollection 2017. doi:10.1038/s41531-017-0011-7 [doi]

Potvin, O., Lorrain, D., Forget, H., Dubé, M., Grenier, S., Préville, M., & Hudon, C. (2012). Sleep quality and 1-year incident cognitive impairment in community-dwelling older adults. *Sleep*, *35*(4), 491-499.

Raats, J. W., Steunenberg, S. L., De Lange, D. C., & Van Der Laan, L. (2016). Risk factors of post-operative delirium after elective vascular surgery in the elderly: a systematic review. *International Journal of Surgery*, *35*, 1-6.

Ram, S., Seirawan, H., Kumar, S. K., & Clark, G. T. (2010). Prevalence and impact of sleep disorders and sleep habits in the United States. *Sleep and breathing*, *14*(1), 63-70.

Ranhoff, A. H., Rozzini, R., Sabatini, T., Cassinadri, A., Boffelli, S., & Trabucchi, M. (2006). Delirium in a sub-intensive care unit for the elderly: occurrence and risk factors. *Aging clinical and experimental research*, *18*(5), 440-445.

Rechtschaffen, A., Bergmann, B. M., Everson, C. A., Kushida, C. A., & Gilliland, M. A. (1989). Sleep deprivation in the rat: X. Integration and discussion of the findings. *Sleep*, *12*(1), 68-87.

Redeker, N. S. (2000). Sleep in acute care settings: an integrative review. *Journal of Nursing Scholarship*, *32*(1), 31-38.

Reid, E. (2001). Factors affecting how patients sleep in the hospital environment. *British Journal of Nursing*, *10*(14), 912-915.

Reynolds III, C. F., & O'Hara, R. (2013). DSM-5 sleep-wake disorders classification: overview for use in clinical practice. *American Journal of Psychiatry*, *170*(10), 1099-1101.

Rinkenauer, G., Osman, A., Ulrich, R., Müller-Gethmann, H., & Mattes, S. (2004). On the locus of speed-accuracy trade-off in reaction time: inferences from the lateralized readiness potential. *Journal of Experimental Psychology: General*, *133*(2), 261.

Robbins, T. W., & Everitt, B. J. (1995). Arousal systems and attention.

Robertson, I. H., Manly, T., Andrade, J., Baddeley, B. T., & Yiend, J. (1997). Oops!': performance correlates of everyday attentional failures in traumatic brain injured and normal subjects. *Neuropsychologia*, *35*(6), 747-758.

Robinson, T. N., Raeburn, C. D., Angles, E. M., & Moss, M. (2008). Low tryptophan levels are associated with postoperative delirium in the elderly. *The American Journal of Surgery*, *196*(5), 670-674.

Rockwood, K., Cosway, S., Carver, D., Jarrett, P, Stadnyk, K., & Fisk, J. (1999). The risk of dementia and death after delirium. *Age and ageing*, *28*(6), 551-556.

Rockwood, K., Song, X., MacKnight, C., Bergman, H., Hogan, D. B., McDowell, I., & Mitnitski, A. (2005). A global clinical measure of fitness and frailty in elderly people. *Cmaj*, *173*(5), 489-495.

Roehrs, T., & Roth, T. (2008). Caffeine: sleep and daytime sleepiness. *Sleep medicine reviews*, *12*(2), 153-162.

Rosenberg, J. (2001). Sleep disturbances after non-cardiac surgery. *Sleep medicine reviews*, *5*(2), 129-137.

Rubin, F. H., Neal, K., Fenlon, K., Hassan, S., & Inouye, S. K. (2011). Sustainability and scalability of the hospital elder life program at a community hospital. *Journal of the American Geriatrics Society*, *59*(2), 359-365.

Sander, B., Markvart, J., Kessel, L., Argyraki, A., & Johnsen, K. (2015). Can sleep quality and wellbeing be improved by changing the indoor lighting in the homes of healthy, elderly citizens?. *Chronobiology international*, *32*(8), 1049-1060.

Serafim, R. B., Soares, M., Bozza, F. A., e Silva, J. R. L., Dal-Pizzol, F., Paulino, M. C., ... & Salluh, J. I. (2017). Outcomes of subsyndromal delirium in ICU: a systematic review and meta-analysis. *Critical Care*, *21*(1), 179.

Shafi, M. M., Santarnecchi, E., Fong, T. G., Jones, R. N., Marcantonio, E. R., Pascual-Leone, A., & Inouye, S. K. (2017). Advancing the Neurophysiological Understanding of Delirium. *Journal of the American Geriatrics Society*. http://doi.org/10.1111/jgs.14748

Siddiqi, N., House, A. O., & Holmes, J. D. (2006). Occurrence and outcome of delirium in medical in-patients: A systematic literature review. *Age and Ageing, 35*(4), 350–364. http://doi.org/10.1093/ageing/afl005

Sinforiani, E., Terzaghi, M., Pasotti, C., Zucchella, C., Zambrelli, E., & Manni, R. (2007). Hallucinations and sleep–wake cycle in Alzheimer's disease: a questionnaire-based study in 218 patients. *Neurological Sciences*, *28*(2), 96-99.

Skapinakis, P., Lewis, G., & Mavreas, V. (2004). Temporal relations between unexplained fatigue and depression: Longitudinal data from an international study in primary care. *Psychosomatic Medicine, 66*(3), 330–335. http://doi.org/10.1097/01.psy.0000124757.10167.b1

SmartDraw [Computer Software]. Retrieved from https://www.smartdraw.com

Stenvall, M., Olofsson, B., Lundström, M., Svensson, O., Nyberg, L., & Gustafson, Y. (2006). Inpatient falls and injuries in older patients treated for femoral neck fracture. *Archives of gerontology and geriatrics*, *43*(3), 389-399.

Stone, K. L., Ensrud, K. E., & Ancoli-Israel, S. (2008). Sleep, insomnia and falls in elderly patients. *Sleep medicine*, *9*, S18-S22.

Tombaugh, T. N. (2004). Trail Making Test A and B: normative data stratified by age and education. *Archives of clinical neuropsychology*, *19*(2), 203-214.

Tractenberg, R. E., Singer, C. M., & Kaye, J. A. (2005). Symptoms of sleep disturbance in persons with Alzheimer's disease and normal elderly. *Journal of sleep research*, *14*(2), 177-185.

Tractenberg, R. E., Singer, C. M., Cummings, J. L., & Thal, L. J. (2003). The sleep disorders inventory: An instrument for studies of sleep disturbance in persons with alzheimer's disease. *Journal of Sleep Research, 12*(4), 331-337. doi:374 [pii]

Trompeo, A. C., Vidi, Y., Locane, M. D., Braghiroli, A., Mascia, L., Bosma, K., & Ranieri, V. M. (2011). Sleep disturbances in the critically ill patients: Role of delirium and sedative agents. *Minerva Anestesiologica, 77*(6), 604–612. http://doi.org/R02116357 [pii]

Trzepacz, P. T. (1994). A review of delirium assessment instruments. *General Hospital Psychiatry*, *16*(6), 397-405.

Trzepacz, P. T., Baker, R. W., & Greenhouse, J. (1988). A symptom rating scale for delirium. *Psychiatry research*, *23*(1), 89-97.

Trzepacz, P. T., Mittal, D., Torres, R., Kanary, K., Norton, J., & Jimerson, N. (2001). Validation of the Delirium Rating Scale-revised-98: comparison with the delirium rating scale and the cognitive test for delirium. *The Journal of neuropsychiatry and clinical neurosciences*, *13*(2), 229-242.

Tune, L., Carr, S., Cooper, T., Klug, B., & Golinger, R. C. (1993). Association of anticholinergic activity of prescribed medications with postoperative delirium. *The Journal of neuropsychiatry and clinical neurosciences*.

Turner-Stokes, L., Nyein, K., Turner-Stokes, T., & Gatehouse, C. (1999). The UK FIM+ FAM: development and evaluation. *Clinical rehabilitation*, *13*(4), 277-287.

Tyler, D. B. (1955). Psychological changes during experimental sleep deprivation. *Diseases of the nervous system*, *16*(10), 293-299.

Tyrer, P. (2014). A comparison of DSM and ICD classifications of mental disorder. *Advances in psychiatric treatment*, *20*(4), 280-285.

Van Den Berg, J. F., Van Rooij, F. J., Vos, H., Tulen, J. H., Hofman, A., Miedema, H. M., . . . Tiemeier, H. (2008). Disagreement between subjective and actigraphic measures of sleep duration in a population-based study of elderly persons. *Journal of Sleep Research, 17*(3), 295-302. doi:10.1111/j.1365-2869.2008.00638.x [doi]

Villalpando-Berumen, J. M., Pineda-Colorado, A. M., Palacios, P., Reyes-Guerrero, J., Villa, A. R., & Gutiérrez-Robledo, L. M. (2003). Incidence of delirium, risk factors, and long-term survival of elderly patients hospitalized in a medical specialty teaching hospital in Mexico City. *International psychogeriatrics*, *15*(4), 325-336.

Vitiello, M. V., & Borson, S. (2001). Sleep disturbances in patients with Alzheimer's disease. *CNS drugs*, *15*(10), 777-796.

Vitiello, M. V., Moe, K. E., & Prinz, P. N. (2002). Sleep complaints cosegregate with illness in older adults: clinical research informed by and informing epidemiological studies of sleep. *Journal of psychosomatic research*, *53*(1), 555-559.

Wagner, S., Helmreich, I., Dahmen, N., Lieb, K., & Tadić, A. (2011). Reliability of three alternate forms of the trail making tests a and B. *Archives of Clinical Neuropsychology*, *26*(4), 314-321.

Wakefield, B. J. (2002). Risk for acute confusion on hospital admission. *Clinical Nursing Research*, *11*(2), 153-172.

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology, 54*(6), 1063–1070. https://doi.org/10.1037/0022-3514.54.6.1063

Watson, P. L., Ceriana, P., & Fanfulla, F. (2012). Delirium: Is sleep important? Best Practice and Research: *Clinical Anaesthesiology, 26*(3), 355–366. http://doi.org/10.1016/j.bpa.2012.08.005

Weinhouse, G. L., Schwab, R. J., Watson, P. L., Patil, N., Vaccaro, B., Pandharipande, P., & Ely, E. W. (2009). Bench-to-bedside review: delirium in ICU patients - importance of sleep deprivation. *Critical Care (London, England), 13*(6), 234. http://doi.org/10.1186/cc8131

Whiting, P., Rutjes, A. W., Reitsma, J. B., Bossuyt, P. M., & Kleijnen, J. (2003). The development of QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. *BMC medical research methodology*, *3*(1), 25.

Wilson, K., Broadhurst, C., Diver, M., Jackson, M., & Mottram, P. (2005). Plasma insulin growth factor—1 and incident delirium in older people. *International Journal of Geriatric Psychiatry: A journal of the psychiatry of late life and allied sciences*, *20*(2), 154-159.

Witlox, J., Eurelings, L. S., de Jonghe, J. F., Kalisvaart, K. J., Eikelenboom, P., & Van Gool, W. A. (2010). Delirium in elderly patients and the risk of postdischarge mortality, institutionalization, and dementia: a meta-analysis. *Jama*, *304*(4), 443-451.

Wolkove, N., Elkholy, O., Baltzan, M., & Palayew, M. (2007). Sleep and aging: 1. Sleep disorders commonly found in older people. *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne*, *176*(9), 1299–1304. https://doi.org/10.1503/cmaj.060792

World Health Organization. (1992). The ICD-10 classification of mental and behavioural disorders: *Clinical descriptions and diagnostic guidelines.* Geneva: World Health Organization.

World Health Organization. (2000). The ICD-10 classification of mental and behavioural disorders: *Clinical descriptions and diagnostic guidelines.* Geneva: World Health Organization.

World Medical Association. (2013). World Medical Association Declaration of Helsinki ethical principles for medical research involving human subjects. *JAMA: Journal of the American Medical Association, 310*(20), 2191–2194. https://doi.org/10.1001/jama.2013.281053

Yaffe, K., Laffan, A. M., Harrison, S. L., Redline, S., Spira, A. P., Ensrud, K. E., ... & Stone, K. L. (2011). Sleep-disordered breathing, hypoxia, and risk of mild cognitive impairment and dementia in older women. *Jama*, *306*(6), 613-619.

Young, T., Shahar, E., Nieto, F. J., Redline, S., Newman, A. B., Gottlieb, D. J., ... & Samet, J. M. (2002). Predictors of sleep-disordered breathing in community-dwelling adults: the Sleep Heart Health Study. *Archives of internal medicine*, *162*(8), 893-900.

Young, T. B. (2004). Epidemiology of daytime sleepiness: definitions, symptomatology, and prevalence. *J Clin Psychiatry*, *65*(Suppl 16), 12-16.

Occupational Health, University of Kent, (2013, March). *University of Kent Campus walks*. Retrieved from www.kent.ac.uk/safety/oh/general-health-topics/Campus%20Walks.html

Appendices

Appendix A: A Systematic Review of Screening tools to detect Sleep Disorders and assess Sleep Quality in Older People

A.1 Systematic review data extraction forms:

Table 33 Systematic review data extraction forms

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**

Insomnia Severity Index (ISI) [2]
(Bastien, Vallieres, & Morin, 2001)
	Source:
	Participants in a trial of Cognitive Behavioural Trial for primary insomnia
	Inclusion:
	DSM III-R and ICSD primary insomnia
	Exclusion:
	Comorbid major psychiatric disorder, medical disorder known to affect sleep, use of medications known to affect sleep, significant cognitive impairment
		Polysomnography
		-3-night on 3 occasions over 3 months
		-Sleep Onset, Wake after Sleep Onset, Early morning awakenings, and Sleep Efficiency
			Insomnia
			-Questionnaire;
			-Seven items (severity of sleep-onset, sleep maintenance, early morning awakening problems, satisfaction with sleep pattern, interference with daily functioning, noticeability of impairment, and level of distress)
			-Each item rated on a scale of 0-4.
			-Total score 0-28 with clinical thresholds provided
				N=78;
				- Mean age, 65 $\pm$ 6.7
				- Mean education, 14.4 $\pm$ 2.4
				- Women, 64%
				- Married, 68%
				- Retired, 47%
					Internal consistency,
					- Cronbach's α, .32 - .9
					Concurrent Validity,
					Bivariate correlations (Pearson's Product Moment)
					- Sleep Onset, initial insomnia, *r* = .39 to .45;
					- Wake after sleep onset, middle insomnia,
					r = .16 to .45;
					- Early morning awakening, terminal insomnia,
					r = .07 to .23;
					- Sleep efficiency, total ISI,
					r= -.09 to -.35

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
Insomnia Severity Index (ISI), [74] (Postuma, Gagnon, Pelletier, & Montplaisir, 2017)	**Source:** -Following a cohort of idiopathic RBD patients -Between 2004 and 2016 following a large cohort -As part of a clinical follow up patients completed sleep scales. **Inclusion:** *RBD group* -Confirmed idiopathic RBD by PSG *Control group* -Confirmed absence of RBD through PSG **Exclusion:** -Parkinson's or Dementia	**Polysomnography** -one night -Sleep latency, TST, SE, Stage 1%, Stage 2%, SWS %, REM %, Phasic REM density %, Tonic REM %	**Insomnia Severity Index** -Questionnaire; -7-items on sleep onset, sleep maintenance, insomnia, sleep satisfaction, impact of sleep disorders on quality of life -Cut-off of 10 indicates insomnia	**RBD Group** -Evaluated N=158, out of this included N=151 -at least one baseline sleep analysis -Mean age, 66.4 ± 8.3 -RBD duration from symptom onset 8.7 ± 9.3 years -Male, 75% -Neurodegenerative disease development from baseline, 3.2 ± 2.4 years (range: 1-11 years) **Control group** -Mean age, 68.9 ± 8.5 -Male, 74%	*ISI mean scores* -Significant difference, with higher scores in idiopathic RBD than controls (10.0 ± 5.5 vs. 6.35 ± 4.66, n=54, p < .001) -A significant difference in the number of abnormal ISI scores in RBD patients compared to controls (46.7% vs 24.5%, *p* = .001) -Differences more marked for general sleep disturbances / worry/ impact than for direct insomnia questions -Significant increase in sleep maintenance insomnia in RBD patients compared to controls (questions 2+3 = 2.7 ± 1.7 vs. 2.1 ± 1.4, *p* = .043) -No significant differences in baseline ISI between those who developed disease vs those who remained disease-free (10.4 ± 5.9 vs. 10.0 ± 5.4, *p* = .76) and no significant differences in single ISI item score -In patients with repeated ISI, significant decline in ISI over time (mean change = -1.43 ±

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
					5.09, *p* = .029) moving towards control values with time, score reduction was primarily driven by questions related to sleep satisfaction/worrying about sleep. -Significant difference in a decline in sleep maintenance insomnia scores in those who developed disease (change = 0.45 ± 1.05 points, *p* = .083)
Observation-Based Nocturnal Sleep Inventory (ONSI) [3] (Onen et al., 2008)	**Source:** Consecutive referrals to a geriatric sleep centre from five geriatric hospitals for suspicion of sleep apnoea (complaints of snoring, excessive daytime sleepiness or overweight/obesity) **Inclusion:** - Aged 70 or older - 'Caucasian race' **Exclusion:**	**Polysomnography** -1-night	**Sleep Apnoea** -Behavioural observation; -5 x 5-minute observations by a nurse (for interrupted breathing, gasping or choking; snoring; and awakening)	N=121 (With SA, n= 68; Without SA, n=43) - Mean age, 79.3 ± 5.2 - Mean MMSE, 25 ± 3.5 - Women, 50%	**Inter-observer reliability** *k* = .89^ **Diagnostic Accuracy** Optimal cut-off: two or more snoring or one or more apnoeas - Sensitivity = 89.7%, - Specificity = 81.4%, - PPV = 88%, - NPV = 83%

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
	- heart failure - nocturnal oxygen supplementation - severe dementia (MMSE <10) - major psychiatric disorder - too sick to be evaluated - having a condition that prevents the use of polysomnography - have previously undergone sleep study - have received care for SA				
Observational Sleep Assessment Instrument (OSAI) [78] (Martin, Mory, & Alessi, 2005)	**Source:** -Residents of community nursing homes -Daytime sleepiness and night-time sleep disruption -Enrolled in a RCT of nonpharmacological interventions to improve sleep **Inclusion:**	**Actigraphy** - 2 nights - TST	**Symptoms of SDB** - Hourly 3-minute observations - Recording snoring, breathing rate, loudness, continuity and chest movements	N=109; -Mean age, 86.2 ± 9.2 -Years in nursing home, 2.9 ± 2.9 -BMI, 25.3 ± 5.6 -MMSE, 11.3 ± 9.6 -No. of medical diagnoses, 9.9 ± 3.9 -No. of routine medications, 9.1 ± 5.2	**Relationship between OSAI and ODI (derived from actigraphy)** -Observed loud breathing was statistically significant related to ODI (r = .28, p = .003). - No statistically significant relationships were found for: number of observations per night (r = .04, p = .71), discontinuity of breathing (r = -.007, p = .94), discontinuity of

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
	-Met criteria for observed daytime sleepiness -Scored asleep <80% of the time between 10:00 pm and 06:00 am **Exclusion:** -Bed bound -In contact isolation -Left facility before screening			-No. of PRN medications, 1.9 ± 1.8 -CIRS-G, 24.6 ± 5.0 -Female, 74.3% -Non-Hispanic White, 92.7% -Taking sedative medications, 17.4% -Cardiac disease, 10.1% -Pulmonary disease, 56.9% -Neurologic disease, 62.4%	chest movement (r = .14, p = .15), percentage of observations with snoring (r = .13, p = .12) and breathing rate (per minute) (r = -.01, p = .91).
Mayo Sleep Questionnaire (MSQ) [5] (Boeve et al., 2011)	**Source:** -Enrolled in the Mayo Alzheimer's Disease Research Centre, Clinic at Rochester or Jacksonville **Inclusion/Exclusion:** -None	1-night **Polysomnography** + comprehensive sleep interview and physical examination (ICSD 2nd Ed criteria used).	**REM Sleep Behaviour Disorder** -Questionnaire (Informant based version) -Sixteen items, (REM Behaviour Disorder, Periodic Limb Movement during sleep; Restless Leg Syndrome; Sleepwalking; Obstructive Sleep Apnoea; Sleep Related Leg Cramps; and Insomnia)	N=176 (no dementia, n=8; mild cognitive impairment, n=44; Alzheimer's disease, n=23; dementia with Lewy bodies, n=74; other dementias and/or parkinsonian syndromes, n=27) - Median age, 71 - Women 15%	**Diagnostic Accuracy** REM Behaviour Disorder, - Sensitivity = 98%; - Specificity = 74%; Sleep Related Breathing, - Sensitivity = 38 to 41%; - Specificity = 29 to 41%

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
Mayo Sleep Questionnaire (MSQ) [52] (Boeve et al., 2013) (NB: Q1 only)	**Source:** - Enrolled in MSCA - Community residents - Aged 70-89 years at baseline - Data for 97 subjects included only as others didn't achieve REM sleep or had EMG tone **Inclusion:** -bed partner/informant competed the MSQ - undergone PSG between 1st January 2003 and 31st December 2008.	**Polysomnography** - Mean AHI	**Screens for presence of RBD** - Q1 only here **-** Have you ever seen the patient appear to "act out his/her dreams" whilst sleeping? (Punched or flailed arms in the air, shouted or screamed) - Responses from bed partners who are asked if a behaviour has been exhibited at least three times in the past. - 'Yes' responses follow sub-questions.	(NB only N=97) N=128; Mean Age at PSG -60-69 N=7 -70-79 N=68 -80-89 N=52 -<90 N=1 -Median age = 77 -Male N=104 (89%) -Bed partner spouse N=126 (99%) **Neurological diagnosis** *Cognitively normal* N=95 (N=3 with single stroke, N=2 with PD) *MCI* *SD-amnestic* N=16 (1 PD) *MD-amnestic* N=9 (N=2 with single stroke, N=1 with PD) *SD-non- amnestic* N=4 (N=1 with single stroke)	**Diagnostic accuracy** (*n*=97) **Q1 Yes** DEB and RSWA = 9, No DEB = 4; Sensitivity = 100% (95%CI: .63-1.0); **Q1 No** DEB and RSWA = 0, No DEB= 84; Specificity = 95% (95%CI: .88-.98)

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
				MD-non-amnestic N=1 *AD* N=3	
REM sleep behaviour disorder Japanese version (RBDSQ-J) [64] (Miyamoto et al., 2009)	**Source:** -Patients with PSG-confirmed iRBD recruited from a University Hospital or Somnology Center	**Polysomnography** - to define presence of iRBD - Criteria as used in ICSD-2	**REM sleep behaviour disorder** - 10-item questionnaire with yes/no responses on sleep behaviour - Frequency and content of dreams and their relationship to nocturnal movements and behaviour (Q1 – 4), (Q5) self‐injuries and injuries of the bed partner, (Q6) 4 subitems assessing nocturnal motor behaviour. (Q7 and 8) nocturnal awakenings, (Q9) disturbed sleep in general, (Q10) presence of any neurological disorder	N=52; -Mean age, 66.4 ± 6.9 -Males, N=36, mean age 66.1 ± 7.0 -Females, N=16, mean age, 67.1 ± 6.8	Test-retest reliability of entire RBDSQ-J for iRBD = .836 (95% CI = .601–.939) AOC = .927 from iRBD vs OSAS AOC = .918 from iRBD (male) vs OSAS **Diagnostic accuracy** **OSAS** - Sensitivity = 11.5 – 88.8% - Specificity = 56.1 – 96.4%

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
REM sleep behaviour disorder screening questionnaire-Japanese version (RBDSQ-J) [6] (Nomura, Inoue, Kagimura, Uemura, & Nakashima, 2011)	**Source:** Consecutive patients admitted to a University Hospital **Inclusion:** People with Parkinson Disease	**Polysomnography** + Clinical Interview, American Sleep Disorders Association Criteria	**REM Sleep Behaviour Disorder** -Questionnaire -Thirteen items	N=76 n=45 with REM SD - Mean age, 72.9 ± 9.1; - women 50% n=31 age and gender matched controls; - Mean age, 67.8 ± 6.5 - Women 29%	**Diagnostic Accuracy** Any RBD symptoms: Optimal cut-off: 6 points, - Sensitivity = 84.2% - Specificity = 95.3%; - ROC AUC, .953 Violent RBD symptoms only: Optimal cut-off: 6 points, - Sensitivity = 100% - Specificity = 87.5%; - ROC AUC, .969
Sleep Interview [60] (Eisensehr, Lindeiner, Jäger, & Noachtar, 2001)	**Source**: -Review of all PSGs performed at the University of Munich Sleep Lab -All scheduled for a PSG for complaints of non-restorative sleep, difficulties in maintaining sleep, excessive daytime sleepiness or complex nocturnal behaviour	**Polysomnography** -at least 2 nights -10pm – 6am - RBD diagnosed according to American Sleep Disorders Association guidelines	**Interview** -With neurologist specialising in sleep medicine prior to PSG and where possible with bedpartners -Questions focused on self-injuries or injuries of the patient's bedpartners during sleep, violent dream content, association of dreams with complains from the patients' bedpartners about complex	N=292; **PD** -N=19 -Mean age, 67.7 ± 9.4 -13 male (68%) -Hoehn and Yahr 1.0 *n* = 2 (1 with RBD) 1.5 *n* = 3 (1 with RBD) 2.0 *n* = 5 (2 with RBD) 2.5 *n* = 7 (4 with RBD) 3.0 *n* = 1 4.0 *n* = 1 (1 with RBD)	**Sensitivity of interview for diagnosing RBD** -PD = 33% -non-PD = 100% **Specificity of interview for diagnosing RBD** -PD = 90% -Non-PD = 99.6%

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
	-Non-PD patients referred to the sleep disorders clinic of the department of neurology of the Ludwig-Maximilans-University of Munich -PD patients recruited from movement disorders outpatient clinic **Exclusion:** -impaired cognitive function or mental deficits -patients taking medications known to induce sleep alternations (except dopaminergic meds in PD)		or even aggressive behaviour during sleep	**Non-PD** -N=273 -Mean age, 55.0 ± 16.0 -168 male (58%)	

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
Sleep Symptom Checklist (SSC) [48] (Bailes et al., 2008)	**Source:** Waiting areas of three family practice centres **Inclusion:** - >50 years and over - Community resident - Volunteer - Sufficient cognitive and language skills to complete measures in English or French	**Polysomnography** -1-night -10pm to 7am	**Presence of sleep disorders** - Self reported questionnaire - 21-items (signs and symptoms of sleep disorders) - Snoring, breathing interruption in sleep, insomnia, daytime fatigue, sleepiness and psychological maladjustment - Check mark next to item if experienced symptom in the prior month - Each item: (a) rated on severity (1 to 3) or 0 if not checked (b) indicate if the symptom was discussed with their physician at the current appointment (c) indicate if the symptom was experienced within the past year - Report what doctor recommended in terms of referral or treatment in open ended format	N=196; (males, n=71, women, n=125) - Mean age of males 69.93 $\pm$ 9.1 - Women mean age 69.96 $\pm$ 10.8	Three-week test re-test (*n* = 21, 14 female, 7 male, mean age 46.1 $\pm$ 12.1) **Internal consistency** - Cronbach's α, .74 (first administration) and 0.68 (second administration) - Cronbach's α, .86 (checked items), .88 (severity ratings) **Concurrent validity** - Pearson product-moment correlation total score $r = 0.79$ $p < 0.1$ **Concurrent validity** - (Pearson test re-test) - Insomnia $r = .79$ - Day time aspects $r = .77$ - Sleep disorder $r = .80$ - Psychological maladjustment $r = .80$

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
PSQI [50] Beaudreau et al. (2012)	**Source:** - Community-dwelling women ≥65 between September 1986 – October 1998 from SOF **Inclusion:** - Women - ≥65 years	**Actigraphy** - ≥72 hours -WASO, day time inactivity	**Sleep Quality** - Questionnaire, - 19 items, generate 7 component scores (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction)	N=2968; - Mean age = 83.4 ± 3.7 years - Years of education = 12.9 ± 2.7 - Race (N=2662 white 89.7%, N=306 black 10.3%)	**Internal consistency** - 17 item PSQI total sample Cronbach's α, .78, older white women α, .78 and in older black women α, .80 - Item-total correlation .12 – .69 -Merged subscales, Cronbach's α = .72 (total sample), α =.72 (older white women) and α = .74 (older black women). **Construct validity** Correlations reported: - PSQI and daytime inactivity *r_s, 0.05; p < .05* - PSQI and total sleep time *r_s, -0.02; p = .34* - PSQI and wake after sleep onset *r_s, 0.14; p < .001* - PSQI and Total Sleep Time n/s
PSQI [53] Buysse et al. (1991)	**Source:** - Identified through presentations to senior citizens' groups, newspaper and poster	**Polysomnography** - 2 nights	**Sleep Quality** - Questionnaire -21 item global score, sum of 7 individual component scores	N=44; -Age, <80 (men n=20, women n=24)	-No significant difference between PSQI and PSG for sleep latency or for sleep efficiency.

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
	advertisements and word of mouth **Inclusion:** -Good health (verified through medical and psychological screening procedures) **Exclusion:** -Any serious or rapidly progressive medical illness (chronic medical conditions did not exclude participants providing the condition is stable without medications or with medications that are not known to have a significant effect on sleep). -No current or life-time history of any psychiatric disorder		- 19 items, generate 7 component scores (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction)		-PSQI habitual sleep duration and sleep efficiency were greater than PSG (sleep duration: t = -3.18, *p* = .002; sleep efficiency: t = - 2.04, *p* = .04) - PSQI global scores were not significantly correlated with PSG sleep variables. **Sleep quality** - Not correlated with any PSG variables
PSQI (*Italian Version*) [9]	**Source:** Not described **Inclusion:**	**Polysomnography** -1-night	**Sleep Quality** - Questionnaire, - 19 items, generate 7 component scores (subjective	N=50 ('healthy elderly', n=10; 'healthy young', n=10; sleep	**Internal consistency**, - Cronbach's α = .835 **Diagnostic Accuracy**

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
(Curcio et al., 2013)	*Healthy* -normal sleep duration and schedule *Dementia* -NINCDS-ADRDA guidelines *SA* -AHI ≥ 30/h *Depression* -Hamilton Depression Rating Scale (No cut-off described) **Exclusion:** *Healthy,* -neurological, psychiatric or any other serious condition -daytime nap habits -excessive daytime sleepiness *Depression,* - other neurological or serious medical condition		sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction) **-** Italian version translated from English to Italian then evaluated by two independent experts in sleep disorders. This was then back-translated from Italian to English	apnoea syndrome patients, n=10; depressed patients, n=10; individuals with dementia, n=10) People with dementia: - Mean age, 75 ± 6.52 Healthy elderly: - Mean age, 68.6 ± 6.98	Sensitivity and specificity reported for various cut-offs on PSQI, but the reference standard is not defined. **Concurrent Validity,** Bi-variate correlations reported between PSG global score: - Stage 2 latency *r, .294; p = .04* - Slow Wave Sleep (SWS) latency *r, .524 ; p = .0001* - Stage 1 % *r, .324; p = .02* - Stage 2 % *r, -.349; p = .01* - Stage 1 latency, REM latency, SWS %, REM%, Awakenings, Total Sleep Time, Total Bed Time, Sleep Efficiency Index *r, between -.222 and .217 all non-significant (p ≥ .05)*
PSQI [54] (Chen, 2013)	**Source:** - Two musculoskeletal clinics in Taiwan	**Actigraphy** - 3 days -SL, TST, SE, WASO, Number of	**Sleep quality** - Questionnaire, - 19 items, generate 7 component scores (subjective	N=30; -Mean age, 65.6 ± 10.6 (range 42–88) - Female 60%	**Spearman's rank correlation coefficient** - *Sleep latency (mins)*

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
	(October 2010 - March 2011) - Those who agreed to take part in a secondary study **Inclusion:** -A diagnosis of OA from radiographic evidence by physicians, -< 40 years of age, -Ability to answer the questions in Mandarin or Taiwanese. -Residing in the community in Taiwan**.** **Exclusion:** -Cognitive impairments or inability to understand instructions.	Awakenings after Sleep Onset	sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction)		Subjective = 46.7 ± 62.3, *p* = .27, *p* = .149 Objective = 21.3 ± 25.0, *p* =.27, *p* = .149 - *TST (hours)* Subjective = 5.3 ± 1.3, *p* = .06, p = .771 Objective = 6.7 ± 1.1, *p* = .06, *p* = .771 - *Sleep efficiency (%)* Subjective = 76.1 ± 18.3, *p* = .28, *p* = .13 Objective = 87.9 ± 9.4, *p* = .28, *p* = .13 **Differences between objective and subjective measures** -Wilcoxon matched pairs signed-ranks test *Sleep latency (mins)* Mean = -25.4 ± 64.6 Median = -6.2 Range = -270.3 – 92.0 *p* = .04 (*p* < .05) *TST (hour)*

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
					Mean = 1.4 ± 1.7 Median = 1.2 Range = -2.3 – 4.5 $p < .001$ ($p < .001$) *Sleep efficiency (%)* Mean = 11.9 ± 18.2 Median = 10.5 Range = -32.9 – 51.8 $p = .002$ ($p < .01$) **Comparison of objective sleep variables by dichotomised global PSQI score** -Mann-Whitney U test -"Good sleep" n=8 -"Poor sleep" n=22 *Sleep latency (mins)* Z = -1.18, $p = .24$ "Good sleep" Median = 9.7 (5.7 – 26.3) Mean = 12.9 ± 8.4 95% CI for mean = 5.9 - 19.9 "Poor Sleep" Median = 13.0 (6 - 122) Mean = 24.4 ± 28.3 95% CU for mean 11.8 - 36.9

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/ Psychometric Properties**
					TST (hours) *Z = -1.08 p = .28* "Good sleep" Median = 7.3 (5.7 – 7.9) Mean = 7.0 ± 0.7 96% CI for mean = 6.4 – 7.7 "Poor sleep" Median = 6.9 (2.7 – 8.5) Mean = 6.6 ± 1.3 96% CI for mean = 6.1 – 7.2 *Sleep efficiency (%)* *Z = -1.97, p = .049* "Good sleep" Median = 94.2 (85.3 – 98.7) Mean = 93.3 ± 4.7 96% CI for mean = 89.3 – 97.2 "Poor sleep" Median = 88.4 (58.0 – 97.9) Mean = 86.0 ± 10.0 96% CI for mean = 81.6 - 90.5 *WASO (mins)* *Z = -2.21, p = .027* "Good sleep" Median = 39.8 (5.7 – 58.3) Mean = 36.7 ± 20.2 96% CI for mean = 19.8 – 53.5 "Poor sleep" Median = 56.7 (14.0 - 168.7)

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
					Mean = 68.3 ± 40.2 96% CI for mean = 50.5 - 86.1 *Number of awakenings after sleep onset* *Z = -2.62, p = .009* "Good sleep" Median = 3.0 (0 - 5) Mean = 2.8 ± 1.5 96% CI for mean = 1.5 - 4.0 "Poor sleep" Median = 5.0 (0 – 9) Mean = 2.8 ± 1.5 96% CI for mean = 4.0 – 5.9
PSQI [56] (Dew et al., 1994)	**Source:** **-**Recruited from prior study on sleep intensity and propensity in later life - Collected during a 12-month period from 57 healthy elders **Exclusion:** -Subjective/wake complaints -Current or past psychiatric disorder	**Polysomnography** - 3 nights -Sleep efficiency, slow-wave sleep, REM sleep, REM latency, number of micro-arousals, number of mini-arousals, AHI, MI	**Sleep quality** - Questionnaire, - 19 items, generate 7 component scores (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction)	N=57; - Mean age, 74.3 ± 7.96 (61-89) -93% high school graduates -95% white -76% retired or homemakers -35% taking at least one prescribed medication	**Baseline** *Good sleepers* (n=34) 3.91 ± 0.35 *Inefficient sleepers* (n=13) 3.84 ± 0.9 *Poorer sleepers* (n=10) 2.30 ± 0.73 Three-group comparison = 3.14, *p < .01* **1-year follow-up** *Good sleepers* (n=34) 5.53 ± .35 *Inefficient sleepers* (n=13) 4.61 ± .79

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
	-Serious or uncontrolled physical health problems -Medications that affect sleep or mood				*Poorer sleepers* (n=10) 3.50 ± .70 Three-group comparison = 1.17, *p = .28*
PSQI [62] (Fung et al., 2012)	**Source:** **-**Prospective, observational cohort study -18 ALFs in California USA -Recruited April 2006 - March 2008 -Proprietary (all but one facility) -Bed size ranged from 60–239. - Residents had control over sleep schedules, including bedtime and wake up time. -Recruited after a 30-minute presentation about sleep research during which the PI described the study **Inclusion:** -≥ 65 years	**Actigraphy** - 3 days and nights -TST, night-time percent sleep	**Sleep quality** - Questionnaire, - 18 items, generate 7 component scores (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction).	N=121; -Mean age, 85.3 ± 6.5 -Female, (n=87, 86%) -Non-Hispanic white race/ethnicity, (n=106, 88%) -Years of residence, 2.6 years ± 2.9 -MMSE score, 26.4 ± 3.1 -GDS-5 score, 1.1 ± 1.2 -ADLs, 6.3 ± 0.7 -IADLs, 5.3 ± 1.5 -Time between baseline and final follow-up visit, 223 days ± 45.3 -Use of night-time sedating medication, (N=39, 33.6%) -High risk of SA, 39 (32.5%)	**Paired t-tests** -No statistically significant relationships between TST, night-time percent sleep and PSQI total score **Bivariate testing** -No statistically significant relationships (using Sidak-corrected p-values for multiple comparisons) between objectively and subjectively measured sleep disturbances and participant characteristics -no statistically significant relationships between objectively-measured sleep variables and PSQI total score

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
	Exclusion: -Inability to communicate with research staff (due to aphasia or non-English-speaking) -Inability of the participant to provide written informed consent.			-Symptoms suggestive of RLS, (N=14, 11.6%)	
PSQI [11] (Landry, Best, & Liu-Ambrose, 2015)	**Source:** Advertising in newspapers, pamphlets distributed at community centres, and word of mouth. **Inclusion:** -Community dwelling adults 55 years or older; - ≥ 24 MMSE; - able to read, write, and speak English **Exclusion:** - People with dementia; or other neurodegenerative or neurological condition	**Actigraphy**: *Good sleep* - fragmentation ≤ 25 - efficiency ≥85 and - duration ≥ 420min *Poor sleep*: - fragmentation ≥40 - efficiency ≤75, or -duration ≤ 360min *Average* -those not covered above	**Sleep Quality** - Questionnaire, - 19 items, generate 7 component scores (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction)	N=78; - Mean age, 71.6 ± 6.6 - Women, 67% - Education (> High School), 82% - MMSE, 28.8 ± 1.2	**Concurrent Validity,** Bi-variate correlations reported: - Sleep efficiency *r, -0.03; not significant* - sleep latency r*, 0.21; not significant* - sleep duration/time r*, 0.29; p < .01* **Diagnostic Cross-tabulation** -2x2: Actigraphy, 2 levels (poor/good); and PSQI cut-off χ^2 (2)= .195; *p* = .907

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/ Psychometric Properties**
	that affects cognitive function and sleep; - Those enrolled on concurrent clinical trial; - Those unable to speak by telephone				
Pittsburgh Sleep Quality Index (PSQI) [67] (Most, Aboudan, Scheltens, & Van Someren, 2012)	**Source:** -Elderly people clinically diagnosed, by a neurologist or geriatrician, with probable Alzheimer disease, (NINCDS–ADRDA18 criteria) -Diagnoses made 1.07 ± 1.11 years prior to participation **Exclusion**: -Diagnosis with other neurologic or psychiatric disorders -SA -RLS	**Actigraph** -2 weeks -TIB, SOL, TST, percentage sleep, average sleep bout duration, percent wake, average wake bout duration, WASO, SE and fragmentation index.	**Sleep quality** - Questionnaire, - 19 items, generate 7 component scores (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction).	N=55; -Men, N=38 -Women, N=17 -Mean age, 70.4 ± 3.2 -MMSE, 22.7 ± 3.7 (14 – 30) **Normal comparison** -N=26 -Men, N=15 -Mean age, 73.0 ± 4.4 -Six partners of the participants and 20 volunteers from the local community -MMSE, 28.9 ± 0.8	**Regression** -PSQI Q4 (TST) predicted actigraphically estimated TST (df = 50, t = 2.57, β = .35, *p* = .01, for AD patients, and df = 24, t = 2.10, β = .40, *p* = .05, for the normal comparison group). -PSQI Q2 (Sleep onset) only in the normal comparison group, predicted actigraphically estimated SOL (df=24, t=3.29, β = .57, *p* = .003).

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
Pittsburgh Sleep Quality Index (PSQI), [74] (Postuma, Gagnon, Pelletier, & Montplaisir, 2017)	**Source:** -Following a cohort of idiopathic RBD patients -Between 2004 and 2016 following a large cohort -As part of a clinical follow up patients completed sleep scales. **Inclusion:** *RBD group* -Confirmed idiopathic RBD by PSG *Control group* -Confirmed absence of RBD through PSG **Exclusion:** -Parkinson's or Dementia	**Polysomnography** -one night -Sleep latency, TST, SE, Stage 1%, Stage 2%, SWS %, REM %, Phasic REM density %, Tonic REM %	**Sleep quality** - Questionnaire, - 25 items, generate 7 component scores (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction). Note: Until 2013 not all patients completed these scales, scales part of clinical assessment and assessed systematically as part of the research evaluation	**RBD Group** -Evaluated N=158, out of this included N=151 -at least one baseline sleep analysis -Mean age, 66.4 ± 8.3 -RBD duration from symptom onset 8.7 ± 9.3 years -Male, 75% -Neurodegenerative disease development from baseline, 3.2 ± 2.4 years (range: 1-11 years) **Control group** -Mean age, 68.9 ± 8.5 -Male, 74%	*PSQI mean scores* -Significant difference, with higher scores in patients than controls (7.2 ± 3.8 vs. 4.9 ± 3.4, p = .004) -A significant difference in the proportion of abnormal PSQI scores in RBD patients than controls (68.5% vs. 44.9%, p = .029). -Differences mainly driven by 'sleep disturbance' (1.49 ± .65 vs 1.21 ± .56, p = .035) and 'sleep medications' (1.51 ± 1.43 vs .28 ± .80). -No significant differences between those who converted and those who did not (7.1 ± 3.8, in convertors vs. 7.7 ± 4.1, in disease free, p = .52) -No significant differences in any subcomponent between those who converted or remained disease-free -No significant change in the total PSQI over time (change = -0.02 ± 30.8 points) or any subcomponent of the PSQI

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
					-No significant change in the total PSQI (change = -.82 ± 3.6, *p* = .36) -Self-reported sleep duration increased significantly over time in those who later developed the disease (+.88 ± 1.26h, *p* = .023), significant improvement in the PSQI sleep duration score (-0.44 ± .66, *p* = .014) and better sleep efficiency (-.44 ± .81, *p* = .04), changes that were also significantly different from those patients who remained diseases-free (sleep duration change in disease-free = .086 ± .72, *p* = .012, efficiency change = +.18 ± 1.19, *p* = .026).
PSQI [70] (Van Den Berg et al., 2008)	**Source:** -Part of the Rotterdam Study, a prospective population-based cohort study started in 1990 -Living in Ommoord -Investigating incidence of and risk factors for chronic and disabling diseases	**Actigraphy** -5-7 consecutive days -Event marker button pressed each night when trying to fall asleep and when they got out of bed each morning	**Sleep quality and disturbance** - Questionnaire, - 1-month period - 19 items, generate 7 component scores (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction).	N = 969; -Mean age, 68.5 ± 6.9 -Female, N= 506, 52.2% -Actigraphic TST (h:min), 6:31 ± 0:50 - Diary TST (h:min), 6:54 ± 0:57 -Difference between actigraphic and diary	**Direction of disagreement** **-**Definition: the average of the normal differences. Signals whether an individual has a tendency to over- or underestimate TST in diary when compared with the actigraphically measured TST. Positive differences indicate that diary estimates are higher than actigraphic parameters,

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
	-December 2004 invited to participant in the actigraphy study **Inclusion**: -At least 3 valid nights of actigraphy	-Bed time, get up time, sleep start, sleep end, TST, SOL, SE	- Global score 0 – 21	TST (h:min), 0:23 ± 1:04 -Actigraphic bed time (h:min), 23:51 ± 0:49 -Actigraphic get up time (h:min), 08:10 ± 0:46 -Actigraphic sleep onset latency (h:min), 0:21 ± 0:14 -Actigraphic sleep efficiency, 78.4% ± 7.4 -PSQI, 3.6 ± 3.5 -Use of sleep medication (≥1 night),	whereas negative differences reflect lower subjective than actigraphic values -Participants with poor perceived PSQI showed shorter diary estimates of TST than their actigraphic measures β = -7.12, (-8.12 – -6.13), $p < .001$ **Level of disagreement** -Definition: the average of the absolute differences between night-by-night diary estimates of TST and actigraphically measured TST. -Poorer PSQI score increased the level of disagreement β = .72, (.02 – 1.42), $p = .04$
Dutch Sleep Disorders Questionnaire (SDQ) [67] (Most, Aboudan, Scheltens, & Van Someren, 2012)	**Source:** -Elderly people clinically diagnosed, by a neurologist or geriatrician, with probable Alzheimer disease, (NINCDS–ADRDA18 criteria) -Diagnoses made 1.07 ± 1.11 years prior to participation	**Actigraph** -2 weeks -TIB, SOL, TST, percentage sleep, average sleep bout duration, percent wake, average wake bout duration, WASO, SE and fragmentation index.	**Sleep quality** -Questionnaire, -75 questions on a Likert scale "never" to "very often or always" -6 types of complaints (insomnia, periodic limb movement, excessive daytime sleepiness, narcolepsy, psychiatric diseases, and sleep apnoea	N=55; -Men, N=38 -Women, N=17 -Mean age, 70.4 ± 3.2 -MMSE, 22.7 ± 3.7 (14 – 30) **Normal comparison** -N=26 -Men, N=15 -Mean age, 73.0 ± 4.4	**Regression** -(AD Patients) SDQ EDS predicted the actigraphically estimated daytime activity level M10 (df = 49, t = −3.19, β = −.42, $p = .002$).

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
	Exclusion: -Diagnosis with other neurologic or psychiatric disorders -SA -RLS		-1 – 5 rating per item, cut-off 3 for likely presence	-Six partners of the participants and 20 volunteers from the local community -MMSE, 28.9 ± 0.8	
Self-rated Sleep Scale (SSA) [68] (Happe et al., 2005)	**Source:** -Patients with PD in Vienna, Austria -Control group data from SIESTA study and PD patients investigated according to same study protocol **Inclusion:** *Control group* -Age matched with PD -Fully completed sleep logs -PSQI score ≤ 5 *PD patients* -Clinically assessed by an experienced neurologist and classified according to Hoehn and Yahr **Exclusion:**	**Polysomnography** -2 nights -Scored accordingly to the Rechtschaffen and Kales criteria - TSP, SE, sleep latency to sleep stage 2, number of awakenings ≥ 30 seconds	**Sleep quality** -Self-rated on scale -Subjective sleep, quality of time awake and somatic disturbances at time of awakening. -Total score (sum of item score)	N=79; *PD patients* -N=17 -Female, N=6, 35.3% -Mean age, 64.1 ± 6.2 -Hoehn and Yahr, 2.1 ± 0.7, (median 2.0) -Disease duration, 5.6 ± 4.8 *Control group* -N=62 -Mean age, 64.4 ± 8.4 -Female N=36, 58.1%	**Subjective VS Objective measures** *Healthy controls* - PSG overestimated sleep latency, sleep efficiency, and sleep period time ($p < .01$) in second night - Significant correlation between objective and subjective sleep period time ($r > .280$, $p < .04$) and sleep efficiency ($r > .381$, $p < .004$) in both nights.

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
	All -Sleep medication *Control Group* -Presence of any relevant somatic and psychiatric disorders				
Sleep Disorders Inventory (SDI) [1] (Tractenberg, Singer, Cummings, & Thal, 2003).	**Source:** A concurrent trial for Melatonin as a therapy for sleep disturbances **Inclusion:** - Probable or Possible Alzheimer's Disease (NINCDS-ADRDA criteria) - average nightly total sleep time <7 hours over previous 2-3 weeks - at least two episodes of night time awakening over previous 2-3 weeks **Exclusion:** - none	**Actigraphy**, sleep time (night time, 8pm:8am; day time, 8am:8pm); wake after sleep onset; sleep efficiency	**Sleep Behaviour** - Questionnaire (Informant based) - Seven items (difficulty falling asleep, getting up during the night, wandering at night, awakening informant at night, awakening at night and thinking it is morning, awakening too early, sleeping excessively, other night time behaviours that bother the informant) - Each item rated for frequency (1 to 4), severity (1 to 3); and its product provides the item level score. Total SDI score is determined by the sum of the item level scores with higher scores indicating greater frequency and severity (0 to 96). Caregivers are also asked to	N=104 - Mean age, 75.5 $\pm$ 8.6 - Mean education, 12.6 $\pm$ 3.8 - Women, 49% - MMSE, 15.5 $\pm$ 8.4	**Concurrent Validity,** Bivariate correlations (Nonparametric), total SDI with: - Night Sleep Time (*rho,* -.244; $p < .01$) - Day Sleep Time (*rho,* .114; not significant) - Sleep Efficiency (*rho,* -.283; $p < .05$) - Wake After Sleep Onset (*rho,* .243; $p < .01$) - Night Sleep Time/Day Sleep Time (*rho,* .215; $p < .01$) - 24hr Sleep Time (*rho,* -.084; n/s)

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
			rate their distress for each item (1 to 5).		
Comprehensive Geriatric Assessment (CGA) [59] (Dos Santos et al., 2015)	**Source:** -Older adult population living in Sao Paulo, Brazil (EPIDOSO) -Underwent medical evaluations with health professionals **Inclusion:** -≤60 years -Responded to the sleep habits questionnaire and acceptance to PSG **Exclusion:** -Refusal to perform PSG -Problems that interfere with the examination (flu or fever)	**PSG** -1 night -awakenings, sleep onset latency, TST, SE, AHI, LM -Decreased SE if blow 85% and awakenings index normal until 10 events per hour -Diagnosis of AHI if ≤15 per hour and PLM ≤15 per hour	**Sleep habits** -Questionnaire in CGA -Questions on perceived sleep (difficulty sleeping, waking up during the night, difficulty to get back to sleep and walking up too early in the morning) -Yes/No responses (to only unusual behaviour during sleep and daytime evidences)	N=40; -Mean age, 73.68 (range = 64-89) -Female 55% -High BMI 27.36	***Relationship between PSG and CGA*** *Difficulty Sleeping* -Sleep onset latency, p = .015* *Waking up at night* -Sleep onset latency, p = .005* *Sleepiness* -Total sleep time, p = .005* -Sleep efficiency, p = .004* *Snoring* -Total sleep time, p = .027* -Sleep efficiency, p = .033* -Stage 2, p = .075* -Awakenings, p = .012* *Pause in breathing* -Sleep efficiency, p = .024* -Apnoea/hypopnea index, p =.001* No relationship between PSG and difficulty sleeping and waking up at night and leg movements **PSG compared with CGA rated normal/changed** -Awakenings, p = -x- -Sleep onset latency, p = .413

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
					-Total sleepy time, *p* =.035 -Sleep efficiency, *p* = .036 -Apnoea/hypopnea index, *p* = .213 -Leg movements, *p* = .496
Sleep Diary/Ecological momentary assessment (EMA) [49] (Baillet et al., 2016)	**Source:** -Subsample from AMImage2 cohort - ≤ 65 years - Retired and worked in agriculture for ≤20 years - Being affiliated to the MSA under own name - Living in rural area **Exclusion:** - Sleep medications - Diagnosed sleep disorders - Depression (CESD < 16)	**Actigraph** - 7 days and 8 nights - TST and SE	**Total sleep time** - 7 days and 8 nights - structured electronic sleep diary using Samsung Galaxy S assessing current context, psychological phenomena and interactions in daily life - 5 times a day over 1-week - Self reported questionnaire - Question: "how many hours did you sleep last night?" - First assessment every morning - Scale: 0h (no sleep at all) – 10h - At least 3 nights of complete objective and subjective evaluations	N=45; - Mean age 75.39 ± 0.62 - 42% women - CESD = 03.4 ± 0.52 - Happiness 05.5 ± 0.08 - MMSE, 27.7 ± 0.25 - Episodic memory 05.0 ± 0.13	**Paired t-test** N=175 nights - *Actigraphic TST* 08:09 ± 00:05 (*p* < .001) - *Self-report TST* 06:40 ± 00:06 (*p* < .001) - Average magnitude of different between objective and subjective TST was 1 hour and 29 minutes (*p* < .001) - *Sleep efficiency as a predictor of discrepancy* Sleep efficiency (ϒ = -.0003, SE = .019; *t* ratio = -.148) (p value not reported just not *p* < .05)

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
Epworth Sleepiness Scale (ESS) [50] (Beaudreau et al., 2012)	**Source:** - Community-dwelling women ≥65 between September 1986 – October 1998 from SOF **Inclusion:** - Women - ≥65 years	**Actigraphy** - ≥72 hours -WASO, day time inactivity	**Excessive daytime sleepiness** - Questionnaire - 8 items on likelihood respondent will fall asleep in eight different situations, each item rated on a scale 0-3 to generate a total score 0-24.	N=2968; - Mean age = 83.4 ± 3.7 years - Years of education = 12.9 ± 2.7 - Race (N=2662 white 89.7%, N=306 black 10.3%)	**Internal consistency ESS** Cronbach's α, .76 Range = .31 – .54 **Construct validity** Correlations reported: - ESS and daytime inactivity *r_s, .15; p < .001* - ESS and total sleep time *r_s, -.19; p < .001* - ESS and wake after sleep onset *r_s, .05; p < .01*
Epworth Sleepiness Scale (ESS) [74] (Postuma et al., 2017)	**Source:** -Following a cohort of idiopathic RBD patients -Between 2004 and 2016 following a large cohort -As part of a clinical follow up patients completed sleep scales. **Inclusion:** *RBD group* -Confirmed idiopathic RBD by PSG *Control group*	**Polysomnography** -one night -Sleep latency, TST, SE, Stage 1%, Stage 2%, SWS %, REM %, Phasic REM density %, Tonic REM %	**Daytime sleepiness** -Sleep propensity in eight standardized daily situations -Self-rated scale 0-3 – -Possible scores range from zero to 24, and higher scores reflect greater sleepiness	**RBD Group** -Evaluated N=158, out of this included N=151 -at least one baseline sleep analysis -Mean age, 66.4 ± 8.3 -RBD duration from symptom onset 8.7 ± 9.3 years -Male, 75% -Neurodegenerative disease development from baseline, 3.2 ± 2.4 years (range: 1-11 years)	*ESS mean scores* -No significant differences between idiopathic RBD patients and controls (7.0 ± 4.6 vs 7.2 ± 4.7, n=57, *p* = .77) -No significant difference in proportion of abnormal ESS (28.7% vs. 28.1%, *p* = 1.0) -No significant differences in baseline scores between those who eventually converted and those still remaining disease-free (6.7 ± 4.4 in convertors vs. 7.1 ± 4.7 in disease free, *p* = 1.0)

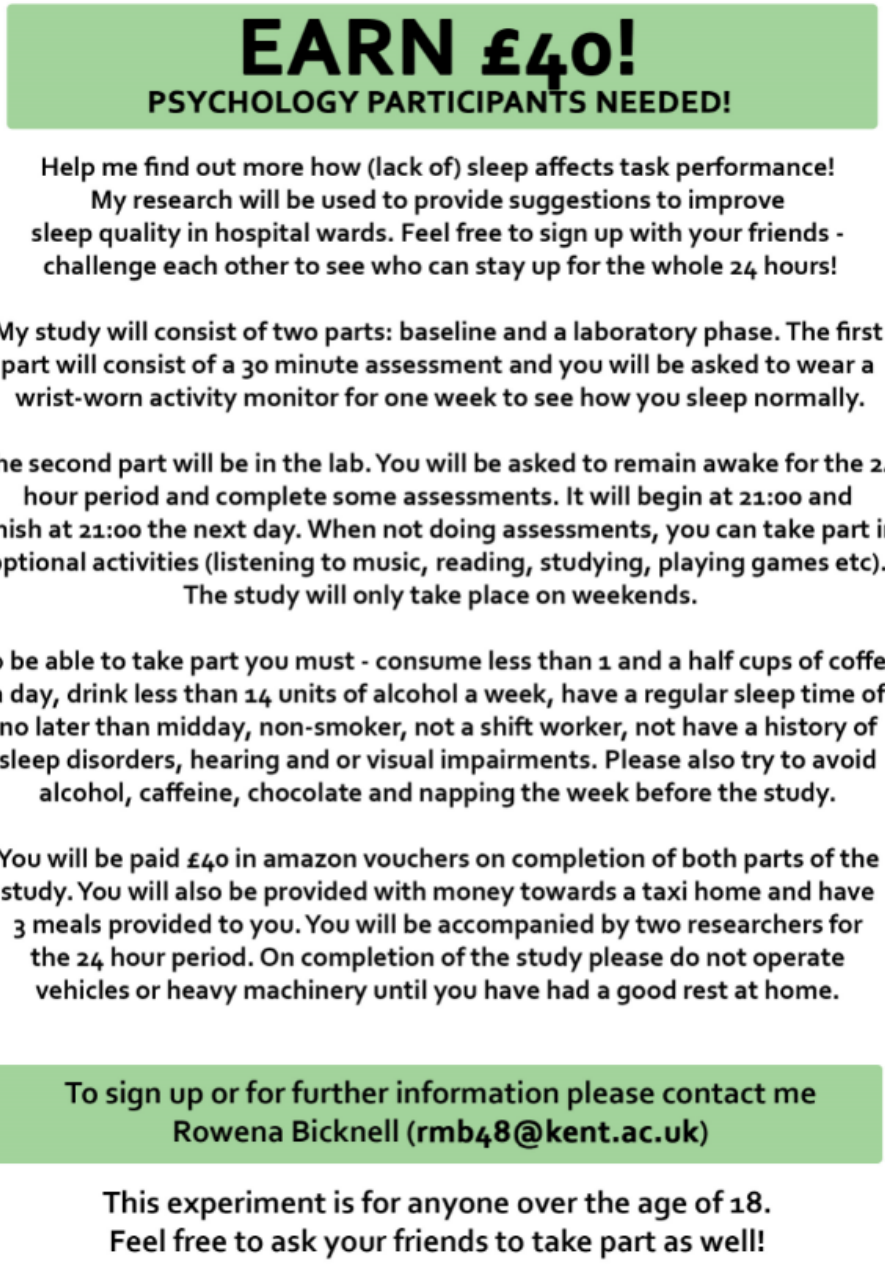
Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/** **Psychometric Properties**
	-Confirmed absence of RBD through PSG **Exclusion:** -Parkinson's or Dementia			**Control group** -Mean age, 68.9 ± 8.5 -Male, 74%	-No significant difference in time (average change = +0.07 ± 3.1 points, *p* = .99) -No significant differences in progression in ESS scores over time in those developing disease (mean change = +0.4 ± 2.1 points, *p* = .45).
Karolinska Sleepiness Scale (KSS) [76] (Paavilainen et al., 2005)	**Source:** -Nursing homes in Finland -Using the IST Vivago -Screened for dementia with CDR (non-demented = CDR ≥ 0.5) and MMSE (non-demented = MMSE ≥ 20) -Depression measured with GDS-5 -Functional ability with BI. **Exclusion:** -Refusal to use the device continuously for 24h per day throughout the study	**IST Vivago 3001** (Includes: wrist unit, a base station, alarm receiving and routing software) -wrist worn device - built in sensor for activity and usage monitoring - online monitoring whenever the wrist unit is worn and within active range of 60m in open space - has alarm to call for help -Activity analysed in periods: full 24h (21:00 – 21:00), day (09:00 to	**Alertness** -in daytime and evening -Questionnaire -9-scale, (1 "very alert", 9 "very sleepy, fighting sleep, an effort to keep awake" -Verbal descriptions with every second point	N=16; -Women, 15, Men, 1 -113 days	**Correlations** *Daytime alertness* -Poincare (min) SD2 = -.12, p < .001 -Poincare (24h-12h) = -.25, p < .001 -SD (24h) -.12, *p* < .001 -Mean (night) = .18, *p* < .001 -SD (night) = .11, *p* < .001 -Median (night) = .19, *p* < .001 -Mean (day) -.09, *p* < .01 -SD (day) = .08, *p* < .01 -Median (day) = -.09, *p* <.01 -Night (normalized) = .23, *p* < .001 -Day (normalized) = -.19, *p* < .001 -Night/day (median) = .23, *p* < .001 -Night/day (mean) = .24, *p* < .001

Scale Name (Authors, Year)	**Recruitment and Selection**	**Reference Measure**	**Disorder/Construct** Index Measure	**Demographic Data**	**Diagnostic Accuracy/ Psychometric Properties**
	-Chronic conditions seriously affecting wrist movements (e.g. Parkinson's disease and un-rehabilitated hemiplegia)	21:00) and night (00:00 to 06:00)			-Sine amplitude = -.20, p < .001 -Sine acrophase = -.17, p < .001 *Evening alertness* -Poincare (min) SD2 = -.10, p < .001 -Poincare (24h – 12h) = -.18, p < .001 -SD (24h) = -.09, p < .001 -Mean (night) = .16, p < .001 -SD night = .09, p < .01 -Median (night) = .16, p < .001 -Mean (day) = -.07, p < .01 -Median (day) = -.08, p < .01 -Night (normalized) = .19, p < .001 -Day (normalized) = -.16, p < .001 -Night/day (median) = .19, p < .001 -Night/day (mean) = .20, p < .001 -Sine amplitude = -.12, p < .001

Appendix B: Investigating the effect circadian rhythm and sleep deprivation has on neuropsychological and neuropsychiatric functioning

B.1 Study call for participation

Call for participation image used on social media



Participant Information Sheet

Dear Sir/Madam,

Please take time to read the following information carefully.

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Please ask if anything is unclear, and do not feel rushed into making a decision. Please ask if anything is unclear, and do not feel rushed into making a decision.

What is the purpose of this study?
The purpose of this study is to find out about how the circadian rhythm (the internal body clock) is affected by sleep deprivation and whether certain symptoms (which come under a term called psychotomimetic states) can be observed in the healthy adult population. We were also looking at your performance in neuropsychological and neuropsychiatric tasks whilst you were sleep deprived and whether this showed a trend in line with your internal body clock.

What would taking part involve?
This study is made up of two parts: screening and baseline and a laboratory phase.

<u>Screening</u>

The Researcher will meet with you in the laboratory to discuss this project with you and be able to answer questions. If you decide to take part, we will ask your permission for us to use your information in the study by asking you to complete a consent form. The Researcher will then take you through a few assessments to make sure the study is right for you.

This will take around 30 minutes and will include

- Some questions on smoking, caffeine, drug and or medication, alcohol intake, recent travel history, the presence of shift-work as well as hearing and visual impairments
- Some questions on the presence of psychiatric disorders, your internal body clock, sleep and mood.

Please note to be included in the study you need to meet some requirements. These are as follows: consume less than 1 ½ cups of coffee a day, less than 14 units of alcohol a week (the government guideline), non-smoker (including e-cigarettes), not a shift worker (e.g. work night shifts), not travelled between significant time-zones in the last 2 months, not have a regular bedtime of later than 12:00 (e.g. you stay up all night and go to bed at midday), not currently on drugs or medication (other than vitamins or the contraceptive pill), not have a medical history of visual (other than glasses or contact lenses, corrected to normal vision) or hearing impairments or a sleep disorder and not have a medical history of a psychiatric disorder.

If you are suitable for the study, we will invite you to complete baseline assessments.

Baseline

The Researcher will conduct some more assessments. It is important that this part of the study takes place seven days before the laboratory phase begins. This will include:

- Questions on psychotic-type experiences such as; false beliefs, changes to your how you view the environment around you, confusion, the inability to feel and experience pleasure, mood and hearing or seeing things which aren't there.
- Measuring your height and weight to work out your BMI

In addition to this, we will also ask you to wear an ActiGraph activity monitor on your non-dominate wrist to measure your sleep (see right). This is a very good way to measure the quality and duration of your sleep and is often used in this type of research. We will ask you to wear the ActiGraph for seven days. The ActiGraph is waterproof so you can even wear it in the shower.

We will also provide you with a sleep diary to help give us a richer understanding of your sleep patterns. We will ask you to complete this for seven days as well alongside the ActiGraph activity monitor.

Please refrain from alcohol, caffeine, chocolate intake and napping between baseline and the laboratory phase.

Laboratory

The Researcher will arrange to meet with you after your baseline assessment has been completed. This will be the day immediately after this period has ended (Day 8 of Baseline) after a night of normal sleep.

We will meet you 21:00 in the laboratory where we will collect the Actigraph activity monitor and diary from you. You will be asked to complete some assessments every four hours during a 24-hour period. These will include:

- Questions on psychotic-type experiences
- Questions on sleep
- Assessments involving pen and paper as well as computerised tasks on reaction time and attention

You will be asked to not sleep for the 24 hours that you spend in the laboratory phase. You will be free to take part in optional activities such as listening to music, reading, studying, playing games and using your mobile phones. Meals will be provided and the lights will be adjusted throughout the day. There will be two researchers in total, one male and one female

supervising you throughout the study to ensure you remain awake at all times and you will be taking part at the same time as other participants. If you require the bathroom, a researcher of the same sex will accompany you and wait outside. Please do not to nap, consume alcohol or drink caffeine in the 24 hours to the run up of the laboratory phase.

In total, the Researcher will need to meet with you two times. The first time will be around 30 minutes and for the second part 24 hours (from 21:00 to 21:00 the following day) in the laboratory. You will need to wear the ActiGraph and use a sleep diary for seven days during the baseline phase of the study.

The research team may advise you to contact your GP to make further investigations if we feel any of our findings from the study are relevant to your health and wellbeing.

What are the possible benefits of taking part?

By taking part in our study you will help us increase our understanding of the relationship between sleep deprivation, neuropsychological and neuropsychiatric tasks and your internal body clock. You will also earn a £40 Amazon voucher for your participation, have a taxi ride home provided to you (unless discussed otherwise) and three meals provided.

What are the possible disadvantages and risks of taking part?

People will feel tired at the end of the laboratory session. Please remember not to operate vehicles or heavy machinery. You will also be provided with taxi home as you may be too tired to drive or cycle after the study (unless otherwise discussed). Please make sure you have a good rest at home after taking part in the study.

What if something goes wrong?

This research project is simply to monitor how you are doing as you are being sleep deprived. It is very unlikely the research itself will cause you harm. If you feel unwell and it is urgent, please contact your General Practitioner. If you believe that it may be related to the research project, please contact Rowena Bicknell.

What will happen if I don't want to carry on with the study?

You will be able to withdraw from the study at any time. If you refuse to take part or if you decide to withdraw, this will not affect the care that you receive. If you do choose to withdraw or are no longer able to participate, the study investigators will keep the data collected up to that point.

How will my information be kept confidential?

All information we collect from you will be kept confidential as required by law. The

information you provide will be kept in password protected computer programs and in locked filing cabinets at the University of Kent. Only the research team will have access to your information. The only thing that will contain your name will be the consent form and all other documents will refer to you by a number to keep data anonymous.

What will happen to the results of this study?

The results from this study will be analysed and reported in publications in medical journals; presented at conferences; and will be included in a doctoral thesis. We will be happy to provide you with a summary of our findings and/or a copy of the published research, should you wish to have one.

Who is organising and funding this study?

This study is organised by Rowena Bicknell, (Research PhD Student, Centre for Health Services) at the University of Kent. The University is providing the funds for this PhD project. You should contact Rowena Bicknell if you require further information relating to the study.

Please contact for further information

Rowena Bicknell (PhD Student) Researcher
Centre for Health Services Studies, 2nd Floor George Allen Wing, Cornwallis Building, University of Kent, Canterbury, CT2 7NF
Phone: 01227 16436 Email: rmb48@kent.ac.uk

Dr David Lowery (Supervisor)
Centre for Health Services Studies, 2nd Floor George Allen Wing, Cornwallis Building, University of Kent, Canterbury, CT2 7NF
Phone: 01227 824908 Email: d.lowery@kent.ac.uk

Dr David Wilkinson (Supervisor)
School of Psychology, Keynes College, University of Kent, Canterbury, Kent, CT2 7NP
Phone: 01227 824772 Email: D.T.Wilkinson@kent.ac.uk.

We thank you for taking time to read this. If you decide to participate in the study, you will receive a copy of this Information Sheet and a Consent Form that you must later sign.

Participant Identification Code:

Consent Form

Name of Researcher: Rowena Bicknell, Centre for Health Services Studies, Rutherford Annexe, University of Kent, Canterbury, CT2 7NX, 01227 16436, rmb48@kent.ac.uk

Supervisors: Dr David Lowery (01227 824908, d.lowery@kent.ac.uk) and Dr David Wilkinson (01227 824772, d.t.wilkinson@kent.ac.uk)

Please initial box

1. I confirm I have read and understand the information sheet. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand I may be too tired to drive or cycle after the study and that I will be offered a taxi home if I live in Canterbury. If I decline this offer I understand it will be my responsibility to make my own travel arrangements home. I understand that I should not operate vehicles or heavy machinery until after I have a good rest at home. ☐
4. I agree to take part in the above study. ☐

_____	_____	_____
Name of Participant	Date	Signature
_____	_____	_____
Name of Person taking consent	Date	Signature

When completed, 1 for participant; 1 for researcher (original).

Participant Identification Code:

Actigraphy monitor

I confirm that I have received the actigraphy monitor

Serial number _____

Participant signature _____

Researcher signature _____

Date _ _ / _ _ / _ _ _ _

Summary for Research Team

Laboratory

This aspect of the study will be conducted in the School of Psychology laboratories on Level 2 (in 2.01 and 2.02) at the University of Kent. The laboratory study will take place after a night of normal sleep which will be assessed using an actigraphy monitor seven days to the run up of the study. Participants will be asked to refrain from alcohol, caffeine, chocolate intake and napping the week before the study. Participants will also be asked to complete a short questionnaire to check whether they had adhered to the study rules (not napping, consuming alcohol or drink caffeine). Participants will still be included even if they have broken these guidelines.

The session will start at 21:00 hours where the participant will be invited to the laboratory to complete the following assessments

To be completed by the participant

- Study adherence questionnaire (to be completed once by the participant at 21:00)
- Psychotomimetic States Inventory (PSI) (paper)
- Stanford Sleepiness Scale (SSS) (paper)
- Positive And Negative Affect Scale (PANAS) (paper)
- Trail Making Test (TMT) (paper) 4 different versions of this, each version will be clearly marked with the participant number and time
- Sustained Attention to Response Task (SART) (computer) repeated 3 times per assessment
- Corsi Block-Tapping Test (CBTT) (computer)

To be completed by the researcher (based on either measurements or observations)

- Delirium Rating Scale (DRS R-98)
- Core body temperature (using a thermometer)

Other

- Pen
- USB stick containing CBTT and SART

Assessments will take place at four-hourly intervals from 21:00. There will be 7 assessments in total and the last assessment phase will be at 21:00 hours. Participants will be supervised at all times.

Rowena will provide the materials for the pen and paper assessments prior to the study and pre-label these with the individualized participant codes. Participants will be reminded of their unique identifier code at the start of the study. For computerized assessments, the program for these will be pre-installed on the PCs being used for assessments. Researchers will be required to guide participants to a PC, open the program and enter the individualized participant code as well as the session number (and number of times, only relevant for the SART). At the end of the assessment the Researcher will check that this has been saved on the PC before guiding the participant back to the main room.

The timings are as follows:

Assessment number	Time
1	21:00
2	01:00
3	05:00
4	09:00
5	13:00
6	17:00
7	21:00

Kent IT services have provided us with a temporary log in to use. The details for this are as follows:

[REDACTED]

Participants will be asked to stay in the laboratory at all times throughout the study. The only exception will be if they need to use the toilet which they will be allowed to do so. There will be two researchers at all times. If a participant needs to go to the toilet a researcher will accompany them (to the unisex bathroom opposite the lab). The researcher will wait outside for the participant. If the participant does not emerge from the bathroom in 10 minutes the researcher will knock and call out to see if the participant is OK. If after repeated knocking there is no reply, the assumption will be made that the participant has fallen asleep. Campus Security will be notified as well in case something has happened to the participant. Campus Security are aware of the study taking place. Their number is 01227 823333 (emergencies). You can also contact for help using the SafeZone app on your phone.

The researcher shifts will be as follows

21:00 – 03:00
03:00 – 09:00
09:00 – 15:00
15:00 – 21:00

When not performing assessments, participants (and researchers) will be free to take part in optional activities such as; listening to music, reading, studying, playing games and they will be allowed to use their mobile phones. In an effort to preserve endogenous circadian rhythms, standard meals will be served to participants in line with their normal meal times. In an effort to preserve established endogenous circadian rhythms, light will be adjusted in line with the external environment. This will be done by observing sunrise and sunset times available online via weather report websites. Lights will therefore be dimmed in the laboratory after sunset (by either adjusting the blinds in the room and or turning off the lights at the switch) and participants will be monitored by researchers to ensure they remain awake at all times. The study will end once the last assessment which will be conducted at 24 hours after their arrival at the laboratory. At the end of the study, participants will be debriefed and reminded to have a good rest at home and not operate vehicles or heavy machinery. Participants will be reminded that it is their own responsibility to make their own travel arrangements home if they are too tired to drive or cycle. This will be made clear in the Participant Information Sheet and in the Informed Consent form. They will also receive payment of £40 and 8 RPS course credits at the end of the study.

Participant Identification Code:

Study Assessment Record - Lab

Time	Assessment	Initials	Comments
21:00	Study adherence questionnaire		
	Retrieve completed sleep diary		
	Retrieve actigraphy monitor		
	Body temperature		
	Psychotomimetic States Inventory		
	Stanford Sleepiness Scale		
	Positive and Negative Affect Scale		
	Trail Making Test Part A		
	Trail Making Test Part B		
	Sustained Attention Task 1		
	Sustained Attention Task 2		
	Sustained Attention Task 3		
	Corsi Block Tapping Task		
	Delirium Rating Scale		
01:00	Body temperature		
	Psychotomimetic States Inventory		
	Stanford Sleepiness Scale		
	Positive and Negative Affect Scale		
	Trail Making Test Part A		
	Trail Making Test Part B		
	Sustained Attention Task 1		

	Sustained Attention Task 2		
	Sustained Attention Task 3		
	Corsi Block Tapping Task		
	Delirium Rating Scale		
05:00	Body temperature		
	Psychotomimetic States Inventory		
	Stanford Sleepiness Scale		
	Positive and Negative Affect Scale		
	Trail Making Test Part A		
	Trail Making Test Part B		
	Sustained Attention Task 1		
	Sustained Attention Task 2		
	Sustained Attention Task 3		
	Corsi Block Tapping Task		
	Delirium Rating Scale		
09:00	Body temperature		
	Psychotomimetic States Inventory		
	Stanford Sleepiness Scale		
	Positive and Negative Affect Scale		
	Trail Making Test Part A		
	Trail Making Test Part B		
	Sustained Attention Task 1		
	Sustained Attention Task 2		
	Sustained Attention Task 3		

	Corsi Block Tapping Task		
	Delirium Rating Scale		
13:00	Body temperature		
	Psychotomimetic States Inventory		
	Stanford Sleepiness Scale		
	Positive and Negative Affect Scale		
	Trail Making Test Part A		
	Trail Making Test Part B		
	Sustained Attention Task 1		
	Sustained Attention Task 2		
	Sustained Attention Task 3		
	Corsi Block Tapping Task		
	Delirium Rating Scale		
17:00	Body temperature		
	Psychotomimetic States Inventory		
	Stanford Sleepiness Scale		
	Positive and Negative Affect Scale		
	Trail Making Test Part A		
	Trail Making Test Part B		
	Sustained Attention Task 1		
	Sustained Attention Task 2		
	Sustained Attention Task 3		
	Corsi Block Tapping Task		
	Delirium Rating Scale		

21:00	Body temperature		
	Psychotomimetic States Inventory		
	Stanford Sleepiness Scale		
	Positive and Negative Affect Scale		
	Trail Making Test Part A		
	Trail Making Test Part B		
	Sustained Attention Task 1		
	Sustained Attention Task 2		
	Sustained Attention Task 3		
	Corsi Block Tapping Task		
	Delirium Rating Scale		
	Reimburse participant and complete reimbursement confirmation		
	Debrief		

Participant Identification Code:

Study adherence questionnaire

This questionnaire is to check whether you have stuck to the pre-study guidelines or not. Please answer these questions as truthfully as possible. Your responses will not affect your eligibility to take part in this study. Thank you.

Within the 7 days, have you …		**Details – amount and date** (only complete if you answer YES)
Consumed alcohol	YES / NO	
Taken a nap	YES / NO	
Drunk caffeine	YES / NO	
Eaten chocolate	YES / NO	

Within the last 24 hours, have you …		**Details - amount and date** (only complete if you answer YES)
Consumed alcohol	YES / NO	
Taken a nap	YES / NO	
Drunk caffeine	YES / NO	

Participant Identification Code:

Body temperature

Time	Temperature	Comments
21:00		
01:00		
05:00		
09:00		
13:00		
17:00		
21:00		

Participant Identification Code:

Stanford Sleepiness Scale

We would like to know how alert you are feeling right now.

This simple seven–point Likert-type scale has descriptors ranging from “feeling active, vital alert, or wide awake” (score = 1) to “no longer fighting sleep, sleep onset soon and having dream-like thoughts” (score = 7). Choose the set of descriptors that best describes your feeling of sleepiness at the time this scale is administered (at the time of the sleep assessment/right now).

Degree of Sleepiness	**Scale Rating**
Feeling active, vital, alert, or wide awake	1
Functioning at high levels, but not at peak; able to concentrate	2
Awake, but relaxed; responsive but not fully alert	3
Somewhat foggy, let down	4
Foggy; losing interest in remaining awake; slowed down	5
Sleepy, woozy, fighting sleep; prefer to lie down	6
No longer fighting sleep, sleep onset soon; having dream-like thoughts	7
Asleep	X

Degree of Sleepiness	**Scale Rating**
Assessment 1 (21:00)	
Assessment 2 (01:00)	
Assessment 3 (05:00)	
Assessment 4 (09:00)	
Assessment 5 (13:00)	
Assessment 6 (17:00)	
Assessment 7 (21:00)	

Participant Identification Code:

Positive and Negative Affect Scale

Worksheet 3.1 The Positive and Negative Affect Schedule (PANAS; Watson et al., 1988)

PANAS Questionnaire

This scale consists of a number of words that describe different feelings and emotions. Read each item and then list the number from the scale below next to each word. **Indicate to what extent you feel this way right now, that is, at the present moment *OR* indicate the extent you have felt this way over the past week (circle the instructions you followed when taking this measure)**

1	2	3	4	5
Very Slightly or Not at All	A Little	Moderately	Quite a Bit	Extremely

Assessment 1: 21:00

_____ 1. Interested	_____ 11. Irritable
_____ 2. Distressed	_____ 12. Alert
_____ 3. Excited	_____ 13. Ashamed
_____ 4. Upset	_____ 14. Inspired
_____ 5. Strong	_____ 15. Nervous
_____ 6. Guilty	_____ 16. Determined
_____ 7. Scared	_____ 17. Attentive
_____ 8. Hostile	_____ 18. Jittery
_____ 9. Enthusiastic	_____ 19. Active
_____ 10. Proud	_____ 20. Afraid

Assessment 2: 01:00

_____ 1. Interested	_____ 11. Irritable
_____ 2. Distressed	_____ 12. Alert
_____ 3. Excited	_____ 13. Ashamed
_____ 4. Upset	_____ 14. Inspired
_____ 5. Strong	_____ 15. Nervous
_____ 6. Guilty	_____ 16. Determined
_____ 7. Scared	_____ 17. Attentive
_____ 8. Hostile	_____ 18. Jittery
_____ 9. Enthusiastic	_____ 19. Active
_____ 10. Proud	_____ 20. Afraid

Assessment 3: 05:00

_____ 1. Interested	_____ 11. Irritable
_____ 2. Distressed	_____ 12. Alert
_____ 3. Excited	_____ 13. Ashamed
_____ 4. Upset	_____ 14. Inspired
_____ 5. Strong	_____ 15. Nervous
_____ 6. Guilty	_____ 16. Determined
_____ 7. Scared	_____ 17. Attentive
_____ 8. Hostile	_____ 18. Jittery
_____ 9. Enthusiastic	_____ 19. Active
_____ 10. Proud	_____ 20. Afraid

Assessment 4: 09:00

_____ 1. Interested	_____ 11. Irritable
_____ 2. Distressed	_____ 12. Alert
_____ 3. Excited	_____ 13. Ashamed
_____ 4. Upset	_____ 14. Inspired
_____ 5. Strong	_____ 15. Nervous
_____ 6. Guilty	_____ 16. Determined
_____ 7. Scared	_____ 17. Attentive
_____ 8. Hostile	_____ 18. Jittery
_____ 9. Enthusiastic	_____ 19. Active
_____ 10. Proud	_____ 20. Afraid

1	2	3	4	5
Very Slightly or Not at All	A Little	Moderately	Quite a Bit	Extremely

Assessment 5: 13:00

_____ 1. Interested	_____ 11. Irritable
_____ 2. Distressed	_____ 12. Alert
_____ 3. Excited	_____ 13. Ashamed
_____ 4. Upset	_____ 14. Inspired
_____ 5. Strong	_____ 15. Nervous
_____ 6. Guilty	_____ 16. Determined
_____ 7. Scared	_____ 17. Attentive
_____ 8. Hostile	_____ 18. Jittery
_____ 9. Enthusiastic	_____ 19. Active
_____ 10. Proud	_____ 20. Afraid

Assessment 6: 17:00

_____ 1. Interested	_____ 11. Irritable
_____ 2. Distressed	_____ 12. Alert
_____ 3. Excited	_____ 13. Ashamed
_____ 4. Upset	_____ 14. Inspired
_____ 5. Strong	_____ 15. Nervous
_____ 6. Guilty	_____ 16. Determined
_____ 7. Scared	_____ 17. Attentive
_____ 8. Hostile	_____ 18. Jittery
_____ 9. Enthusiastic	_____ 19. Active
_____ 10. Proud	_____ 20. Afraid

Assessment 7: 21:00

_____ 1. Interested	_____ 11. Irritable
_____ 2. Distressed	_____ 12. Alert
_____ 3. Excited	_____ 13. Ashamed
_____ 4. Upset	_____ 14. Inspired
_____ 5. Strong	_____ 15. Nervous
_____ 6. Guilty	_____ 16. Determined
_____ 7. Scared	_____ 17. Attentive
_____ 8. Hostile	_____ 18. Jittery
_____ 9. Enthusiastic	_____ 19. Active
_____ 10. Proud	_____ 20. Afraid

Participant Identification Code:
Time:

Delirium Rating Scale R-98

Name of Rater: _____

SEVERITY SCORE: [ ] **TOTAL SCORE:** [ ]

Severity Item	Item Score				Optional Information
Sleep-wake cycle	0	1	2	3	Naps Nocturnal disturbance only Day-night reversal
Perceptual disturbances	0	1	2	3	Sensory type of illusion or hallucination: auditory visual olfactory tactile Format of illusion or hallucination: simple complex
Delusions	0	1	2	3	Type of delusion: persecutory Nature: poorly formed systematized
Lability of affect	0	1	2	3	Type: angry anxious dysphoric elated irritable
Language	0	1	2	3	Check here if intubated, mute, etc.
Thought process	0	1	2	3	Check here if intubated, mute, etc.
Motor agitation	0	1	2	3	Check here if restrained *Type of restraints:*
Motor retardation	0	1	2	3	Check here if restrained *Type of restraints:*
Orientation	0	1	2	3	Date: Place: Person:
Attention	0	1	2	3	
Short-term memory	0	1	2	3	Record # of trials for registration of items: Check here if category cueing helped
Long-term memory	0	1	2	3	Check here if category cueing helped
Visuospatial ability	0	1	2	3	Check here if unable to use hands
Diagnostic Item	**Item Score**				**Optional Information**
Temporal onset of symptoms	0	1	2	3	Check here if symptoms appeared on a background of other psychopathology
Fluctuation of symptom severity	0	1	2		Check here if symptoms only appear during the night

Participant Identification Code:
Time:

Psychotomimetic States Inventory

Please complete the following questions by circling the number that best describes your experience <u>at the moment</u>

	Not at all	*Slightly*	*Moderately*	*Strongly*
1. You enjoy mixing with people	3	2	1	0
2. You hesitate even when you know what you are going to say	0	1	2	3
3. Your mood is going up and down a lot	0	1	2	3
4. You feel that you can predict what is about to happen	0	1	2	3
5. You feel more sensitive to light or the colour or brightness of things	0	1	2	3
6. You feel close to people	3	2	1	0
7. You think you are being talked about	0	1	2	3
8. It is more difficult than normal to follow conversations with people	0	1	2	3
9. You feel rather indifferent about things	0	1	2	3
10. Your mind jumps a lot from one thing to another	0	1	2	3
11. You think people are saying or doing things to annoy you	0	1	2	3
12. You think other people can read your mind	0	1	2	3
13. You find it more difficult than usual to start doing things	0	1	2	3
14. You are bothered by the idea that people are watching you	0	1	2	3
15. You find activities less enjoyable than usual	0	1	2	3
16. Your mind is so full of ideas that you can't concentrate on one thing	0	1	2	3
17. You feel that people have it in for you	0	1	2	3
18. It is fun to do things with other people	3	2	1	0
19. You feel that you have special or magical powers	0	1	2	3
20. Your sense of smell is unusually strong or different	0	1	2	3
21. You want to be the centre of attention more than usual	0	1	2	3
22. Your experience of time is unnaturally fast or slow	0	1	2	3
23. You feel that no one understands you	0	1	2	3

Please turn over

	Not at all	*Slightly*	*Moderately*	*Strongly*
24. You feel rather uninvolved with other people	0	1	2	3
25. People can put thoughts into your mind	0	1	2	3
26. You are experiencing something very special or important	0	1	2	3
27. Your hearing has become very sensitive	0	1	2	3
28. You find it difficult to think clearly	0	1	2	3
29. You stop to think things over before doing them	3	2	1	0
30. Your speech is difficult to understand because your words are all mixed up	0	1	2	3
31. You feel that you might cause something to happen just by thinking about it	0	1	2	3
32. You feel as though your head, limbs or body have somehow changed	0	1	2	3
33. You feel that you deserved to be punished in some way	0	1	2	3
34. When you try to concentrate many unrelated thoughts pop into your mind	0	1	2	3
35. Your thoughts are sometimes so strong that you can almost hear them	0	1	2	3
36. You have seen a person's face in front of you when no one was in fact there	0	1	2	3
37. Your thoughts stop suddenly, interrupting what you are saying	0	1	2	3
38. You have a vague sense of danger or sudden dread for reasons you don't understand	0	1	2	3
39. You would feel uncomfortable if your friends were to touch you	0	1	2	3
40. You feel that you can read other people's minds	0	1	2	3
41. Ideas and insights come to you so fast that you can't express them all	0	1	2	3
42. You think people are laughing about you behind your back	0	1	2	3
43. You have the feeling of gaining or losing energy when people look at or touch you	0	1	2	3
44. You can sense an evil presence around you, even though you cannot see it	0	1	2	3
45. You can see shapes and forms even though they aren't there	0	1	2	3
46. You are easily distracted when doing something or talking to someone	0	1	2	3
47. You are confused by too much happening at the same time	0	1	2	3
48. You believe you are a special person with an important mission	0	1	2	3

University of Kent
School of Psychology

Circadian rhythm and Sleep Deprivation on Psychotomimetic States

CHSS
University of Kent
Centre for Health Services Studies

Sleep Diary

Participant identification code:				
Day (i.e. Monday) Date (i.e. 01/07/16)	**Example** Day 1: Monday Date: 01/08/17	**Day 1:** **Date: _ _ / _ _ / _ _**	**Day 2:** **Date: _ _ / _ _ / _ _**	**Day 3:** **Date: _ _ / _ _ / _ _**
Time woke in the morning	7:30 am			
Time, length and location of sleeps in the day (including naps)	1:00 – 1:20pm, 20 minutes, on the sofa 4:35 – 5:00pm, 25 minutes, in bed			
Time started preparing for bed	09:30pm			
Any problems	No			
Where you went to bed	Bed			
Time went to sleep	10:00pm			

Day (i.e. Monday) Date (i.e. 01/07/16)	Day 4: Date: _ _ / _ _ / _ _	Day 5: Date: _ _ / _ _ / _ _	Day 6: Date: _ _ / _ _ / _ _	Day 7: Date: _ _ / _ _ / _ _
Time woke in the morning				
Time, length and location of sleeps in the day (including naps)				
Time started preparing for bed				
Any problems				
Where you went to bed				
Time went to sleep				

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School of Psychology

Circadian rhythm and Sleep Deprivation on Psychotomimetic States

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University of Kent
Centre for Health Services Studies

Participant Identification code:

Did you take the sleep watch off? If so, please fill in the details below for each time you took it off

Example **Date:** 01/08/17	**Date:** _ _ / _ _ / _ _	**Date:** _ _ / _ _ / _ _	**Date:** _ _ / _ _ / _ _	**Date:** _ _ / _ _ / _ _
Time (start): 7:35am	**Time (start):**	**Time (start):**	**Time (start):**	**Time (start):**
Time (end): 7:55am	**Time (end):**	**Time (end):**	**Time (end):**	**Time (end):**
Reason: took a bath	**Reason:**	**Reason:**	**Reason:**	**Reason:**
Date: _ _ / _ _ / _ _	**Date:** _ _ / _ _ / _ _	**Date:** _ _ / _ _ / _ _	**Date:** _ _ / _ _ / _ _	**Date:** _ _ / _ _ / _ _
Time (start):	**Time (start):**	**Time (start):**	**Time (start):**	**Time (start):**
Time (end):	**Time (end):**	**Time (end):**	**Time (end):**	**Time (end):**
Reason:	**Reason:**	**Reason:**	**Reason:**	**Reason:**

University of Kent
School of Psychology

Circadian rhythm and Sleep Deprivation on Psychotomimetic States

CHSS
University of Kent
Centre for Health Services Studies

Participant Identification code:

Did you take the sleep watch off? If so, please fill in the details below for each time you took it off

Example **Date:** 01/08/17	**Date:** _ _ / _ _ / _ _	**Date:** _ _ / _ _ / _ _	**Date:** _ _ / _ _ / _ _	**Date:** _ _ / _ _ / _ _
Time (start): 7:35am	**Time (start):**	**Time (start):**	**Time (start):**	**Time (start):**
Time (end): 7:55am	**Time (end):**	**Time (end):**	**Time (end):**	**Time (end):**
Reason: took a bath	**Reason:**	**Reason:**	**Reason:**	**Reason:**
Date: _ _ / _ _ / _ _	**Date:** _ _ / _ _ / _ _	**Date:** _ _ / _ _ / _ _	**Date:** _ _ / _ _ / _ _	**Date:** _ _ / _ _ / _ _
Time (start):	**Time (start):**	**Time (start):**	**Time (start):**	**Time (start):**
Time (end):	**Time (end):**	**Time (end):**	**Time (end):**	**Time (end):**
Reason:	**Reason:**	**Reason:**	**Reason:**	**Reason:**

Participant Identification Code:

Pre-study guideline questionnaire

1. Do you smoke? YES/NO
2. Do you drink caffeine? YES/NO Details:
3. Do you currently take any drugs or medication (other than vitamins?) YES/NO Details
4. Do you drink alcohol? YES/NO Details:
5. In the last two months have you had trans-meridian travel? YES/NO
6. Are you a shift worker? YES/NO
7. Have you have a history of sleep disorders? YES/NO
8. Do you have a medical history of hearing impairments? YES/NO
9. Do you have a medical history of visual impairments (other than glasses or contact lenses, corrected to normal vision)? YES/NO
10. Do you usually go to bed later than 12:00 (midday)? YES/NO
11. (If applicable) When was your last period? Details:

Participant Identification Code:

Mini International Psychiatric Interview

	MODULES	TIME FRAME	MEETS CRITERIA	DSM-IV	ICD-10	
A	MAJOR DEPRESSIVE EPISODE	Current (2 weeks)	☐	296.20-296.26 Single	F32.x	☐
		Recurrent	☐	296.30-296.36 Recurrent	F33.x	☐
	MDE WITH MELANCHOLIC FEATURES Optional	Current (2 weeks)	☐	296.20-296.26 Single	F32.x	☐
				296.30-296.36 Recurrent	F33.x	☐
B	DYSTHYMIA	Current (Past 2 years)	☐	300.4	F34.1	☐
C	SUICIDALITY	Current (Past Month) Risk: ☐ Low ☐ Medium ☐ High	☐			☐
D	MANIC EPISODE	Current	☐	296.00-296.06	F30.x-F31.9	☐
		Past	☐			
	HYPOMANIC EPISODE	Current	☐	296.80-296.89	F31.8-F31.9/F34.0	☐
		Past	☐			
E	PANIC DISORDER	Current (Past Month)	☐	300.01/300.21	F40.01-F41.0	☐
		Lifetime	☐			
F	AGORAPHOBIA	Current	☐	300.22	F40.00	☐
G	SOCIAL PHOBIA (Social Anxiety Disorder)	Current (Past Month)	☐	300.23	F40.1	☐
H	OBSESSIVE-COMPULSIVE DISORDER	Current (Past Month)	☐	300.3	F42.8	☐
I	POSTTRAUMATIC STRESS DISORDER	Current (Past Month)	☐	309.81	F43.1	☐
J	ALCOHOL DEPENDENCE	Past 12 Months	☐	303.9	F10.2x	☐
	ALCOHOL ABUSE	Past 12 Months	☐	305.00	F10.1	☐
K	SUBSTANCE DEPENDENCE (Non-alcohol)	Past 12 Months	☐	304.00-.90/305.20-.90	F11.1-F19.1	☐
	SUBSTANCE ABUSE (Non-alcohol)	Past 12 Months	☐	304.00-.90/305.20-.90	F11.1-F19.1	☐
L	PSYCHOTIC DISORDERS	Lifetime	☐	295.10-295.90/297.1/ 297.3/293.81/293.82/ 293.89/298.8/298.9	F20.xx-F29	☐
		Current	☐			
	MOOD DISORDER WITH PSYCHOTIC FEATURES	Lifetime	☐	296.24/296.34/296.44	F32.3/F33.3/ ☐	
		Current	☐	296.24/296.34/296.44	F30.2/F31.2/F31.5 F31.8/F31.9/F39 ☐	
M	ANOREXIA NERVOSA	Current (Past 3 Months)	☐	307.1	F50.0	☐
N	BULIMIA NERVOSA	Current (Past 3 Months)	☐	307.51	F50.2	☐
	ANOREXIA NERVOSA, BINGE EATING/PURGING TYPE	Current	☐	307.1	F50.0	☐
O	GENERALIZED ANXIETY DISORDER	Current (Past 6 Months)	☐	300.02	F41.1	☐
P	ANTISOCIAL PERSONALITY DISORDER Optional	Lifetime	☐	301.7	F60.2	☐

Which problem troubles you the most? Indicate your response by checking the appropriate check box(es).

Participant Identification Code:

Morningness-Eveningness Questionnaire

For each question, please select the answer that best describes you by circling the point value that best indicates how you have felt in recent weeks.

1. *Approximately* what time would you get up if you were entirely free to plan your day?

   [5] 5:00 AM–6:30 AM *(05:00–06:30 h)*
   [4] 6:30 AM–7:45 AM *(06:30–07:45 h)*
   [3] 7:45 AM–9:45 AM *(07:45–09:45 h)*
   [2] 9:45 AM–11:00 AM *(09:45–11:00 h)*
   [1] 11:00 AM–12 noon *(11:00–12:00 h)*

2. *Approximately* what time would you go to bed if you were entirely free to plan your evening?

   [5] 8:00 PM–9:00 PM *(20:00–21:00 h)*
   [4] 9:00 PM–10:15 PM *(21:00–22:15 h)*
   [3] 10:15 PM–12:30 AM *(22:15–00:30 h)*
   [2] 12:30 AM–1:45 AM *(00:30–01:45 h)*
   [1] 1:45 AM–3:00 AM *(01:45–03:00 h)*

3. If you usually have to get up at a specific time in the morning, how much do you depend on an alarm clock?

   [4] Not at all
   [3] Slightly
   [2] Somewhat
   [1] Very much

4. How easy do you find it to get up in the morning (when you are not awakened unexpectedly)?

   [1] Very difficult
   [2] Somewhat difficult
   [3] Fairly easy
   [4] Very easy

5. How alert do you feel during the first half hour after you wake up in the morning?

   [1] Not at all alert
   [2] Slightly alert
   [3] Fairly alert
   [4] Very alert

6. How hungry do you feel during the first half hour after you wake up?

   [1] Not at all hungry
   [2] Slightly hungry
   [3] Fairly hungry
   [4] Very hungry

7. During the first half hour after you wake up in the morning, how do you feel?

   [1] Very tired
   [2] Fairly tired
   [3] Fairly refreshed
   [4] Very refreshed

8. If you had no commitments the next day, what time would you go to bed compared to your usual bedtime?

   [4] Seldom or never later
   [3] Less that 1 hour later
   [2] 1-2 hours later
   [1] More than 2 hours later

9. You have decided to do physical exercise. A friend suggests that you do this for one hour twice a week, and the best time for him is between 7-8 AM *(07-08 h)*. Bearing in mind nothing but your own internal "clock," how do you think you would perform?

   [4] Would be in good form
   [3] Would be in reasonable form
   [2] Would find it difficult
   [1] Would find it very difficult

10. At *approximately* what time in the evening do you feel tired, and, as a result, in need of sleep?

    [5] 8:00 PM–9:00 PM *(20:00–21:00 h)*
    [4] 9:00 PM–10:15 PM *(21:00–22:15 h)*
    [3] 10:15 PM–12:45 AM *(22:15–00:45 h)*
    [2] 12:45 AM–2:00 AM *(00:45–02:00 h)*
    [1] 2:00 AM–3:00 AM *(02:00–03:00 h)*

11. You want to be at your peak performance for a test that you know is going to be mentally exhausting and will last two hours. You are entirely free to plan your day. Considering only your "internal clock," which one of the four testing times would you choose?

    [6] 8 AM–10 AM *(08–10 h)*
    [4] 11 AM–1 PM *(11–13 h)*
    [2] 3 PM–5 PM *(15–17 h)*
    [0] 7 PM–9 PM *(19–21 h)*

12. If you got into bed at 11 PM *(23 h)*, how tired would you be?

    [0] Not at all tired
    [2] A little tired
    [3] Fairly tired
    [5] Very tired

13. For some reason you have gone to bed several hours later than usual, but there is no need to get up at any particular time the next morning. Which one of the following are you most likely to do?

[4] Will wake up at usual time, but will not fall back asleep
[3] Will wake up at usual time and will doze thereafter
[2] Will wake up at usual time, but will fall asleep again
[1] Will not wake up until later than usual

14. One night you have to remain awake between 4-6 AM *(04-06 h)* in order to carry out a night watch. You have no time commitments the next day. Which one of the alternatives would suit you best?

[1] Would not go to bed until the watch is over
[2] Would take a nap before and sleep after
[3] Would take a good sleep before and nap after
[4] Would sleep only before the watch

15. You have two hours of hard physical work. You are entirely free to plan your day. Considering only your internal "clock," which of the following times would you choose?

[4] 8 AM–10 AM *(08–10 h)*
[3] 11 AM–1 PM *(11–13 h)*
[2] 3 PM–5 PM *(15–17 h)*
[1] 7 PM–9 PM *(19–21 h)*

16. You have decided to do physical exercise. A friend suggests that you do this for one hour twice a week. The best time for her is between 10-11 PM *(22-23 h)*. Bearing in mind only your internal "clock," how well do you think you would perform?

[1] Would be in good form
[2] Would be in reasonable form
[3] Would find it difficult
[4] Would find it very difficult

17. Suppose you can choose your own work hours. Assume that you work a five-hour da (including breaks), your job is interesting, and you are paid based on your performance. At *approximately* what time would you choose to begin?

[5] 5 hours starting between 4–8 AM *(05–08 h)*
[4] 5 hours starting between 8–9 AM *(08–09 h)*
[3] 5 hours starting between 9 AM–2 PM *(09–14 h)*
[2] 5 hours starting between 2–5 PM *(14–17 h)*
[1] 5 hours starting between 5 PM–4 AM *(17–04 h)*

18. At *approximately* what time of day do you usually feel your best?

[5] 5–8 AM *(05–08 h)*
[4] 8–10 AM *(08–10 h)*
[3] 10 AM–5 PM *(10–17 h)*
[2] 5–10 PM *(17–22 h)*
[1] 10 PM–5 AM *(22–05 h)*

19. One hears about "morning types" and "evening types." Which one of these types do you consider yourself to be?

[6] Definitely a morning type
[4] Rather more a morning type than an evening type
[2] Rather more an evening type than a morning type
[1] Definitely an evening type

____ Total points for all 19 questions

Participant Identification Code:

Pittsburgh Sleep Quality Index

Instructions: The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. **Please answer all questions.**

1. During the past month, what time have you usually gone to bed at night? _____
2. During the past month, how long (in minutes) has it usually taken you to fall asleep each night? _____
3. During the past month, what time have you usually gotten up in the morning? _____
4. During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spent in bed.) _____

5. During the past month, how often have you had trouble sleeping because you…	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
a. Cannot get to sleep within 30 minutes				
b. Wake up in the middle of the night or early morning				
c. Have to get up to use the bathroom				
d. Cannot breathe comfortably				
e. Cough or snore loudly				
f. Feel too cold				
g. Feel too hot				
h. Have bad dreams				
i. Have pain				
j. Other reason(s), please describe:				
6. During the past month, how often have you taken medicine to help you sleep (prescribed or "over the counter")?				
7. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?				
	No problem at all	Only a very slight problem	Somewhat of a problem	A very big problem
8. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?				
	Very good	Fairly good	Fairly bad	Very bad
9. During the past month, how would you rate your sleep quality overall?				

Participant Identification Code:

Sleep Disorders Questionnaire

Instructions:

This questionnaire will give your doctor a good understanding about your problems with sleeping and waking. It is very important to answer every question, because some disorders show up as a pattern of answers to different questions.

In answering the questions, consider each question as applying to the ***past six months*** of your life, unless you have been told differently by the person who gave you this booklet.

Some people work night shift, or rotating shifts. Others have a very changeable bedtime. For these people, questions which ask about "day, daytime, morning, etc." will mean the time when they wake from their longest sleep of the day and become active. Similarly, "night, nighttime, bedtime, nocturnal" would refer to whenever they are having their longest sleep of the day.

Most of the questions are simple statements. You answer by circling a number from 1 to 5. If you strongly disagree with the statement, or if it never happens to you, answer "1". If the statement is always true in your case, or you agree strongly with it, answer "5". You may also choose "2 rarely", "3 sometimes", or "4 usually" as your answer. Notice that an "answer key" appears at the bottom of each page to remind you what is meant by the numbers. Please answer all of the questions.

Here is an example of how to fill out a question:

1. How often does it snow in Florida in July? (1) 2 3 4 5

IF YOU ARE CERTAIN THAT A QUESTION DOES NOT APPLY TO YOU, LEAVE IT BLANK. But . . . try to answer every question if at all possible. This is important. Notice that answer "1" can mean that the things asked in the question ***never*** happen to you.

If you are using the computerized answer sheet, blacken the space which corresponds to your answer, "1 to 5", instead of circling the answer in this booklet.

********** Key for answers **********

1	2	3	4	5
NEVER	RARELY	SOMETIMES	USUALLY	ALWAYS
(strongly disagree)	(disagree)	(not sure)	(agree)	(agree strongly)

1. I get too little sleep at night	1 2 3 4 5
2. I often have a poor night's sleep	1 2 3 4 5
3. I have trouble getting to sleep at night	1 2 3 4 5
4. I wake up often during the night	1 2 3 4 5
5. My bedtime varies a lot	1 2 3 4 5
6. At bedtime, thoughts race through my mind	1 2 3 4 5
7. At bedtime, I feel sad and depressed	1 2 3 4 5
8. At bedtime, I worry about things	1 2 3 4 5
9. At bedtime, I feel muscular tension	1 2 3 4 5
10. At bedtime, I'm afraid of not being able to go to sleep	1 2 3 4 5
11. When falling asleep, I feel paralyzed (unable to move)	1 2 3 4 5
12. When falling asleep, I have "restless legs" (a feeling of crawling, aching, or inability to keep legs still)	1 2 3 4 5
13. After waking at night, I fear I will not be able to get back to sleep	1 2 3 4 5
14. My night sleep is restless and disturbed	1 2 3 4 5
15. At night, my sleep disturbs my bed partner's sleep	1 2 3 4 5
16. My night sleep is disturbed by light	1 2 3 4 5
17. My night sleep is disturbed by noise	1 2 3 4 5
18. My sleep is disturbed by severe heartburn and choking ("regurgitation", bringing up bitter stomach fluid)	1 2 3 4 5
19. I often wake up because I am hungry	1 2 3 4 5
20. I snore in my sleep	1 2 3 4 5
21. I am told I snore loudly and bother others	1 2 3 4 5
22. I am told I stop breathing ("hold my breath") in sleep	1 2 3 4 5
23. I awake suddenly gasping for breath, unable to breathe	1 2 3 4 5

********** Key for answers **********

1	2	3	4	5
NEVER (strongly disagree)	RARELY (disagree)	SOMETIMES (not sure)	USUALLY (agree)	ALWAYS (agree strongly)

24. At night my heart pounds, beats rapidly, or beats irregularly ("palpitations")	1 2 3 4 5
25. I sweat a great deal at night	1 2 3 4 5
26. I walk in my sleep	1 2 3 4 5
27. I grind my teeth while I sleep	1 2 3 4 5
28. I wake from sleep screaming, confused, and at times violent ("night terrors")	1 2 3 4 5
29. My sleep is disturbed because of pain in the neck, back, muscles, joints, legs or arms	1 2 3 4 5
30. My sleep is disturbed by chest pain (not angina)	1 2 3 4 5
31. My sleep is disturbed by "restless legs" (a feeling of crawling, aching, inability to keep legs still)	1 2 3 4 5
32. My sleep is disturbed by thoughts racing through my mind	1 2 3 4 5
33. My sleep is disturbed by sadness or depression	1 2 3 4 5
34. My sleep is disturbed by worrying about things	1 2 3 4 5
35. My sleep is disturbed by muscular tension	1 2 3 4 5
36. My sleep is disturbed by fears that I might not be able to get back to sleep if I should wake up	1 2 3 4 5
37. I often have a night full of intense vivid dreams	1 2 3 4 5
38. I have a lot of nightmares (frightening dreams)	1 2 3 4 5
39. I feel unable to move (paralyzed) after a nap	1 2 3 4 5
40. I have dream-like images (hallucinations) when I awaken in the morning even though I know I am not asleep	1 2 3 4 5
41. I am sometimes very sleepy in the daytime, and this seems to go in cycles at regular intervals	1 2 3 4 5
42. I have slept for several days at a time, or at least I have been overwhelmingly sleepy for that long	1 2 3 4 5
43. I have been unable to sleep at all for several days	1 2 3 4 5
44. I feel that my sleep is abnormal	1 2 3 4 5

********** Key for answers **********

1	2	3	4	5
NEVER (strongly disagree)	RARELY (disagree)	SOMETIMES (not sure)	USUALLY (agree)	ALWAYS (agree strongly)

45. I feel that I have insomnia	1 2 3 4 5
46. As a child, I had difficulty waking up in the morning	1 2 3 4 5
47. As a child, I had sleepiness during the day	1 2 3 4 5
48. I have a problem because of headaches while sleeping	1 2 3 4 5
49. As a child, I was fatigued during the day	1 2 3 4 5
50. As a child, I rocked myself to get to sleep	1 2 3 4 5
51. I used to bang my head as a child	1 2 3 4 5
52. I used to sleepwalk in childhood	1 2 3 4 5
53. As a child, I had convulsions (seizures) during sleep	1 2 3 4 5
54. As a child, I would grind my teeth while asleep	1 2 3 4 5
55. Now, I am very sleepy during the day and I struggle to stay awake	1 2 3 4 5
56. In the past 6 months, I have fallen asleep accidentally in some of these situations: eating a meal, talking on the phone, talking to someone, riding in a bus or car, watching TV, at a theater, reading a book, at a lecture.	1 2 3 4 5
57. I got bad grades in school because I was too sleepy	1 2 3 4 5
58. I now have trouble doing my job because of sleepiness or fatigue	1 2 3 4 5
59. I often have to let someone else drive the car because I am too sleepy to do it	1 2 3 4 5
60. I see vivid dream-like images (hallucinations) either just before or just after a daytime nap, yet I am sure I am awake when they happen	1 2 3 4 5
61. I have vivid dreams during my daytime naps	1 2 3 4 5
62. I am often unable to move (paralyzed) when I am waking up in the morning	1 2 3 4 5
63. Sometimes I realize I have driven my car to the wrong place, and I can't remember how I did it	1 2 3 4 5
64. I find myself doing things which make no sense, such as writing nonsense instead of notes, or mixing together chocolate and gravy	1 2 3 4 5
65. People tell me that I act strangely at times, and yet I was not aware of it when it happened	1 2 3 4 5

********** Key for answers **********

1	2	3	4	5
NEVER	RARELY	SOMETIMES	USUALLY	ALWAYS
(strongly disagree)	(disagree)	(not sure)	(agree)	(agree strongly)

66. I get "weak knees" when I laugh	1 2 3 4 5
67. I get sudden muscular weakness (or even a brief period of paralysis, being unable to move) when laughing, angry, or in situations of strong emotion	1 2 3 4 5
68. I am excessively sleepy during the daytime	1 2 3 4 5
69. I have at some time had trouble with my bladder	1 2 3 4 5
70. I have had problems with tonsils or adenoids	1 2 3 4 5
71. I have high blood pressure (or once had it)	1 2 3 4 5
72. My tonsils and/or adenoids have been removed	1 2 3 4 5
73. I get pains in my abdomen (stomach)	1 2 3 4 5
74. I have had a head injury	1 2 3 4 5
75. I have been knocked unconscious (knocked out)	1 2 3 4 5
76. I suffer from dizzy spells	1 2 3 4 5
77. I have seizures ("fits", convulsions, epilepsy)	1 2 3 4 5
78. I have problems with clumsiness, incoordination	1 2 3 4 5
79. I feel that I have a sexual problem	1 2 3 4 5
80. My desire or interest in sex is less than it used to be	1 2 3 4 5
81. I have pain or discomfort during sexual intercourse	1 2 3 4 5
82. I sleep better after having sex	1 2 3 4 5
83. I am unhappy about my social life	1 2 3 4 5
84. I am unhappy about loving relationships in my life	1 2 3 4 5
85. I am unhappy about my sex life	1 2 3 4 5
86. I am dissatisfied with my job	1 2 3 4 5
87. I have a problem with my sleep	1 2 3 4 5
88. I wake up in the morning with a headache	1 2 3 4 5
89. I have considered or attempted suicide	1 2 3 4 5

********** Key for answers **********

1	2	3	4	5
NEVER (strongly disagree)	RARELY (disagree)	SOMETIMES (not sure)	USUALLY (agree)	ALWAYS (agree strongly)

90. I feel I am useful and needed	1 2 3 4 5
91. I am sleeping more than I used to	1 2 3 4 5
92. Someone in my immediate family has trouble with insomnia (brother/sister, father/mother, son/daughter, grandparent)	1 2 3 4 5
93. Someone in my immediate family is very sleepy during the day	1 2 3 4 5
94. Someone in my immediate family has psychiatric or emotional illness (e.g.: depression, alcoholism)	1 2 3 4 5
95. Some of my other relatives have trouble with insomnia (uncles, aunts, cousins)	1 2 3 4 5
96. Some of my other relatives are very sleepy during the day	1 2 3 4 5
97. Some of my other relatives have psychiatric illness	1 2 3 4 5
98. Some family member has died suddenly in their sleep	1 2 3 4 5
99. Some family member has "restless legs" while sleeping (a feeling of crawling, aching, inability to keep the legs still)	1 2 3 4 5
100. A child in my family died from "crib death" (sudden infant death syndrome, SIDS)	1 2 3 4 5
101. Someone in my family has been hospitalized for a psychiatric illness or "nervous breakdown".	1 2 3 4 5
102. People in my family seem to be worriers	1 2 3 4 5
103. Someone in my family has diabetes	1 2 3 4 5
104. Someone in my family has had a stroke ("apoplexy")	1 2 3 4 5
105. I often use alcohol in order to get to sleep	1 2 3 4 5
106. I use alcohol to steady my nerves	1 2 3 4 5
107. While drinking alcohol, I have carried out actions without being aware of them, and not remembered them the next day	1 2 3 4 5
108. I smoke tobacco within two hours of bedtime	1 2 3 4 5
109. I have used "street drugs" (marijuana, "uppers", "downers", narcotics, hallucinogens, cocaine)	1 2 3 4 5
110. I have used tobacco to help me go to sleep	1 2 3 4 5

********** Key for answers **********

1	2	3	4	5
NEVER (strongly disagree)	RARELY (disagree)	SOMETIMES (not sure)	USUALLY (agree)	ALWAYS (agree strongly)

111. I have used marijuana to help me go to sleep	1 2 3 4 5
112. I currently take a non-prescription drug from the pharmacy in order to help me sleep	1 2 3 4 5
113. I currently take a non-prescription drug to stop me being so sleepy and fatigued in the daytime	1 2 3 4 5
114. I take a prescription drug which the doctor gave me mainly to help me sleep (sleeping pills, anti-depressants, tranquilizers)	1 2 3 4 5
115. I take a prescription drug which the doctor gave me mainly to keep me awake during the day (e.g.: ritalin)	1 2 3 4 5
116. I take some drugs at night for my other illnesses, not related to sleep, yet I find they help me sleep	1 2 3 4 5
117. I have taken drugs for my heart	1 2 3 4 5
118. I use relaxation techniques or mental imagery (e.g.: counting sheep) to help me sleep	1 2 3 4 5
119. I use non-drug therapies in order to get to sleep (e.g.: biofeedback, acupuncture, electrosleep)	1 2 3 4 5
120. I exercise regularly	1 2 3 4 5
121. I was born as part of a multiple birth (twins, or triplets, etc. Includes cases where the others died at birth or afterwards)	1 2 3 4 5
122. My family was emotionally close in my childhood	1 2 3 4 5
123. I got along well with my parents while growing up	1 2 3 4 5
124. I am currently unemployed	1 2 3 4 5
125. I am working at a job with rotating shifts	1 2 3 4 5
126. I have had a job where I worked at unusual times	1 2 3 4 5
127. I am presently living in a house	1 2 3 4 5
128. I get along well with my husband / wife / friend, who is currently living with me	1 2 3 4 5
129. Coffee, tea, or cola drinks seem to worsen my sleep	1 2 3 4 5
130. Mental stress, worry, or anxiety worsens my sleep	1 2 3 4 5

********** Key for answers **********

1	2	3	4	5
NEVER (strongly disagree)	RARELY (disagree)	SOMETIMES (not sure)	USUALLY (agree)	ALWAYS (agree strongly)

131. Physical exercise helps my sleep	1 2 3 4 5
132. A daytime nap worsens my nighttime sleep	1 2 3 4 5
133. Mental stress, worry, or anxiety makes me feel sleepy during the day	1 2 3 4 5
134. After a nap, I feel less sleepy in the daytime	1 2 3 4 5
135. Hot weather makes me sleepy during the day	1 2 3 4 5
136. When doing shift work, I am sleepy during the day	1 2 3 4 5
137. I have a small jaw, or other abnormality of the bones in my head or neck	1 2 3 4 5
138. I have a chronic chest disease (bronchitis, asthma, emphysema)	1 2 3 4 5
139. I have a problem with my nose blocking up when I am trying to sleep (allergies, infections)	1 2 3 4 5
140. I wake up with "attacks" which are different from those described anywhere else in this questionnaire	1 2 3 4 5
141. My snoring or my breathing problem is much worse if I sleep on my back	1 2 3 4 5
142. My snoring or my breathing problem is much worse if I fall asleep right after drinking alcohol	1 2 3 4 5
143. My snoring or my breathing problem is much worse when I have an allergy or infection in the nose, throat, or chest	1 2 3 4 5

********** Key for answers **********

1	2	3	4	5
NEVER (strongly disagree)	RARELY (disagree)	SOMETIMES (not sure)	USUALLY (agree)	ALWAYS (agree strongly)

****

THE FOLLOWING QUESTIONS ARE FOR WOMEN ONLY:

144. I have gone through the menopause ("change of life")	1 2 3 4 5
145. My sleep at night is affected by my menstrual cycle	1 2 3 4 5
146. My daytime sleepiness worsens with pregnancy	1 2 3 4 5
147. My daytime sleepiness is worse since my menopause	1 2 3 4 5

****

THE FOLLOWING QUESTIONS ARE FOR MEN ONLY:

148. I often have problems getting an erection	1 2 3 4 5
149. I have trouble maintaining an erection	1 2 3 4 5
150. I have trouble with ejaculation (either I can't do it at all, or it happens too soon)	1 2 3 4 5
151. My erections are physically distorted	1 2 3 4 5
152. I often awaken with an erection during the night or in the morning	1 2 3 4 5

********** Key for answers **********

1	2	3	4	5
NEVER (strongly disagree)	RARELY (disagree)	SOMETIMES (not sure)	USUALLY (agree)	ALWAYS (agree strongly)

IN THE NEXT SECTION, PLEASE CIRCLE THE ITEM (NUMBERED 1-5) WHICH BEST MATCHES YOUR ANSWER.

---

153. How many hours of sleep do you get at night, not including time spent awake in bed?

1.) Less than 4 hrs. 2.) Four to 5 hrs. 3.) Six hrs.
4.) Seven hrs. 5.) Eight or more

154. How long is your longest wake period at night?

1.) Less than 5 min. 2.) Six to 19 min. 3.) 20 to 59 min.
4.) One to 2 hrs. 5.) More than 2 hrs.

155. How many times in a night do you get up to urinate?

1.) None. 2.) One time 3.) Two times
4.) Three times 5.) Four or more times

156. How many work accidents have you had as a result of sleepiness or fatigue?

1.) None 2.) One 3.) Two
4.) Three 5.) Four or more

157. How many car accidents or "near misses" have you had because of excessive sleepiness?

1.) None 2.) One 3.) Two
4.) Three 5.) Four or more

158. How many daytime naps (asleep for 5 minutes or more) do you take on an average working day?

1.) None 2.) One 3.) Two
4.) Three or four 5.) Five or more

159. How many rest periods do you take on an average working day (but do not sleep during them)?

1.) None 2.) One 3.) Two or three
4.) Four or five 5.) Six or more

160. How many times, in an average working day, do you try to nap but find that you can't fall asleep?

1.) None 2.) One 3.) Two
4.) Three 5.) Four or more

161. How long do you remain restored (refreshed, alert) after a daytime nap?

1.) Less than 1 hr. 2.) One to 2 hours 3.) Three hours
4.) Four or 5 hours 5.) Six hours or more

162. How long do you remain restored after a rest?

1.) Less than 30 min. 2.) 30-59 minutes 3.) One to 2 hrs.
4.) Three to 4 hrs. 5.) Five hours or more

163. What is your current weight (in lb.)?

1.) 134 lb. or less 2.) 135-159 lb. 3.) 160-183 lb.
4.) 184-209 lb. 5.) 210 lb. or more

164. What was your weight six months ago?

1.) 134 lb. or less 2.) 135-159 lb. 3.) 160-183 lb.
4.) 184-209 lb. 5.) 210 lb. or more

165. What was your weight at age 20?

1.) 125 lb. or less 2.) 126-139 lb. 3.) 140-155 lb.
4.) 156-175 lb. 5.) 176 lb. or more

166. How many cups of regular coffee do you have in a day?

1.) None 2.) One cup 3.) Two cups
4.) 3 to 5 cups 5.) Six cups or more

167. How many of the coffees are within 2 hrs. of bedtime?

1.) None 2.) One cup 3.) Two cups
4.) 3 to 5 cups 5.) Six cups or more

168. How many glasses/cans of cola drinks do you have in a day (do not include decaffeinated types)?

1.) None 2.) One can 3.) Two cans
4.) 3 to 5 cans 5.) Six cans or more

169. How many of these colas are within 2 hrs. of bedtime?

1.) None 2.) One can 3.) Two cans
4.) 3 to 5 cans 5.) Six cans or more

170. How many years were you a smoker?

1.) None 2.) One year 3.) 2 to 12 years
4.) 13 to 25 years 5.) 26 years or more

171. How long does it take you to adjust after traveling across time zones (especially 4 or more zones)?

1.) No time at all 2.) One day 3.) Two days
4.) Three to 4 days 5.) Five or more days

172. How tall are you?

1.) 63 in. or less 2.) 64 to 66.5 in. 3.) 67 to 69.5 in.
4.) 70 to 71 in. 5.) 71.5 inches or taller

173. How old are you now?

1.) 25 or under 2.) 26-35 yr. 3.) 36-44 yr.
4.) 45-50 yr. 5.) 51 yr. or older

174. How many years did you go to school? Include years of college and university too.

1.) 4 yr. or less 2.) 5-11 yr. 3.) 12 yr.
4.) 13-14 yr. 5.) 15 yr. or more

175. Before this visit, how many "therapists" (doctor, psychiatrist, psychologist, nurse, counselor, osteopath, chiropractor) have you ever seen about a problem of sleeping too much or too little?

1.) None 2.) One only 3.) Two
4.) Three or 4 5.) Five or more

Participant Identification Code:

Beck Depression Inventory

Instructions: This questionnaire consists of 21 groups of statements. Please read each group of statements carefully, and then pick out the **one statement** in each group that best describes the way you have been feeling during the **past two weeks, including today.** Circle the number beside the statement you have picked. If several statements in the group seem to apply equally well, circle the highest number for that group. Be sure that you do not choose more than one statement for any group, including Item 16 (Changes in Sleeping Pattern) or Item 18 (Changes in Appetite).

1. Sadness
- 0 I do not feel sad.
- 1 I feel sad much of the time.
- 2 I am sad all the time.
- 3 I am so sad or unhappy that I can't stand it.

2. Pessimism
- 0 I am not discouraged about my future.
- 1 I feel more discouraged about my future than I used to be.
- 2 I do not expect things to work out for me.
- 3 I feel my future is hopeless and will only get worse.

3. Past Failure
- 0 I do not feel like a failure.
- 1 I have failed more than I should have.
- 2 As I look back, I see a lot of failures.
- 3 I feel I am a total failure as a person.

4. Loss of Pleasure
- 0 I get as much pleasure as I ever did from the things I enjoy.
- 1 I don't enjoy things as much as I used to.
- 2 I get very little pleasure from the things I used to enjoy.
- 3 I can't get any pleasure from the things I used to enjoy.

5. Guilty Feelings
- 0 I don't feel particularly guilty.
- 1 I feel guilty over many things I have done or should have done.
- 2 I feel quite guilty most of the time.
- 3 I feel guilty all of the time.

6. Punishment Feelings
- 0 I don't feel I am being punished.
- 1 I feel I may be punished.
- 2 I expect to be punished.
- 3 I feel I am being punished.

7. Self-Dislike
- 0 I feel the same about myself as ever.
- 1 I have lost confidence in myself.
- 2 I am disappointed in myself.
- 3 I dislike myself.

8. Self-Criticalness
- 0 I don't criticize or blame myself more than usual.
- 1 I am more critical of myself than I used to be.
- 2 I criticize myself for all of my faults.
- 3 I blame myself for everything bad that happens.

9. Suicidal Thoughts or Wishes
- 0 I don't have any thoughts of killing myself.
- 1 I have thoughts of killing myself, but I would not carry them out.
- 2 I would like to kill myself.
- 3 I would kill myself if I had the chance.

10. Crying
- 0 I don't cry any more than I used to.
- 1 I cry more than I used to.
- 2 I cry over every little thing.
- 3 I feel like crying, but I can't.

_____ Subtotal Page 1 Continued on Back

11. Agitation

0 I am no more restless or wound up than usual.
1 I feel more restless or wound up than usual.
2 I am so restless or agitated that it's hard to stay still.
3 I am so restless or agitated that I have to keep moving or doing something.

12. Loss of Interest

0 I have not lost interest in other people or activities.
1 I am less interested in other people or things than before.
2 I have lost most of my interest in other people or things.
3 It's hard to get interested in anything.

13. Indecisiveness

0 I make decisions about as well as ever.
1 I find it more difficult to make decisions than usual.
2 I have much greater difficulty in making decisions than I used to.
3 I have trouble making any decisions.

14. Worthlessness

0 I do not feel I am worthless.
1 I don't consider myself as worthwhile and useful as I used to.
2 I feel more worthless as compared to other people.
3 I feel utterly worthless.

15. Loss of Energy

0 I have as much energy as ever.
1 I have less energy than I used to have.
2 I don't have enough energy to do very much.
3 I don't have enough energy to do anything.

16. Changes in Sleeping Pattern

0 I have not experienced any change in my sleeping pattern.
1a I sleep somewhat more than usual.
1b I sleep somewhat less than usual.
2a I sleep a lot more than usual.
2b I sleep a lot less than usual.
3a I sleep most of the day.
3b I wake up 1–2 hours early and can't get back to sleep.

17. Irritability

0 I am no more irritable than usual.
1 I am more irritable than usual.
2 I am much more irritable than usual.
3 I am irritable all the time.

18. Changes in Appetite

0 I have not experienced any change in my appetite.
1a My appetite is somewhat less than usual.
1b My appetite is somewhat greater than usual.
2a My appetite is much less than before.
2b My appetite is much greater than usual.
3a I have no appetite at all.
3b I crave food all the time.

19. Concentration Difficulty

0 I can concentrate as well as ever.
1 I can't concentrate as well as usual.
2 It's hard to keep my mind on anything for very long.
3 I find I can't concentrate on anything.

20. Tiredness or Fatigue

0 I am no more tired or fatigued than usual.
1 I get more tired or fatigued more easily than usual.
2 I am too tired or fatigued to do a lot of the things I used to do.
3 I am too tired or fatigued to do most of the things I used to do.

21. Loss of Interest in Sex

0 I have not noticed any recent change in my interest in sex.
1 I am less interested in sex than I used to be.
2 I am much less interested in sex now.
3 I have lost interest in sex completely.

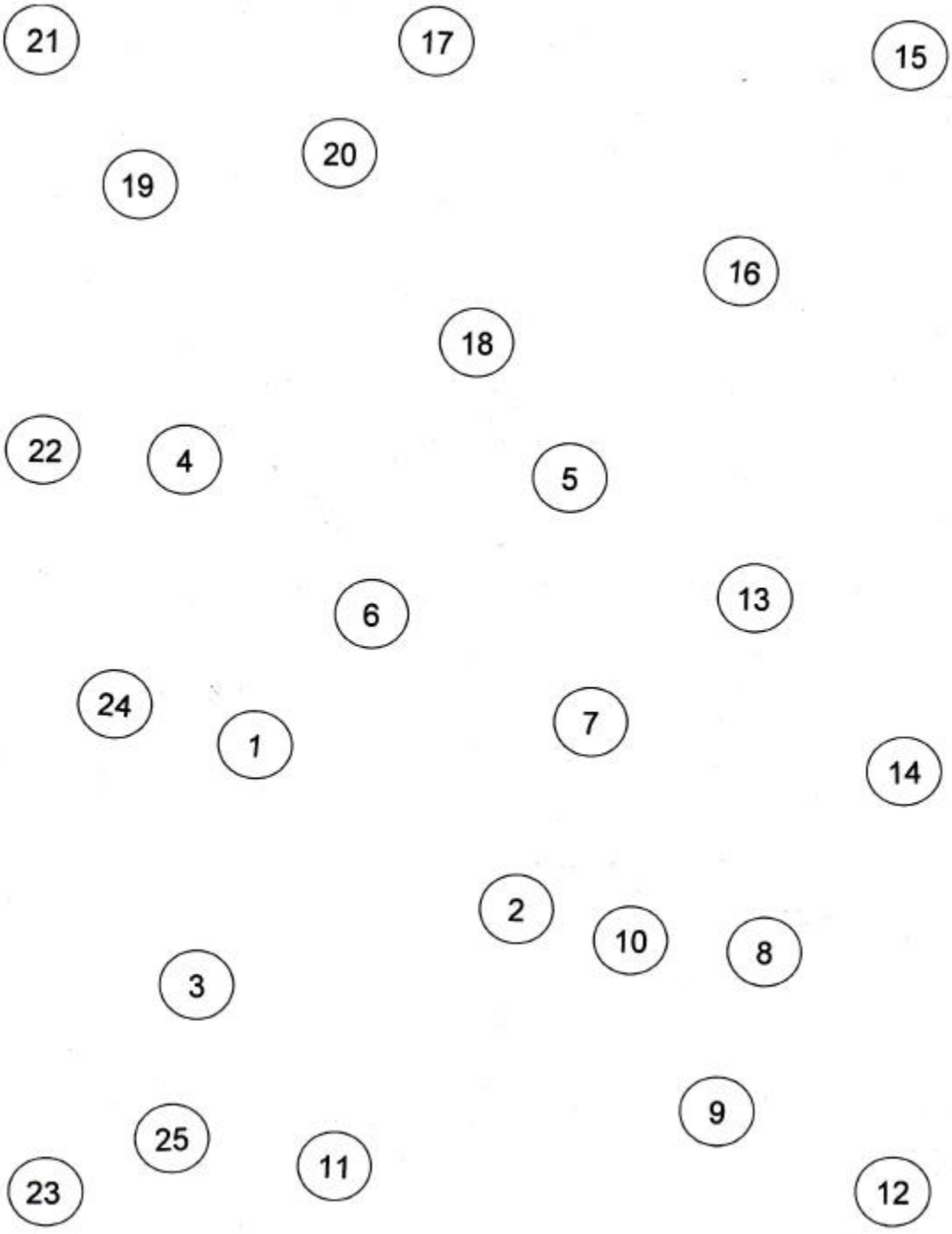
_____ Subtotal Page 2

_____ Subtotal Page 1

_____ Total Score

Participant Identification Code:

Trail Making Test (AA)



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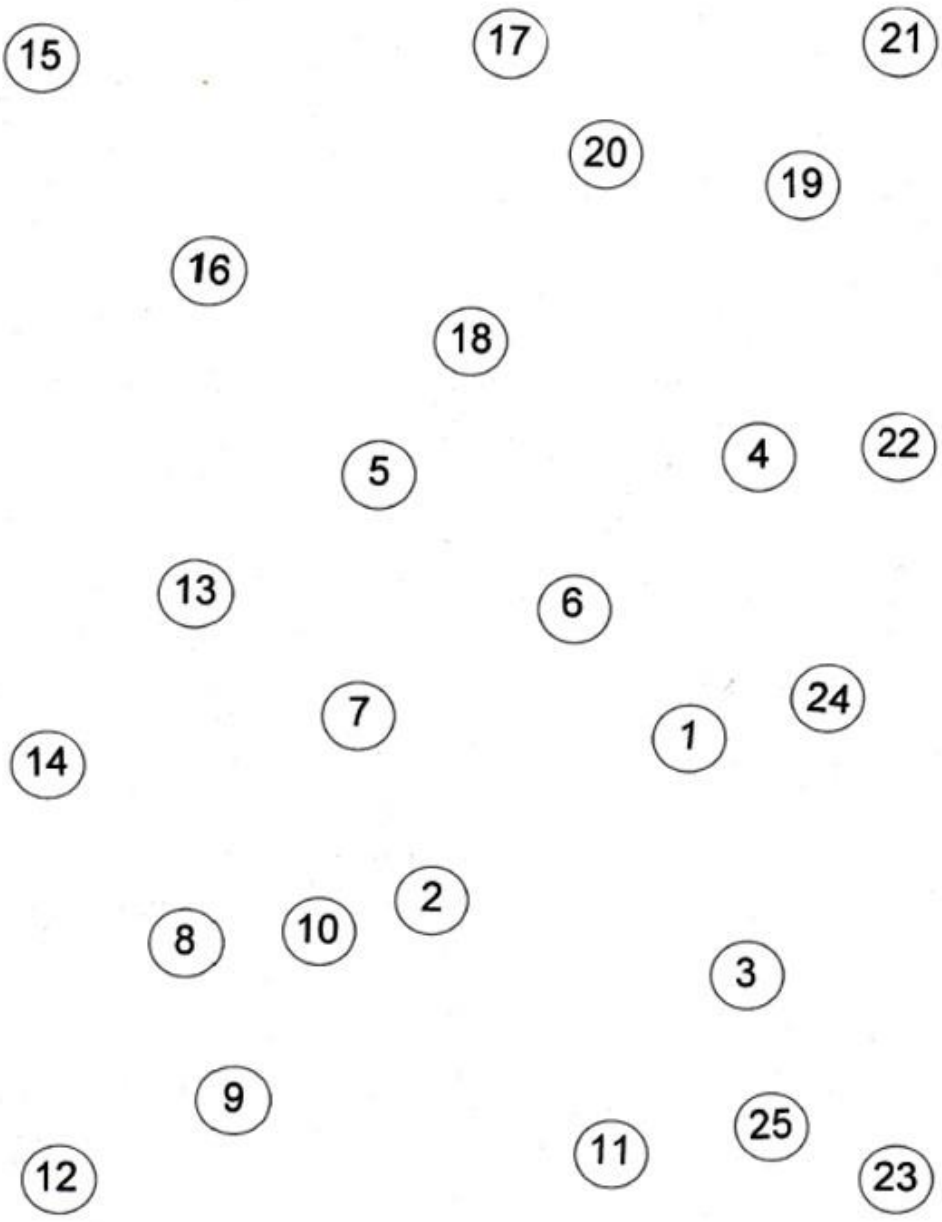

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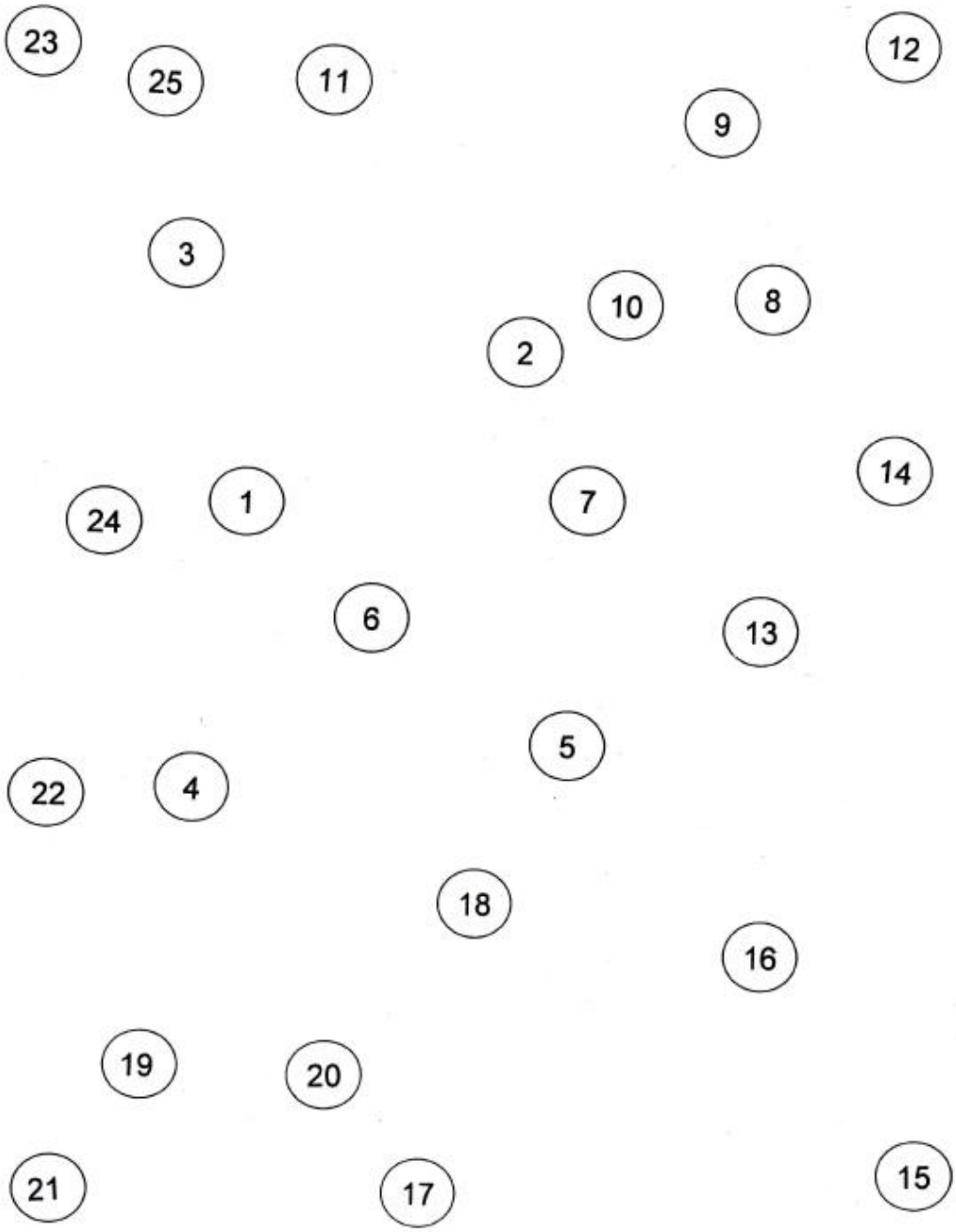

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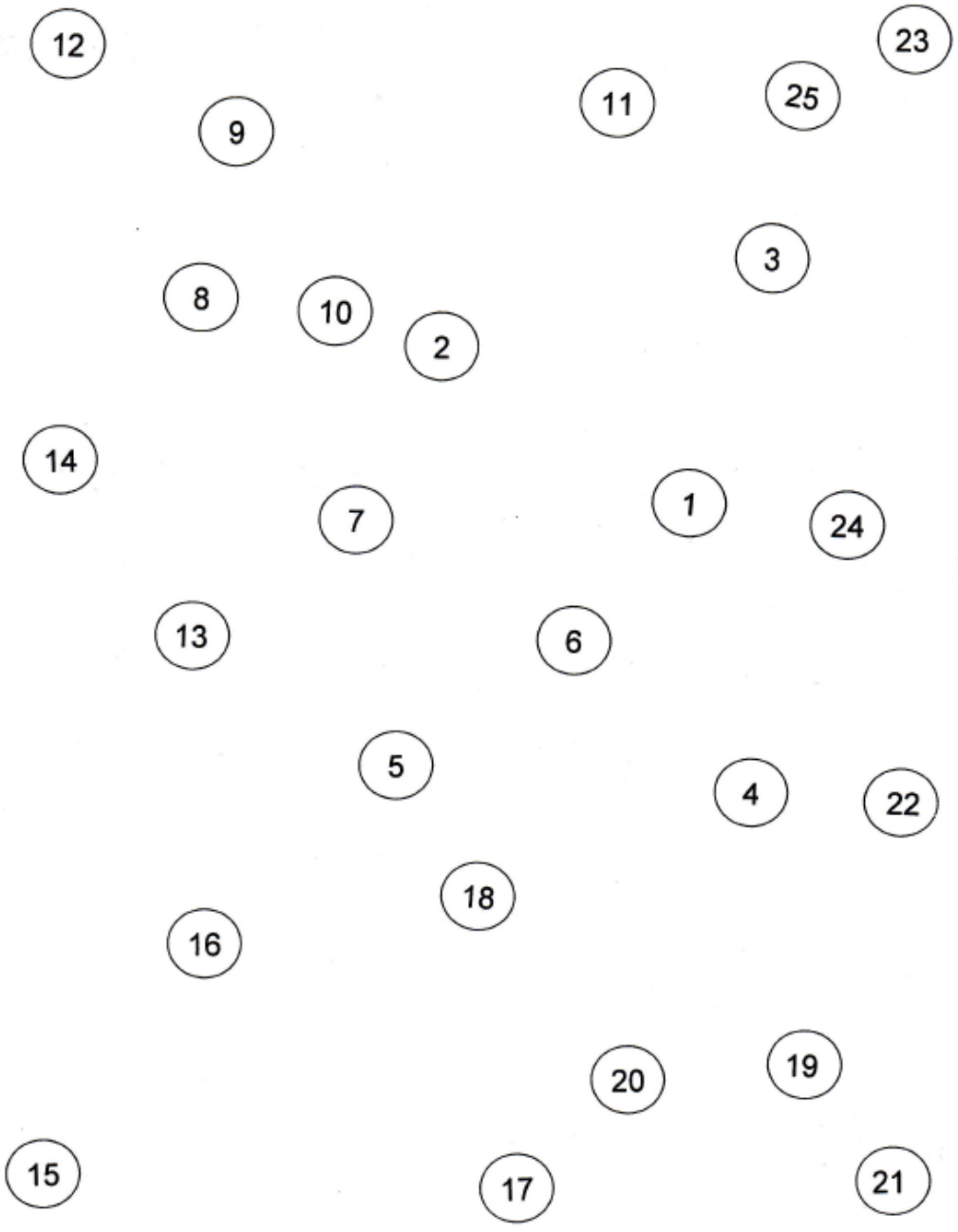

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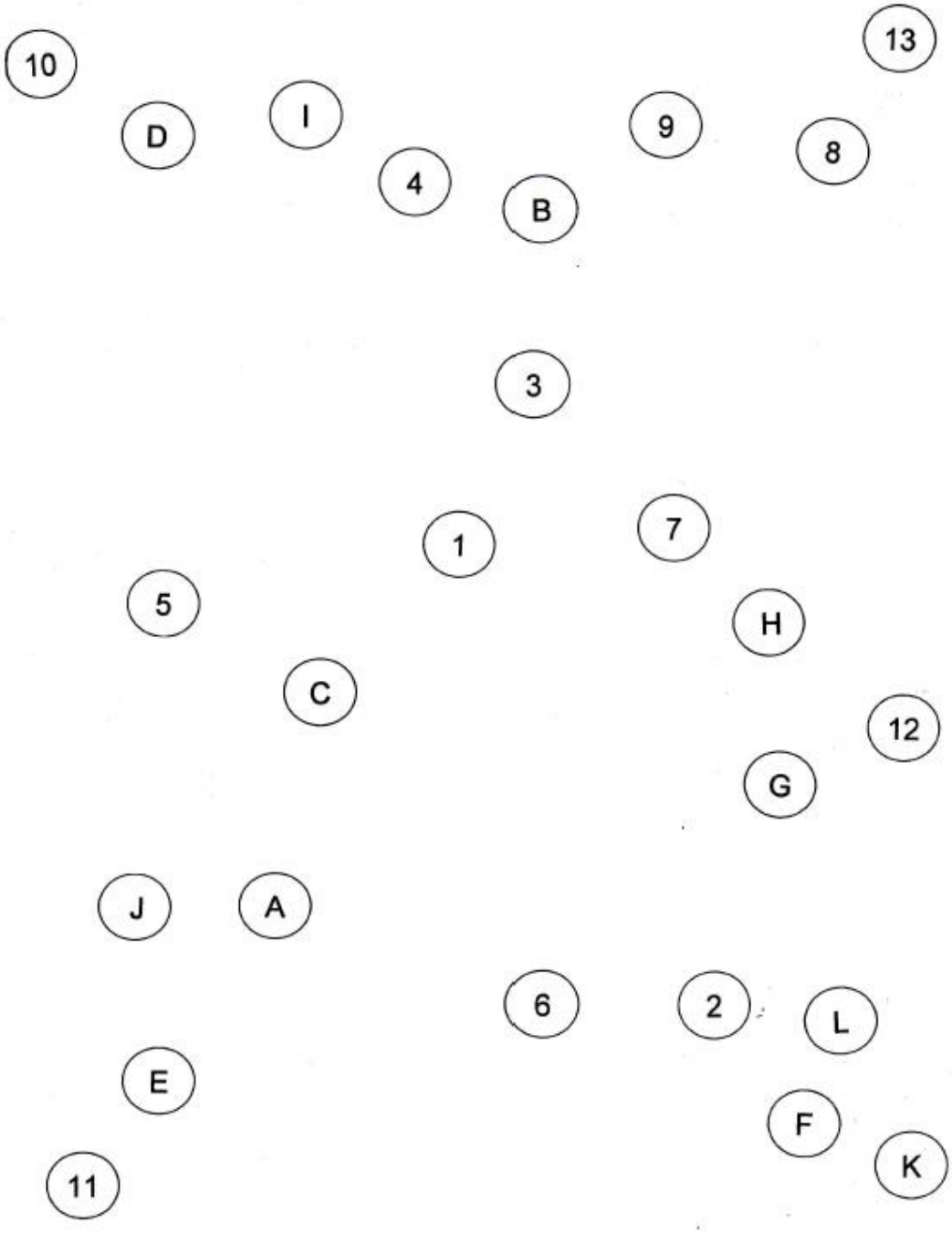

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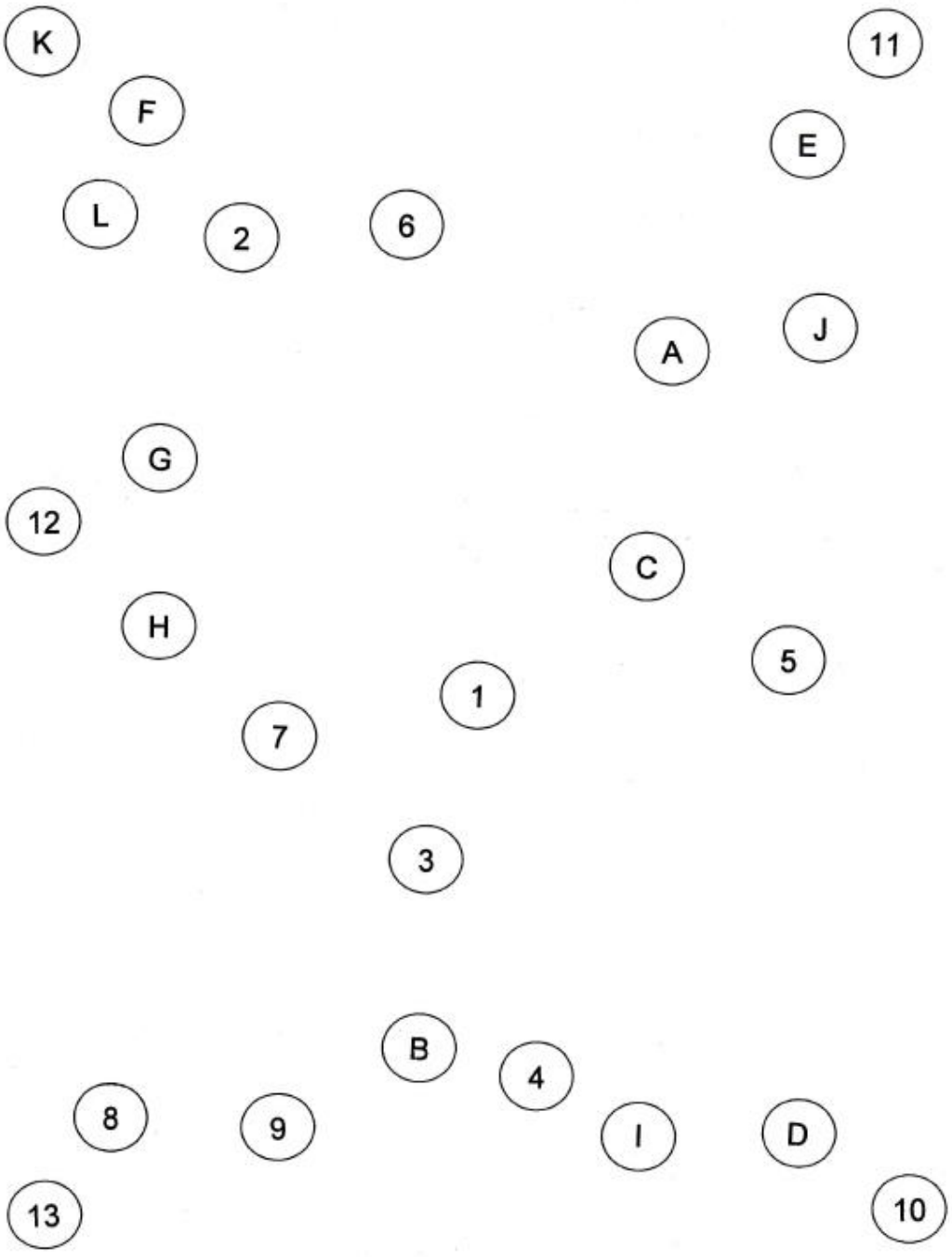

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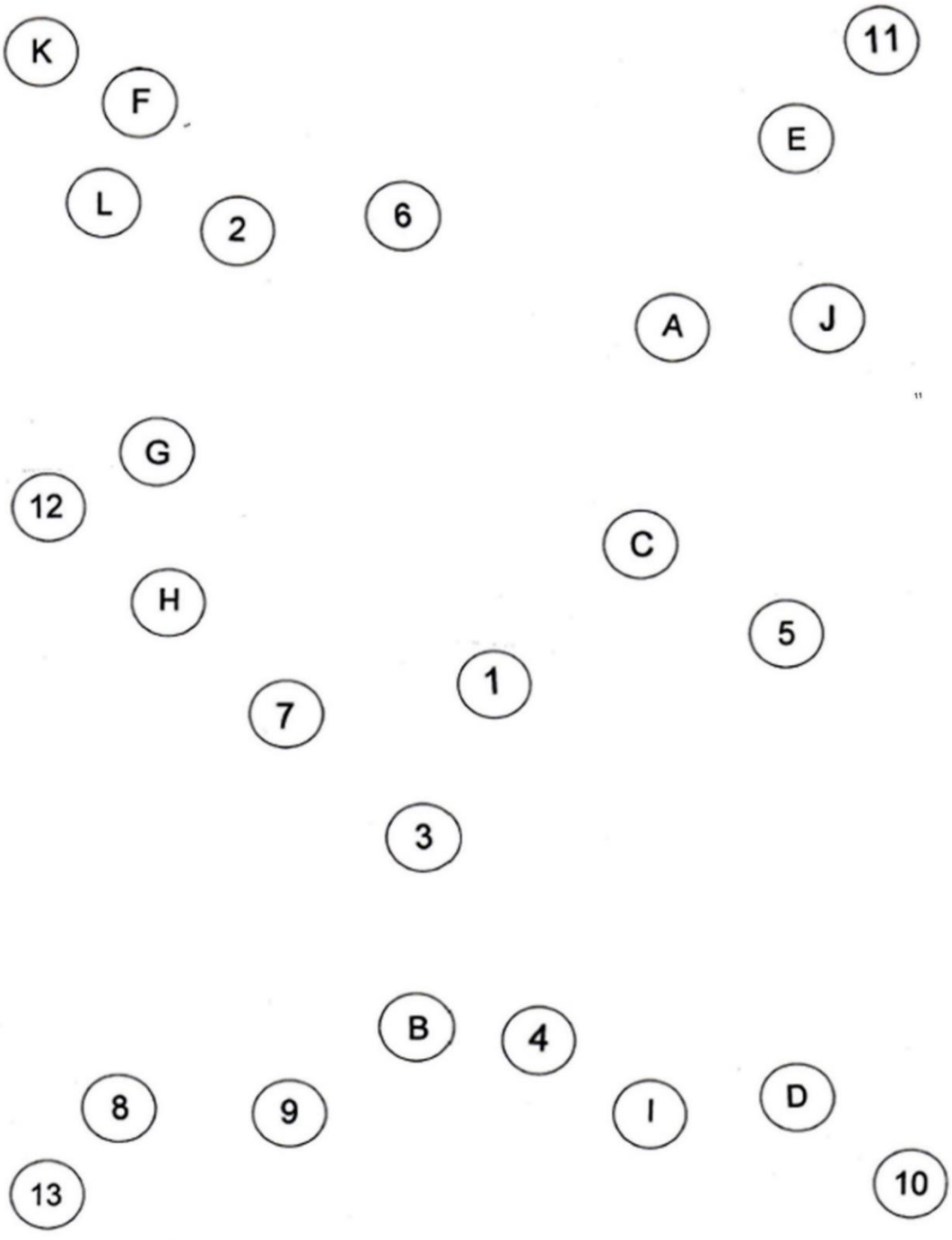

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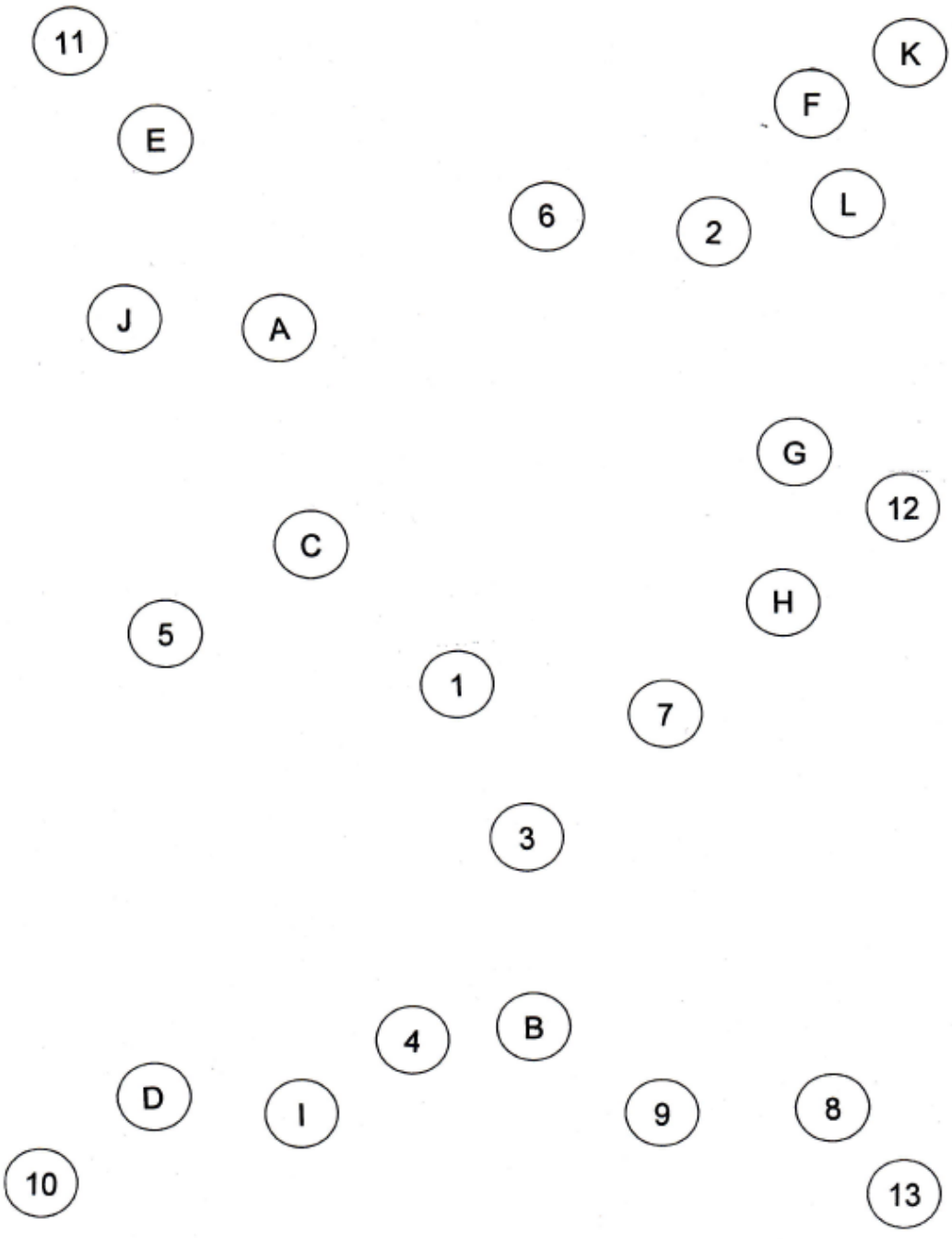

Participant Identification Code:

Reimbursement Confirmation

I confirm that I have received a £40 Amazon voucher for my participation and have been offered a taxi journey home following the study

Participant signature _____

Researcher signature _____

Date _ _ / _ _ / _ _ _ _

Participant Identification Code:

Reimbursement Confirmation

I confirm that I have received £40 for my participation and have been offered a taxi journey home following the study

Participant name _____

Participant signature _____

Researcher signature _____

Date _ _ / _ _ / _ _ _ _

Debrief

Thank you for taking part in this study. Please remember not to operate vehicles or heavy machinery and ensure that you take up the offer of the taxi journey home as you may be too tired to drive or cycle after the study. Please make sure you have a good rest at home.

Sleep is really important, particularly the quality of sleep. Research has shown that performance in certain tasks are affected to a greater degree by sleep deprivation than others, especially tasks which require sustained attention. The aim of the experiment was to see how the circadian rhythm (the internal body clock) is affected by sleep deprivation and whether certain symptoms (which come under a term called psychotomimetic states) can be observed in the healthy adult population. We were also looking at your performance in neuropsychological and neuropsychiatric tasks whilst you were sleep deprived to see whether this showed a trend in line with your internal body clock.

We expect to observe a variability in reaction time scores with this increasing the longer you have been sleep deprived for, higher scores on the psychotomimetic scale, higher scores on subjective sleepiness the longer you have been taking part, poorer performance in neuropsychological and neuropsychiatric tasks and for your performance on these measures to fluctuate depending on your body clock. We expected to see you perform the worst at two specific time points where both your circadian rhythm and sleepiness are at its highest.

Information collected during this study will be held confidentially in line with the UK Data Protection Act (1998). Once the data is analysed, a report of the findings may be submitted for publication. Only broad trends will be reported and it will not be possible to identify any individuals. If you would like a summary of the results this can be made available to you on request.

If you have any questions, please do not hesitate to contact me (Rowena Bicknell) at the University of Kent on 01227 816436 or via email: rmb48@kent.ac.uk.

You can also get in touch with my Supervisors, Dr David Lowery at the University of Kent on 01227 824908 or via email: d.lowery@kent.ac.uk and Dr David Wilkinson on 01227 824772 or via email: D.T.Wilkinson@kent.ac.uk.

Appendix C: The Role of Sleep as a Predictive and Precipitating Factor for Delirium in the Hospitalised Older Adult Population

C.1 Adverse events and risk management

An AE **does include** a / an:

1. Exacerbation of a pre-existing illness
2. Increase in frequency or intensity of a pre-existing episodic event or condition
3. Condition detected or diagnosed after intervention even though it may have been present prior to the start of the study
4. Continuous persistent disease or symptoms present at baseline that worsen following the start of the trial

*An AE **does not include** a / an:*

1. Medical or surgical procedure (e.g., surgery, endoscopy, tooth extraction, transfusion); but the condition that lead to the procedure is an AE;
2. Pre-existing disease or conditions present or detected at the start of the trial that did not worsen;
3. Situations where an untoward medical occurrence has not occurred (e.g., hospitalisations for cosmetic elective surgery, social and / or convenience admissions)

A Serious Adverse Event (SAE) is defined as any adverse event occurring following study mandated procedures, that results in any of the following outcomes:

1. Death;
2. A life-threatening adverse event;
3. Inpatient hospitalisation for non-elective procedures;
4. Sudden or rapidly progressive major disablement;
5. An event that caused the participant to seek non-routine medical treatment.

Important medical events that may not have resulted in death, be life-threatening, or require hospitalisation may be considered a serious adverse event when, based upon appropriate medical judgment, they may jeopardize the patient or participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. All adverse events were assessed for seriousness, expectedness and causality by a study Principal Investigator. A distinction

was drawn between serious and severe AEs. Severity is a measure of intensity whereas seriousness is defined using the criteria above. Hence, a severe AE need not necessarily be serious.

Reporting of adverse events

All research study related SAEs were recorded and reported to the REC as part of the annual reports. Unexpected serious adverse events were reported within the timeframes to the REC as stated below. The Principal Investigator was responsible for all adverse event reporting. During the study**,** we conducted monitoring of adverse events. Participants were asked to contact the study site immediately in the event of any serious adverse event. Adverse Events (AEs) were brought to the attention of the study team by either:

- *Telephone call to the study team*. Participants were encouraged to call the study team if they experience any adverse effects during the study.
- *Notification by GP*. Participant's doctors were encouraged to contact the study team of any AEs they are made aware of.
- *Notification by clinical care team at hospital*. The participant's clinical care team were encouraged to contact the study team, either in person or by telephoning the researcher, if they observe any AEs in the participant.

On notification of an AE at the study centre, the Principal Investigator called the subject for further information. The Principal Investigator shall determine seriousness and causality in conjunction with any treating medical practitioners. All adverse events were recorded and closely monitored until resolution, stabilisation, or it has been demonstrated that the study treatment is not the cause.

Risk management

To safeguard the research team, the primary care team were asked whether patients recruited for the study had a previous history of violence and exclude them if this was the case. This was not included in the exclusion criteria as the exclusion of patients deemed inappropriate to approach had already been highlighted.

Risk issues

The below issues were deemed to be of low risk due to the nature of the study being observational in nature.

- Inadvertent disclosure of dementia - (disclosure of diagnosis rests with lead clinician (GP)
- Carer suffering from undiagnosed dementia – (excluded those for whom an appropriate representative with capacity to consent cannot be identified)
- Initiation or worsening of other behavioural and psychological symptoms, e.g., agitation/aggression (Clinical Team and Chief Investigator to monitor; adverse event reporting)
- Worsening of sleep disturbances (adverse event reporting)
- Accidents – Chief Investigator assessed hospital and home environment to undertake a risk assessment for potential hazards which could have contributed to an increased risk of slips, trips and falls

Due to the nature of the study, with home visits to participants where members of the research team were unaccompanied, the study adhered to the 'Lone workers and the avoidance of violence at work Performance Standard' as part of the Health, Safety and Risk Management Regulations at the University of Kent. Further information on this can be found here: www.kent.ac.uk/safety/hs/pages/loneworking/loneworking.html. The study adhered to the General Health and Safety regulations of the University of Kent. In instances where an AE occurs, the Risk Assessment Pathway will be followed and events were logged and recorded using the incident report form depending on severity. Logged issues were reported to the Safety, Health and Environment Unit at the University of Kent and raised with the rest of the research team at the first available instance.

Study intervention related Serious Adverse Events

A SAE that was deemed directly related to or suspected to be related to the study intervention was reported to the Study Steering Committee and ethics committee. The event was reported immediately to the site Principal Investigator and Study Chief Investigator.

The Principal Investigator:

- Assessed the event for seriousness, expectedness and relatedness to the research study.
- Took appropriate medical action, which may have included halting the study and informing the sponsor of such action.

- If the event was deemed related to the study participation, the Principal Investigator informed the REC using the reporting form found on the NRES web page within seven days of knowledge of the event. Within a further 8 days, any follow-up information and reports were sent to the REC.
- Make any amendments as required to the study protocol and inform the REC as required.

C.2 Authorship / Acknowledgment policy

Purpose

This policy sets out the criteria and requirements whereby authorship, acknowledgement and responsibilities for the publication of findings arising from 'The Role of Sleep as a Predictive and Precipitating Factor for Delirium in the Hospitalised Older Adult Population' are properly credited.

Authorship/Acknowledgment Criteria and Contributions.

To qualify for authorship, an individual must be able to check at least 1 area for each of the following 3 categories:

1. Contributed substantially to the intellectual content through: conception and design; acquisition of data; and/or analysis and interpretation of data
2. Contributed substantially to the intellectual content through: drafting of the manuscript; and/or critical revision of the manuscript for important intellectual content
3. Contributed substantial intellectual input through: statistical expertise; obtaining funding; administrative, technical or material support; supervision; or other (specify)

Where an individual or group's contributions do not meet criteria for full authorship, but have contributed to at least one of the above categories, acknowledgement of this contribution should be made. All acknowledgments must be approved by those being acknowledged.

Authorship Responsibilities

Authors agree that they will, if requested:

- provide the data or co-operate fully in obtaining and providing the data on which publications are to be based;
- allow the corresponding author to serve as the primary correspondent with the respective editorial office, to review the edited typescript and proof, and to make decisions regarding release of information in the manuscript where there are more than 1 author; or if the individual is sole author, will be the corresponding author and agree to serve in the roles described above.
- Give final approval of the submitted manuscript.

Process of manuscript drafting

All proposed publications relating to the work of 'The Role of Sleep as a Predictive and Precipitating Factor for Delirium in the Hospitalised Older Adult Population' are to be identified and described to

the authors of this protocol prior to any submission. This should be in the form of a bulleted summary which includes the following information:

- Title
- Authors
- Target Journal
- Outline of content, including: rationale, method, outcome measures, key findings and implications

* Writing of the first draft of any paper to be submitted confers right to be listed as 1st named author. The Chief Investigator reserves the right to be named 2nd or last in the list of authors.

Monitoring Outputs and Dispute Resolution

The steering group will monitor and ensure the study team adequately report findings arising from the trial. Also, where there is a dispute of authorship or acknowledgement, the steering group agrees to act as arbitrator and the study team agrees to abide by decisions made by the Steering Group.

C.3 Study materials

Participant Information Sheet

Re: The Role of Sleep as a Predictive and Precipitating Factor for Delirium in the Hospitalised Older Adult Population

Dear Sir/Madam,
Please take time to read the following information carefully.

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others if you wish.

Please ask if anything is unclear, and do not feel rushed into making a decision.

What is the purpose of this study?

The purpose of this study is to find out about how staying in hospital affects sleep in older people. We will also look at whether poorer sleep will have an effect on developing delirium.

Delirium is a medical term used to describe people who have lost the ability to concentrate or remember things in the way they normally can. It is a symptom, not a disease. It happens in a small number of people who have surgery like yours. It usually does not last long, and most people quickly recover their ability to concentrate and remember things. We would like to learn about this so that we can help improve the care people staying in hospital.

Why have I been chosen and how many will be involved in the study?

Sometimes people experience delirium when they go into hospital and older people have a greater chance of this happening. You have been chosen because you are over the age of 70 and are due to have hip or knee replacement surgery.

We will ask 104 people like you to take part in this study.

What would taking part involve?

Pre-admission clinic

The research team will meet you at your pre-admission clinic after you have seen your doctor. We will discuss this project with you and be able to answer questions. If you decide to take part, we will ask your permission for us to use your information in the study.

We will then take you through a few brief assessments on delirium, thinking, mood and your sleep to make sure this study is right for you. This will take around 20 minutes in total and will include:

- Some thinking and memory questions, this will take about 10 minutes

- Some questions about how your mood has been, this will take about 10 minutes

At home before surgery

The research team will arrange to visit you at home before you go into hospital. We will conduct some more assessments which will take around 1 hour and 20 minutes in total. This will include:

- Some thinking and memory questions, this will take about 10 minutes
- Some questions on how your sleep is, this will take about 20 minutes
- Questions on how you manage everyday tasks and daily living, this will take about 35 minutes
- Two tasks to measure your reaction time. These will on pen and paper and also on a computer, this will take around 20 minutes

In addition to these assessments, we will also ask you to wear an ActiGraph activity monitor to measure your sleep. This is a very good way to measure the quality and duration of your sleep and is often used in this type of research. We will ask you to wear the ActiGraph for three days. The ActiGraph (see inset picture) is waterproof so you can even wear it in the shower. Wearing the ActiGraph could cause discomfort.

We will also provide you with a sleep diary to help give us a richer understanding of your sleep patterns

In hospital after surgery

After you have had your surgery the research team will visit you in hospital again one day after your surgery to repeat some of the assessments you did at home. These will include:

- Some thinking and memory questions, this will take about 10 minutes
- Some questions on your daily living, this will take about 5 minutes
- Two tasks to measure your reaction time. These will on pen and paper and also on a computer, this will take around 20 minutes

These assessments will take no more than 35 minutes to complete.

You will once again be asked to wear the ActiGraph to monitor your sleep and be given a sleep diary. You will wear the ActiGraph and use the sleep diary for three days.

We will visit you again after a further three days'. This will be 4 days after your surgery and repeat the assessments you did 3 days earlier. These will include:

- Some thinking and memory questions, this will take about 10 minutes
- Some questions on your daily living, this will take about 5 minutes

- Two tasks to measure your reaction time. These will on pen and paper and also on a computer, this will take around 20 minutes

These assessments will take no more than 35 minutes to complete.

At the end of these assessments we will collect the Actigraph activity monitor and diary from you.

At home after surgery

The last visit will be three months after your surgery where the research team will visit again for the final assessments. These assessments will include:

- Some thinking and memory questions, this will take about 10 minutes
- Some questions on how your sleep is, this will take about 20 minutes
- Some questions on your daily living, this will take about 5 minutes
- Two tasks to measure your reaction time. These will on pen and paper and also on a computer, this will take around 20 minutes

In total the research team will need to meet with you five times for around 20 to 1 hour and 20 minutes on each occasion. You will need to wear the ActiGraph and use a sleep diary for 2 periods of 3 days during the study.

Your GP will also receive an information sheet similar to this one which explains the research study and informs them that you have been invited to take part. The research team may contact your GP if you are not eligible to take part and may advise they make further investigations. If we feel your health may be in danger, we may have to report the results to your GP.

What are the possible benefits of taking part?

By taking part in our study you will help us increase our understanding of the relationship between sleep and delirium. Your support may help us improve the care people for people who need surgery.

What are the possible disadvantages and risks of taking part?

Some people may feel a little more tired at the end of the session. You may take a rest break if you become tired.

What if something goes wrong?

This research project is simply to monitor how you are doing and how your hospital stay affects you. It is very unlikely the research itself will cause you harm. However, a senior consultant from NHS East Kent Trusts will be monitoring your safety with respect to the research project. Taking part will not affect the care you would otherwise receive as part of your surgery and recovery.

If you feel unwell and it is urgent, please contact your General Practitioner. If it is specific to your hospitalization, please contact Chris Farmer. If it is related to the research project, please contact Rowena Bicknell.

What happens if I experience delirium during the study?

Sometimes people experience delirium when they go into hospital. This is a risk for everyone. When people experience delirium, they may lose the ability to make everyday decisions in the way they previously would have (lose the capacity to consent). This condition is temporary, and typically resolves within hours.

It is important that people who experience delirium remain in the study as this condition is the main focus of the research. Therefore, we will continue to attempt to assess you, even if you are having problems with your thinking and memory.

To help support you during any periods where you may be having problems with thinking and memory, we would like you to nominate a personal consultee and give permission to that consultee to provide an opinion on the appropriateness of your participation in the event that you lose capacity during the course of the study. We would like you to nominate someone close to you, such as a family member or friend. We will ask them to provide an opinion on whether you would want to continue to take part.

We will always keep your best interests in mind, and if we think you are showing signs of stress or distress, we will make arrangements to see you another time.

What will happen if I don't want to carry on with the study?

You will be able to withdraw from the study at any time. If you refuse to take part or if you decide to withdraw, this will not affect the care that you receive. If you do choose to withdraw or are no longer able to participate, the study investigators will keep the data collected up to that point.

How will my information be kept confidential?

All information we collect from you will be kept confidential as required by law. The information you provide will be kept in password protected computer programs and in locked filing cabinets at the University of Kent. Only the research team will have access to your information. The only thing that will contain your name will be the consent form and all other documents will refer to you by a number to keep data anonymous. However, if we feel your health may be in danger, we may have to report your results to your GP.

What will happen to the results of this study?

The results from this study will be analysed and reported in publications in medical journals; presented at conferences; and will be included in a doctoral thesis.

We'd be happy to provide you with a summary of our findings and/or a copy of the published research, should you wish to have one. We will keep personal identifiable data

including your name and address for 3-6 months to provide the research team sufficient time to analyse the data and be able to contact you when the outcomes of the study are available. This data will only be accessible by the Chief Investigator and the identifiable information will be destroyed after 6 months.

Who is organising and funding this study?

This study is organised by Rowena Bicknell, (Research PhD Student, Centre for Health Services) at the University of Kent. The University is providing the funds for this PhD project. You should contact Rowena Bicknell if you require further information relating to the study.

Please contact for further information

Rowena Bicknell (PhD Student) Study Chief Investigator

Centre for Health Services Studies, 2nd Floor George Allen Wing, Cornwallis Building, University of Kent, Canterbury, CT2 7NF

Phone: 01227 16436 Email: rmb48@kent.ac.uk

Professor Chris Farmer MD FRCP

Centre for Health Services Studies, 2nd Floor George Allen Wing, Cornwallis Building, University of Kent, Canterbury, CT2 7NF

Phone: 01227 816439 Email: C.Farmer-357@kent.ac.uk

Patient advice and liaison services (PALS): Queen Elizabeth The Queen Mother Hospital

Queen Elizabeth The Queen Mother Hospital, St Peters Road, Margate, Kent, CT9 4AN

Phone: 01227 783145 Email: ekh-tr.patientexperienceteam@nhs.net

We thank you for taking time to read this sheet. If you decide to participate in the study, you will receive a copy of both this Information Sheet and the consent form that you must later sign. You will also be asked to nominate a relative/friend as a consultee and give permission for that consultee to make decisions on your behalf with regard to the study should you lose the capacity to consent. Your General Practitioner will also be informed of your participation.

CHSS University of Kent

Centre for Health Services Studies

Dear Sir/Madam,

Thank you for taking the time to read this letter. The University of Kent are conducting research to look at how staying in hospital affects sleep in older people.

You have been invited to take part in this study because we feel that your experiences will contribute to our understanding and knowledge of sleep and delirium, and also enhance our understanding of hospital environments, and how this can be improved in the future. Your support will help us improve the care of people who need surgery.

Please try and complete the assessments given to you which will look at delirium, thinking, mood and your sleep. We will also ask you to wear an activity monitor. This is a very good way to measure the quality and duration of your sleep and is often used in this type of research.

The information that we collect from the questionnaires will be kept private. Any information about you will have a number on it instead of your name (for example, participant #1). Only the research team at the University of Kent will know what your number is and we will keep that information strictly confidential. It will not be shared with or given to anyone. A final report will be created from the data – which will not include access to the individual questionnaires or any data that could identify you.

If you have any questions, please do not hesitate to contact me (Rowena Bicknell) at the University of Kent on 01227 816436 or via email: rmb48@kent.ac.uk. Please see the enclosed Participant Information Sheet for more information.

Yours faithfully,

[REDACTED]

Rowena Bicknell

PhD Student, University of Kent

Version 2.0 14/03/2017

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WHO COLLABORATING CENTRE

University of Kent
George Allen Wing
Canterbury
Kent CT2 7NF
United Kingdom

General Practitioner Information Sheet

Re: The Role of Sleep as a Predictive and Precipitating Factor for Delirium in the Hospitalised Older Adult Population

Dear General Practitioner,

You are being contacted because a patient under your care has been invited to take part in a research study.

What is the purpose of this study?

The purpose of this study is to find out about how staying in hospital affects sleep in older people. It will also look at whether poorer sleep will have an effect on developing delirium. Delirium is a medical term to describe a temporary confused state. Doctors use this to describe people who have lost the ability to concentrate or remember people or things. It is a symptom, not a disease. We would like to learn about this so that we can help improve the care people who experience delirium receive.

Why has your patient been chosen and how many patients will be involved in the study?

Sometimes people experience delirium when they go into hospital and research has suggested that older people have a greater likelihood of this. Your patient has been chosen because they are over the age of 70 and are scheduled to have hip or knee replacement surgery. We aim to involve a total of 104 patients in this study.

What would taking part as a <u>patient</u> involve?

- The research team will meet your patient at their pre-admission clinic to discuss the project and answer questions. If they decide to take part, we will ask them to provide consent so their information can be used in the study. We will then conduct some assessments on delirium, thinking, mood and sleep.
- The research team will contact your patient to arrange a visit them on four occasions (at pre-surgery, 1-day post-surgery, 4-days post-surgery and 3-months post-surgery).
- At each visit the research team will conduct a series of assessments lasting for around 20 minutes to 1 hour 20 minutes. We will also put on an ActiGraph activity monitor on their wrist to measure their sleep and provide them with a sleep diary. This ActiGraph (see right) needs to be worn all the time and will not affect their daily life. Wearing the ActiGraph could cause discomfort. The ActiGraph and sleep diary will be worn/used for three days.

What will taking part as a <u>General Practitioner</u> involve?

GP involvement in this study will be minimal and not require anything in addition to your normal day-to-day work. There are no aspects within this observational study which directly involve the GP. In instances where your patient feels unwell and it is not specific to their hospitalization and or research project they have been advised to contact you, their General Practitioner. If it is specific to their hospitalization, please contact Chris Farmer. If it is related to the research project, please contact Rowena Bicknell.

What are the possible benefits of taking part?

By taking part in our study you will help us increase our understanding of the relationship between sleep and delirium. Your support may help us improve the care people for people who need surgery.

What are the possible disadvantages and risks of taking part?

Some patients may feel a little more tired at the end of the session. Your patient may take a rest break if they become tired.

What if something goes wrong?

This research project is simply to monitor how your patient is doing and how their hospital stay affects them. It is very unlikely the research itself will cause your patient harm however a senior consult from NHS East Kent Trusts will be monitoring their safety with respect to the research project.

What will happen if my patient doesn't want to carry on with the study?

Your patient will be able to withdraw from the study at any time. If they refuse to take part or if they decide to withdraw, it will not affect the care that they receive. If your patient chooses to withdraw or are no longer able to participate, the study investigators will keep the data collected up to that point.

How will my patient's information be kept confidential?

All information we collect will be kept confidential as required by law. The information your patient provides will be kept in password protected computer programs and in locked filing cabinets. Only the research team will have access to the information. The only thing that will contain your patient's name will be the consent form and all other documents will refer to your patient by a number to keep data anonymous.

What will happen to the results of this study?

The results from this study will be analysed and reported in publications in medical journals; presented at conferences; and will be included in a doctoral thesis.

Who is organising and funding this study?

This study is organised by Rowena Bicknell, (Research PhD Student, Centre for Health Services) at the University of Kent. The University is providing the funds for this PhD project. You should contact Rowena Bicknell if you require further information relating to the study.

Please contact for further information

Rowena Bicknell (PhD Student) Study Chief Investigator

Centre for Health Services Studies, 2nd Floor George Allen Wing, Cornwallis Building, University of Kent, Canterbury, CT2 7NF

Phone: 01227 16436 Email: rmb48@kent.ac.uk

Professor Chris Farmer MD FRCP

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Phone: 01227 816439 Email: C.Farmer-357@kent.ac.uk

Patient advice and liaison services (PALS): Queen Elizabeth The Queen Mother Hospital

Queen Elizabeth The Queen Mother Hospital, St Peters Road, Margate, Kent, CT9 4AN

Phone: 01227 783145 Email: ekh-tr.patientexperienceteam@nhs.net

We thank you for taking time to read this sheet. Your patient, if they decide to take part, will receive a copy of both an Information Sheet and a signed copy of the consent form. Your patient has been informed that you have notified of their participation.

Participant Identification Code:

Consent Form

Name of Chief Investigator: Rowena Bicknell

Please initial box

5. I confirm I have read and understand the information sheet. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

6. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐

7. I understand that relevant sections of my medical notes collected during the study may be looked at by responsible individuals from the study team and regulatory authorities. I give permission for these individuals to have access to this information. ☐

8. I agree to my GP being informed of my participation in the study, should the research team believe this to be appropriate. ☐

9. I agree to my bed manager informing the Chief Investigator of the date I will be admitted into hospital. ☐

10. I understand if I lose the capacity to consent I will remain in the study and the research team will continue to attempt to obtain data in accordance to the Mental Capacity Act 2005 Code of Practice. I understand I have the right to withdraw data retrospectively. ☐

11. I agree to take part in the above study. ☐

_____	_____	_____
Name of Participant	Date	Signature
_____	_____	_____
Name of Person taking consent	Date	Signature

When completed, 1 for patient; 1 for researcher site file; 1 (original) to be kept in medical notes.

Consultee Information Sheet

Re: The Role of Sleep as a Predictive and Precipitating Factor for Delirium in the Hospitalised Older Adult Population

Dear Sir/Madam,
Please take time to read the following information carefully.

Why have I been approached?

We identified a friend or relative of yours as a person who might like to take part in the Sleep as a Factor for Delirium in the Hospitalised Older Adult Population study. They have previously nominated you to be their personal consultee. You can find the details of this study on page 2 of this information sheet.

When carrying out research, we only involve people who agree to take part in the full knowledge of what we are asking them to do, including all the risks and benefits. However, we feel that your relative/friend is unable to decide for himself/herself whether to participate in this research.

It is important that your friend/relative still has an opportunity to take part. To help decide if your friend/relative should join the study, we would like to ask your opinion whether or not they would want to be involved. We would ask you to consider what you know of their wishes and feelings, and to consider their interests. Please let us know of any advance decisions they may have made about participating in research. These should take precedence.

If you decide that your friend/relative would not wish to take part, it will not affect the standard of care they receive in any way.

If you decide your relative/friend would have no objection to taking part, we will ask you to read and sign the record of consultation that accompanied this information sheet. We will then give you a copy to keep. We will keep you fully informed during the study so you can let us know if you have any concerns or if you think your relative/friend should be withdrawn. The final decision about whether your friend or relative takes part in the research rests with the Research team.

Do I have to give my opinion?

No, it is entirely up to you whether you decide to give your opinion or not. We will understand if you do not want to take on this responsibility.

If you are unsure about taking the role of consultee you may seek independent advice.

Will I have to do anything else, other than give my opinion?

We will ask you to sign a record of consultation form and provide you space on the document to give your advice. You will not be asked to do anything else.

What is the purpose of this study?

The purpose of this study is to find out about how staying in hospital affects sleep in older people. We will also look at whether poorer sleep will have an effect on developing delirium.

Delirium is a medical term used to describe people who have lost the ability to concentrate or remember things in the way they normally can. It is a symptom, not a disease. It happens in a small number of people who have surgery like yours. It usually does not last long, and most people quickly recover their ability to concentrate and remember things. We would like to learn about this so that we can help improve the care people staying in hospital.

Why have I been chosen and how many will be involved in the study?

Sometimes people experience delirium when they go into hospital and older people have a greater chance of this happening. Your relative/friend has been chosen because they are over the age of 70 and are due to have hip or knee replacement surgery.

We will ask 104 people like your relative/friend to take part in this study.

What would taking part involve?

Pre-admission clinic

The research team will meet your relative/friend at their pre-admission clinic after they have seen their doctor. We will discuss this project with them and be able to answer questions. If your relative/friend decides to take part, we will ask your relative/friend's permission for us to use their information in the study.

We will then take your relative/friend through a few brief assessments on delirium, thinking, mood and their sleep to make sure this study is right for them. This will take around 20 minutes in total and will include:

- Some thinking and memory questions, this will take about 10 minutes
- Some questions about how their mood has been, this will take about 10 minutes

At home before surgery

The research team will arrange to visit your relative/friend at home before they go into hospital. We will conduct some more assessments which will take around 1 hour and 20 minutes in total. This will include:

- Some thinking and memory questions, this will take about 10 minutes
- Some questions on how their sleep is, this will take about 20 minutes

- Questions on how they manage everyday tasks and daily living, this will take about 35 minutes
- Two tasks to measure their reaction time. These will on pen and paper and also on a computer, this will take around 20 minutes

In addition to these assessments, we will also ask your relative/friend to wear an ActiGraph activity monitor to measure their sleep. This is a very good way to measure the quality and duration of their sleep and is often used in this type of research. We will ask them to wear the ActiGraph for three days. The ActiGraph (see inset picture) is waterproof so it can even be worn in the shower. Wearing the ActiGraph could cause discomfort.

We will also provide your relative/friend with a sleep diary to help give us a richer understanding of their sleep patterns.

<u>In hospital after surgery</u>

After your relative/friend have had their surgery, the research team will visit them in hospital again one day after their surgery to repeat some of the assessments they did at home. These will include:

- Some thinking and memory questions, this will take about 10 minutes
- Some questions on their daily living, this will take about 5 minutes
- Two tasks to measure their reaction time. These will on pen and paper and also on a computer, this will take around 20 minutes

These assessments will take no more than 35 minutes to complete.

Your relative/friend will once again be asked to wear the ActiGraph to monitor their sleep and be given a sleep diary. They will wear the ActiGraph and use the sleep diary for three days.

We will visit your relative/friend again after a further four days'. This will be 3 days' after their surgery and repeat the assessments they did 3 days earlier. These will include:

- Some thinking and memory questions, this will take about 10 minutes
- Some questions on their daily living, this will take about 5 minutes
- Two tasks to measure their reaction time. These will on pen and paper and also on a computer, this will take around 20 minutes

These assessments will take no more than 35 minutes to complete.

At the end of these assessments we will collect the Actigraph activity monitor and diary from them.

At home after surgery

The last visit will be three months after your relative/friend's surgery where the research team will visit again for the final assessments. These assessments will include:

- Some thinking and memory questions, this will take about 10 minutes
- Some questions on how their sleep is, this will take about 20 minutes
- Some questions on their daily living, this will take about 5 minutes
- Two tasks to measure their reaction time. These will on pen and paper and also on a computer, this will take around 20 minutes

In total the research team will need to meet with your relative/friend five times for around 20 to 1 hour and 20 minutes on each occasion. They will need to wear the ActiGraph and use a sleep diary for 2 periods of 3 days during the study.

Their GP will also receive an information sheet similar to this one which explains the research study and informs them that you have been invited to take part. The research team may contact their GP if you are not eligible to take part and may advise they make further investigations. If we feel your relative/friend's health may be in danger, we may have to report the results to their GP.

What are the possible benefits of taking part?

By taking part in our study your relative/friend will help us increase our understanding of the relationship between sleep and delirium. Their support may help us improve the care people for people who need surgery.

What are the possible disadvantages and risks of taking part?

Some people may feel a little more tired at the end of the session. Your relative/friend may take a rest break if they become tired.

What if something goes wrong?

This research project is simply to monitor how your relative/friend is doing and how their hospital stay affects them. It is very unlikely the research itself will cause them harm. However, a senior consultant from NHS East Kent Trusts will be monitoring their safety with respect to the research project. Taking part will not affect the care they would otherwise receive as part of their surgery and recovery.

If your relative/friend feels unwell and it is urgent, please contact their General Practitioner. If it is specific to their hospitalization, please contact Chris Farmer. If it is related to the research project, please contact Rowena Bicknell.

What happens if my relative/friend experiences delirium during the study?

Sometimes people experience delirium when they go into hospital. This is a risk for everyone. When people experience delirium, they may lose the ability to make everyday decisions in the way they previously would have (lose the capacity to consent). This condition is temporary, and typically resolves within hours.

It is important that people who experience delirium remain in the study as this condition is the main focus of the research. Therefore, we will continue to attempt to assess your relative/friend, even if they are having problems with their thinking and memory.

To help support your relative/friend during any periods where they may be having problems with thinking and memory, we have asked for their permission to nominate a personal consultee to provide an opinion on the appropriateness of their participation in the event that they lose capacity during the course of the study. If you are receiving this information sheet, our participant has nominated you to be their consultee. We will ask them to provide an opinion on whether you would want to continue to take part.

We will always keep your relative/friend's best interests in mind, and if we think they are showing signs of stress or distress, we will make arrangements to see them another time.

What will happen if my relative/friend doesn't want to carry on with the study?

Your relative/friend will be able to withdraw from the study at any time. If they refuse to take part or if they decide to withdraw, this will not affect the care that they receive. If they do choose to withdraw or are no longer able to participate, the study investigators will keep the data collected up to that point.

How will my relative/friend's information be kept confidential?

All information we collect from them will be kept confidential as required by law. The information provided will be kept in password protected computer programs and in locked filing cabinets at the University of Kent. Only the research team will have access to the information. The only thing that will contain your relative/friend's name will be the consent form and all other documents will refer to you by a number to keep data anonymous. However, if we feel your relative/friend's health may be in danger, we may have to report the results to their GP.

What will happen to the results of this study?

The results from this study will be analysed and reported in publications in medical journals; presented at conferences; and will be included in a doctoral thesis. We'd be happy to provide you with a summary of our findings and/or a copy of the published research, should you wish to have one.

Who is organising and funding this study?

This study is organised by Rowena Bicknell, (Research PhD Student, Centre for Health Services) at the University of Kent. The University is providing the funds for this PhD project. You should contact Rowena Bicknell if you require further information relating to the study.

Please contact for further information

Rowena Bicknell (PhD Student) Study Chief Investigator

Centre for Health Services Studies, 2nd Floor George Allen Wing, Cornwallis Building, University of Kent, Canterbury, CT2 7NF

Phone: 01227 16436 Email: rmb48@kent.ac.uk

Professor Chris Farmer MD FRCP

Centre for Health Services Studies, 2nd Floor George Allen Wing, Cornwallis Building, University of Kent, Canterbury, CT2 7NF

Phone: 01227 816439 Email: C.Farmer-357@kent.ac.uk

Patient advice and liaison services (PALS): Queen Elizabeth The Queen Mother Hospital

Queen Elizabeth The Queen Mother Hospital, St Peters Road, Margate, Kent, CT9 4AN

Phone: 01227 783145 Email: ekh-tr.patientexperienceteam@nhs.net

We thank you for taking time to read this sheet. If you agree to act as the consultee on behalf of your relative/friend, please read and sign the record of consultation form and provide your advice.

The Role of Sleep as a Predictive and Precipitating Factor for Delirium in the Hospitalised Older Adult Population

Participant Identification Code:

Record of Consultation Form

Name of Chief Investigator: Rowena Bicknell

Please initial box

12. I confirm I have read and understand the information provided to me. ☐

13. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily and to give advice. ☐

If you would like to express your views, please use the space below.

In your opinion, should your friend or relative take part in the research?

What in your opinion do you think your friend or relative's wishes and feelings about taking part in the research would be likely to be, if your friend or relative had capacity in relation to the matter?

_____	_____	_____
Name of Consultee	Date	Signature
_____	_____	_____
Name of Chief Investigator	Date	Signature

When completed, 1 for patient; 1 for researcher site file; 1 (original) to be kept in medical notes.

Case Notes

Date:

Participant Identification Code:

DOB: _ _/ _ _/ _ _
Age:
Sex: Male / Female

Ethnicity:
White
[ ] English/Welsh/Scottish/Northern Irish/ British
[ ] Irish
[ ] Gypsy, Traveller or Irish Traveller
[ ] Any other White background

Mixed/Multiple ethnic groups
[ ] White and Black Caribbean
[ ] White and Black African
[ ] White and Asian
[ ] Any other Mixed/Multiple ethnic background

Asian/Asian British
[ ] Indian
[ ] Pakistani
[ ] Bangladeshi
[ ] Chinese
[ ] Any other Asian background

Black/African/Caribbean/Black British
[ ] African
[ ] Caribbean

Marital Status:

[ ] Single (never married or never in a civil partnership)
[ ] Married (including those in civil partnerships)
[ ] Separated (but still legally married or in a civil partnership)
[ ] Divorced (including formerly in a civil partnership which is now legally dissolved)
[ ] Widowed (including surviving partner from a civil partnership)

Schooling:

[ ] None
[ ] Primary
[ ] Secondary
[ ] Further Education
[ ] Vocational Qualification
[ ] Higher Education (i.e., degree/diploma)
[ ] Post Graduate Qualification (Higher degree)

Total years of education:

Past Medical History:

[ ] Myocardial infarction (history, not ECG changes only)
[ ] Congestive heart failure
[ ] Peripheral disease (includes aortic aneurysm >= 6 cm)
[ ] Cerebrovascular disease: CVA with mild or no residua or TIA
[ ] Dementia
[ ] Chronic pulmonary disease
[ ] Connective tissue disease
[ ] Peptic ulcer disease
[ ] Mild liver disease (without portal hypertension, inlcudes chronic hepatitis)
[ ] Diabetes without end-organ damage (excludes diet-controlled alone)
[ ] Hemiplegia
[ ] Moderate or severe renal disease
[ ] Diabetes with end-organ damage (retinopathy, neuropathy, nephropathy, or brittle diabetes)
[ ] Tumor without metastasis (exclude if > 5 y from diagnosis)
[ ] Leukemia (acute or chronic)
[ ] Lymphoma
[ ] Moderate or severe liver disease
[ ] Metastatic solid tumour
[ ] AIDS (not just HIV positive)

Past Psychiatric History:

[ ] Anxiety Disorders
[ ] Disruptive, Impulse-Control, and Conduct Disorders

[ ] Dissociative Disorders
[ ] Feeding and Eating Disorders
[ ] Mood Disorders
[ ] Neurocognitive Disorders
[ ] Neurodevelopmental Disorders
[ ] Personality Disorders
[ ] Sleep-Wake Disorders
[ ] Somatic Symptoms and Related Disorders
[ ] Substance-Related and Addictive Disorders
[ ] Trauma and Stressor-Related Disorders

Medication

Medication	Start date	Course details	Discontinuation date
	__/__/__		__/__/__
	__/__/__		__/__/__
	__/__/__		__/__/__
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	__/__/__		__/__/__

Sepsis Screening

Symptom	Tick if present, include details
Abnormal body temperature - Hyperthermia greater than or equal to 38.3°C or Hypothermia less than or equal to 36°C	
Tachycardia (heart rate greater than 90 bpm)	
Leukocytosis (WBC count greater than or equal to 12,000/ mm3) or Leukopenia (less than or equal to 4,000 mm3 or greater than 0.5 K/uL bands)	
Tachypnea (respiratory rate greater than 20 breaths per minutes)	
Hyperglycemia (blood glucose levels greater than 140 ml/Dl in non-diabetic patient	
Suspected or documented infection	
Antibiotic therapy (not prophylaxis)	
Respiratory: oxygen saturation less than 90% or increasing oxygen requirements	
Cardiovascular: systolic blood pressure less than 90mmHg or 40mmHg less than baseline or mean arterial pressure less than 65mmHg	

Renal: urine output less than 0.5ml/kg/hr; creatinine increase of greater than 0.5mg/dl from baseline	
Central nervous system: altered consciousness or Glasgow Coma Score less than or equal to 12.	
Hematologic: platelets less than 100,000; International Normalized Ratio greater than 1.5	
Hepatic: Serum total bilirubin greater than or equal to 4mg/dl	
Metabolic: Serum lactic acid greater than or equal to 2mEq/L	

Delirium risk factors

Risk Factors	Tick if present, include details
Old age	
History of depression	
History of alcohol abuse	
Presence of dementia	
Presence of medical illnesses	
Poor physical status prior to surgery (including malnutrition, immobility and presence of fractures pre-surgery)	
Use of physical restraints	
Diminished FIM+FAM scores	
History of sleep disturbances	
Presence of sleep deprivation	
Addition of more than three medications	
Use of 'high-risk medications' e.g. narcotics, major tranquilisers	
Use of catheters	
Unplanned surgeries associated with this operation	
Increased number of admissions in previous 2 years (including urgent admissions)	
Abnormal blood urea nitrogen / creatinine ratio	

Sodium abnormalities	
Potassium abnormalities	
Hypoxia	
Abnormal cerebrospinal fluid	
Abnormal electrocardiogram	
Abnormal chest x-ray findings	
Low mobility after surgery	
Presence of medical complications following surgery	

Other factors	**Details**
Anaesthetic type	
Operation duration	
Presence of sepsis	
Duration of hospital stay	

Clinical Record Form

Participant Identification Code:

Screening and recruitment process

Test site:

	Sign with initials and date when completed	
Clinical team to identify patient	_ _/ _ _/ _ _	
Clinical team to send out information sheet	_ _/ _ _/ _ _	
Researcher to attend pre-admission clinic to ask patient if they have received, read and understood the information sheet	_ _/ _ _/ _ _	
Collect informed consent from patient 1 – for patient; 2 – for patient medical records; 3 – for researcher	_ _/ _ _/ _ _	
Complete Delirium Rating Scale	_ _/ _ _/ _ _	
Complete Mini Mental State Examination	_ _/ _ _/ _ _	
Complete Beck Depression Inventory	_ _/ _ _/ _ _	
Complete Clinical Frailty Scale	_ _/ _ _/ _ _	
Is the patient still suitable for the study? (circle)	YES	NO
Researcher to arrange 2 follow-up home visits with patient	_ _/ _ _/ _ _	
Researcher to inform patient's care team of study participation & liaise with bed manager	_ _/ _ _/ _ _	

Baseline Pre-surgery

Test site:

	Sign with initials and date when completed	
Attach actigraphy monitor to patient's non-dominate arm	_ _/ _ _/ _ _	
Provide a copy of the sleep diary to patient	_ _/ _ _/ _ _	
Complete Delirium Rating Scale	_ _/ _ _/ _ _	

Complete Sleep Disorders Questionnaire	_ _/ _ _/ _ _	
Complete Mini Mental State Examination	_ _/ _ _/ _ _	
Complete FIM + FAM	_ _/ _ _/ _ _	
Complete Clinical Frailty Scale	_ _/ _ _/ _ _	
Complete Trail Making Test	_ _/ _ _/ _ _	
Complete Sustained Attention to Response Task	_ _/ _ _/ _ _	

Pre-admission (actigraphy monitor and sleep diary pick-up)

Test site:

	Sign with initials and date when completed	
Remove actigraphy monitor from patient	_ _/ _ _/ _ _	
Retrieve completed sleep diary from patient	_ _/ _ _/ _ _	
Researcher to enter data obtained from the visit to a password protected encrypted folder once back at the University of Kent	_ _/ _ _/ _ _	

1-day~~s~~ post-surgery

Test site:

	Sign with initials and date when completed	
Attach actigraphy monitor to patient's non-dominate arm	_ _/ _ _/ _ _	
Provide a copy of the sleep diary to patient	_ _/ _ _/ _ _	
Complete Delirium Rating Scale	_ _/ _ _/ _ _	
Complete Mini Mental State Examination	_ _/ _ _/ _ _	
Complete Clinical Frailty Scale	_ _/ _ _/ _ _	
Complete Trail Making Test	_ _/ _ _/ _ _	
Complete Sustained Attention to Response Task	_ _/ _ _/ _ _	

4-days post-surgery

Test site:

	Sign with initials and date when completed	
Remove actigraphy monitor from patient	_ _/ _ _/ _ _	
Retrieve completed sleep diary from patient	_ _/ _ _/ _ _	
Complete Delirium Rating Scale	_ _/ _ _/ _ _	
Complete Mini Mental State Examination	_ _/ _ _/ _ _	
Complete Clinical Frailty Scale	_ _/ _ _/ _ _	
Complete Trail Making Test	_ _/ _ _/ _ _	
Complete Sustained Attention to Response Task	_ _/ _ _/ _ _	

Extract information from discharge summary report	_ _/ _ _/ _ _	

3-months post-surgery

Test site:

	Sign with initials and date when completed	
Complete Delirium Rating Scale	_ _/ _ _/ _ _	
Complete Sleep Disorders Questionnaire	_ _/ _ _/ _ _	
Complete Mini Mental State Examination	_ _/ _ _/ _ _	
Complete FIM + FAM	_ _/ _ _/ _ _	
Complete Clinical Frailty Scale	_ _/ _ _/ _ _	
Complete Sustained Attention to Response Task	_ _/ _ _/ _ _	
Complete Trail Making Test	_ _/ _ _/ _ _	
Complete case notes analysis	_ _/ _ _/ _ _	

Researcher to inform patient care-team of study trial completion	_ _/ _ _/ _	

Sleep Diary

Participant identification code:				
Day (i.e. Monday) Date (i.e. 01/07/16)	**Example** Day 1: Monday Date: 01/08/16	**Day 1:** **Date: _ _ / _ _ / _ _**	**Day 2:** **Date: _ _ / _ _ / _ _**	**Day 3:** **Date: _ _ / _ _ / _ _**
Time woke in the morning	7:30 am			
Time, length and location of sleeps in the day (including naps)	1:00 – 1:20pm, 20 minutes, on the sofa 4:35 – 5:00pm, 25 minutes, in bed			
Time started preparing for bed	09:30pm			
Any problems	No			
Where you went to bed	Bed			
Time went to sleep	10:00pm			

Participant Identification code:

Did you take the sleep watch off? If so, please fill in the details below for each time you took it off

Example **Date:** 01/08/16	**Date:** __/__/__	**Date:** __/__/__	**Date:** __/__/__	**Date:** __/__/__
Time (start): 7:35am	**Time (start):**	**Time (start):**	**Time (start):**	**Time (start):**
Time (end): 7:55am	**Time (end):**	**Time (end):**	**Time (end):**	**Time (end):**
Reason: took a bath	**Reason:**	**Reason:**	**Reason:**	**Reason:**
Date: __/__/__	**Date:** __/__/__	**Date:** __/__/__	**Date:** __/__/__	**Date:** __/__/__
Time (start):	**Time (start):**	**Time (start):**	**Time (start):**	**Time (start):**
Time (end):	**Time (end):**	**Time (end):**	**Time (end):**	**Time (end):**
Reason:	**Reason:**	**Reason:**	**Reason:**	**Reason:**

Participant ID:

Delirium Severity Scale R-98

Name of Rater: _____

SEVERITY SCORE: ☐ **TOTAL SCORE:** ☐

Severity Item	Item Score				Optional Information
Sleep-wake cycle	0	1	2	3	Naps Nocturnal disturbance only Day-night reversal
Perceptual disturbances	0	1	2	3	Sensory type of illusion or hallucination: auditory visual olfactory tactile Format of illusion or hallucination: simple complex
Delusions	0	1	2	3	Type of delusion: persecutory Nature: poorly formed systematized
Lability of affect	0	1	2	3	Type: angry anxious dysphoric elated irritable
Language	0	1	2	3	Check here if intubated, mute, etc.
Thought process	0	1	2	3	Check here if intubated, mute, etc.
Motor agitation	0	1	2	3	Check here if restrained *Type of restraints:*
Motor retardation	0	1	2	3	Check here if restrained *Type of restraints:*
Orientation	0	1	2	3	Date: Place: Person:
Attention	0	1	2	3	
Short-term memory	0	1	2	3	Record # of trials for registration of items: Check here if category cueing helped
Long-term memory	0	1	2	3	Check here if category cueing helped
Visuospatial ability	0	1	2	3	Check here if unable to use hands
Diagnostic Item	**Item Score**				**Optional Information**
Temporal onset of symptoms	0	1	2	3	Check here if symptoms appeared on a background of other psychopathology
Fluctuation of symptom severity	0	1	2		Check here if symptoms only appear during the night

Participant ID:

Instructions:

This questionnaire will give your doctor a good understanding about your problems with sleeping and waking. It is very important to answer every question, because some disorders show up as a pattern of answers to different questions.

In answering the questions, consider each question as applying to the ***past six months*** of your life, unless you have been told differently by the person who gave you this booklet.

Some people work night shift, or rotating shifts. Others have a very changeable bedtime. For these people, questions which ask about "day, daytime, morning, etc." will mean the time when they wake from their longest sleep of the day and become active. Similarly, "night, nighttime, bedtime, nocturnal" would refer to whenever they are having their longest sleep of the day.

Most of the questions are simple statements. You answer by circling a number from 1 to 5. If you strongly disagree with the statement, or if it never happens to you, answer "1". If the statement is always true in your case, or you agree strongly with it, answer "5". You may also choose "2 rarely", "3 sometimes", or "4 usually" as your answer. Notice that an "answer key" appears at the bottom of each page to remind you what is meant by the numbers. Please answer all of the questions.

Here is an example of how to fill out a question:

1. How often does it snow in Florida in July? (1) 2 3 4 5

IF YOU ARE CERTAIN THAT A QUESTION DOES NOT APPLY TO YOU, LEAVE IT BLANK. But . . . try to answer every question if at all possible. This is important. Notice that answer "1" can mean that the things asked in the question ***never*** happen to you.

If you are using the computerized answer sheet, blacken the space which corresponds to your answer, "1 to 5", instead of circling the answer in this booklet.

********** Key for answers **********

1	2	3	4	5
NEVER	RARELY	SOMETIMES	USUALLY	ALWAYS
(strongly disagree)	(disagree)	(not sure)	(agree)	(agree strongly)

1. I get too little sleep at night	1 2 3 4 5
2. I often have a poor night's sleep	1 2 3 4 5
3. I have trouble getting to sleep at night	1 2 3 4 5
4. I wake up often during the night	1 2 3 4 5
5. My bedtime varies a lot	1 2 3 4 5
6. At bedtime, thoughts race through my mind	1 2 3 4 5
7. At bedtime, I feel sad and depressed	1 2 3 4 5
8. At bedtime, I worry about things	1 2 3 4 5
9. At bedtime, I feel muscular tension	1 2 3 4 5
10. At bedtime, I'm afraid of not being able to go to sleep	1 2 3 4 5
11. When falling asleep, I feel paralyzed (unable to move)	1 2 3 4 5
12. When falling asleep, I have "restless legs" (a feeling of crawling, aching, or inability to keep legs still)	1 2 3 4 5
13. After waking at night, I fear I will not be able to get back to sleep	1 2 3 4 5
14. My night sleep is restless and disturbed	1 2 3 4 5
15. At night, my sleep disturbs my bed partner's sleep	1 2 3 4 5
16. My night sleep is disturbed by light	1 2 3 4 5
17. My night sleep is disturbed by noise	1 2 3 4 5
18. My sleep is disturbed by severe heartburn and choking ("regurgitation", bringing up bitter stomach fluid)	1 2 3 4 5
19. I often wake up because I am hungry	1 2 3 4 5
20. I snore in my sleep	1 2 3 4 5
21. I am told I snore loudly and bother others	1 2 3 4 5
22. I am told I stop breathing ("hold my breath") in sleep	1 2 3 4 5
23. I awake suddenly gasping for breath, unable to breathe	1 2 3 4 5

********** Key for answers **********

1	2	3	4	5
NEVER (strongly disagree)	RARELY (disagree)	SOMETIMES (not sure)	USUALLY (agree)	ALWAYS (agree strongly)

24. At night my heart pounds, beats rapidly, or beats irregularly ("palpitations")	1 2 3 4 5
25. I sweat a great deal at night	1 2 3 4 5
26. I walk in my sleep	1 2 3 4 5
27. I grind my teeth while I sleep	1 2 3 4 5
28. I wake from sleep screaming, confused, and at times violent ("night terrors")	1 2 3 4 5
29. My sleep is disturbed because of pain in the neck, back, muscles, joints, legs or arms	1 2 3 4 5
30. My sleep is disturbed by chest pain (not angina)	1 2 3 4 5
31. My sleep is disturbed by "restless legs" (a feeling of crawling, aching, inability to keep legs still)	1 2 3 4 5
32. My sleep is disturbed by thoughts racing through my mind	1 2 3 4 5
33. My sleep is disturbed by sadness or depression	1 2 3 4 5
34. My sleep is disturbed by worrying about things	1 2 3 4 5
35. My sleep is disturbed by muscular tension	1 2 3 4 5
36. My sleep is disturbed by fears that I might not be able to get back to sleep if I should wake up	1 2 3 4 5
37. I often have a night full of intense vivid dreams	1 2 3 4 5
38. I have a lot of nightmares (frightening dreams)	1 2 3 4 5
39. I feel unable to move (paralyzed) after a nap	1 2 3 4 5
40. I have dream-like images (hallucinations) when I awaken in the morning even though I know I am not asleep	1 2 3 4 5
41. I am sometimes very sleepy in the daytime, and this seems to go in cycles at regular intervals	1 2 3 4 5
42. I have slept for several days at a time, or at least I have been overwhelmingly sleepy for that long	1 2 3 4 5
43. I have been unable to sleep <u>at all</u> for several days	1 2 3 4 5
44. I feel that my sleep is abnormal	1 2 3 4 5

********** Key for answers **********

1	2	3	4	5
NEVER	RARELY	SOMETIMES	USUALLY	ALWAYS
(strongly disagree)	(disagree)	(not sure)	(agree)	(agree strongly)

45. I feel that I have insomnia	1 2 3 4 5
46. As a child, I had difficulty waking up in the morning	1 2 3 4 5
47. As a child, I had sleepiness during the day	1 2 3 4 5
48. I have a problem because of headaches while sleeping	1 2 3 4 5
49. As a child, I was fatigued during the day	1 2 3 4 5
50. As a child, I rocked myself to get to sleep	1 2 3 4 5
51. I used to bang my head as a child	1 2 3 4 5
52. I used to sleepwalk in childhood	1 2 3 4 5
53. As a child, I had convulsions (seizures) during sleep	1 2 3 4 5
54. As a child, I would grind my teeth while asleep	1 2 3 4 5
55. Now, I am very sleepy during the day and I struggle to stay awake	1 2 3 4 5
56. In the past 6 months, I have fallen asleep accidentally in some of these situations: eating a meal, talking on the phone, talking to someone, riding in a bus or car, watching TV, at a theater, reading a book, at a lecture.	1 2 3 4 5
57. I got bad grades in school because I was too sleepy	1 2 3 4 5
58. I now have trouble doing my job because of sleepiness or fatigue	1 2 3 4 5
59. I often have to let someone else drive the car because I am too sleepy to do it	1 2 3 4 5
60. I see vivid dream-like images (hallucinations) either just before or just after a daytime nap, yet I am sure I am awake when they happen	1 2 3 4 5
61. I have vivid dreams during my daytime naps	1 2 3 4 5
62. I am often unable to move (paralyzed) when I am waking up in the morning	1 2 3 4 5
63. Sometimes I realize I have driven my car to the wrong place, and I can't remember how I did it	1 2 3 4 5
64. I find myself doing things which make no sense, such as writing nonsense instead of notes, or mixing together chocolate and gravy	1 2 3 4 5
65. People tell me that I act strangely at times, and yet I was not aware of it when it happened	1 2 3 4 5

********** Key for answers **********

1	2	3	4	5
NEVER	RARELY	SOMETIMES	USUALLY	ALWAYS
(strongly disagree)	(disagree)	(not sure)	(agree)	(agree strongly)

66. I get "weak knees" when I laugh	1 2 3 4 5
67. I get sudden muscular weakness (or even a brief period of paralysis, being unable to move) when laughing, angry, or in situations of strong emotion	1 2 3 4 5
68. I am excessively sleepy during the daytime	1 2 3 4 5
69. I have at some time had trouble with my bladder	1 2 3 4 5
70. I have had problems with tonsils or adenoids	1 2 3 4 5
71. I have high blood pressure (or once had it)	1 2 3 4 5
72. My tonsils and/or adenoids have been removed	1 2 3 4 5
73. I get pains in my abdomen (stomach)	1 2 3 4 5
74. I have had a head injury	1 2 3 4 5
75. I have been knocked unconscious (knocked out)	1 2 3 4 5
76. I suffer from dizzy spells	1 2 3 4 5
77. I have seizures ("fits", convulsions, epilepsy)	1 2 3 4 5
78. I have problems with clumsiness, incoordination	1 2 3 4 5
79. I feel that I have a sexual problem	1 2 3 4 5
80. My desire or interest in sex is less than it used to be	1 2 3 4 5
81. I have pain or discomfort during sexual intercourse	1 2 3 4 5
82. I sleep better after having sex	1 2 3 4 5
83. I am unhappy about my social life	1 2 3 4 5
84. I am unhappy about loving relationships in my life	1 2 3 4 5
85. I am unhappy about my sex life	1 2 3 4 5
86. I am dissatisfied with my job	1 2 3 4 5
87. I have a problem with my sleep	1 2 3 4 5
88. I wake up in the morning with a headache	1 2 3 4 5
89. I have considered or attempted suicide	1 2 3 4 5

********** Key for answers **********

1	2	3	4	5
NEVER	RARELY	SOMETIMES	USUALLY	ALWAYS
(strongly disagree)	(disagree)	(not sure)	(agree)	(agree strongly)

90. I feel I am useful and needed	1 2 3 4 5
91. I am sleeping more than I used to	1 2 3 4 5
92. Someone in my immediate family has trouble with insomnia (brother/sister, father/mother, son/daughter, grandparent)	1 2 3 4 5
93. Someone in my immediate family is very sleepy during the day	1 2 3 4 5
94. Someone in my immediate family has psychiatric or emotional illness (e.g.: depression, alcoholism)	1 2 3 4 5
95. Some of my other relatives have trouble with insomnia (uncles, aunts, cousins)	1 2 3 4 5
96. Some of my other relatives are very sleepy during the day	1 2 3 4 5
97. Some of my other relatives have psychiatric illness	1 2 3 4 5
98. Some family member has died suddenly in their sleep	1 2 3 4 5
99. Some family member has "restless legs" while sleeping (a feeling of crawling, aching, inability to keep the legs still)	1 2 3 4 5
100. A child in my family died from "crib death" (sudden infant death syndrome, SIDS)	1 2 3 4 5
101. Someone in my family has been hospitalized for a psychiatric illness or "nervous breakdown".	1 2 3 4 5
102. People in my family seem to be worriers	1 2 3 4 5
103. Someone in my family has diabetes	1 2 3 4 5
104. Someone in my family has had a stroke ("apoplexy")	1 2 3 4 5
105. I often use alcohol in order to get to sleep	1 2 3 4 5
106. I use alcohol to steady my nerves	1 2 3 4 5
107. While drinking alcohol, I have carried out actions without being aware of them, and not remembered them the next day	1 2 3 4 5
108. I smoke tobacco within two hours of bedtime	1 2 3 4 5
109. I have used "street drugs" (marijuana, "uppers", "downers", narcotics, hallucinogens, cocaine)	1 2 3 4 5
110. I have used tobacco to help me go to sleep	1 2 3 4 5

********** Key for answers **********

1	2	3	4	5
NEVER	RARELY	SOMETIMES	USUALLY	ALWAYS
(strongly disagree)	(disagree)	(not sure)	(agree)	(agree strongly)

111. I have used marijuana to help me go to sleep	1 2 3 4 5
112. I currently take a non-prescription drug from the pharmacy in order to help me sleep	1 2 3 4 5
113. I currently take a non-prescription drug to stop me being so sleepy and fatigued in the daytime	1 2 3 4 5
114. I take a prescription drug which the doctor gave me mainly to help me sleep (sleeping pills, anti-depressants, tranquilizers)	1 2 3 4 5
115. I take a prescription drug which the doctor gave me mainly to keep me awake during the day (e.g.: ritalin)	1 2 3 4 5
116. I take some drugs at night for my other illnesses, not related to sleep, yet I find they help me sleep	1 2 3 4 5
117. I have taken drugs for my heart	1 2 3 4 5
118. I use relaxation techniques or mental imagery (e.g.: counting sheep) to help me sleep	1 2 3 4 5
119. I use non-drug therapies in order to get to sleep (e.g.: biofeedback, acupuncture, electrosleep)	1 2 3 4 5
120. I exercise regularly	1 2 3 4 5
121. I was born as part of a multiple birth (twins, or triplets, etc. Includes cases where the others died at birth or afterwards)	1 2 3 4 5
122. My family was emotionally close in my childhood	1 2 3 4 5
123. I got along well with my parents while growing up	1 2 3 4 5
124. I am currently unemployed	1 2 3 4 5
125. I am working at a job with rotating shifts	1 2 3 4 5
126. I have had a job where I worked at unusual times	1 2 3 4 5
127. I am presently living in a house	1 2 3 4 5
128. I get along well with my husband / wife / friend, who is currently living with me	1 2 3 4 5
129. Coffee, tea, or cola drinks seem to worsen my sleep	1 2 3 4 5
130. Mental stress, worry, or anxiety worsens my sleep	1 2 3 4 5

********** Key for answers **********

1	2	3	4	5
NEVER	RARELY	SOMETIMES	USUALLY	ALWAYS
(strongly disagree)	(disagree)	(not sure)	(agree)	(agree strongly)

131. Physical exercise helps my sleep	1 2 3 4 5
132. A daytime nap worsens my nighttime sleep	1 2 3 4 5
133. Mental stress, worry, or anxiety makes me feel sleepy during the day	1 2 3 4 5
134. After a nap, I feel less sleepy in the daytime	1 2 3 4 5
135. Hot weather makes me sleepy during the day	1 2 3 4 5
136. When doing shift work, I am sleepy during the day	1 2 3 4 5
137. I have a small jaw, or other abnormality of the bones in my head or neck	1 2 3 4 5
138. I have a chronic chest disease (bronchitis, asthma, emphysema)	1 2 3 4 5
139. I have a problem with my nose blocking up when I am trying to sleep (allergies, infections)	1 2 3 4 5
140. I wake up with "attacks" which are different from those described anywhere else in this questionnaire	1 2 3 4 5
141. My snoring or my breathing problem is much worse if I sleep on my back	1 2 3 4 5
142. My snoring or my breathing problem is much worse if I fall asleep right after drinking alcohol	1 2 3 4 5
143. My snoring or my breathing problem is much worse when I have an allergy or infection in the nose, throat, or chest	1 2 3 4 5

********** Key for answers **********

1	2	3	4	5
NEVER	RARELY	SOMETIMES	USUALLY	ALWAYS
(strongly disagree)	(disagree)	(not sure)	(agree)	(agree strongly)

****

THE FOLLOWING QUESTIONS ARE FOR WOMEN ONLY:

144. I have gone through the menopause ("change of life")	1 2 3 4 5
145. My sleep at night is affected by my menstrual cycle	1 2 3 4 5
146. My daytime sleepiness worsens with pregnancy	1 2 3 4 5
147. My daytime sleepiness is worse since my menopause	1 2 3 4 5

****

THE FOLLOWING QUESTIONS ARE FOR MEN ONLY:

148. I often have problems getting an erection	1 2 3 4 5
149. I have trouble maintaining an erection	1 2 3 4 5
150. I have trouble with ejaculation (either I can't do it at all, or it happens too soon)	1 2 3 4 5
151. My erections are physically distorted	1 2 3 4 5
152. I often awaken with an erection during the night or in the morning	1 2 3 4 5

********** Key for answers **********

1	2	3	4	5
NEVER	RARELY	SOMETIMES	USUALLY	ALWAYS
(strongly disagree)	(disagree)	(not sure)	(agree)	(agree strongly)

IN THE NEXT SECTION, PLEASE CIRCLE THE ITEM (NUMBERED 1-5) WHICH BEST MATCHES YOUR ANSWER.

---

153. How many hours of sleep do you get at night, not including time spent awake in bed?

1.) Less than 4 hrs. 2.) Four to 5 hrs. 3.) Six hrs.
4.) Seven hrs. 5.) Eight or more

154. How long is your longest wake period at night?

1.) Less than 5 min. 2.) Six to 19 min. 3.) 20 to 59 min.
4.) One to 2 hrs. 5.) More than 2 hrs.

155. How many times in a night do you get up to urinate?

1.) None. 2.) One time 3.) Two times
4.) Three times 5.) Four or more times

156. How many work accidents have you had as a result of sleepiness or fatigue?

1.) None 2.) One 3.) Two
4.) Three 5.) Four or more

157. How many car accidents or "near misses" have you had because of excessive sleepiness?

1.) None 2.) One 3.) Two
4.) Three 5.) Four or more

158. How many daytime naps (asleep for 5 minutes or more) do you take on an average working day?

1.) None 2.) One 3.) Two
4.) Three or four 5.) Five or more

159. How many rest periods do you take on an average working day (but do not sleep during them)?

1.) None 2.) One 3.) Two or three
4.) Four or five 5.) Six or more

160. How many times, in an average working day, do you try to nap but find that you can't fall asleep?

1.) None 2.) One 3.) Two
4.) Three 5.) Four or more

161. How long do you remain restored (refreshed, alert) after a daytime nap?

1.) Less than 1 hr. 2.) One to 2 hours 3.) Three hours
4.) Four or 5 hours 5.) Six hours or more

162. How long do you remain restored after a rest?

1.) Less than 30 min. 2.) 30-59 minutes 3.) One to 2 hrs.
4.) Three to 4 hrs. 5.) Five hours or more

163. What is your current weight (in lb.)?

1.) 134 lb. or less 2.) 135-159 lb. 3.) 160-183 lb.
4.) 184-209 lb. 5.) 210 lb. or more

164. What was your weight six months ago?

1.) 134 lb. or less 2.) 135-159 lb. 3.) 160-183 lb.
4.) 184-209 lb. 5.) 210 lb. or more

165. What was your weight at age 20?

1.) 125 lb. or less 2.) 126-139 lb. 3.) 140-155 lb.
4.) 156-175 lb. 5.) 176 lb. or more

166. How many cups of regular coffee do you have in a day?

1.) None 2.) One cup 3.) Two cups
4.) 3 to 5 cups 5.) Six cups or more

167. How many of the coffees are within 2 hrs. of bedtime?

1.) None 2.) One cup 3.) Two cups
4.) 3 to 5 cups 5.) Six cups or more

168. How many glasses/cans of cola drinks do you have in a day (do not include decaffeinated types)?

1.) None 2.) One can 3.) Two cans
4.) 3 to 5 cans 5.) Six cans or more

169. How many of these colas are within 2 hrs. of bedtime?

1.) None 2.) One can 3.) Two cans
4.) 3 to 5 cans 5.) Six cans or more

170. How many years were you a smoker?

1.) None
2.) One year
3.) 2 to 12 years
4.) 13 to 25 years
5.) 26 years or more

171. How long does it take you to adjust after traveling across time zones (especially 4 or more zones)?

1.) No time at all
2.) One day
3.) Two days
4.) Three to 4 days
5.) Five or more days

172. How tall are you?

1.) 63 in. or less
2.) 64 to 66.5 in.
3.) 67 to 69.5 in.
4.) 70 to 71 in.
5.) 71.5 inches or taller

173. How old are you now?

1.) 25 or under
2.) 26-35 yr.
3.) 36-44 yr.
4.) 45-50 yr.
5.) 51 yr. or older

174. How many years did you go to school? Include years of college and university too.

1.) 4 yr. or less
2.) 5-11 yr.
3.) 12 yr.
4.) 13-14 yr.
5.) 15 yr. or more

175. Before this visit, how many "therapists" (doctor, psychiatrist, psychologist, nurse, counselor, osteopath, chiropractor) have you ever seen about a problem of sleeping too much or too little?

1.) None
2.) One only
3.) Two
4.) Three or 4
5.) Five or more

Participant ID:

Mini-Mental State Examination (MMSE)

Patient name:

Date: Visit 1: Visit 2: Visit 3: Visit 4:

Maximum score	Visit 1	Visit 2	Visit 3	Visit 4	
					ORIENTATION
5	( )	( )	( )	( )	What (year) (season) (date) (day) (month) is it? *(1 point for each correct answer.)*
5	( )	( )	( )	( )	Where are we: (province) (country) (town or city) (hospital or clinic) (floor)? *(1 point for each correct answer.)*
					REGISTRATION
3	( )	( )	( )	( )	Listen to the following: "apple," "table," "penny." Repeat all 3. *(1 point for each correct answer.)*
# Trials:	( )	( )	( )	( )	(Repeat the objects until the patient learns all 3. Make a maximum of 6 trials. Record the number of trials.)
					ATTENTION AND CALCULATION
5	( )	( )	( )	( )	Spell "world" backwards. *(1 point for each letter in correct order.)* **Alternate:** Subtract 7 from 100. Take the result and subtract 7 from that. Continue until I ask you to stop. *(Continue for 5 subtractions. 1 point for each correct subtraction.)*
					RECALL
3	( )	( )	( )	( )	What were the 3 objects we repeated earlier? *(1 point for each correct answer.)* (Note: Recall cannot be tested if all 3 objects were not remembered during registration.)
					LANGUAGE
2	( )	( )	( )	( )	What are these? (pencil) (watch).
1	( )	( )	( )	( )	Repeat the following: "No ifs, ands, or buts."
3	( )	( )	( )	( )	Take a piece of paper in your right hand, fold it in half and put it on the floor. *(1 point for each section of the command performed.)*
					READ AND OBEY
1	( )	( )	( )	( )	Read the following ("Close your eyes.") and do as it says.
1	( )	( )	( )	( )	Write a sentence.
1	( )	( )	( )	( )	Copy the following design on the back of this page:  No construction problem
Total score (max. score 30)					

Adapted from Folstein MF *et al.* "Mini-Mental State": A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189-198, and Cockrell JR, Folstein MF. Mini-Mental State Examination (MMSE). *Psychopharm Bull* 1988;24(4):689-692.

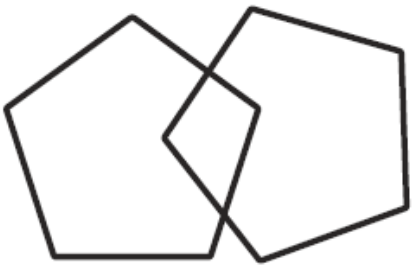
Mini-Mental State Examination (MMSE)

READING:

Close your eyes.

WRITING:

COPYING:



Participant ID:

Self-care
1) Eating
2) Grooming
3) Bath/showering
4) Dressing upper body
5) Dressing lower body
6) Toileting
7) Swallowing[a]

Sphincters
8) Bladder management
9) Bowel management

Mobility
10) Transfers: bed/chair/wheelchair
11) Transfers: toilet
12) Transfers: tub/shower
13) Transfers: car[a]
14) Locomotion: walking/wheelchair
15) Locomotion: stairs
16) Community mobility[a]

Communication
17) Expression
18) Comprehension
19) Reading[a]
20) Writing[a]
21) Speech intelligibility[a]

Psychosocial
22) Social interaction
23) Emotional status[a]
24) Adjustment to limitations[a]
25) Use of leisure time (replaces 'Employability' in original version)[a]

Cognition
26) Problem solving
27) Memory
28) Orientation[a]
29) Concentration (replaces 'Attention' in original version)[a]
30) Safety awareness (replaces 'Safety Judgement' in original version)[a]

[a]FAM items

Seven levels for each item

Level		Description
7	Complete independence	Fully independent
6	Modified independence	Requiring the use of a device, but no physical help
5	Supervision/set-up	Requiring only stand-by assistance or verbal prompting or just help with set-up
4	Minimal assistance	Requiring incidental hands-on help only (performs >75% of the task)
3	Moderate assistance	Subject still performs more than half the task (50–74%)
2	Maximal assistance	Subject provides less than half of the effort of the task (25–49%)
1	Total assistance	Subject contributes less than 25% or is unable to do the task at all

Participant ID:

Beck Depression Inventory

Instructions: This questionnaire consists of 21 groups of statements. Please read each group of statements carefully, and then pick out the **one statement** in each group that best describes the way you have been feeling during the **past two weeks, including today.** Circle the number beside the statement you have picked. If several statements in the group seem to apply equally well, circle the highest number for that group. Be sure that you do not choose more than one statement for any group, including Item 16 (Changes in Sleeping Pattern) or Item 18 (Changes in Appetite).

1. Sadness
- 0 I do not feel sad.
- 1 I feel sad much of the time.
- 2 I am sad all the time.
- 3 I am so sad or unhappy that I can't stand it.

2. Pessimism
- 0 I am not discouraged about my future.
- 1 I feel more discouraged about my future than I used to be.
- 2 I do not expect things to work out for me.
- 3 I feel my future is hopeless and will only get worse.

3. Past Failure
- 0 I do not feel like a failure.
- 1 I have failed more than I should have.
- 2 As I look back, I see a lot of failures.
- 3 I feel I am a total failure as a person.

4. Loss of Pleasure
- 0 I get as much pleasure as I ever did from the things I enjoy.
- 1 I don't enjoy things as much as I used to.
- 2 I get very little pleasure from the things I used to enjoy.
- 3 I can't get any pleasure from the things I used to enjoy.

5. Guilty Feelings
- 0 I don't feel particularly guilty.
- 1 I feel guilty over many things I have done or should have done.
- 2 I feel quite guilty most of the time.
- 3 I feel guilty all of the time.

6. Punishment Feelings
- 0 I don't feel I am being punished.
- 1 I feel I may be punished.
- 2 I expect to be punished.
- 3 I feel I am being punished.

7. Self-Dislike
- 0 I feel the same about myself as ever.
- 1 I have lost confidence in myself.
- 2 I am disappointed in myself.
- 3 I dislike myself.

8. Self-Criticalness
- 0 I don't criticize or blame myself more than usual.
- 1 I am more critical of myself than I used to be.
- 2 I criticize myself for all of my faults.
- 3 I blame myself for everything bad that happens.

9. Suicidal Thoughts or Wishes
- 0 I don't have any thoughts of killing myself.
- 1 I have thoughts of killing myself, but I would not carry them out.
- 2 I would like to kill myself.
- 3 I would kill myself if I had the chance.

10. Crying
- 0 I don't cry any more than I used to.
- 1 I cry more than I used to.
- 2 I cry over every little thing.
- 3 I feel like crying, but I can't.

_____ Subtotal Page 1 Continued on Back

11. Agitation

0 I am no more restless or wound up than usual.
1 I feel more restless or wound up than usual.
2 I am so restless or agitated that it's hard to stay still.
3 I am so restless or agitated that I have to keep moving or doing something.

12. Loss of Interest

0 I have not lost interest in other people or activities.
1 I am less interested in other people or things than before.
2 I have lost most of my interest in other people or things.
3 It's hard to get interested in anything.

13. Indecisiveness

0 I make decisions about as well as ever.
1 I find it more difficult to make decisions than usual.
2 I have much greater difficulty in making decisions than I used to.
3 I have trouble making any decisions.

14. Worthlessness

0 I do not feel I am worthless.
1 I don't consider myself as worthwhile and useful as I used to.
2 I feel more worthless as compared to other people.
3 I feel utterly worthless.

15. Loss of Energy

0 I have as much energy as ever.
1 I have less energy than I used to have.
2 I don't have enough energy to do very much.
3 I don't have enough energy to do anything.

16. Changes in Sleeping Pattern

0 I have not experienced any change in my sleeping pattern.

1a I sleep somewhat more than usual.
1b I sleep somewhat less than usual.

2a I sleep a lot more than usual.
2b I sleep a lot less than usual.

3a I sleep most of the day.
3b I wake up 1–2 hours early and can't get back to sleep.

17. Irritability

0 I am no more irritable than usual.
1 I am more irritable than usual.
2 I am much more irritable than usual.
3 I am irritable all the time.

18. Changes in Appetite

0 I have not experienced any change in my appetite.

1a My appetite is somewhat less than usual.
1b My appetite is somewhat greater than usual.

2a My appetite is much less than before.
2b My appetite is much greater than usual.

3a I have no appetite at all.
3b I crave food all the time.

19. Concentration Difficulty

0 I can concentrate as well as ever.
1 I can't concentrate as well as usual.
2 It's hard to keep my mind on anything for very long.
3 I find I can't concentrate on anything.

20. Tiredness or Fatigue

0 I am no more tired or fatigued than usual.
1 I get more tired or fatigued more easily than usual.
2 I am too tired or fatigued to do a lot of the things I used to do.
3 I am too tired or fatigued to do most of the things I used to do.

21. Loss of Interest in Sex

0 I have not noticed any recent change in my interest in sex.
1 I am less interested in sex than I used to be.
2 I am much less interested in sex now.
3 I have lost interest in sex completely.

_____ Subtotal Page 2

_____ Subtotal Page 1

_____ Total Score

Participant ID:

Clinical Frailty Scale*

1 Very Fit – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2 Well – People who have **no active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g. seasonally.

3 Managing Well – People whose **medical problems are well controlled,** but are **not regularly active** beyond routine walking.

4 Vulnerable – While **not dependent** on others for daily help, often **symptoms limit activities.** A common complaint is being "slowed up", and/or being tired during the day.

5 Mildly Frail – These people often have **more evident slowing,** and need help in **high order IADLs** (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6 Moderately Frail – People need help with **all outside activities** and with **keeping house**. Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.

7 Severely Frail – **Completely dependent for personal care**, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8 Very Severely Frail – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

9. Terminally Ill - Approaching the end of life. This category applies to people with **a life expectancy <6 months**, who are **not otherwise evidently frail.**

Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia**, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

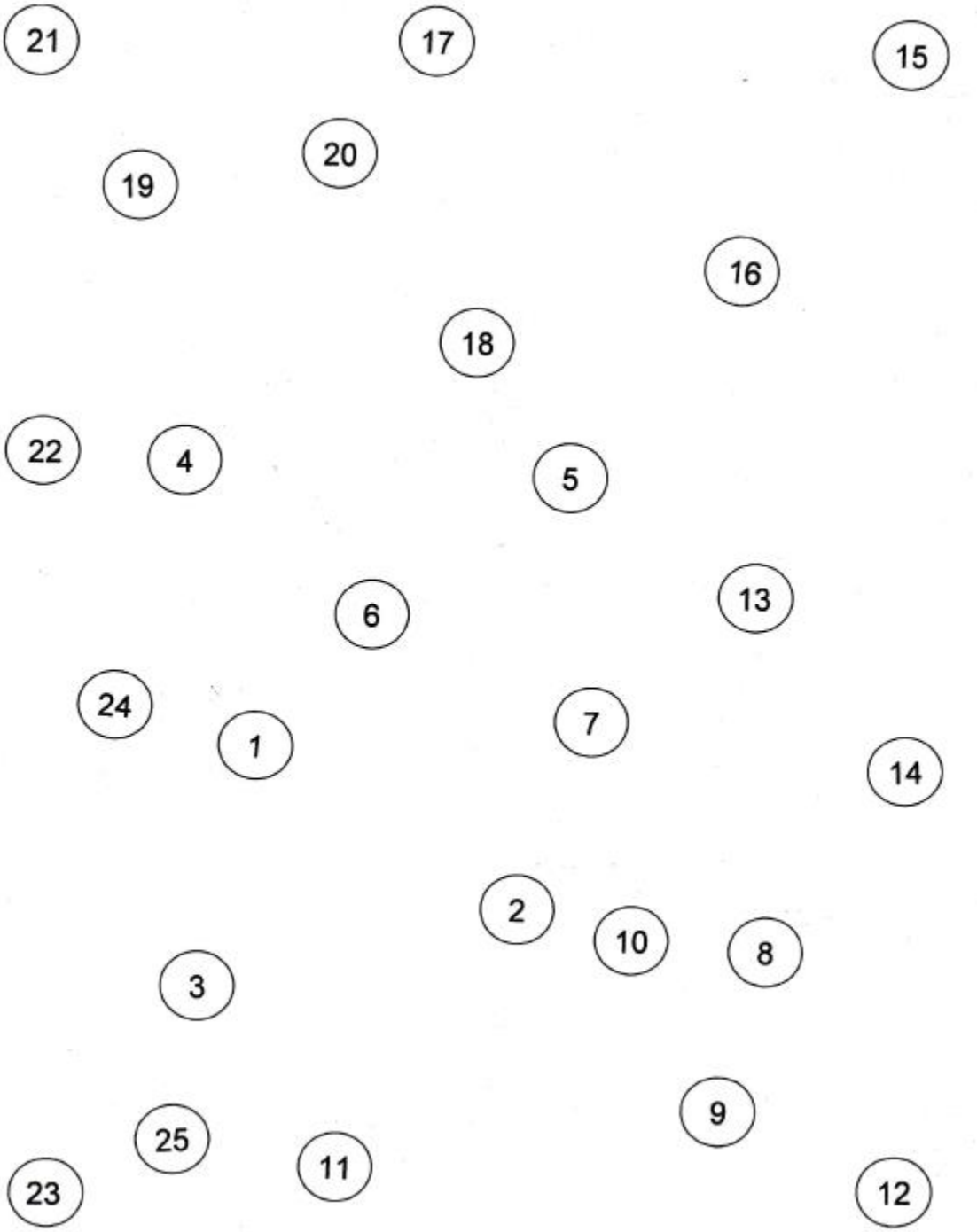
In **severe dementia**, they cannot do personal care without help.

* 1. Canadian Study on Health & Aging, Revised 2008.
2. K. Rockwood et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489-495.

DALHOUSIE UNIVERSITY *Inspiring Minds*

Participant ID:

Trail Making Test (AA)



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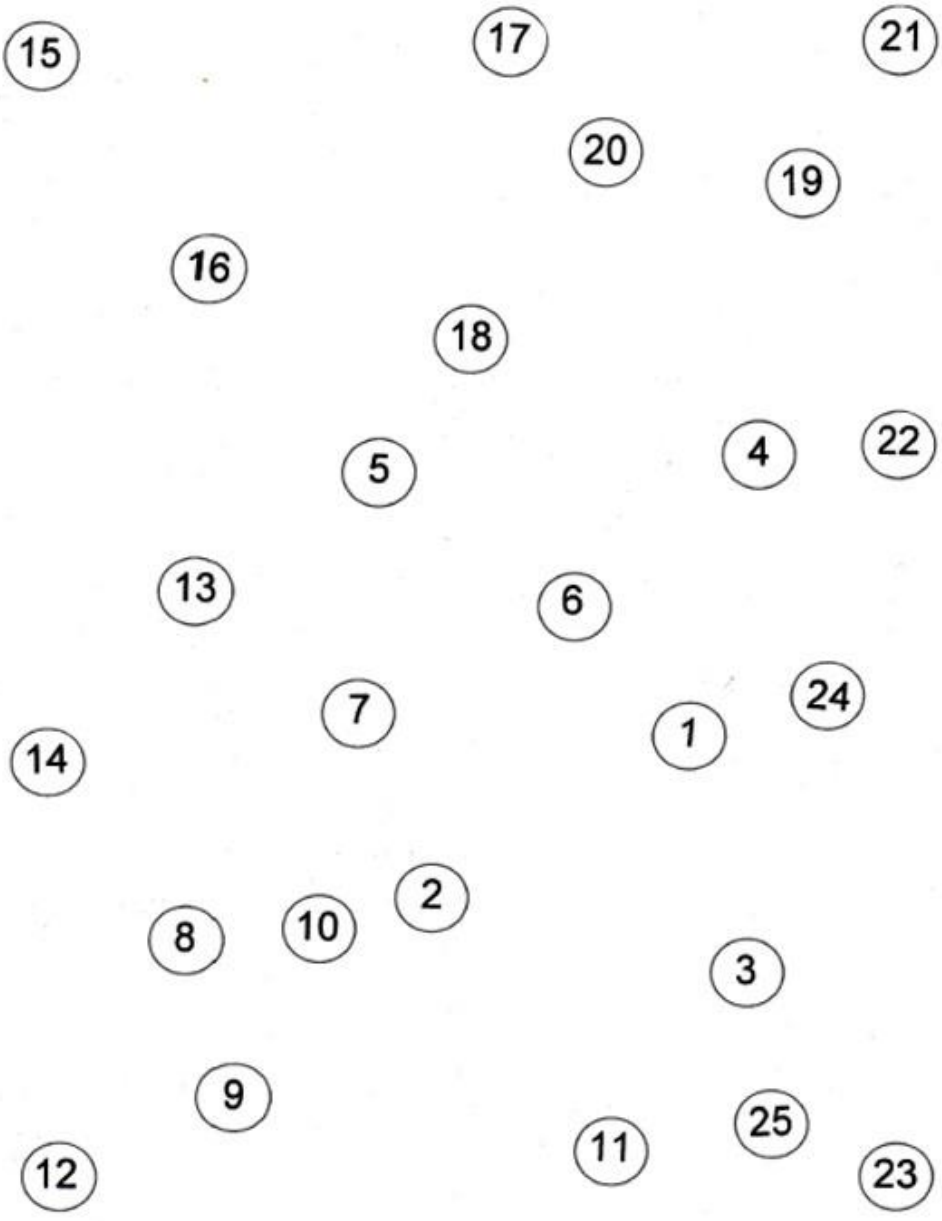

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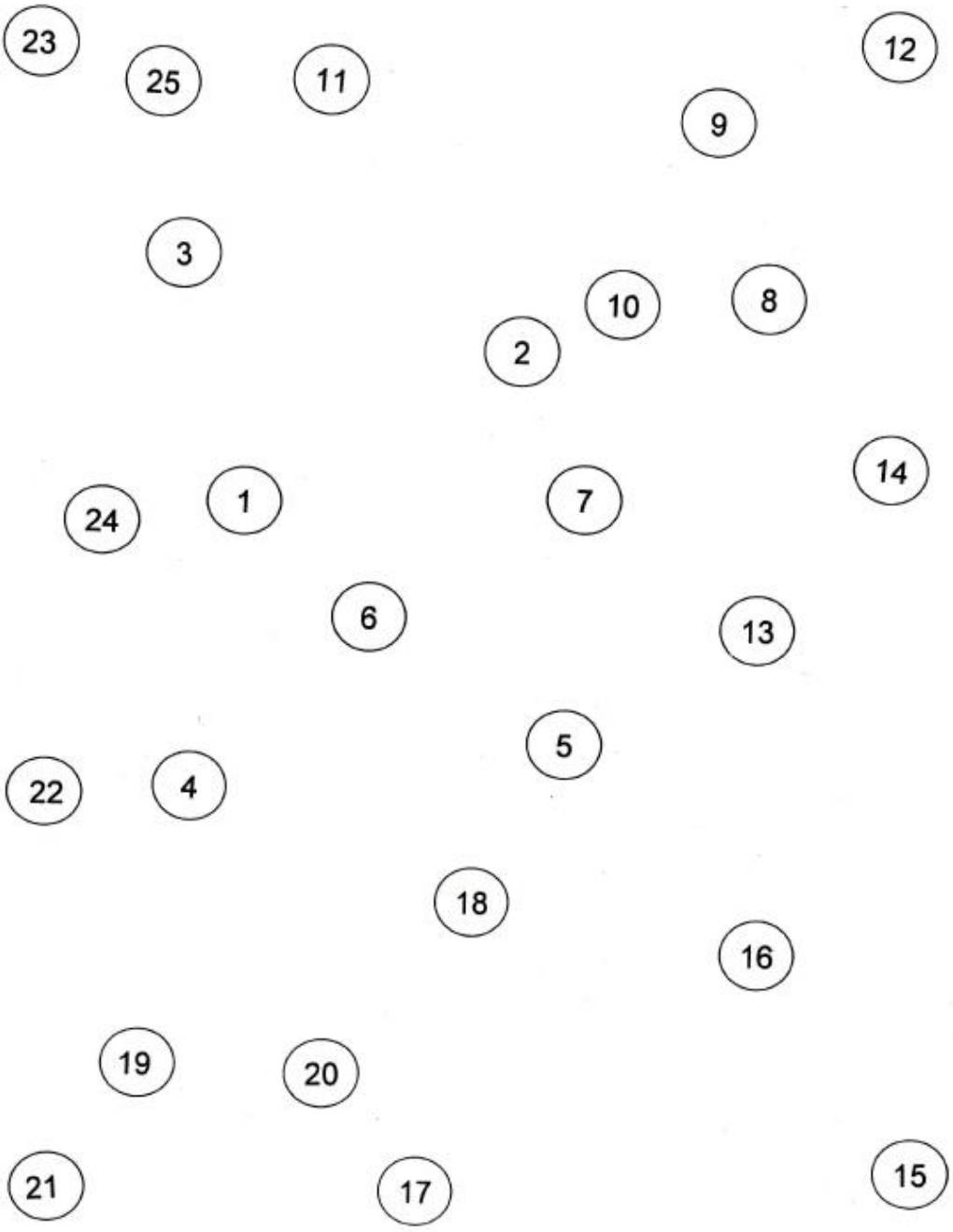

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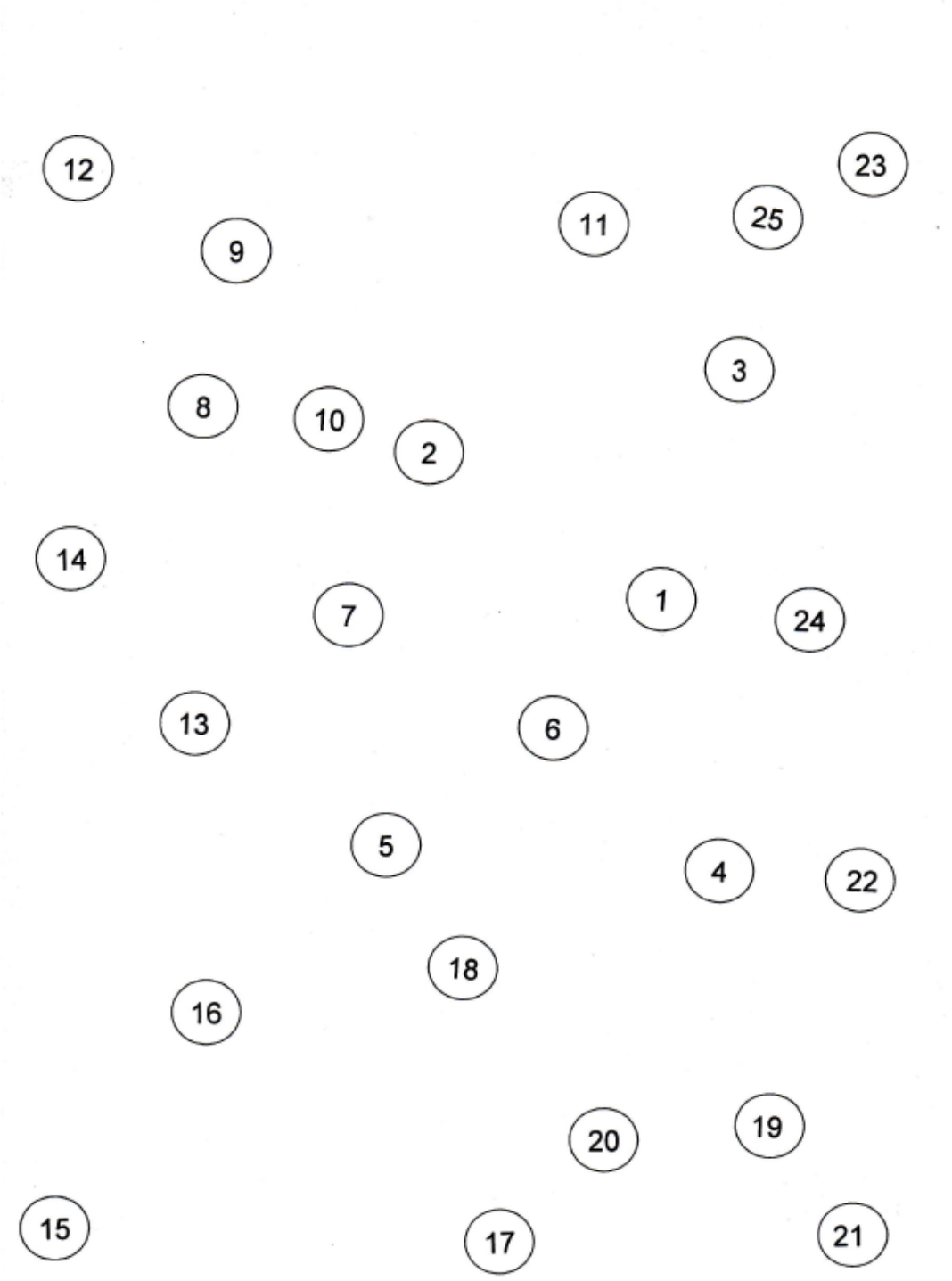

Participant ID:

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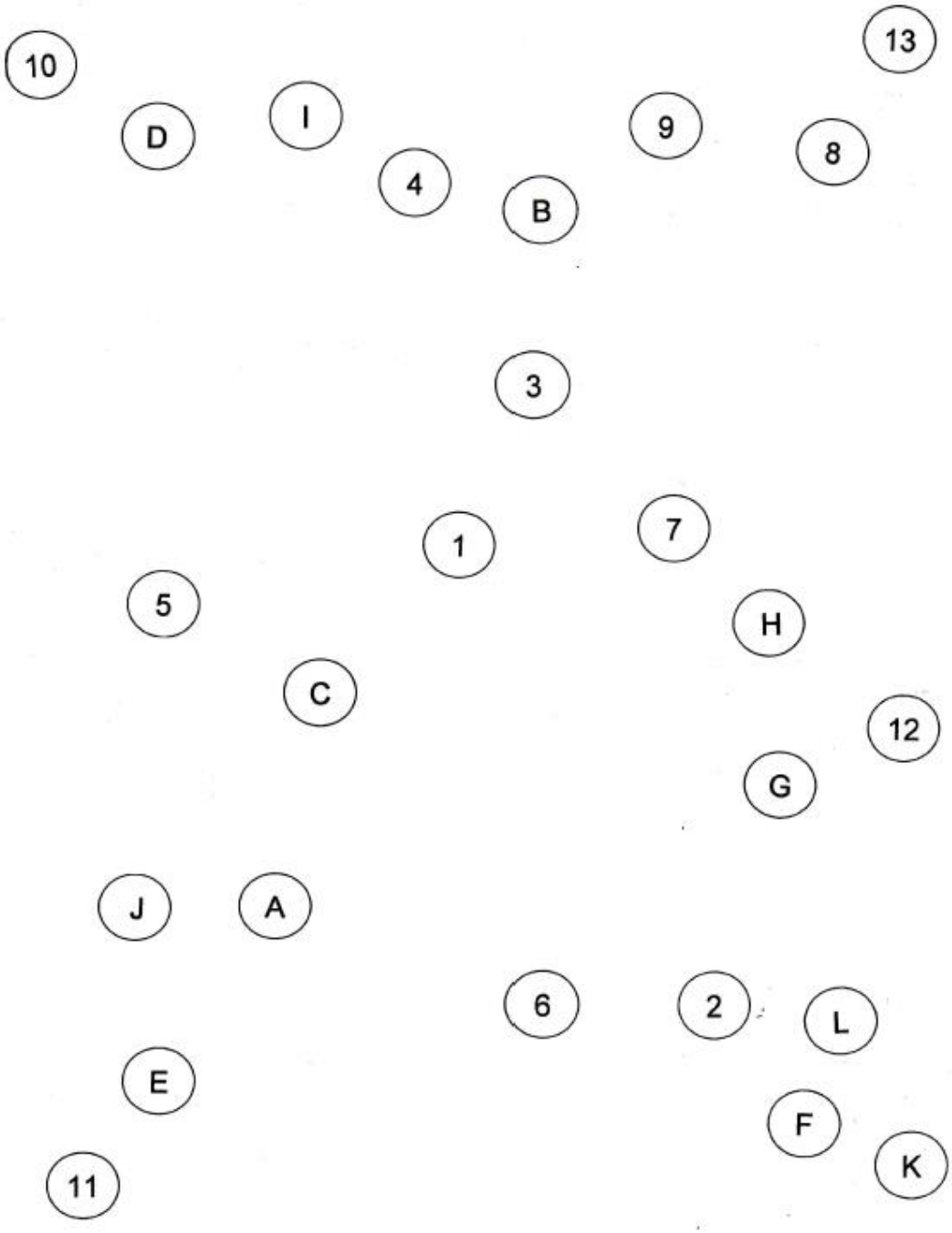

Participant ID:

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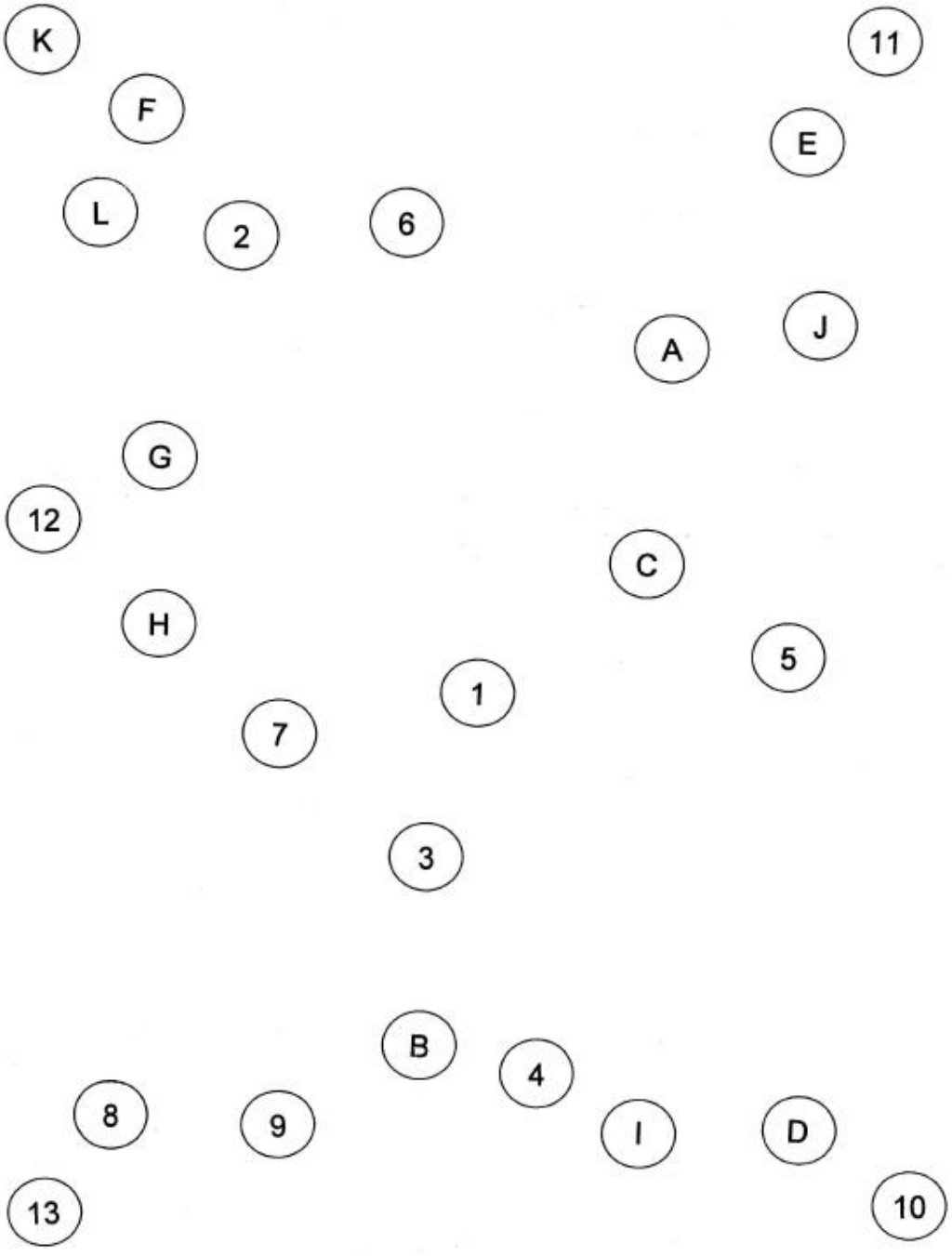

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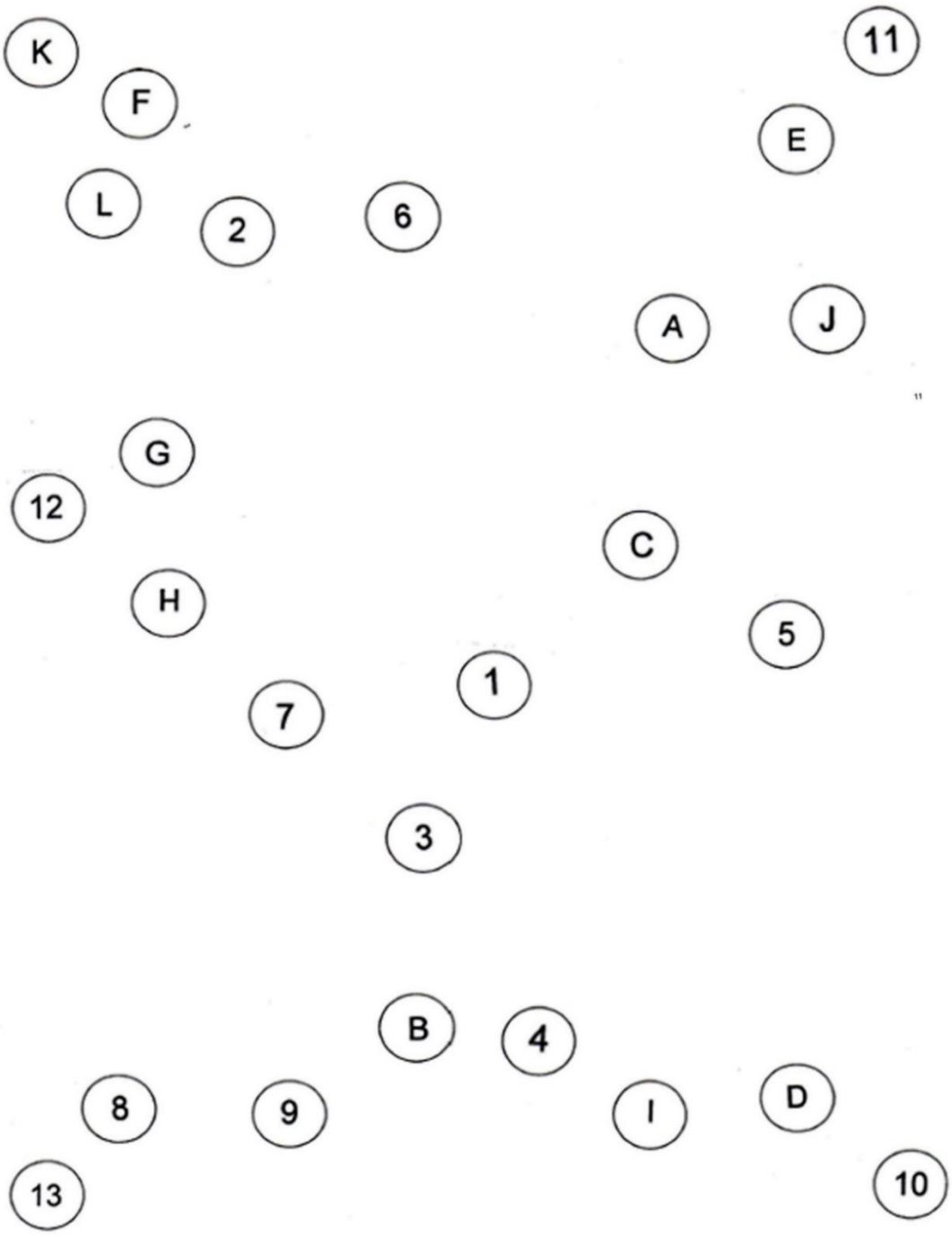

Participant ID:

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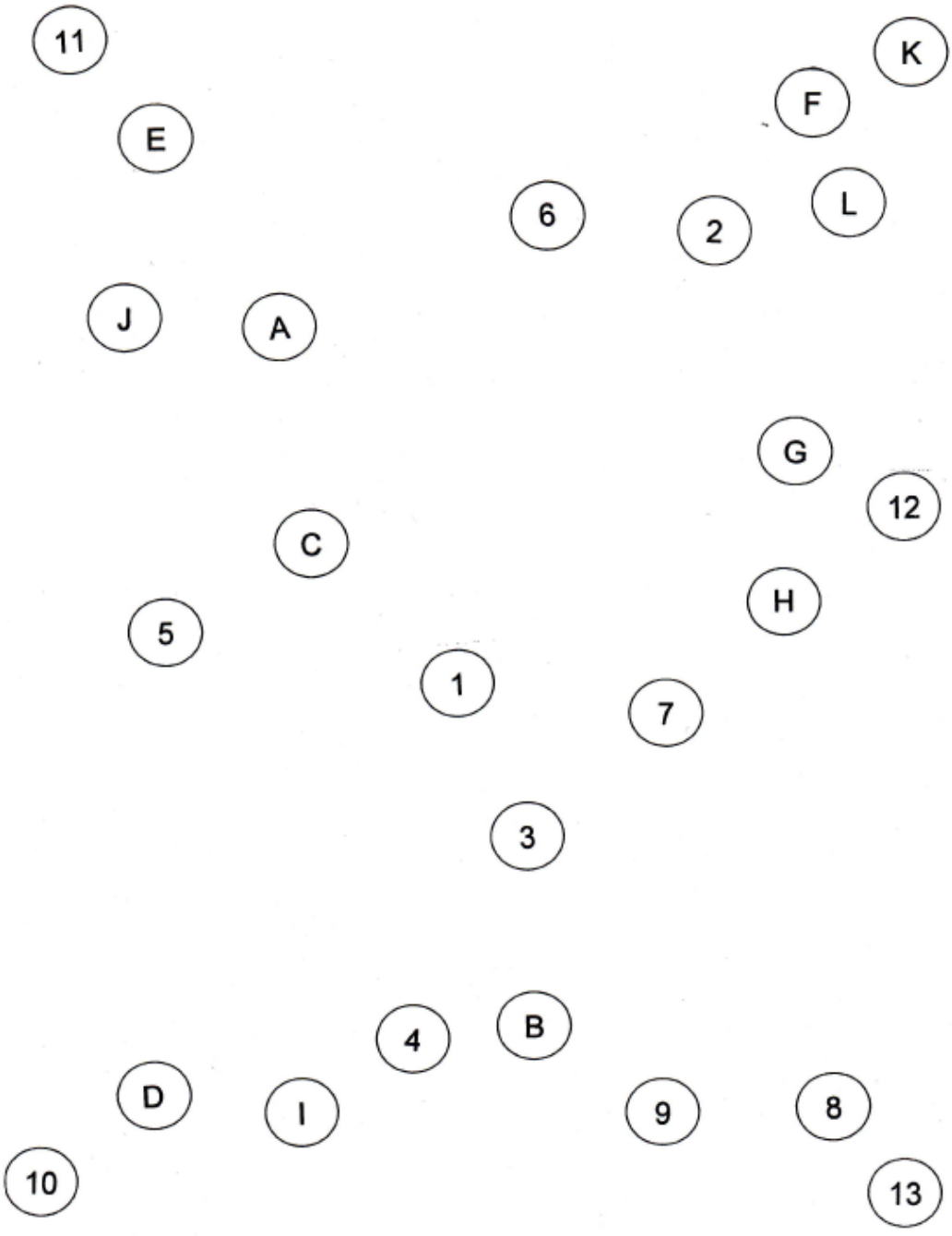
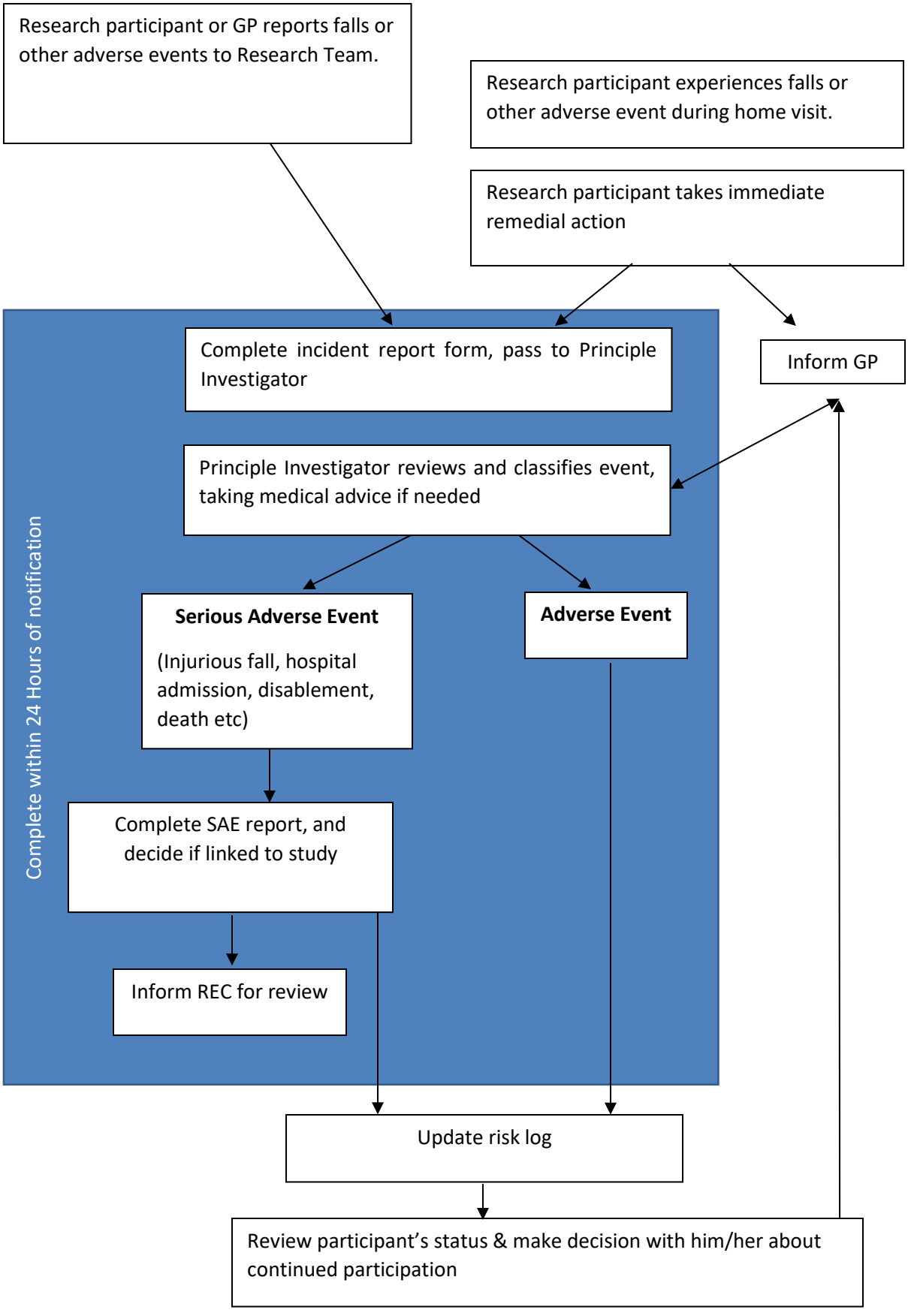


Risk Assessment Pathway



Incident Report Form

Incident Report Form	
Participant identification Code:	
Incident Reported by:	
Date of incident:	_ _ / _ _ / _ _
Details of incident: Actions Taken Witness name and role in study:	
Outcome	
Form completed by: Print name Signed Date _ _ / _ _ / _ _	Principle Investigator Print name Signed Date_ _ / _ _ / _ _

Serious Adverse Event Reporting Form

Participant study ID: _____ Participant Initials: _____ Date of Birth:___/_____/_____

Which period of the study did the event occur in?

Has the participant died? Yes ☐ No☐

Date:___/_____/_____
Cause/Description:_____
_____

Was the participant admitted to hospital? Yes ☐ No☐

Date:___/_____/_____
Description:_____
_____

Was the admission as a result of any of the following: severe migraine; psychotic episode; mania; hallucinations; suicidal ideation; falls? Yes ☐ No☐

Has the participant incurred injury or illness without hospital admission? Yes ☐ No☐

Date:___/_____/_____
Description:_____
_____

Form completed by:

(Signature) _____ (Print name)_____ Date:___/_____/_____

Form reviewed by

(Signature) _____ (Print name)_____ Date:___/_____/_____

To be completed by the site Principal Investigator:

Is this event an SAE relating to patient safety in the study?

☐ Yes –convene meeting to discuss study safety, inform ethics committee

☐ No – no further action required

(Signature) _____ (Print name)_____ Date:___/_____/_____

Signed by Chief Investigator

(Signature) _____ (Print name)_____ Date:___/_____/_____

CHSS
University of Kent

Centre for Health Services Studies

Dear Participant,

Thank you for your interest in participating in this study on how staying in hospital affects sleep in older people. Unfortunately, we are no longer recruiting for this particular study as we have enough participants. There is a possibility that we may contact you again in the future to participant in a second study following the findings of this initial study.

If you have any questions, please do not hesitate to contact me (Rowena Bicknell) at the University of Kent on 01227 816436 or via email: rmb48@kent.ac.uk.

Yours faithfully,

[REDACTED]

Rowena Bicknell

PhD Student, University of Kent

50
1965-2015
THE UK'S EUROPEAN UNIVERSITY

WHO COLLABORATING CENTRE

Version 1.0 5/3/2016

University of Kent
George Allen Wing
Canterbury
Kent CT2 7NF
United Kingdom

C.4 Study amendments

The following amendments were submitted:

1. On the 20th February 2017, a substantial amendment was submitted to change the study design. The study assessment timeline was altered to be in line with hospital admission length; from 3-days and 6-days post op to 1-day and 4-days post-surgery. The GP information sheet, clinical record form, participant information sheet, consultee information sheet and protocol was amended to reflect this change.
2. On the 15th March 2017, a non-substantial amendment was submitted to change minor typographic errors in the Accompanying Letter. The wording initially implied the prospective participant had already been approached regarding the study and recruited when in fact they had not. A similar change was made to clarify how the data was be stored and anonymised as well as the actigraphy monitor being referred to as an 'activity monitor' as opposed to a 'special watch'.
3. On the 17th August 2017, a non-substantial amendment was submitted to include a new site, William Harvey Hospital. The protocol was amended to reflect this change.
4. On the 2nd January 2018, a non-substantial amendment was submitted to extend the study beyond the point initially specified in the application form to August 2018. The statement of activities was amended to reflect these changes.

C.5 Study results

Table 34 Summary of study recruitment numbers between February 2017 and June 2018

	Participants Recruited
February 2017	2
March 2017	1
April 2017	4
May 2017	2
June 2017	0
July 2017	0
August 2017	3
September 2017	10
October 2017	10
November 2017	6
December 2017	8
January 2018	1
February 2018	1
March 2018	1
April 2018	3
June 2018	1