

CLINICAL CARE STRATEGIES FOR THE DIAGNOSIS AND MANAGEMENT OF ADULT PATIENTS WITH RESPIRATORY SLEEP DISORDERS

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Statement of originality

I, Sulaiman Saleh S Alsaif, hereby declare that the work presented in this Thesis is my own, except where explicit reference or acknowledgement is made to the contribution of others, and that no part of this Thesis has previously been submitted in application for a higher degree. Publications and presentations arising from this work are listed on **page 8**. Information from other sources is referenced accordingly.

The mandibular movement monitors used in **Chapter 2** were donated, plus home respiratory polygraphy monitors were loaned to our research group by Sunrise SA, Belgium to conduct the investigator-led randomised controlled study.

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Abstract

Many patients with obstructive sleep apnoea (OSA) in the UK remain undiagnosed, and untreated. Conventional clinical care for OSA diagnosis and management is insufficient to meet the increasing demand, which has been exponentially rising post-pandemic.

This Thesis investigated new clinical care strategies for the diagnosis and management of OSA and evaluated patient experiences with, and preferences for, these strategies. Quantitative and qualitative investigations in adult patients with suspected or existing OSA diagnosis were conducted.

In a randomised controlled pilot study, patients referred for suspected OSA were investigated using novel mandibular movement (MM) monitoring with automated machine-learning analysis. Reduced time to treatment decision and saved healthcare professionals' time, were found compared to conventional home respiratory polygraphy.

In a qualitative evaluation, nested study, within the randomised controlled study, patients described their journeys to OSA diagnosis. They expressed their preference for home OSA testing with the “*unobtrusive*” MM monitor, compared to the more “*cumbersome and restrictive*” respiratory polygraphy.

In a systematic review and meta-analysis, virtual care *via* telephone or video consultations was found to be as effective as in-person consultations for improving subjective sleepiness in patients treated with continuous positive airway pressure (CPAP). Virtual care also appeared to be less costly than in-person care strategies.

In a UK survey of patients with self-reported OSA treated with CPAP, most patients reported being satisfied with their CPAP initiation experience. Most patients also expressed their preference for in-person CPAP initiation and follow-up care, compared to remote care strategies.

These findings show that digitally-enabled clinical care can be considered for OSA diagnosis and management. However, remote care pathways for OSA may not accommodate the preferences and needs of all patients, specifically those at higher risk of being digitally excluded. Thus, future investigations should address potential health inequalities associated with widespread implementation of remote care pathways for OSA.

Publications arising from this Thesis

Published paper

- Sulaiman S. Alsaif, Julia L. Kelly, Stuart Little, Hilary Pinnock, Mary J. Morrell, Michael I. Polkey, Phyllis Murphie. (2022). *Virtual consultations for patients with obstructive sleep apnoea: a systematic review and meta-analysis*. European Respiratory Review (166) 220180; DOI: 10.1183/16000617.0180-2022

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- Sulaiman S. Alsaif, Wendy Douglas, Joerg Steier, Mary J. Morrell, Michael I. Polkey[†], Julia L. Kelly[†]. (2023). *Mandibular movement monitor provides faster, yet accurate diagnosis, for obstructive sleep apnoea: a randomised controlled study*. Manuscript submitted to Clinical Medicine Journal in November 2023.

Presented abstracts

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This Thesis is dedicated to my late grandmothers, Modhi and Muznah. I wish I could tell you that I made it...

Sulaiman S. Alsaif
London, UK

Dedication

In memory of the most resilient people I knew, my late grandmothers.

Modhi A. Alfnikh (1958 - 2013)

Muznah A. Aljutaily (1953 - 2015)

I would not be where I am now if they had not directly and indirectly taught me how to turn challenging experiences and difficult times into immeasurable grit and lifelong wisdom.

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Abbreviations

AASM	American Academy of Sleep Medicine
AHI	Apnoea-Hypopnoea Index
BLF	British Lung Foundation
BMI	Body Mass Index
CCG	Clinical Commissioning Group
CPAP	Continuous Positive Airway Pressure
DVLA	Driver and Vehicle Licensing Agency
EDS	Excessive Daytime Sleepiness
ESS	Epworth Sleepiness Scale
G&STT	Guy's and St Thomas' NHS Foundation Trust
GCP	Good Clinical Practice
GP	General Practitioner
HRA	Health Research Authority
HRQoL	Health-related Quality of Life
HSAT	Home Sleep Apnoea Testing
HTA	Health Technology Appraisal
ICF	Informed Consent Form
ICT	Information and Communication Technologies
ID	Identification
MM	Mandibular Movements
NHS	National Health Service
NICE	National Institute of Clinical Excellence
ORDI	Obstructive Respiratory Disturbance Index
OSA	Obstructive Sleep Apnoea
PIS	Participant Information Sheet
PM	Portable Monitors
PSG	Polysomnography
RBH	Royal Brompton Hospital
RCT	Randomised Control Trial
RDI	Respiratory Disturbance Index
RERA	Respiratory Effort-Related Sleep Arousal
SDB	Sleep-Disordered Breathing
SOSAT	The Sunrise OSA Trial
UK	United Kingdom
US	United States
VAS	Visual Analogue Scale

Chapter 1 – General Introduction

1.1. Overview of Chapter 1

This general introduction provides a background to the research within this Thesis, starting with the definition, pathophysiology, sequelae, and prevalence of obstructive sleep apnoea (OSA). This is followed by a discussion of the provision of clinical care for OSA in the United Kingdom (UK) and the role of the National Institute for Health and Care Excellence (NICE). Additionally, an overview of conventional and newer diagnostic and clinical management strategies for OSA, as well as the role of patient experiences and preferences are presented.

This chapter also includes a synopsis of focused informal discussions with sleep clinical leads in the UK, as a real-world background to the challenges sleep services are facing post-Coronavirus Disease 2019 (COVID-19) pandemic.

1.2. Spectrum of sleep-disordered breathing

Sleep-disordered breathing (SDB) covers a spectrum of respiratory disorders that occur during sleep (Ioachimescu and Collop, 2012). In the 3rd edition of the International Classification of Sleep Disorders (ICDS-3), SDB disorders were categorised into five groups, including OSA disorders, central sleep apnoea syndromes, sleep-related hypoventilation disorders, sleep-related hypoxemia disorder, and isolated symptoms and normal variants (American Academy of Sleep Medicine, 2014).

1.3. Overview of obstructive sleep apnoea

Although sleep medicine is a relatively new field of medical research and practice (Schulz, 2022), the evidence of SDB manifestations existed as early as the Ptolemaic Dynasty era (305 to 30 BC) (Michalopoulos et al., 2003). OSA, which dominates the current demand for respiratory sleep services, was not officially described as a '*sleep-induced apnoea*' until 1965 in Europe (Dement, 1998). Later in 1976, Guilleminault et al. (1976) published a review that described the '*sleep apnoea syndrome*' and its clinical manifestations and symptomatology. Since then, the definition of this syndrome and other SDB disorders have evolved due to the

progress of scientific knowledge, which is also linked to advances in investigative technologies (Mann et al., 2020).

1.3.1. Definition of OSA

OSA is characterised by recurring partial (hypopnoea) or complete (apnoea) closure of the upper airway during sleep (Guilleminault et al., 1977), as illustrated in **Figure 1.1**. A diagnosis of ‘*obstructive sleep apnoea syndrome*’ is made if a patient, with sleep-related respiratory events, also has symptoms such as excessive daytime sleepiness (EDS), the commonest symptom of OSA (Ioachimescu and Collop, 2012). Other nocturnal and daytime symptoms commonly associated with OSA include snoring, choking during sleep (Schlosshan and Elliott, 2004), nocturia (Romero et al., 2010), unrefreshing sleep, waking headaches, irritability, cognitive dysfunction, and memory impairment (Osman et al., 2018).

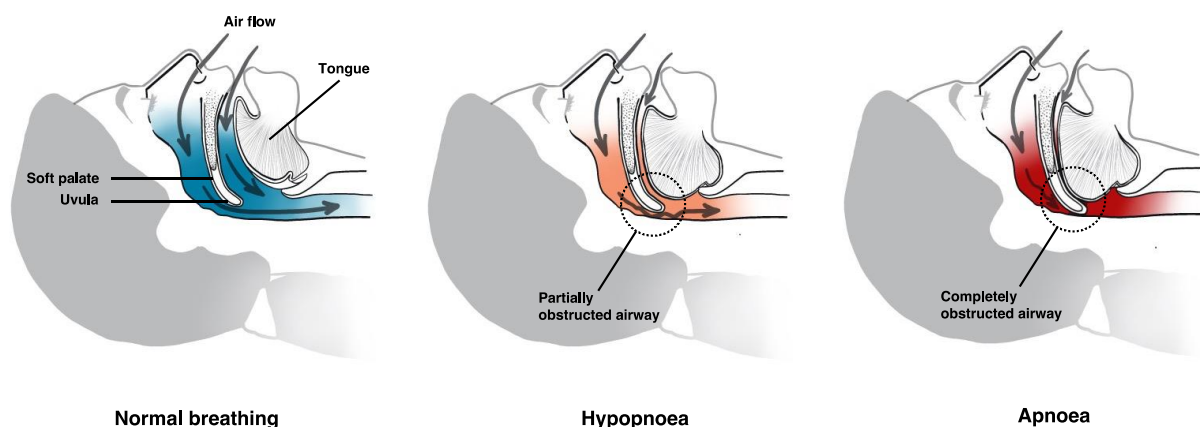


Figure 1.1 An original illustration of normal breathing during sleep (**Left**). Partial closure of the upper airway with reduced airflow results in hypopnoea (**Middle**) and complete closure of the upper airway with no airflow results in apnoea (**Right**).

1.3.2. Pathophysiology of OSA

OSA is a heterogenous disorder, with multiple pathophysiologic mechanisms and clinical manifestations. In healthy individuals, sleep onset is associated with a loss of the ‘*wakefulness drive to breathe*’, a decreased tone of the upper airway dilator muscles, and reduced chemosensitivity, which result in normal pharyngeal airway narrowing and a reduction in ventilation (Stradling et al., 1985, Morrell et al., 1996, Fogel et al., 2005).

The mechanisms of OSA pathophysiology include (Malhotra et al., 2020, Eckert et al., 2013):

- anatomically compromised upper airway
- inadequate upper airway dilator muscle activity during sleep
- low respiratory arousal threshold
- oversensitive and unstable ventilatory control

Additional physiological factors such as end-expiratory lung volume, intensity of arousals, and redistribution of body fluids may also contribute to the occurrence and severity of OSA (Malhotra et al., 2020).

In brief, patients with OSA are more susceptible to collapsibility of the pharyngeal airway, which is determined by the transmural pressure across the airway lumen (Morrell et al., 2020). The repetitive collapse of the pharyngeal airway leads to intermittent hypoxemia, recurrent changes in intrathoracic pressure, and frequent arousals with sleep fragmentation (Dewan et al., 2015). The arousals and airway pressure changes may contribute to the activation of the sympathetic nervous system and consequent comorbidity (Rossi et al., 2013). Additionally, intermittent hypoxemia may promote increased oxidative stress, systemic and vascular inflammation (Dewan et al., 2015). These factors are likely to contribute to OSA morbidity, specifically related to cardiovascular and metabolic diseases (Dewan et al., 2015).

1.3.3. Global and UK prevalence of OSA

OSA is the most common type of respiratory sleep disorders (Peppard et al., 2013). The global prevalence of mild to severe OSA, with and without symptoms, has been estimated to affect nearly one billion adults aged 30 – 69 years; with wide geographical variation in the prevalence estimates across countries (Benjafield et al., 2019). Notably, more than 45% of these individuals (425 million adults) were estimated to have moderate or severe OSA, when using an apnoea-hypopnoea index (AHI) cutoff value of ≥ 15 events per hour of sleep (Benjafield et al., 2019).

If OSA symptoms are considered along with AHI, then the prevalence of OSA is estimated at a mean (range) of 4% (1 – 17%) in females and 6% (3 – 18%) in males (Young et al., 1993, Franklin and Lindberg, 2015). Whilst these data reported that males are nearly twice as likely as females to have OSA, recent epidemiological studies reported a marginally lower male-to-female ratio (Quintana-Gallego et al., 2004, Heinzer et al., 2015, Donovan and Kapur, 2016).

The higher proportion of male patients with OSA is attributed to anatomical and physiological features of the upper airway, and sex-dependent fat distribution (Lozo et al., 2017). Sex hormones may also explain the difference in OSA prevalence between males and females. Whilst androgens are thought to stimulate upper airway collapsibility, progesterone has been found to have a protective effect against OSA, through its role as a respiratory drive stimulant (Sigurðardóttir et al., 2022, Jordan and Doug McEvoy, 2003). These findings may also explain the increased prevalence and severity of OSA amongst postmenopausal females (Sigurðardóttir et al., 2022, Jordan and Doug McEvoy, 2003).

1.3.3.a: Prevalence of OSA in the UK

In the UK, moderate or severe OSA is estimated to affect 1.5 million (4.8%) of the 33 million adults aged 30 – 69 years, and if those with mild OSA are included, the estimated prevalence is over 8 million people, equating to 24.5% of all adults aged 30 – 69 years (Benjafield et al., 2019). However, it should be noted that there will undoubtedly be additional people aged below 30 and over 69 years who also have OSA. Therefore, these estimates only consider half of the UK population i.e. 33 out of 67 million people (Office for National Statistics, 2022). Therefore, it is notable that we do not have complete estimates for the prevalence of OSA in the UK.

1.3.3.b: Rising prevalence of OSA

Global prevalence rates of OSA have markedly increased over the last three decades and are expected to further increase due in part to the improved sensitivity of sleep apnoea testing (Heinzer et al., 2015), and primarily due to the increasing rates of obesity and the

ageing populations, both of which are closely associated with OSA (Senaratna et al., 2017, Punjabi, 2008). Obesity is regarded as the most important risk factor for developing OSA, and it has been reported that a 10% weight gain is associated with a six-fold increase in the risk of developing OSA (Deegan and McNicholas, 1996, Peppard et al., 2000a).

Ageing is also a risk factor for OSA and previous studies have reported an increase in the prevalence of OSA with age, even in the healthy elderly, with people aged >65 years being at least twice more likely than their younger counterparts to have OSA (Hoch et al., 1990, Glasser et al., 2011). However, the magnitude of daytime symptoms may be lower in older patients with OSA, compared to younger patients (Glasser et al., 2011). This may influence how older people with OSA symptoms seek medical help, and how their symptoms are recognised when presenting to healthcare services.

1.3.3.c: Limitations of epidemiological studies on OSA prevalence

It is important to recognise the limitations of the epidemiological studies to date, including those in the global prevalence review by Benjafield et al. (2019). Many of these studies were carried out in geographically different regions, and have some representation of different ethnic groups and populations; however, the generalisability of their findings may be limited by participation and selection bias. The studies also used inconsistent methodologies and definitions to assess the prevalence of OSA. One possible way to minimise these limitations is to exploit emerging digital health technologies, which may offer an opportunity to assess the prevalence of this condition amongst the general population, using scalable, reliable, and consistent methods for sleep apnoea screening.

1.3.4. Clinical sequelae of OSA

Underdiagnosed and, thus untreated, OSA represents a substantial clinical and public health burden (Rejón-Parrilla et al., 2014). As discussed in **Section 1.3.2**, the recurrent apnoeas and hypopnoeas during sleep lead to intermittent oxygen desaturations, intrathoracic pressure

changes, and arousals (Sánchez-de-la-Torre et al., 2013); resulting in sleep fragmentation, poor quality sleep, and EDS (Ayas et al., 2014).

Figure 1.2 shows a putative mechanism leading to intermediate mechanisms such as overactivation of the sympathetic system (Somers et al., 1995), oxidative stress, and increased cardiac preload and afterload (Sánchez-de-la-Torre et al., 2013, Gottlieb and Punjabi, 2020). These, in turn, contribute to the development of consequences, such as elevated blood pressure, metabolic dysregulation, and systemic and vascular inflammation (Gottlieb and Punjabi, 2020), and also serious health consequences and diseases including, cardiovascular (Phillips and O'Driscoll, 2013, Peppard et al., 2000b), cerebrovascular (Arzt et al., 2005), metabolic (Reichmuth et al., 2005), and mental health disorders (Wheaton et al., 2012) in some people.

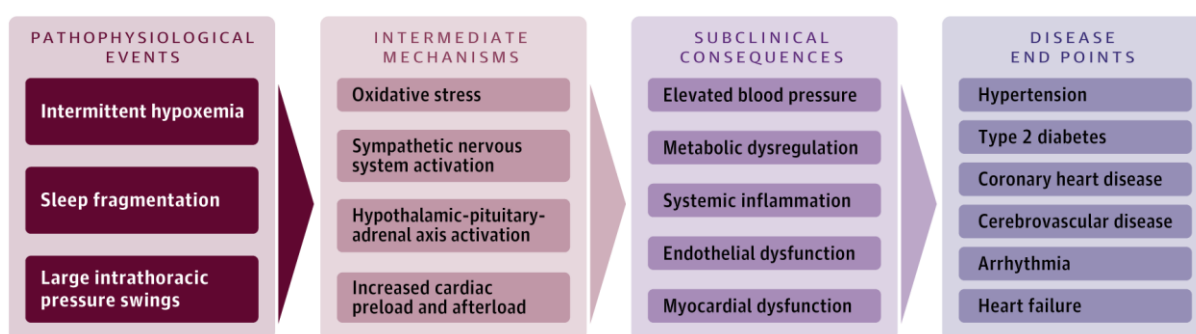


Figure 1.2 Putative mechanism of how physiological alterations in the form of intermittent oxygen desaturations, sleep fragmentation, and intrathoracic pressure changes that are caused by obstructive sleep apnoea (OSA) lead to intermediate mechanisms, resulting in serious subclinical consequences and diseases. Adapted from Gottlieb and Punjabi (2020) and reproduced with permission of the American Medical Association.

Untreated OSA is also associated with increased healthcare utilisation (Wickwire et al., 2020), increased risk of work-related and motor vehicle accidents (Karimi et al., 2013, Antonopoulos et al., 2011, Garbarino et al., 2016, Maria et al., 2021), and reduced vitality and work productivity (Mulgrew et al., 2007, Baldwin et al., 2001, Jurado-Gómez et al., 2015). These, in turn, can significantly contribute to the impairment of all domains of the patient's health-related quality of life (HRQoL).

1.3.4.a: Daytime somnolence as a feature of OSA

Somnolence, sleepiness, or '*the desire to sleep*' is a normal physiological state, experienced by humans. Excessive and persistent sleepiness is estimated to affect 12% – 18% of the population, and is often regarded as the commonest symptom that patients present with in sleep clinics (Roth and Roehrs, 1996, Slater and Steier, 2012).

OSA is the most prevalent condition associated with EDS (Bonsignore et al., 2021), however, the estimates of EDS prevalence amongst patients with OSA are inconsistent (Rosenberg et al., 2021). Some studies suggested that up to 80% of patients with OSA self-report experiencing EDS prior to being treated, and other community-based studies reported that approximately 55% of patients with OSA do not self-report symptoms of EDS (Gottlieb et al., 1999, Kapur et al., 2005, Bailly et al., 2016). In a large UK-wide survey of patients living with OSA (n= 2,671 participants), 79% of participants reported that they experienced daytime sleepiness prior to receiving their OSA diagnosis and 11% reported falling asleep whilst driving (British Lung Foundation, 2014), which highlights the potential consequences of EDS. It has been estimated that patients with untreated OSA are at a two-fold greater risk of motor vehicle accidents, compared to the general population, and this risk may be further exacerbated in excessively sleepy patients (Bonsignore et al., 2022).

1.3.4.b: Quality of life impairment due to OSA

Quality of life (QoL) is a broad concept that has gained popularity in recent decades. It is a multidimensional, subjective and dynamic concept, which aims to assess an individual's perception of their well-being, relative to both positive and negative dimensions, at a specific point in time (Teoli and Bhardwaj, 2023).

The World Health Organization (WHO) defines QoL as "*individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns*" (World Health Organization, 1995). The multidimensional nature of QoL emphasises the importance of incorporating

broad-ranging domains, including physical, psychological, social, environmental, and spiritual (World Health Organization, 1995). HRQoL however, is difficult to clearly define but may be thought of as the assessment of the QoL domains *“that are related to or affected by the presence of disease or treatment”* (Ebrahim, 1995), including patients’ perceived physical functioning, emotional state, and social interactions (Knauert et al., 2015, Lacasse et al., 2002).

HRQoL is commonly assessed, in both clinical practice and health research, using validated instruments that have been developed to measure the health dimensions of QoL (Sheats, 2016). These instruments can be either generic such as the EuroQol EQ-5D (EuroQol Group, 1990) and the 12-Item Short-Form Health Survey (SF-12) (Ware et al., 1996), or disease-specific such as the Functional Outcomes of Sleep Questionnaire (FOSQ) (Weaver et al., 1997) and the OSA Patient-Oriented Severity Index (OSAPOS) (Piccirillo et al., 1998). In patients with OSA, the impact of the condition on HRQoL is not limited to the effects of EDS, the commonest symptom of OSA, rather the sequelae of this condition lead to detrimental impairment in all the domains of HRQoL (Lacasse et al., 2002), and this can be both an advantage and a disadvantage in assessing the impact of disease, on a personal or population level.

1.3.5. Economic burden of OSA

The direct and indirect economic burden of undiagnosed and untreated sleep disorders, including OSA, have been investigated in different regions worldwide. The economic assessment analyses typically include direct health costs related to diagnosing and managing OSA, and the comorbidities associated with the condition such as cardiovascular disease and stroke (McDaid et al., 2009). Indirect or attributable financial costs, such as those related to reduced HRQoL and workplace productivity, higher healthcare utilisation, and increased risk of traffic and occupational accidents, may also be included in these economic assessments.

Earlier OSA-related economic data from the UK, including that of a cost-effectiveness analysis by the National Health Service (NHS) Centre for Reviews and Dissemination (University of York, UK), found that continuous positive airway pressure (CPAP) treatment for patients with moderate or severe OSA was associated with higher costs and health benefits (in terms of cardiovascular events, stroke, road traffic accidents, and mortality) from the UK NHS perspective, compared to non-treatment or lifestyle management (National Institute for Health Care Excellence, 2008, Guest et al., 2008, McDaid et al., 2009).

In 2014, an OSA Health Economics Report, published by the British Lung Foundation (BLF; *now known as Asthma + Lung UK*), assessed the economic burden of OSA in the UK, based on a conservative OSA prevalence estimate; 1.5 million adults with OSA of whom 667,000 had moderate or severe OSA. It was estimated that in 2012-2013 patients with moderate or severe OSA cost the NHS £483 million per annum in England, £49.2 million in Scotland, £28.2 million in Wales, and £16.1 million in Northern Ireland. The total annual NHS direct cost was estimated to be £577 million (Rejón-Parrilla et al., 2014). The report concluded that if all patients with moderate or severe OSA were to be diagnosed and thus treated, the NHS would incur annual savings of £55 million, and 40,000 quality-adjusted life-year gained (QALY).

It was also estimated that approximately 40,000 road traffic accidents could be prevented in the UK if all patients with OSA were treated, and this would likely result in both considerable economic and health gains (Rejón-Parrilla et al., 2014). In addition, the economic benefits of treating patients with OSA extend beyond the cost savings related to healthcare utilisation and road traffic safety, and also include societal benefits. The treatment of OSA with CPAP therapy (see **Section 1.7.1** for a description of CPAP therapy) improves patients' vitality and workplace productivity, enhances their partners' QoL, and was also estimated to decrease societal costs of occupational injuries by £491 million (Rejón-Parrilla et al., 2014).

In another report commissioned by the American Academy of Sleep Medicine (AASM), it was estimated that undiagnosed OSA cost the United States (US) economy \$149.6 billion per annum (~ £120 billion UK Pound Sterling) (Frost & Sullivan, 2016). The majority of this economic burden was due to lost productivity at work (\$86.9 billion), whereas the cost of increased healthcare utilisation due to comorbidities and mental health disorders associated with OSA was \$30 billion per annum. Road traffic and workplace accidents related to undiagnosed and untreated OSA cost the US \$26.2 billion and \$6.5 billion, respectively. Interestingly, their financial modelling also calculated the costs of undiagnosed *versus* diagnosed and treated OSA, estimating that the treatment costs are equivalent to only a third (33%) of non-treatment costs. Thus, diagnosing and treating all patients with OSA would result in considerable net cost savings to the nation (Frost & Sullivan, 2016).

The economic modelling in these assessments involves perceived assumptions and may inevitably rely on conjecture, therefore, the above estimates need to be interpreted with caution. However, based on the international economic data available to date, it is likely that OSA is associated with a profound direct and indirect economic burden on individuals, healthcare systems, and society. These economic implications are likely to further increase due to the increasing prevalence of OSA, which highlights the need to investigate alternative clinical and cost-effective strategies that address OSA underdiagnosis and undertreatment in the UK, and worldwide.

1.4. Provision of diagnosis and clinical management of OSA

This section provides a discussion on the mismatch in OSA healthcare delivery, and a summary of NICE clinical guidelines for OSA and its role in reducing the ‘*unwarranted*’ variations in clinical practice.

1.4.1. The burden of undiagnosed OSA

Despite the increasing recognition of OSA and its clinical and economic consequences, OSA remains underdiagnosed. An earlier population-based study of nearly 5,000 employed adults

in the US, estimated that over 80% of males and more than 90% of females with moderate or severe OSA remain without a clinical diagnosis (Young et al., 1997). In 2014, the BLF (*now known as Asthma + Lung UK*) suggested that although OSA affects approximately 1.5 million adults in the UK, up to 85% of people with OSA remain undiagnosed, and consequently not receiving the treatment they need (Rejón-Parrilla et al., 2014). These high estimates of undiagnosed and untreated OSA, despite its rising prevalence, represent a growing national and global public health concern, not only at an individual level but also for healthcare systems.

Historically, and primarily due to a lack of OSA awareness amongst the public and healthcare professionals, along with the social stigma associated with snoring and obesity, patients tend to go for a long time before seeking medical help after noticing their OSA symptoms (British Lung Foundation, 2014, Williams et al., 2008, Boccabella and Malouf, 2017).

The treatment delay is further prolonged once patients get into the clinical care pathway, whereby timely referral to specialist care is not only dependent on the General Practitioner (GP) or health professionals' awareness of the clinical manifestations of OSA; but also, on '*where the patient lives*' and whether the required diagnostic services are available nearby. Consequently, patients who are being investigated for suspected OSA experience long waiting times before being offered a diagnostic assessment. For example, the current waiting time for a sleep study is over 12 months in an NHS Highlands sleep service. This is compared to a waiting time of 6 months in a tertiary referral centre in inner London (*Personal communication with the clinical leads at these sleep services, 2022*). In the case where an OSA diagnosis is then confirmed, patients may incur a further delay before their treatment is initiated, which may exacerbate their health burden.

1.4.2. The increasing demand for OSA healthcare delivery

In recent years, and specifically post-COVID-19 pandemic, there has been a growing awareness of the national need for improved healthcare delivery for OSA. Currently, referrals to sleep services account for one-third of all referrals to respiratory medicine (Allen, 2021). Additionally, the commissioning of diagnostic sleep studies in the UK increased by 70% between 2007 and 2013 (Public Health England, 2016). This could be explained by the increased awareness of the health and economic implications of OSA, along with the introduction of the constitutional right for a maximum diagnostic waiting time from referral to treatment (Public Health England, 2016). However, despite the increasing number of sleep studies performed in recent years, the number of patients awaiting their sleep study in the UK has also been exponentially rising, particularly post-COVID-19 pandemic, with a yearly growth rate exceeding 74% (NHS England and NHS Improvement, 2022). It has also been reported that each year in England, only 18% (121,000 out of 666,000 people) of those who present to healthcare services with symptoms of OSA get referred to sleep services for a diagnostic sleep study and further investigation (National Institute for Health and Care Excellence, 2021b).

In addition to the increasing demand for OSA diagnosis, there is a variation in the number of diagnostic sleep studies performed across the different regions in England, as illustrated in **Figure 1.3**. The NHS Atlas of Variation in Healthcare reported in 2019 that the magnitude of variation in the provision of diagnostic sleep studies across the country ranged from 4.3 to 1,312 per 100,000 population, equating to a 305-fold difference amongst the 211 clinical commissioning groups (CCGs) (Public Health England, 2019). The quoted reasons for such variation included the absence of national standardised guidelines, differences in service availability, the prevalence of risk factors and associated comorbidities, and symptom recognition and appropriate referral by GPs (Public Health England, 2019).

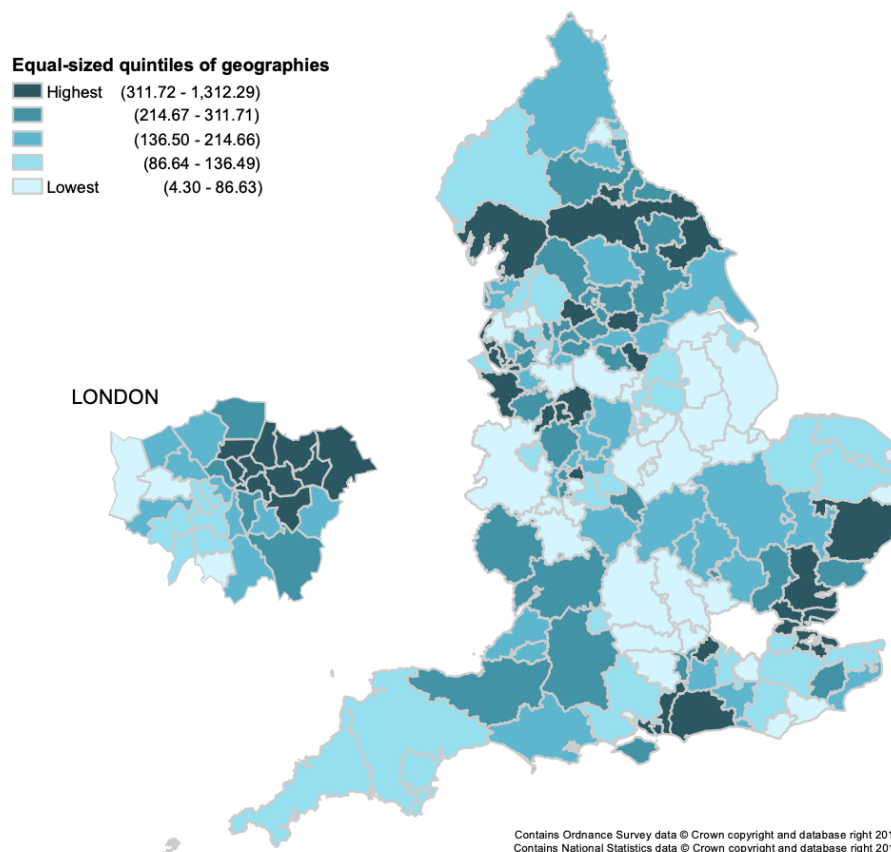


Figure 1.3 The variation in the rates of diagnostic sleep studies undertaken per 100,000 of the population by clinical commissioning groups in England (2018-2019). The legend on the left shows the rates of diagnostic sleep studies in 5 quintiles, ranging from lowest to highest. The darker the colour, the higher the rate of diagnostic sleep studies undertaken. Figure from the 2nd Atlas of Variation in Risk Factors and Healthcare for Respiratory Disease in England (2019). Reproduced from Public Health England under an [Open Government Licence V3.0](#).

1.4.3. The mismatch in OSA healthcare delivery across the UK

The ability to provide equitable and high-quality sleep services requires the identification of ‘unwarranted’ variations in healthcare provision whilst also considering the different regional requirements for these services. In 2014, Steier et al. (2014) in collaboration with the BLF (now known as *Asthma + Lung UK*) produced an overall risk map for OSA, based on the five most common factors associated with the condition. These were obesity, type II diabetes, age, hypertension, and sex. This map was then used to illustrate the predictive prevalence estimates of OSA and the available sleep services in the UK (**Figure 1.4**).

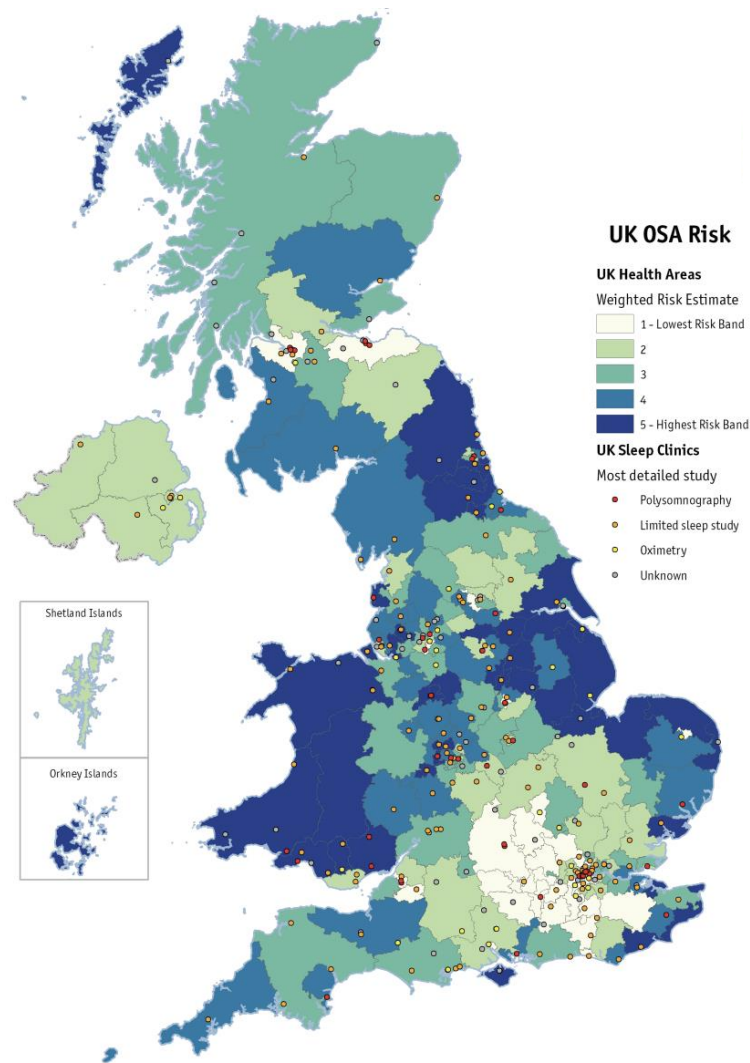


Figure 1.4 The predicted prevalence estimates for obstructive sleep apnoea (OSA) and the available sleep services across the UK. Areas on the map are displayed for health authorities. The legend on the right shows relative risk bands in quintiles of 1 – 5; the darker the colour the higher the predicted prevalence estimates. Adapted from British Lung Foundation and Steier et al. (2014) and reproduced with permission of BMJ Publishing Group Ltd.

Steier et al. (2014) found significant variations in the predictive prevalence of OSA across the UK regions, and also a mismatch between the predicted regional healthcare requirements and the distribution of existing sleep services.

In 2008, which was a landmark year for the UK sleep community, NICE published its first technology appraisal guidance for OSA, in which CPAP treatment was recommended for adult patients with symptomatic moderate or severe OSA (National Institute for Health Care Excellence, 2008). Since then, testing for respiratory sleep disorders, particularly OSA, has

markedly improved. However, unfortunately, patient access to diagnostic and treatment sleep services in the UK remains subject to a '*postcode lottery*' (Ghiassi, 2014). Geographical '*hotspots*' that have been identified as regions with high predicted OSA prevalence such as rural Scottish Islands, large parts of Wales, North West of England, and East Anglia have reduced service provision and, consequently increased travel requirements in order to access care. This not only poses a potential safety risk to patients with excessive sleepiness but also undermines the equity of access to healthcare in the NHS, which has promised to "*meet the needs of everyone*" with equal access for equal needs (Wenzl et al., 2015).

In the absence of national guidelines for OSA diagnosis and management at the time of publishing their report, the NHS Atlas of Variation in Healthcare (2019) emphasised the need for an assessment of the demand and available resources in local sleep services, and a comprehensive review of the referral and diagnostic pathways used in clinical practice (Public Health England, 2019). However, it is envisaged that national efforts to reduce inequalities in sleep services provision and improve access to OSA diagnosis and treatment, may be hindered due to insufficient resources and shortage of staff in sleep services. In addition, discrepancies in sleep services' documentation of both clinical and financial activity data (e.g. the actual number of diagnostic sleep studies being performed *versus* the number of studies being paid for) will inevitably influence financial reimbursements, and any reliable analysis of service delivery in the UK (Allen, 2021). Whilst recognising these limitations, the recently published Respiratory Medicine 'Getting It Right First Time' (GIRFT) review report has made several recommendations (Allen, 2021). These were:

- *ensure the infrastructure for delivering a sleep service is sufficient to meet demand,*
- *improve care for patients in sleep medicine by addressing delays in diagnosis of sleep problems, ensuring the activity is captured and coded,*
- *deliver an optimal and expedited pathway with direct-to-test and, with appropriately trained physiologists in place, direct-to-CPAP-treatment,*
- *and ensure timely initiation of CPAP with a device that allows remote monitoring.*

The latter was specifically highlighted as an effective management strategy that should become a standard practice. A discussion of the clinical management for patients with OSA, including follow-up care of those treated with CPAP therapy, is presented in **Section 1.7** below.

1.4.4. NICE clinical guidelines for reducing ‘unwarranted’ variations in OSA healthcare delivery

NICE is an executive non-departmental public body, established in 1999, and is sponsored by the UK Department of Health and Social Care. It facilitates the delivery of high-quality healthcare by developing and providing national evidence-based clinical guidelines, health technology appraisals, public health guidance, and quality standards for the NHS, local authorities, and other healthcare providers (Rawlins, 1999).

Clinical guidelines, also known as clinical practice guidelines, are “*statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options*” (Institute of Medicine, 2011). NICE clinical guidelines are ‘*advisory rather than compulsory*’ sets of recommendations for the initial assessment, diagnosis, and management of people with specific conditions.

The development of these clinical guidelines is based on rigorous, transparent, and pre-specified methods, to systematically search, critically appraise and synthesise the best available evidence on the guideline topic. This reproducible and transparent systematic approach is at the top of the hierarchy of evidence, which is central to the provision of evidence-based clinical practice (Burns et al., 2011). In addition to their robust methodology, NICE continuously seeks input from all relevant stakeholders, including patient and carer organisations, healthcare professionals’ representatives, NHS, and other entities throughout the different stages of developing the clinical guidelines.

1.4.4.a: NICE clinical guidelines for OSA

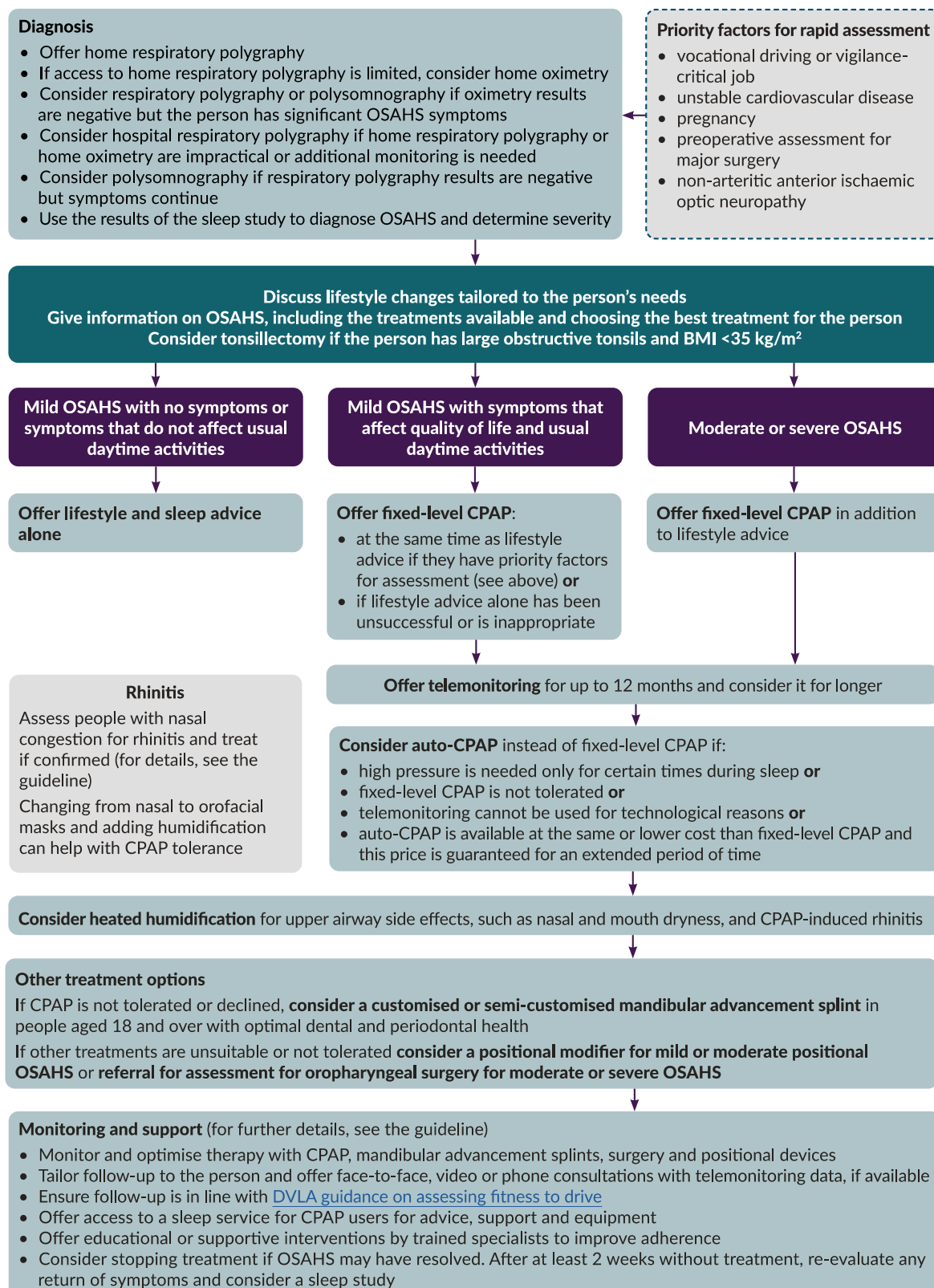
In the UK, OSA is typically diagnosed based on a combination of subjective and objective clinical assessments such as sleep history, physical examination, the presence of related symptoms and comorbidities associated with the condition, and the findings from a diagnostic sleep study (Greenstone and Hack, 2014). A visual summary of NICE guidance on OSA diagnosis and management is presented in **Figure 1.5**. Further details on conventional diagnostic and management strategies and their supporting evidence will be discussed in **Sections 1.5** and **1.7** below.

In brief, NICE clinical guidelines recommend using subjective questionnaires (Epworth Sleepiness Scale, with or without STOP-Bang Questionnaire; see **Section 1.5.1** for a description of the subjective questionnaires) for the preliminary assessment of sleepiness and risk of disease in people with suspected OSA (National Institute for Health and Care Excellence, 2021a). The recommended initial diagnostic strategy for suspected OSA is home respiratory polygraphy, and only if access to respiratory polygraphy is limited, nocturnal home oximetry alone may be considered. If suggestive symptoms persist, despite negative results from the sleep study, further detailed investigation should then be considered.

In the UK, home sleep apnoea testing with respiratory polygraphy or nocturnal oximetry as the initial diagnostic strategy has been increasingly used. NICE's review of evidence found that home respiratory polygraphy was more clinically and cost-effective than both in-hospital respiratory polygraphy and home nocturnal oximetry (NICE Diagnostic Evidence Review, 2021a). Thus, their recommendation is likely to move OSA diagnosis from sleep laboratories into patients' homes, encouraging the use of home respiratory polygraphy over other diagnostic strategies.

OSAHS: investigations and treatment

NICE National Institute for Health and Care Excellence



Published date: August 2021. This is a summary of the advice on OSAHS investigation and treatment in NICE's guideline on obstructive sleep apnoea-hypopnoea syndrome and obesity hypoventilation syndrome

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Figure 1.5 Summary of the National Institute for Health and Care Excellence (NICE) guidance on obstructive sleep apnoea (OSA) diagnosis and management. Reproduced under NICE UK open content license, from ©NICE [2021] OSAHS: investigations and treatment. Available from www.nice.org.uk/guidance/ng202 all rights reserved. Subject to [Notice of Rights](#).

Following a diagnosis of OSA, NICE recommends initiating a discussion of lifestyle modification, tailored to the patient's needs. Health information on OSA and its treatment should also be provided to patients to facilitate shared decision-making on the best treatment options available to patients.

In addition to lifestyle advice, NICE recommends CPAP therapy with up to 12 months of telemonitoring as the first-line treatment strategy for patients with moderate or severe OSA (see **Section 1.7.1** for a discussion on CPAP therapy). This treatment strategy is also recommended for patients diagnosed with symptomatic mild OSA that affects their QoL and usual daytime activities. However, if the mild OSA is associated with no symptoms or symptoms that do not affect daytime functioning, then lifestyle and sleep advice alone is recommended.

NICE also recommends that all treated patients should be monitored and supported to optimise their therapy, using follow-up management strategies that are tailored to each patient with either in-person or virtual (video or phone) consultations plus telemonitoring data, if available.

1.5. Overview of conventional diagnostics for OSA

This section provides an overview of the conventional subjective and objective assessments used for OSA diagnosis, and a discussion of their limitations.

Investigation of suspected OSA in the UK is recommended in patients presenting with two or more of the following clinical manifestations (National Institute for Health and Care Excellence, 2021a):

- snoring,
- witnessed apnoeas,
- unrefreshing sleep,
- waking headaches,
- unexplained excessive sleepiness, tiredness or fatigue,

- nocturia,
- choking during sleep,
- sleep fragmentation or insomnia,
- or cognitive dysfunction or memory impairment.

OSA should also be suspected if the above clinical manifestations are present in the patient populations that have been identified to have a higher prevalence of OSA (National Institute for Health and Care Excellence, 2021a). These may include patients with obesity or overweight, hypertension, diabetes, stroke or transient ischaemic attack, chronic heart failure, or Down's syndrome.

1.5.1. Subjective assessment scales for suspected OSA

Many scales have been developed to assess sleep, sleepiness, and/or sleep disorders. Shahid et al. (2012) published a textbook that provides a compilation of over 100 different sleep and sleep disorders scales used in clinical settings and/or health research. Their textbook discusses the purpose, methods for administration, and reliability and validity of these scales.

In clinical settings, subjective scales such as the STOP-Bang (**S**nororing, **T**iredness, **O**bserved apnoea, **B**lood **P**ressure, **B**ody mass index, **A**ge, **N**eck circumference, **G**ender) and Berlin Questionnaires are widely used as screening instruments to assess the risk of having OSA (Chung et al., 2008, Netzer et al., 1999). However, their diagnostic accuracy has been criticised for their high sensitivity for identifying patients with severe OSA and low specificity impacting their value in screening out patients without OSA (Chiu et al., 2017, Ahmadi et al., 2008).

NICE clinical guidelines for OSA diagnosis recommend using the Epworth Sleepiness Scale (ESS) for the initial assessment of sleepiness in patients with suspected OSA, as discussed in **Section 1.4.4** above. Healthcare professionals are also advised to consider using the STOP-Bang Questionnaire along with ESS, which has been suggested to improve the specificity of

STOP-Bang for predicting OSA (National Institute for Health and Care Excellence, 2021a, Zheng et al., 2022).

Although other subjective sleepiness scales such as the Stanford Sleepiness Scale and Karolinska Sleepiness Scale are being used in some sleep services worldwide, ESS is the most widely used in both clinical practice and health research (Åkerstedt and Gillberg, 1990, E Hoddes, 1971, Johns, 1991). *In this Thesis, I have used ESS for the initial eligibility assessment for participation in the randomised controlled study (presented in **Chapter 2**). I have also used the results of ESS as a co-primary outcome in the systematic review and meta-analysis (presented in **Chapter 4**).*

ESS is used to assess the level of sleepiness (sleep propensity) in patients with sleep disorders, rather than to diagnose OSA. It is a patient-reported scale, consisting of eight items, that asks individuals about the likelihood of them dozing off or falling asleep whilst engaged in a variety of daily situations. **Figure 1.6** shows the original ESS scale, which was first developed in English for Australia in 1990 but has subsequently been translated into more than 50 languages (Buysse et al., 2008).

Each item is rated on a 4-point scale (0 – 3), with 0 being “*would never doze*”, 1 = “*slight chance of dozing*”, 2 = “*moderate chance of dozing*”, and 3 = “*high chance of dozing*”. The summary or overall score is an integer value, ranging from 0 to 24, and is derived from the calculation of the scores of all items in the scale. ESS scores of 11 or more represent increasing levels of EDS, whereas scores of 16 – 24 indicate severe EDS (Johns, 1991).

When assessing the clinical improvement in daytime sleepiness, a reduction of 2 – 3 points in the ESS score has been estimated to represent the minimum clinically important difference (MCID), using distribution- and anchor-based methods (Patel et al., 2018). However, it is recognised that patients with OSA present with multifaceted symptoms, and excessive sleepiness is one common symptom that may or (may not) be experienced by patients,

irrespective of their OSA severity (see **Section 1.5.3** for a discussion on the severity classification of OSA).

Epworth Sleepiness Scale (ESS)

Name: _____ Today's date: _____

Your age (Yrs): _____ Your sex (Male = M, Female = F): _____

How likely are you to doze off or fall asleep in the following situations, in comparison to feeling just tired?

This refers to your usual way of life in recent times.

Even if you have not done some of these things recently try to work out how they would have affected you.

Use the following scale to choose the **most appropriate number** for each situation:

- 0 = would **never** doze
- 1 = **slight chance** of dozing
- 2 = **moderate chance** of dozing
- 3 = **high chance** of dozing

It is important that you answer each question as best as you can

Situation	Chance of Dozing (0-3)
Sitting and reading _____	_____
Watching TV _____	_____
Sitting still in a public place (e.g., a theatre, a cinema or a meeting) _____	_____
As a passenger in a car for an hour without a break _____	_____
Lying down to rest in the afternoon when circumstances allow _____	_____
Sitting and talking to someone _____	_____
Sitting quietly after a lunch without having drunk alcohol _____	_____
In a car, while stopped for a few minutes in traffic _____	_____

THANK YOU FOR YOUR CO-OPERATION

ESS © MW Johns 1990-1997. Used under License

Figure 1.6 The Epworth Sleepiness Scale. Participants are asked to rate each scenario on a 4-point scale, with higher numbers representing increased likelihood of daytime sleepiness. The scores of all items are then summed to produce a total ESS score, ranging from 0 to 24 points. Reproduced with permission of ©Mapi Research Trust.

The popularity of ESS to assess daytime sleepiness in clinical settings is perhaps due to its simplicity, however, the lack of reliable and easy-to-use screening tools for OSA led to using ESS for purposes it was never designed for. One example I have seen in clinics is using ESS

as a definitive decision-support tool for referring patients for OSA investigation, or for assessing the presence of OSA. It has also found its use beyond the realms of clinical care settings, and is now used as part of the medical information required by the Driver and Vehicle Licensing Agency (DVLA) to assess fitness-to-drive and confirm control of OSA symptoms (DVLA, 2016).

Using ESS for other purposes than assessing the level of sleepiness may be problematic due to its limitations. A recent NICE diagnostic meta-analysis of three clinical studies in 2,067 adult patients found that ESS had low pooled sensitivity (52%) and specificity (50%) in diagnosing OSA (Hesselbacher et al., 2012, Vana et al., 2013, Cowan et al., 2014). In addition, other studies reported contradictory findings on the correlation between subjective sleepiness, assessed by ESS, and objective sleepiness, measured using the multiple sleep latency test (MSLT) which is considered to be the gold standard measure of sleepiness (Carskadon, 1986, Aurora et al., 2011, Johns, 1994, Chervin and Aldrich, 1999).

A further systematic review of ESS measurement properties (Kendzerska et al., 2014) reported that in addition to having a weak, or at best, a modest association with MSLT, ESS had no or weak association with the severity of OSA, measured objectively by AHI. Additionally, ESS may be a more sensitive measure of subjective sleepiness in males than in females, and it may also underestimate the level of sleepiness in older people (Onen et al., 2013, Baldwin et al., 2004).

Taken together, these limitations warrant consideration when interpreting ESS results as a definitive marker of excessive sleepiness, the presence of OSA, or the severity of the condition. However, ESS can be useful in the preliminary assessment of sleepiness in patients with suspected OSA, and in determining treatment and assessing patient response to treatment (NICE Diagnostic Evidence Review, 2021a).

1.5.2. Objective assessment tests for suspected OSA

OSA diagnosis requires confirmation of the presence of respiratory disturbances during sleep, in the form of abnormal snoring, apnoeas, hypopnoeas, and respiratory effort-related arousals (RERAs). In 1994, the American Sleep Disorders Association (*now known as the AASM*), published a statement on standards of practice which classified objective sleep studies into four major levels, based on the number and type of bio-parameters that are monitored during sleep (Ferber et al., 1994, American Sleep Disorders Association, 1994). These levels were:

- **Level I** (standard in-laboratory polysomnography)
- **Level II** (comprehensive portable polysomnography)
- **Level III** (modified portable sleep apnoea testing)
- **Level IV** (continuous single- or dual-bioparameter recording)

The AASM statement was amongst the first attempts to address inconsistencies in the terminology used to describe different sleep testing devices, by determining the levels of sleep studies and providing the specifications of diagnostic devices used in each one of those levels (Ferber et al., 1994). However, OSA diagnostic devices have since then developed, due to the introduction of technological advances in biosignal detection and processing, sleep monitoring, sleep data analysis, and data transmission (Penzel et al., 2021).

Figure 1.7 shows the different types of sleep studies currently used in clinical practice and health research. Whilst Level I sleep study is still recognised as the standard diagnostic test for OSA, the remaining 3 levels which have been collectively termed portable monitors (PM) or home sleep apnoea testing devices, are also used for the diagnosis of OSA in uncomplicated symptomatic adult patients (Kapur et al., 2017).

Many of the emerging OSA diagnostic devices are based on technological features that were not included in the original 1994 AASM classification of portable sleep studies, and this led to the development of new and inclusive classification systems. In 2011, Collop et al. (2011) proposed the SCOPER classification framework, which categorises the diagnostic devices

based on their direct or surrogate measurement of **S**leep, **C**ardiovascular, **O**ximetry, **P**osition, **E**ffort, and **R**espiratory (SCOPER) bio-parameters. This physiologically-oriented framework facilitates the evaluation of the emerging digital technologies that are being developed as alternatives to conventional diagnostics for OSA.

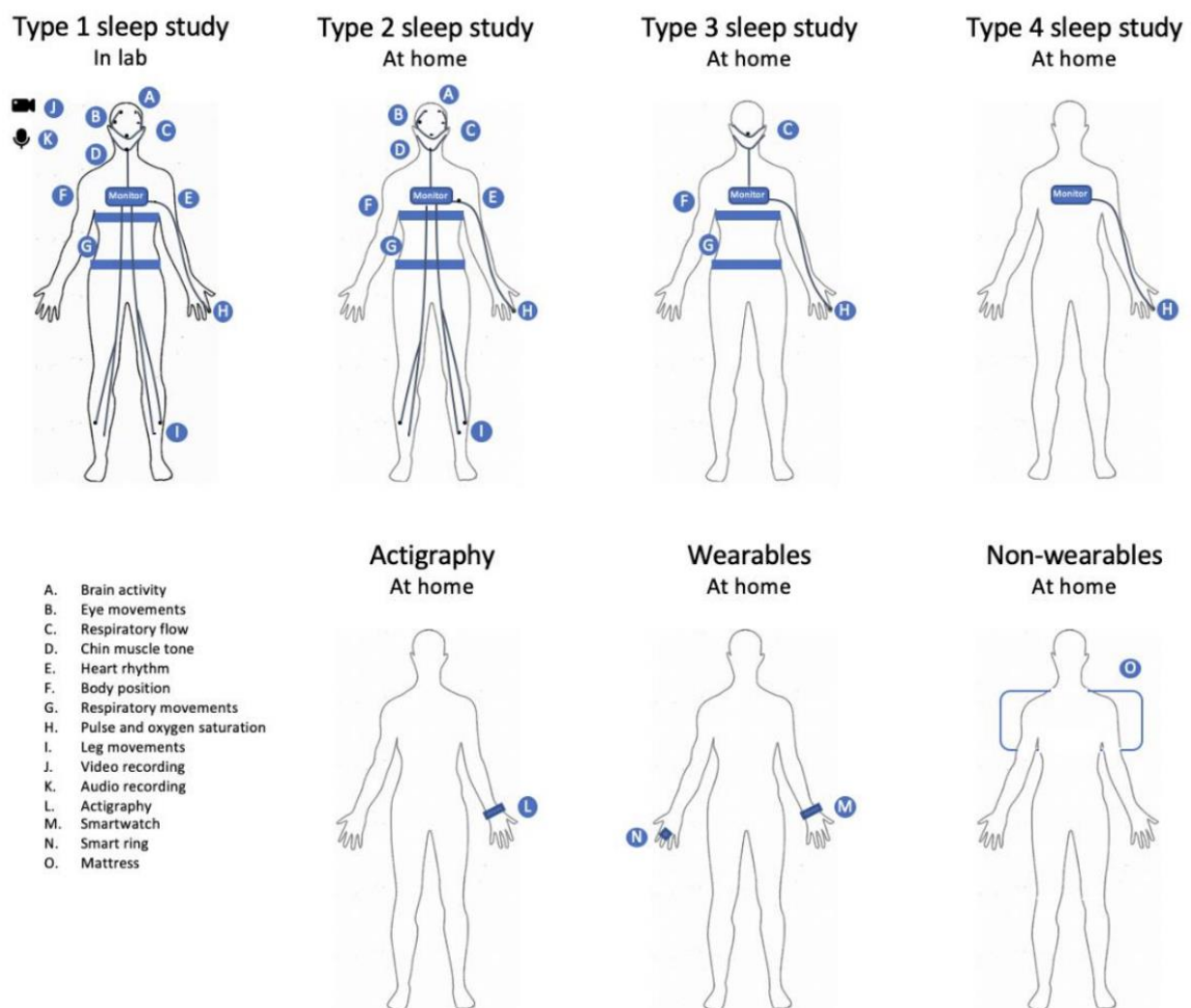


Figure 1.7 Illustration of the different types of sleep studies with their associated bio-parameters that are monitored during the recording of the sleep study. Adapted from Arnardottir et al. (2021) and reproduced with permission of Elsevier.

1.5.2.a: Level I – Polysomnography: the gold-standard diagnostic test

Polysomnography (PSG) is the most comprehensive diagnostic sleep test, and it has been used in clinical practice since the 1950s (Shepard et al., 2005). In-laboratory PSG (Level I) is considered the ‘gold’ standard for the evaluation of sleep and respiratory sleep disorders. It

refers to an attended sleep study performed in a hospital or laboratory setting with continuous overnight monitoring by a trained sleep specialist to ensure the quality of the recordings (Kushida et al., 2005).

A PSG sleep study typically records a minimum of seven sleep and respiratory-related bio-parameters. These include:

- electroencephalogram (EEG) – brain activity,
- electrooculogram (EOG) – eye movements,
- electromyogram (EMG) – muscle tone,
- electrocardiogram (ECG) – heart rate and rhythm,
- airflow and respiratory effort,
- oxygen saturation,
- and body position.

These bio-parameters are simultaneously monitored during the sleep study (Gottlieb and Punjabi, 2020, Rundo and Downey, 2019). In a portable PSG (Level II), the same bio-parameters recorded in Level I sleep studies are also monitored; however, Level II sleep studies may be performed outside of the hospital or sleep laboratory (e.g. in the patient's own home) and it is unattended by a trained sleep specialist.

1.5.2.b: Limitations of polysomnography

Level I and Level II PSG sleep studies can often be burdensome, and inconvenient for patients who are expected to sleep normally whilst being attached to multiple wires, usually away from their home environment.

PSG is also expensive, time-consuming, and requires specialised and trained personnel to operate equipment, score and interpret the sleep study data (Gottlieb and Punjabi, 2020, Corral et al., 2017). In addition, most countries, including the UK, have a limited number of facilities that are equipped for PSG testing; thus, leading to delays in diagnosis (Flemons et al., 2004). In a study published nearly a decade ago, Steier et al. (2014) reported that only 50 out of 289 sleep services in the UK offered PSG sleep studies. This was 10 times higher than

the US ratio of sleep services offering PSG per population served. In the UK, each accredited sleep service serves 1.25 million people, compared to 126,000 people in the US (Steier et al., 2014). The limited availability of these services has stimulated the development of alternative sleep testing devices to meet the increasing demand for the diagnosis and management of respiratory sleep disorders.

1.5.2.c: OSA diagnosis in the patient's home

Some of the challenges associated with Level I and Level II PSG testing for OSA diagnosis can be mitigated through alternative home sleep apnoea tests, a term used by the AASM to describe the sleep studies that are routinely performed at home (Rosen et al., 2018). These include Level III and Level IV sleep studies which are often less complex, less costly, and more convenient to patients than PSG (El Shayeb et al., 2014, Guerrero et al., 2014). However, conventional home sleep apnoea testing devices do not monitor EEG, EOG, or EMG signals, therefore, these devices lack the ability to distinguish between sleep and wake states, and cannot determine the actual sleeping time i.e. total sleep time (TST).

Level III modified portable sleep apnoea testing devices are commonly known as respiratory polygraphy or cardiorespiratory sleep study (Arnardottir et al., 2021). *In this Thesis, I used a Level III home respiratory polygraphy for OSA diagnosis in the randomised controlled study* (presented in **Chapter 2**). Home respiratory polygraphy has been well-validated in the screening and diagnosis of sleep apnoea (Masa et al., 2011), and in line with NICE clinical guidelines, many sleep services in the UK use it for routine screening of suspected OSA (National Institute for Health and Care Excellence, 2021a). Respiratory polygraphy records a minimum of four bio-parameters, and the device typically consists of:

- nasal cannula to monitor nasal airflow and snoring,
- oximeter to measure heart rate and oxygen saturation,
- chest band to measure respiratory effort,
- and body position.

Figure 1.8 shows the sensors and components of the ApneaLink™ Air (ResMed Ltd, Australia), the Level III home respiratory polygraphy used in the research conducted for this Thesis.

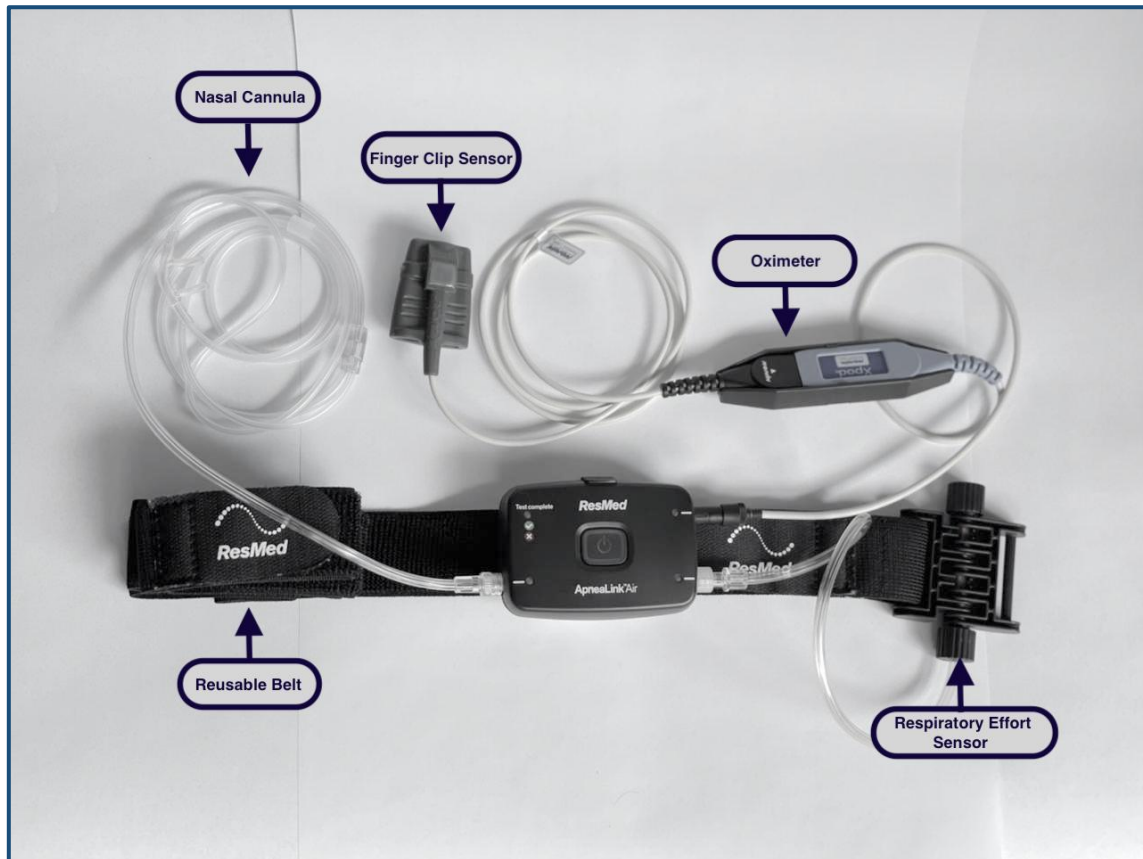


Figure 1.8 The sensors and components of the Level III home respiratory polygraphy monitor (ApneaLink™ Air; ResMed Ltd, Australia) used in the research conducted for this Thesis.

Recently developed Level III devices are typically linked with software that allows for automated analysis of the data recorded during the sleep study. The automated analysis can often be manually reviewed and modified *via* a dedicated platform. However, it is recognised that the limitations of these automated analysis algorithms may restrict their diagnostic accuracy and, therefore, the AASM position is that raw data should be reviewed and interpreted by a sleep specialist (Rosen et al., 2018).

Figure 1.9 shows an example of an original diagnostic report generated by AirView (ResMed Ltd, Australia), the platform used to set up, download, analyse, and report the sleep studies performed by ApneaLink™ Air (ResMed Ltd, Australia).



AirView™

Diagnostic Report

Recording details				07/02/2023			
Device				ApneaLink Air			
Recording	Start:	11:28pm	End:	7:01am	Duration - hr:	7:33	
Flow evaluation	Start:	11:38pm	End:	6:59am	Duration - hr:	7:10	
Oxygen saturation evaluation	Start:	11:38pm	End:	7:01am	Duration - hr:	7:22	
Statistics							
							
Events index	AHI:		46.5		AI:	5.0	
Supine	AHI:		24.7		AI:	16.4	
Non-supine	AHI:		48.2		AI:	4.9	
Upright	AHI:		0.0		AI:	0.0	
Events totals	Apnoeas:		36		Hypopnoeas:	298	
Apnoea Index	Obstructive:	4.3	Central:	0.4	Mixed:	0.1	
Cheyne-Stokes respiration	Time - hr:		0:00		Percentage:	0	
Oxygen desaturation	ODI:		52.7		Total:	389	
Oxygen saturation %	Baseline:	96		Avg:	92		
Oxygen saturation - eval time %	<=90%sat:	23		<=85%sat:	3		
	<=88%sat:	10		<=88%Time - hr:	0:43		
Breaths	Total:	6180		Avg/min:	14.4		
Pulse - bpm	Min:	51		Avg:	65		
Analysis guidelines: AASM 2012, Manual scoring							
Apnoea[10%; 10s; 80s; 1.0s; 20%; 60%; 8%]; Hypopnoea[70%; 10s; 100s; 1.0s]; Snoring[6.0%; 0.3s; 3.5s; 0.5s]; Desaturation[3.0%]; CSR[0.5]. Airflow sensor and respiratory effort sensor: Pressure transducer. Hypopnoeas were scored only if there was valid oximetry data.							



AirView™

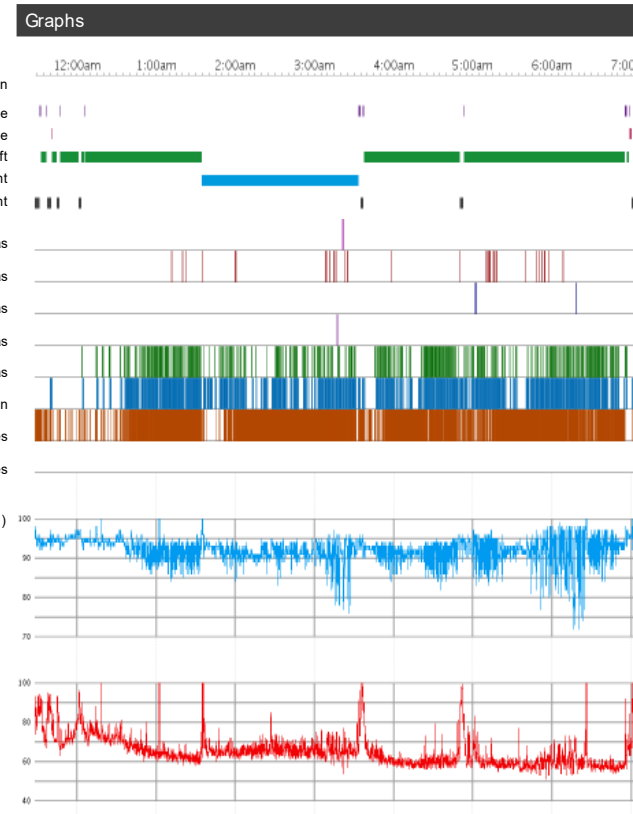


Figure 1.9 An anonymised original diagnostic report generated following an overnight home sleep study using respiratory polygraphy (ApneaLink™ Air; ResMed Ltd, Australia). The diagnostic report suggests the presence of severe obstructive sleep apnoea (OSA) in an adult patient referred for investigation of suspected OSA. Repetitive obstructive apnoeas and hypopnoeas with an apnoea-hypopnoea index (AHI) of 46.5 events per hour are seen. Associated oxyhaemoglobin desaturations with an oxygen desaturation index (ODI) of 52.7 events per hour are also seen.

Level IV sleep study devices typically involve limited-channel monitoring, with continuous single- or dual-bioparameter recording during sleep. The most commonly measured bioparameter is nocturnal oximetry, which can be coupled with airflow, pulse rate, peripheral arterial tonometry, or tracheal sound (Riha, 2023). These devices do not directly measure sleep-related respiratory events such as apnoeas and hypopneas but rather provide surrogate indices such as baseline peripheral capillary oxygen saturation (SpO_2), oxyhaemoglobin desaturation index (ODI), and the duration of desaturations, derived from the nocturnal oximetry. These bio-parameters are then used to assist in the diagnosis of patients with high pre-test probability of OSA. However, nocturnal oximetry should only be used if access to home respiratory polygraphy is limited. In addition, nocturnal oximetry may also be inaccurate in differentiating between OSA and other health conditions (e.g. chronic obstructive pulmonary disease) that can result in nocturnal oxygen desaturations (NICE Diagnostic Evidence Review, 2021a, Riha, 2023).

1.5.2.d: Limitations of home sleep apnoea testing devices

A major limitation of all sleep studies is that they are typically performed for one night only in clinical practice. This strategy does not account for night-to-night variability in the sleep bioparameters being monitored, and also the potential first-night effect, both of which may lead to misdiagnosis or misclassification of patients with OSA (Arnardottir et al., 2021, Roeder et al., 2020, Stradling et al., 2004).

Home sleep apnoea testing devices generally lack the ability to distinguish between sleep and wake states, measure TST, and detect hypopneas that are associated with cortical arousals (Rosen et al., 2018). Such limitations restrict their ability to provide accurate measurement of sleep-related respiratory events, thus, their estimates which are based on total recording time and hypopnoeas associated with oxygen desaturations only, may inevitably underestimate the severity of OSA (Lévy and Schiza, 2023).

Whilst home respiratory polygraphy has become the mainstay for OSA screening and diagnosis, this diagnostic device has additional limitations that I have personally encountered during my research experience in the UK.

As seen in **Figure 1.8** above, this device involves several sensors and components with wires that must be properly attached to the patient's nostrils, chest, and finger whilst asleep. Although this can be uncomfortable, it may also make patients feel apprehensive about the success of their sleep study which, in turn, leads to interrupted sleep. In addition, home respiratory polygraphy has a higher technical failure rate than in-hospital PSG and respiratory polygraphy (El Shayeb et al., 2014), which may consequently result in requiring patients to do one or more repeat sleep studies.

Asking patients to repeat their sleep study may exacerbate the burden of the diagnostic pathway, potentially leading to a delayed conclusive diagnosis and, thus, delaying the initiation of appropriate treatment. Whilst this may be minimised and partly addressed by providing increased training and support to patients, ensuring they can accurately set up the device and initiate the sleep study at their home; however, requiring further resources and time allocation would likely incur additional financial and organisational implications for sleep services.

Sleep services typically require patients with suspected OSA to attend the hospital to receive the sleep testing device and step-by-step instructions, and then to return the device after their overnight sleep study, for manual download and review of the sleep data before a diagnosis can be confirmed. This strategy is burdensome on sleep service staff, patients, and carers. It can also be a risk to ask those prone to excessive sleepiness to drive for a long distance to pick up their sleep testing device. Some sleep services mitigate these concerns by posting the sleep testing devices directly to patients, with prepaid reply envelopes for the return of equipment. Whilst this alternative strategy may replace patient travel, it incurs

considerable financial costs to sleep services due to postal services expenses and any sleep testing devices that may be lost on the way.

1.5.3. Severity classification of OSA

The severity of OSA is typically quantified by the measurements of PSG. The most commonly used metric is AHI, which is defined as the number of apnoeas and hypopnoeas per hour of sleep. Alternatively, respiratory disturbance index (RDI) may be used to classify OSA severity. RDI is defined as the number of apnoeas and hypopnoeas plus RERAs per hour of sleep (Kushida et al., 2005). However, if the sleep study was conducted using a sleep testing device that does not measure the TST, then the AHI and RDI are calculated based on the number of sleep-related respiratory events (apnoeas, hypopneas, and RERAs) per hour of total recording time (Kushida et al., 2005). By expert consensus, AASM proposed the following AHI thresholds for categorising the severity of OSA (Kapur et al., 2017):

- **Normal:** AHI of <5 events per hour
- **Mild OSA:** AHI of ≥ 5 to <15 events per hour
- **Moderate OSA:** AHI of ≥ 15 to <30 events per hour
- **Severe OSA:** AHI of ≥ 30 events per hour

Although widely used in health research, clinical practice, and medicolegal aspects of sleep apnoea, AHI has often been criticised for solely reflecting the total number of apnoeas and hypopnoeas that occur during sleep, and not capturing the effects of other relevant physiological and clinical features of OSA (Pevernagie et al., 2020, Soori et al., 2022). Thus, sleep researchers have been actively developing and investigating alternative metrics that incorporate the effects of hypoxic burden, arousal intensity, respiratory events, acute systemic effects, and chronic end-organ impact on patients with OSA; these metrics may become more widely used in the future (Malhotra et al., 2021, Randerath et al., 2018).

1.6. Digitally-enabled diagnostics for OSA

This section provides an overview of the implementation of digitally-enabled healthcare services within the NHS, a discussion of the COVID-19 pandemic impact on OSA clinical care delivery, and a description of a novel digitally-enabled diagnostic device for OSA.

1.6.1. Overview of digitally-enabled healthcare provision across the NHS

The use of digital technologies to improve healthcare services and experience of care is now a central principle of the NHS and the UK Department of Health strategies. In 2008, the “*High Quality Care For All*” report was published with a strategic and clear emphasis on the importance of ensuring timely access to care, improving diagnostics, and providing convenient care closer to home (Department of Health, 2008).

Several subsequent nationwide initiatives to explore the untapped potential of digital technologies to improve the safety, quality, and accessibility of healthcare, preceded the announcement of the NHS Long Term Plan in 2019 (National Health Service, 2019). This plan placed a national and strategic focus on utilising digital technologies; envisioning a markedly different model of care where digitally-enabled healthcare services are mainstream across the NHS, with a ‘digital first’ option being offered for most patients.

In 2023, the NHS Long Term Workforce Plan was launched (NHS England, 2023b), with a reiteration of the NHS intention to take full advantage of digital and technological innovations as set out in the policy paper: a plan for digital health and social care (2022). These reports highlighted that the safe widespread and accelerated adoption of reliable and effective innovations will change how healthcare services are delivered, enabling close-to-home and streamlined care pathways, faster diagnoses, and improved care in underserved areas (NHS England, 2023b).

Digital health is an umbrella term for the application of digital technologies in wellbeing and health care, which includes the use of wearables and mobile health, telehealth, and

telemedicine (Ronquillo et al., 2021). Virtual care, however, is often used interchangeably with telehealth or telemedicine to describe the provision of synchronous or asynchronous health and social care using a ‘*virtual*’ technology-enabled platform (Bhavnani and Sitapati, 2019). These emerging applications are changing how healthcare is delivered, and they have the potential to enable patient-centred, efficient, and cost-effective care even for hard-to-reach populations i.e. those who live in remote or rural areas (Jandoo, 2020, Imison et al., 2016, Peck et al., 2015).

Respiratory sleep medicine is regarded as a leading speciality in the utilisation of digital health technologies and virtual care strategies in a variety of settings. These include, but are not limited to, tediagnosis (Coma-Del-Corral et al., 2013), teleconsultation (Murphie et al., 2017), teletherapy, mobile health, and telemonitoring of patients using CPAP therapy (Hwang, 2016). Earlier studies suggested that the implementation of these approaches is potentially useful and effective in improving access to care, without impacting patient satisfaction and adherence to therapy (Isetta et al., 2014, Parikh et al., 2011).

An example of how digitally-enabled care has been effectively used within the NHS is the intelligent clinical decision support system, developed by Liverpool Sleep Centre at Aintree University Hospital NHS Foundation Trust (Biswajit et al., 2020). Liverpool Sleep Centre is one of the UK’s busiest sleep services, serving some of the most socioeconomically deprived areas in England (Liverpool City Council, 2019). The demand for their sleep services has markedly increased from 1,400 referrals in 2012 to over 5,000 in 2019. This increase can be partly explained by the increased awareness and recognition of OSA (Craig, 2022). The socioeconomic status of the population served may also be a contributing factor, whereby socioeconomic deprivation has been shown to be associated with an increased risk of OSA (Guglielmi et al., 2019, Soso and Matos, 2021).

The newly created end-to-end sleep management system that has been developed in Liverpool addresses this increase in demand by providing a digitally-enabled streamlined

pathway for the assessment, diagnosis, management and follow-up of patients with OSA. The system was designed to be used during both remote or in-person (face-to-face) consultations by either specialist or non-specialist sleep personnel, facilitating a faster initial assessment of suspected OSA and efficient CPAP therapy initiations (Chakrabarti et al., 2022).

In a patient cohort of 1,591 adults, less than 8% of patients required a virtual or in-person outpatient clinic appointment with a sleep consultant, compared to over 80% of patients prior to the implementation of the digitally-enabled sleep management system (Keane et al., 2022). Such a reduction in the number of consultant-review clinics (post-diagnostic sleep apnoea testing) with no safety concerns, liberates time to care for patients with complex sleep problems. An additional feature of this digitally-enabled system was the ability to generate a '*clinical dashboard*', allowing for real-time monitoring of both service-level and patient-level activities.

1.6.2. Digitally-enabled healthcare provision in the COVID-19 era

The use of digital health and virtual care in the treatment and management of OSA accelerated during the COVID-19 pandemic (British Sleep Society, 2020, Schiza et al., 2021). The priority of controlling the coronavirus infection placed digital health and virtual care at the forefront of both national and international healthcare responses (Gunasekeran et al., 2021), accelerating the acceptance and adoption of these care strategies by governments, healthcare professionals, and patients (Ting et al., 2020).

The COVID-19 pandemic has profoundly impacted respiratory sleep services provision in the UK (British Sleep Society, 2020), where some centres had to move from in-person care to remote care – a shift in practice that is likely to persist (National Institute for Health and Care Excellence, 2021a, Schiza et al., 2021). Currently, sleep services in the UK are utilising advanced technologies for treating, monitoring, and managing patients with OSA. However, diagnostic pathways for OSA remain heavily reliant on sleep apnoea testing devices that are time-consuming and potentially costly, even when performed in patients' own homes.

Therefore, innovative digital health technologies for the provision of OSA diagnosis were explored in this Thesis.

1.6.3. Novel digitally-enabled diagnostics for OSA

In recent years, researchers and manufacturers have developed several efficient and reliable digital health technologies for the diagnosis of OSA (Verbraecken, 2013). Mandibular movement (MM) monitoring, coupled with automated machine-learning analysis, is one of the novel digital health technologies that has been developed for remote OSA diagnosis. It is categorised in the SCOPER framework (described in **Section 1.5.2**) as $S_3C_0O_0P_2E_4R_5$ (Pépin et al., 2020). *In this Thesis, I have used MM monitoring in the randomised controlled study of a remote diagnostic pathway for OSA (presented in **Chapter 2**).*

1.6.4. Physiology of mandibular movement monitoring

In **Section 1.3.2**, I discussed the pathophysiology of OSA, including how pharyngeal airway narrowing is partly caused by the decreased tone of upper airway dilator muscles during sleep, in some patients with OSA. Many of the upper airway muscles are attached directly to the mandible, or indirectly *via* the hyoid bone (Rivlin et al., 1984), as illustrated in **Figure 1.10**. Thus, mandibular movement plays a role in stabilising the pharynx and maintaining upper airway patency during sleep (Martinot and Pépin, 2023, Malhotra et al., 2023).

The neural and anatomical interactions between the mandible and hyoid bone, and multiple muscles surrounding the upper airway contribute to airway patency (Ayappa and Rapoport, 2003). In a complex interaction, the mandible provides an anchoring structure to the upper airway muscles, plus the surrounding soft tissues, whilst also acting as an intricate lever where muscle contractions result in either movement of the mandible or stiffening of the upper airway dilator muscles (Ayappa and Rapoport, 2003). The position of the mandible is, therefore, central for supporting the function of these muscles and determining the patency and collapsibility of the airway (Isono et al., 2004), closely reflecting the central respiratory control during sleep.

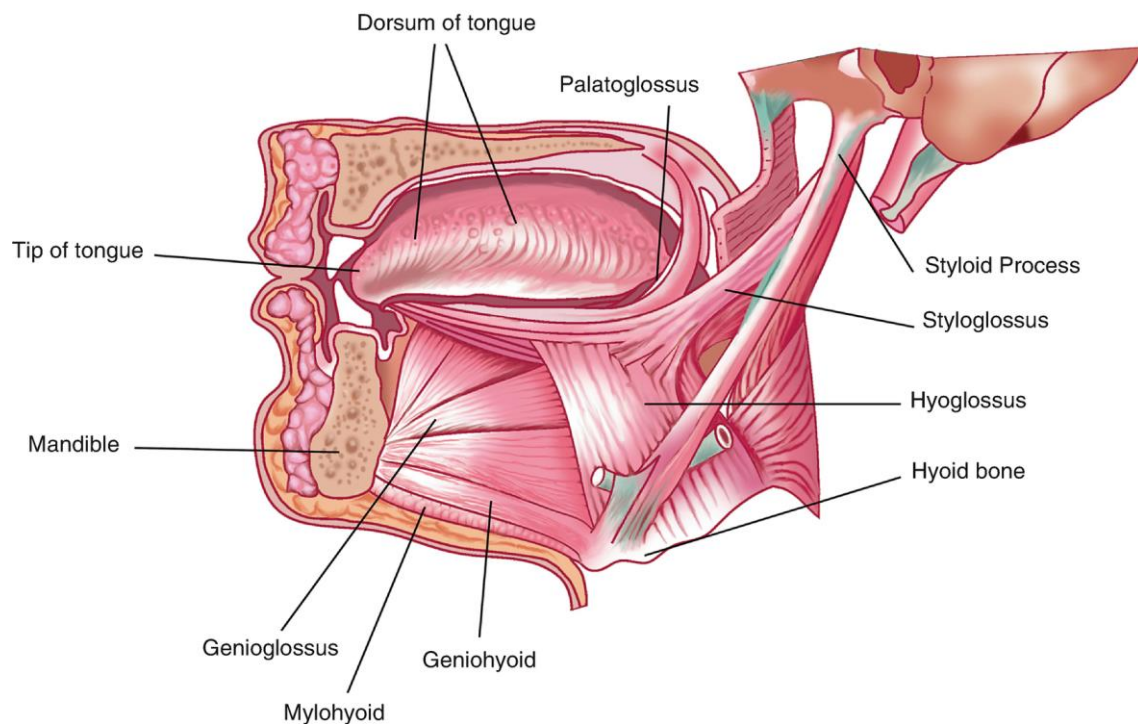


Figure 1.10 A lateral view anatomical illustration of some of the important upper airway dilator muscles that intricately work together to maintain upper airway patency during sleep. These muscles are attached directly to the mandible, or indirectly via the hyoid bone. Adapted from (Rathod et al., 2018) and reproduced with permission of Springer Nature.

Respiratory-related mandibular movement during sleep, in both healthy subjects and patients with OSA, was first described by Hollowell and Suratt (1991). Subsequent physiological studies that investigated the association between MM biosignals and sleep-related respiratory activities demonstrated that MM monitoring may:

- distinguish between sleep and wake states (Senny et al., 2009),
- differentiate between different sleep stage-related respiratory events (Tsuda et al., 2011),
- detect salient MM patterns as a surrogate measure for arousals (Maury et al., 2013),
- and closely correlate with crural diaphragmatic EMG in identifying changes in respiratory effort during normal sleep and sleep-related respiratory events (Martinot et al., 2017).

These studies have used either magnetometry techniques or a single point-of-contact sensor to record the MM biosignals, demonstrating that these biosignals exhibit distinct MM patterns, frequencies, and amplitudes during different sleep stages and sleep-related respiratory

events (Martinot and Pépin, 2023). The analysis of MM biosignals may therefore provide information for the diagnosis of OSA, and other forms of respiratory sleep disorders.

Figure 1.11 shows an example of MM biosignals embedded within a PSG epoch of obstructive apnoea and hypopnea episodes. It can be seen that increasing respiratory effort, during obstructive events, is also depicted by MM biosignals, which measure the rotational speed movement of the mandibular jaw. MM biosignals also reflect the position of the mandibular jaw relative to gravity, whereby a negative signal indicates that the mouth is opening until an arousal occurs, which results in an abrupt mouth closure followed by airflow restoration (Martinot and Pépin, 2023). The opposite pattern is observed during central events which are characterised by a decreased or absent MM amplitude with a slight passive mouth opening due to the decreased respiratory central drive (Martinot et al., 2019).

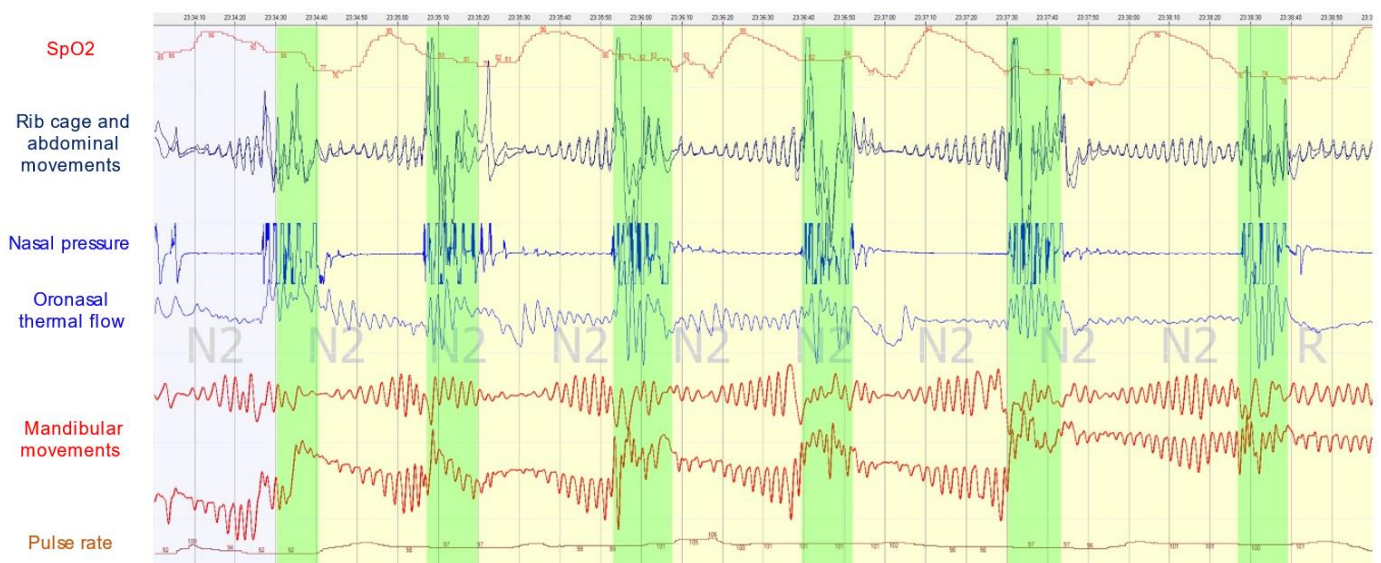


Figure 1.11 An epoch of polysomnography (PSG) with mandibular movements (MM) biosignals embedded to illustrate the relationship between MM and other bio-parameters during obstructive apnoea and hypopnea episodes. MM biosignals are captured by a gyroscope that measures the rotational speed movement of the mandibular jaw (**Top**) and an accelerometer that reflects the position of the mandibular jaw relative to gravity (**Bottom**). Adapted from Pepin et al. (2022) and reproduced under the CC BY-NC Licence.

1.6.5. The use of mandibular movement monitoring for the diagnosis of OSA

The MM monitor used in this Thesis was the Sunrise solution (Sunrise SA, Belgium), which was developed and validated as part of the 'SENSAPNEA' entrepreneurship grant, sponsored by the European Institute of Innovation and Technology (EIT), a body of the European Union.

The SENSAPNEA project was set up in 2019 to develop and validate a simple, end-to-end, digitally-enabled solution for sleep apnoea diagnosis and this objective was driven by the EIT Health focus areas: bringing care to home and improving care pathways for value-based care (EIT Health, 2019). The project was coordinated by Prof Jean-Louis Pepin from Grenoble Alpes University and was carried out in collaboration with a consortium of international and leading experts in various fields, including our research group at Imperial College London for clinical research, Fondation de l'Avenir for economic analysis, Docapost for data storage, and Neoma and Probayes for artificial intelligence (AI) solutions (EIT Health, 2019).

Data arising from this work added to the preliminary effectiveness evidence of the Sunrise solution, which is now an FDA-cleared, CE-marked, and commercially available medical device for the diagnosis of sleep apnoea in adults (Pépin et al., 2020). *The Sunrise solution monitors used in this Thesis were donated to our research group by Sunrise SA, Belgium to conduct the investigator-led randomised controlled study (presented in **Chapter 2**), with no other input to the research I carried out.*

Figure 1.12 shows the MM monitor (Sunrise solution) which comprises of (EIT Health, 2019):

- a novel, 3-gram, recyclable chin sensor for the measurement of MM,
- a smartphone application (compatible with both Android and iOS) for external control and data recording,
- and a secure cloud-based platform for patient data management.



Figure 1.12 *The Sunrise solution sensor with the associated smartphone application (Sunrise SA, Belgium) used in the research conducted for this Thesis (Top). An individual wearing the single-use, coin-sized, recyclable sensor, attached to the chin at the mentolabial sulcus to allow for the measurement of mandibular movements during sleep (Bottom). Adapted from the Clinical Compendium of Sunrise (2022) and reproduced with permission of Sunrise SA.*

The non-invasive measurement of MM is based on the position and rotational movements of the mandible, which are captured by an accelerometer and a gyroscope (see **Figure 1.11** above). These biosignals are then processed using validated machine-learning algorithms to allow for the identification and classification of sleep and wakefulness states (TST), sleep stages (wakefulness, light, deep, or rapid eye movement sleep), sleep-related respiratory events (obstructive respiratory disturbance index [ORDI], estimated AHI, and RERAs), respiratory effort, arousal movements, and body position (Pépin et al., 2020).

The sleep study, with the MM monitor (Sunrise solution), is typically performed at home. Patients are required to download a smartphone application first, which helps onboard users with step-by-step instructions and also collects demographic data. ESS, insomnia severity index (ISI), and other patient-reported data such as symptoms are also recorded. Patients are then asked to apply the coin-sized sensor to their chin at the mentolabial sulcus before initiating the overnight sleep study, which requires a continuous internet connection with Wi-Fi or 3G/4G.

The measurement unit inside the sensor connects *via* Bluetooth to a smartphone application. The recorded data is then transferred into a secure cloud-based platform, which uses dedicated machine-learning algorithms for automated analysis. Immediately after the sleep study, the associated platform generates a diagnostic report made available to both healthcare providers and patients. If needed, raw sleep data may be accessed and manually reviewed by the healthcare provider. **Figure 1.13** shows an example of an original diagnostic report generated automatically by the Sunrise solution platform, which is the platform used to access and review the sleep studies performed by the MM monitor (Sunrise solution).



sleep report

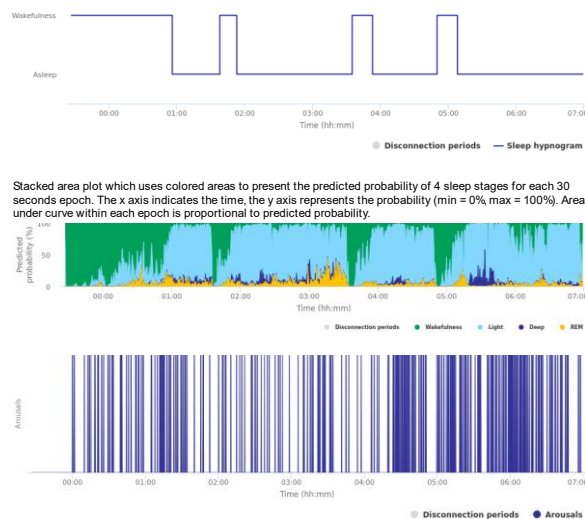
Summary (1/3)

Complaints	I snore - I stop breathing at night - I feel unusually tired during the day
Epworth sleepiness scale	20 points - Severe excessive daytime sleepiness
Insomnia severity index	20 points - Moderate insomnia
Date of the test (dd/mm/yyyy - end of the recording)	08/02/2023
TST (hh:mm)	06:05
Total sleep time	
Arl (events/hour)	49.9
Arousal index	
ORDI (events/hour)	36.2
Obstructive respiratory disturbance index	
Estimated AHI (events/hour)	60.6 [58.9 - 62.2]
Estimated apnea hypopnea index	
RE (% of TST)	78%
Cumulative duration of increased respiratory effort	
Alcoholic drinks before going to bed	No
Stimulants or sedatives before going to bed	No
Medical treatment impacting sleep	No
Comment	-
How did the test go?	
No problem occurred during the sleep test.	



Sunrise sleep report

Summary (2/3)



Sunrise sleep report

Summary (3/3)

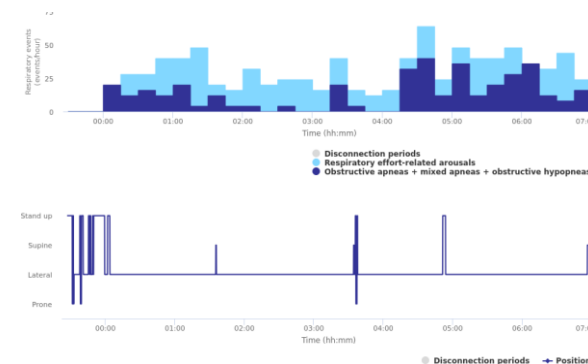


Figure 1.13 An anonymised original diagnostic report generated automatically following an overnight home sleep study using the mandibular movement monitor (Sunrise solution; Sunrise SA, Belgium). The diagnostic report suggests the presence of severe obstructive sleep apnoea (OSA) in an adult patient referred for investigation of suspected OSA. Repetitive obstructive apnoeas and hypopnoeas with an obstructive respiratory disturbance index (ORDI) of 36.2 events per hour and an estimated apnoea-hypopnoea index (AHI) of 60.6 events per hour are seen. Associated respiratory effort-related arousals (RERAs) are also seen.

1.6.5.a: Clinical validation studies of the Sunrise solution for OSA diagnosis

Sunrise solution incorporates both OSA diagnostics and remote delivery of healthcare. The development of this novel digital health technology was based on the physiological association between MM biosignals and sleep-related respiratory events (Malhotra et al., 2023); see **Section 1.6.4** for further details.

Sunrise solution may support the diagnosis of OSA due to its ability to identify obstructive and mixed apnoeas and hypopnoeas, plus RERAs based on stereotypical MM patterns (Martinot et al., 2017b, Martinot et al., 2015). It also distinguishes between sleep and wakefulness states, enabling accurate measurement of TST for precise estimates of sleep-related respiratory indices (Le-Dong et al., 2021). This novel diagnostic device has been validated in clinical and real-world settings.

In a prospective, diagnostic study of a clinical referral population ($n = 376$) of adult participants with suspected OSA in Belgium, Pépin et al. (2020) compared the automated analysis of MM by the Sunrise solution with a simultaneous in-laboratory PSG. The PSG data were manually and independently scored by two experienced professionals. MM-derived RDI reliably identified patients with PSG-RDI of ≥ 5 events per hour or ≥ 15 events per hour, with a high accuracy of 0.92 and 0.88, respectively. This agreement between the two diagnostic strategies in detecting RDI showed reliable agreement in patients without OSA (mean difference [95% confidence intervals]: 1.31 [−1.05 to 3.66] events per hour) and those with mild OSA (mean difference [95% CI]: −0.69 [−3.77 to 2.38] events per hour). However, MM monitoring was also found to systematically underestimate RDI by a mean difference of −11.74 (95% CI: −20.83 to −2.67) events per hour, compared to in-laboratory PSG, in patients with moderate or severe OSA (predominantly in those with PSG-RDI of ≥ 40 events per hour). The authors argued that the underestimation may not be clinically relevant, in terms of treatment decisions for those with moderate or severe OSA. In addition, they

highlighted that these discrepancies would be addressed in the ongoing iterative algorithmic development of the Sunrise solution (Pépin et al., 2020).

A further cross-sectional study of adult patients ($n = 38$) with mild to severe OSA compared MM biosignals, recorded by the Sunrise solution, with esophageal pressure signals (P_{es}), the gold standard method for measuring respiratory effort changes during sleep (Pépin et al., 2022). Participants underwent a simultaneous overnight sleep study using the Sunrise solution, and in-laboratory PSG with an invasive intrathoracic catheter measuring P_{es} . The resultant 8,042 signal sequences extracted from both MM and P_{es} monitoring were analysed. The findings demonstrated that MM biosignals reliably differentiate between normal breathing, obstructive, mixed, and central apnoea periods. Thus, MM monitoring could be used as a non-invasive surrogate of P_{es} for reliable measurement of respiratory effort (Pépin et al., 2022).

In a recent diagnostic study, the Grenoble group, in collaboration with our research group, evaluated the applicability of MM monitoring for OSA diagnosis in real-world settings (Kelly et al., 2022). Adult patients ($n = 40$) with suspected OSA underwent a single overnight in-home PSG with simultaneous MM monitoring. The automated MM analysis, recorded by the Sunrise solution, was compared to the in-home PSG sleep studies, which were manually and independently scored by two international sleep services (Royal Brompton Hospital in London, UK and Grenoble Alpes University Hospital in Grenoble, France). This study showed that MM monitoring coupled with automated machine-learning analysis was comparable to manually scored in-home PSG for the diagnosis of patients with suspected OSA, with good agreement between MM-derived ORDI and the 2-scorers averaged PSG-ORDI (median bias [95% CI]: 0.00 [−23.25 to 9.73] events per hour).

The agreement in ORDI between the two diagnostic devices was similar to the agreement in PSG scoring between the two sleep services, London and Grenoble (median [95% CI]: −3.40 [−22.80 to 14.00] events per hour). Consistent with the findings from previous validation

studies, Kelly et al. (2022) reported systematic bias across OSA severity, whereby MM monitoring underestimated ORDI by -8.70 (95% CI: -28.46 to 4.01) events per hour, compared to in-home PSG, in patients with moderate or severe OSA (those with a PSG-ORDI of ≥ 15 events per hour). In terms of the diagnostic performance of MM-derived ORDI for the OSA severity thresholds based on PSG-ORDI of 5, 15, and 30 events per hour, the receiver operating characteristic (ROC) analysis showed high performance for each threshold; 0.92, 0.90, and 0.91, respectively.

Taken together, the clinical validation studies of the MM monitor coupled with automated machine-learning analysis (Sunrise solution) demonstrate its applicability and reliability for the diagnosis of OSA. The use of this novel digital health technology could modify the diagnostic pathway for adult patients with suspected OSA, potentially providing timely access to diagnosis and, thus, accelerating treatment provision. It may also be a cost-effective alternative to the commonly used respiratory polygraphy. In the UK, the cost of an in-hospital sleep study with respiratory polygraphy is approximately £636, which is three times the cost of a home respiratory polygraphy sleep study (*based on data from 2020*: National Institute for Health and Care Excellence, 2021), and seven times the cost of the Sunrise solution which is commercially available at £89 for a one-night single-use sleep study (excluding clinical time).

1.6.5.b: Ongoing evaluation of the Sunrise solution for OSA diagnosis

Further to the physiological and clinical studies conducted to evaluate its validity as a diagnostic device, Sunrise solution is currently being evaluated from a healthcare provision perspective. It is now being evaluated within the OSA diagnostic pathways of four regional healthboards across NHS Scotland (Glasgow, Edinburgh, Dundee, and Inverness). The interim results of the randomised controlled study (presented in **Chapter 2**) informed this ongoing service evaluation, which aims to assess the clinical applicability of Sunrise solution as a first-line screening tool for adult patients with suspected OSA in Scotland.

Furthermore, the NICE Diagnostics Assessment Programme recently commissioned an evidence assessment and analysis report. The *Southampton Health Technology Assessments Centre* is leading the project, as an external assessment group. This diagnostic assessment aims to assess the clinical effectiveness and cost-effectiveness of several novel home-testing devices in diagnosing and assessing the severity of OSA.

Sunrise solution is amongst the selected diagnostic devices for this assessment, and I have been approached to share the results of the randomised controlled study (presented in **Chapter 2**) to be included in their analysis. They stated that the evidence arising from this analysis will support the NICE Diagnostics Assessment Programme in the development of their guidance on using these novel diagnostic devices in the NHS.

1.6.5.c: Limitations of the Sunrise solution

Sunrise solution is not recommended for use in patients with anatomical abnormalities affecting the rotational movement of the mandible and those with thick beards; both of which may impact the quality of the MM sensor recordings. Whilst, in principle, the neural and anatomical interactions between the mandible and upper airway dilator muscles during sleep are likely to be similar across individuals, suggesting no systematic reason that MM monitoring would operate differently in males and females, and across different ethnicities, there is a lack of published data on the validity of the Sunrise solution in detecting OSA or assessing its severity in specific patient subgroups, such as those with severe obesity and individuals from different ethnic backgrounds. Another limitation of the Sunrise solution, and most emerging digital health technologies, is the requirement for digital literacy and connectivity, which may exacerbate the '*digital divide*' and health inequalities in the delivery of OSA care. Although there has been a rising adoption of online 'internet' use across all ages, it was reported in 2017 that 1 in 10 UK households do not have internet access (Office for National Statistics, 2017), and they may potentially be digitally excluded. This data makes the point that widespread implementation of these diagnostic devices within the NHS may

restrict access to OSA care, specifically in rural and socioeconomically deprived areas with limited access to quality internet, and possibly lower digital literacy (Blanc et al., 2023).

1.7. Overview of clinical management for OSA

Following the diagnosis of OSA, appropriate treatment and subsequent monitoring of the effectiveness of the treatment prescribed are needed. This section provides an overview of currently available OSA treatments and follow-up management strategies for patients with OSA.

Prior to the 1980s, the treatment options for patients with severe OSA were limited to chronic tracheostomy (Dement, 1998). This treatment was considered unacceptable amongst many in the clinical community and patients, which posed a barrier to the expansion of OSA care (Dement, 1998).

In 1981, an alternative treatment was introduced in the US (Fujita et al., 1981). This was uvulopalatopharyngoplasty (UPPP), a surgical approach to correct the anatomical abnormalities in patients with OSA. Despite its short-lived popularity at the time, subsequent surgical techniques have been developed and some data on UPPP effectiveness in ameliorating OSA consequences has been published (Dement, 1998, Caples et al., 2010).

CPAP therapy is the first-line treatment for OSA. It was introduced in 1981 in Australia (Sullivan et al., 1981). This treatment was relatively more tolerable than tracheostomy or surgical UPPP, and its positive effectiveness in treating OSA accelerated the diagnosis of OSA worldwide (Dement, 1998).

1.7.1. Current treatments for OSA

Current treatment options for OSA can be broadly categorised into three types of interventions: behavioural, medical, and surgical. This section will briefly discuss these interventions and will also provide a summary of evidence for CPAP therapy, which is considered the treatment of choice for most patients with OSA.

The goal of all treatments for OSA is to establish a stable breathing pattern and normalise oxyhaemoglobin levels and cardiovascular parameters during sleep, prevent snoring, eliminate sleep fragmentation, and promote enhanced alertness during daytime (Verbraecken et al., 2023).

Behavioural interventions, specifically lifestyle modifications, are commonly used as an adjunct ‘*add-on*’ treatment for OSA. These interventions may include advice on physical activity, weight management, smoking cessation, alcohol intake, and sleep hygiene.

NICE clinical guidelines recognise the importance of such interventions due to their association with the presence or severity of OSA, thus, a personalised discussion of appropriate lifestyle changes is recommended for all patients newly diagnosed with OSA. Lifestyle advice should be provided along with the appropriate primary treatment chosen with the patient, except in patients with asymptomatic mild OSA where lifestyle advice alone can help prevent the condition from worsening (National Institute for Health and Care Excellence, 2021a). However, whilst these interventions alone may lead to improvement in OSA symptoms and severity, they are insufficient as the sole treatment strategy for symptomatic OSA (Araghi et al., 2013, Jung et al., 2019).

Medical treatments include CPAP therapy, the recommended first-line treatment for OSA. **Figure 1.14** shows an original illustration of the mechanism of CPAP therapy, which works as a pneumatic splint, considerably decreasing or eliminating respiratory-related events during sleep, by maintaining upper airway patency through the constant delivery of positive pressure, *via* a mask interface over the mouth, nose, or both (Pavwoski and Shelgikar, 2017).

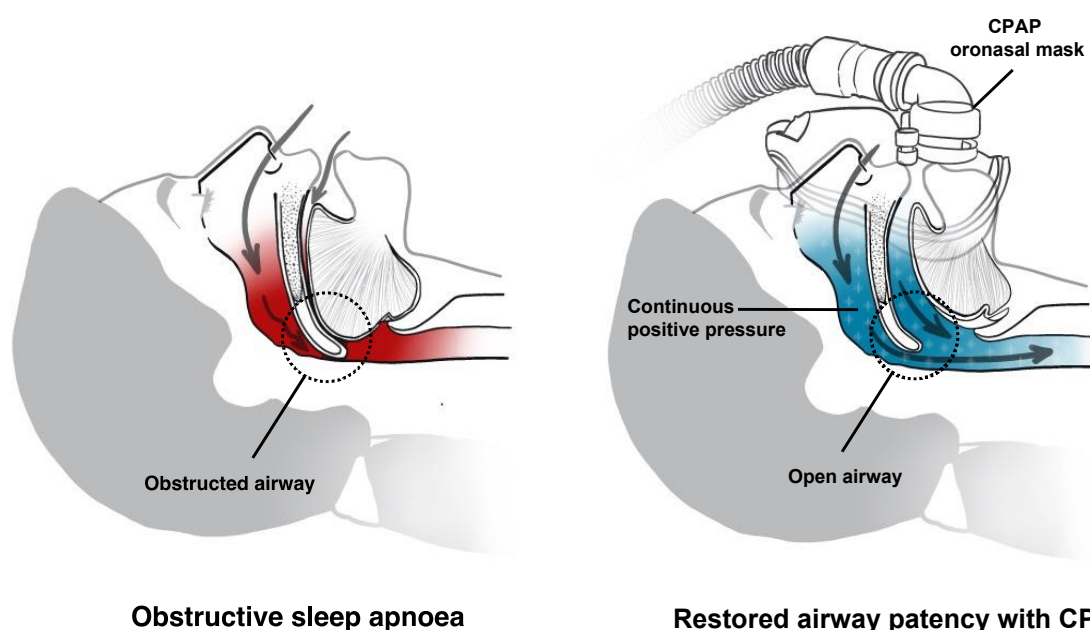


Figure 1.14 An original illustration of the mechanism of the treatment of obstructive sleep apnoea (OSA) with continuous positive airway pressure (CPAP) therapy. Note the obstructed airway due to the sleep-related respiratory events associated with OSA (**Left**). Positive pressure delivered by the CPAP therapy via an oronasal mask restores the patency of the upper airway (**Right**).

1.7.1.a: The therapeutic benefit of CPAP therapy for OSA

Nearly two decades after the first publication (Sullivan et al., 1981) on the use of CPAP therapy in OSA, the Centre for Reviews and Dissemination (University of York, UK) published a review of evidence on CPAP therapy effectiveness (Wright et al., 1997). This review highlighted a lack of robust clinical and cost-effectiveness evidence, concluding that the role of “CPAP therapy in improving health outcomes has been poorly evaluated” in patients with OSA.

The Wright report provoked a scientific debate and motivated further research on the topic (Simonds, 2008). Subsequent systematic reviews and meta-analyses have evaluated the effectiveness of CPAP therapy in patients with OSA (Neil, 1998, Giles et al., 2006) and, in 2008, NICE issued its landmark Health Technology Appraisal (HTA) of CPAP therapy. Their HTA guidance, which was based on both a systematic review and economic analysis (see **Section 1.4.4** for details on NICE guidelines development), provided unequivocal evidence supporting the use of CPAP therapy as a cost-effective treatment of choice for adults with

moderate or severe symptomatic OSA (National Institute for Health Care Excellence, 2008). Such evidence-based recommendations have markedly impacted the provision of sleep services in the UK.

The therapeutic benefit of CPAP treatment has traditionally been investigated by evaluating improvements in daytime symptoms. The assessment of subjective daytime sleepiness, using ESS scores (see **Section 1.5.1** for a detailed description), was therefore highlighted in the NICE HTA review. The meta-analysis of 23 randomised controlled trials (RCTs) showed a significant reduction in daytime sleepiness in patients treated with CPAP therapy, compared to those allocated to placebo or usual care (weighted mean difference in ESS scores [95% CI]: -2.7 [-3.5 to -2.0] points). This reduction lies within the MCID of ESS improvement, which was estimated to be between -2 and -3 points (Patel et al., 2018).

In a later UK multicentre RCT of patients with minimally symptomatic OSA ($n = 391$), Craig et al. (2012a) reported that CPAP therapy was associated with improvements in both subjective and objective daytime sleepiness, despite a relatively-low CPAP usage (median [IQR]: 2:39 [0:36 – 4:59] hours per night). In addition to ameliorating daytime sleepiness, CPAP therapy also improves HRQoL, daily functioning, vitality and workplace productivity, and significantly reduces the risk of occupational injuries (Siccoli et al., 2008, Schein et al., 2014, National Institute for Health and Care Excellence, 2008, Antonopoulos et al., 2011, Rejón-Parrilla et al., 2014). The initiation of CPAP therapy was also found to decrease accident rates, both in real-life and virtual simulation environments; supporting the role of OSA treatment in preventing road traffic accidents (Antonopoulos et al., 2011). Treating patients with CPAP may also reduce the risk of OSA-related comorbidities such as stroke, hypertension, and cardiovascular disease (Chaiard and Weaver, 2019).

Due to a lack of evidence at the time, the effectiveness of CPAP therapy in patients with mild OSA was not covered in the 2008 NICE HTA guidance. Several subsequent studies have addressed this gap in knowledge, including a recent multicentre RCT, published by our

research group in collaboration with the UK Respiratory Sleep Research Network. Participants in the MERGE trial (n= 233) were allocated to either 3 months of CPAP plus standard care (sleep counselling), or standard care alone (Wimms et al., 2020). A significant improvement in vitality, measured by the 36-Item Short Form Health Survey (SF-36), was observed in patients treated with CPAP, compared to those allocated to standard care alone.

The centralised ongoing patient support protocol, implemented during the MERGE trial, resulted in good CPAP usage (median [IQR]: 4:00 [1:36 – 5:44] hours per night) at 3 months. These findings, along with data from five additional studies, were incorporated into the current NICE clinical guidelines, which now recommends CPAP therapy for patients with mild symptomatic OSA that affects their QoL and usual daytime activities (National Institute for Health and Care Excellence, 2021a).

1.7.1.b: Adherence to CPAP therapy

The therapeutic benefit of CPAP is contingent on optimal adherence to treatment (Rotenberg et al., 2016b). However, adherence to CPAP therapy remains a challenge despite its positive effects on health and HRQoL, and the ongoing advances in technology such as the user interface (Weaver and Sawyer, 2010). It has been suggested that higher CPAP usage is associated with greater objective and subjective therapeutic benefits, with ≥ 4 hours per night for $\geq 70\%$ of nights being the generally accepted minimum (Weaver, 2019). Although this adherence threshold is commonly used, the impact on daytime outcomes, compared to other lower or higher cutoff values has not been extensively investigated and, therefore, modifications to this current threshold may be warranted to address what matters most to patient clinical outcomes (May et al., 2023).

Newer CPAP therapy machines have the advantage of facilitating continuous monitoring of treatment usage, with objective data on a nightly and monthly basis (*via* telemonitoring). Unfortunately, adherence rates remain low in the UK, with less than half of patients using their CPAP therapy for ≥ 4 hours per night for $\geq 70\%$ of nights (Dielesen et al., 2021, Cowen

et al., 2023). This not only affects patient clinical and economic outcomes, but also underestimates the therapeutic effect size, limiting the evaluation of CPAP therapy effects on OSA-related comorbidities in clinical trials (Weaver, 2019).

Patients with OSA tend to overestimate their CPAP therapy adherence when assessed *via* self-reported means as opposed to objective monitoring (Rotenberg et al., 2016b). Thus, reliable assessment of CPAP therapy adherence may require the use of machine-documented data either through downloadable SD cards or telemonitoring. Low adherence to CPAP therapy is difficult to predict in advance, however, previous data suggest that adherence may be influenced by several patient and clinical characteristics, including socioeconomic status, smoking, social support, OSA severity, the initial 90-day compliance, and treatment side effects (Mehrtash et al., 2019, Kohler et al., 2010, Cowen et al., 2023).

1.7.1.c: Non-CPAP therapies for OSA

If patients with OSA do not accept or tolerate the use of CPAP therapy, alternative treatment options may be offered. These interventions include MADs, which prevent upper airway collapse by the displacement of soft tissue and mandibular protrusion (Basyuni et al., 2018). Positional therapy, which prevents patients from sleeping in the supine position, may also be a treatment option for patients with positional OSA (ALQarni et al., 2023). In selected patients, surgical interventions may be suitable to treat their OSA. These surgical approaches and procedures are typically performed to correct anatomical abnormalities in the upper airway, using a variety of procedures which require different expertise (Carvalho et al., 2012). The selection of which alternative treatment option is appropriate for the patient depends on their OSA clinical phenotype, anatomical traits, health status, and preferences.

1.7.2. Follow-up management for OSA

NICE clinical guidelines recommend that all treated patients should be monitored and supported to optimise their therapy, as discussed in **Section 1.4.4** above. Ongoing support and follow-up management vary from centre to centre, and may include evaluation of

treatment tolerance and acceptability, usage of CPAP therapy, OSA-related symptoms, daytime sleepiness, HRQoL, driving status, and disease severity in terms of improvement in AHI or ODI (Murphie et al., 2018, Maury and Testelmans, 2023).

Follow-up care of patients treated with CPAP therapy has traditionally been conducted during an in-person visit at their local sleep service, which can be burdensome for patients and healthcare professionals. Remote follow-up visits, also known as virtual or tele consultations, have been increasingly used in recent years as an acceptable alternative to in-person follow-up care, and are viewed to facilitate additional opportunities for timely patient support, education, and early intervention for treatment adherence issues (Bruyneel, 2019, Weaver, 2019).

Virtual consultations, using technology-enabled CPAP therapy monitoring, as occurred during the COVID-19 pandemic, reduce the number of patient visits to the sleep service and, consequently, reduce departmental footfall (Allen, 2021). This advantage was critical to preventing the spread of COVID-19 infections in hospitals whilst having the option to continue supporting patients with their CPAP therapy, albeit remotely.

Current NICE clinical guidelines recommend an initial (in-person, video, or phone) consultation with a review of telemonitoring data, if available, within one month of initiating CPAP therapy in patients with OSA. Further follow-up should be tailored to patients' needs, and once effective CPAP treatment is achieved, a yearly follow-up of patients is recommended. In addition, these patients should have access to their local sleep service for additional advice, support, and treatment equipment when needed (National Institute for Health and Care Excellence, 2021a).

This intensive management strategy adds to the strain on respiratory sleep services already coping with the increasing demand, as discussed in **Section 1.4.2** above. Therefore, further investigation of these follow-up management strategies from patient, clinical, and economic

perspectives is needed. *In this Thesis, I have investigated the effectiveness of virtual consultations, compared to in-person consultations, on patient-reported sleepiness and cost-effectiveness (see **Chapter 4**). I have also investigated patient experiences of, and preferences for, remote versus in-person CPAP therapy initiation and follow-up care (see **Chapter 5**).*

1.8. The role of patient experiences and preferences in the management of OSA

This section highlights the importance of understanding healthcare delivery from patient perspectives to facilitate the provision of person-centred care, which relies on ensuring that the preferences, needs, and values of people are incorporated into their personalised clinical care (Health Education England, 2017). *Further discussion on the quantitative and qualitative methodologies used for the evaluation of patient experiences and preferences is presented in the relevant chapters of this Thesis (see **Chapters 3 and 5**).*

The notion of person-centred care is not new to today's healthcare, rather it has been advocated for since the classical period, as depicted in a hypothesis commonly ascribed to Hippocrates (460-377 BCE): "*It is more important to know what sort of person has a disease than to know what sort of disease a person has*" (Coulter and Oldham, 2016). Thus, the provision of person-centred care requires a comprehensive understanding of patient perspectives, and active collaboration between patients, their families, and healthcare professionals to allow for the provision of personalised diagnostic and management care, encouraging shared decision-making (Coulter and Oldham, 2016). This is particularly important for patients with chronic conditions that typically involve continuity of care.

As set out in the NHS Long Term Plan, discussed in **Section 1.6.1**, digitally-enabled healthcare services will facilitate the redesign of clinical care pathways (National Health Service, 2019); with a '*digital first*' option being offered to most patients. This is likely to

change how healthcare is delivered and will inevitably, positively or negatively, impact patient experiences of care.

The NHS defines patient experience as “*what the process of receiving care feels like for the patient, their family and carers.*”, and, indeed, it describes “*each patient’s experience as the final arbiter in everything the NHS does*” (NHS Institute for Innovation and Improvement, 2013). Patient experience is also regarded as the third pillar that completes the triangle of high-quality care (NHS Institute for Innovation and Improvement, 2013, Kruk et al., 2018, Department of Health, 2008). Therefore, the evaluation of patient experience may be considered as essential as that of clinical effectiveness and patient safety.

Additionally, a systematic review of the relationship between these pillars of high-quality care showed a positive association between patient experience and both clinical effectiveness and patient safety (Cathal et al., 2013). The review also reported that patient experience was positively associated with subjectively and objectively measured health outcomes, including adherence to prescribed treatment and utilisation of healthcare services (Cathal et al., 2013). These findings encourage a comprehensive evaluation of all the pillars of high-quality care, rather than investigating them in silos, particularly when designing or assessing clinical care pathways for patients with specific conditions.

Although OSA is a common chronic condition with multiple clinical consequences that impact patients differently, little is currently known about patient experiences and preferences for OSA clinical care in the UK.

A notable report on the experiences of patients living with OSA was published by the BLF (now known as Asthma + Lung UK) as part of a wider OSA awareness campaign in 2014 (British Lung Foundation, 2014). This UK-wide survey (n= 2,671 participants) considered the lack of nationally agreed minimum standards for OSA referral, assessment, diagnosis, treatment, and management at that time. The survey, therefore, was conducted to explore

patient experiences throughout the clinical care pathway, from initial symptom recognition to treatment and management. The findings will be discussed further in **Chapter 5**; however, they are now outdated and, therefore, are unlikely to reflect current patient perspectives due to the considerable changes in OSA clinical care in recent years, specifically post-COVID-19 pandemic.

*In this Thesis, I have addressed this gap in knowledge by evaluating patient experiences of, and preferences for, OSA diagnostic and clinical management pathways in adult patients with a suspected, or existing OSA diagnosis (see **Chapters 3** and **5**).*

1.9. Real-world background on OSA clinical care pathways: a review of focused discussions with clinical leads within the UK

1.9.1. Rationale

I started my PhD programme of research in January 2021, during the second wave of the COVID-19 pandemic in the UK, with the first month of my studies spanning both the highest peak of positive COVID-19 cases and the introduction of a nationwide lockdown (Office for National Statistics, 2021).

Respiratory sleep services were profoundly impacted and most of their respiratory personnel were deployed to COVID-19 care, placing a huge burden on most sleep centres (see **Section 1.6.2** for further details). This has resulted in widening the variation in sleep services provision, and potentially increasing the backlog of demand across the UK. Some sleep centres had the infrastructure and capacity to move to remote care, whilst others had to pause their services.

My research group and I anticipated that these substantial changes would affect OSA care provision, however, nationwide data were lacking. Thus, whilst working remotely, I proactively investigated ways in which I could further my understanding of healthcare delivery for patients with OSA in the UK. With the support of my supervisors, and the UK Respiratory

Sleep Research Network, I was able to investigate OSA clinical care pathways from healthcare professionals' perspectives *via* informal remote discussions.

This section presents a synopsis of the real-world delivery of OSA clinical care in the UK as a background to the research presented in my Thesis. The collected information helped inform and provide the context for the subsequent studies of my PhD programme of research.

1.9.2. Methods

A purposeful sample of sleep consultants in different sleep services across the UK were invited to one-to-one informal discussions. The semi-structured interview guide shown in **Figure 1.15** was developed following discussions within our research group (see **Chapter 3, Section 3.2.3** for a discussion on semi-structured interviews and topic guide development). The informal discussions (duration 20-30 minutes) were carried out remotely *via* a secure platform (Microsoft Teams, Microsoft Corporation, Washington, USA), to understand the impact of the COVID-19 pandemic on OSA patient care pathways and to gain insight into the current referral, diagnostic, and management strategies. In addition, the sleep consultants' views on the challenges and opportunities of the current clinical care pathways, and their thoughts on how to optimise sleep services provision and patient experience, were also explored (see **Chapter 3** for further details on qualitative research in healthcare).

**Informal discussions with clinical leads within the UK about
OSA clinical care pathways**

Interview Topic Guide

Introductory

[confirm consent for recording]

Introductory question:

1- Tell me about the current care pathway for OSA in your sleep service?

Key questions:

Challenges and opportunities of the current patient care pathway

2- What do you think are the main strengths of the current patient pathway in your sleep service?

3- What do you think are the current and future challenges in OSA care provision in your sleep service?

4- How would you optimise sleep services provision and ensure a positive patient experience?

Ending question:

5- How is digital health technology utilised in the current pathway?

Conclusion remarks

[Thank the participant]

Figure 1.15 Interview guide for the informal remote discussions with sleep consultants within the UK to investigate obstructive sleep apnoea clinical care pathways.

1.9.3. Summary of findings

Seven sleep consultants agreed to take part in the one-to-one informal discussions, which took place between September and November 2021. **Figure 1.16** shows a UK map of the geographical locations of the sleep services with which these consultants were affiliated.

Table 1.1 shows the characteristics of these sleep services.

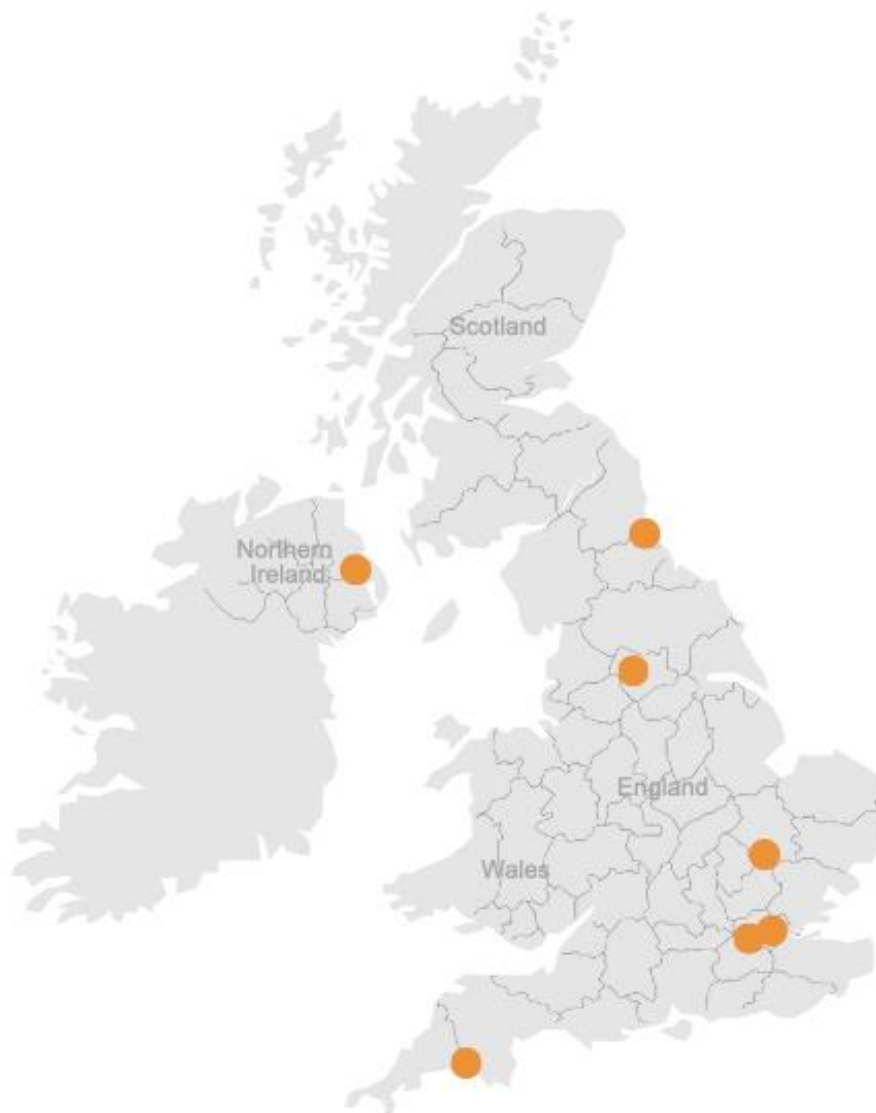


Figure 1.16 A UK map showing the geographical locations of the sleep consultants who participated in the remote informal discussions on obstructive sleep apnoea clinical care pathways. They were from Belfast, Bradford, Cambridge, London (Hospital 1), London (Hospital 2), Newcastle, and Plymouth.

Table 1.1 Sleep services' characteristics

Location	UK region	Clinical commissioning group (CCG)	Population served by the CCG [#]	Diagnostic sleep studies performed in 2018/19 [¶] (Crude rate per 100,000 people)
Belfast	Northern Ireland	Belfast Local Commissioning Group	> 340,000	NA
Bradford	Yorkshire and the Humber	NHS Bradford District and Craven	600,000	532.1
Cambridge	East of England	NHS Cambridgeshire and Peterborough	1,005,341	187
London (<i>Hospital 1</i>)	Greater London	NHS South East London	1,900,000	1,398
London (<i>Hospital 2</i>)	Greater London	NHS West London	> 260,279	114.8
Newcastle	North East England	NHS Newcastle Gateshead	495,781	54.2
Plymouth	South West England	NHS Devon	1,200,000	232.7

UK: United Kingdom. [#]Data taken from the sleep services or CCGs' official websites in 2021. [¶] Rate of diagnostic sleep studies undertaken per population (crude rate per 100,000 people) by CCG (data from the NHS Atlas of Variation in Healthcare in 2018/19). Please note that these figures may not be representative of the actual diagnostic sleep studies performed due to discrepancies in sleep services' documentation of clinical and financial activities; see **Section 1.4.3** for further details.

1.9.3.a: Variations in OSA clinical care pathways

The sleep consultants were asked to provide a summary of the typical patient care pathway for OSA in their sleep services. Their responses were gathered into one visual clinical care pathway. The variations between the seven sleep services in the referral, assessment, diagnosis, treatment, and management of patients with OSA are shown in **Figure 1.17**.

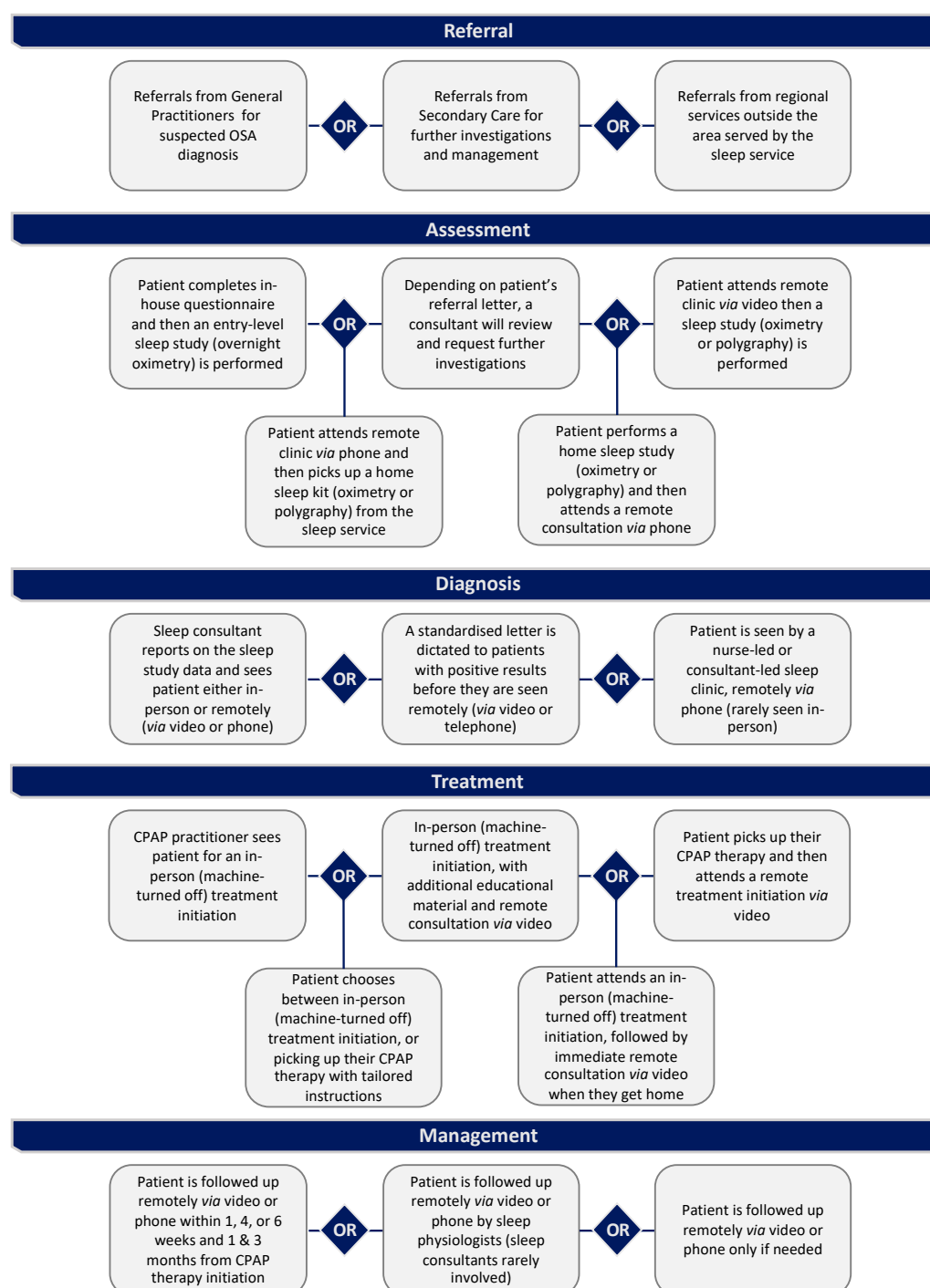


Figure 1.17 A summary of the variations in obstructive sleep apnoea clinical care pathways in the UK. Data from seven sleep services: Belfast, Bradford, Cambridge, London (Hospital 1), London (Hospital 2), Newcastle, and Plymouth.

1.9.3.b: Strengths of the clinical care pathways

When asked about the strengths of the OSA clinical care pathway in their sleep service, all the sleep consultants reported the important role of digitally-enabled healthcare i.e. virtual clinics, telephone consultations, remote diagnosis, and telemonitoring, in facilitating convenient and flexible care for both patients and clinicians.

One of the sleep consultants suggested that digitally-enabled healthcare may also expedite treatment provision for patients with OSA. When commenting on the strengths of current clinical care pathways in their sleep service, they stated: *“It also means that when I get results back for a patient, I don't necessarily have to wait until my next clinic gap. I can respond more rapidly and give the results and get them onto treatment more rapidly, so I don't have that access barrier that I had with physical clinic space, and a lot of patients like it.”*. However, the sleep consultants also highlighted the limitations that come with virtual care, including the inability to perform a proper clinical examination and the potential loss of the *“human touch”*.

Whilst considering the limited resources in most sleep services, having the ability to monitor patients remotely was seen as an advantage that could allow for triaging patients who need further support. One consultant commented on their experience prior and during the COVID-19 pandemic: *“...we didn't used to have the personnel time to access the telemonitoring data, and we could never work out how we were going to change our system to do that. So that's now happened, and I think whilst it's not perfect for all problems, it's pretty good in identifying the people who are doing well, who don't need to attend the hospital, and also identifying the people who do need to come in”*.

In addition, a patient-initiated follow-up system was considered to be a strength of a clinical care pathway in a tertiary hospital in London. Other strengths that were also highlighted by the sleep consultants included having access to dedicated CPAP professionals, employing a

direct-to-test streamlined local care pathway, and implementing a physiologist-led follow-up programme.

1.9.3.c: Current and future challenges of the clinical care pathways

The increasing demand for sleep apnoea services and issues with the national supply of CPAP machines were regarded as two current challenges in OSA care. In addition, challenges with virtual care included difficulties with training future healthcare professionals if no, or fewer, patients were coming to clinics, potential staff exhaustion due to remote delivery of care, and issues with health inequalities, health, and digital literacy.

Another challenging aspect that was frequently mentioned by the sleep consultants was patient selection regarding who may need further support and how to accommodate their choices and preferences, as one consultant commented: *"...do patients like the remote clinics, for which point I don't know. I know in the first wave everyone wanted to be remote because they didn't want to come to hospital at all. Do they still feel like that, or do they feel we're short-changing? Then? There's obviously a lot being said about General Practice, but I don't know about our patients. Should we be giving them a choice? I think we probably should"*. The sleep consultants also highlighted the current and future challenges with services integration, access to care and long waiting times, and public health issues; with one ending the conversation by saying that *"the biggest problem and public health challenge is obesity"*.

1.9.3.d: Suggested areas for improvement

The sleep consultants were asked to share their insights on how to optimise OSA care in the UK. One started with the recommendation to encourage evidence-supported elimination of unnecessary variations in healthcare delivery whilst providing options for OSA care to account for the limited resources in different sleep services. Other recommendations included the need for optimal integration of services, timeliness across the clinical care pathway, and access to non-CPAP therapies; with one consultant suggesting that *"we need*

to be rapid in our diagnosis and treatment. So, I think once the patients are in our pathway, they need to feel that they are going to be moved through really quite quickly. So, if there is any interruption in their everyday life, it's going to be minimal". Another consultant highlighted the need for an optimal clinical care pathway, where community diagnostic centres are utilised to perform diagnostic sleep studies at the beginning of the care pathway to reduce unnecessary appointments in secondary care.

Sleep consultants also thought that ensuring the provision of person-centred care with equity of access is of key importance, especially when delivering digitally-enabled care, as one consultant emphasised: *"...so I think it's really important that we don't develop a pathway that potentially excludes patients who, for whatever reason don't have this; the access to digitally enabled care that other patients do, and so there's just a kind of thread underlying everything that we're doing that looks at equitability in access"*. Another consultant also referred to implementing the British Sleep Society (BSS) strategy and its commitment to optimising healthcare delivery for OSA. In addition, improving public awareness and tackling public health issues, specifically obesity, were highlighted along with putting research upfront to inform any improvement in OSA care.

1.9.4. Conclusion

The findings of these informal discussions with the sleep consultants provided me with ideas for investigations to understand the delivery of OSA care from both patient and clinical perspectives. I was able to gain first-hand insights into the variations in the clinical care pathways for patients with OSA across the UK. In addition, the sleep consultants shared their views on the opportunities and challenges of pre- and post-COVID-19 pandemic OSA care, highlighting the benefits of utilising digitally-enabled healthcare and the need for investigating patient preferences and providing them with expedited and equitable clinical care pathways. These insights helped inform and provide the context for the next studies of my PhD programme of research, and I am very grateful to all the consultants for their valuable time.

1.10. Aims and structure of the Thesis

1.10.1. Rationale for research

OSA is a prevalent respiratory sleep disorder, and many patients with OSA in the UK remain undiagnosed and, thus, untreated. Conventional clinical care for OSA diagnosis and management is currently insufficient to meet the increasing demand, which has been exponentially rising post-COVID-19 pandemic. Digitally-enabled diagnosis and management may address these challenges and improve the delivery of OSA care.

1.10.2. Aim of Thesis

The overall aim of this PhD was to investigate new clinical care strategies for the diagnosis and management of OSA and evaluate patient experiences with, and preferences for, these clinical care strategies.

1.10.3. Structure of Thesis

This PhD Thesis contains four experimental chapters, split into two parts; plus a general introduction and a general discussion.

Chapter 1: General background to the research in the Thesis.

Part One – comprises two chapters investigating the diagnosis of OSA:

Chapter 2: A two-centre, randomised controlled pilot study investigating a remote diagnostic pathway for OSA using a novel MM monitor, compared to home respiratory polygraphy, in adult patients with suspected OSA.

Time to treatment decision was compared between the diagnostic devices, and across two geographically distinct UK regions: Highlands and Islands of Scotland and inner London.

Chapter 3: A nested qualitative evaluation investigating patient experiences of remote diagnostic pathways using both the MM monitor and home respiratory polygraphy.

Part Two – comprises two chapters investigating the clinical management of OSA:

Chapter 4: A systematic review and meta-analysis investigating the effectiveness of virtual consultations, compared to in-person consultations, on patient-reported sleepiness and the cost-effectiveness for adult patients with OSA treated with CPAP therapy.

Chapter 5: A UK survey of patients with self-reported OSA treated with CPAP therapy investigating their experiences of, and preferences for, remote versus in-person CPAP therapy initiation.

Chapter 6: General discussion, providing a summary of the findings presented in this Thesis and discussing their implications and the future directions for research in this area.

Part One

Investigations of the diagnosis for OSA

Chapter 2

Mandibular movement monitor provides faster, yet accurate diagnosis, for obstructive sleep apnoea: a randomised controlled study

*The randomised controlled pilot study described in this chapter was submitted for publication in the **Clinical Medicine Journal** in November 2023*

2.1 Introduction

OSA is estimated to affect nearly one in seven people worldwide, with increasing prevalence, as discussed in **Chapter 1 (Section 1.3.3)**; (Benjafield et al., 2019 and Peppard et al., 2013). In the UK, moderate or severe OSA affects approximately 1.5 million adults and if those with mild OSA are included, the estimated prevalence is in excess of 8 million adults (Benjafield et al., 2019). However, up to 85% of patients with OSA remain undiagnosed, and untreated (Rejón-Parrilla et al., 2014). This in part relates to a delay in diagnosis; novel diagnostic strategies may improve access to OSA diagnosis for patients with suspected OSA.

MM monitoring is a novel digital health technology that has been used for the diagnosis of OSA (this was discussed in **Chapter 1, Section 1.6.3**). In brief, sleep-related respiratory events such as apnoeas and hypopnoeas are associated with mandibular jaw movements, which can be detected by a sensor worn on the chin overnight and thus, by quantifying these events, diagnose OSA using automated machine-learning algorithms (Martinot et al., 2017a, Martinot et al., 2015, Pepin et al., 2022, Maury et al., 2014, Maury et al., 2013, Senny et al., 2008, Pépin et al., 2020). MM analysis can also distinguish between sleep and wakefulness, enabling accurate measurement of TST for precise estimates of sleep-related respiratory indices (Senny et al., 2012, Le-Dong et al., 2021). In a recent study, our research group reported on the applicability of MM monitoring for the diagnosis of OSA (Kelly et al., 2022). The findings of the study suggested that MM monitoring coupled with automated machine-learning analysis is comparable to manually scored in-home PSG for the diagnosis of patients with suspected OSA.

NICE clinical guidelines for OSA diagnosis in adults with suspected OSA recommend that home sleep apnoea testing with respiratory polygraphy should be used as the initial diagnostic strategy (National Institute for Health and Care Excellence, 2021a). However, home respiratory polygraphy requires staff time to set up and analyse, and patients must either attend the sleep centre, or have the diagnostic device posted to them. In rural

locations, this may involve travelling long distances to collect, and then return, the diagnostic device (see **Chapter 1, Section 1.4.3** for a discussion on the existing mismatch between regional healthcare requirements for OSA and the distribution of sleep services in the UK).

The hypothesis for this study was that MM monitoring might reduce time to diagnosis and save staff time, compared with home respiratory polygraphy. This hypothesis was tested using a randomised controlled design comparing time to treatment decision between the two sleep study devices in two geographically distinct UK regions: Highlands and Islands of Scotland and inner London.

2.2 Methods

2.2.1 Study design

The Sunrise OSA Trial (SOSAT) was a prospective, randomised, blinded pilot study of OSA diagnosis using a MM monitor (Sunrise solution; Sunrise SA, Belgium), compared to home respiratory polygraphy (ApneaLink™ Air; ResMed Ltd, Australia).

2.2.1.a: Regulatory procedures

This study, which was conducted remotely, was sponsored by the Research Office at Guy's and St Thomas' NHS Foundation Trust (Project reference: 296444). The study was approved by Health Research Authority and Health and Care Research Wales (REC reference: 21/WA/0162) in June 2021 and then received approval for non-commercial research from NHS Highland (RD&I reference: H1754) in November 2021 (see **Appendix 2.1.1** for ethical approval letter). A substantial amendment (Amendment 1; REC reference: 21/WA/0162) was submitted in June 2022 to extend the study duration due to unexpectedly slow recruitment, and also to include a new recruiting site, Guy's Hospital, part of Guy's & St Thomas' NHS Foundation Trust. The study was also registered on Clinicaltrials.gov (ID: NCT05204004). This was an investigator-led study, and the MM monitors were donated, plus respiratory polygraphy monitors were loaned by Sunrise SA, Belgium.

Signed written informed consent was obtained from all participants and the study is reported according to the Consolidated Standards of Reporting Trials (CONSORT) statement, a widely used evidence-based minimum set of recommendations for reporting RCTs (Eldridge et al., 2016). Ethical approval letters, the participant information sheet (PIS), and consent forms are presented in **Appendix 2.1**.

2.2.2 Participants

Adult patients referred with suspected OSA to the Royal Brompton Hospital (RBH) and Guy's Hospital (Guy's and St Thomas' NHS Foundation Trust, London, England), or Raigmore Hospital's sleep service (NHS Highland, Inverness, Scotland) were considered for participation. Inclusion criteria were: ≥ 18 years old, reported snoring, body mass index (BMI) of ≥ 28 kg/m², and ESS score of ≥ 12 points (see **Chapter 1, Section 1.5.1** for a description of ESS). These criteria were deliberately chosen to identify patients with high pre-test probability of OSA. Participants also had to be able to use a smartphone application and have internet access.

Exclusion criteria: previous treatment for OSA, secondary sleep pathology (e.g. periodic limb movement syndrome, narcolepsy), and concerns about sleepy driving. Patients were also excluded if they were unwilling to shave a thick beard or remove acrylic or painted fingernails, both of which may impede the recordings of the sleep studies (see **Table 2.1** for the full inclusion and exclusion criteria).

Table 2.1 Inclusion and exclusion criteria for eligibility in the randomised controlled study

Inclusion criteria:	▪ Aged ≥ 18 ▪ Ability and willingness to provide informed consent ▪ Patient referred for suspected OSA ▪ BMI ≥ 28 kg/m² ▪ Epworth Sleepiness Score ≥ 12 ▪ Reported snoring (criterion may be ignored if patient sleeps alone) ▪ Patient able to use a smartphone application and having an internet connection at home
Exclusion criteria:	▪ Patient already treated for OSA ▪ Patient has PSV or HGV driving license ▪ Unstable cardiac disease ▪ Supplemental oxygen ▪ Known secondary sleep pathology e.g. Periodic Limb Movement Syndrome, Narcolepsy, Circadian Disorder, Obesity Hypoventilation Syndrome ▪ Concerns about sleepy driving or any other potentially dangerous symptom from physician or urgent referral from GP when patient has been told to stop driving ▪ Pregnant woman, parturient, nursing mother, person deprived of liberty by judicial or administrative decision, person subject to a legal protection measure ▪ Patient whose beard is too thick to wear the Sunrise device, and who does not wish to shave ▪ Patient with acrylic or painted fingernails, who does not wish to remove acrylic or paint

OSA: obstructive sleep apnoea; BMI: body mass index; PSV: Public Service Vehicle; HGV: Heavy Goods Vehicle; GP: General Practitioner

2.2.3 Randomisation and blinding

Eligible patients were randomised (1:1) to receive their treatment decision based on results from either the MM monitor or respiratory polygraphy. Participants were stratified according to their location (Scottish Highlands and Islands versus inner London) to allow for permuted block randomisation, with n=20 participants in each group (Broglia, 2018). Participants were then randomised using the sealed envelope technique (Beller et al., 2002), in which sequentially numbered, opaque, sealed envelopes containing group allocations were pre-prepared. Once a patient had consented, a random envelope was opened, and the

participant was then allocated to receive their treatment decision based on results from either the MM monitor (n=10 participants in each group) or respiratory polygraphy (n=10 participants in each group). The treating clinicians were blinded to the results collected simultaneously by the alternative device when reviewing sleep study data during the multi-disciplinary team (MDT) meetings. Dr Julia Kelly and I were not blinded to participant randomisation and the results of the sleep studies as we prepared the diagnostic sleep reports for the MDT meetings; however, we were not involved in direct patient care. Participants remained blinded to their allocation of the diagnostic device upon which their treatment decision was based.

2.2.4 Procedures

Local clinical teams at each participating site screened the referrals of patients with suspected OSA and reviewed their medical history to identify potential participants based on the pre-specified inclusion criteria (**Table 2.1**). Potential participants received a PIS with an invite, by email or post, to contact the research team in London if they were interested in taking part in the study. Patients underwent an initial assessment by phone to verify their eligibility for the study, and their informed consent was obtained remotely, by email. I then sent, *via* postal services, the necessary equipment and written instructions to participants to perform a simultaneous overnight home sleep study using both diagnostic devices (see **Appendix 2.2** for patient instructions). **Figure 2.1** demonstrates the setup of both sleep study devices, the MM monitor and respiratory polygraphy.



Figure 2.1 An individual wearing the white single-sensor mandibular movement monitor (Sunrise solution; Sunrise SA, Belgium), attached to the chin, and the multichannel respiratory polygraphy monitor (ApneaLink™ Air; ResMed Ltd, Australia) to demonstrate the complete setup for the simultaneous overnight home sleep study. The individual gave permission for this photo to be included in this Thesis.

Patient experience was assessed using a bespoke short self-administered questionnaire consisting of Visual Analogue Scales (VAS), binary, and open questions, to assess the following outcomes:

- The **ease of use** for each diagnostic device (the MM monitor and respiratory polygraphy) was measured by a VAS, with a horizontal line ranging from 0 (very easy) to 100 mm (very difficult).
- The **comfort** of each diagnostic device (the MM monitor and respiratory polygraphy) was measured by a VAS, with a horizontal line ranging from 0 (very uncomfortable) to 100 mm (very comfortable).
- **Participants' preferred sleep study diagnostic device:** (the MM monitor or respiratory polygraphy) was measured by a binary choice.

- **Participants' preferred sleep study setting:** (in-hospital or at home) was measured by a binary choice.
- **Travel time and distance:** Participants were asked, using open questions, to provide the approximate distance (km) from their house to the sleep service, and how long (min) it would normally take them to travel to their sleep service.

Participants were asked to complete the short patient questionnaire in the morning following their overnight home sleep study. The questionnaire, which took approximately 3-5 minutes to complete, also included questions about participants' demographics, specifically age, gender, anthropometric measures (i.e. height, weight, and neck circumference), and geographic location. The patient questionnaire is shown in **Appendix 2.3**. *Additionally, a qualitative evaluation, nested within this randomised controlled study, was performed to further investigate patient experiences of the remote diagnostic pathway using both the MM monitor and home respiratory polygraphy. This nested qualitative evaluation is presented in Chapter 3.*

Participants returned sleep study devices to the research team in a pre-paid postal envelope. Participants were excluded from the study and referred back to their local sleep service if their sleep study was unsuccessful with both sleep study devices. However, if only the device that was being used to determine the outcome of the study was unsuccessful, participants were offered a repeat sleep study using the same device.

In conjunction with the initial comprehensive medical evaluation conducted remotely or in-person by the treating clinician, a multi-disciplinary team comprising the treating physicians, a nurse consultant, and a physiotherapist, met weekly to review participants' sleep study results from the diagnostic device allocated at randomisation, before making a decision on how to treat. When results from the alternative device became available, they were retrospectively compared to the results from the initial diagnostic device.

2.2.4.a: Mandibular movement monitoring

The MM monitor (Sunrise solution) is a novel, CE-marked, and commercially available medical device for the diagnosis of sleep apnoea in adults (see **Chapter 1, Section 1.6.5** for further details). It was developed and validated as part of an entrepreneurship grant, sponsored by EIT (Pépin et al., 2020, Kelly et al., 2022). Patients download a mobile application, which guides them to set up the device, apply the small non-invasive sensor on their chin at the mentolabial sulcus, and then initiate the sleep study. The inertial measurement unit inside the sensor enables the detection of mandibular movements, whilst communicating with the smartphone application for external control *via* Bluetooth. The data is transferred to a secure cloud-based platform, which uses machine-learning algorithms for automated analysis and generates a detailed sleep report, made available to the research team the morning after the sleep study. The mobile application also collects demographic data, scores from the ESS and ISI, and other patient-reported data e.g. participants' symptoms and complaints; see **Section 1.5.1** for a discussion on subjective assessment scales for suspected OSA.

2.2.4.b: Respiratory polygraphy monitoring

Level III home respiratory polygraphy has been validated in the screening and diagnosis of sleep apnoea (Masa et al., 2011) (see **Chapter 1, Section 1.5.2** for further details). ApneaLink™ Air (ResMed Ltd, Australia) was used in this study. On return of the diagnostic device, the data were manually downloaded and uploaded to a central server (AirView, ResMed Ltd), which allowed for the sleep studies to be analysed using automated algorithms based on the AASM 2012 scoring criteria (Berry et al., 2012). Together with Dr Kelly, we manually reviewed the raw data of all the sleep studies, independently. Dr Kelly and I were not involved in direct patient care.

2.2.5 Study outcomes

Primary outcome of the study was:

- Time to treatment decision (measured in days) from sleep study device dispatch to treatment decision

Secondary outcomes of the study were:

- Difference in time to treatment decision between the Scottish Highlands and inner London
- Agreement between the diagnostic devices for the measurement or estimation of the AHI, and the clinical decision to treat (or not)
- Time required to prepare and manually review the sleep studies
- Patient experiences with both diagnostic devices

2.2.6 Analysis

There were no available data to calculate the sample size for the primary outcome of the study and, therefore, no formal sample size calculation was performed. The pragmatic target of n=40 participants was based in part on feasibility considerations and, judged by our research group's prior experience with the MM monitoring device (Kelly et al., 2022), to likely obtain sufficient data to assess the feasibility of this diagnostic strategy in remote rural regions.

De-identified data were entered onto a secure, Good Clinical Practice (GCP)-compliant electronic database; Microsoft Excel (Version 16.65, Microsoft Corporation, Washington, USA). I conducted all the statistical analyses using GraphPad Prism (Version 9, GraphPad Software, California, USA).

Descriptive statistics were reported for baseline and clinical characteristics, and study outcomes including the number of participants (n), mean and standard deviation (SD), median and interquartile range (IQR), or frequencies and percentages (%). The primary outcome was analysed using the Mann-Whitney test, and the secondary outcomes were

analysed using the unpaired t-test or Mann-Whitney test for between-group comparisons, and correlation analysis and Bland-Altman plot to evaluate the agreement in AHI between the diagnostic devices.

2.2.7 Patient and public involvement

This study was designed to evaluate the use of MM monitoring in real-world clinical settings, and patient experience was assessed as a secondary outcome of the study. *Patient experiences of the remote diagnostic pathway used in this study was further investigated in the nested qualitative evaluation (presented in **Chapter 3**)*. Members of the public provided input to the development of the study materials and educational support for study participants.

2.3 Results

Between 22nd September 2021 and 8th March 2023, 40 patients were recruited and randomised; 20 from the Scottish Highlands and Islands and 20 from inner London. In each location, 10 participants were allocated to receive their treatment decision based on the MM monitor and 10 from the respiratory polygraphy. All participants completed the study, however, data for primary outcome analysis was available for 90% (n= 36/40) of participants; see CONSORT diagram (**Figure 2.2**).

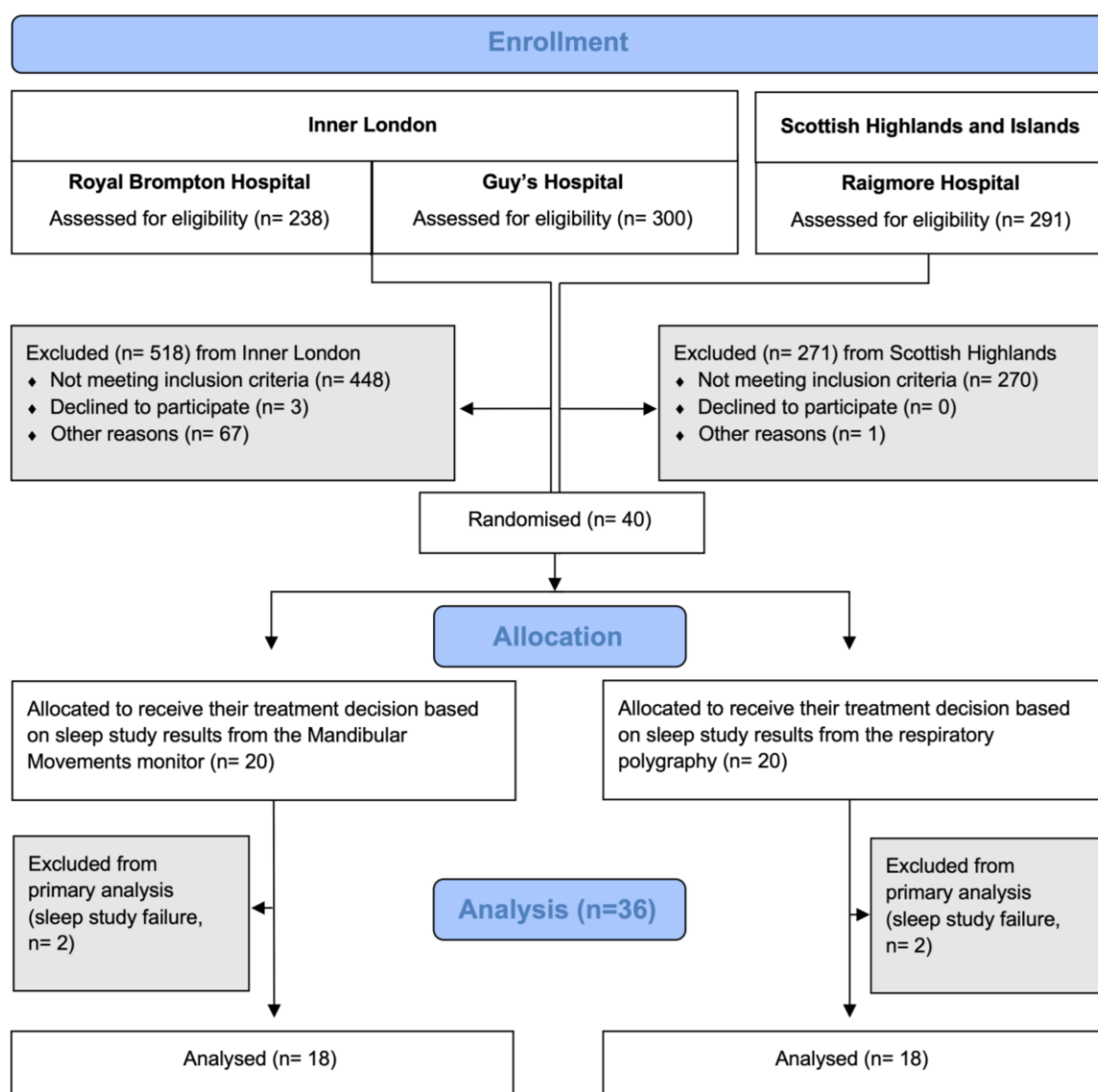


Figure 2.2 Consolidated Standard of Reporting Trials (CONSORT) flow diagram for the Sunrise Obstructive Sleep Apnoea Trial (SOSAT).

2.3.1 Technical failures

Technical failure rates were similar between the study diagnostic devices. 15% (n= 6/40) of participants failed their MM monitor sleep studies due to inability to associate the sensor with the mobile application (n=2), loss of connection resulting in significant data loss (n=3), or human error 'difficulty setting up the monitor' (n=1). Similarly, 17% (n= 7/40) of participants failed their respiratory polygraphy sleep studies due to signal failure resulting in significant data loss (n=5), human error 'difficulty setting up the monitor' (n=1), or patient intolerance (n=1).

2.3.2 Participant characteristics

Baseline characteristics are presented in **Table 2.2**. Participants ($n=40$) had a mean $\pm$ SD age of 46.8 ± 12.9 years, and 70% were male, with a BMI of 36.9 ± 7.5 kg/m², and ESS score of 14.9 ± 4.1 points. Raw data for participants' baseline characteristics is presented in **Appendix 2.4, Table A.2.4.1**.

Table 2.2 Baseline characteristics of participants randomised to receive their treatment decision based on sleep study results from the MM monitor or respiratory polygraphy

	MM monitor ($n=20$)	Respiratory polygraphy ($n=20$)	All participants ($n=40$)
Age (years)	45.9 ± 12.4	47.7 ± 13.7	46.8 ± 12.9
Gender (%)			
<i>Male</i>	15 (75%)	13 (65%)	28 (70%)
<i>Female</i>	5 (25%)	7 (35%)	12 (30%)
BMI (kg/m ²)	35.7 ± 7.4	38.2 ± 7.6	36.9 ± 7.5
Neck Circumference (cm)	43.6 ± 4.0 °	44.0 ± 4.4 #	43.8 ± 4.2 ¶
Epworth Sleepiness Scale (12-24) points	14.8 ± 4.1	15.0 ± 4.2	14.9 ± 4.1
Insomnia severity Index (0-28) points	20.8 ± 5.0 °	18.2 ± 5.6 #	19.5 ± 5.4 ¶

Data are presented as mean $\pm$ SD or n (percentage). MM: mandibular movement; BMI: body mass index. °Data available for $n=18$ participants. #Data available for $n=19$ participants. ¶Data available for $n=37$ participants.

2.3.3 Primary outcome: time to treatment decision

Time to treatment decision was significantly less with the MM monitor, compared to home respiratory polygraphy (n=36 participants; median [IQR]: 13.5 [7.0 – 21.5] vs. 19.5 [13.7 – 35.5] days, $P=0.017$) (**Figure 2.3**). Raw data for time to treatment decisions is presented in **Appendix 2.4, Table A.2.4.2**.

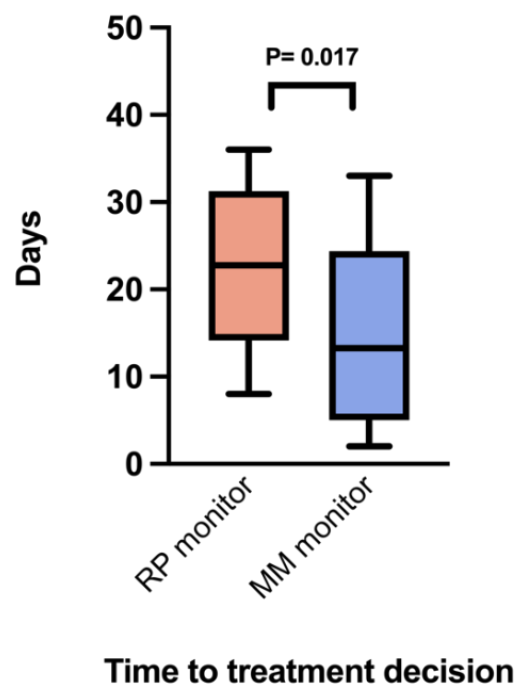


Figure 2.3 shows a significant reduction in time to treatment decision (measured in days) when using sleep study results from the mandibular movement (MM) monitor (n=18 participants; median [IQR]: 13.5 [7.0 – 21.5] days), compared to the home respiratory polygraphy (RP) monitor (n=18 participants; median [IQR]: 19.5 [13.7 – 35.5] days).

2.3.4 Secondary outcomes

2.3.4.a: Time to treatment decision: Scottish Highlands versus inner London

Secondary analysis showed no difference when the time to treatment decision was compared across locations (Scottish Highlands and Islands n=19 participants; median [IQR]: 15.0 [8.0 – 21.0] vs. inner London n=17 participants: 16.0 [13.0 – 31.0] days, $P=0.341$) (**Figure 2.4**).

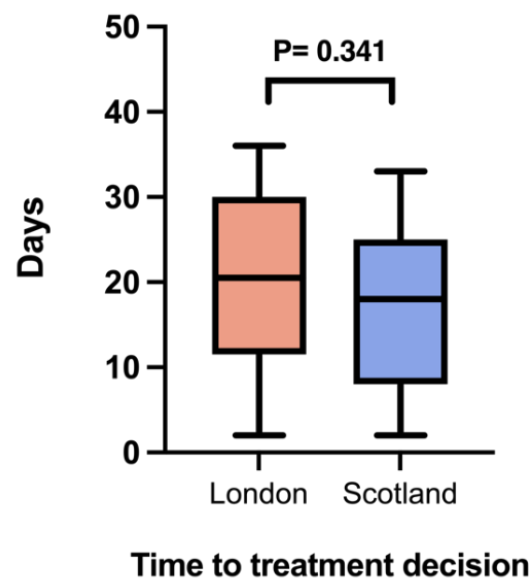


Figure 2.4 There was no difference in time to treatment decision (measured in days) between participants recruited from Scottish Highlands and Islands ($n=19$ participants; median [IQR]: 15.0 [8.0 – 21.0] days), and those recruited from inner London ($n=17$ participants; median [IQR]: 16.0 [13.0 – 31.0] days).

2.3.4.b: Agreement in AHI between the diagnostic devices

Using the available paired data from both diagnostic devices ($n=30$ participants), the MM-estimated AHI was a mean $\pm$ SD of 32.0 ± 20.0 and the respiratory polygraphy AHI was 27.5 ± 25.1 events per hour. The MM monitor overestimated AHI, compared to respiratory polygraphy (mean bias [95% Limits of Agreement]: $+4.47$ [-29.3 to $+38.2$] events per hour). The variance was greater with higher AHIs (>15 events per hour), and the MM monitor tended to overestimate AHI in mild disease and underestimate AHI in severe OSA (**Figure 2.5**). Correlation analysis of the relationship between MM-estimated AHI and respiratory polygraphy AHI is shown in **Figure 2.6** (Raw data is also presented in **Appendix 2.4, Table A.2.4.2**).

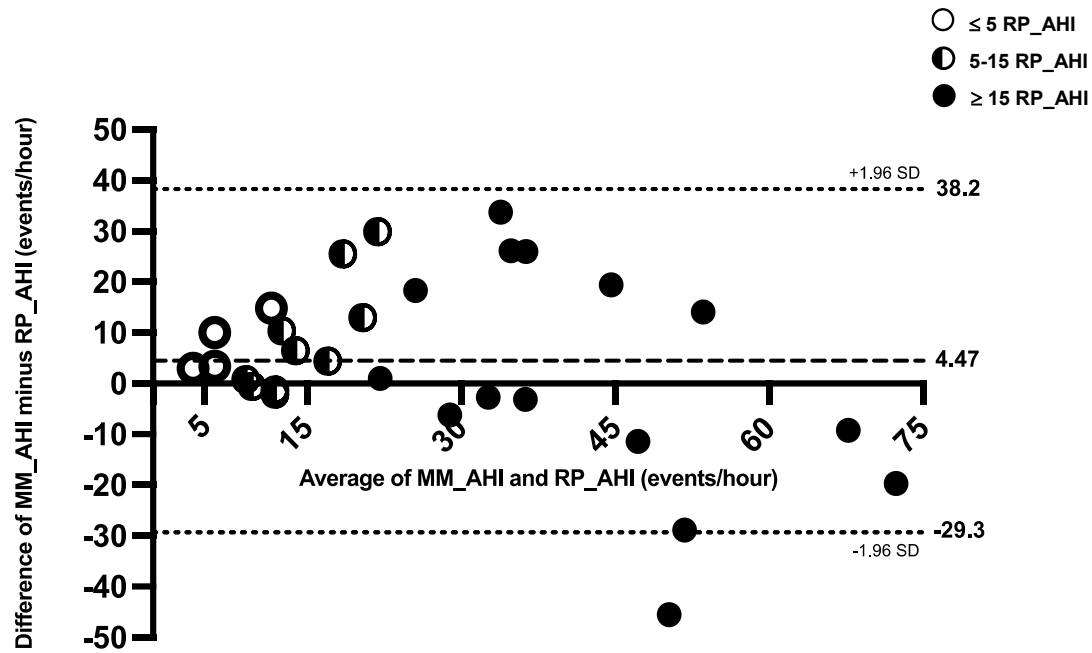


Figure 2.5 Bland-Altman plot of the difference (MM monitor estimated AHI minus RP AHI) vs average AHI of both diagnostic devices ($n=30$ participants). MM monitor overestimated AHI, compared to respiratory polygraphy; the dashed black line in the middle indicates the mean bias of +4.47 (SD: 17.24) events per hour. The 95% limits of agreement are marked by the above and below dotted lines. Shapes are based on the RP AHI thresholds. MM: mandibular movement; RP: respiratory polygraphy.

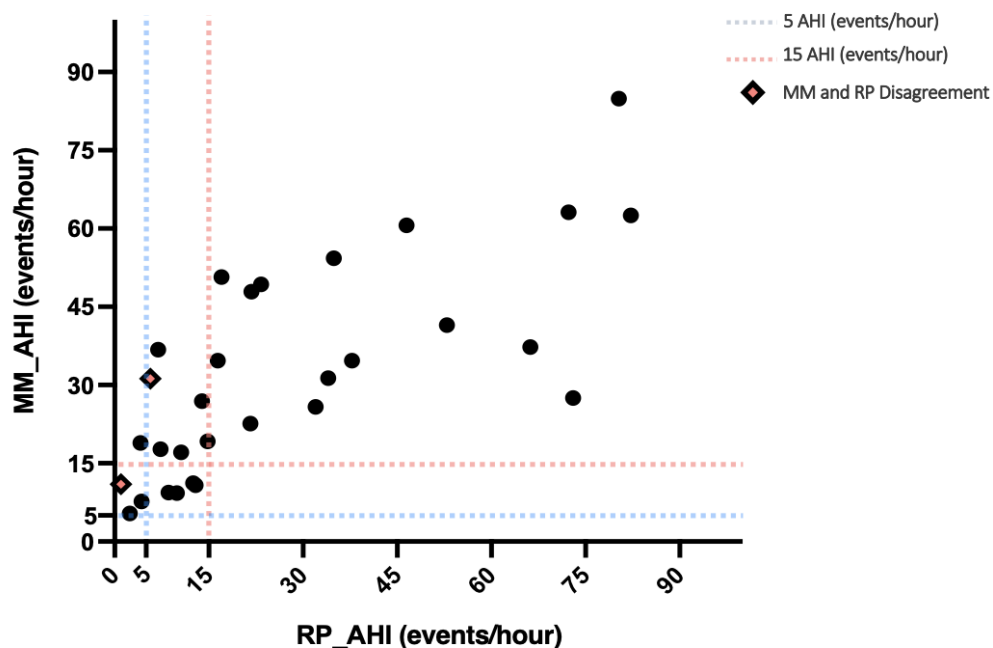


Figure 2.6 shows a positive correlation ($r=0.73$, $p<0.0001$) between MM monitor estimated AHI and RP AHI ($n=30$ participants). The dotted blue line represents the 5 events per hour cut-off (the threshold for which treatment may be indicated). The dotted red line at 15 events per hour represents the threshold where treatment is usually started for obstructive sleep apnoea. Rhombus shapes represent participants where the clinical treatment decision differed between results obtained from each diagnostic device. AHI: apnoea-hypopnoea index; MM: mandibular movements; RP: respiratory polygraphy.

2.3.4.c: Clinical decision to treat (or not)

The MDT clinical decision was the same in 30 out of 33 (91%) participants, irrespective of which sleep study device was used to determine the outcome of the study. For participants where treatment decisions differed, two were randomised to treatment decision based on the MM monitor and one was randomised to treatment decision based on respiratory polygraphy.

Table 2.3 shows the MM-estimated AHI and the respiratory polygraphy AHI for three participants where the MDT treatment decisions differed.

Table 2.3 AHI values for the participants where the MDT treatment decisions differed

Participant ID	Randomisation	AHI (events per hour)		MDT clinical decision
		MM monitor	RP monitor	
SOSAT-17 (<i>Scottish Highlands</i>)	RP monitor	11	1	Patient was referred for further investigation outwith this study
SOSAT-18 (<i>Scottish Highlands</i>)	MM monitor	31.2	5.7	Patient was offered a trial of CPAP therapy
SOSAT-24 (<i>Inner London</i>)	MM monitor	13.3	4.9	Patient was offered a trial of CPAP therapy

AHI: apnoea hypopnoea index; MDT: multi-disciplinary team; MM: mandibular movements; RP: respiratory polygraphy; CPAP: continuous positive airway pressure

2.3.4.d: Clinical time saved

MM monitor sleep reports were automatically generated, immediately after the sleep study. The time required to prepare and manually review the automated analysis of each respiratory polygraphy test, including the preparation of the sleep report for the MDT discussion took myself and Dr Kelly, on average, 29 minutes per patient.

2.3.4.e: Patient experience

Participants reported that the MM monitor was easier to set up than respiratory polygraphy (n=35 participants; median [IQR]: 1.3 [0.1 – 2.5] vs. 2.7 [1.4 – 4.9] cm, P=0.014) (**Figure 2.7**), and was also thought to be more comfortable to sleep with than respiratory polygraphy (n=35

participants; mean $\pm$ SD: 6.9 ± 3.1 vs. 4.1 ± 2.7 cm, $P=0.0002$) (**Figure 2.7**). The MM monitor was preferred by 85.7% of participants, the respiratory polygraphy by 5.7%, and the remaining 8.5% had no preference (**Figure 2.8**).

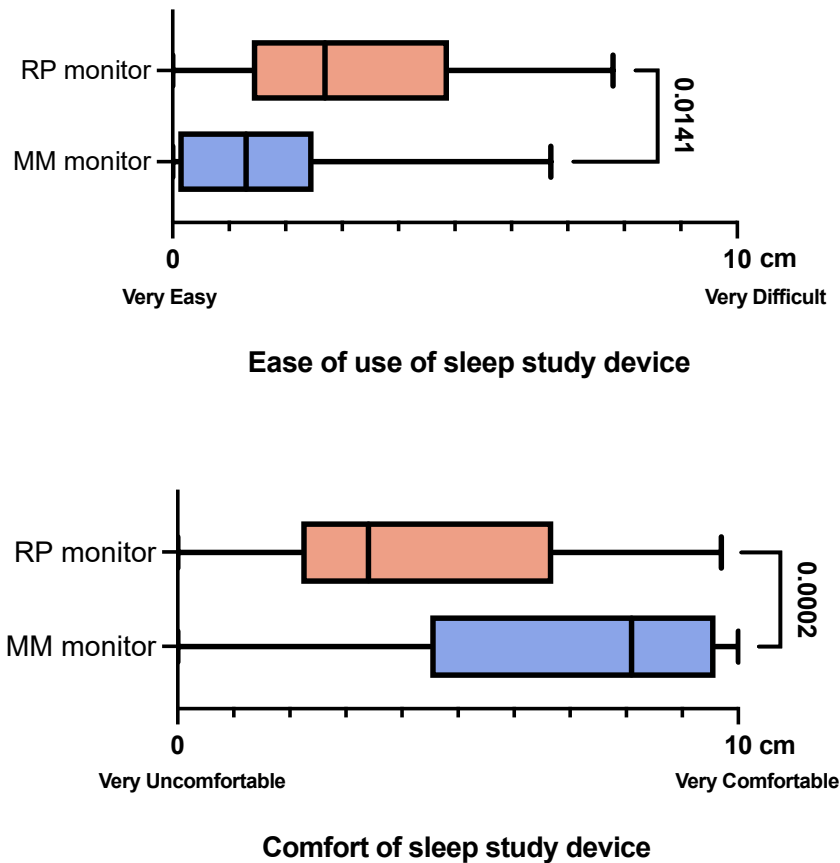


Figure 2.7 shows the ease of use and comfort of the sleep study devices. Participants ($n=35$) made a vertical mark on (10 cm) Visual Analogue Scales. (**Top**) Participants reported that the MM monitor was easier to set up compared to RP monitor ($P=0.0141$). (**Bottom**) Participants found the MM monitor more comfortable to sleep with compared to RP monitor ($P=0.0002$). MM: mandibular movement; RP: respiratory polygraphy.

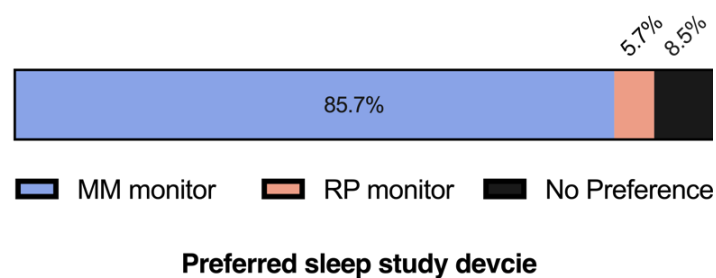


Figure 2.8 Participants ($n=35$) expressed their preference for the sleep study devices, favouring the mandibular movement (MM) monitor over the home respiratory polygraphy (RP) monitor.

Most participants (94%) preferred having an in-home sleep study compared to in-hospital testing (**Figure 2.9**). Participants also preferred having the sleep study device posted to their home with written instructions and over-the-phone assistance if needed (91.5%), as compared to collecting the device from the hospital and receiving face-to-face instruction (5.7%). One patient (2.8%) had no preference.

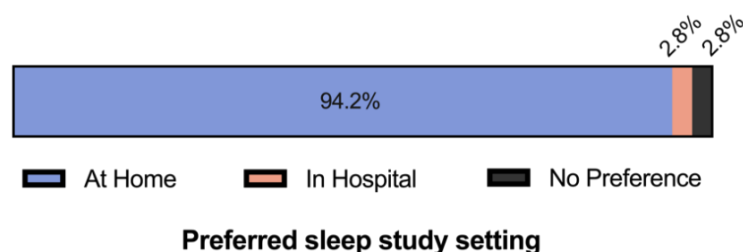


Figure 2.9 Participants ($n=35$) expressed their preference for home-based sleep studies over in-hospital sleep studies.

The distance from participants' houses to their local sleep service was a median (IQR) of 19.5 (5.0 – 60.1) km, potentially saving on average mean $\pm$ SD of 57.3 ± 47.7 minutes of self-reported travel time per one-way trip. **Table 2.4** shows the self-reported distance and travel time according to participants' location (Scottish Highlands and Islands vs. inner London).

Table 2.4 Self-reported distance and travel time (km and mins) from participants' houses to their local sleep service

	Participants location		
	inner London ($n= 16$)	Scottish Highlands ($n= 19$)	All participants ($n= 35$)
Distance (km)	17.6 (8.2 – 49.5)	20.0 (5.0 – 120.0)	19.5 (5.0 – 60.1)
Travel time (min)	60.1 $\pm$ 34.7	55.0 $\pm$ 57.2	57.3 $\pm$ 47.7
<i>Data are presented as median (IQR) or mean $\pm$ SD</i>			

2.4 Discussion

The main finding of this study is that MM monitoring with automated machine-learning analysis gave a six-day reduction in time to treatment decision, compared to home respiratory polygraphy, in adult patients referred for investigation of suspected OSA, and saved 29 minutes of a healthcare professional's time per patient. This finding was irrespective of location with no difference in the time to treatment decision for patients in the Scottish Highlands and Islands, compared to patients in inner London. There was good agreement between the MM monitor and home respiratory polygraphy for the clinical treatment decision.

2.4.1 Significance of the findings

In this study, an accelerated treatment decision, by nearly a week, was accompanied by an average time-saving of 29 minutes per sleep test from a skilled healthcare professional's time when using the MM monitor, compared to respiratory polygraphy. This finding is of relevance to sleep service delivery in the UK (also see **Chapter 1, Section 1.4.2**); the number of patients awaiting a sleep test has been exponentially rising, particularly post-COVID-19 pandemic, with a yearly growth rate exceeding 74% (NHS England and NHS Improvement, 2022).

UK sleep services commonly use respiratory polygraphy for routine screening of OSA, in accordance with the NICE clinical guidelines (National Institute for Health and Care Excellence, 2021a); see **Chapter 1, Section 1.4.4**. Although the respiratory polygraphy device was posted in this study, most sleep services do not do this routinely due to concerns about the loss of expensive equipment or its delayed return, which makes patient testing scheduling difficult. Instead, patients are usually required to attend the hospital to receive the device with face-to-face instruction and then return the device the next day. This approach is burdensome on staff and patients, and may also be dangerous if those prone to sleepiness have to drive for long distances (Tregear et al., 2009). In this study, patient travel was

replaced by postage of sleep study devices, saving patients approximately an hour for each one-way hospital trip.

Moreover, unlike respiratory polygraphy, healthcare professionals do not spend time preparing the MM monitor, instructing patients on attaching the sensor, or manually downloading and reviewing the automated analysis of sleep studies. This meant that the MM monitor was less time-consuming, compared to respiratory polygraphy, thereby potentially freeing up staff for other tasks (e.g. CPAP therapy initiation and monitoring) which could enhance sleep services provision. The time-saving benefits of using the MM monitor are likely to be higher in real-world clinical practice because in sleep services with limited resources, there may be delays in downloading and preparing the respiratory polygraphy sleep reports, even after the device is returned. Indeed, since no skilled time is required for the MM monitor, it could conceivably be used in general practice prior to referral to secondary care.

The findings of this study showed reasonable agreement between MM-estimated AHI and respiratory polygraphy AHI, despite an overestimation of AHI by the MM monitor. Sleep testing devices that do not measure neurophysiological data to distinguish between sleep and wakefulness, inherently underestimate the severity of OSA as quantified conventionally by AHI (Bianchi and Goparaju, 2017), as discussed in **Chapter 1 (Section 1.5.2)**. This is because the total recording time includes periods where the patient is awake. Since AHI is the number of apnoeas and hypopnoeas divided by the TST (expressed as events per hour of sleep) and if the denominator is overestimated because the patient is awake, AHI will be reduced. Specifically, respiratory polygraphy can underestimate AHI by 30% compared to polysomnography; thus resulting in underdiagnosis and misclassification of OSA (Escourrou et al., 2015). By contrast, MM can identify sleep and wake states, allowing for a more accurate estimate of TST and thus more accurate calculation of sleep-related respiratory indices (Senny et al., 2012, Le-Dong et al., 2021).

The clinical decision regarding treatment was the same in 30 out of 33 (91%) participants, irrespective of which sleep study device was used. Where the MM monitor and respiratory polygraphy differed, the MM monitor yielded a higher AHI in all three cases. Considering the patients' history and symptoms, the MDT offered two of these a trial of CPAP therapy and successful treatment with CPAP therapy suggested that the MM data had led to correct treatment. However, the MDT was reluctant to start the third patient on treatment; further investigation outside of this study confirmed a diagnosis of mild OSA, indicating that the patient was borderline with regard to an indication for CPAP therapy.

Finally, this study demonstrated that a remote diagnostic pathway with MM monitoring for the investigation of suspected OSA has the potential for other patient-reported advantages including ease of use, comfort, and overall improved patient experience.

2.4.2 Critique of the method

In addition to time to treatment decisions, and the agreement in treatment decisions, between the diagnostic devices, this study investigated other outcomes related to patient-reported experience and time saved by patients and healthcare professionals. However, the findings of this study must be interpreted with caution due to several limitations.

Firstly, the small sample size, with recruitment being targeted at those with higher pre-test probability of OSA, may limit the generalisability of the findings. Generalisability may also be limited by the low recruitment rate, with only 40 participants recruited out of 829 patients assessed for eligibility. Whilst access to the screening logs used by the local clinical teams at each participating site was not possible, the low recruitment rate may in part be explained by patient referrals received at each centre. Patients with complex sleep problems or comorbid conditions are typically referred to tertiary referral centres for specialist care, and these patients were likely to be excluded based on the exclusion criteria (see **Table 2.1** for the full inclusion and exclusion criteria).

Secondly, weekly MDT meetings may be viewed as a limitation that systemically biased the primary outcome (time to treatment decision) by underestimating the benefits of the automated machine-learning analysis and the cloud-based nature of the MM monitor, as frequently in real-world clinical practice there may be greater time delays with the analysis of sleep study data. However, this approach was chosen to reflect the existing care pathways in the participating sites. Thirdly, a greater difference in time to diagnosis between the study recruitment locations was anticipated because of both distance and travel time requirements, which were thought to be longer in rural areas such as the Scottish Highlands and Islands, compared to inner London. However, this was not observed. In practice, a proportion of the Scottish patients in this study lived in or near the major population centre (Inverness), whereas few of the London patients lived close to the Royal Brompton Hospital or Guy's Hospital (both of which are located in central London).

Notably, MM monitoring (and other emerging digital health technologies) may exacerbate health inequalities (*'the digital divide'*) as they require digital skills and connectivity (National Voices, 2021). However, of the participants who were remotely assessed for eligibility in the study, only three did not own a smartphone or have access to one and had to be referred back to the usual diagnostic pathway.

Furthermore, this study was aimed at the diagnosis of OSA, and did not address remote management and follow-up strategies for patients with OSA, which I have investigated in the systematic review and meta-analysis presented in **Chapter 4** (Alsaif et al., 2022).

2.5 Conclusion

The findings of this study show that a MM monitor can be safely used to reduce the time to treatment decision, compared to home respiratory polygraphy, in patients with suspected OSA, with saving of healthcare professionals' time which could then be reallocated to the treatment and management part of the care pathway. MM monitoring can, therefore, be

considered as an alternative primary diagnostic strategy in this population of patients with high pre-test probability of OSA.

Chapter 3

A nested qualitative study of patient experiences with a remote diagnostic pathway for obstructive sleep apnoea using a mandibular movement monitor and respiratory polygraphy

3.1 Introduction

The NHS Long Term Plan states that digital health technologies will enable and facilitate the redesign of clinical care pathways (National Health Service, 2019), as discussed in **Chapter 1, Section 1.6.1**. It is envisaged that this will provide convenient and timely access to healthcare services. The patient experience, which is defined as “*what the process of receiving care feels like for the patient, their family and carers*” (NHS Institute for Innovation and Improvement, 2013), is a core pillar of quality in healthcare, along with clinical effectiveness and patient safety (Department of Health, 2008). Thus, exploring patient experiences of the remote diagnostic pathways, that utilise emerging digital health technologies, is central to understanding healthcare delivery from patient perspectives.

The results of the randomised controlled study (presented in **Chapter 2, Section 2.3**) demonstrated that a remote diagnostic pathway, using a MM monitor with automated machine-learning analysis, accelerated OSA diagnosis, and thus, treatment decisions by 6 days. This novel digital health technology has the potential to be used as an alternative diagnostic strategy in adult patients with suspected OSA. It is also currently being evaluated within the diagnostic pathways for OSA in four regional healthboards across NHS Scotland (Glasgow, Edinburgh, Dundee, and Inverness). The interim results of the randomised controlled study (**Chapter 2**) helped to inform this ongoing Scottish service evaluation, which aims to assess the clinical applicability of MM monitoring as a first-line screening tool for adult patients with suspected OSA (also see **Chapter 1, Section 1.6.5**).

The patient experience data presented in the randomised controlled study (**Chapter 2, Section 2.3.4**) showed that most participants preferred the MM monitor, finding it easier to set up and more comfortable to sleep with, compared to home respiratory polygraphy. Most participants also expressed their preference for a remote diagnostic pathway, favouring home sleep apnoea testing over in-hospital testing. These data were collected using a quantitative short self-administered questionnaire; however, it is important to seek a better

understanding of the contextual factors influencing patients' experiences of, and preference for, remote diagnostic strategies.

Qualitative research, in health and social care, is used to understand the 'how' and 'why' of human behaviours, describe their lived experiences within personal and social contexts, explore the factors influencing these experiences, and inform the design of healthcare interventions (Gelling, 2014, Renjith et al, 2021). These applications of qualitative research enable and facilitate the provision of person-centred care. This is central to the NHS Constitution, which emphasises that the *“NHS services must reflect, and should be coordinated around and tailored to, the needs and preferences of patients, their families and their carers”* (Department of Health & Social Care, 2009).

Earlier studies, focusing primarily on patient experiences with OSA treatment and adherence, have used a variety of qualitative research methods, including focus groups and individual interviews (Almeida et al., 2013, Bakker et al., 2014, Sawyer et al., 2010, Zarhin and Oksenberg, 2017). Additional studies have also provided data on the awareness and perceptions of OSA (Firestone and Gander, 2010), as well as gender-based experiences, and behaviours of care-seeking (Zarhin, 2018). However, to date, little is known about the patient experiences of OSA diagnostic pathways. Rodgers (2014) used in-depth interviews to explore patient experiences of living with OSA, highlighting patients' struggle with the unknowns; which were specifically related to “delayed diagnosis, lack of knowledge before and after diagnosis, and lack of support and follow-up after diagnosis”. *Therefore, the aim of this qualitative evaluation, nested within the randomised controlled study (presented in Chapter 2), was to further explore patient experiences of an OSA remote diagnostic pathway using both the MM monitor and home respiratory polygraphy.*

3.2 Methods

3.2.1 Study design

A nested qualitative evaluation, based on individual semi-structured online interviews, was carried out concurrently with the randomised controlled study (presented in **Chapter 2**) using an embedded mixed method (1) research design.

3.2.1.a: Embedded mixed method research

Mixed methods research refers to the process of combining both qualitative and quantitative data to address the aims of a research study or a series of related studies, incorporating a thorough understanding of the patient's lived experience with the broader, aggregated quantitative findings. Creswell and Plano Clark (2011) proposed six major designs for mixed methods research, including sequential and concurrent designs. Embedded mixed method research design can, therefore, be either sequential or concurrent, and it typically consists of a smaller qualitative or quantitative component embedded (or nested) within a larger qualitative or quantitative study, and the same participants are involved in both (Bishop, 2015). Thus, the smaller component is designed to complement the findings of the larger component and is explicitly viewed as supporting the parent study (Bishop, 2015), resulting in a granular interpretation of the findings (Creswell and Clark, 2010). In this qualitative evaluation, I used a concurrent embedded mixed method research design to further explore patient experiences of the OSA remote diagnostic pathway used in the parent study (presented in **Chapter 2**).

3.2.1.b: Regulatory procedures

Ethical approval for the parent randomised controlled study was obtained from Health Research Authority and Health and Care Research Wales (REC reference: 21/WA/0162) in June 2021 and the study received approval for non-commercial research from NHS Highland (RD&I reference: H1754) in November 2021 (see **Appendix 2.1.1** for ethical approval letters for the RCT). A substantial amendment was approved in April 2022 by the same ethics

committees (Amendment 1; REC reference: 21/WA/0162) to conduct the semi-structured individual interviews for this nested qualitative evaluation. The ethical approval was received after n=18 out of n=40 participants had already been recruited for the parent study; therefore, only the remaining n=22 patients were identified as potential participants. All participants gave signed written informed consent prior to their participation in the online interviews. Ethical amendment approval letters, the PIS, and consent forms are presented in **Appendix 3.1**.

The data arising from each interview was handled in accordance with GCP and the British Sociological Association Ethical Practice Statement (BSA, 2017). The anonymised data were stored securely with password-protected access.

3.2.2 Participants

Participants were recruited from the parent study (presented in **Chapter 2**), and they were from two different clinical settings: a geographically dispersed region in the Highlands and Islands of Scotland, or a densely populated region – inner London.

All potential participants had recently (successfully or unsuccessfully) completed an overnight home diagnostic sleep study, using a MM monitor and respiratory polygraphy simultaneously. Potential participants were then invited to take part in the optional online individual interviews and were asked to provide separate informed consent, either by post or email. Once specific consent was obtained, I contacted the participants by phone and/or email to arrange the interview at a time suitable for them. The aim was to conduct the interviews within 4-8 weeks after they completed the diagnostic sleep study, which would potentially ensure a better recall of their experiences of care.

3.2.2.a: Sample size

In qualitative research, there are no widely accepted standards for formal sample size calculation (Vasileiou et al., 2018). Rather, the final sample size is typically determined by

data saturation i.e the point of '*informational redundancy*' where no new information is being discovered from the interviews (Saunders et al., 2018). I therefore, planned to conduct online individual interviews with up to 12 participants, which was anticipated to be sufficient to achieve data saturation in this patient population.

3.2.3 Data collection

Overnight home diagnostic sleep studies were carried out using the MM monitor (Sunrise solution; Sunrise SA, Belgium) and respiratory polygraphy (ApneaLink™ Air; ResMed Ltd, Australia) simultaneously (see **Chapter 2, Section 2.2.4** for further details). The outcomes of the diagnostic sleep studies from each device are reported for all participants in the parent study (**Appendix 2.4**).

3.2.3.a: Semi-structured interviews

This qualitative evaluation was carried out using semi-structured interviews (duration 30 – 40 minutes). I conducted all interviews remotely *via* a secure platform (Zoom, California, USA), which allowed for the recording and automated transcription of the interviews. Participants received step-by-step instructions *via* email with a link to join the call (without having to download any software). Additional technical support was provided when needed. To ensure participant confidentiality, all interviews were conducted remotely using a Royal Brompton Hospital computer. I was in a private, access-controlled room with no one else present; participants were in their own homes.

The semi-structured interview guide shown in **Figure 3.1** was developed following discussions with an experienced qualitative researcher (Dr Jillian Riley, Imperial College London). The interview guide included pre-specified open-ended questions to guide the discussion with participants. The nature of the semi-structured interviews provided an opportunity to improvise and ask additional questions based on the interviewee's responses to the pre-specified questions. This allowed for further exploration of patient experiences and views on the remote diagnostic pathway. Each interview started with an introductory open-

ended question to establish a rapport with participants, which helped ensure that they could freely share their experiences and thoughts.

The Sunrise OSA TRIAL (SOSAT)

Participants Interview Topic Guide

Introduction

[Confirm consent for recording]

Introductory question:

1. Tell me what you understand about sleep apnoea?

Key questions:

2. Why did you seek medical help for your sleep problem?
3. How did you expect it to be diagnosed?
4. **You used two different devices for your sleep test (the Sunrise and respiratory polygraphy).** Can you tell me about your experiences using both study devices?
5. What do you think are the skills needed to set up and use the home sleep testing devices?

Ending question:

6. Overall, how did you feel about the remote diagnostic pathway for your sleep apnoea, and how could it be improved?

Conclusion remarks

[Thank the participant]

Figure 3.1 Interview guide for the qualitative evaluation nested within the randomised controlled study (presented in **Chapter 2**).

3.2.4 Analysis

3.2.4.a: Transcription of the qualitative data

Interviews were recorded with permission from participants and were transcribed verbatim using an automated transcription feature, integrated within the secure platform. I then manually checked the transcripts against the original recordings to ensure accuracy, and all identifiable characteristics and details were removed.

3.2.4.b: Analysis of the qualitative data

Anonymised transcripts were imported onto a qualitative data analysis software, NVivo (Version 14.23, QSR International, Colorado, USA). Analysis began simultaneously with the first individual interview using a constant comparative analysis approach to capture participants' experiences as they perceived them.

3.2.4.c: Principles of constant comparison analysis

In brief, constant comparative analysis is a method of qualitative data analysis, traditionally used in grounded theory, to perform coding and form categories; and is key to developing a theoretical model that is grounded in the data (Charmaz, 2014, Glaser and Strauss, 2017). Tesch (1990) embraces the importance of constant comparison and describes it as the main intellectual tool used for all intellectual activities whilst conducting the analysis. The process of constant comparative analysis begins simultaneously with data collection. Once the initial qualitative data is collected or generated, coding commences by identifying incidents or concepts. The initial phase of the analysis involves constant comparison of incidents to incidents within the data, and then a comparison between initial codes and subsequent codes. Codes are subsequently grouped into provisional categories, which are then compared with other codes and categories that emerge from successive data (Birks and Mills, 2015, Chun Tie et al, 2019). This process of iterative analysis requires the researcher to utilise both inductive and deductive thinking (Charmaz, 2014).

Constant comparative analysis can, therefore, be used to identify similarities and discrepancies within the data, using an iterative process to continuously refine concepts and categories which leads to the development of a theoretical model, and in this qualitative evaluation, the development of key themes and subthemes relevant to the aim of the study.

3.2.4.d: Development of themes and subthemes

The first part of the analysis for these data involved reading and re-reading each transcript. I then carried out the initial open coding. Phrases and sentences from participants were

examined and labelled with specific codes that reflected each individual concept or incident. Initial coding was performed on the first four interviews, and this was then followed by clustering of the initial codes into provisional categories. Comparison between the codes and any new concepts was carried out for the remaining interviews. The provisional categories were then grouped into key themes and subthemes.

The four earlier transcripts were then re-evaluated to consider any emerging concepts identified in the subsequent interviews. The overall analysis of the qualitative data and the final coding framework were reviewed by an experienced qualitative researcher (Dr Sohag Saleh, Imperial College London) to ensure the rigor of the coding process.

3.3 Results

3.3.1 Participant characteristics

Between 3rd June 2022 and 17th March 2023, 22 of the 40 participants in the parent randomised controlled study were approached to take part in this nested qualitative evaluation. Seven (31%) of the 22 participants agreed to take part in the online individual interviews. These participants (n=7; 71% male) were representative of those in the parent study, however, n=5 (71%) participants were from inner London and n=2 (29%) from Scottish Highlands and Islands. A summary of the participants' characteristics are presented in **Table 3.1**. The baseline characteristics of all participants in the parent study are shown in **Chapter 2, Section 2.3.2**.

Three participants were diagnosed with mild OSA and three were diagnosed with severe OSA based on the sleep study results from the MM monitor or home respiratory polygraphy (see **Chapter 1, Section 1.5.3** for further details on OSA severity). The remaining participant failed both of his sleep studies and was referred for further investigation at his local sleep service. The outcomes of the diagnostic sleep studies, including the unsuccessful attempts, are shown in **Table 3.1**.

Table 3.1 Participants’ characteristics and the outcomes of their diagnostic sleep studies							
Participant ID	Age (Years)	Gender	ESS (0-24)	Location	Overnight sleep study		Diagnosis
					MM monitor	RP monitor	
SOSAT-12	62	Female	14	inner London	Failed	Successful	Mild OSA
SOSAT-15	53	Male	12	Scottish Highlands	Failed	Failed	NA
SOSAT-31	66	Male	21	Scottish Highlands	Successful	Successful	Severe OSA
SOSAT-33	52	Male	20	inner London	Successful	Successful	Severe OSA
SOSAT-36	63	Female	14	inner London	Successful	Successful	Mild OSA
SOSAT-39	62	Male	22	inner London	Successful	Successful	Mild OSA
SOSAT-40	48	Male	20	inner London	Successful	Successful	Severe OSA

ESS: Epworth Sleepiness Scale; MM: mandibular movement; RP: respiratory polygraphy; OSA: obstructive sleep apnoea. Mild OSA: Apnoea-hypopnoea index of 5-15 events per hour; Severe OSA: Apnoea-hypopnoea index of ≥ 30 events per hour.

3.3.2 Key themes and subthemes

The qualitative data analysis resulted in the identification of three key themes and eight subthemes, related to participants' experiences of the OSA remote diagnostic pathway using both the MM monitor and home respiratory polygraphy, and these are shown in **Table 3.2**.

Table 3.2 Key themes and subthemes identified using constant comparative analysis of individual interviews of a subgroup of participants from the randomised controlled study

Themes	Subthemes
Theme 1: Existing knowledge and (un)planned discovery of the sleep problem	▪ Knowledge of sleep apnoea ▪ Experience of symptoms ▪ Seeking medical attention ▪ Expectations of care
Theme 2: Concerns and benefits of home sleep apnoea testing	▪ A Dickensian contraption or an unobtrusive gadget ▪ Home sleep apnoea testing is the way forward
Theme 3: Factors influencing the experience of care	▪ Barriers to a positive diagnosis experience ▪ Facilitators of a positive diagnosis experience

Additional information on key themes and subthemes, plus data synthesis, are presented in **Table 3.3**, **Table 3.4**, and **Table 3.5**. Quotations from participants are used in the tables as anecdotal statements to illustrate the subthemes.

Table 3.3 Theme 1 – Existing knowledge and (un)planned discovery of the sleep problem with four subthemes described

Subthemes	Data synthesis	Anecdotal statements
1- Knowledge of sleep apnoea	All participants had recently completed a diagnostic sleep test for investigation of high pre-test probability OSA, and were either diagnosed with mild to severe OSA or waiting for further investigation to rule in or rule out suspected OSA. However, despite this, participants' lack of OSA knowledge was evident. Most participants vaguely described the condition, and their understanding was limited to “<i>stopping breathing</i>” and “<i>inadequate oxygen</i>” during sleep. This occurred if they knew someone with the condition, or not. One participant highlighted the “<i>knock-on effects</i>” of sleep apnoea symptoms on her life, and another one who works as a medical interpreter demonstrated a clear understanding of the condition and its potential consequences. Only one participant clearly recognised the seriousness of OSA, commenting that “<i>it can be quite serious, I believe</i>”. Another participant who was recently diagnosed with severe OSA, stated that, despite receiving a formal OSA diagnosis more than a decade ago, he did not think that starting treatment was practical due to his occupation, delaying his treatment until retirement (see <i>anecdotal statement</i>):	“... I actually had a test some time ago, 10-15 years ago, and I was diagnosed then but I was working on a ship and it wasn't practical to have a machine so I kind of like put that on hold but now that I am retired from the sea, I found my condition was getting worse and my wife was struggling to cope with the noise.” (SOSAT-31)
2- Experience of symptoms	The symptoms experienced by most participants started years before their referral for investigation of suspected OSA. Nearly all of these patients had been struggling with common symptoms such as excessive daytime sleepiness, tiredness, and snoring, all of which had an impact on their professional and social lives. Participants described their night struggles as	

having “*difficulty sleeping*” or “*staying asleep*”, an example from one patient was:

“...it's very rare I have a decent night's sleep. It's just broken at the best of times.” (SOSAT-15)

In addition, others highlighted the impact of OSA sequelae on their professional activities. One participant, undeniably explained that as a result of “*a real struggle just to keep ‘her’ eyes open*”, her work life also suffered:

“...It's just a struggle, it's a real struggle to concentrate. I mean, I have had to phone in to work and just haven't been able to work in the morning.” (SOSAT-12)

A central feature of OSA, and a common symptom, that made patients live with a “*guilty conscience*” was **snoring**. Whether they were in a waiting room or in the comfort of their homes, it is a constant battle between the feelings of “*embarrassment*” and “*worry*”, as described by a participant:

“...it's (the snoring) getting so bad I don't let other people sleep I mean like my wife and my son and probably I have to separate my bedroom, and sleep in the living room, yeah, to let them sleep. Yeah, so it's getting really bad. And, and I, I don't, and sometimes you have a kind of a guilty conscience. When you want to go back to sleep you can't. You're worried to wake the other people up. And it's not, it's not very good, it's not very good.” (SOSAT-39)

For other participants, the struggle of dealing with these debilitating symptoms extended beyond their nightly and daytime battles to their time of leisure. This struggle was made vivid by a statement from a recently retired patient:

“SOSAT-31: *Because I feel so tired, I feel that sort of life's passing us by, you know? Even when I do my hobbies, I would feel tired and feel like I would, that I would sleep at any time.*

Interviewer: *Could you please tell me more about it?*

SOSAT-31: *Even things that interested me, and I like. I'm quite keen on fishing and boating. I'd be out on the boat going fishing. I have my own boat and I would start feeling drowsy sort of halfway through the day. And I mean, that would be supposedly my enjoyment and I was falling asleep.”*

3- Seeking medical attention

In some cases, participants' realisation of the serious impact of their worsening OSA symptoms on their life and safety, prompted them to seek medical support. One patient who was recently diagnosed with severe OSA, described his concerns and experience with **excessive daytime sleepiness** that led him to seek medical attention:

“...I used to drive hundreds and hundreds of miles without any problem. And it was getting so bad recently that if I just drove 10 miles, sometimes I had to stop because I was feeling sleepy. and started to get a little bit concerned obviously that I wasn't safe driving...”

but not only that it was the fact that I was so tired all the time. I would wake up from a night's sleep and I wouldn't feel like I'd slept I would feel like I was still tired. And if I if I just sat down again I would fall asleep straight after a full night of sleep. So, you know, it's the feeling of not having any energy to do anything.” (SOSAT-31)

In other cases, relatives' recognition of the symptoms, and thus their concern about the health of their loved ones, encouraged participants to seek medical attention for their sleep problem:

“...my wife said that she has very often woken up and she has been very concerned because I've not been breathing to the point of where she was going to wake me up. But then I started breathing again. So, as I say, it's been ongoing for some time and now having a diagnosis has made me feel a lot better.” (SOSAT-33)

For most participants, their recognition of OSA symptoms and their keenness to alleviate the significant impact on their professional and social lives led them to seek medical advice from healthcare professionals. However, for some patients, it was a “by-product” of receiving medical support for another health condition, which therefore, resulted in an *unplanned discovery* of the sleep apnoea, as one participant described it:

“...I just happened to be in the right place at the right time” (SOSAT-15).

4- Expectations of care

Upon their referral for a diagnostic sleep study, most participants appeared to have different expectations of the diagnostic pathway. These expectations were largely influenced by the participants' or their partners' previous knowledge of, and experiences with, the same or similar sleep condition. Here, one patient who had undergone an in-hospital sleep testing years ago commented on what he expected:

"...I honestly thought that I would have to go to hospital and maybe spend the night there or certainly a few hours while I undergo tests."
(SOSAT-31)

Participants highlighted that although they would have liked a "quicker" referral and diagnosis process, they understand that the journey to treatment may require long waiting times. As one patient commented:

"...I know that a lot of people with sleep apnea have waited a considerable time for their testing and then a considerable time for treatment afterwards."
(SOSAT-33)

Despite the delay, they expected, in getting the care they needed, participants looked forward to getting their "normal" life back. This feeling of hope whilst being in the middle of the care pathway was pointed out by a patient recently diagnosed with OSA, describing what he was most looking for:

"... I know that there's treatment for it. I know that we can move forward and hopefully get some sort of semblance back, of normality, back in my life."
(SOSAT-33)

Table 3.4 Theme 2 – Concerns and benefits of home sleep apnoea testing with two subthemes described

Subthemes	Data synthesis	Anecdotal statements
1- A Dickensian contraption or an unobtrusive gadget	All participants have recently completed an overnight diagnostic sleep study using a MM monitor and respiratory polygraphy, simultaneously. The experiences of the patients in this study reveal similar insights and views on these sleep testing devices. Participants highlighted that the respiratory polygraphy was “<i>quite straightforward</i>” to wear and set up, however, they described it as “<i>cumbersome and restrictive</i>”, exacerbating the “<i>anxiety</i>” of being tested for “<i>something which relatively can be quite serious</i>”. The struggle of dealing with this diagnostic device was depicted with great clarity by one patient who described his experience with respiratory polygraphy: Additionally, another participant who made the decision to take off the respiratory polygraphy device nearly an hour after initiating the sleep test, explained how it was not possible for him to sleep due to the test indicator lights being lit and bright green in his countryside dark bedroom:	<i>“... it (the respiratory polygraphy) gave me a hard time and I couldn't and I didn't have a comfortable night; I mean usually I don't have a comfortable night but that was extra uncomfortable because this thing like you have three connections, one in your finger, one on your nose, and one on your heart. The one in your finger, every time you want to turn right, left, that cable, you know, it goes around your body or is pushing, and it keeps waking you up.” (SOSAT-39)</i> <i>“...I mean I could almost see the inside of my eyelids with that bright light, and I had no chance of sleeping with it.” (SOSAT-15)</i>

Reflecting on their experiences with the MM monitor, participants appreciated the “*unobtrusive*” nature of this diagnostic device. Some participants also acknowledged that setting up the MM monitor may be challenging for those who are not “*technically minded*” due to requiring a smartphone application to activate the sleep test. As described by a 63-year-old female, who clearly preferred the “*very simple*” MM monitor but also needed additional support to successfully complete her overnight sleep study:

“...I had to get help in order to get the application downloaded and make sure the Wi-Fi, what is it?, the Bluetooth I think is on. Yes. So, I'm not very good with these technologies. So, if someone has not helped me with it, I don't think I would have been able to do anything.” (SOSAT-36)

Compared to respiratory polygraphy, the MM monitor was largely preferred by patients because it did not impede their sleep, where they explained that “*you hardly notice you're wearing it*”. One participant commented on his experience with both diagnostic devices and his “*concerns*” during the night:

“...I did not have any kind of concern that it (the MM monitor) would move in the night and in fact, the other device (the respiratory polygraphy) when I sometimes would kind of wake up and then I looked down a couple of times and the monitor was flashing red and it had only moved slightly and I thought oh I'm kind of glad I woke up now because it might have invalidated the whole night.” (SOSAT-40)

Despite voicing their preference for the “easy to use”, “unobtrusive”, and “comfortable” sleep diagnostic device, participants emphasised the importance of validating the accuracy of the MM monitor against “standard procedures” for OSA diagnosis. If it works, then it was seen by the participants as a “superior” alternative to the respiratory polygraphy, as one of them commented:

“So, the Sunrise (the MM monitor), the one on your chin. In theory, I think was far superior to the quite Dickensian contraption. That is the old system (the respiratory polygraphy).” (SOSAT-15)

2- Home sleep apnoea testing is the way forward

The participants in this qualitative evaluation expressed a preference for carrying out sleep apnoea testing at their own homes. For some, it’s a two-way benefit for the patients and the healthcare providers i.e. NHS, when considering costs. For others, it’s the notion of having a very difficult time when trying to sleep whilst away from home. Most participants clearly emphasised that a home sleep test would result in a better reflection of one’s normal sleep, which is central to an accurate diagnosis. This view was summarised by the statement of this participant commenting on home sleep testing:

“...I do think that’s the way to go because people are going to sleep in a normal sleep pattern better at home. In their normal environment. Then, you know, if I had to go to a centre somewhere with kit bags, you know. I mean, who can sleep if they go to a hospital, no one sleeps anyway!” (SOSAT-15)

Table 3.5 Theme 3 – Factors influencing the experience of care with two subthemes described

Subthemes	Data synthesis	Anecdotal statements
1- Barriers to a positive diagnosis experience	The “<i>inflexibility</i>” of the referral process and the long waiting times for a diagnostic sleep study appeared to have an impact on patients' experiences of the care received. While they may understand the reasons behind the inevitable long waiting times, participants expressed their hopes for a “<i>quicker</i>” care pathway to alleviate their struggles. Here, in spite of having an urgent referral, a patient recently diagnosed with OSA described her experience: In addition, the perception of stigma related to a failed sleep study resulted in negative feelings, potentially impacting the provision of a positive patient experience. Participants described feelings of guilt and disappointment, whether the sleep study failure was due to human error or unavoidable technical issues with the diagnostic devices, as commented by a patient who failed to complete both of his sleep studies: Some participants also highlighted that having only one chance, a “<i>one-time deal</i>”, to successfully complete their sleep studies exacerbated the pressure exerted on them. Having the opportunity to repeat the study if needed was perceived as a positive factor that would take some of that pressure off.	“...It (the waiting time) took few months, and I was absolutely struggling with it because it was at that time when I was really struggling. And I kept asking the team, the respiratory team here to try to, try to, you know, give me an appointment.” (SOSAT-36) “...I actually felt quite guilty because I know that you guys, you know, have been very good, you've done all this. You've organised it, you've sent it out, and really what I've done is wasted your time because of not being successful in doing what, was needed to be achieved.” (SOSAT-15)

Further issues with accessibility were also reported by other participants. These included a lack of digital connectivity due to living in the “*countryside with poor phone signals*” and limited digital literacy, both of which may impede the successful set-up and activation of the MM monitor. Additional accessibility concerns highlighted the difficulty of following combined sets of instructions for patients with attention deficit disorders, which were important to successfully complete the overnight sleep study.

2- Facilitators of a positive diagnosis experience

Most participants reported that having their sleep study at home, with clear and easy-to-follow instructions to set up the sleep testing devices, would facilitate a seamless diagnostic experience. In addition to sleeping in the comfort of their own homes, participants highlighted additional safety and financial benefits of undertaking home sleep testing. One participant described how the home sleep testing saved him, and his wife, a long journey to the hospital:

“...that would take us nearly two hours to get there. So to go there and have a test it's a 150-mile round trip. And it's a full day, you know, even if you just went for a few hours. We would probably have to stay overnight you know which incurs additional costs. Yeah. Whereas by doing it's a home, it's so much easier.”
(SOSAT-31)

Partners were also identified as a key factor supporting the patient throughout the diagnostic pathway. When describing their experiences of setting up and putting on the sleep testing devices, participants often highlighted the importance of family members' involvement. As one participant commented:

“...I had help from my partner to put on the chest device (the respiratory polygraphy). I think I could have done it by myself, but it would have been trickier.”
(SOSAT-40)

	Expediating the process from referral to diagnosis, and thus accelerating treatment, was appreciated by participants, facilitating their “pleasant” diagnostic experience. Here, one patient reflected on the speed of the process:	<i>“...I just want to say thank you for doing everything so fast. Because I was expecting this to take months and months of waiting, and everything seems to have gone so fast. And as I say, I got my machine yesterday, and I'm looking forward now to, well, getting a proper night's sleep for the next, for the foreseeable future.” (SOSAT-31)</i>
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3.4 Discussion

The participants in this qualitative evaluation, nested within the randomised controlled study (presented in **Chapter 2**), described their experiences of the OSA remote diagnostic pathway, giving a clear preference for home sleep testing with the “*unobtrusive*” MM monitor, compared to the more “*cumbersome and restrictive*” respiratory polygraphy monitor. Participants also provided insights into some of the barriers and facilitators of a positive OSA diagnosis experience. In addition, participants showed an overall lack of knowledge about sleep apnoea. Taken together, these findings provide further understanding of the factors influencing patients’ experiences of the remote diagnostic pathway and expand on the findings of the parent study.

3.4.1 Significance of the findings

Consistent with the results from the parent study (presented in **Chapter 2, Section 2.3.4**), participants in this qualitative evaluation favoured home sleep testing, emphasising their preference for sleeping in their own environment. Earlier studies have also shown that patients prefer in-home sleep testing, compared to in-hospital testing (Garg et al., 2014, Campbell and Neill, 2011, Bruyneel et al., 2011). Interestingly, these participants highlighted that a remote diagnostic pathway is not only cheaper for the NHS but was also associated with time and financial savings for themselves, compared to having to travel to their local sleep service to collect their sleep testing device for a home sleep study, or to undergo an in-hospital sleep testing. In addition, NICE clinical guidelines report that home sleep testing for OSA diagnosis, using respiratory polygraphy, is indeed cost-effective compared to in-hospital testing using the same device (NICE Diagnostic Evidence Review, 2021b).

The majority of participants in the parent study expressed their preference for the MM monitor, finding it easier to set up and more comfortable to sleep with, compared to respiratory polygraphy. The main reason for favouring the MM monitor over respiratory polygraphy was its “*unobtrusive*” nature; which meant that it did not impede participants’

sleep during the night. However, these potential patient-reported advantages may come with the risk of exacerbating health inequalities (*'the digital divide'*) (Farre et al., 2023). Some participants highlighted that setting up and activating the MM monitor may be challenging for those who are not *"technically minded"* or those who live in rural areas with poor connectivity. Although this was not an issue for most of the participants recruited for this study, care should be taken when using such digital health technologies, where additional support or alternative diagnostic strategies may be needed for some patients.

The participants in this nested study described a number of barriers and facilitators of a positive OSA diagnosis experience. These included factors that were external to healthcare providers such as partners and family involvement in supporting patients during the diagnostic pathway. Other factors were internal, and these included the inflexibility of the referral process and the pressure of having only one chance to successfully complete the diagnostic sleep study at home. It is also worth noting that although participants were expecting their care in the NHS to be lengthy, with long waiting times for their appointments, they also expressed their need for a diagnostic pathway that is faster than currently experienced. As discussed in **Chapter 1 (Section 1.4)**, access to OSA care and sleep study waiting times vary across the UK, with the current waiting time for a sleep study through a sleep service in the Scottish Highlands being over 12 months. This is compared to a waiting time of 6 months in a tertiary referral centre in inner London (*Personal communication with the clinical leads at these sleep services, 2022*). Therefore, accelerating the time to OSA diagnosis, and thus treatment, may contribute to facilitating a positive patient experience, which is one of the NHS's core pillars of high-quality care (Department of Health, 2008).

Although most of the participants had received a formal diagnosis of OSA, there was a clear lack of knowledge about OSA and its consequences. This was consistent with Rodgers (2014) who reported participants' lack of knowledge both before and after OSA diagnosis. It also aligns with previous UK data highlighting poor awareness and knowledge of OSA

amongst both patients and the general population (British Lung Foundation, 2014, Sia et al., 2017). This is particularly important as a lack of OSA knowledge and awareness may lead to delayed symptom recognition, resulting in delayed opportunities for diagnosis. Patients with OSA usually experience symptoms for long periods of time, due to delayed identification and misdiagnosis (Rahaghi and Basner, 1999). Such delays may have a negative impact on patients' HRQoL, and add to the substantial clinical and public health burden of undiagnosed and untreated OSA (Rejón-Parrilla et al., 2014); also see **Chapter 1, Section 1.4.1**. On the other hand, by communicating OSA diagnosis to patients with OSA-related symptoms, their HRQoL improved regardless of the severity of their condition (Isidoro et al., 2015). Therefore, a review of the strategies currently used to educate the public and communicate a new diagnosis to patients may be of value for improving OSA clinical care in the UK, or elsewhere.

3.4.2 Critique of the method

The patients invited to participate in this qualitative evaluation were from a clinical population and were recruited from rural Scottish Highlands and Islands and urban inner London, enabling the evaluation of patient experiences across geographically distinct UK regions. However, the findings of this evaluation are reported with caution due to several limitations.

Firstly, the small sample size, together with the majority of participants being male and from inner London, may increase the risk of bias and limit the variation and diversity of the study population; which may also limit the applicability of the findings (Noble and Smith, 2015). Secondly, all interviews were conducted remotely in line with the parent study protocol (presented in **Chapter 2**). Although this remote approach may have led to communication challenges between myself and some of the interviewees, it had the advantage of speeding up the recruitment process (Engward et al., 2022) and the ability to interview hard-to-reach patients living in rural areas, which would not have been possible if these were in-person interviews.

In addition, I personally conducted all the interviews for this nested qualitative evaluation. Whilst this provided a standardised interview approach, it may have also introduced bias, with a tendency to put more emphasis on certain aspects as influenced by my personal biases and existing assumptions; impacting the “*truth value*” of this qualitative evaluation (Morse et al., 2002). Using multiple investigators to minimise bias was not possible due to the COVID-19 pandemic. Therefore, my use of an embedded mixed method research design facilitated the triangulation of both quantitative and qualitative data, which has enabled a more comprehensive interpretation of the findings; ensuring the trustworthiness of the evaluation outcomes (Noble and Smith, 2015).

3.5 Conclusion

The findings of this nested qualitative evaluation expand our understanding of patient experiences with remote diagnostic pathways for OSA. Participants expressed their preference for home sleep apnoea testing, using the “*unobtrusive*” MM monitor. Participants also described their planned or unplanned personal journeys to OSA diagnosis, however, despite receiving a formal diagnosis, their lack of sleep apnoea knowledge was evident. These findings, along with other specific facilitators of a positive patient experience such as a flexible referral process, expedited home-based diagnostics, and family involvement and support, may enable the redesign of OSA clinical care pathways by matching available diagnostic strategies with the preferences, needs, and expectations of patients.

Part Two

Investigations of the clinical management for OSA

Chapter 4

Virtual consultations for patients with obstructive sleep apnoea: a systematic review and meta-analysis

*The systematic review and meta-analysis in this chapter was published (under CC BY-NC Licence) in the **European Respiratory Review Journal** in December 2022*

4.1 Introduction

OSA is estimated to affect nearly one billion adults worldwide, with increasing prevalence, as discussed in **Chapter 1 (Section 1.3.3)**; (Benjafield et al., 2019 and Peppard et al., 2013). It is also associated with debilitating symptoms, reduced neurocognitive performance and HRQoL, increased risk of cardiovascular and metabolic morbidity and occupational accidents (Garbarino et al., 2016, Lévy et al., 2015), and overall represents a major public health concern (Lyons et al., 2020).

NICE clinical guidelines recommend CPAP therapy as the first-line treatment for adult patients with symptomatic OSA (National Institute for Health and Care Excellence, 2021a). As discussed in **Chapter 1 (Section 1.7.1)**, CPAP therapy improves daytime sleepiness, daily functioning, and HRQoL, however, its effectiveness is contingent on optimal adherence (Rotenberg et al., 2016a). NICE clinical guidelines also recommend a consultation with the patient within one month of CPAP therapy initiation, and subsequent follow-ups based on patients' needs until optimal outcomes are achieved (National Institute for Health and Care Excellence, 2021a). This intensive management strategy adds to the strain on respiratory sleep services already coping with the increasing demand, as discussed in **Chapter 1, Section 1.4.2**.

Accelerated by the COVID-19 pandemic, digital health interventions such as telemonitoring and virtual consultations have been introduced into sleep medicine to meet this growing demand (Johnson et al., 2021, Turnbull et al., 2022, Pinnock et al., 2022). Such transition has the potential to revolutionise the way healthcare is delivered, improving accessibility and affordability (World Health Organization, 2019), though there are concerns about exacerbating health inequalities, particularly in disadvantaged communities such as minorities and rural populations (Litchfield et al., 2021).

In a previous systematic review, our research group reported on the applicability and feasibility of telemonitoring and virtual consultations in reviewing patients with OSA using

CPAP therapy (Murphie et al., 2017). At the time, evidence on clinical and cost-effectiveness of these management strategies was scarce. Subsequent reviews have reported promising findings on the potential of digital health interventions to improve adherence to CPAP therapy, but have not evaluated the effectiveness of such strategies on patient-reported outcomes and cost-effectiveness (Aardoom et al., 2020, Hu et al., 2021, Labarca et al., 2021, Verbraecken, 2021). *Therefore, the aim of this systematic review and meta-analysis was to investigate the effectiveness of virtual consultations compared to in-person consultations on patient-reported sleepiness and cost-effectiveness for adults with OSA treated with CPAP therapy.*

4.2 Methods

This systematic review and meta-analysis was registered in the International Prospective Register of Systematic Reviews (PROSPERO), an open-access international database of prospectively registered systematic reviews in health and social care. The review protocol (PROSPERO ID: CRD42022297532) is presented in **Appendix 4.1**. The review was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement, an evidence-based guideline comprising a minimum set of items for reporting in systematic reviews and meta-analyses (Page et al., 2021).

4.2.1 Systematic review: search strategy and data sources

A comprehensive search of six electronic databases (*MEDLINE, EMBASE, Scopus, Cochrane Library [Central], CINAHL, and medRxiv*) was conducted from database inception to 10th January 2022. No limits on publication year or language were imposed. The search strategy, developed in consultation with an Imperial College London medical librarian, used the search terms and keywords: “*Sleep Apnoea, Obstructive*”, “*OSA*”, “*OSAHS*”, “*Sleep-disordered breathing*” AND “*Positive airway pressure*”, “*PAP*”, “*CPAP*” AND “*Virtual consultation*”, “*Remote consultation*”, “*Telemedicine*” (See **Appendix 4.2** for the full search strategy).

The search results were de-duplicated in EndNote (Version 20, Clarivate, Philadelphia, United States). I then manually searched the reference lists of the included studies, other published reviews, and relevant sleep medicine and respiratory journals (e.g. *SLEEP*, *Sleep Medicine*, *Thorax*) to identify any additional relevant studies.

4.2.2 Eligibility criteria

The PICO framework, which encapsulates key components of the eligibility criteria for including studies in the review, was used to prespecify the review **P**opulation, **I**ntervention, **C**ontrol, and **O**utcomes. This commonly used framework is outlined in the Cochrane Handbook for Systematic Reviews as a proposed method for determining whether studies are eligible for inclusion (Thomas et al., 2019). In addition to the review PICO, shown in **Table 4.1**, studies were included if they were RCTs, quasi-RCTs, or controlled clinical trials (CCTs) of adult patients with OSA using CPAP, comparing virtual consultations to in-person consultations for the follow-up of CPAP therapy.

Table 4.1 PICO framework for inclusion and exclusion criteria

Population	Adults with a clinical diagnosis of OSA, either naïve or established users of CPAP; recruited from any healthcare or community setting. Studies were excluded if they investigated patients with other types of sleep disorders such as Central Sleep Apnoea.
Intervention	Any form of a virtual consultation between a patient and a healthcare provider. This included either synchronous or asynchronous communications made via telephone or videoconferencing, with or without real-time telemonitoring of CPAP. No limitations were imposed regarding the number of consultations, methods of CPAP initiation, or the duration of consultations. Trials that investigated automated interventions, without direct input from a healthcare professional, were excluded.
Comparator	The comparator group were allocated to a clinical in-person consultation, with or without real-time telemonitoring of CPAP therapy.
Outcomes	The primary clinical outcome was subjective sleepiness, assessed by the Epworth Sleepiness Scale, and the primary organisational outcome was cost-effectiveness of the intervention. Additional outcomes were clinical, patient and/or clinician-reported, and environmental impact outcomes.
Study design	Studies were included if they were randomised controlled trials (RCTs), quasi-randomised controlled trials (quasi-RCTs), or controlled clinical trials (CCTs)

OSA; obstructive sleep apnoea, CPAP; continuous positive airway pressure.

4.2.3 Study selection and data extraction

The study selection process was conducted using the software Covidence® (Veritas Health Innovation, Melbourne, Australia). Once the studies had been uploaded onto the software, two reviewers were required to independently carry out the study selection and data extraction to reduce the possibility of omitting relevant studies or data, as outlined in the Cochrane Collaboration guidance (Lefebvre et al., 2019). Together with Dr Phyllis Murphie, I reviewed all the studies. We independently screened titles and abstracts using the predefined inclusion and exclusion criteria (**Table 4.1**). We then independently assessed the full-text reports of potentially eligible studies to determine inclusion eligibility. Any discrepancies

between ourselves at either stage were resolved by a third reviewer (Dr Julia Kelly), or the wider review team (Dr Stuart Little, Prof Hilary Pinnock, Prof Mary Morrell, and Prof Michael Polkey).

Dr Murphie and I performed data extraction independently using a customisable form in Covidence® software (Veritas Health Innovation, Melbourne, Australia), with comparison and discussion of the findings. The following data were extracted:

- Study design, methodology, follow-up duration, and participants' demographic and baseline data
- Details of intervention, including mode of delivery, intensity, and duration
- Details of comparator
- Relevant findings, specifically those related to our primary and additional outcomes

When needed, corresponding authors were contacted to either seek missing data or clarify unclear methodologies. If the required data were not available in the correct format, the study was excluded from the quantitative meta-analysis.

4.2.4 Risk of bias assessment

Dr Murphie and I independently assessed the risk of bias (RoB) for each included trial by using the Cochrane Collaboration's tool for assessing risk of bias in randomised trials (Higgins et al., 2011). In the event of a disagreement, Dr Kelly arbitrated. The assessment of reporting bias through funnel plots was not appropriate in this review due to the small number of studies included in the meta-analyses (Higgins JPT, 2022).

4.2.5 Data synthesis

Data focusing on clinically relevant outcomes, including patient-reported sleepiness, cost-effectiveness, and adherence to CPAP therapy, are reported in this review. Where appropriate data (i.e. mean $\pm$ SD) were available for the key outcomes, findings were pooled for a meta-analysis. I used a random-effects model, with mean differences for continuous data, to pool the results and to calculate 95% CI and the P values for key outcomes between

the virtual consultations group and the control group. The endpoint data after exposure to the intervention were used for these analyses. I^2 statistic was used to assess the statistical heterogeneity of the included studies; a value greater than 50% was considered an indicator of substantial heterogeneity. Subgroup analyses by the mode of delivery of the virtual intervention and by study follow-up duration were performed. I conducted all the statistical analyses using the review manager software, RevMan (Version 5.4.1, Cochrane Collaboration, Copenhagen, Denmark).

4.3 Results

4.3.1 Overview of eligible studies

The literature search identified 875 records. After deduplication, 324 studies were retained for initial title and abstract screening. Of these, 63 studies were retrieved for full-text review and assessment for eligibility. 51 studies did not meet the inclusion criteria, and a total of 12 studies (Taylor et al., 2006, Stepnowsky et al., 2007, Isetta et al., 2015, Fields et al., 2016, Frasnelli et al., 2016, Turino et al., 2017, Lugo et al., 2019, Nilius et al., 2019, Pépin et al., 2019, Tamisier et al., 2020, Kooij et al., 2021, Fietze et al., 2022) were included in the review as outlined in the PRISMA flow diagram (**Figure 4.1**). The commonest reason for exclusion was '*wrong intervention*' (n=16 studies). Nine of these studies appeared initially to meet the inclusion criteria, but were excluded because they required an in-person consultation for patients randomised to virtual care; see **Appendix 4.3** for further details.

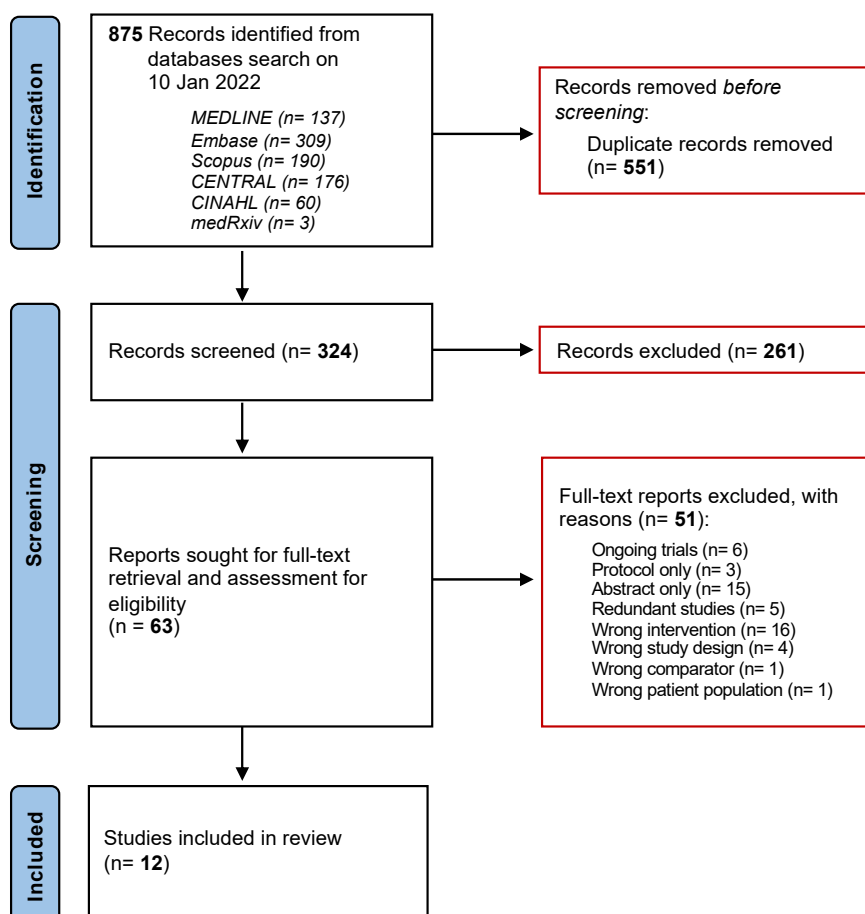


Figure 4.1 PRISMA flow diagram of the records identified and assessed during the study selection process. PRISMA; Preferred Reporting Items for Systematic Reviews and Meta-Analyses, CENTRAL; Cochrane Central Register of Controlled Trials, CINAHL; Cumulative Index to Nursing and Allied Health Literature.

4.3.2 Study characteristics

A summary of the included studies is presented in **Table 4.2**. 11 of the 12 studies were RCTs and one was a CCT, published between 2006 and 2021. These trials had study sample sizes ranging between 45 to 306 participants and follow-up durations spanning 30 days to 6 months. In these trials, multimodal digital health interventions were used to deliver virtual consultations to patients with OSA using CPAP. In total, the 12 included studies represented 1,823 adult participants with the majority being male (averaging 78% of trials participants) and overweight, diagnosed with moderate to severe OSA (**Table 4.3**). Only four studies reported ethnicity data (Taylor et al., 2006, Stepnowsky et al., 2007, Fields et al., 2016, Fietze et al., 2022), and two (Taylor et al., 2006, Kooij et al., 2021) reported only minimal data on socioeconomic status.

Table 4.2 Summary of the studies included in the systematic review and meta-analysis

Study (Country)	Study design and overall risk of bias	Number of participants (n= 1,823)	Population description	Intervention	Intensity and duration	Mode of delivery	Main findings
Taylor et al 2006 (USA)	RCT FU: 30 days High RoB	Total: 114 VC: 56 IP: 58	Adult patients with OSAS who were initiating CPAP therapy	Telemonitoring via the Health Buddy OSAS + Patients with 'high-risk' responses were contacted within 24 h	Patients were contacted as needed to resolve issues	Telephone consultation	ESS was not reported for post-intervention follow-up
Stepnowsky et al 2007 (USA)	RCT FU: 2 months Moderate RoB	Total: 45 VC: 24 IP: 21	Adult patients newly diagnosed with OSA	Telemonitoring via a flow generator data + Objective and subjective patient reports triggered patient contact	Patients were contacted as needed based on a pre-defined clinical pathway	Telephone consultation	No significant differences in ESS scores between the study groups at baseline and post-intervention
Isetta et al 2015 (Spain)	RCT FU: 6 months Moderate RoB	Total: 139 VC: 69 IP: 70	Adult OSA patients requiring CPAP treatment	Telemonitoring via a website developed for this study + input evaluation triggered patient contact	Virtual consultations via skype were scheduled at 1 and 3 months Consultation duration: 38.97 ± 12.04 mins	Video consultation	Improvement in ESS at 6 months, but no significant difference in change from baseline between the study groups The telemedicine-based strategy had a lower total cost compared to standard care
Frasnelli et al 2015 (Switzerland)	CCT FU: 30 days High RoB	Total: 223 VC: 113 IP: 110	Adult patients with sleep apnoea	Telemonitoring via CPAP + A colour-coded algorithm triggered patient contact	Patients were contacted as needed for a duration of ~30 mins	Telephone consultation	ESS was not reported for post-intervention follow-up

Fields et al 2016 (USA)	RCT FU: 3 months Moderate to high RoB	Total: 60 VC: 32 IP: 28	Adult patients with OSA from two community-based outpatient centres	Telemonitoring via APAP + scheduled follow-up contact and if needed	Initial evaluation visit for 40 min with a 10 min (or less) follow up call at week 1. Virtual consultations scheduled at 1 and 3 months for 20 mins each	Initial evaluation via real-time CVT + telephone consultation for follow up	No significant difference in the change of ESS scores from baseline to 3-months follow-up between the study groups
Turino et al 2016 (Spain)	RCT FU: 1 and 3 months Moderate RoB	Total: 100 VC: 52 IP: 48	Adult patients with newly diagnosed OSA requiring treatment with CPAP	Telemonitoring via MyOSA – Oxigen Salud web database + Automatic alarms triggered patient contact	Patients were contacted as needed to resolve issues	Telephone consultation	ESS was not reported for post-intervention follow-up The total average cost per randomised patient was 28% lower in the VC group than in the IP standard care group
Lugo et al 2019 (Spain)	RCT FU: 3 months Moderate RoB	Total: 186 VC: 94 (32 with CPAP) IP: 92 (40 with CPAP)	Adult patients with suspected OSA who were referred to the Sleep Unit	Telemonitoring via CPAP and + input in a custom web application triggered patient contact	Virtual consultations were scheduled at 3, 6, 12 weeks for no more than 15 mins each	Video or Telephone consultation	No significant differences in the ESS scores between the study groups The costs of the VC were cheaper than those for IP standard care, and the Bayesian analysis showed that the VC was cost-effective
Nilius et al 2019 (Germany)	RCT FU: 6 months Moderate to high RoB	Total: 80 VC: 40 IP: 40	Adult OSA patients who had suffered an ischemic stroke within the last 3 months	Telemonitoring + A colour-coded algorithm triggered a more detailed evaluation and patient contact if needed	Patients were contacted as needed for a duration of 5 mins	Telephone consultation	VC group had a significantly lower ESS scores at 6-months follow up

Pepin et al 2019 (France)	RCT FU: 6 months Moderate RoB	Total: 306 VC: 157 IP: 149	Adult patients with severe OSA and high cardiovascular risk	Telemonitoring via CPAP and the multimodal system + Automatic algorithms triggered patient contact	Patients were contacted as needed + regular assessments at day 8 and months 1 and 6	Telephone or teleconsultation	ESS scores significantly improved in both study groups, but the size of improvement was significantly higher in the VC group
Tamisier et al 2020 (France)	RCT FU: 6 months Moderate RoB	Total: 206 VC: 102 IP: 104	Newly diagnosed adult patients with OSA and low cardiovascular risk who were referred for CPAP therapy.	Telemonitoring via CPAP and the multimodal system + Automatic algorithms triggered patient contact	Patients were contacted as needed based on an automatic algorithm	Telephone or teleconsultation	ESS scores significantly improved in both study groups, with no significant difference between the groups.
Fietze et al 2021 (Germany)	RCT FU: 6 months Moderate to high RoB	Total: 224 VC: 110 IP: 114	Adult patients with moderate to severe OSA	Telemonitoring via APAP + predefined criteria triggered patient contact	Patients were contacted as needed based on predefined criteria	Telephone consultation	Change from baseline to 6 months in ESS scores was not significantly different between the two groups
Kooij et al 2021 (Netherlands)	RCT FU: 4 weeks 12 weeks 24 weeks Moderate RoB	Total: 140 VC: 70 IP: 70	Adult patients diagnosed with moderate or severe OSA who require CPAP treatment	Telemonitoring + not achieving pre-defined objectives (e.g adherence and residual AHI) triggered patient contact	Patients were contacted as needed + scheduled follow-ups at 1 and 4 weeks	Video and Telephone consultation	ESS was not reported for post-intervention follow-up

RCT; randomised controlled trial, CCT; controlled clinical trial, FU; follow up duration, RoB; risk of bias, ESS, Epworth Sleepiness Scale, VC; virtual consultations, IP; in-person consultations, OSA; obstructive sleep apnoea, AHI; apnoea-hypopnoea index, CPAP; continuous positive airway pressure.

Table 4.3 Baseline characteristics of the participants in the included studies

Study	Number of participants (n= 1,823)	Age (years)		Gender (Male %)		BMI (kg/m ²)		AHI (events per hour)	
		Virtual	In-person	Virtual	In-person	Virtual	In-person	Virtual	In-person
Taylor et al 2006	Total: 114 VC: 56 IP: 58	45.8 ± 10	44.6 ± 8.5	66%	71%	NR	NR	NR	NR
Stepnowsky et al 2007	Total: 45 VC: 24 IP: 21	60 ± 10.8	58 ± 13.7	98%	98%	33.3 ± 4.9	30.5 ± 5.1	44.8 ± 17.9	37.6 ± 14.3
Isetta et al 2015	Total: 139 VC: 69 IP: 70	51.0 ± 8.9	47.0 ± 10.9[†]	85%	87%	32.8 ± 7.3	33.6 ± 8.3	45 (35; 70) [#]	52 (35; 62) [#]
Frasnelli et al 2015	Total: 223 VC: 113 IP: 110	55 (47; 63) [#]	55 (45; 61) [#]	76%	78%	NR	NR	37 (23; 62) [#]	40 (20; 69) [#]
Fields et al 2016	Total: 60 VC: 32 IP: 28	46.7 ± 13.1	58.2 ± 14.4	93%	94%	33.2 ± 6.0	32.9 ± 3.8	32.0 ± 33.9	30.1 ± 30.0
Turino et al 2016	Total: 100 VC: 52 IP: 48	56 ± 13	54 ± 12	77%	77%	35 ± 7	35 ± 7	52 ± 25	53 ± 26
Lugo et al 2019	Total: 186 VC: 94 (32 with CPAP) IP: 92 (40 with CPAP)	50.39 ± 11.31	50.82 ± 12.15	70%	66%	29.97 ± 6.19	31.50 ± 10.91	24.68 ± 21.01	33.60 ± 28.96
Nilius et al 2019	Total: 80 VC: 40 IP: 40	55.4 ± 10.4	58.6 ± 9.3	73%	73%	31.7 ± 5.4	30.1 ± 6.6	41.2 ± 19.0	37.6 ± 18.4
Pepin et al 2019	Total: 306 VC: 157 IP: 149	60.8 (53.8; 66) [#]	61.8 (54.7; 66.1) [#]	73%	74%	32.4 (29.6; 36.5) [#]	31.4 (28.1; 35) [#]	47 (35; 60.5) [#]	45 (35.4; 61.2) [#]

Tamisier et al 2020	Total: 206 VC: 102 IP: 104	51.9 (44.8; 58.8) #	49.4 (40; 57.9) #	58%	68.3%	30.5 (27.5; 34.9) #	31.3 (26.6; 35.2) #	45 (34; 58) #	42.3 (33; 57.6) #
Fietze et al 2021	Total: 224 VC: 110 IP: 114	53.6 ± 11.8	53.1 ± 10.6	83%	79%	32.8 ± 6.4	31.7 ± 5.6	35.3 ± 17.6	37.0 ± 20.3
Kooij et al 2021	Total: 140 VC: 70 IP: 70	52.3 ± 12.4	54.3 ± 11.9	83%	76%	BMI > 30: n = 51 (73%)	BMI > 30 n = 46 (66%)	31 (22; 46) #	30.5 (20; 42) #

Data are presented as n or mean ± SD, unless otherwise stated. VC; virtual consultation, IP; in-person consultation, BMI; body mass index AHI; apnoea-hypopnoea index, NR; not reported. #; median (interquartile range), †; Significantly different value from the other group

4.3.3 Risk of bias and quality of evidence assessment

A summary of the RoB assessment for the included studies is provided in **Figure 4.2**.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective Reporting (reporting bias)	Other Bias
<i>Taylor et al 2006</i>	+	?	-	+	-	+	-
<i>Stepnowsky et al 2007</i>	+	+	-	+	?	+	+
<i>Isetta et al 2015</i>	+	+	-	+	+	+	+
<i>Frasnelli et al 2015</i>	-	-	-	+	+	+	+
<i>Fields et al 2016</i>	+	?	-	+	-	+	+
<i>Turino et al 2016</i>	?	?	-	+	+	+	+
<i>Lugo et al 2019</i>	+	+	-	+	+	+	+
<i>Nilius et al 2019</i>	+	?	-	+	-	+	+
<i>Pepin et al 2019</i>	+	?	-	+	+	+	+
<i>Tamisier et al 2020</i>	+	?	-	+	+	+	+
<i>Fietze et al 2021</i>	?	?	-	-	+	+	+
<i>Kooij et al 2021</i>	+	?	-	+	+	+	+

 Low risk of bias
 High risk of bias
 Not Clear

Figure 4.2 A summary of risk of bias assessment for the included studies.

Overall, the assessment showed variation in the RoB amongst the included studies due to the complex nature of the intervention. As would be expected, there was a high RoB in all included studies, because of the inability to blind participants and personnel to allocation. Additionally, the RoB arising from allocation concealment was found to be unclear. Imprecision of the findings is unlikely due to the large sample size in the meta-analysis. However, the certainty of evidence was rated down because of the indirectness in the studies. There was variation in how the intervention of interest, virtual consultations, were delivered. Additionally, all the trials recruited the population of interest (patients with OSA using CPAP) and investigated the outcomes of interest. Taken together, with reference to the

Grading Recommendations, Assessment, Development and Evaluations (GRADE) framework, the evidence to support the use of virtual consultations for improving the primary outcome, ESS scores, in patients with OSA is moderate.

4.3.4 Primary outcomes

4.3.4.a: Patient-reported sleepiness

The change in subjective sleepiness, assessed by ESS, was reported by eight studies (Stepnowsky et al., 2007, Isetta et al., 2015, Fields et al., 2016, Lugo et al., 2019, Nilius et al., 2019, Pépin et al., 2019, Tamisier et al., 2020, Fietze et al., 2022). These studies found an improvement in ESS scores from baseline to follow-up in both virtual and in-person consultation groups, with two trials (Nilius et al., 2019, Pépin et al., 2019) reporting a significantly greater reduction in ESS scores in the virtual consultation group. No difference was observed in the ESS scores for virtual compared to in-person consultations (mean difference [95% CI]: -0.39 [-1.38 to 0.60] points, $p = 0.44$; moderate-certainty evidence) in the seven studies ($n=1089$) that had the endpoint data in the correct format for a meta-analysis (Figure 4.3). However, considerable statistical heterogeneity was observed ($I^2=72\%$).

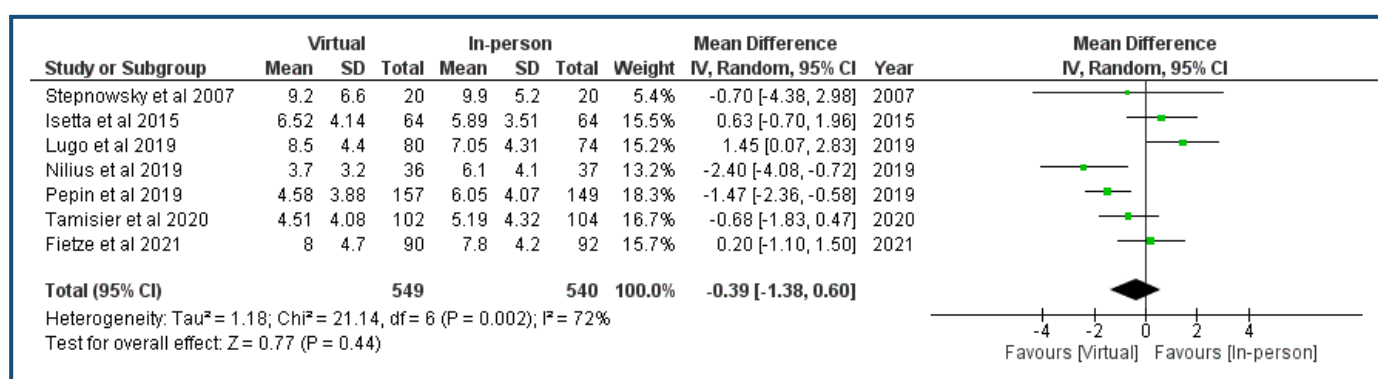


Figure 4.3 Forest plot of the mean difference in patient-reported sleepiness scores, assessed by Epworth Sleepiness Scale (ESS), in patients randomised to virtual compared to in-person consultations for the management of obstructive sleep apnoea. The diamond represents the 95% confidence interval (95% CI) of the pooled estimate of the mean difference.

Subgroup analysis by the mode of delivery of the virtual intervention showed no differences in the ESS scores for virtual compared to in-person consultations in the three studies (n=295 patients) of telephone consultations alone (mean difference [95% CI]: -0.96 [-2.89 to 0.97] points, $p = 0.33$) and the four studies (n=794 patients) of video and/or telephone consultations (mean difference [95% CI]: -0.09 [-1.39 to 1.22] points, $p = 0.89$) (**Figure 4.4**).

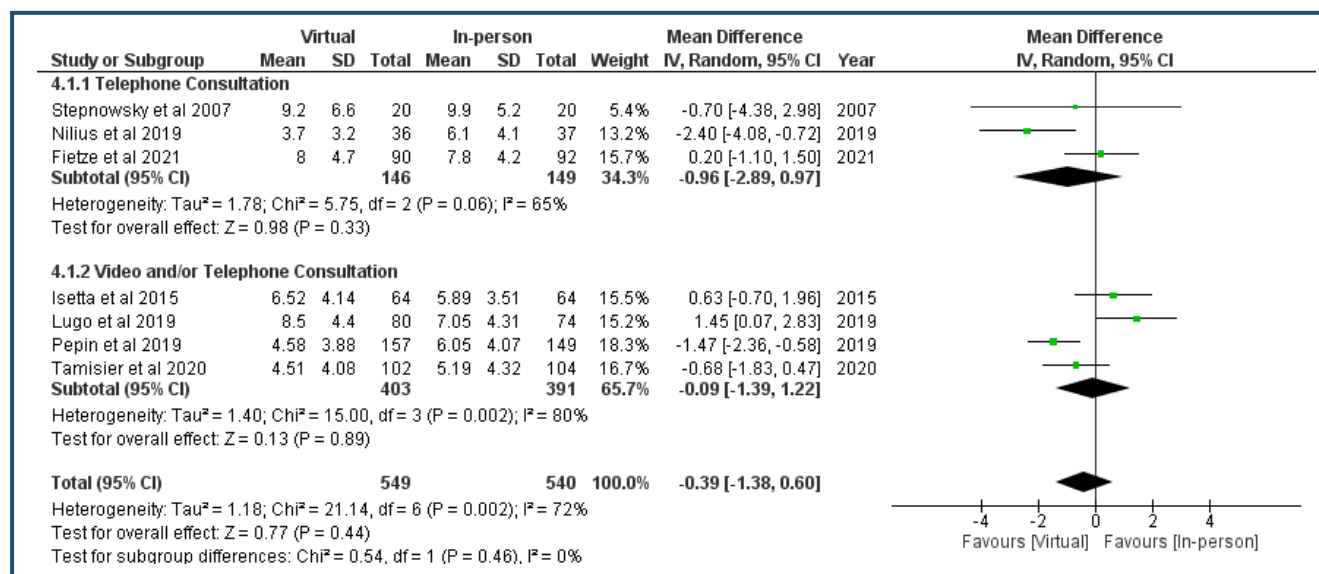


Figure 4.4 Forest plot of the subgroup analysis for the mode of delivery of virtual consultations in the included studies. The diamonds represent the 95% confidence interval (95% CI) of the pooled estimate of the mean differences in patient-reported sleepiness scores, assessed by Epworth Sleepiness Scale, in patients randomised to virtual compared to in-person consultations for the management of obstructive sleep apnoea.

A further subgroup analysis by study follow-up duration also showed no differences in the ESS scores for virtual compared to in-person consultations in the two studies (n=194 patients) with ≤ 3 months follow-up duration (mean difference [95% CI]: 1.08 [-0.51 to 2.67] points, $p = 0.18$) and the five studies (n=895 patients) with a 6-month follow-up duration (mean difference [95% CI]: -0.76 [-1.74 to 0.22] points, $p = 0.13$) (**Figure 4.5**).

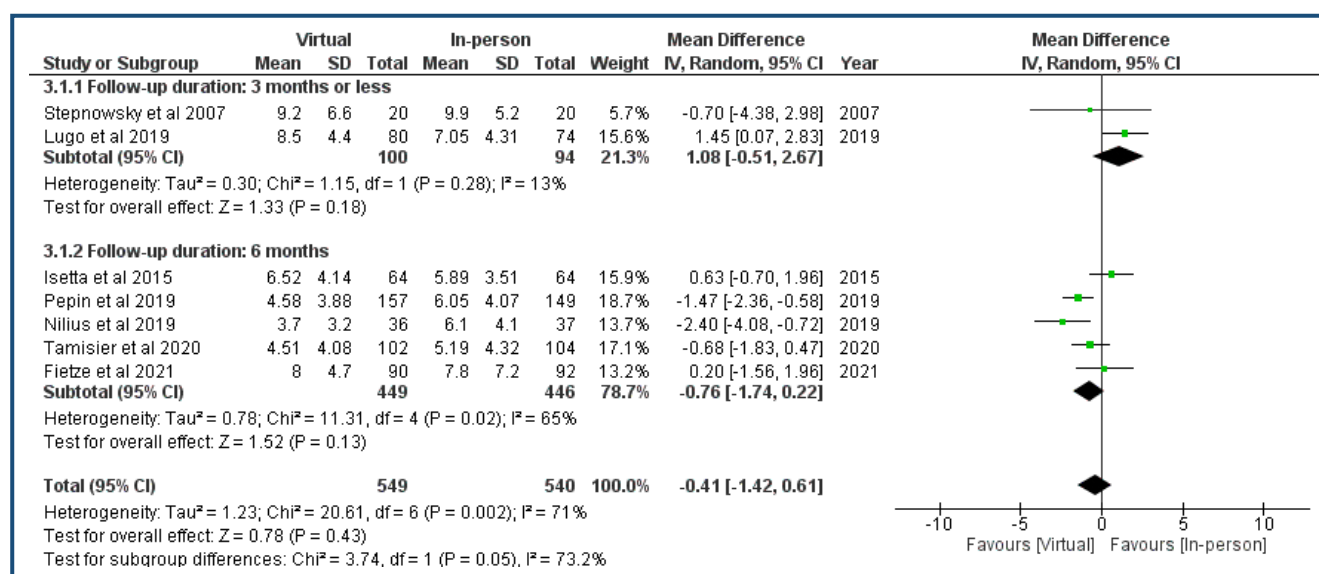


Figure 4.5 Forest plot of the subgroup analysis for the follow-up duration in the included studies. The diamonds represent the 95% confidence interval (95% CI) of the pooled estimate of the mean differences in patient-reported sleepiness scores, assessed by Epworth Sleepiness Scale, in patients randomised to virtual compared to in-person consultations for the management of obstructive sleep apnoea.

5.3.4.b: Cost-effectiveness

Three trials (Isetta et al., 2015, Turino et al., 2017, Lugo et al., 2019) from Spain investigated the cost-effectiveness of virtual compared to in-person care for patients with OSA, from patient and provider perspectives. Isetta et al. (2015) reported that a telemedicine-based strategy had a slightly lower total cost, with a 69% estimated probability that it would be cheaper than in-person care. When considering only OSA-related costs, the probability increased to 98% with estimated costs of €150.90 and €114.00 respectively for the in-person and virtual care strategies. In another RCT, Turino et al. (2017) found the total average cost for each randomised participant to be 28% lower in the virtual care group (€123.60) than in the in-person care group (€170.90), with a €47.32 difference between the two study groups. The investigators also reported the Incremental Cost-effectiveness Ratio (ICER) per Quality-Adjusted Life Year which was estimated at €17,358.65 (QALY). The third study conducted by Lugo et al. (2019) showed, using Bayesian analysis, that the telemedicine-based strategy was

cost-effective; OSA-related costs for the virtual and in-person care groups were €264.96 and €412.03, respectively.

4.3.5 Secondary outcomes

4.3.5.a: Adherence to CPAP therapy

CPAP therapy usage, assessed objectively, was reported by all included studies (n=12). The average CPAP usage at follow-up assessment ranged from 3.5 to 5.6 hours per night with virtual consultations and 2.1 to 5.6 hours per night with in-person consultations. Nine studies (Taylor et al., 2006, Stepnowsky et al., 2007, Isetta et al., 2015, Fields et al., 2016, Turino et al., 2017, Lugo et al., 2019, Tamisier et al., 2020, Kooij et al., 2021, Fietze et al., 2022) found no statistically significant difference in the mean hours of CPAP usage between the two care strategies, while the other three studies (Frasnelli et al., 2016, Nilius et al., 2019, Pépin et al., 2019) showed a significantly higher adherence amongst participants randomised to virtual consultations.

The pooled analysis of 10 RCTs (Taylor et al., 2006, Stepnowsky et al., 2007, Isetta et al., 2015, Fields et al., 2016, Turino et al., 2017, Lugo et al., 2019, Nilius et al., 2019, Pépin et al., 2019, Tamisier et al., 2020, Fietze et al., 2022) comprising 1299 patients demonstrated a significant difference in favour of virtual consultations (mean difference [95% CI]: +0.43 [0.06 to 0.80] hours per night, $p = 0.02$; moderate-certainty evidence); see **Figure 4.6**. This equates to an average of a 26 (04 to 48) minute increase in CPAP usage per night. However, considerable statistical heterogeneity was observed ($I^2 = 68\%$).

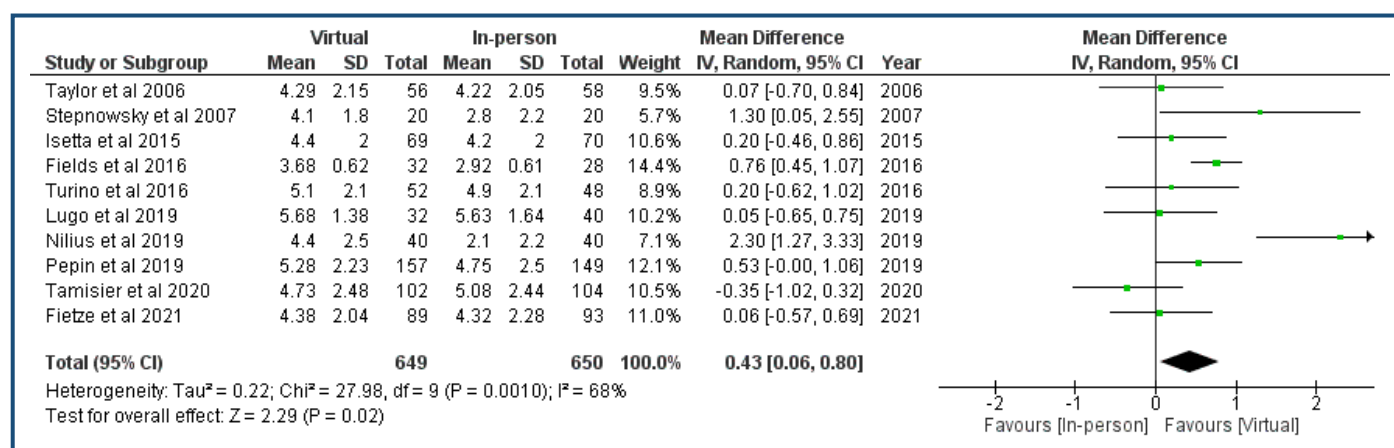


Figure 4.6 Forest plot of the mean difference in continuous positive airway pressure (CPAP) usage (hours per night) in virtual compared to in-person consultations. The diamond represents the 95% confidence interval (CI) of the pooled estimate of the mean difference.

Subgroup analysis by the mode of delivery of the virtual intervention showed no differences in the CPAP usage for virtual compared to in-person consultations in the three studies ($n=302$ patients) of telephone consultations alone (mean difference [95% CI]: 1.17 [-0.28 to 2.63] hours per night, $p = 0.11$) and the seven studies ($n=997$ patients) of video and/or telephone consultations (mean difference [95% CI]: 0.28 [-0.05 to 0.61] hours per night, $p=0.09$) (**Figure 4.7**).

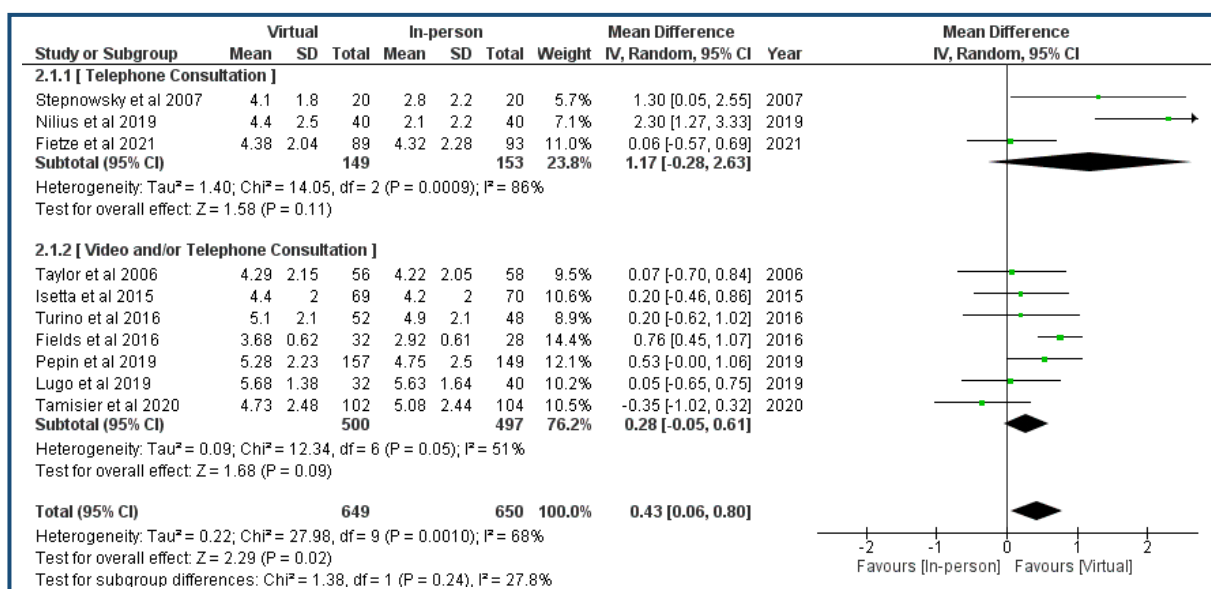


Figure 4.7 Forest plot of the subgroup analysis for the mode of delivery of virtual consultations in the included studies. The diamonds represent the 95% confidence interval (95% CI) of the pooled estimate of the mean differences in continuous positive airway pressure (CPAP) usage (hours per night) in patients randomised to virtual compared to in-person consultations for the management of obstructive sleep apnoea.

A further subgroup analysis by study follow-up duration showed a significant difference in the CPAP usage for virtual compared to in-person consultations in the five studies (n=386 patients) with ≤ 3 months follow-up duration (mean difference [95% CI]: 0.45 [0.04 to 0.86] hours per night, $p = 0.03$). However, there was attenuation of the effect size in the other five studies (n=913 patients) with a 6-month follow-up duration (mean difference [95% CI]: 0.47 [-0.20 to 1.13] hours per night, $p = 0.17$) (**Figure 4.8**).

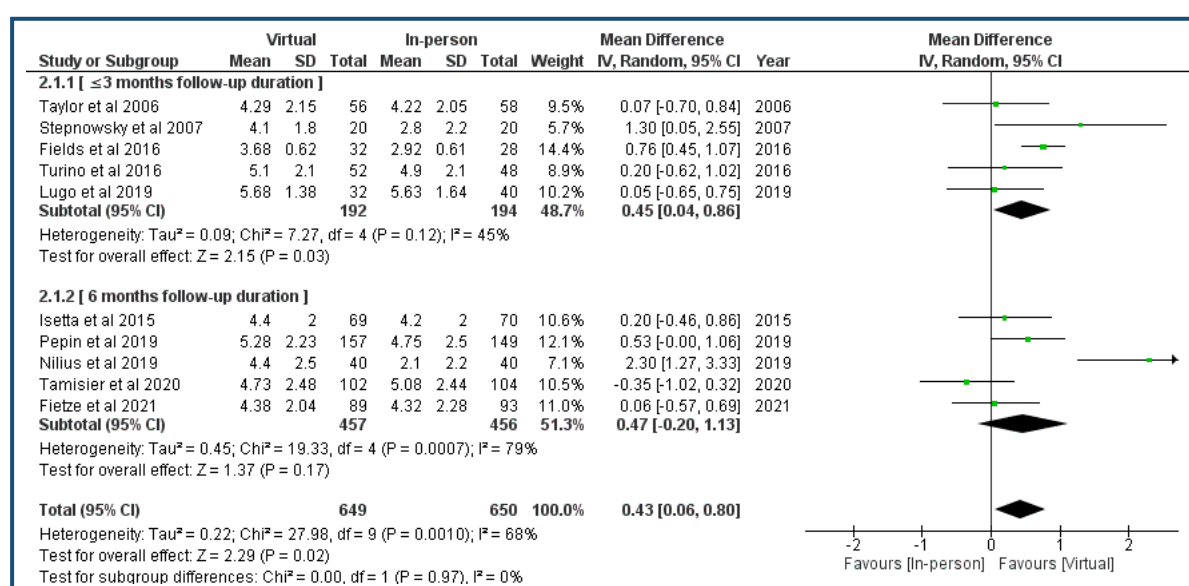


Figure 4.8 Forest plot of the subgroup analysis for the follow-up duration in the included studies. The diamonds represent the 95% confidence interval (CI) of the pooled estimate of the mean differences in continuous positive airway pressure (CPAP) usage (hours per night) in patients randomised to virtual compared to in-person consultations for the management of obstructive sleep apnoea.

4.3.5.b: Change in quality of life

10 trials (Taylor et al., 2006, Stepnowsky et al., 2007, Isetta et al., 2015, Fields et al., 2016, Turino et al., 2017, Lugo et al., 2019, Pépin et al., 2019, Tamisier et al., 2020, Fietze et al., 2022, Nilius et al., 2019) reported the change in HRQoL from baseline using multiple different generic and disease-specific instruments, including EQ-5D (n=2), SF-12 (n=3), FOSQ (n=4), and a modified FOSQ (M-FOSQ) (n=1) (see **Chapter 1, Section 1.3.4** for further details on HRQoL assessment). Seven of these trials reported a general improvement in HRQoL amongst participants randomised to both virtual and in-person consultations, with no statistically significant differences between the two groups (EQ-5D n=1/2; SF-12 n=2/3;

FOSQ n=3/4; and M-FOSQ n=1/1). Three trials found a greater improvement of HRQoL in the virtual consultations group compared to the in-person consultations group (EQ-VAS n=1/2; SF-12 physical component n=1/3; and FOSQ n=1/4).

4.3.5.c: Environmental impact outcomes

None of the trials reported environmental impact outcomes (including travel distances from home to clinic, mode of transport, and carbon-footprint emissions).

4.3.6 Sensitivity analyses

Due to the substantial heterogeneity amongst the included studies in the meta-analyses, I performed post-hoc sensitivity analyses after seeking input from Dr Kelly and then the wider review team. Nilius et al. (2019) met the inclusion criteria, but was thought on clinical grounds to be an outlier due to its specific patient population (OSA patients with recent ischemic stroke), which may have resulted in unexpected between-group differences in the study outcomes, specifically ESS scores and CPAP adherence. However, when this study was removed from the meta-analyses, the results remained unchanged: the pooled weighted mean difference for subjective sleepiness was (mean difference [95% CI]: -0.09 [-1.07 to 0.89] points, $p=0.86$) and for CPAP usage was (mean difference [95% CI]: +0.30 [0.00 to 0.60] hours per night, $p=0.05$).

4.3.7 Deviations from protocol

Although the heterogeneity assessment was higher than specified in the protocol ($I^2 > 50\%$), I decided to perform the meta-analyses due to the complex nature of the intervention; this decision was after seeking input from the wider review team. I have also conducted subgroup and sensitivity analyses.

4.3.8 Inter-reviewer agreement

The degree of agreement between Dr Murphie and myself was high (>90%), and any discrepancies amongst us were resolved by consensus without further input, except in two instances where arbitration and input were sought from Dr Kelly and the wider review team.

4.4 Discussion

To my knowledge, this is the first systematic review and meta-analysis to evaluate the effectiveness of virtual compared to in-person consultations on both patient-reported sleepiness and also cost-effectiveness. The main findings are that virtual consultations using telephone or videoconferencing are as effective as in-person consultations for improving patient-reported sleepiness (*moderate-certainty evidence*) in patients with OSA treated with CPAP therapy and appear to be cost-effective. Additionally, virtual consultations, modestly increased the average CPAP usage by nearly half an hour per night when compared to in-person consultations. No published studies compared the environmental impact of virtual versus in-person follow-up strategies.

4.4.1 Significance of the findings

Subjective sleepiness, assessed by the ESS, is an important outcome for the management and monitoring of patients with OSA (see **Chapter 1, Section 1.3.4** and **1.5.1**). In this meta-analysis, there was no difference in the magnitude of improvement of ESS scores between virtual and in-person consultations, though ESS decreased in both groups. Importantly, this observation persisted with subgroup analyses by the mode of delivery of the virtual consultation (telephone alone or video and/or telephone consultations) and by study follow-up duration (≤ 3 months or 6 months), suggesting that virtual care delivered in a variety of strategies remained as effective as in-person care.

CPAP therapy adherence was higher in the virtual consultations group than the in-person consultations group, although the 26 minute increase in CPAP usage is slightly lower than the minimal clinically important improvement of 30 minutes per night (Patil et al., 2019). This

increase in CPAP usage is consistent with earlier meta-analyses which focused on the use of virtual care strategies specifically to investigate the effect on CPAP adherence (Aardoom et al., 2020, Hu et al., 2021, Labarca et al., 2021). However, recent post-COVID-19 data has shown a reduction in CPAP adherence with remote CPAP set-up, compared to in-person (Stanchina et al., 2022, Turnbull et al., 2022). Whilst CPAP set-up is just one part of the process of initiation onto therapy, these data highlight the need for robust assessment of new healthcare strategies, before they become mainstream. In this meta-analysis, assessment of whether specific characteristics of the virtual consultation could have influenced the adherence to CPAP therapy were performed. Subgroup analysis by follow-up duration showed a trend for the effect size to attenuate in studies with 6 month compared to ≤ 3 month follow-up durations, which may support the efficacy of long-term follow-up interventions (Patel et al., 2022).

Virtual care strategies were less costly than in-person strategies in the three studies that reported cost-effectiveness (Isetta et al., 2015, Turino et al., 2017, Lugo et al., 2019). Whilst these data need to be interpreted with caution, it is reassuring that there is no suggestion that virtual follow-up is more costly. The cost savings were mainly driven by fewer in-person follow-up visits, savings on transport, and less loss of productivity. However, the cost-utility analyses were limited to one healthcare context (i.e. Spain) and there was little clarity in how all the calculations of the mean cost per patient were performed. Further global data is likely to emerge as such virtual care strategies are continued following the COVID-19 pandemic. Well-designed studies are important to establish whether virtual consultations are a clinically and cost-effective strategy for the management of patients with OSA using CPAP, particularly from the patient, societal, and healthcare provider perspectives.

There has been a growing interest in the importance of reporting ethnicity and socioeconomic status data in clinical trials as well as addressing their potential effect on health inequalities (Buttery et al., 2021). A concerning finding of this review is that only one-

third of the studies reported data on ethnicity and two studies presented minimal data on socioeconomic status. This reduces interpretability and generalisability of their findings, emphasising the need for explicit reporting of trial participants' demographics. Such data facilitates investigations of OSA phenotypes, where heterogeneous clinical manifestations exist. This data will also inform discussions around health inequalities as we move towards personalised medicine approaches for OSA care (Edwards et al., 2019); see **Chapter 6, Section 6.4** for further details on future directions for research in this area.

Virtual care strategies have the potential to improve access to healthcare services and address geographical barriers to delivering high-quality care (Barbosa et al., 2021, Greenhalgh et al., 2012). However, patient-focused concerns exist, specifically about increasing health inequalities (*'the digital divide'*) (Greenhalgh et al., 2021), emphasising the need to ensure that the care is tailored to patients' context, needs, and preferences.

One unanticipated finding in this review was that none of the included studies reported data on any of the environmental impact outcomes, despite increased awareness of the climate emergency (Purohit et al., 2021). This observation signifies a potential gap in evidence related to virtual care strategies for the management of OSA. A critical and interesting direction for future research would be to assess the impact of virtual compared to in-person consultations on the environment, reinforcing the need for sustainable delivery of healthcare.

4.4.2 Critique of the method

This review was conducted in accordance with current recommendations and guidelines (Page et al., 2021, Higgins JPT, 2022). However, there are several limitations to consider when interpreting the findings.

The studies were relatively small in size, with most containing between 100 and 200 participants. They were also varied in terms of the methodologic quality, identified by the RoB assessment. The studies were heterogeneous in type, intensity, and duration of both virtual

and in-person care strategies; potentially limiting the interpretation of the results. Care should also be taken when interpreting the subgroup analyses due to the small number of included studies. I suggest future studies should, therefore, be powered to evaluate the different techniques, cost-effectiveness, and the environmental impact of delivering virtual consultations for the management of patients with OSA. This is to identify the most efficacious components of these virtual care strategies from patient, clinical, and economic perspectives.

Finally, it is important to stress that this review did not address the diagnosis of OSA, and therefore cannot be used to support a virtual diagnostic pathway; which I was concurrently investigating in the randomised controlled study presented in **Chapter 2**.

4.5 Conclusion

The findings of this systematic review and meta-analysis suggest that virtual patient care delivered by telephone or video consultations is as effective as in-person consultations for improving subjective sleepiness in patients with OSA treated with CPAP. Moreover, virtual consultations modestly increased CPAP therapy adherence, compared to in-person consultations, and were not associated with reduced cost-effectiveness. Virtual follow-up of patients with OSA using CPAP therapy should be available as an alternative care strategy to in-person follow-up, where patients prefer it.

Chapter 5

**A UK survey of experiences with, and preferences for,
remote versus in-person continuous positive airway
pressure therapy initiation in patients with
obstructive sleep apnoea**

5.1 Introduction

Clinical care pathways for the diagnosis and treatment of sleep apnoea vary across the UK regions, as illustrated in **Figure 1.17 (Chapter 1, Section 1.9.3)**. The COVID-19 pandemic has also led to increased utilisation of digitally-enabled respiratory sleep services, as part of the national mitigation strategies for coronavirus infection control (British Sleep Society, 2020, Schiza et al., 2021). Consequently, clinical care pathways for the diagnosis, treatment, and management of OSA have been modified, with virtual care strategies being prioritised as the means of service delivery, particularly in the initiation of CPAP therapy for newly diagnosed patients (Turnbull et al., 2022, Schiza et al., 2021, Craig et al., 2020). These changes in the clinical care pathway could impact patient experiences of care and, therefore, investigating patients' perspectives is of importance for post-pandemic OSA clinical care delivery; particularly, the impact on engagement with the treatment.

Digitally-enabled healthcare services are in line with the NHS Long Term Plan (National Health Service, 2019), discussed in **Chapter 1, Section 1.6.1**. However, recent post-pandemic data found a reduction in CPAP therapy adherence, with higher discontinuation rates when CPAP therapy was initiated remotely (Turnbull et al., 2022, Stanchina et al., 2022). Contrary to these findings, Meurling et al. (2023) reported that remote CPAP education for newly diagnosed patients during the COVID-19 pandemic did not significantly impact short-term adherence, compared to in-person CPAP education. However, adherence to CPAP therapy was modest, with only 38% of the patients achieving good adherence (≥ 4 hours per night for $\geq 70\%$ of nights); see **Chapter 1, Section 1.7.1** for a discussion on the recommended adherence threshold.

The systematic review and meta-analysis that I carried out (presented in **Chapter 4**), investigated the clinical and cost-effectiveness of virtual consultations, compared to in-person consultations for the management of patients with OSA (Alsaif et al., 2022). The main finding was that virtual care, delivered by telephone or video consultations, was as effective as in-

person consultations for improving subjective sleepiness in patients with OSA treated with CPAP. In addition, I found that this management strategy modestly improved adherence to CPAP therapy by an average of 26 (95% CI: 4 to 48) minutes per night, without increasing the costs (see **Chapter 4, Section 4.3**). These findings support the use of virtual care as a clinical management strategy for patients with OSA treated with CPAP, and are at odds with the recent findings of Turnbull et al. (2022) and Stanchina et al. (2022).

Patients' insights on clinical management strategies can provide essential information to healthcare providers to help inform the redesign of clinical care pathways for improved health outcomes (Paul and Glenn, 2006), as discussed in **Chapter 1, Section 1.8**. In general, it is known that people with chronic diseases are likely to be more adherent to medical treatment if it is tailored to their choices and preferences (Losi et al., 2021) and although the NHS regards "*each patient's experience as the final arbiter in everything the NHS does*" (Department of Health, 2011), the role of patient experiences and preferences in the clinical management of OSA is currently unclear. It is, therefore, important to consider what matters most to patients. *The aim of this UK patient survey was to investigate the experiences of, and preferences for, remote versus in-person CPAP therapy initiation in patients with OSA.*

5.2 Methods

5.2.1 Study design

An anonymous, self-administered online survey was carried out to explore experiences with, and preferences for CPAP therapy initiation in patients with self-reported sleep apnoea, and experience of using CPAP therapy in the UK.

5.2.1.a: Regulatory procedures

Participation in the survey was voluntary, and potential participants were recruited using a community-based approach *via* two UK charities that support patients with sleep apnoea (the Sleep Apnoea Trust and Hope2Sleep); see **Sections 5.2.3.a and 5.2.3.b** for more information about these patient-support charities. The survey was approved by Imperial College

Research Governance and Integrity Team on 1st February 2023 (Imperial College Research Ethics Committee Reference number: 6363566); the ethical approval letter is presented in **Appendix 5.1.1**. An online invitation included a summary of the survey, a link to the PIS, plus an online consent statement (see **Appendix 5.1.2**). The invitation and the PIS also explained the confidentiality and anonymity of the survey. In addition, our research group's contact details were provided in case potential participants had any further queries about the survey.

The survey responses were collected anonymously *via* a secure online survey platform, Qualtrics XM (Qualtrics, Washington, USA), which was General Data Protection Regulation (GDPR)-compliant. The anonymised dataset arising from the survey was uploaded to a cloud-service, OneDrive (Microsoft Corporation, Washington, USA), using an Imperial College account to facilitate secure storage of the dataset; with password-protected access.

5.2.2 Survey objectives

Primary objectives of the survey were:

- To investigate participant-reported satisfaction with their CPAP initiation
- To investigate participant preferences for CPAP initiation: remote versus in-person

Secondary objective of the survey was:

- To explore factors that may influence participant satisfaction and preferences

5.2.3 Participants

Members of the UK patient-support charities, the Sleep Apnoea Trust and Hope2Sleep, were invited to participate in this survey. Potential participants were eligible if they were ≥ 18 years old, with self-reported sleep apnoea, and experience of using CPAP therapy. Participants also had to be able and willing to complete the self-administered online survey. These criteria were assessed by filtering questions before they could continue to the survey (see **Appendix 5.2**). Exclusion criteria were inability or unwillingness to respond to the self-administered online survey, no self-reported sleep apnoea, and no previous experience of using CPAP therapy.

5.2.3.a: The Sleep Apnoea Trust (www.sleep-apnoea-trust.org/about-us)

The Sleep Apnoea Trust (SATA) is a Charitable Incorporated Organisation (Charity number: 1186235, Charity Commission) that was founded as a patient group in 1993 to support sleep apnoea patients and their families through education, advocacy, raising awareness, and assisting research and development. SATA is primarily run by sleep apnoea patients (8 Trustees and 15 Volunteers) and they currently support more than 1,300 members. Their social media platforms (i.e. Facebook and Twitter) have in excess of 1,800 followers.

5.2.3.b: Hope2Sleep (www.hope2sleep.co.uk/about-us)

Hope2Sleep was founded as a non-profit company in 2009 and it became a registered charity and a Charitable Incorporated Organisation in 2016 (Charity number: 1168089, Charity Commission). Hope2Sleep is run by sleep apnoea patients and sleep professionals (4 Trustees, and 5 Volunteers) to support people with all forms of SDB. The patient-support charity currently has more than 8,600 members, and their social media platforms (i.e. Facebook and Twitter) have more than 9,100 followers.

5.2.3.c: Sample size

A convenience sampling approach was used for this survey, and no formal sample size calculation was performed. All active online members of SATA and Hope2Sleep were invited to complete the anonymous, self-administered online survey (approximately 17,000 potential recipients). I anticipated a conservative response rate of between 5-10% of those who were invited to take part in the survey (850 to 1,700 of 17,000 potential recipients), with a pragmatic target of at least 500 responses.

5.2.4 Data collection

5.2.4.a: Survey development

The aim and objectives of this survey were informed by the focused informal discussions with sleep consultants from different sleep services across the UK (see **Chapter 1, Section 1.9**), and the findings of the systematic review and meta-analysis (presented in **Chapter 4**).

A bespoke survey was developed, as no validated questionnaires have been published to assess patient perspectives of the clinical management of OSA, specifically their experiences with, and preferences for CPAP therapy initiation. The survey development was based on a framework, adapted from that described by Gehlbach et al. (2010).

- **Literature review:** The first stage of the survey development included a literature review, with reference to existing patient surveys and frameworks e.g. the OSA patient experience survey by the BLF (*now known as Asthma + Lung UK*), and the NHS patient experience book (British Lung Foundation, 2014, NHS Institute for Innovation and Improvement, 2013).
- **Focused discussions:** A series of focused discussions within our research group, and across other UK sleep services were also carried out. All questions in the survey were patient-focused, to explore OSA clinical care pathways and evaluate participants' experiences and preferences.
- **The first draft:** This was independently reviewed by my supervisors (Prof Morrell and Dr Kelly) and was discussed amongst our research group. The feedback from the initial reviews was collated and a second draft was produced.
- **The second draft:** This draft of the survey was reviewed by two independent expert collaborators:
 - **Dr Annabel Nickol** – Lead Consultant in Respiratory and Sleep Medicine, Oxford Centre for Respiratory Medicine, Oxford University Hospitals NHS Foundation Trust
 - **Prof Joerg Steier** – Professor of Respiratory and Sleep Medicine, Lane Fox Respiratory Service, Guy's & St Thomas' NHS Foundation Trust

Feedback was provided on the overall content and face validity (Boateng et al., 2018), focusing on question relevancy and importance, clarity and comprehensibility, and any missing content (Streiner et al., 2015). The feedback from the second round of reviews was used to produce a third draft of the survey.

- **The third draft:** This draft of the survey was reviewed by patient representatives from the patient-support charities (SATA and Hope2Sleep) to ensure that the questions

were relevant from the patients' perspectives, readable, and sufficiently comprehensive to assess their experiences and preferences.

- **Pilot testing:** The survey was then transferred from a Microsoft Word-based document (Version 16.65, Microsoft Corporation, Washington, USA) onto the online survey platform, Qualtrics XM (Qualtrics, Washington, USA). A pilot test was carried out with five laypeople to identify and troubleshoot any technical issues before disseminating the survey to potential participants.

The final bespoke survey consisted of three sections*, with a total of 31 questions that took approximately 15-30 min to complete (see **Appendix 5.2**).

- **Section 1** asked participants about the pathway and the care they received for their OSA diagnosis and treatment
- **Section 2** assessed participants' experiences of the care they received, including their satisfaction with, and preferences for CPAP therapy initiation and follow-up care
- **Section 3** collected sociodemographic and patient-reported clinical data e.g. comorbidities

***Please note:** *the results of the survey will not be presented based on the above sections, however, the data will be presented in reverse order according to the stratification of participants based on satisfaction; see Section 5.2.5.*

All the survey questions were closed with pre-specified response options, except where numerical values or qualitative insights were sought; these queries were open, with a space for participants to write their responses.

5.2.4.b: Survey distribution

The anonymous, self-administered online survey was distributed *via* the patient-support charities, SATA and Hope2Sleep. Their active online members received an email invitation and/or an advert with a link to participate in the survey *via* the online survey platform. Potential participants had the opportunity to read the PIS and the consent statement before agreeing to take part in the survey by ticking a 'YES' box (see **Appendix 5.1.2**).

Participants were able to stop answering the survey questions at any time, and their answers were not recorded unless the survey was submitted. If participants submitted their answers to the survey, their anonymous responses were kept and used for data analysis.

5.2.5 Analysis

The anonymised survey data were exported from the online survey platform, Qualtrics XM (Qualtrics, Washington, USA) onto a secure, GCP-compliant electronic database; Microsoft Excel (Version 16.65, Microsoft Corporation, Washington, USA) for data cleaning and management. Statistical analyses were carried out using GraphPad Prism (Version 9, GraphPad Software, California, USA). A data visualisation software, Tableau Desktop (Version 2022.1, Tableau Software, Washington, USA) was used to generate a UK map of the locations of the participants in the survey.

Descriptive statistics were used to report sociodemographic data, clinical characteristics, and other survey outcomes. Data are presented as number of participants (n), frequencies and percentages (%), or median and interquartile range (IQR), where appropriate, as all continuous data were non-parametric. In the case of missing data in any of the survey variables (i.e. unanswered questions), the results were reported for the available data including information on the number of participants who provided their answers to the question.

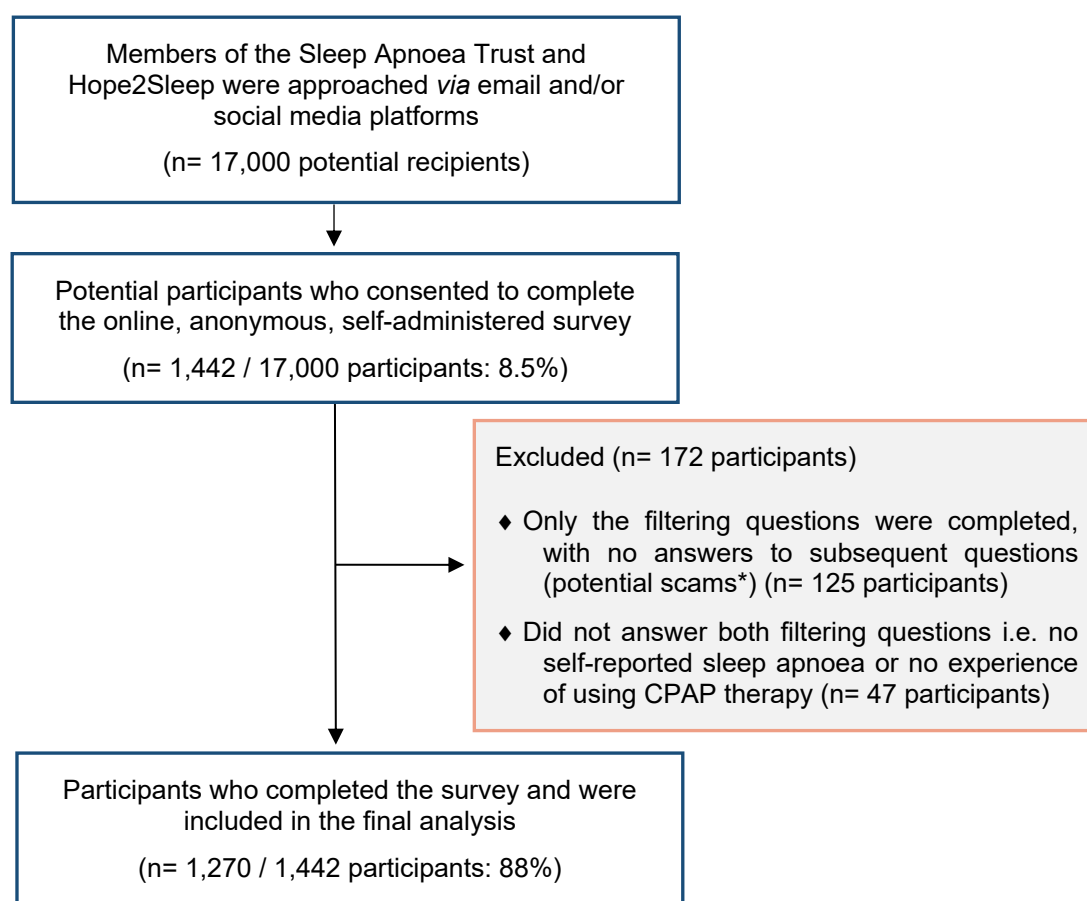
Participants' overall satisfaction with the CPAP therapy initiation experience, was used to stratify participants into *satisfied* or *unsatisfied* groups. Participants who were *neither satisfied nor unsatisfied* were removed from the data analysis (see **Section 5.3.3** for further details). Mann-Whitney tests were then carried out to compare the quantitative variables between *satisfied* and *unsatisfied* groups. Chi-square or Fisher's exact tests were used to test the association between *satisfaction* and the other categorical variables.

Further exploratory analysis was carried out to explore potential predictors of participants' dissatisfaction with their CPAP therapy initiation experience; a series of unadjusted logistic regression analyses were performed to derive odds ratios (OR) and 95% CI. These were carried out for all independent variables that had a statistically significant difference between the *satisfied* and *unsatisfied* groups, or a significant association with the *satisfaction* variable in the previous analyses. Logistic regression analysis was not performed if the independent variable had perfect separation, or if both the independent variable and *satisfaction* variable were linearly dependent.

5.3 Results

5.3.1 Survey response

A flow diagram of the survey responses is shown in **Figure 5.1**. The self-administered online survey was open for 10 weeks (data collection from 2nd February 2023 to 10th April 2023). 1,442 of 17,000 potential recipients consented to participate (8.5% response rate); 1,270 participants completed the survey (88% of those who consented), and their responses were included in the analysis. The survey was predominantly completed by the participants themselves (99%), and the remaining (1%) had help from a carer or a family member.



**These 125 responses had a similar pattern and were likely to be automated fraudulent attempts to fill the survey, where only the filtering questions were answered, and the rest of the questions remained unanswered.*

Figure 5.1 Flow diagram of the data included in the analysis of patient experiences with, and preferences for continuous positive airway pressure (CPAP) therapy initiation in patients with obstructive sleep apnoea.

5.3.2 Survey participants

5.3.2.a: Geographical distribution of participants

The geographical location data for the survey participants is shown in **Figure 5.2**. The majority of participants (84%) were living in England, and the others were from Scotland (6%), Wales (2%), Northern Ireland (2%), and other UK isles and territories (6%).

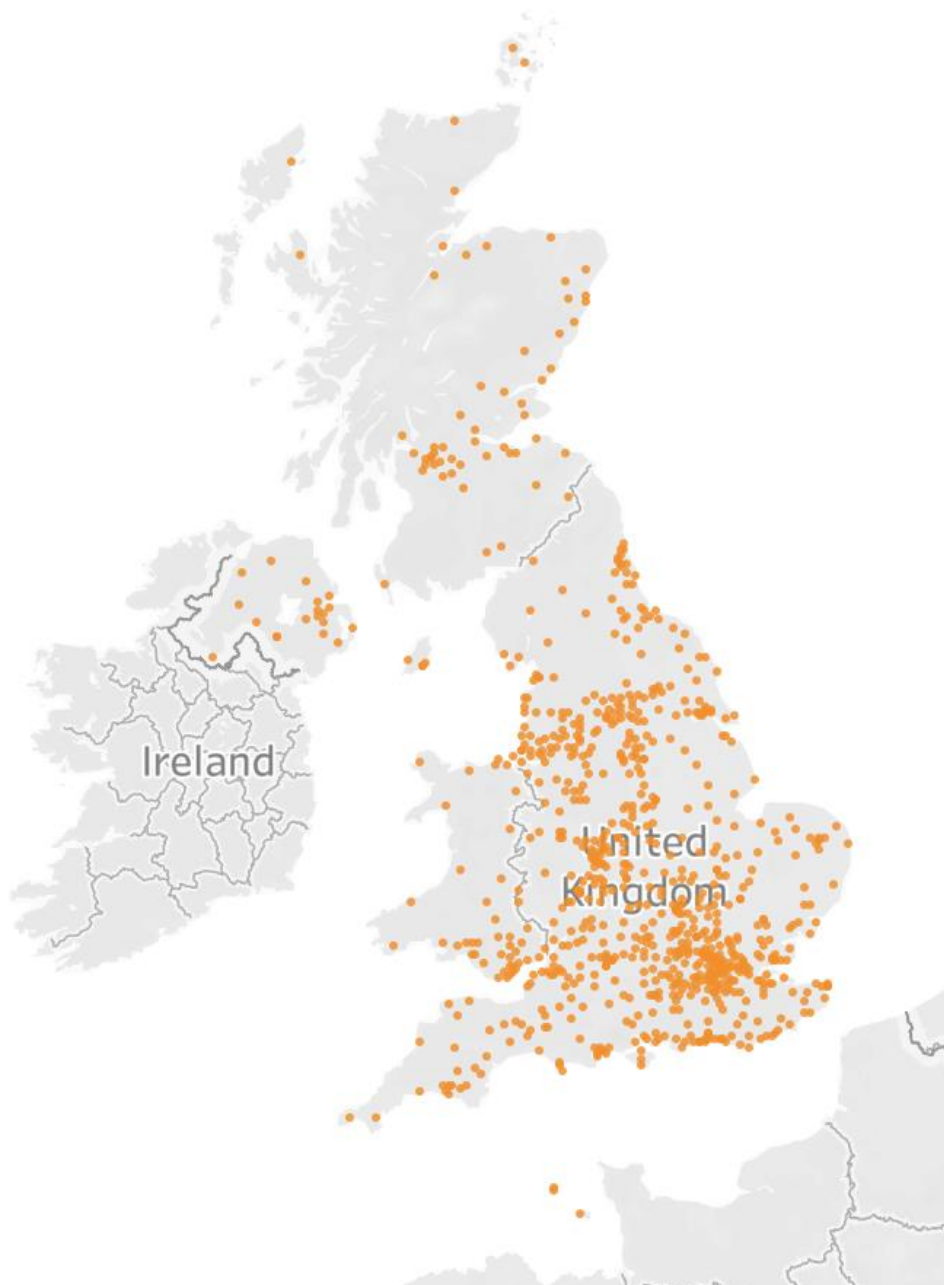


Figure 5.2 Map of the UK showing the geographical distribution of the participants that completed the online, anonymous, self-administered survey. Each dot represents an outward code (first half of the postcode) provided by the participants ($n= 1,136$ of $1,270$; 89%).

5.3.2.b: Sociodemographic characteristics of participants

The sociodemographic characteristics of the survey participants are shown in **Table 5.1**. The table also shows the sociodemographic characteristics associated with participants' overall satisfaction with their CPAP therapy initiation experience; see **Section 5.2.5** for further details on participant stratification.

The majority of participants were aged between 40 and 79 years (40-59 years: 41% of participants; 60-79 years: 51% of participants). Participants had an even gender distribution (53% female) and were predominantly white (97%), with the majority being either retired from work (43%) or unable to work because of a health condition (12%).

Table 5.1 Sociodemographic characteristics of the survey participants, stratified by their overall satisfaction with their continuous positive airway pressure therapy initiation experience

	All participants (n= 1051)	Satisfied participants (n= 907)	Unsatisfied participants (n= 144)	P-value ¹
Q22. In which age group are you?	n= 1038	n= 895 (86%)	n= 143 (14%)	0.25
18-39	46	37 (80%)	9 (20%)	
40-59	426	366 (86%)	60 (14%)	
60-79	525	453 (86%)	72 (14%)	
80 and above	41	39 (95%)	2 (5%)	
Q23. Are you?	n= 1039	n= 896 (86%)	n= 143 (14%)	0.008*
Male	491	438 (89%)	53 (11%)	
Female	548	458 (84%)	90 (16%)	
Q24. What do you consider to be your ethnic group?	n= 1037	n= 894 (86%)	n= 143 (14%)	0.27
White	1008	871 (86%)	137 (14%)	
Other ethnic groups ϕ	29	23 (79%)	6 (21%)	
Q27. What is the highest education level you completed?	n= 1032	n= 890 (86%)	n= 142 (14%)	0.89
GCSE, O level, A level or equivalent	279	240 (86%)	39 (14%)	
Professional qualification below degree level	235	207 (88%)	28 (12%)	
Degree level qualification or higher	456	389 (85%)	67 (15%)	
No formal qualification	41	36 (88%)	5 (12%)	
Other	21	18 (86%)	3 (14%)	

Q28. What is your current employment status?	<i>n</i> = 1037	<i>n</i> = 894 (86%)	<i>n</i> = 143 (14%)	0.12
<i>Employed</i>	383	330 (86%)	53 (14%)	
<i>Retired from work</i>	441	390 (88%)	51 (12%)	
<i>Unemployed</i>	12	11 (92%)	1 (8%)	
<i>Unable to work because of a health condition</i>	126	104 (83%)	22 (17%)	
<i>Student</i>	2	1 (50%)	1 (50%)	
<i>Other</i>	73	58 (79%)	15 (21%)	
Q29. Which of these best describe the area where you live?	<i>n</i> = 1038	<i>n</i> = 895 (86%)	<i>n</i> = 143 (14%)	0.50
<i>Urban i.e. city/large town</i>	220	189 (86%)	31 (14%)	
<i>Suburban i.e. suburbs of city/large town</i>	432	374 (87%)	58 (13%)	
<i>Rural area</i>	350	304 (87%)	46 (13%)	
<i>Other</i>	36	28 (78%)	8 (22%)	

Data are presented as *n* (percentage of all participants). ¹ *p*-value is derived from Chi-square or Fisher's exact tests, comparing satisfied vs. unsatisfied groups. *Statistically significant at ($P < 0.05$).

∅ Other ethnic groups include Asian or Asian British, Black or Black British or Caribbean or African, and Mixed or multiple ethnic groups. GCSE: general certificate of secondary education.

5.3.2.c: Clinical characteristics of participants

The clinical characteristics of the survey participants, stratified by their overall satisfaction with the CPAP therapy initiation experience, are shown in **Table 5.2**. Further details on participants' stratification are given in **Section 5.2.5**. The majority of participants (80%) self-reported their OSA as moderate or severe, and 8% self-reported that they had mild OSA. A further 8% of the participants did not remember their OSA severity. Notably, more than 3% of the participants self-reported that the severity of their condition was not described nor discussed.

The majority of participants (86%) self-reported that they had one or more health conditions, with obesity or overweight being the most frequently cited comorbidity (71%), followed by high blood pressure (44%), and then diabetes (22%).

The most cited reasons for seeking medical help for the sleep problem were “*unexplained excessive sleepiness, tiredness or fatigue*” (68%), followed by “*snoring*” (66%), “*unrefreshing sleep*” (61%), and “*witnessed apnoeas*” (56%).

Table 5.2 Clinical characteristics of the survey participants, stratified by their overall satisfaction with their continuous positive airway pressure therapy initiation experience

	All participants (n= 1051)	Satisfied participants (n= 907)	Unsatisfied participants (n= 144)	P-value ¹
Q26. Which of the following did your sleep specialist use to describe the severity of your sleep apnoea?	n= 1037	n= 894 (86%)	n= 143 (14%)	<0.0001*
<i>Mild</i> (5-15 AHI)	84	66 (79%)	18 (21%)	
<i>Moderate</i> (15-30 AHI)	261	228 (87%)	33 (13%)	
<i>Severe</i> (>30 AHI)	574	503 (88%)	71 (12%)	
<i>My condition's severity was not described or discussed</i>	36	20 (56%)	16 (44%)	
<i>I do not remember</i>	82	77 (94%)	5 (6%)	
Q25. Do you have any of these health conditions? ϕ	n= 1039	n= 896 (86%)	n= 143 (14%)	0.38
<i>Obesity or overweight</i>	734	636 (87%)	98 (13%)	
<i>Diabetes</i>	225	204 (91%)	21 (9%)	
<i>High blood pressure</i>	461	395 (86%)	66 (14%)	
<i>Heart disease</i>	115	100 (87%)	15 (13%)	
<i>Stroke</i>	32	28 (88%)	4 (12%)	
<i>None of the above</i>	147	122 (83%)	25 (17%)	
Q2. Which of the following reasons led you to seek medical help? ϕ	n= 1050	n= 906 (86%)	n= 144 (14%)	0.06
<i>Unexplained excessive sleepiness, tiredness or fatigue</i>	712	623 (88%)	89 (12%)	
<i>Snoring</i>	698	618 (89%)	80 (11%)	
<i>Unrefreshing sleep</i>	644	559 (87%)	85 (13%)	
<i>Witnessed apnoeas</i>	592	524 (89%)	68 (11%)	
<i>Waking up with headaches</i>	327	277 (85%)	50 (15%)	
<i>Nocturia</i>	315	275 (87%)	40 (13%)	
<i>Choking during sleep</i>	239	199 (83%)	40 (17%)	
<i>Memory problems</i>	224	183 (82%)	41 (18%)	
<i>Insomnia</i>	191	159 (83%)	32 (17%)	
<i>Other</i>	180	150 (83%)	30 (17%)	

Data are presented as n (percentage of all participants). ¹ p-value is derived from Chi-square or Fisher's exact tests, comparing satisfied vs. unsatisfied groups. ϕ Multiple answers were allowed for these questions; AHI: apnoea hypopnoea index.

5.3.3 Participant-reported satisfaction with their CPAP therapy initiation experience

The participants' overall satisfaction with the CPAP therapy initiation experience, stratified according to their answers to *Question 15* on the survey (see **Appendix 5.2**), is shown in **Figure 5.3**. Participants were generally satisfied with their CPAP therapy initiation experience, with most participants (77%; $n=907/1,186$) being “satisfied” or “very satisfied”, and a smaller number were “neither satisfied nor unsatisfied” (11%; $n=135/1,186$). The remaining participants (12%; $n=144/1,186$) were “unsatisfied” or “very unsatisfied” with their CPAP therapy initiation experience.

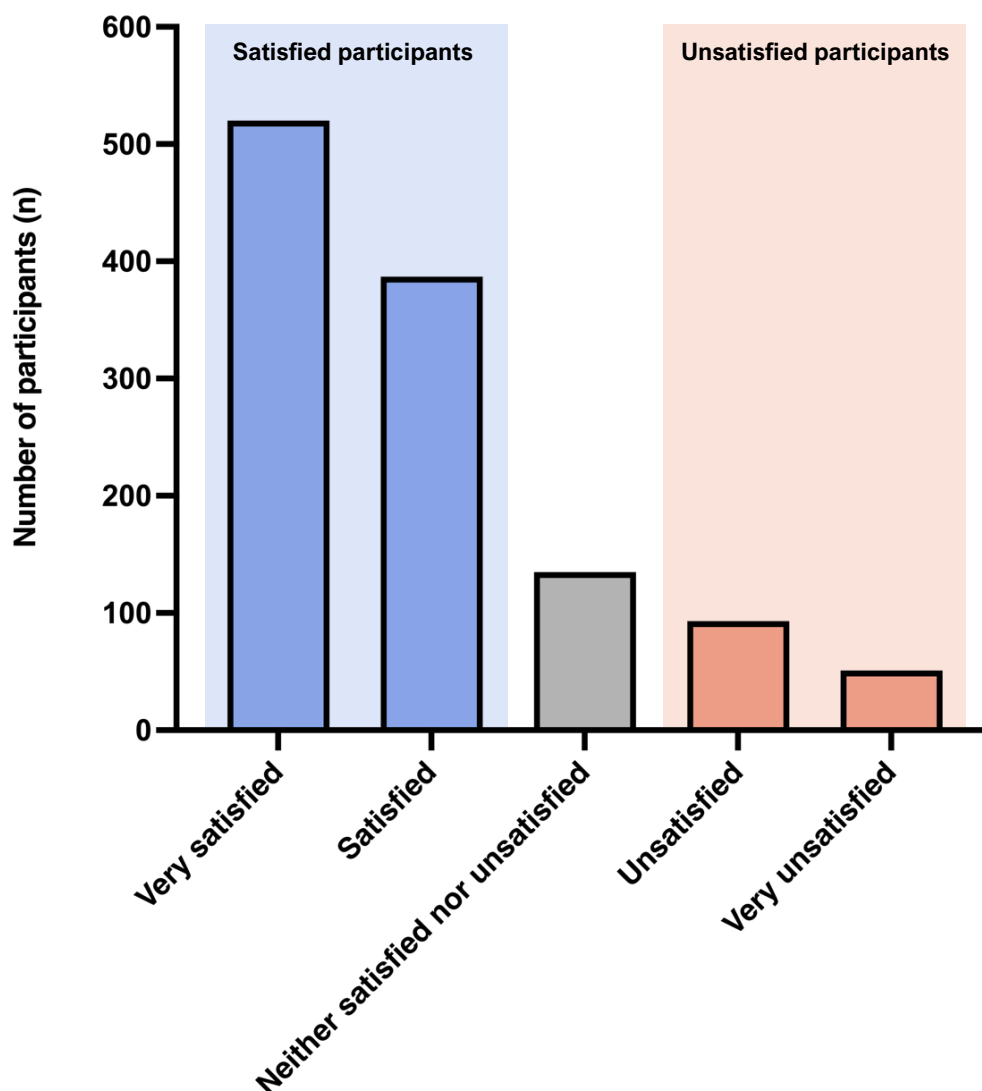


Figure 5.3 Participants were asked, using a five-point Likert scale, “(Q15) How satisfied are you with your overall experience of the CPAP therapy set-up and training?”. Data was available for $n=1,186$ participants and their answers were used to group them into satisfied or unsatisfied.

5.3.4 Potential influencers of participants' satisfaction with their CPAP therapy initiation experience

The unadjusted logistic regression analyses are presented below in separate tables within each of the subsections for clarity. A full table of the unadjusted logistic regression analyses of potential predictors of participants' dissatisfaction with their CPAP therapy initiation experience is provided in **Appendix 5.3**.

5.3.4.a: Sociodemographic and clinical characteristics

The sociodemographic and clinical characteristics of the survey participants, stratified by their overall satisfaction with the CPAP therapy initiation experience are shown in **Table 5.1** and **Table 5.2**.

There was a significant difference in the distribution of severity between *satisfied* and *unsatisfied* groups (X^2 : 37.92, *df*: 4, $P = <0.0001$). The *unsatisfied* group had a higher proportion of participants with self-reported mild OSA, compared to the *satisfied* group (13% vs. 7% of participants, $P = <0.0001$). Similarly, the *unsatisfied* group had a higher proportion of those whose OSA severity was not described nor discussed by their sleep specialist (11% vs. 2% of participants, $P < 0.0001$). Logistic regression analysis was not possible for OSA severity; see **Section 5.2.5** for further details.

There was a significant association between gender and satisfaction ($P = 0.008$) (**Table 5.1**). The number of female participants was higher than males in the *unsatisfied* group, and female participants were more likely to be dissatisfied with their CPAP therapy initiation experience (OR [95% CI]: 1.62 [1.13 – 2.34], $P = 0.009$; **Table 5.3**).

Table 5.3 Unadjusted logistic regression analysis of gender as a predictor of participants' dissatisfaction

	OR	95% CI	P-value ¹
Q23. Gender			
Male	Ref	Ref	Ref
Female	1.62	1.13 – 2.34	0.009*

¹ p-value is derived from unadjusted logistic regression, with the most frequent variable set as the reference value. *Statistically significant at (P<0.05). OR: odds ratio of the logistic regression; 95% CI: confidence intervals of the odds ratio.

5.3.4.b: Involvement of participants in the decisions about their sleep apnoea care

The self-reported involvement in the decision-making of OSA care is shown in **Figure 5.4**. There was a significant difference in the distribution of the levels of involvement between the *satisfied* and *unsatisfied* groups (X^2 : 465, *df*: 2, $P = <0.0001$). 63% of the *satisfied* participants felt “*definitely*” involved in the decision-making of their OSA care. This is compared to only 2% of the *unsatisfied* participants. Moreover, the *unsatisfied* group had a significantly higher proportion of those who did not feel involved in their OSA care. These participants were more likely to be dissatisfied with their CPAP therapy initiation experience, compared to those who felt involved in their OSA care (OR [95% CI]: 509.3 [156.4 – 3132], $P = <0.0001$; **Table 5.4**).

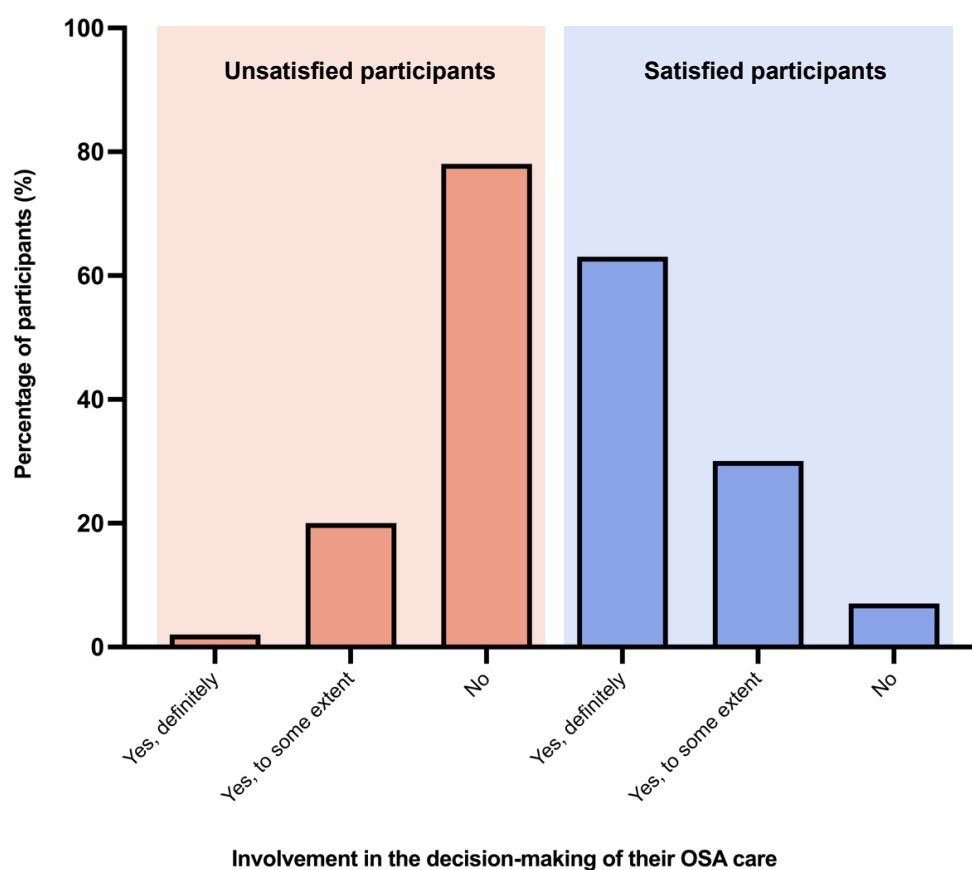


Figure 5.4 Participants were asked “(Q19) Did you feel involved as much as you wanted to be in the decisions about your sleep apnoea care?”. Data was available for $n = 1,046$ participants, and the answers were stratified by participants’ overall satisfaction with their CPAP therapy initiation experience (unsatisfied: $n = 143$ and satisfied: $n = 903$ participants). Data are presented as percentages (%) based on the number of participants in each corresponding group.

Table 5.4 Unadjusted logistic regression analysis of the involvement of participants in the decisions about their sleep apnoea care as a predictor of participants’ dissatisfaction

	OR	95% CI	P-value ¹
Q19. Did you feel involved as much as you wanted to be in the decisions about your sleep apnoea care?			
Yes, definitely	Ref	Ref	Ref
Yes, to some extent	31.12	9.28 - 193.4	<0.0001*
No	509.3	156.4 - 3132	<0.0001*

¹ p-value is derived from unadjusted logistic regression, with the most frequent variable set as the reference value. *Statistically significant at ($P < 0.05$). OR: odds ratio of the logistic regression; 95% CI: confidence intervals of the odds ratio.

5.3.4.c: Provision of amount and type of educational information about sleep apnoea and CPAP use

Information on the provision of educational information that participants self-reported receiving is shown in **Table 5.5**. There was a significant difference in the distribution of the **amount** of educational information given to the *satisfied and unsatisfied* groups (X^2 : 396.5, df : 3, $P = <0.0001$). 1% of the participants in both groups self-reported receiving “*too much*” or “*did not need any information*” about OSA and CPAP use. 86% of the *satisfied* participants self-reported being given the “*right amount*” of information, compared to 9% of the *unsatisfied* participants (**Figure 5.5**). Moreover, the *unsatisfied* group had a significantly higher proportion of those who did not receive enough educational information. These participants were more likely to be dissatisfied with their CPAP therapy initiation experience, compared to those who received the “*right amount*” of educational information (OR [95% CI]: 63.2 [35.86 – 120.8], $P = <0.0001$; **Table 5.6**).

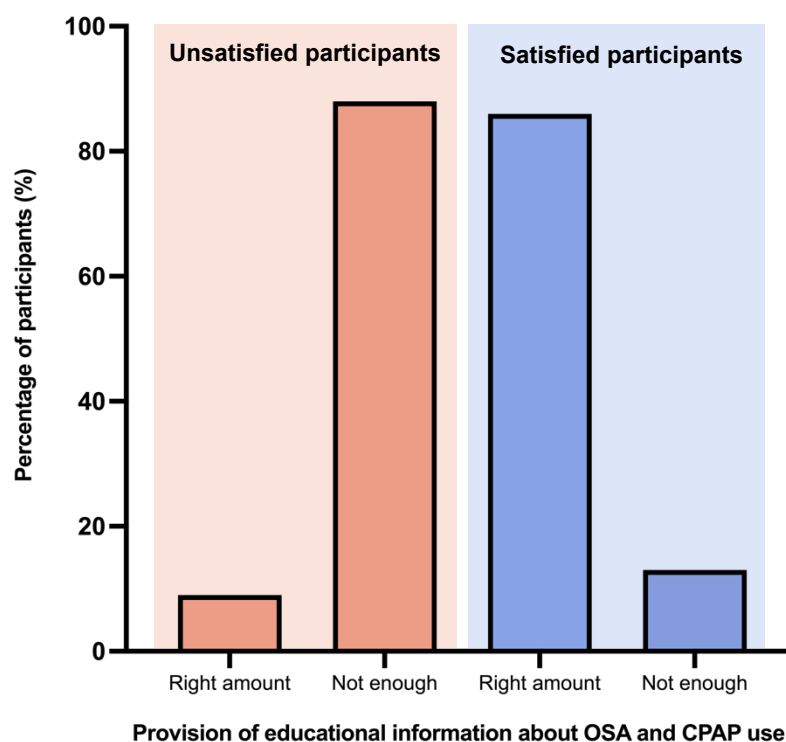


Figure 5.5 Participants were asked “(Q8) How much information was given to you about sleep apnoea and CPAP use?”. Data was available for $n = 1,034$ participants, and the answers were stratified by participants’ overall satisfaction with their continuous positive airway pressure (CPAP) therapy initiation experience (unsatisfied: $n = 139$ and satisfied: $n = 895$ participants). Data are presented as percentages (%) based on the number of participants in each corresponding group.

There was a significant difference in the distribution of the **type** of information given to the *satisfied* and *unsatisfied participants* (X^2 : 44.46, *df*: 2, $P < 0.0001$; **Table 5.5**). Whilst most participants (80%) in both the *satisfied* and *unsatisfied* groups were given “*written Information e.g. patient leaflet or booklet*” to support them with using their CPAP therapy, 27% were directed to “*online health information e.g. link to a website or a video*”. Notably, the *satisfied* group had a higher proportion of those who received written or online health information (written: 84% vs. 58% of participants, $P < 0.0001$; online: 29% vs. 17% of participants, $P < 0.0001$). Logistic regression analysis was not possible for the variable of the **type** of educational information given to participants; see **Section 5.2.5** for further details.

Table 5.5 Provision of educational information on sleep apnoea and its treatment, stratified by participants' overall satisfaction with their continuous positive airway pressure therapy initiation experience

	All participants (<i>n</i> = 1051)	Satisfied participants (<i>n</i> = 907)	Unsatisfied participants (<i>n</i> = 144)	<i>P</i> -value ¹
Q8. How much information was given to you about sleep apnoea and CPAP use?	<i>n</i> = 1046	<i>n</i> = 903 (86%)	<i>n</i> = 143 (14%)	<0.0001*
Too much	3	2 (67%)	1 (33%)	
Right amount	789	776 (98%)	13 (2%)	
Not enough	245	119 (49%)	126 (51%)	
I did not need any information	9	6 (67%)	3 (33%)	
Q9. Besides your training, what other sources of information were you given to support you with using your CPAP therapy? ϕ	<i>n</i> = 980	<i>n</i> = 855 (87%)	<i>n</i> = 125 (13%)	<0.0001*
Written Information ∇	788	716 (91%)	72 (9%)	
Online health information #	265	244 (92%)	21 (8%)	
Other	188	140 (74%)	48 (26%)	

Data are presented as *n* (percentage of all participants). CPAP: continuous positive airway pressure. ¹ *p*-value is derived from Chi-square or Fisher's exact tests, comparing satisfied vs. unsatisfied groups. *Statistically significant at ($P < 0.05$). ϕ Multiple answers were allowed for this question. ∇ Written Information such as patient leaflet or booklet. # Online health information such as a link to a website or a video.

Table 5.6 Unadjusted logistic regression analysis of the provision of educational health information as a predictor of participants' dissatisfaction

	OR	95% CI	P-value ¹
Q8. How much information was given to you about sleep apnoea and CPAP use?			
<i>Too much</i>	29.85	1.34 - 331.1	0.006*
<i>Right amount</i>	Ref	Ref	Ref
<i>Not enough</i>	63.20	35.86 - 120.8	<0.0001*
<i>I did not need any information</i>	29.85	5.82 - 127.1	<0.0001*

¹ p-value is derived from unadjusted logistic regression, with the most frequent variable set as the reference value. *Statistically significant at (P<0.05). OR: odds ratio of the logistic regression; 95% CI: confidence intervals of the odds ratio; CPAP: continuous positive airway pressure.

5.3.4.d: Diagnostic care pathways experienced by participants

Information on participants' diagnostic pathway(s) is shown in **Table 5.7**. The duration since the participants received their OSA diagnosis was significantly shorter in the *unsatisfied* group, compared to those who were *satisfied* (*unsatisfied*: median [IQR]: 5.0 [2.0-8.7] vs. *satisfied*: 7.0 [4.0-13.0] years, P<0.0001). A shorter duration since OSA diagnosis was found to increase the likelihood of being dissatisfied with the CPAP therapy initiation experience (OR [95% CI]: 0.93 [0.90 – 0.96], P= <0.0001; **Table 5.8**).

The majority of participants (76%) in both the *satisfied* and *unsatisfied* groups received their OSA diagnosis prior to the COVID-19 pandemic (i.e. *before 2020*). However, the *unsatisfied* group had a higher proportion of those who were diagnosed post-COVID-19 pandemic (35% vs. 22% of participants, P<0.002). These participants were more likely to be dissatisfied with their CPAP therapy initiation experience, compared to those diagnosed pre-pandemic (OR [95% CI]: 1.84 [1.26 – 2.68], P=0.001; **Table 5.8**).

Most participants (67%) in both the *satisfied* and *unsatisfied* groups had a home sleep apnoea test, and 31% had their sleep apnoea test carried out in a hospital. There was a significant difference in the distribution of the type of sleep test between *satisfied* and *unsatisfied* participants (X^2 : 6.07, *df*: 2, P= 0.048). Although the *unsatisfied* group had a

higher proportion of those who had home sleep apnoea testing (72% vs. 66% of participants, $P=0.048$), the logistic regression analysis for this variable was not statistically significant (**Table 5.8**).

The majority of participants (85%) in both the *satisfied* and *unsatisfied* groups were told about their OSA diagnosis during an in-person appointment at the clinic, and the remaining 15% were told about their diagnosis remotely through a phone or a video call. There was a significant difference in the distribution of the diagnosis communication strategies between *satisfied* and *unsatisfied* participants (X^2 : 21.17, df : 2, $P<0.0001$). The *unsatisfied* group had a higher proportion of those who were told about their diagnosis remotely (28% vs. 13% of participants, $P<0.0001$). These participants were more likely to be dissatisfied with their CPAP therapy initiation experience, compared to those who received in-person diagnosis communication (*via* phone call: OR [95% CI]: 2.39 [1.53 – 3.68], $P= <0.0001$; *via* video call: 3.94 [1.21 – 11.35], $P= 0.01$; **Table 5.8**).

Table 5.7 Participants' diagnostic and treatment pathway, stratified by their overall satisfaction with their continuous positive airway pressure therapy initiation experience

	All participants (n= 1051)	Satisfied participants (n= 907)	Unsatisfied participants (n= 144)	P-value ¹
Q1. When did your sleep doctor tell you that you had sleep apnoea? (Duration in years)	n= 1042	n= 898 (86%)	n= 144 (14%)	<0.0001*
	7.0 (4.0-12.2)	7.0 (4.0-13.0)	5.0 (2.0-8.7)	
Time of OSA diagnosis	n= 1042	n= 898 (86%)	n= 144 (14%)	0.002*
Pre-Covid-19 pandemic	791	697 (88%)	94 (12%)	
Post-Covid-19 pandemic	251	201 (80%)	50 (20%)	
Q3. Where did you have your sleep test?	n= 1050	n= 906 (86%)	n= 144 (14%)	0.048*
Sleep test carried out in hospital	327	292 (89%)	35 (11%)	
Sleep test carried out at home	700	597 (85%)	103 (15%)	
Other	23	17 (74%)	6 (26%)	
Q4. How did your sleep specialist tell you that you had sleep apnoea?	n= 1042	n= 904 (87%)	n= 138 (13%)	<0.0001*
F2F (in-person) appointment at the clinic	881	782 (89%)	99 (11%)	
Remote appointment through a phone call	146	112 (77%)	34 (23%)	
Remote appointment through a video call	15	10 (67%)	5 (33%)	
Q5. How long after your sleep test was it until you received your (CPAP) therapy? (Duration in weeks) ▽	n= 1000	n= 859 (86%)	n= 141 (14%)	0.0004*
	4.0 (2.0-8.0)	4.0 (2.0-8.0)	4.0 (2.5-12.0)	

Q7. If you have been given training on using your CPAP therapy, how did you receive your training?	<i>n</i> = 1045	<i>n</i> = 902 (86%)	<i>n</i> = 143 (14%)	<0.0001*
<i>F2F (in-person): CPAP machine was turned on during training</i>	717	660 (92%)	57 (8%)	
<i>F2F (in-person): CPAP machine was not turned on during training</i>	223	185 (83%)	38 (17%)	
<i>Remote training through a phone or a video call</i>	14	11 (79%)	3 (21%)	
<i>I did not receive training for my CPAP</i>	70	35 (50%)	35 (50%)	
<i>Other</i>	21	11 (52%)	10 (48%)	
Q6. What other treatments did you try for your sleep apnoea? ϕ	<i>n</i> = 1041	<i>n</i> = 900 (86%)	<i>n</i> = 141 (14%)	0.84
<i>Lifestyle advice e.g. weight loss and sleep hygiene</i>	320	280 (87%)	40 (13%)	
<i>Positional modifier</i>	44	37 (84%)	7 (16%)	
<i>Mouth guard (Mandibular Advancement Devices)</i>	133	114 (86%)	19 (14%)	
<i>Electrical stimulation</i>	6	6 (100%)	0 (0%)	
<i>Surgery</i>	27	25 (93%)	2 (7%)	
<i>None of the above</i>	624	538 (86%)	86 (14%)	
<i>Other</i>	47	38 (81%)	9 (19%)	

Data are presented as median (interquartile range) or *n* (percentage of all participants). ¹ *p*-value is derived from the Mann-Whitney, Chi-square, or Fisher's exact tests, comparing satisfied vs. unsatisfied groups. *Statistically significant at ($P < 0.05$). ∇ The face validity of this statistical findings was checked due to the similarity of the medians, suggesting a comparable central tendency. The variability of the IQR in both groups makes this result possible. ϕ Multiple answers were allowed for these questions. CPAP: continuous positive airway pressure; F2F: face-to-face; AHI: apnoea-hypopnoea index.

Table 5.8 Unadjusted logistic regression analyses of the diagnostic and treatment care pathways as predictors of participants' dissatisfaction

	OR	95% CI	P-value ¹
Q1. When did your sleep doctor tell you that you had sleep apnoea? (Duration in years)			
	0.93	0.90 - 0.96	<0.0001*
Time of OSA diagnosis			
Pre-Covid-19 pandemic	Ref	Ref	Ref
Post-Covid-19 pandemic	1.84	1.26 - 2.68	0.001*
Q3. Where did you have your sleep test?			
Sleep test carried out in hospital	0.69	0.45 - 1.03	0.08
Sleep test carried out at home	Ref	Ref	Ref
Other	2.04	0.19 - 1.38	0.14
Q4. How did your sleep specialist tell you that you had sleep apnoea?			
F2F (in-person) appointment at the clinic	Ref	Ref	Ref
Remote appointment through a phone call	2.39	1.53 - 3.68	<0.0001*
Remote appointment through a video call	3.94	1.21 - 11.35	0.01*
Q5. How long after your sleep test was it until you received your (CPAP) therapy? (Duration in weeks)			
	1.00	0.99 - 1.01	0.07

¹ p-value is derived from unadjusted logistic regression, with the most frequent variable set as the reference value. *Statistically significant at (P<0.05). OR: odds ratio of the logistic regression; 95% CI: confidence intervals of the odds ratio; CPAP: continuous positive airway pressure; F2F: face-to-face.

5.3.4.e: Treatment care pathways experienced by participants

Information on participants' treatment pathway(s) is also shown in **Table 5.7** above. The duration between the sleep apnoea testing and CPAP therapy initiation was significantly different between the *unsatisfied* and *satisfied* groups (*unsatisfied*: median [IQR]: 4.0 [2.5-12.0] vs. *satisfied*: 4.0 [2.0-8.0] weeks, P= 0.0004). However, the logistic regression analysis for this variable was not statistically significant (**Table 5.8**).

Most participants (69%) in both the *satisfied* and *unsatisfied* groups received in-person training with the CPAP machine turned on, and 21% had in-person training without turning the CPAP machine on. Notably, only 1% of participants received remote CPAP training

through a phone or a video call. Logistic regression analysis was not possible for this variable, however, there was a significant difference in the distribution of the CPAP initiation strategies between *satisfied* and *unsatisfied participants* (X^2 : 109.5, *df*: 2, $P < 0.0001$). The *satisfied* group had a higher proportion of those who received in-person training for CPAP therapy (94% vs. 66% of participants, $P < 0.0001$). Notably, the *unsatisfied* group had a higher proportion of those who reported not receiving any training for their CPAP therapy (24% vs. 4% of participants, $P < 0.0001$; **Table 5.7**).

5.3.5 Adherence to therapy and utilisation of healthcare services associated with participants' satisfaction

5.3.5.a: Participants reported adherence to CPAP therapy

Participants' self-reported adherence to CPAP therapy is shown in **Table 5.9**. The nightly and weekly usage of CPAP therapy was similar between the *satisfied* and *unsatisfied* groups. Their nightly CPAP usage was self-reported as a median (IQR) of 7.0 (6 – 8) hours per night, and their weekly CPAP usage was a median (IQR) of 7.0 (7 – 7) nights per week.

Although participants self-reported good adherence to CPAP therapy ($\geq 70\%$ of nights with ≥ 4 hours of usage), their subjective rating of their CPAP usage varied. Whilst 90% of all participants rated their usage of CPAP therapy as “good” or “very good”, 5% of them rated their CPAP usage as “poor” or “very poor”, and the remaining 5% were neutral. There was a significant difference in the distribution of the subjective rating of CPAP usage between *satisfied* and *unsatisfied participants* (X^2 : 175.6, *df*: 2, $P < 0.0001$). The *unsatisfied* group had a significantly higher proportion of those who rated their CPAP usage as “poor” or “very poor” (27% vs. 2% of participants, $P < 0.0001$). These participants were more likely to be dissatisfied with their CPAP therapy initiation experience, compared to those who rated their CPAP usage as “very good” (poor: OR [95% CI]: 22.64 [10.42 – 52.35], $P = < 0.0001$; very poor: 27.72 [11.58 – 73.81], $P = < 0.0001$; **Table 5.10**).

Table 5.9 Participant-reported adherence to continuous positive airway pressure (CPAP) therapy, stratified by their overall satisfaction with their CPAP therapy initiation experience

	All participants (n= 1051)	Satisfied participants (n= 907)	Unsatisfied participants (n= 144)	P-value ¹
Q11. On average, how many hours per night do you use your CPAP therapy?	n= 1043	n= 901 (86%)	n= 142 (14%)	0.01*
	7.0 (6 – 8)	7.0 (6 – 8)	7.0 (6 – 8)	
Q12. On average, how many nights per week do you use your CPAP therapy?	n= 1043	n= 900 (86%)	n= 143 (14%)	<0.0001*
	7.0 (7 – 7)	7.0 (7 – 7)	7.0 (7 – 7)	
Q10. How would you rate your current use of the CPAP therapy?	n= 1045	n= 903 (86%)	n= 142 (14%)	<0.0001*
Very Good	695	636 (92%)	59 (8%)	
Good	239	211 (88%)	28 (12%)	
Neither good nor poor	55	39 (71%)	16 (29%)	
Poor	31	10 (32%)	21 (68%)	
Very Poor	25	7 (28%)	18 (72%)	

Data are presented as n (percentage of all participants) or median (interquartile range). ¹ p-value is derived from the Mann-Whitney, Chi-square, or Fisher's exact tests, comparing satisfied vs. unsatisfied groups. *Statistically significant at (P<0.05). CPAP: continuous positive airway pressure.

Table 5.10 Unadjusted logistic regression analyses of the adherence to continuous positive airway pressure therapy and utilisation of healthcare services as predictors of participants' dissatisfaction

	OR	95% CI	P-value ¹
Q10. How would you rate your current use of the CPAP therapy?			
Very Good	Ref	Ref	Ref
Good	1.430	0.87 - 2.28	0.14
Neither good nor poor	4.422	2.28 - 8.26	<0.0001*
Poor	22.64	10.42 - 52.35	<0.0001*
Very Poor	27.72	11.58 - 73.81	<0.0001*
Q13. Over the last 12 months, how many times have you contacted your sleep clinic or CPAP provider to seek medical support?			
0	Ref	Ref	Ref
1-2	1.05	0.71 - 1.55	0.80
3-4	3.43	1.84 - 6.23	<0.0001*
5 or more	6.90	2.76 - 17.07	<0.0001*

¹ p-value is derived from unadjusted logistic regression, with the most frequent variable set as the reference value.

*Statistically significant at (P<0.05). OR: odds ratio of the logistic regression; 95% CI: confidence intervals of the odds ratio; CPAP: continuous positive airway pressure.

5.3.5.b: Patient-initiated follow up for medical support

The participant-initiated contacts to seek medical support within the last 12 months are shown in **Figure 5.6**. 48% of the participants in both the *satisfied* and *unsatisfied* groups did not contact their sleep clinic or CPAP provider to seek medical support. 44% sought medical support between 1-2 times, and 8% had 3 or more contacts with their sleep clinic or CPAP provider.

There was a significant difference in the distribution of the frequency of patient-initiated contacts for medical support between *satisfied* and *unsatisfied* participants (X^2 : 38.87, *df*: 3, $P = <0.0001$). The *unsatisfied* group had a significantly higher proportion of those with 3 or more patient-initiated contacts within the last 12 months (20% vs. 6% of participants, $P < 0.0001$). These participants were more likely to be dissatisfied with their CPAP therapy initiation experience, compared to those who did not seek medical support, and as the

number of patient-initiated contacts increased the likelihood of being dissatisfied also increased (3-4 contacts: OR [95% CI]: 3.43 [1.84 – 6.23], $P = <0.0001$; 5 or more contacts: 6.90 [2.76 – 17.07], $P = <0.0001$; **Table 5.10**).

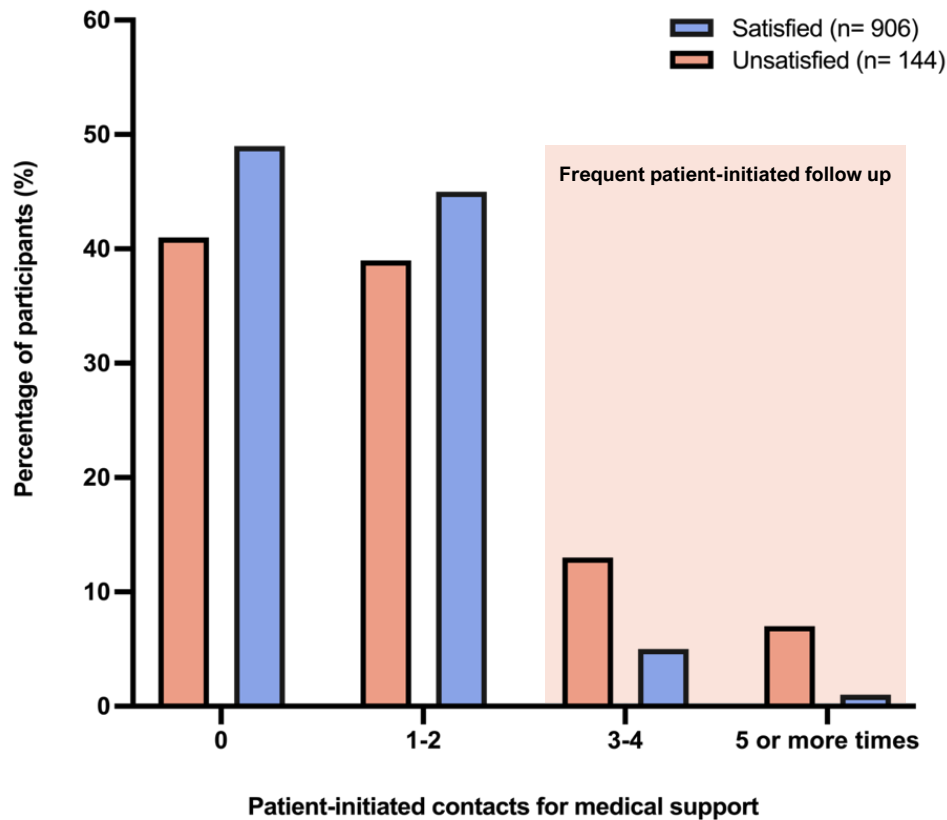


Figure 5.6 Participants were asked “(Q13) Over the last 12 months, how many times have you contacted your sleep clinic or CPAP provider to seek medical support?”. Data was available for $n = 1,050$ participants, and the answers were stratified by participants’ overall satisfaction with their CPAP therapy initiation experience (satisfied: $n = 906$ and unsatisfied: $n = 144$ participants). Data are presented as percentages (%) based on the number of participants in each corresponding group.

5.3.6 Participants' preferences for CPAP therapy initiation and follow-up care

The participants' preferences for CPAP therapy initiation and follow-up care are shown in **Figure 5.7** and **Table 5.11**. There was no association between participants' level of satisfaction with their CPAP therapy initiation experience and their preferences for in-person or remote CPAP therapy initiation ($P= 0.08$), and follow-up care ($P= 0.39$). Most participants (91%) expressed their preference for an in-person CPAP therapy initiation, compared to remote CPAP initiation through a phone or a video call (3%). The remaining 6% of participants had no preference. Similarly, the majority of participants (70%) preferred to receive in-person appointments for their follow-up care, and 19% of them indicated their preference for remote follow-up care through a phone or a video call. The remaining 11% of participants had no preference.

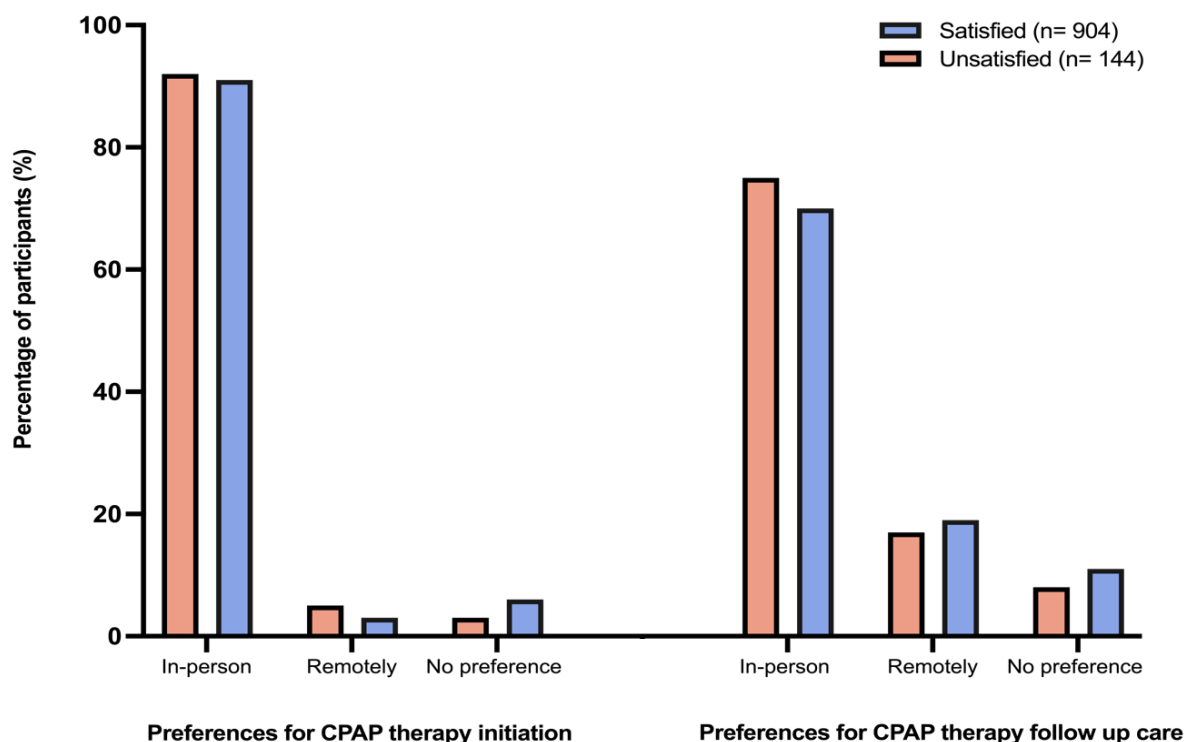


Figure 5.7 Participants were asked “(Q20A and B) If you had to receive your care again (for the same/similar condition), how would you prefer to receive your therapy and follow-up care?”. Data was available for $n=1,048$ participants. **(Left)** shows participants' preferences for continuous positive airway pressure (CPAP) therapy initiation. **(Right)** shows participants' preferences for CPAP therapy follow-up care. Data are presented as percentages (%) based on the number of participants in each corresponding group.

Table 5.11 Participants' preferences for therapy initiation and follow-up care, stratified by their overall satisfaction with their continuous positive airway pressure therapy initiation experience

	All participants (n= 1051)	Satisfied participants (n= 907)	Unsatisfied participants (n= 144)	P-value ¹
Q20A. If you had to receive your care again (for the same/similar condition), how would you prefer to receive your therapy?	n= 1048	n= 904 (86%)	n= 144 (14%)	0.08
Face-to-Face (in-person) appointment	955	822 (86%)	133 (14%)	
Remotely through a phone call	9	7 (78%)	2 (22%)	
Remotely through a video call	22	17 (77%)	5 (23%)	
No preference	62	58 (94%)	4 (6%)	
Q20B. If you had to receive your care again (for the same/similar condition), how would you prefer to receive your follow-up care?	n= 1048	n= 904 (86%)	n= 144 (14%)	0.39
Face-to-Face (in-person) appointment	737	629 (85%)	108 (15%)	
Remotely through a phone call	107	102 (95%)	5 (5%)	
Remotely through a video call	93	74 (80%)	19 (20%)	
No preference	111	99 (89%)	12 (11%)	

Data are presented as n (percentage of all participants). ¹ p-value is derived from Chi-square or Fisher's exact tests, comparing satisfied vs. unsatisfied groups. *Statistically significant at (P<0.05). CPAP: continuous positive airway pressure.

5.3.7 Additional data on participants' satisfaction with specific domains

Further data on participants' satisfaction with other specific domains is shown in **Table 5.12**.

These domains include participants' satisfaction with the duration before they received their CPAP therapy, how the clinical care team communicated with them during the CPAP therapy initiation, and the support they received from the clinical care team after the CPAP therapy initiation. Similar patterns of satisfaction levels were found between the *satisfied* and *unsatisfied* groups; compared to the *satisfied* group, the *unsatisfied* group had higher proportions of those who were dissatisfied with the waiting time for their CPAP therapy, and the communication and support during and after their CPAP therapy initiation.

Table 5.12 Participants' satisfaction with treatment waiting times, communication, and clinical support, stratified by their overall satisfaction with their continuous positive airway pressure therapy initiation experience

	All participants (n= 1051)	Satisfied participants (n= 907)	Unsatisfied participants (n= 144)	P-value ¹
Q16. How satisfied are you with how long it took to receive your CPAP therapy?	n= 1051	n= 907 (86%)	n= 144 (14%)	<0.0001*
Very satisfied	564	534 (95%)	30 (5%)	
Satisfied	304	267 (88%)	37 (12%)	
Neither satisfied nor unsatisfied	77	44 (57%)	33 (43%)	
Unsatisfied	71	45 (63%)	26 (37%)	
Very unsatisfied	35	17 (49%)	18 (51%)	
Q17. How satisfied are you with the way your clinical care team communicated with you during your CPAP therapy set-up and training?	n= 1051	n= 907 (86%)	n= 144 (14%)	<0.0001*
Very satisfied	537	534 (99%)	3 (1%)	
Satisfied	320	308 (96%)	12 (4%)	
Neither satisfied nor unsatisfied	80	48 (60%)	32 (40%)	
Unsatisfied	71	15 (21%)	56 (79%)	
Very unsatisfied	43	2 (5%)	41 (95%)	
Q18. How satisfied are you with the support you received from the clinical care team after your CPAP therapy set-up and training?	n= 1050	n= 906 (86%)	n= 144 (14%)	<0.0001*
Very satisfied	442	436 (99%)	6 (1%)	
Satisfied	311	299 (96%)	12 (4%)	
Neither satisfied nor unsatisfied	133	115 (86%)	18 (14%)	
Unsatisfied	103	44 (43%)	59 (57%)	
Very unsatisfied	61	12 (20%)	49 (80%)	

Data are presented as n (percentage of all participants). ¹ p-value is derived from Chi-square or Fisher's exact tests, comparing satisfied vs. unsatisfied groups. *Statistically significant at (P<0.05). CPAP: continuous positive airway pressure.

5.4 Discussion

The main findings of this UK survey were that over 75% of participants with self-reported OSA were satisfied with their CPAP therapy initiation experience, regardless of their sociodemographic and clinical characteristics. Notably, participants diagnosed post-COVID-19 pandemic were more likely to be dissatisfied with their CPAP therapy initiation experience, compared to those diagnosed pre-pandemic. Participants' dissatisfaction with their CPAP therapy initiation experience was also associated with not feeling involved in the decision-making of their OSA care and not receiving enough educational information about OSA and CPAP therapy. In addition, dissatisfied participants were more likely to rate their CPAP therapy usage as poor and require further medical support from their sleep clinic or CPAP provider, compared to those who were satisfied. Most participants expressed their clear preference for an in-person CPAP therapy initiation and follow-up care, compared to remote strategies through a phone or a video call.

5.4.1 Are the findings of the survey representative?

The geographical distribution of the participants in this survey closely reflected the UK population density; most participants were from England, followed by Scotland, Wales and Northern Ireland (Office for National Statistics, 2022). The participants in this survey were predominantly white, with little representation of other ethnic backgrounds. In typical OSA populations, higher representation of other ethnic groups would be expected, particularly those from Asian or African ethnicities (Johnson et al., 2022). The participants in the current survey had similar sociodemographic and clinical characteristics to those of a previous study, which is the largest UK-wide survey to date (n= 2,671 patients with OSA) published a decade ago by the BLF (*now known as Asthma + Lung UK*) (British Lung Foundation, 2014). The participants in both surveys also experienced similar symptoms leading up to their OSA diagnosis. However, in the current survey, the gender distribution was even, whereas in the BLF survey the majority of participants were male (78%). This may in part be due to the

increasing recognition of gender-related differences in symptomatology and clinical presentations leading to OSA diagnosis in female patients (Bonsignore et al., 2019).

5.4.2 Patient satisfaction as a measure of patient experience

Patient experience is regarded as a pillar of high-quality care, both in the UK and globally (also see **Chapter 1, Section 1.8**). Indeed, the NHS Constitution commits to encouraging the continuous collection of patients' feedback on their experiences of healthcare, and using their insights to improve services (Department of Health & Social Care, 2009). Whilst patient satisfaction is not a synonym for patient experience, it is an important outcome measure of patient experience (Kruk et al., 2018). To date, there is limited available data on patient experiences and satisfaction with CPAP therapy initiation and follow-up care. The findings of this survey allow hypotheses generation, specifically to address potential predictors of dissatisfaction with the experiences of care.

Previous data from a US study of patients newly diagnosed with OSA showed the effects of virtual care strategies on patient satisfaction and CPAP adherence (Parikh et al., 2011). The study found no differences in satisfaction and CPAP therapy adherence between patients allocated to virtual consultations and those who had in-person consultations. In another US study, the researchers investigated patient satisfaction with sleep apnoea testing, finding that patients who had an in-hospital sleep apnoea test were more likely to be satisfied with their experience, compared to those who had their sleep apnoea test carried out at home (Kapur et al., 2018). Previous studies also demonstrated that patient satisfaction was associated with objective measures of quality care and patient health outcomes (Cathal et al., 2013). However, it is important to consider that satisfaction with experiences of care can be influenced by numerous factors including patients' sociodemographics, geographical location, health status, previous experiences of care, and existing expectations (Batbaatar et al., 2017). Some of these factors were explored as potential predictors of dissatisfaction with the CPAP therapy initiation experience, in the current survey. I found that participant

dissatisfaction was associated with poor subjective rating of their CPAP therapy usage and increased demand for more medical support from their sleep clinic or CPAP provider.

Further investigation of this data is of importance to the delivery of person-centred OSA care in the UK, as both patient experience and satisfaction may be positively associated with improved patient health outcomes including adherence to treatment (Barbosa et al., 2012). This may be of particular importance to patient populations who are subject to more pronounced health inequalities in terms of their experiences of care and health outcomes, such as those living in socioeconomically disadvantaged communities (Morris and Scobie, 2020); see **Chapter 6, Section 6.4** for further details on future directions for the clinical management of OSA.

5.4.3 Patient involvement in the decision-making of their OSA care

The findings of this survey highlight the importance of shared decision-making and educational information provision in OSA care. Participants who did not feel involved as much as they wanted to be in the decisions about their OSA care and those who reported not receiving enough educational information about OSA and CPAP use, were more likely to be dissatisfied with their CPAP therapy initiation experience. Involving patients in the decision-making about their care is central to providing the personalised, person-centred care, promised by the NHS Long Term Plan (National Health Service, 2019). It has also been on the agenda of key national and international health policies and is often advocated for in the health and social care principles across the UK countries (Department of Health & Social Care, 2009, The Scottish Government, 2019, Northern Ireland Department of Health, 2016, The Welsh Government, 2018).

NICE has recently developed guidance and a standards framework to support shared decision-making (NICE, 2021). This framework emphasises the importance of health information sharing with patients and the need to understand their values and preferences, to enable active involvement (NICE, 2021). However, despite decades of research and policy

support, involving people in their care has been, unfortunately, slow (Coulter et al., 2022). Therefore, it is envisaged that this may lead to patients' lack of knowledge about their condition and the available care options. But also healthcare providers' lack of awareness about their patients' preferences and needs, which may in turn, result in uninformed decisions about patient care, resulting in uninformed demand for healthcare services. In the current survey, dissatisfied participants were more likely to rate their CPAP usage as poor, and were also more likely to require frequent contact with their sleep clinic or CPAP provider to seek medical support. Increased healthcare utilisation would, therefore, contribute to the economic burden of OSA, as discussed in **Chapter 1, Section 1.3.5**.

5.4.4 Patient preferences for their OSA care

Patient preferences are dynamic, and therefore, may change over time. In the BLF survey, published a decade ago, only one percent of participants wanted to receive telephone or video services for their OSA care, and ongoing support (British Lung Foundation, 2014). Interestingly, the findings of this survey showed a 19-fold increase in the number of participants who prefer to receive their follow-up care remotely through a phone or a video call. This increase is in part explained by technological advances and improved digital literacy. It is also likely due, in part, to the COVID-19 pandemic, which necessitated an abrupt adoption of digital health and virtual care by healthcare professionals and patients (Clipper, 2020), as discussed in **Chapter 1, Section 1.6.2**.

In addition to being a valuable outcome for patient experience, and thus for quality of care, patient satisfaction may also play a central role as a mediator between patient preferences and adherence to treatment (Konerding, 2016). Therefore, care strategies that are aligned with patients' preferences may result in higher satisfaction, which may, in turn, lead to better health outcomes by motivating treatment adherence. The findings of the current survey may demonstrate this relationship. Participants clearly expressed their preferences for in-person CPAP initiation and follow-up care, and most of them reported receiving an in-person CPAP

therapy initiation. Whether their preferences are based on their past experiences, individual expectations, or other factors is unknown. However, receiving their preferred choice of care may explain the high level of satisfaction, which may have consequently resulted in the good CPAP therapy adherence reported by most participants. Yet, it is important to note that patient satisfaction may also be influenced by numerous factors, hence, why a smaller number of the survey participants remained dissatisfied, despite receiving in-person care and reporting good treatment adherence. It is possible that these participants received what they would consider suboptimal care, impacting their satisfaction, and thus, developing an espoused expectation that in-person care, with its perceived traditional benefits, outweighs the advantages of remote strategies of care.

5.4.5 Patient-reported adherence to CPAP therapy is unreliable

Previously, the reliability of CPAP therapy adherence monitoring was hindered by relying on patient-reported estimates, which were thought to be unreliable in distinguishing between adherent and non-adherent patients (Rauscher et al., 1993). This was subsequently superseded by the newer generations of CPAP machines, which can provide objective and reliable estimates of patient adherence to CPAP therapy. Previous data suggested that subjectively reported adherence to CPAP therapy did not always accurately reflect the objectively measured adherence (Salepci et al., 2013). Patients tend to overestimate their CPAP usage, compared to the usage values measured objectively by the CPAP machine (Rotenberg et al., 2016b).

In the current survey, the participants reported CPAP therapy adherence was a median (IQR) of 7.0 (6.0 – 8.0) hours per night across 7.0 (7.0 – 7.0) nights per week. This level of adherence would be considered good due to being higher than the often-reported clinical threshold of ≥ 4 hours per night for $\geq 70\%$ of nights (Weaver, 2019); see **Chapter 1, Section 1.7.1** for further details. It is also higher than the objectively measured CPAP therapy adherence levels reported in several CPAP trials; MOSAIC (median [IQR]: 2:39 [0:36 – 4:59]

hours per night) at 6 months, PREDICT (median [IQR]: 1:33 [0:13 – 5:00] hours per night) at 3 months, and MERGE (median [IQR]: 4:00 [1:36 – 5:44] hours per night) at 3 months; all of which were conducted in real-world clinical settings across the UK (Craig et al., 2012b, McMillan et al., 2014, Wimms et al., 2018). The higher levels of adherence reported in the current survey might be related to the more severe levels of OSA reported by the survey participants, compared to the patient populations in the trials which recruited patients with minimally symptomatic OSA, older patients with OSA, and patients with mild OSA, respectively. Most participants in this survey self-reported their OSA as moderate or severe; a variable that has been previously reported as an independent predictor of long-term adherence to CPAP therapy (Kohler et al., 2010). However, the substantial difference between the patient-reported and objectively measured adherence to CPAP therapy reinforces what has been previously reported in earlier studies (Salepci et al., 2013, Rotenberg et al., 2016b), suggesting that patient-reported adherence may be unreliable for monitoring their treatment usage. Therefore, healthcare providers should consider using objectively measured data to monitor CPAP therapy adherence.

5.4.6 Critique of the method

As far as I am aware, this survey is the largest since the BLF's patient experience survey (2014). In addition, whilst the BLF survey recruited patients from 53 out of the 289 sleep clinics across the UK, the participants in the current survey were distributed throughout the regions of England and countries of the UK. The survey population was also representative of the patients presenting to sleep services in the UK, in terms of sociodemographic and clinical characteristics; however, the findings of this survey must be interpreted with caution due to several limitations.

Firstly, the findings are limited by selection bias, due to recruiting participants online, which requires a level of digital literacy. Secondly, participants were members of OSA patient-support charities, who may be more engaged with their care than the patients who would

have been inevitably excluded due to our recruitment strategy; this may explain the high levels of participants' satisfaction in the survey. Thirdly, the generalisability of the findings is limited by the participants being predominately white, which inevitably excluded the insights from patients of other ethnic backgrounds. Patients affected by these biases, and therefore not well-represented in this survey, may include those at a higher risk of being digitally excluded such as ethnic minority communities, socioeconomically disadvantaged populations, and people living in remote or rural areas (NHS England, 2023a, Honeyman et al., 2020). Additionally, the findings of this survey may be limited by recall bias (Schmier and Halpern, 2004). The majority of participants received their OSA diagnosis prior to the COVID-19 pandemic, with a median [IQR] of 7.0 [4.0 – 12.2] years since diagnosis, and this may have affected not only their ability to accurately recall their experiences of care but also the applicability of the findings to post-pandemic delivery of OSA care. Finally, the analyses of the data were exploratory in nature and hypothesis-generating and did not adjust for potential confounders.

Despite these limitations, the survey findings offer important clinical and research insights by providing an exploration of participants' experiences with, and preferences for, remote versus in-person CPAP therapy initiation and follow-up care. Additional research is needed to further examine the relationship between participants' satisfaction, preferences, and the potential predictors of dissatisfaction with the experiences of care.

5.5 Conclusion

The findings of this UK survey showed a high level of satisfaction amongst patients with self-reported sleep apnoea and experience of using CPAP therapy. The survey also identified potential predictors of participants' dissatisfaction with their CPAP therapy initiation experience, such as not feeling involved in the decision-making of their OSA care, and not receiving enough educational information about OSA and CPAP therapy use. In addition, participants diagnosed post-COVID-19 pandemic were more likely to be dissatisfied with their

CPAP therapy initiation experience, compared to those diagnosed pre-pandemic. These factors may be of value to clinical care providers since low levels of satisfaction were associated with poor subjective rating of CPAP therapy usage and increased demand for more medical support from the sleep clinics or CPAP providers. Participants expressed a clear preference for in-person CPAP therapy initiation and follow-up care, compared to remote care strategies through a phone or a video call. These findings, together with findings of the systematic review and meta-analysis (presented in **Chapter 4**), could help in developing and evaluating clinical care strategies for the management of patients with OSA.

Chapter 6 – General Discussion

6.1 Quest for understanding OSA clinical care strategies in the UK

The aim of this programme of research was to understand the delivery of OSA care from both patient and clinical perspectives, this required investigations using different research methodologies.

In a training programme on value-based healthcare, Professor Sir Muir Gray, the former Chief Knowledge Officer of the NHS, reminded us that “*knowledge is the enemy of disease*”. Knowledge in the context of healthcare delivery is typically derived from research, organisational audits and routinely collected data, or the experiences of patients and healthcare professionals (De Brún, 2013). I hope that the research contained within this Thesis will be of value for evaluating and improving post-pandemic delivery of OSA clinical care in the UK.

In this PhD Thesis, specific clinical care pathways for OSA diagnosis and management were investigated using both quantitative and qualitative study designs, including a *self-administered online survey*, a *nested qualitative evaluation*, a *randomised controlled study*, and a *systematic review and meta-analysis*.

The study designs for the experimental chapters were chosen based on the aims of the studies. They also highlight the principles of evidence-based clinical practice, moving up the hierarchy of evidence (**Figure 6.1**). Each study design has unique strengths and, therefore, this approach enabled my investigations of OSA clinical care delivery in the UK to be as robust as possible (Burns et al., 2011, Garattini et al., 2016).

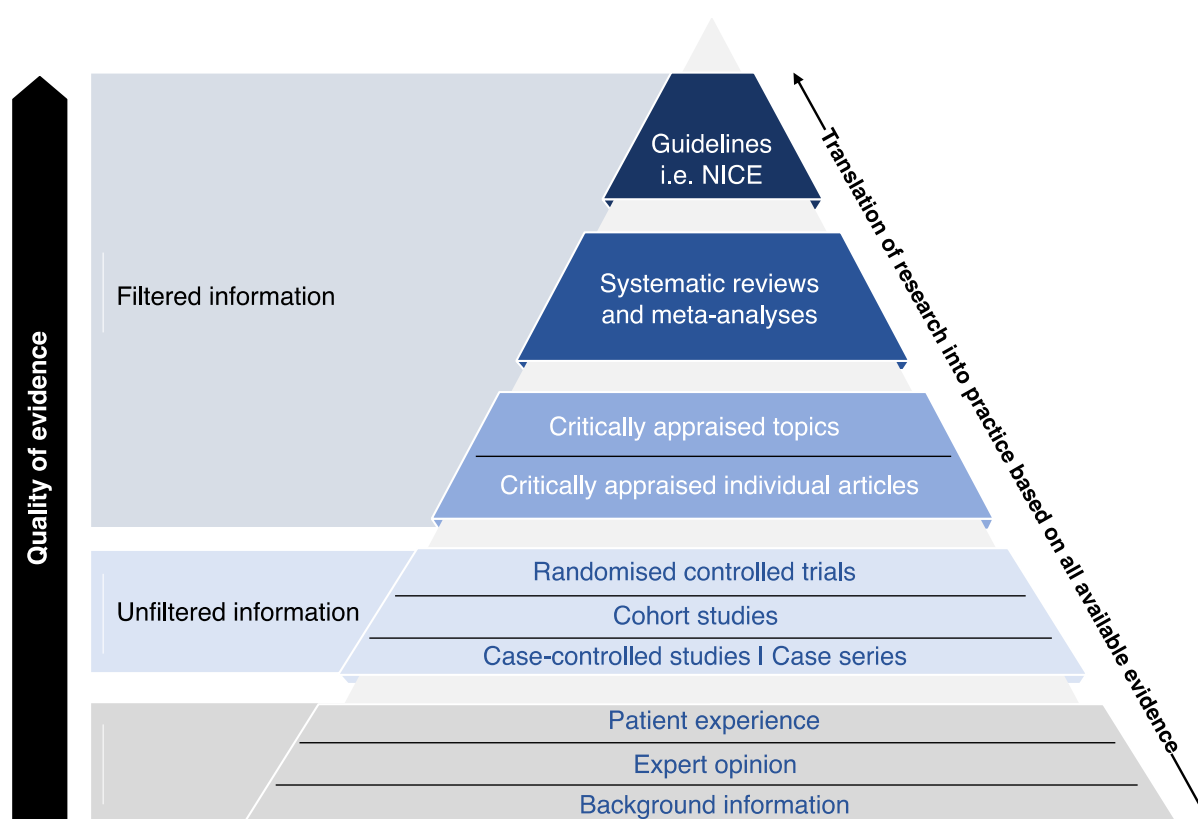


Figure 6.1 The hierarchy of evidence-based clinical practice. Modified from (Garattini et al., 2016) and reproduced with permission of Elsevier.

6.2 Summary of aims

Many patients with OSA in the UK remain undiagnosed and, thus, untreated. Conventional clinical care for OSA diagnosis and management is currently insufficient to meet the increasing demand, which has been exponentially rising post-COVID-19 pandemic. Digitally-enabled diagnosis and management may address these challenges and improve the delivery of OSA care.

In this PhD Thesis, I aimed to investigate new clinical care strategies for the diagnosis and management of OSA and evaluate patient experiences with, and preferences for these strategies. In order to address these aims, I carried out investigations, in adult patients with suspected, or existing OSA diagnosis.

6.3 Summary of findings

Part One – Investigations of the diagnosis for OSA

Chapter 2: *A two-centre, randomised controlled pilot study investigating a remote diagnostic pathway for OSA using a novel MM monitor, compared to home respiratory polygraphy.*

This study found that in adult patients referred for investigation of suspected OSA, MM monitoring with automated machine-learning analysis reduced time to treatment decision by an average of 6 days, compared to home respiratory polygraphy (median [IQR]: 13.5 [7.0 – 21.5] vs. 19.5 [13.7 – 35.5] days, $P=0.017$). MM monitoring was also associated with an average time-saving of 29 minutes per sleep test for a skilled healthcare professional. These findings were irrespective of geographical location, with no difference in time to treatment decision for patients in the Scottish Highlands and Islands, compared to patients in inner London.

Chapter 3: *A qualitative evaluation investigating patient experiences of remote diagnostic pathways using both the MM monitor and home respiratory polygraphy. This was a nested study within the randomised controlled study reported in **Chapter 2**.*

This study found that most participants (86%; $n=6 / 7$) preferred home sleep apnoea testing with the “unobtrusive” MM monitor, compared to the more “cumbersome and restrictive” respiratory polygraphy monitor. Participants also described their planned or unplanned personal journeys to OSA diagnosis. Of note, despite receiving a formal diagnosis, there was a lack of knowledge about sleep apnoea and its consequences. The findings of the study provide insights into some of the barriers and facilitators for a positive OSA diagnosis experience.

Part Two – Investigations of the clinical management for OSA

Chapter 4: *A systematic review and meta-analysis investigating the effectiveness of virtual consultations, compared to in-person consultations, on patient-reported sleepiness and the cost-effectiveness.*

This study found that in adult patients with OSA treated with CPAP therapy, virtual care delivered by telephone or video consultations was as effective as in-person consultations for improving their subjective sleepiness, assessed by ESS (mean difference [95% CI]: -0.39 [-1.38 to 0.60] points, $P=0.44$). Virtual care also appeared to be less costly than in-person care strategies*. In addition, virtual consultations modestly increased the average CPAP therapy usage by nearly half an hour per night (mean difference [95% CI]: +26 [04 to 48] minutes per night, $P=0.02$), compared to in-person consultations.

**This is based on a qualitative synthesis of the findings in three trials (Isetta et al., 2015, Turino et al., 2017, Lugo et al., 2019), no statistical analysis was performed.*

Chapter 5: *A survey of experiences with, and preferences for, remote versus in-person CPAP therapy initiation in adult patients with self-reported OSA treated with CPAP therapy.*

This survey found that most participants (77%; $n=907 / 1,186$) were satisfied with their CPAP therapy initiation experience, regardless of their sociodemographic and clinical characteristics. Participants' dissatisfaction with their experience of care was associated with not feeling involved in the decision-making of their OSA care and not receiving enough educational information about OSA and CPAP therapy. In addition, dissatisfied participants were more likely to rate their CPAP therapy usage as poor and require further medical support from their sleep clinic or CPAP provider, compared to those who were satisfied. Most participants expressed their preference for in-person CPAP therapy initiation (91%; $n=955 / 1,048$) and in-person follow-up care (70%; $n=737 / 1,048$), compared to remote care strategies.

6.4 Future directions: ‘Digital first’ for the clinical management of OSA is not everyone’s first choice.

The findings of the studies in this Thesis provide insights into both clinical and patient perspectives of conventional compared to newer clinical care strategies for OSA diagnosis and management in the UK. Building on the above findings, along with the lessons learned throughout this PhD, I have proposed a two-phase future investigation:

6.4.1 Background

In this Thesis, I found that most patients preferred home sleep apnoea testing, however, they expressed their preference for in-person CPAP therapy initiation and follow-up management strategies, compared to remote care strategies. I also found that some patients reported lack of involvement in the decision-making of their OSA care and insufficient provision of educational information about OSA and CPAP therapy. Both of these factors were associated with dissatisfaction with their experiences of care, which was also associated with poor subjective rating of CPAP therapy usage and increased requirements for further medical support. These findings are important for OSA clinical care because they suggest that patient preferences and needs can be dynamic and context-dependent, thus, the provision of person-centred care requires active involvement of patients in order to understand their preferences and needs.

The shift to remote care pathways for OSA treatment and follow-up management, which was accelerated by the COVID-19 pandemic, may not accommodate all patient preferences and needs. Although the NHS Long Term Plan envisions a different model of care with a ‘*digital first*’ option being offered to most patients by 2029, the NHS Constitution, however, is committed to providing healthcare services that are tailored to the needs and preferences of patients, their families, and their carers (Department of Health & Social Care, 2009, National Health Service, 2019). Indeed, this is central to equitable healthcare provision in the UK, specifically when caring for those at a higher risk of being digitally excluded such as

socioeconomically disadvantaged populations and people living in remote or rural areas (NHS England, 2023a, Honeyman et al., 2020, Office for Health Improvement and Disparities, 2022). Whilst the relationship between rurality and OSA treatment outcomes is unclear, recent UK data suggest that patients living in socioeconomically deprived areas are more likely to experience difficulties with their CPAP therapy usage (Cowen et al., 2023); consequently requiring further support tailored to their needs.

As a next step in developing OSA clinical care pathways for this patient population, I propose carrying out a two-phase study to address potential health inequalities associated with implementing remote care pathways for OSA in the UK. This would be achieved using an experience-based co-design approach (Raynor et al., 2020), in socioeconomically disadvantaged patients. **The aim of the study would be to gain an in-depth understanding of their preferences and needs, identify barriers to treatment adherence and key priorities for improvement, and then co-design a person-centred clinical management intervention to enhance their treatment acceptance and adherence.**

6.4.2 Phase 1: Active collaboration with the patient population to inform the design of their own OSA clinical care

Post-hoc analysis of the survey data (reported in **Chapter 5**) for the most deprived 20% of the participants, will be compared to the least deprived 20%, according to the official English measure of relative deprivation (Index of Multiple Deprivation). This exploratory analysis would then inform the development of a further qualitative study, using in-person or remote focus group discussions with socioeconomically disadvantaged patients and their carers, to investigate the contextual factors influencing:

- patient preferences for in-person versus remote clinical care,
- patient involvement in the decision-making of their OSA care,
- and patient acceptance and adherence to their OSA treatment.

6.4.2.a: Proposed protocol for the qualitative study

I plan to use a community-based approach, working in tandem with patient-support charities (e.g. SATA and Hope2Sleep; see **Chapter 5, Section 5.2.3** for their details) and faith settings, to facilitate the recruitment of this patient population which may be hard-to-reach. A purposive sampling technique would be used to conduct four to six focus group discussions, lasting no more than 90 minutes with up to eight participants per group, and these are anticipated to be sufficient for this study (Onwuegbuzie et al., 2009). The final sample size would be determined by data saturation; see **Chapter 3, Section 3.2.2** for sample size considerations in qualitative research.

The focus group discussions would need to be conducted by at least two researchers (a moderator and an assistant moderator) using a semi-structured topic guide (see **Chapter 3, Section 3.2.3** for a discussion on topic guide development). The use of two or more researchers would facilitate the collection of individual data, group data, and/or group interaction data (Onwuegbuzie et al., 2009), providing further insights from different perspectives.

6.4.3 Phase 2: Co-designing the future of OSA clinical care with the patient population

The findings of the investigations in **Phase 1** would inform the development of a clinical management intervention for OSA, co-designed with socioeconomically disadvantaged patients and tailored to their preferences and needs, to enhance their treatment acceptance and adherence. This approach may be key to the effectiveness of the care they receive since it has been reported that people with chronic conditions are likely to be more adherent to their medical treatment if it is tailored to their preferences and needs (Losi et al., 2021).

6.4.3.a: Proposed methodology for subsequent testing

A prospective, randomised controlled study would then be needed to assess the applicability and acceptability (e.g. by patients and healthcare professionals) of the co-designed clinical management intervention in real-world settings:

- **Preliminary hypothesis:** A clinical care management intervention co-designed with patients, improves treatment adherence and daytime functioning, compared to usual clinical care, at 3 months; specifically in socioeconomically disadvantaged OSA patients who experience difficulties with their CPAP usage.

6.4.4 Building on past experiences

The delivery of this study could be supported by our research group's previous experience in completing trials that inform clinical practice guidelines. These trials have been carried out in collaboration with the UK Respiratory Sleep Research Network.

In the PREDICT trial (McMillan et al., 2014), our research group addressed the inequality of health research in older patients with OSA and showed that CPAP therapy with standard supportive care was clinically effective in reducing sleepiness and marginally more cost-effective, compared to standard supportive care alone, in this patient population. However, their CPAP usage was low (median [IQR]: 1:33 [0:13 – 5:00] hours per night) at 3 months. Conversely, the MERGE trial (Wimms et al., 2020) achieved a relatively-good adherence using a centralised patient support protocol for patients with mild OSA (median [IQR]: 4:00 [1:36 – 5:44] hours per night) at 3 months; see **Chapter 1, Section 1.7.1** for further details.

6.4.5 Relevance of proposed investigations for OSA clinical care in the UK

NICE clinical practice guidelines stated that “*because there was no evidence for people who have difficulty using CPAP, the committee made a research recommendation on interventions to improve CPAP adherence to inform future guidance*” (NICE Adherence Evidence Review, 2021). In addition, the NHS’s *Core20PLUS* initiative, which aims to inform actions for reducing health inequalities at both national and healthcare system level, also highlights the importance of targeting the most deprived 20% of the national population plus other minoritised communities (NHS England and NHS Improvement, 2021). These people are subject to more pronounced health inequalities in terms of access to NHS services, experience of care, and health outcomes (Morris and Scobie, 2020). Therefore, the evidence

from the proposed investigations could inform the redesign of clinical care pathways for patients with OSA in the UK.

6.5 Expanding the horizons of my research and professional endeavours in Saudi Arabia

In 2013, a few days before I left home for the first time to study abroad, my late grandmother, who had been actively involved in raising me, shared her wisdom one more time and indirectly conveyed a message, by saying: *“Your pursuit of knowledge is a compass that can take you far, but returning home crowned with that knowledge and life experiences should be your ultimate destination”*. Now, as I begin the transition back to my home country after 11 years of steep education and learning, the knowledge, skills, and insights I gained during my time in the US and UK will provide me with valuable guidance in navigating the complexities of OSA clinical care delivery in the Saudi healthcare system, which is undergoing transformational changes.

Saudi Arabia (SA) has recently launched the delivery plan for its Healthcare Sector Transformation Programme, as part of *Saudi Vision 2030* (Saudi Ministry of Health, 2021). The programme aims to restructure the Saudi health ecosystem, enhancing its capabilities through building digital infrastructure and expanding the provision of virtual care, which will facilitate guaranteed access to free healthcare services, with comprehensive geographical coverage across the kingdom (Saudi Ministry of Health, 2021). This has led to the establishment of SEHA Virtual Hospital, which utilises digital health technologies to connect more than 130 geographically distributed hospitals with over 30 specialised healthcare services (SEHA Virtual Hospital, 2022).

Notably, both the Saudi Healthcare Sector Transformation Plan and the UK NHS Long Term Plan have placed a national and strategic focus on utilising digital health technologies; envisioning different models of care – where digitally-enabled healthcare services are mainstream across both countries. In addition, similar logistical and operational challenges

are faced by both healthcare systems. People in rural areas in SA and those in certain parts of the UK may have limited access to high-quality healthcare services, thus, widespread implementation of reliable and effective; person-centered, digitally-enabled care will change how healthcare services are delivered in the future. It is anticipated that this will facilitate improved access to healthcare services in underserved areas.

Comparison of future healthcare delivery between SA and the UK illustrates the applicability and relevance of my UK-based programme of research on a global scale, surpassing geographical boundaries to inform my future professional activities.

6.6 Conclusion

The findings of this Thesis contribute to our understanding of conventional compared to newer clinical care strategies for OSA in the UK. The use of both MM monitoring for remote diagnosis and virtual consultations for CPAP therapy follow-up can be considered for the delivery of OSA clinical care. However, digitally-enabled care may not accommodate all patient preferences and needs. Although most patients preferred home OSA diagnosis, they expressed their preference for in-person CPAP initiation and follow-up management strategies, compared to remote care strategies. In addition, lack of patient involvement in the decision-making of their OSA care and insufficient provision of educational information about OSA and its treatment, were associated with dissatisfaction with their experiences of care. Patient dissatisfaction was also associated with poor subjective rating of their CPAP usage and increased demand for more medical support from their sleep clinic or CPAP provider. Therefore, future investigations should address potential health inequalities associated with widespread implementation of remote care pathways for OSA in the UK, using a community-based approach to co-design a clinical management intervention with patient populations at higher risk of being digitally excluded, such as those living in socioeconomically disadvantaged communities, to enhance their OSA treatment acceptance and adherence.

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Expected presentation date	Feb 2024
Order reference number	Figure for General Introduction - 1
Portions	Figure 2 - Different types of objective sleep measurements
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Appendix 2.1 Regulatory documents for the randomised controlled study

2.1.1 Ethical approval letters



N/ADr Julia L Kelly
Academic Unit of Sleep and Breathing
National Heart and Lung Institute
Royal Brompton Hospital, London
SW3 6NPN/A

Email: Wales.REC3@wales.nhs.uk

16 June 2021

Dear Dr Kelly

**HRA and Health and Care
Research Wales (HCRW)
Approval Letter**

Study title:	A prospective, multicentre, randomised, blinded study of obstructive sleep apnoea detection using the Sunrise solution: The Sunrise OSA Trial (SOSAT)
IRAS project ID:	296444
Protocol number:	N/A
REC reference:	21/WA/0162
Sponsor	Royal Brompton Hospital

I am pleased to confirm that [HRA and Health and Care Research Wales \(HCRW\) Approval](#) has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

Please now work with participating NHS organisations to confirm capacity and capability, [in line with the instructions provided in the "Information to support study set up" section towards the end of this letter.](#)

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?

HRA and HCRW Approval does not apply to NHS/HSC organisations within Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) have been sent to the coordinating centre of each participating nation. The relevant national coordinating function/s will contact you as appropriate.

Please see [IRAS Help](#) for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

How should I work with participating non-NHS organisations?

HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your non-NHS organisations to [obtain local agreement](#) in accordance with their procedures.

What are my notification responsibilities during the study?

The standard conditions document “[After Ethical Review – guidance for sponsors and investigators](#)”, issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The [HRA website](#) also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

Who should I contact for further information?

Please do not hesitate to contact me for assistance with this application. My contact details are below.

Your IRAS project ID is **296444**. Please quote this on all correspondence.

Yours sincerely,

Ann Parry
Approvals Specialist

Email: Wales.REC3@wales.nhs.uk

Copy to: Mr. Patrik Pettersson, Guy's and St Thomas' NHS Foundation Trust

List of Documents

The final document set assessed and approved by HRA and HCRW Approval is listed below.

<i>Document</i>	<i>Version</i>	<i>Date</i>
Instructions for use of medical device [SOSAT_Participant Instructions]	v1.0	27 April 2021
Instructions for use of medical device [SOSAT_Apnoealink Air Instructions]	v1.0	16 March 2021
Instructions for use of medical device [SOSAT_Sunrise Guide_v2.0]	v2.0	24 May 2021
IRAS Application Form [IRAS_Form_29042021]		29 April 2021
IRAS Application Form XML file [IRAS_Form_29042021]		29 April 2021
Letter from funder [SOSAT_Letter of Agreement]		23 April 2021
Letter from statistician [SOSAT_Stats Letter]		23 April 2021
Letters of invitation to participant [SOSAT_Invitation Letter]	v1.0	16 March 2021
Non-validated questionnaire [SOSAT_Patient Questionnaire_v2.0]	v2.0	24 May 2021
Organisation Information Document [SOSAT_OID v3_12May2021]	v3	12 May 2021
Other [Response to REC]	v1.0	04 June 2021
Other [SOSAT_Protocol_v2.0]	v2.0	04 June 2021
Participant consent form [SOSAT_ICF_v3.0]	v3.0	16 June 2021
Participant information sheet (PIS) [SOSAT_PIS_v2.0]	v2.0	24 May 2021
Referee's report or other scientific critique report [SOSAT_Peer Review]		21 March 2021
Schedule of Events or SoECAT [SOSAT - Schedule of Events (SoE) v2 07May2021]	2	07 May 2021
Summary CV for Chief Investigator (CI) [SOSAT_CI_CV]		19 April 2021
Summary CV for student [SOSAT_Student CV]		
Summary CV for supervisor (student research) [SOSAT_Supervisor CV]		19 April 2021

TEMP009 Version 6 July 2021

Dr Beth Sage
Research, Development & Innovation Director
NHS Highland RD&I Office
Centre for Health Science
Old Perth Road
Inverness
IV2 3JH

E-mail: beth.sage@nhs.scot

2nd November 2021

NHS Highland RD&I Ref: **HIGHLAND 1754**
NRSPCC Ref: **NRS 21/296444**

Dr Beth Sage
Respiratory Consultant
Raigmore Hospital
Old Perth Road
Inverness
IV2 3JH

Dear Dr Sage,

Management Approval for Non-Commercial Research

I am pleased to tell you that you now have Management Approval for the research project entitled: 'A prospective, multicentre, randomised, blinded study of obstructive sleep apnoea detection using the Sunrise solution: The Sunrise OSA Trial' **(SOSAT) [Protocol V2.0 04/06/2021]**.

I acknowledge that:

- The project is sponsored by Guy's and St Thomas' NHS Foundation Trust.
- The project has no external funding.
- Ethics approval for the project has been obtained from the Wales REC 3 Research Ethics Committee (Reference Number: 21/WA/0162).
- The project has a signed Organisational Information Document.

The following conditions apply:

- The responsibility for monitoring and auditing this project lies with Guy's and St Thomas' NHS Foundation Trust.
- This study will be subject to ongoing monitoring for Research Governance purposes and may be audited to ensure compliance with the UK Policy Framework for Health and Social Care Research (2018, V3.3 07/11/17, however prior written notice of audit will be given).



Headquarters: Assynt House, Beechwood Park, INVERNESS IV2 3BW

Chair: Professor Boyd Robertson
Chief Executive: Pam Dudek

- **Any researchers coming into NHS Highland, or accessing data from NHS Highland, for the purposes of carrying out research with patients will require a Letter of Access before starting the study at this site. Please contact a member of the RD&I Governance team at nhsh.nhshighlandresearchpassports@nhs.scot for further assistance.**
- The paperwork concerning all incidents, adverse events and serious adverse events thought to be attributable to a NHS Highlands participant's involvement in this project should be notified to the NHS Highland RD&I Governance team. Please email documents to nhsh.RandD@nhs.scot.
- You are reminded that all amendments (substantial or non-substantial) to the protocol and associated study documents or to the REC application should be notified to the NHS Highland RD&I Governance team to obtain amendment approval (nhsh.RandD@nhs.scot). Guidance can be found at <https://www.nhsresearchscotland.org.uk/services/permissions-co-ordinating-centre/permissions>
- Monthly recruitment rates should be notified to the NHS Highland RD&I Governance team, detailing date of recruitment and the participant trial ID number (please do not include names or other identifiable information). This should be done by e-mail on the first week of the following month, to Marion Bamford, RD&I Facilitator at nhsh.RandD@nhs.scot. Please quote your RD&I Highland reference number (Highland 1754).
- Please report any other changes in resources used, or staff involved in the project, to myself at nhsh.RandD@nhs.scot.

Please quote your RD&I Highland reference number (Highland 1754) on all correspondence.

Yours sincerely,



Laura McIlhatton
RD&I Governance Manager
NHS Highland

cc

Mr. Sulaiman S. Alsaif, PhD Student, Academic Unit of Sleep and Breathing, National Heart and Lung Institute, Royal Brompton Campus, London - s.alsaif18@imperial.ac.uk

Marion Bamford, RD&I Facilitator, NHS Highland Research, Development & Innovation Division - nhsh.randd@nhs.scot

Mrs Wendy Douglas, Sleep Nurse Specialist, Raigmore Hospital, NHS Highland – wendy.douglas2@nhs.scot

Jo Fraser, RD&I Administration Assistant, NHS Highland Research, Development & Innovation Division – nhsh.randd@nhs.scot

Dr J Kelly, Chief Investigator/Academic Supervisor, Guys' and St Thomas' NHS Foundation Trust & Academic Unit of Sleep and Breathing, National Heart and Lung Institute, Royal Brompton Hospital, London j.kelly@rbht.nhs.uk

Professor M Morrell – Academic Supervisor, Academic Unit of Sleep and Breathing, National Heart and Lung Institute, Royal Brompton Hospital, London m.morrell@imperial.ac.uk

Mr Patrik Pettersson, Sponsor Representative, Guy's and St Thomas' NHS Foundation Trust Research Office, Sydney Street, London – research@rbht.nhs.uk

2.1.2 Participant information sheet



Royal Brompton
and Harefield



IRAS ID: 296444

Participant Information Sheet (PIS)

Part 1

Study Title: Obstructive sleep apnoea detection using the Sunrise device

The Sunrise Obstructive Sleep Apnoea Trial (SOSAT)

Invitation to participate in the above study:

You are invited to take part in a research study known as the as the Sunrise OSA Trial (SOSAT) study. Obstructive sleep apnoea (OSA) is when people have trouble with their breathing when they are sleeping, which can lead to poor sleep and daytime symptoms such as sleepiness. OSA is usually diagnosed using results from a sleep test. The purpose of this study is to compare a new sleep testing device (called the Sunrise device) to a standard home sleep testing device (called polygraphy). We want to compare several outcomes including how long it takes for you to get a treatment decision and whether the treatment decision is the same using the results from each device. We also want to know about your experience using both devices.

This information sheet is designed to explain what will happen if you agree to participate in the study. Before you decide to enter this study, it is important to understand why the research is being done and what it will involve. Please read the following information carefully and discuss it with whoever you choose: friends; relatives and/or your doctor. Please ask if you want us to clarify anything or if you would like more information. **We will go through the information sheet with you and answer any questions you have.**

Part 1 of the PIS tells you the purpose of this study and what will happen to you if you take part.

Part 2 gives you more detailed information about the conduct of the study.

Please ask us if there is anything that is not clear. Take time to decide whether or not you wish to take part.



What is the purpose of the study?

Obstructive Sleep Apnoea (OSA) is when the muscles in your throat relax during sleep which leads to narrowing or closing of your airway resulting in a drop in your oxygen level and then an awakening from sleep. This happens repetitively throughout every hour of your sleep and can lead to poor sleep and daytime symptoms. We can measure the amount of times these breathing events occur by monitoring your breathing during sleep using a home sleep test.

The standard sleep test includes several sensors that measure breathing including nasal airflow, chest movements and oxygen levels. The device is returned to the sleep department where the data is downloaded and analysed by specially trained professionals who produce a sleep report.



Figure 1: A standard home polygraphy sleep test kit

A new, smaller device with a single sensor has been developed. The Sunrise™ device, is a small sensor that is applied to the chin, measures chin movements during sleep and uses artificial intelligence to automatically detect breathing events. It communicates with a mobile app. for automatic data transfer and provides a detailed report to doctors and patients the day after the test.



Figure 2: The new Sunrise device

We want to find out whether this new technology, using the Sunrise device, is useful for patients undergoing investigation for OSA. We want to compare several outcomes including how long it takes for you to get a treatment decision and whether the treatment decision is



the same using the results from each device. We also want to know about your experience using both devices.

Why have I been invited?

You have been referred for investigation for suspected obstructive sleep apnoea (OSA). As part of our clinical pathway, you will be asked to undertake a home sleep test to help your team decide if you have OSA and whether you need treatment. We would like to ask you to consider wearing two home sleep test devices on the same night so that we can compare the results. If you give permission, then you will be invited to join our study. This study will provide information for a larger study, but in the first instance we are studying 40 patients.

Do I have to take part?

No. Participation in this study is optional and it is entirely up to you whether you would like to take part or not. If you do wish to take part, you will sign a consent form and enter into the study. You are free to withdraw from the study at any time without a reason and this will not affect the care you subsequently receive.

What will happen to me if I take part?

As the first step, we will make sure that you understand the study, and ask you to provide Informed Consent. If you received this information sheet by post or email, your clinician or a designated researcher may contact you to further discuss the study and to ask for your verbal consent to begin the study. If this is the case, we will also ask for your written consent at a later stage remotely via email or post.

You will be posted the two home sleep study devices, **the Sunrise™ device** and the **polygraphy device**, along with written instructions for how to use them. You will be asked to wear both devices at the same time while you sleep for one night. The next morning we will ask you to complete a questionnaire to let us know about your experience using both devices. We will ask you to send back both sleep test devices and your questionnaire in a reply-paid envelope.

Other information:

All study kit, including the sleep study devices will be clean in line with COVID-19 precautions. The polygraphy device is a standard home sleep test that you would usually be undertaking. The Sunrise device is the additional test and requires you to download a phone application and answer some online questions before the sleep test. You will also need to associate your phone with the Sunrise device via Bluetooth when you go to bed.

Following the overnight sleep study, the Sunrise report of your sleep data will be available for review via a secure online cloud transfer system. Your sleep data from the polygraphy device will also be downloaded for review. Results from the sleep tests will be given to your clinical team for them to decide which treatment is best for you.

You will be randomly allocated to receive your treatment decision based on the data from either the Sunrise device, or the polygraphy device. You will have a 50% chance of having



your treatment decision based on data from the Sunrise device and a 50% chance of having your treatment decision based on data from the polygraphy device. This is a 'blind trial' and therefore you will not know which data was used to make your treatment decision.

Your participation in the study is then complete. You will revert to routine clinical care at your local centre, where you will discuss ongoing management and treatment options with your local team.

Follow-up:

For further information on your experiences, preferences, and insights, you will be invited to participate in an optional remote individual interview. A separate consent will be required to participate in the interview.

Expenses and payments

You will not be paid for your involvement in the study. We will, however, provide you with reply-paid envelopes to post the sleep kit back to us so that you will not need to make any trial-related hospital visits.

What do I have to do?

Usually when patients are investigated for OSA, they undertake a home sleep test. In this study we are asking you to use two home sleep test devices on the same night so that we can compare a new device with the standard one. You do not have to undertake any additional nights' test or any further invasive testing.

The new sleep test device (Sunrise) is already CE marked and is commercially available in the UK. It is a single-use simple non-invasive sensor that has already been tested for safety. Therefore, we are not testing its safety, but we want to know whether it will speed up the testing process and lead to a faster treatment decision. We also want to know about your experience using the new device, compared to the standard polygraphy test. We ask that you complete the questionnaire in the morning following the sleep test.

We will also ask you to consider taking part in an optional remote individual interview that will occur up to 3 months after your sleep test.

What are the alternatives for diagnosis or treatment?

In the UK there are various sleep tests that are used for the investigation of OSA. These include oximetry (small sensor on the finger), polygraphy (as in this study – see Figure 1), or a full polysomnography which involves more sensors that collect brain signals to determine sleep. Some of these tests, like the polysomnography, need to be done in hospital and are complex and expensive.

New devices are aimed to make it simpler and easier for the patient to use at home. The Sunrise device is one such device.

What are the possible disadvantages and risks of taking part?



The devices used in this study are CE-marked, commercially available devices used to detect OSA in adults. No major risks have been reported. There is a small risk that the adhesive for the Sunrise device may irritate very sensitive skin. If this occurs, you should remove the device.

The new Sunrise device might give a different result compared to the standard polygraphy device. We will compare all the results to ensure that you receive an appropriate treatment decision based on standard clinical care.

What are the side-effects of any treatment received when taking part?

There is no treatment given as part of this study.

What are the possible benefits of taking part?

The benefits of using the Sunrise device compared to standard polygraphy in the diagnosis of OSA have not been fully determined, which is our reason for carrying out the study. It is possible that you may experience a reduction in waiting-time, leading to earlier detection and treatment of OSA. We are also interested in any benefits that you might report by using the device, whether either device is easier or preferable compared to the other.

What happens when the research study stops?

After completion of the study, you will return to routine clinical care. Your ongoing care will be provided by your sleep service.

What if there is a problem?

Any complaint about the way you have been dealt with or any possible harm you might suffer will be addressed. The detailed information on this is given in part 2

Will my taking part in the study be kept confidential?

Yes, we will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

This completes Part 1. If the information in Part 1 has interested you and you are considering participation, please read the additional information in part 2 before making any decision.



Part 2

What if relevant new information becomes available?

Sometimes we get new information. If this happens your research doctor will tell you and discuss whether you should continue in the study. Because this is not a treatment study, this is an unlikely scenario

What will happen if I don't want to carry on with this study?

Your participation is voluntary and you may change your mind at any time. If you do decide to take part you are free to withdraw at any time during the study without providing a reason and this will not affect your clinical care in any way. If you withdraw we will continue to use all data collected up to your withdrawal if you consent for us to do so. If you lose capacity during the duration of the study, you will be withdrawn from the study but any identifiable data already collected would be kept confidentially and used in the study.

What if there is a problem?

Complaints:

If you have a concern about any aspect of this study you should ask to speak with the researchers who will do their best to answer your questions juliakelly2@nhs.net. If you remain unhappy and wish to complain formally, you can do this.

- Royal Brompton Hospital patients, please contact the hospital Patient Advice and Liaison Service (PALS): pals@rbht.nhs.uk
- NHS Highlands patients, please contact the hospital Patient Advice Support Service (PASS)

Inverness Badenoch and Strathspey Citizens Advice Bureau
29-31 Union Street
Inverness IV1 1QA
01463 237664
enquiries@invernesscab.casonline.org.uk

Harm:

In the event that something goes wrong, and you are harmed during the research and this is due to someone's negligence then you may have grounds for legal action for compensation against the study Sponsor, Guys' and St Thomas' NHS Foundation Trust, but you may have to pay your legal costs.

The normal NHS complaints mechanism will still be available to you.

Will my taking part in the study be kept confidential

The records obtained while you are in this study will remain strictly confidential at all times. Personal information, including name, phone number, email and address will be shared with the central research team who will post the sleep study devices and collect the sleep study data. This team may be employees of NHS Highland or the Royal Brompton Hospital.



All other study documentation will be coded only with your unique study ID number, and will contain no personal identifiers. We will ask for your postcode (only the first half). This information will not be used to identify you, however, it will help us to understand the differences in access to healthcare across various parts of the UK. Additionally, your sleep study data from polygraphy will be downloaded and stored with only your study ID number.

We will follow standard ethical and legal practice and all information about you will be handled in confidence. Our procedures for handling, processing, storage and destruction of their data match the General Data Protection Regulations (GDPR). Your identifiable data will only be accessed by authorised persons such as researchers, sponsors, regulatory authorities and Research & Development (R&D) audit (for monitoring of the quality of the research). Published results will not contain any names of study participants.

Sunrise sleep study data:

When registering to use the Sunrise device, you must set up a user account which includes giving explicit consent. This must occur before your registration data is temporarily stored on your phone and then sent to the Application Programming Interface (API) to be recorded. Without this consent, this data is neither stored on the phone, nor sent to the API and your user account cannot be created.

At the end of the night, a wireless connection (WiFi or 3G/4G) is required to establish communication between the smartphone and the cloud server. Recording data is temporarily stored on the phone overnight but is sent to cloud storage after the night is over.

All transfers and communications with the API are carried out using HTTPS (HyperText Transfer Protocol Secure), an encrypted and secure communication protocol.

The cloud service used ensures compliance with European GDPR directives in terms of data protection. Anonymised data are stored in the EU. Your data, identifiable only by your study identification number, will be available to the researchers via a secure nhs.net email account.

How will we use information about you?

This study is sponsored by the Royal Brompton Hospital, Guys' and St Thomas' NHS Foundation Trust. We will need to use information from you and from your medical records for this research project. This information will include your initials/ name/ contact details. People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead. We will keep all information about you safe and secure.



Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

What are your choices about how your information is used?

- You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.

Where can you find out more about how your information is used?

You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/
- our leaflet available from <https://www.rbht.nhs.uk/patients-visitors/patients/patient-support-services/your-personal-information>
- by asking one of the research team

You can also email the trust Data Protection Officer: ig@rbht.nhs.uk, who can listen to your concerns or give you advice about your rights in respect to the data we hold about you.

What will happen to any samples I give?

This study does not collect any samples.

Will any genetic tests be done?

No

What will happen to the results of the research study?

We intend to publish the results in peer-reviewed publications. Your anonymised data may also be included as part of an Imperial College PhD thesis. You will not be identified in any report/publication. We also intend to use this pilot data to apply for a larger trial in the UK.

Who is organising and funding the research?

This study is not receiving any external funding. The Sunrise devices have been donated by Sunrise SA (Belgium).

Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee (REC), to protect your interests. This study has been reviewed and given favorable opinion by Wales REC 3 Research Ethics Committee (REC).

Further Information and Contact Details

For further information about the study, please contact Dr Julia Kelly:
juliakelly2@nhs.net Ph: 0207 3528121 ext 84183

2.1.3 Informed consent form



Royal Brompton
and Harefield



IRAS ID: 296444

Patient Identification Number for this trial: _____

INFORMED CONSENT FORM

Title: Obstructive sleep apnoea detection using the Sunrise solution **The SOSAT Trial**

Name of Researcher:

Dr Julia Kelly, PhD
Clinical and Academic Unit of Sleep and Breathing
Royal Brompton Hospital, London, SW3 6NP

	Please initial box
1. I confirm that I have read and understand the information sheet dated _____ (Version ____) for the above study and have had the opportunity to consider the information, ask questions and have 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 medical care or legal rights being affected.	☐
3. I understand that relevant sections of any of my medical notes and data collected during the study may be looked at by responsible individuals from Guys' and St Thomas' NHS Foundation Trust or from regulatory authorities where it is relevant to my taking part in research. I give permission to these individuals to have access to my records.	☐
4. I agree with the publication of the results of this study in a medical journal (all data will be published anonymously).	☐
5. I understand that my sleep study results will be analysed anonymously, by researchers outside my local hospital, potentially including Belgium. Sunrise sleep study data will be stored anonymously in cloud storage in the EU. I also understand that after the end of the study sleep study results will be stored and may be used, anonymously, in future ethically approved research.	☐
6. I agree to my contact details (name, address) being passed securely to the Central Research Team at the Royal Brompton Hospital	☐



Royal Brompton
and Harefield



7. Optional: I agree to my contact details (name, telephone number) being passed to the Central Research Team at the Royal Brompton Hospital in order to contact me regarding potential participation in an individual interview. This will require separate consent.	☐
8. I agree to take part in the above study.	☐

Royal Brompton Hospital is part of Guy's and St Thomas' NHS Foundation Trust

Name of Patient

Date

Signature

Name of person taking consent

Date

Signature

When completed 1 for patient; 1 for researcher; 1 (original) to be kept with hospital notes

Appendix 2.2 Patient instructions for the randomised controlled study

Royal Brompton
and Harefield



The SOSAT Trial: Patient Instructions

Thank you for participating in the SOSAT trial. You are helping us to investigate a new sleep study technology, the Sunrise™ Solution. We are comparing the **Sunrise™ Solution** to our standard clinical **Polygraphy device** for the investigation of patients for obstructive sleep apnoea.

The Sunrise™ Solution



Polygraphy - ApneaLink Air



What do I do now?

You will need to wear both sleep study devices together for one night while you sleep. We ask you to follow your typical routine before going to sleep, so you do not have to make any adjustment to your nightly routine or sleep schedule.

Please read the following instructions carefully before starting your sleep study. Please **DO NOT** turn on the devices until your bedtime.

- **Using the Sunrise™ Solution device:**

You will receive a new single-use device in a package with a quick guide on how to set up and use the device

During the day:

- You will need to download a smartphone application and create an account – this will take approximately 5–10 minutes. You will also be asked to answer a number of questions on the app about your normal sleep. You will identify yourself only by your trial identification number eg: SOSAT-01. Please **DO NOT** use your own personal details. If prompted for an email address or phone number, please **DO NOT** use your own
- Please **DO NOT** take the device out of the package or remove the sticker from the device until it is time start your sleep study at night.

Before bedtime:

- Scan the QR code on the instructions packet and put on the Sunrise device following the in-app instructions. Ensure you click *NEXT* through the instructions until you reach the final page where you can start the recording.
- You can start the recording when you are ready.
- Please **DO NOT** press the stop button until you have fully woken up the next morning as this will irreversibly end the recording and you will not be able to re-link the device.

SOSAT_Patient_Instructions_v1.0_27Apr2021

Pg 1

Royal Brompton and Harefield



- You will need to place your phone on standby but **DO NOT** close the app or turn the phone off. You may need to keep your phone on charge.
- Before you go to sleep, you will also need to put on the Polygraphy device (see below)
- **Using the Polygraphy - ApneaLink Air device:**
 - You will receive the device which has been set up for you to use.
 - Please follow the specific ApnoeaLink Air instructions to put the device on and get your sleep study started.
 - Please ensure that the green light is ON, confirming the start of the sleep study recording.

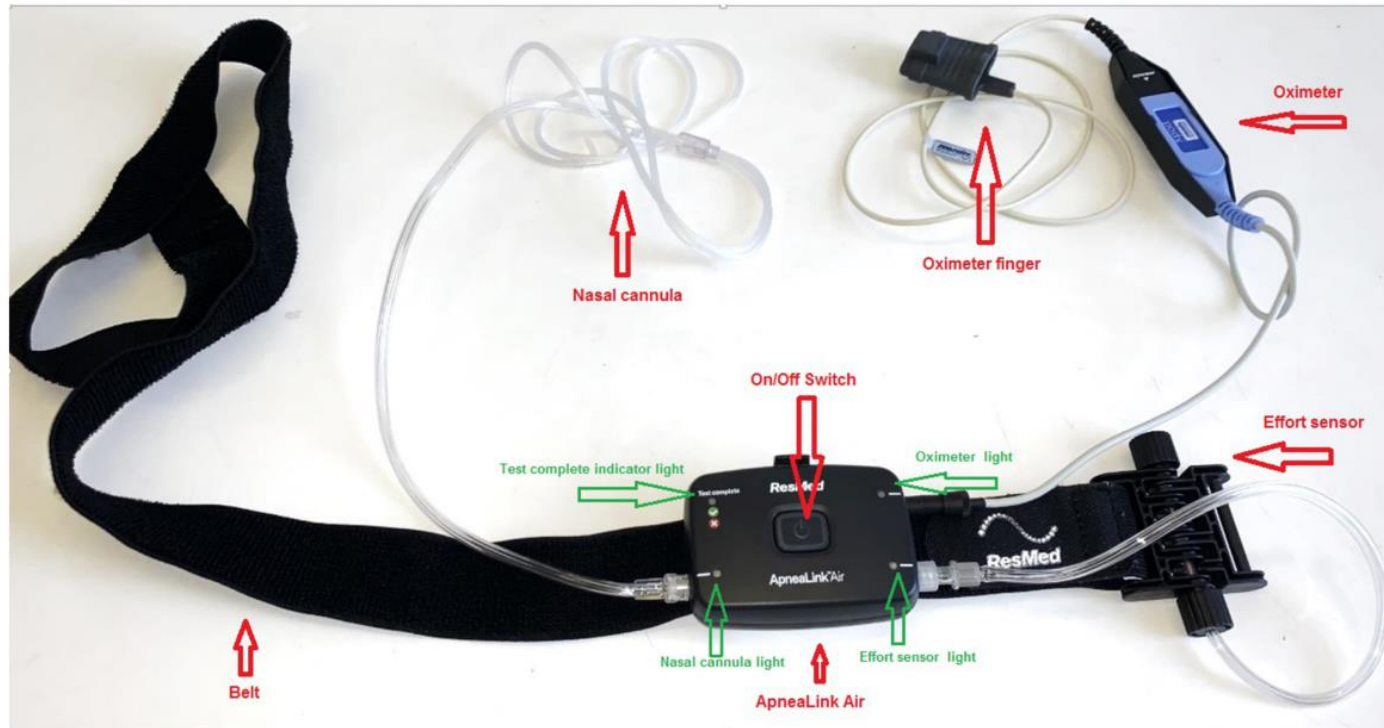
Good Night

- **In the morning:**
 - When you are fully awake, please follow the instructions to turn OFF the Sunrise™ Solution device, then the polygraphy device.
 - Complete the questionnaire to let us know about your experience with both devices.
 - Put both devices and completed questionnaires into the prepaid envelope and post them back to us.

If you have any concerns or questions, you can contact Julia Kelly on 0207 3528121 extn 84183 or juliakelly2@nhs.net.

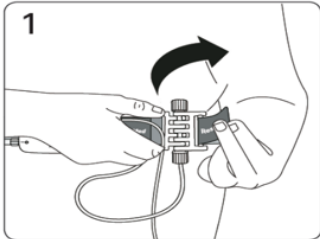
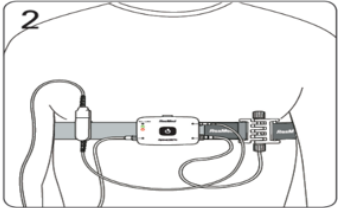
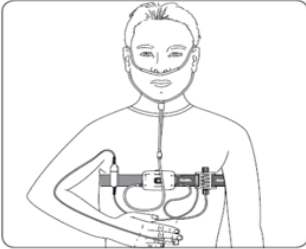
Thank you for participating in the study

Polygraphy: ApneaLink Air Sleep Test Instructions

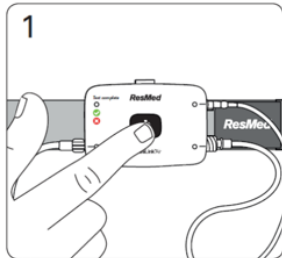
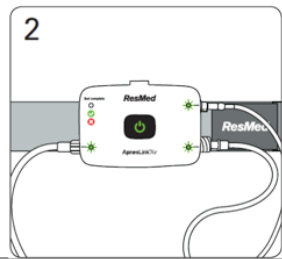


Thank you for completing this sleep test for the SOSAT Study;
Please do not forget to also wear the Sunrise™ device before you go to sleep.

Polygraphy: ApneaLink Air Sleep Test Instructions

Fitting the kit	
• The sleep test has been setup for you to use. • Pull the belt around your body. • Thread the end of the belt through the slot on the effort sensor and fasten the tab to the belt.	
• Check that the belt is secure and comfortable, firm but not tight and that the device is positioned over the centre of your chest.	
• Put the oximeter on any finger with the lead on the top of your finger • Place the nasal cannula into your nostrils, then loop over your ears and under your chin. • Pull the toggle under your chin to keep the cannula in place. • When complete, setup should look like this. • It is recommended that you place small pieces of micropore tape on your cheeks to help hold the nasal cannulae in place and on your finger to hold the oximeter on. • Please do not wear nail polish as the oximeter will not work.	

Polygraphy: ApneaLink Air Sleep Test Instructions

Starting the test	
Press and hold the power button in the centre of the device for about three seconds or until the light turns on.	
- Check that the 3 small lights (left lower, right upper and lower) are GREEN. - If any of these lights are red and blinking, the accessories are not attached correctly. - After a few minutes, all the lights might turn off so that they do not disturb your sleep	
In the morning, please press and hold the power button in the centre of the device for about 3 seconds until the lights turn off. If the sleep test has worked, the light in the top left corner will be green. If it is red this means that something went wrong, please contact juliakelly2@nhs.net; you may be able to repeat the test the next night (the batteries should last for 2 nights).	

Specific instructions for patients participating in a clinical study

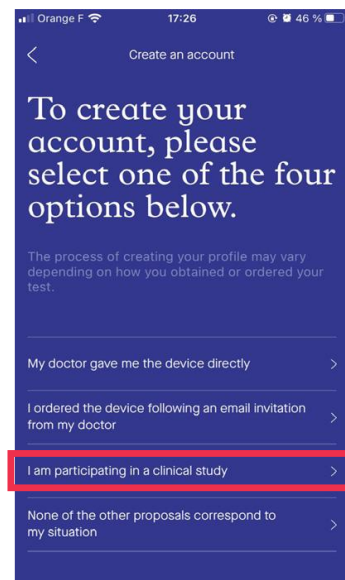


A step-by-step instructional video is available by scanning the QR code or via the URL <http://onboarding-video-en.hellosunrise.com>. This video will guide you step by step through the correct use of the Sunrise device.

01. To create your account, please select the option «I am participating in a clinical study».

02. Next, please enter the email address and password provided by the research team.
Do not enter your name or personal email address.

The results of your test will automatically be uploaded to the server and an email will be sent to the research team notifying them that you have completed your sleep test and that your results are available.



What to do in a case of trouble?

If there is a problem with the device, don't do your sleep test. The next morning, please contact the research team who will assist you in resolving the issue.

sun*rise

Ref : instructions patients clinical trials_V02

Appendix 2.3 Patient questionnaire for the randomised controlled study

Royal Brompton
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NHS

Guy's and St Thomas'
NHS Foundation Trust

Patient ID:

The SOSAT Trial

QUESTIONNAIRE

To be completed after the sleep test

Please could you answer the following questions:

1. DATE OF BIRTH:

2. SEX:

Male

Female

Prefer not to say

3. WEIGHT:

kg

4. HEIGHT:

cm

The following information will not be used to identify you. It will help us to understand the differences in access to healthcare across various parts of the UK.

5. UK POSTCODE

Please enter only the first half of your postcode

6. Approximate distance from your house to your sleep service:

Km

7. How long does it take you to travel to your sleep service?

Min

Royal Brompton
and Harefield

NHS
Guy's and St Thomas'
NHS Foundation Trust

Patient ID:

Please reflect on your overall impression of the Sunrise Device.

Sunrise™ Device



Please answer the following questions by making a vertical mark at a point on the horizontal line.

Q8. How easy was it to set up the device?

Very Easy

Very Difficult

Q9. How comfortable did you find the device to sleep with?

Very uncomfortable

Very comfortable

SOSAT_Patient_Questionnaire_v2.0_24May2021

2

Royal Brompton
and Harefield

NHS
Guy's and St Thomas'
NHS Foundation Trust

Patient ID:

Please reflect on your overall impression of the Polygraphy Device.

Polygraphy - ApneaLink Air Device



Please answer the following questions by making a vertical mark at a point on the horizontal line.

Q10. How easy was it to set up the device?

Very Easy

Very Difficult

Q11. How comfortable did you find the device to sleep with?

Very uncomfortable

Very comfortable

SOSAT_Patient_Questionnaire_v2.0_24May2021

3

Royal Brompton
and Harefield

NHS
Guy's and St Thomas'
NHS Foundation Trust

Patient ID:

Please answer the following questions by ticking one box only.

Q12. Which device did you prefer using?

☐

Sunrise™ Device

☐

Polygraphy - ApneaLink Air Device



Q13. In which setting would you prefer having your sleep study?

☐

In Hospital

☐

At Home

Q14. How would you prefer to receive the sleep study device?

☐

I prefer to pick up the device from the hospital and receive face-to-face instruction

☐

I prefer to have the device posted to my house with written instruction and over the phone assistance, if required

Q15. Is there anything else you would like to tell us?

Appendix 2.4 Raw data of the randomised controlled study

Table A.2.4.1 Raw data for the baseline characteristics of the participants in the randomised controlled study

Participant ID	Recruiting site	Randomised to	Age (Years)	Gender	BMI (kg/m ²)	Neck Circumference (cm)	ESS (0-24)	ISI (0-28)
SOSAT-01	London (RBH)	Sunrise	47	Male	32.7	43	23	20
SOSAT-02	Scotland	Polygraphy	49	Female	39.3	42	12	18
SOSAT-03	Scotland	Sunrise	38	Male	40.9	48	15	21
SOSAT-04	Scotland	Polygraphy	58	Female	35.4	37	14	22
SOSAT-05	Scotland	Sunrise	38	Male	37	42	10	15
SOSAT-06	Scotland	Sunrise	27	Female	55.2	38.3	19	24
SOSAT-07	Scotland	Polygraphy	35	Male	29.6	42	19	26
SOSAT-08	Scotland	Sunrise	54	Male	39.2	46	19	20
SOSAT-09	Scotland	Sunrise	29	Male	36.2	48	11	24
SOSAT-10	London (RBH)	Sunrise	44	Female	37.3	38	13	12
SOSAT-11	Scotland	Polygraphy	31	Male	48.9	46.5	18	18
SOSAT-12	London (RBH)	Polygraphy	62	Female	34.1	42	14	15
SOSAT-13	London (RBH)	Sunrise	58	Female	27.6	37	9	14
SOSAT-14	London (RBH)	Polygraphy	37	Female	31.1	37	18	10
SOSAT-15	Scotland	Sunrise	53	Male	33	NA	12	NA
SOSAT-16	Scotland	Sunrise	36	Male	38.1	50	16	12
SOSAT-17	Scotland	Polygraphy	39	Female	55.9	41	16	26
SOSAT-18	Scotland	Sunrise	46	Male	43.2	43	16	26
SOSAT-19	Scotland	Polygraphy	34	Male	47.8	49	14	16
SOSAT-20	Scotland	Sunrise	31	Male	26.9	44	18	26

SOSAT-21	London (RBH)	Sunrise	68	Male	43	NA	13	NA
SOSAT-22	Scotland	Polygraphy	55	Male	37.3	45	9	15
SOSAT-23	London (GSTT)	Polygraphy	44	Female	45.5	41	19	23
SOSAT-24	London (RBH)	Sunrise	58	Male	25.4	41	11	28
SOSAT-25	London (GSTT)	Sunrise	27	Male	30.4	47	14	26
SOSAT-26	Scotland	Polygraphy	39	Male	35.1	51	9	17
SOSAT-27	London (RBH)	Polygraphy	48	Male	37.2	46	5	5
SOSAT-28	London (GSTT)	Sunrise	49	Male	25.6	42	13	19
SOSAT-29	London (GSTT)	Polygraphy	35	Male	30.7	44	12	17
SOSAT-30	Scotland	Sunrise	42	Female	44.1	47	9	23
SOSAT-31	Scotland	Polygraphy	66	Male	33.5	47	21	23
SOSAT-32	London (RBH)	Polygraphy	46	Male	34.4	48.5	15	21
SOSAT-33	London (RBH)	Polygraphy	52	Male	38.5	44	20	21
SOSAT-34	Scotland	Polygraphy	62	Male	28	NA	14	NA
SOSAT-35	London (GSTT)	Polygraphy	35	Male	42	50.8	17	20
SOSAT-36	London (RBH)	Sunrise	63	Female	31.3	39	14	19
SOSAT-37	London (RBH)	Polygraphy	85	Female	48.6	36	21	24
SOSAT-38	London (GSTT)	Polygraphy	43	Male	31	47	13	10
SOSAT-39	London (RBH)	Sunrise	62	Male	30.2	44	22	26
SOSAT-40	London (GSTT)	Sunrise	48	Male	38.2	49	20	20

SOSAT: Sunrise OSA Trial; RBH: Royal Brompton Hospital; GSTT: Guy's and St Thomas' Hospital; BMI: body mass index; ESS: Epworth Sleepiness Scale; ISI: Insomnia Severity Index

Table A.2.4.2 Raw data for time to treatment decisions, MM-estimated AHI and respiratory polygraphy AHI values, and the MDT clinical decisions to treat

Participant ID	Recruiting site	Randomised to	Sleep kit posted to patient on	Sunrise-estimated AHI	Respiratory polygraphy AHI	MDT clinical decision based on	Date of MDT clinical decision	Same MDT clinical decision
SOSAT-01	London (RBH)	Sunrise	29/09/2021	10.8	12.9	Sunrise	06/10/2021	Yes
SOSAT-02	Scotland	Polygraphy	23/11/2021	26.9	13.9	Polygraphy	08/12/2021	Yes
SOSAT-03	Scotland	Sunrise	01/12/2021	49.3	23.3	Sunrise	15/12/2021	Yes
SOSAT-04	Scotland	Polygraphy	09/12/2021	27.5	73	Polygraphy	05/01/2022	Yes
SOSAT-05	Scotland	Sunrise	14/12/2021	7.7	4.3	Sunrise	26/01/2022	Yes
SOSAT-06	Scotland	Sunrise	05/01/2022	5.4	2.4	Sunrise	12/01/2022	Yes
SOSAT-07	Scotland	Polygraphy	25/01/2022	34.7	16.4	Polygraphy	09/02/2022	Yes
SOSAT-08	Scotland	Sunrise	10/02/2022	19.2	14.8	Sunrise	16/02/2022	Yes
SOSAT-09	Scotland	Sunrise	10/02/2022	37.3	66.2	Sunrise	16/02/2022	Yes
SOSAT-10	London (RBH)	Sunrise	17/02/2022	25.8	32	Sunrise	16/03/2022	Yes
SOSAT-11	Scotland	Polygraphy	22/02/2022	34.7	37.8	Polygraphy	02/03/2022	Yes
SOSAT-12	London (RBH)	Polygraphy	20/02/2023	F	10.4	Polygraphy	08/03/2023	NA
SOSAT-13	London (RBH)	Sunrise	23/03/2022	11.2	12.5	Sunrise	30/03/2022	Yes
SOSAT-14	London (RBH)	Polygraphy	13/04/2022	9.4	8.6	Polygraphy	27/04/2022	Yes
SOSAT-15	Scotland	Sunrise	13/04/2022	F	F	NA	NA	NA
SOSAT-16	Scotland	Sunrise	19/05/2022	62.5	82.2	Sunrise	15/06/2022	Yes
SOSAT-17	Scotland	Polygraphy	19/05/2022	11.0	1	Polygraphy	01/06/2022	No
SOSAT-18	Scotland	Sunrise	06/06/2022	31.2	5.7	Sunrise	22/06/2022	No
SOSAT-19	Scotland	Polygraphy	08/08/2022	54.3	34.9	Polygraphy	14/09/2022	Yes

SOSAT-20	Scotland	Sunrise	09/08/2022	31.3	34	Sunrise	17/08/2022	Yes
SOSAT-21	London (RBH)	Sunrise	25/08/2022	F	F	NA	NA	NA
SOSAT-22	Scotland	Polygraphy	16/09/2022	47.9	21.8	Polygraphy	05/10/2022	Yes
SOSAT-23	London (GSTT)	Polygraphy	16/09/2022	5.6	F	Sunrise*	12/10/2022	NA
SOSAT-24	London (RBH)	Sunrise	30/09/2022	13.3 ^(F)	4.9	Sunrise	26/10/2022	No
SOSAT-25	London (GSTT)	Sunrise	12/10/2022	41.5	52.9	Sunrise	26/10/2022	Yes
SOSAT-26	Scotland	Polygraphy	13/10/2022	22.6	21.6	Polygraphy	02/11/2022	Yes
SOSAT-27	London (RBH)	Polygraphy	02/11/2022	36.8	6.9	Polygraphy	01/02/2023	Yes
SOSAT-28	London (GSTT)	Sunrise	01/11/2022	25.7	F	Sunrise	16/11/2022	NA
SOSAT-29	London (GSTT)	Polygraphy	01/11/2022	7.1	12.4 ^(F)	Polygraphy	28/12/2022	Yes
SOSAT-30	Scotland	Sunrise	01/11/2022	50.7	17	Sunrise	09/11/2022	Yes
SOSAT-31	Scotland	Polygraphy	10/11/2022	63.1	72.3	Polygraphy	23/11/2022	Yes
SOSAT-32	London (RBH)	Polygraphy	15/11/2022	9.3	9.9	Polygraphy	07/12/2022	Yes
SOSAT-33	London (RBH)	Polygraphy	10/11/2022	84.9	80.3	Polygraphy	23/11/2022	Yes
SOSAT-34	Scotland	Polygraphy	23/11/2022	F	14.1	Polygraphy	14/12/2022	NA
SOSAT-35	London (GSTT)	Polygraphy	14/12/2022	48.8	97.9 ^(F)	Polygraphy	01/02/2023	Yes
SOSAT-36	London (RBH)	Sunrise	19/01/2023	17.1	10.6	Sunrise	25/01/2023	Yes
SOSAT-37	London (RBH)	Polygraphy	14/12/2022	18.9	4.1	Polygraphy	18/01/2023	Yes
SOSAT-38	London (GSTT)	Polygraphy	22/12/2022	F	F	NA	NA	NA
SOSAT-39	London (RBH)	Sunrise	12/01/2023	17.7	7.3	Sunrise	25/01/2023	Yes
SOSAT-40	London (GSTT)	Sunrise	19/01/2023	60.6	46.5	Sunrise	08/02/2023	Yes

SOSAT: Sunrise OSA Trial; RBH: Royal Brompton Hospital; GSTT: Guy's and St Thomas' Hospital; AHI: apnoea-hypopnoea index; MDT: multi-disciplinary team; F: Failed.
^(F) failed first sleep study—result from a repeat study. * Patient did not repeat a failed sleep study and the MDT clinical decision was based on alternative device.

Appendix 3.1 Regulatory documents for the nested qualitative study

3.1.1 Ethical approval letters



Wales Research Ethics Committee 4
Cardiff

Mailing address:
Health and Care Research Wales
Castlebridge 4
15-19 Cowbridge Road East
Cardiff, CF11 9AB

Email: Wales.REC3@wales.nhs.uk
Website: www.hra.nhs.uk

08 April 2022

Dr Julia L Kelly
Academic Unit of Sleep and Breathing
National Heart and Lung Institute
Royal Brompton Campus, London
SW3 6NP

Dear Dr Kelly

Study title: A prospective, multicentre, randomised, blinded study of obstructive sleep apnoea detection using the Sunrise solution: The Sunrise OSA Trial (SOSAT)
REC reference: 21/WA/0162
Protocol number: N/A
Amendment number: Amendment 1
Amendment date: 22 March 2022
IRAS project ID: 296444

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Completed Amendment Tool [296444_Amendment 1]	Amendment 1	22 March 2022
Interview schedules or topic guides for participants [SOSAT_Interview_Topic_Guide_Clean]	V1.0	22 March 2022
Participant consent form [SOSAT_Main ICF_Clean]	V4.0	22 March 2022
Participant consent form [SOSAT_Main ICF_Track Changes]	V4.0	22 March 2022
Participant consent form [296444 21WA0162AM01 SOSAT Interviews ICF V1.0 22Mar2022 Clean.doc]	1	22 March 2022
Participant information sheet (PIS) [SOSAT_Main PIS_Clean]	V3.0	22 March 2022

Participant information sheet (PIS) [SOSAT_Main PIS_Track Changes]	V3.0	22 March 2022
Participant information sheet (PIS) [296444 21WA0162AM01 SOSAT Interviews PIS V2.0 6April2022 TC.doc]	2	06 April 2022
Research protocol or project proposal [SOSAT_Protocol_Clean]	V3.0	22 March 2022
Research protocol or project proposal [SOSAT_Protocol_Track Changes]	V3.0	22 March 2022

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

Working with NHS Care Organisations

Sponsors should ensure that they notify the R&D office for the relevant NHS care organisation of this amendment in line with the terms detailed in the categorisation email issued by the lead nation for the study.

Amendments related to COVID-19

We will update your research summary for the above study on the research summaries section of our website. During this public health emergency, it is vital that everyone can promptly identify all relevant research related to COVID-19 that is taking place globally. If you have not already done so, please register your study on a public registry as soon as possible and provide the HRA with the registration detail, which will be posted alongside other information relating to your project.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at: <https://www.hra.nhs.uk/planning-and-improving-research/learning/>

IRAS Project ID - 296444:	Please quote this number on all correspondence
----------------------------------	---



PP: Miss Megan Jones
Dr Kath Clarke
Chair

E-mail: Wales.REC3@wales.nhs.uk

Enclosures: *List of names and professions of members who took part in the review*

Copy to: *Mr. Sulaiman S. Alsaif*

TEMP006 Version 5 May 2021

NHS Highland

R&D Ref No: **H1754**
 REC Ref No: **21/WA/0162**
 NRS Ref No: **NRS21/296444**
 EudraCT Ref No: **NA**
 MHRA Ref No: **NA**
 Today's Date: **18/04/2022**

Frances Hines
 Research, Development & Innovation Manager
 NHS Highland Research, Development &
 Innovation Department
 Centre for Health Science
 Old Perth Road
 Inverness
 IV2 3JH

Tel: 01463 255912
 E-mail: frances.hines@nhs.scot
 www.nhshighland.scot.nhs.uk



Dr Beth Sage
 Respiratory Consultant
 Raigmore Hospital
 Old Perth Road
 Inverness IV2 3JH
 By email: beth.sage@nhs.scot

Dear Dr Sage,

LETTER OF APPROVAL OF YOUR RESEARCH STUDY AMENDMENT

STUDY TITLE: A prospective, multicentre, randomised, blinded study of obstructive sleep apnoea detection using the Sunrise solution: The Sunrise OSA Trial (SOSAT)

REC: 21/WA/0162
NHS Highland R&D Ref Number: H1754

Amendment Type:	Substantial (SA)	✓
	Modified SA	
	Non-substantial (NSA)	
Amendment No:	AM01	
Amendment Date:	22/03/22	
Current Protocol Version No:	V3.0 dated 22/03/22	



Headquarters: Assynt House, Beechwood Park, INVERNESS IV2 3BW

Chair: Professor Boyd Robertson
 Chief Executive: Pam Dudek

TEMP006 Version 5 May 2021



We have been notified of the above amendment to your research project and have received the following documents:

- Notification of Substantial Amendment.
- Amended documents corresponding with those approved in the REC amendment approval letter (Wales Research Ethics Committee 4 Cardiff) dated 08/04/22.

The **RD&I Division**, NHS Highland, is happy to **approve** this amendment as it is within the scope of the original Management Approval Letter (02/11/21).

Yours sincerely,



Frances Hines
NHS Highland Research, Development & Innovation Manager

cc Sulaiman Alsaif, PhD Student, Academic Unit of Sleep and Breathing, National Heart and Lung Institute, Royal Brompton Campus, London
By email: s.alsaif18@imperial.ac.uk

Wendy Douglas, Sleep Nurse Specialist, Raigmore Hospital, NHS Highland
By email: wendy.douglas2@nhs.scot

Dr Julia Kelly, Chief Investigator/Academic Supervisor, Guys' and St Thomas' NHS Foundation Trust & Academic Unit of Sleep and Breathing, National Heart and Lung Institute, Royal Brompton Hospital, London
By email: j.kelly@rbht.nhs.uk

3.1.2 Participant information sheet



Royal Brompton
and Harefield



IRAS ID: 296444

Participant Information Sheet (PIS) For SOSAT Individual Interview

Part 1

Parent Study Title: Obstructive sleep apnoea detection using the Sunrise device

The Sunrise Obstructive Sleep Apnoea Trial (SOSAT)

Invitation to participate in a sub-study of SOSAT:

You are invited to take part in an **individual interview** as part of the Sunrise OSA Trial (SOSAT) study. Before you decide whether to participate in the interview, it is important to understand why the research is being done and what it will involve. Please read the following information carefully and discuss it with whoever you choose: friends; relatives and/or your doctor. Please ask if you want us to clarify anything or if you would like more information. ***We will go through the information sheet with you and answer any questions you have.***

Part 1 of the PIS tells you the purpose of this study and what will happen to you if you take part.

Part 2 gives you more detailed information about the conduct of the study.

Please ask us if there is anything that is not clear. Take time to decide whether or not you wish to take part.



What is the purpose of the individual interview?

The parent SOSAT study aims to find out whether a new technology, using the Sunrise device, is useful for patients undergoing investigation for sleep apnoea. We want to compare several outcomes including how long it takes for you to get a treatment decision and whether the treatment decision was the same using the results of both devices (Sunrise device and polygraphy). We also want to know about your experience using both devices. ***For further details, please refer back the participant information sheet that you were given when you were asked to participate in the parent study.***

The purpose of the **individual interview** is to further understand your experience during the investigation for your sleep apnoea. It will be an opportunity for you to share and discuss your experiences using the devices, your preferences, and your views on how your care could be improved.

Why have I been invited?

You have been invited because you have previously participated in the SOSAT study, and you gave us consent to contact you. We would now like to ask you to consider participating in an interview which will allow us to further explore your perspectives. If you give us your permission, you will be invited for a one-to-one remote interview with one of our researchers.

Do I have to take part?

No. Participation in the interview is optional and it is entirely up to you whether you would like to take part or not. If you do wish to take part, you will be asked to sign a consent form. You are free to withdraw from the study at any time without a reason and this will not affect the care you subsequently receive.

What will happen to me if I take part?

As the first step, we will make sure that you understand the study, and ask you to provide an informed consent.

Once we have received your consent, your contact information, including your email address and phone number will be held by the research team. This is so that we can provide you with the information on the set-up and scheduling of the interview. Your contact information will be treated confidentially and will not be shared with anyone else.

The remote interview should last no longer than 40 minutes and will be conducted *via* a secure online platform such as Microsoft Teams. The discussion will be audio recorded to allow for full transcription and data analyses at a later stage by the researchers. Once the transcription is complete, the recordings will be processed according to Guys' and St Thomas' NHS Foundation Trust data policy. Your data will be anonymised, and you will not be identified in any direct quotations used in any report/publication.

**What topics will be asked during the interview?**

Some or all the following topics will be covered during the individual interview:

- Your views and expectations of the sleep apnoea diagnostic pathway
- Your experiences and views of the sleep apnoea testing devices used in the study
- Your overall experience and your views on improving the patient experience of sleep apnoea care

At the end of the interview, your participation in the study is complete. You will continue your routine clinical care at your local centre, where you will receive ongoing management by your local team.

Expenses and payments

No expenses or payments will be available for participating in the individual interviews.

What do I have to do?

You will take part in a remote individual interview lasting no more than **40 minutes**, which is an optional part of the SOSAT study. We will ask you to sign an informed consent before taking part. The interview will take place at a date and time that is suitable for you and the researcher.

What are the possible disadvantages and risks of taking part?

There are no anticipated disadvantages or risks from taking part in this sub-study.

What are the side-effects of any treatment received when taking part?

There is no treatment given as part of this study.

What are the possible benefits of taking part?

We are interested in any benefits that you might report about using the sleep testing devices, and whether either device is easier or preferable compared to the other. Your experiences and views will contribute to improve our understanding of sleep apnoea care from a patient perspective and may also inform sleep apnoea care improvements.

What happens when the research study stops?

During and after the completion of the study, you will continue your routine clinical care. Your ongoing care will be provided by your local sleep service.

What if there is a problem?



Any complaint about the way you have been dealt with or any possible harm you might suffer will be addressed. The detailed information on this is given in part 2

Will my taking part in the study be kept confidential?

Yes, we will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

This completes Part 1. If the information in Part 1 has interested you and you are considering participation, please read the additional information in part 2 before making any decision.



Part 2

What if relevant new information becomes available?

Sometimes we get new information. If this happens your research doctor will tell you and discuss whether you should continue in the study. Because this is not a treatment study, this is an unlikely scenario.

What will happen if I don't want to carry on with this study?

Your participation is voluntary, and you may change your mind at any time. If you do decide to take part, you are free to withdraw at any time during the study without providing a reason and this will not affect your clinical care in any way. If you withdraw, we will continue to use all data collected up to your withdrawal if you consent for us to do so.

What if there is a problem?

Complaints:

If you have a concern about any aspect of this study you should ask to speak with the researchers who will do their best to answer your questions juliakelly2@nhs.net. If you remain unhappy and wish to complain formally, you can do this.

- Royal Brompton Hospital patients, please contact the hospital Patient Advice and Liaison Service (PALS): pals@rbht.nhs.uk
- NHS Highlands patients, please contact the hospital Patient Advice Support Service (PASS)

Inverness Badenoch and Strathspey Citizens Advice Bureau
29-31 Union Street
Inverness IV1 1QA
01463 237664
enquiries@invernesscab.casonline.org.uk

Harm:

In the event that something goes wrong, and you are harmed during the research and this is due to someone's negligence then you may have grounds for legal action for compensation against the study Sponsor, Guys' and St Thomas' NHS Foundation Trust, but you may have to pay your legal costs.

The normal NHS complaints mechanism will still be available to you.



Will my taking part in the study be kept confidential?

The records obtained while you are in this study will remain strictly confidential at all times. Personal information, including name, phone number, email and address will only be shared with the central research team who will contact you to obtain an informed consent, and agree a time and date for the individual interview. This team will be employees or researchers of the Royal Brompton Hospital. All other study documentation will be coded only with your unique study ID number and will contain no personal identifiers. Additionally, all data (recordings/transcripts) from the individual interview will be treated in accordance with Good Clinical Practice and Guys' and St Thomas' NHS Foundation Trust data policy.

To ensure your confidentiality, the interview will be conducted in a room where no one else is present, using a Royal Brompton Hospital trust computer. We will follow standard ethical and legal practice and all information about you will be handled in confidence. Our procedures for handling, processing, storage and destruction of their data match the General Data Protection Regulations (GDPR). Your identifiable data will only be accessed by authorised persons such as researchers, sponsors, regulatory authorities and R&D audit (for monitoring of the quality of the research). Published results will not contain any names of study participants.

How will we use information about you?

This study is sponsored by the Royal Brompton Hospital, Guys' and St Thomas' NHS Foundation Trust. We will need to use information from you and from your medical records for this research project. This information will include your initials/ name/ contact details. People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead. We will keep all information about you safe and secure.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

What are your choices about how your information is used?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.

Where can you find out more about how your information is used?

You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/

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- our leaflet available from <https://www.rbht.nhs.uk/patients-visitors/patients/patient-support-services/your-personal-information>
- by asking one of the research team

You can also email the trust Data Protection Officer: ig@rbht.nhs.uk , who can listen to your concerns or give you advice about your rights in respect to the data we hold about you.

What will happen to any samples I give?

This study does not collect any samples.

Will any genetic tests be done?

No

What will happen to the results of the research study?

We intend to publish the results in peer-reviewed publications. Your anonymised data, including any direct quotations, may also be included as part of an Imperial College PhD thesis. You will not be identified in any report/publication. We also intend to use this pilot data to apply for a larger trial in the UK.

Who is organising and funding the research?

This study is not receiving any external funding. The Sunrise devices have been donated by Sunrise SA (Belgium).

Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee (REC), to protect your interests. This study has been reviewed and given favourable opinion by the Wales Research Ethics Committee (REC) in June 2021 (REC reference: 21/WA/0162).

Further Information and Contact Details

For further information about the study, please contact Dr Julia Kelly:
juliakelly2@nhs.net Ph: 0207 3528121 ext 84183

3.1.3 Informed consent form



IRAS ID: 296444

Royal Brompton
and Harefield



Patient Identification Number for this trial: _____

INFORMED CONSENT FORM FOR INDIVIDUAL PARTICIPANT INTERVIEW

Title: Obstructive sleep apnoea detection using the Sunrise solution **The SOSAT Trial**

Chief Investigator:

Dr Julia Kelly, PhD
Clinical and Academic Unit of Sleep and Breathing
Royal Brompton Hospital, London, SW3 6NP

	Please initial box
1. I confirm that I have read and understand the information sheet dated _____ (Version ____) for the above study and have had the opportunity to consider the information, ask questions and have these answered satisfactorily.	☐
2. I understand that my participation in an individual interview is voluntary and that I am free to withdraw at any time, without giving any reason, without medical care or legal rights being affected.	☐
3. I understand that relevant sections of any of my medical notes and data collected during the study may be looked at by responsible individuals from Guys' and St Thomas' NHS Foundation Trust or from regulatory authorities where it is relevant to my taking part in research. I give permission to these individuals to have access to my records.	☐
4. I understand that in taking part in an individual interview I agree for my participation to be audio recorded to allow for transcription and analysis of data.	☐
5. I understand that in taking part in this trial I agree for my anonymised data, including any direct quotations to be used in reports(s) and/or publication(s). I also understand that after the end of the trial data will be stored and may be used, anonymously, in future ethically approved research.	☐
6. I understand that all my information will be treated confidentially and in any report on the results of this research my identity will remain anonymous.	☐
7. I agree to take part in an individual interview.	☐



Royal Brompton
and Harefield



Name of Patient

Date

Signature

Name of person taking consent

Date

Signature

When completed 1 for patient; 1 for researcher; 1 (original) to be kept with hospital notes

Appendix 4.1 Systematic review protocol in the International Prospective Register of Systematic Reviews (PROSPERO)

**Imperial College
London**

A systematic review of virtual compared to in-person consultations for the management of Continuous Positive Airway Pressure therapy in patients with Obstructive Sleep Apnoea/Hypopnea Syndrome

Review Protocol

Citation

Sulaiman S Alsaif, Phyllis Murphie, Julia Kelly. A systematic review of virtual compared to in-person consultations for the management of Continuous Positive Airway Pressure therapy in patients with Obstructive Sleep Apnoea/Hypopnea Syndrome. PROSPERO 2022 CRD42022297532 Available from: https://www.crd.york.ac.uk/prospERO/display_record.php?ID=CRD42022297532

Review question

This systematic review aims to systemically evaluate the published and unpublished literature on the utilisation of virtual consultations, with or without real-time telemonitoring, for Continuous Positive Airway Pressure (CPAP) therapy management compared to in-person consultations for patients with Obstructive Sleep Apnoea/Hypopnea Syndrome (OSAHS).

The overarching question for this review:

What is the effectiveness of virtual consultations compared to in-person consultations for the management of Continuous Positive Airway Pressure (CPAP) therapy in adult patients with Obstructive Sleep Apnoea/Hypopnea Syndrome (OSAHS)?

Additional question:

Is virtual consultation non-inferior to in-person consultation for the management of Continuous Positive Airway Pressure (CPAP) therapy, including sleepiness and cost-effectiveness, in adult patients with Obstructive Sleep Apnoea/Hypopnea Syndrome (OSAHS)?

Searches

MEDLINE, EMBASE, Scopus, Cochrane Library (Central), CINAHL, and medRxiv will be searched from their inception to December 2021. Text words and indexed terms related to "Obstructive sleep apnoea/hypopnea syndrome" and "Virtual consultation" will be searched. A detailed search strategy will be provided at a later stage. The search will be limited to full articles. Two researchers (SA and PM) will independently screen potential studies for eligibility in this systematic review. In the event of a disagreement between the researchers, a third team member (JK) and/or the wider team will be brought into the discussion until an agreement is achieved. The reference lists of all included studies will be manually reviewed to identify any other relevant studies. Authors of the included studies may be contacted if we needed to request any relevant missing data.

Types of study to be included

This systematic review will include published and unpublished randomised controlled trials (RCTs), quasi-randomised controlled trials (quasi-RCTs), and controlled clinical trials (CCTs)— for which a full report is available.

Condition or domain being studied

Obstructive sleep apnoea/hypopnea syndrome (OSAHS) is one of the most common respiratory disorders, and its prevalence has been rising due to increasing rates of obesity and ageing society. This chronic condition is associated with serious health and economic consequences. However, despite the availability of a clinical and cost-effective treatment (Continuous Positive Airway Pressure), adherence to therapy is generally low. The recently published NICE guidelines recommend a consultation within 1 month of CPAP initiation, and subsequent follow-ups based on patients' needs until optimal symptom control is achieved. Meeting the increasing demand on respiratory sleep services is challenging, highlighting the need for appropriate and cost-effective strategies to effectively manage patients with OSAHS using CPAP. One of these strategies is the utilisation of telemedicine approaches, including virtual consultations, which has recently become mainstream in many sleep services due to the COVID-19 pandemic. This shift in practice to increased utilisation of virtual consultations must be evidence-based. This systematic review will evaluate the use of virtual consultations for the management of CPAP and its effectiveness on clinical and patient-

reported outcomes.

Participants/population

The inclusion criteria for this review will be studies of adult patients, with a clinical diagnosis of Obstructive Sleep Apnoea/Hypopnea Syndrome (OSAHS), both naïve and established users of Continuous Positive Airway Pressure (CPAP). Trials will be included whether the diagnosis of OSAHS was made using in-laboratory or in-home sleep testing.

Intervention(s), exposure(s)

The intervention will be virtual consultations that take place between a patient and a healthcare provider. This can be either synchronous or asynchronous communication made via telephone or videoconferencing, with or without real-time telemonitoring of CPAP use. No limitations will be imposed regarding the number of consultations, methods of initiation, or duration of visits. We will exclude trials that used automated remote interventions, without input by a healthcare professional.

Comparator(s)/control

A non-exposed control group will act as the comparator in this review. These patients will have been allocated to a clinical in-person consultation with or without real-time telemonitoring data of CPAP use.

Main outcome(s)

The primary outcomes will include a patient-reported outcome measure and an organisational outcome; 1) the change in Epworth sleepiness scale (ESS) 2) the cost-effectiveness of the intervention. The ESS is a widely used self-reported sleep propensity scale, which can be utilised to assess the effectiveness of OSAHS treatment. The cost-effectiveness of the intervention can be measured by the mean total costs of the intervention compared to in-person, or other outcomes of healthcare cost-effectiveness e.g. healthcare utilisation and analyses based on quality-adjusted life-years (QALYs).

Measures of effect

The above outcomes will be extracted in means ($\pm$ SD) or percentages/proportions based on the type of variable i.e continuous or categorical. Results of any meta-analysis will be presented as mean difference (95% CI). A meta-analysis will be performed only if the participants, interventions, comparisons, and outcomes in the trials are deemed to be sufficiently similar.

Additional outcome(s)

The additional outcomes that will be explored in this review will include clinical, patient and/or clinician-reported, and environmental impact outcomes.

Clinical outcomes:

- Change in quality of life (disease-specific or general scales: FOSQ, SAQLI, SF-36)
- Change in apnoea-hypopnoea index (AHI)

Process outcomes:

- Average of CPAP usage (minutes/hours) – Intermediate outcome
- Proportion of adherence to therapy (%) at (>3 and >4 hr/night)
- Not attending an allocated consultation / Uncontactable patients

Patient and/or clinician-reported outcomes:

- Change in sleep quality
- Satisfaction and acceptability of virtual consultations

- Treatment side effects
- Number of patient-initiated follow-up appointments
- Number of healthcare contacts
- Total time saved

Environmental impact outcomes:

- Travel distances from home to the clinic
- Reduced travel
- Mode of transport
- Carbon-footprint emissions

Trials that do not report either of the primary and/or any of the secondary outcome measures will be excluded from this review.

Measures of effect

The above outcomes will be extracted in means ($\pm$ SD) or percentages/proportions based on the type of variable i.e continuous or categorical. Results of any meta-analysis will be presented as mean difference (95% CI). A meta-analysis will be performed only if the participants, interventions, comparisons, and outcomes in the trials are deemed to be sufficiently similar.

Data extraction (selection and coding)

Study selection:

Two reviewers (SA and PM) will independently perform an initial screening of search records to remove duplicates and exclude any unrelated studies. To ensure that we do not overlook potentially eligible trials we will consider any trial in which OSAHS, CPAP therapy, virtual (remote) consultations keywords are explicitly mentioned in the abstract. The full text of potentially eligible studies will be assessed against the predefined inclusion and exclusion criteria by the two independent reviewers. In the event of a disagreement between reviewers, a third team member (JK) and/or the wider team will be involved to arbitrate until an agreement is achieved

Data extraction:

A customised data extraction spreadsheet will be used, following a pilot testing to ensure that it easily and consistently captures all relevant data for the review. The following data will be extracted from included studies (if available):

- Details of study design, methodology, setting, and participants demographic data and baseline characteristics.
- Details of the intervention, including mode of delivery, characteristics of providers, duration of consultations, and study follow up duration.
- Details of the comparison
- Details of relevant findings, specifically those related to our primary and secondary outcomes.

Two reviewers (SA and PM) will independently extract trials data, with constant comparison and discussion of the findings.

Risk of bias (quality) assessment

The risk of bias of trials included in this review will be assessed independently by two reviewers (SA and PM) using the tools and guidance provided in the Cochrane Handbook for Systematic Reviews of Interventions (Cochrane, 2021). For each trial, we will assess any bias arising from the following domains: bias from randomization process and blinding, bias due to deviations from intended interventions, bias due to missing outcome data, bias in the measurement of the outcome, bias in the selection of the reported result. An overall risk-of-bias judgement will be made for each trial. This can be one of the following: 'Low', or 'Some concerns' or 'High' risk of bias. In the event of a disagreement between the reviewers, a third member from the review team (JK) and/or the wider team will be brought in to arbitrate if needed.

Strategy for data synthesis [1 change]

The review will be reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement.

A narrative synthesis of the findings from the included studies will be provided. The synthesis strategy is informed by Cochrane Data Synthesis and Analysis Guidelines 2013, and it will be structured around the type of intervention (e.g. virtual consultation), mode of delivery (e.g. videoconferencing or telephone), characteristics of study participants (OSAHS severity, and naïve or established CPAP users), and outcomes (e.g. sleepiness, adherence to therapy, and patient/clinician acceptability). We will start by systematically investigating the similarities and differences between the findings of the included studies, as well as exploring the data in the context of theoretical bases of the intervention. We will then provide a summary of the characteristics of the included studies, and assess the quality of evidence using the Cochrane Risk of Bias tool and the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach. We will also provide a summary of the intervention effects for each one of the included studies.

We anticipate that there will be a limited scope for meta-analysis because of the substantial heterogeneity across a number of existing trials. However, if we find that the included studies are deemed to be sufficiently similar in terms of participants characteristics, interventions, comparisons, and outcomes then a quantitative synthesis will be performed. I^2 statistic will be used to assess the heterogeneity of the studies; a value greater than 50% will be considered as a substantial heterogeneity. We will use a random-effects meta-analysis, with standardised mean differences, to pool the results, and to calculate 95% confidence intervals and two-sided P values for the main outcomes.

Analysis of subgroups or subsets

If sufficient data are available, subgroup analyses will be conducted to compare between studies.

Where feasible, we will make a comparison between patient groups based on the following stratification:

- Mild OSAHS (AHI $\geq$ 5, but $<$ 15 per hour)
- Moderate and severe (AHI $\geq$ 15)

Where feasible, we will also make a comparison at the following specific follow-up durations from CPAP initiation:

- Short term ($\geq$ 3 months)
- Medium term (3-12 months)
- Long term ($\geq$ 12 months)

Additionally, subgroup analyses will be conducted to compare between naïve and established CPAP users as well as between age and gender groups, rural and urban populations.

Contact details for further information

Sulaiman S Alsaif
s.alsaif18@imperial.ac.uk

Organisational affiliation of the review

Airways Disease Section | National Heart and Lung Institute | Faculty of Medicine | Imperial College London
<https://www.imperial.ac.uk/nhli/research/research-sections/airways-disease/>

Review team members and their organisational affiliations

Mr Sulaiman S Alsaif. Imperial College London
Dr Phyllis Murphie. Independent Respiratory Nurse Consultant
Dr Julia Kelly. Royal Brompton Hospital, London

Collaborators

Dr Stuart Little. NHS Dumfries and Galloway
Professor Hilary Pinnock. The University of Edinburgh
Professor Michael Polkey. Imperial College London
Professor Mary Morrell. Imperial College London

Type and method of review

Intervention, Meta-analysis, Systematic review

Anticipated or actual start date

10 December 2021

Anticipated completion date

10 April 2022

Funding sources/sponsors

The initiation of the review is a collaboration between Imperial College London, Royal Brompton Hospital, University of Edinburgh, and NHS Dumfries and Galloway. The responsibility for managing the review will reside with Imperial College London. Sulaiman Alsaif is a recipient of a full scholarship to complete his doctoral research programme; the scholarship was awarded by King Saud University, Saudi Arabia. Dr Phyllis Murphie is a co-Lead for Sleep Medicine Improvement Work Plan and is funded by Modernising Patient Pathways Programme, Scottish Government. Dr Julia Kelly holds an NIHR RfPB grant investigating treatment in positional OSA.

Conflicts of interest**Language**

English

Country

England, Scotland

Stage of review

Review Ongoing

Subject index terms status

Subject indexing assigned by CRD

Subject index terms

Continuous Positive Airway Pressure; Humans; Referral and Consultation; Respiratory Rate; Sleep Apnea, Obstructive; Syndrome

Date of registration in PROSPERO

04 January 2022

Date of first submission

10 December 2021

Stage of review at time of this submission

Preliminary searches	Yes	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

The record owner confirms that the information they have supplied for this submission is accurate and complete and they understand that deliberate provision of inaccurate information or omission of data may be construed as scientific misconduct.

The record owner confirms that they will update the status of the review when it is completed and will add publication details in due course.

Versions

04 January 2022

Appendix 4.2 Literature search strategy for the systematic review

MEDLINE (1946 to January 10, 2022)

Host: Ovid

The following search strategy was used to search MEDLINE *via* Ovid:

1. (OSAHS or OSAS or OSA).mp. [Keyword]
2. (Sleep* adj3 (apn?ea* or hypopn?ea*).mp. [Keyword]
3. (Sleep* adj3 disorder* adj3 breath*).mp. [Keyword]
4. "Sleep Apnea, Obstructive" [Subject heading]
5. "Sleep Apnea Syndromes" [Subject heading]
6. (1 OR 2 OR 3 OR 4 OR 5)
7. (CPAP OR PAP).mp. [Keyword]
8. (Positive Airway Pressure.mp.).mp. [Keyword]
9. "Continuous Positive Airway Pressure" [Subject heading]
10. (7 OR 8 OR 9)
11. (Telemonitor* or Teleconsult* or Telemedicine or Telehealth or Tele monitor* or Tele consult* or Tele medicine or Tele health).mp. [Keyword]
12. (Virtual consult* or Remote consult* or Remote review* or Video consult* or Telephone consult*).mp
13. Telemedicine [Subject heading]
14. Remote consultation [Subject heading]
15. (11 OR 12 OR 13 OR 14)
16. (6 AND 10 AND 15)

*The above search strategy was adapted to the other electronic databases, listed in **Chapter 4, Section 4.2.1.***

Appendix 4.3 Studies excluded from the systematic review

Table A4.3. Studies excluded due to including at least one in-person consultation for patients randomised to virtual consultations

	Study author and title	Reason for exclusion	Notes (excerpt from study)
1	Fox et al 2012 <i>The Impact of a Telemedicine Monitoring System on Positive Airway Pressure Adherence in Patients with Obstructive Sleep Apnea: A Randomized Controlled Trial</i>	TM group were asked to come to clinic (in-person) at 4-6 weeks and 3 months	"After 4-6 wk of therapy, patients returned to the clinic to see their regular doctor and information was reviewed (including CPAP pressure, mask leak, residual respiratory events, and compliance). Any problems with treatment were also addressed at this time. After 3 mo of treatment patients came to see their sleep specialist, who reviewed the data received via the modem. Surveys and Epworth Sleepiness Scale score (ESS) were completed (same as the standard group)."
2	Mendelson et al 2014 <i>CPAP Treatment Supported by Telemedicine Does Not Improve Blood Pressure in High Cardiovascular Risk OSA Patients: A Randomized, Controlled Trial</i>	TM group were also seen in-person at 4 weeks	"After 4 weeks of treatment, patients met with their sleep specialist and information was reviewed. After 4 months of treatment, patients consulted their sleep specialist and were re-evaluated."
3	Hoet et al 2017 <i>Telemonitoring in continuous positive airway pressure-treated patients improves delay to first intervention and early compliance: a randomized trial</i>	TM group were asked to come to clinic in case of CPAP-related issues	"Sleep laboratory technical staff were instructed to connect to the Web portal and to analyze individual patient's data each Tuesday and Friday. In case of air leaks >50 L/min, residual AHI >10/h, or CPAP use <3 h on 3 consecutive days, they were required to call the patient and to set up a visit with the staff of the sleep laboratory"
4	Schoch et al 2019 <i>Telemedicine for Continuous Positive Airway Pressure in Sleep Apnea. A Randomized, Controlled Study</i>	TM group were also seen in clinic at 1 and 6 months after CPAP initiation	"At 1 and 6 months after CPAP initiation, scheduled follow-up visits in the sleep center were arranged for both groups."
5	Kotzian et al 2019 <i>Proactive telemedicine monitoring of sleep apnea treatment improves adherence in people with stroke: a randomized controlled trial (HOPES study)</i>	TM group were also seen in-person at 3 months	"Patients were asked to return to the hospital after three months for evaluation of therapy"

6	Murase et al 2019 <i>A Randomized Controlled Trial of Telemedicine for Long-Term Sleep Apnea Continuous Positive Airway Pressure Management</i>	TM group were followed up in-person at 3 months	“TM-group patients visited the clinic at 3-month intervals. In the months without a clinic visit, the physicians checked CPAP adherence data monthly using a telemonitoring system and called patients to improve adherence only when good adherence (percentage of days with >4 h/ night of CPAP use > 70%) was not achieved.”
7	Turino et al 2021 <i>Management and treatment of patients with obstructive sleep apnea using an intelligent monitoring system based on machine learning aiming to improve continuous positive airway pressure treatment compliance: randomized controlled trial</i>	MiSAOS-platform group were also seen in-person at 3 and 6 months	“At 3 and 6 months all patients, regardless of the study arm, were visited at the sleep unit. Patients were checked about progress and compliance with therapy and any problems with their CPAP machine. During these visits we collected data on treatment compliance (number of hours/day), ESS score, OSA-related symptoms, EQ-5D, BP, and anthropometric variables”
8	Contal et al 2021 <i>One-Year Adherence to Continuous Positive Airway Pressure With Telemonitoring in Sleep Apnea Hypopnea Syndrome: A Randomized Controlled Trial</i>	TM group were also seen in-person at 3 and 12 months	“Abstract: Face-to-face consultations were scheduled at 3 and 12 months after CPAP initiation.” “all patients were scheduled for follow-up physical appointments with their pulmonologist 3 and 12 months after the beginning of CPAP therapy. CPAP usage data were collected and clinical evaluation (ESS and QD2A) was performed.”
9	Chumpangern et al 2021 <i>Efficacy of a telemonitoring system in continuous positive airway pressure therapy in Asian obstructive sleep apnea</i>	TM group were also seen in clinic at 2 and 4 weeks	“The patients were enrolled in the study for 4 weeks after randomization. Regular visits to the investigator were scheduled at 2 and 4 weeks after randomization”

OSA; obstructive sleep apnoea TM; telemedicine, CPAP; continuous positive airway pressure, ESS; Epworth Sleepiness Scale

Appendix 5.1 Regulatory documents for the anonymous, self-administered survey

5.1.1 Ethical approval letter

**Imperial College
London**

**Imperial College Research Ethics
Committee**
Imperial College London
Room 221
Medical School Building St Marys Campus
London
W2 1PG
Tel: +44 (0)207 594 1862

researchethicscommittee@imperial.ac.uk

01/02/2023

Dear Alsaif Sulaiman

Study Title: A survey of Continuous Positive Airway Pressure therapy initiation

ICREC Reference number: 6363566

The above study was approved by your Head of Department on 01/02/23 and by the Research Governance and Integrity Team (RGIT) on 01/02/23.

Under the Imperial College Research Ethics Committee process, a study that has been reviewed by the Research Governance and Integrity Team (RGIT) and Head of Division/Department, where no significant ethical issues have been identified in the protocol or ethics application, can be granted RGIT approval without requiring it to go to full committee.

Documents

The documents reviewed were:

- Application form (v0.2, 25/01/2023)
- Protocol (v1.0, 11/01/2023)
- Online Participant Information Sheet (v1.0, 11/01/2023)
- Online Consent and Qualtrics Survey (v2.0, 11/01/2023)
- Support Group Recruitment Email and Advert (v2.0, 11/01/2023)

Yours sincerely

Keith Boland
Head of Research Governance and Integrity
Imperial College London

5.1.2 Survey online invitation and participant information sheet

A survey of Continuous Positive Airway Pressure therapy initiation

Study background

We are inviting you to take part in an online (anonymous) survey about your experience of sleep apnoea.

We especially want to ask you about your experiences with Continuous Positive Airway Pressure (CPAP) therapy. Your answers will help us understand how we can improve sleep apnoea care.

The survey will take you approximately 15-30 minutes to complete.

There will be some questions about your sleep apnoea and experience of using CPAP. We will also ask you for some information about yourself.

Your answers will be anonymous and confidential.

You will be able to stop answering the survey questions at any time, and your answers will not be recorded unless you submit the survey. However, once you have submitted the survey, it will not be possible to track or locate your individual answers and therefore we will not be able to remove them.

If you are interested in taking part in this survey, please download a copy of the participant information sheet [here](#) and retain this for your records before providing your consent to start the survey.

If you have any questions or queries, please contact:

Mr Sulaiman Alsaif (PhD Research Fellow at the National Heart and Lung Institute, Faculty of Medicine, Imperial College London: s.alsaif18@imperial.ac.uk)

Consent:

By submitting my answers, I confirm I am at least 18 years of age and provide consent for the information I provide to be used by Imperial College researchers.

I understand that my participation is voluntary, my data are anonymous, and that I will not be personally identified from my responses to the survey.

Do you agree to take part in this survey?

- ☐ Yes
- ☐ No

Imperial College London

Participant Information Sheet (PIS)

Study Title: A survey of Continuous Positive Airway Pressure therapy initiation

Principal Investigator:

Mary J Morrell

Professor of Sleep Physiology (Imperial College London, London)

Co-investigators:

Sulaiman S Alsaif

PhD Research Fellow (Imperial College London, London)

Annabel Nickol

Consultant in Respiratory Medicine (Churchill Hospital, Oxford)

Joerg Steier

Professor of Respiratory and Sleep Medicine (King's College London, London)

Julia Kelly

Clinical Research Fellow (Royal Brompton Hospital, London)

- **Invitation to participate in this survey:**

You are being invited to take part in an online anonymous survey about your experience of sleep apnoea. We especially want to ask you about your experiences with Continuous Positive Airway Pressure (CPAP) therapy. Your answers will help us understand how we can improve sleep apnoea care. This information sheet explains what will happen if you agree to participate in the survey.

Imperial College London

Before you decide, it is important to understand why the survey is being done and what it will involve. Please read the following information carefully and discuss it with others if you wish.

Part 1 of the Participant Information Sheet tells you the purpose of this survey and what will happen to you if you take part.

Part 2 gives you more detailed information about the conduct of the survey.

Please ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this.

Part 1

- **What is the purpose of the survey?**

Obstructive Sleep Apnoea (OSA) is when the muscles in your throat relax during sleep which leads to narrowing or closing of your airway resulting in a drop in your oxygen level and then awakening from sleep. This can happen repetitively throughout your sleep and can lead to daytime sleepiness. There is an effective therapy for OSA called continuous positive airway pressure (CPAP).

CPAP therapy is delivered in many ways, for example in a clinic or remotely, in the United Kingdom. This project is a survey to investigate your experiences with CPAP therapy and your preference for CPAP initiation. It is part of an Imperial College PhD.

- **Why have I been invited?**

You are a member of a UK group that supports people with sleep apnoea, and you have experience using CPAP therapy. We aim to recruit at least 500 participants in this study.

- **Do I have to take part?**

It is up to you to decide whether or not to take part. If you do decide to take part you can download a copy of this information sheet to keep, and online consent. If you decide to take part you are still free to withdraw at any time prior to submitting the survey and without giving a reason.

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- **What will happen to me if I take part?**

You will be asked to complete an online anonymous survey which will take you approximately 15-30 minutes. You will be able to stop answering the survey questions at any time, and your answers will not be recorded unless you submit the survey. However, once you have submitted the survey, your participation is complete, and it will not be possible to track or locate your individual answers and therefore we will not be able to remove them.

- **What do I have to do?**

Your participation is voluntary, and your answers will be anonymous and confidential. You will need to answer questions about your experiences with sleep apnoea and using CPAP. We will also ask you for some information about yourself. Once you submit your answers to the survey, your participation is complete.

Part 2

- **What are the possible disadvantages and risks of taking part?**

There is no disadvantage or risk in taking part in this survey. However, if you feel uncomfortable answering the questions, please do withdraw from the survey at any time and reach out to your support group (The Sleep Apnoea Trust or Hope2Sleep) if needed.

- **What are the possible benefits of taking part?**

The survey may not directly help you, but the information may help improve the experiences of care for people with sleep apnoea.

- **What will happen to the results of the survey?**

The anonymised data will be published in peer-reviewed publications and included in a PhD thesis. We will also provide reports to the support groups that we work with.

- **What if something goes wrong?**

If you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should

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immediately inform the Investigator (Prof Mary J Morrell, Email: m.morrell@imperial.ac.uk).
If you are still not satisfied with the response, you may contact the Imperial College Research Governance and Integrity Team (rgitcoordinator@imperial.ac.uk).

- **Who is organising and funding the survey?**

Imperial College London is the study sponsor. The study is unfunded.

- **Who has reviewed the survey?**

This study was given approval by the Head of National Heart and Lung Institute, Faculty of Medicine, Imperial College London and the Research Governance Integrity Team at Imperial College London.

Further Information and Contact Details

For further information about the survey, please contact:

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Prof Mary J Morrell

Professor of Sleep Physiology

National Heart and Lung Institute

Imperial College London

Email: m.morrell@imperial.ac.uk

Thank you for taking part in this study!

A copy of the written information and online informed consent can be downloaded for you to keep.

Appendix 5.2 The bespoke self-administered survey



This survey is divided into 3 sections:

1. We will ask you about the care you received for your sleep apnoea
2. We will ask you about your satisfaction and preferences
3. We will ask you some information about yourself

The survey will take approximately 15-30 mins to complete

(Filtering Question): Have you been told that you have sleep apnoea by a sleep specialist in the UK?

- ☐ Yes (continue to survey)
☐ No (Thank you and end Survey)

(Filtering Question): Have you used a continuous positive airway pressure (CPAP) machine for your sleep apnoea?

- ☐ Yes (continue to survey)
☐ No (Thank you and end Survey)

Section 1.1: Your sleep apnoea care

Questions 1 to 4 will ask you about the care you received for your sleep apnoea, which is likely to be different in different areas of the UK.

1. When did your sleep doctor tell you that you had sleep apnoea?

Please provide an approximate date:

Month	Year
-------	------

2. Which of the following reasons led you to seek medical help?

Check all that apply.

- ☐ Snoring
☐ Witnessed apnoeas (stopping breathing during your sleep)
☐ Unrefreshing sleep
☐ Waking up with headaches
☐ Unexplained excessive sleepiness, tiredness or fatigue
☐ Nocturia (waking frequently from sleep to urinate)
☐ Choking during sleep
☐ Insomnia (trouble with falling or staying asleep)
☐ Memory problems
☐ Other (Please Specify)

3. Where did you have your sleep test?

- ☐ Sleep test carried out in hospital
☐ Sleep test carried out at home
☐ Other (please specify)

4. How did your sleep specialist tell you that you had sleep apnoea?

"A remote appointment is between a patient and a clinician over the telephone or using video, as opposed to face-to-face (NHS England)."

- ☐ Face-to-Face (in-person) appointment
☐ Remote appointment through a phone call
☐ Remote appointment through a video call

Section 1.2: Your sleep apnoea care

Questions 5 to 13 will ask you about your CPAP and how you use it.

5. How long after your sleep test was it until you received your (CPAP) therapy?

Please provide an approximate duration:

Weeks	Months
-------	--------

6. What other treatments did you try for your sleep apnoea?

Check all that apply.

- ☐ Lifestyle advice e.g. weight loss and sleep hygiene
☐ Positional modifier
☐ Mouth guard (Mandibular Advancement Devices)
☐ Electrical stimulation
☐ Surgery
☐ None of the above
☐ Other (please specify)

7. If you have been given training on using your CPAP therapy, how did you receive your training?
- ☐ Face-to-face (in-person): CPAP machine was **turned on** during the training
- ☐ Face-to-face (in-person): CPAP machine was **not turned on** during the training
- ☐ Remote training through a phone call
- ☐ Remote training through a video call
- ☐ I did not receive training for my CPAP
- ☐ Other (please specify)

8. How much information was given to you about sleep apnoea and CPAP use?
- ☐ Too much
- ☐ Right amount
- ☐ Not enough
- ☐ I did not need any information

9. Besides your training, what other sources of information were you given to support you with using your CPAP therapy?

Check all that apply.

- ☐ Written Information *e.g. patient leaflet or booklet*
- ☐ Online health information *e.g. link to a website or a video*
- ☐ Other (Please Specify)

10. How would you rate your current use of the CPAP therapy?
- ☐ Very Good
- ☐ Good
- ☐ Neither good nor poor
- ☐ Poor
- ☐ Very Poor

11. On average, how many hours per night do you use your CPAP therapy?

 Hours/Night

12. On average, how many nights per week do you use your CPAP therapy?

 Nights/Week

13. Over the last 12 months, how many times have you contacted your sleep clinic or CPAP provider to seek medical support?

- ☐ 0
- ☐ 1-2
- ☐ 3-4
- ☐ 5 or more

14. *Would you like to tell us more about your CPAP therapy initiation experience?*

Section 2: Your experience of your care

We are interested in how your care made you feel.

Questions 15 to 21 will ask you about your satisfaction and preferences.

15. How satisfied are you with your overall experience of the CPAP therapy set-up and training?

- ☐ Very satisfied
- ☐ Satisfied
- ☐ Neither satisfied nor unsatisfied
- ☐ Unsatisfied
- ☐ Very unsatisfied

16. How satisfied are you with how long it took to receive your CPAP therapy?

- ☐ Very satisfied
- ☐ Satisfied
- ☐ Neither satisfied nor unsatisfied
- ☐ Unsatisfied
- ☐ Very unsatisfied

17. How satisfied are you with the way your clinical care team communicated with you during your CPAP therapy set-up and training?

- ☐ Very satisfied
- ☐ Satisfied
- ☐ Neither satisfied nor unsatisfied
- ☐ Unsatisfied
- ☐ Very unsatisfied

18. How satisfied are you with the support you received from the clinical care team after your CPAP therapy set-up and training?

- ☐ Very satisfied
- ☐ Satisfied
- ☐ Neither satisfied nor unsatisfied
- ☐ Unsatisfied
- ☐ Very unsatisfied

19. Did you feel involved as much as you wanted to be in the decisions about your sleep apnoea care?

- ☐ Yes, definitely
- ☐ Yes, to some extent
- ☐ No

20. If you had to receive your care again (for the same/similar condition), how would you prefer to receive your therapy and follow-up care?

A) Therapy set-up and training

- ☐ Face-to-Face (in-person) appointment
- ☐ Remotely (online) through a phone call
- ☐ Remotely (online) through a video call
- ☐ I have no preference

B) Follow up with therapy

- ☐ Face-to-Face (in-person) appointment
- ☐ Remotely (online) through a phone call
- ☐ Remotely (online) through a video call
- ☐ I have no preference

21. *Thinking about your overall experience*, how would you improve the care for your sleep apnoea therapy and follow-up?

Section 3: Information about you

Questions 22 to 31 will ask you some information about yourself. This information will not be used to identify you.

22. In which age group are you?

- ☐ 18-29 years old
- ☐ 30-39 years old
- ☐ 40-49 years old
- ☐ 50-59 years old
- ☐ 60-69 years old
- ☐ 70-79 years old
- ☐ 80 years old and above

23. Are you?

- ☐ Male
- ☐ Female
- ☐ Prefer not to say

24. What do you consider to be your ethnic group?

Please choose the answer that best describes your ethnic group.

- ☐ Asian or Asian British
- ☐ Black or Black British or Caribbean or African
- ☐ Mixed or multiple ethnic groups
- ☐ White
- ☐ Other ethnic group

25. Do you have any of these health conditions?

- ☐ Diabetes
- ☐ High blood pressure
- ☐ Heart disease
- ☐ Obesity or overweight
- ☐ Stroke
- ☐ None of the above

26. Which of the following did your sleep specialist use to describe the severity of your sleep apnoea?

- ☐ **Mild** (5-15 AHI)
- ☐ **Moderate** (15-30 AHI)
- ☐ **Severe** (>30 AHI)
- ☐ My condition's severity was not described or discussed
- ☐ I do not remember

27. What is the highest education level you completed?

- ☐ GCSE, O level, A level or equivalent
☐ Professional qualification below degree level
☐ Degree level qualification or higher or equivalent
☐ No formal qualification
☐ Other (please specify)

28. What is your current employment status?

- ☐ Employed
☐ Retired from work
☐ Unemployed
☐ Unable to work because of a health condition
☐ Student
☐ Other (please specify)

29. Which of these best describe the area where you live?

- ☐ Urban i.e. city/large town
☐ Suburban i.e. suburbs of city/large town
☐ Rural area
☐ Other (please specify)

30. What is the first half of your postcode? (optional)

Providing the first half of your postcode will help us to explore how your experiences vary across the UK

31. Who was the main person answering the questions of this survey?

- ☐ Myself
☐ Carer/ Family member
☐ Both myself and a carer
☐ Other

End of survey

Thank you for taking the time to complete this survey. The information you have provided will be treated confidentially.

If you have any queries about the survey, please do not hesitate to contact:

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PhD Research Fellow

National Heart and Lung Institute

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Prof Mary J Morrell

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Appendix 5.3 Unadjusted logistic regression analyses of the predictors of participants' dissatisfaction with their CPAP therapy initiation experience

Table A.5.3.1 Unadjusted logistic regression analyses of the predictors of participants' dissatisfaction with their continuous positive airway pressure therapy initiation experience

	OR	95% CI	P-value ¹
Sociodemographic and clinical characteristics			
Q23. Are you?			
Male	Ref	Ref	Ref
Female	1.62	1.13 - 2.34	0.009*
Q26. Which of the following did your sleep specialist use to describe the severity of your sleep apnoea?			
Mild (5-15 AHI)			
Moderate (15-30 AHI)			
Severe (>30 AHI)			
Severity was not described or discussed			
I did not remember			
	Logistic regression analysis could not be performed		
Involvement in the decisions about their sleep apnoea care			
Q19. Did you feel involved as much as you wanted to be in the decisions about your sleep apnoea care?			
Yes, definitely	Ref	Ref	Ref
Yes, to some extent	31.12	9.28 - 193.4	<0.0001*
No	509.3	156.4 - 3132	<0.0001*
Provision of educational information about sleep apnoea and CPAP use			
Q8. How much information was given to you about sleep apnoea and CPAP use?			
Too much	29.85	1.34 - 331.1	0.006*
Right amount	Ref	Ref	Ref
Not enough	63.20	35.86 - 120.8	<0.0001*
I did not need any information	29.85	5.82 - 127.1	<0.0001*
Q9. Besides your training, what other sources of information were you given to support you with using your CPAP therapy?			
Written Information e.g. patient leaflet or booklet			
Online health information e.g. link to a website or a video			
Other			
	Logistic regression analysis could not be performed		

¹ p-value is derived from unadjusted logistic regression, with the most frequent variable set as the reference value.
 *Statistically significant at (P<0.05). OR: odds ratio of the logistic regression; 95% CI: confidence intervals of the odds ratio;
 CPAP: continuous positive airway pressure; AHI: apnoea-hypopnoea index.

Table A.5.3.2 Unadjusted logistic regression analyses of the predictors of participants' dissatisfaction with their continuous positive airway pressure therapy initiation experience

	OR	95% CI	P-value ¹
Diagnostic and treatment care pathways			
Q1. When did your sleep doctor tell you that you had sleep apnoea? (Duration in years)			
	0.93	0.90 - 0.96	<0.0001*
Time of OSA diagnosis			
Pre-Covid-19 pandemic	Ref	Ref	Ref
Post-Covid-19 pandemic	1.84	1.26 - 2.68	0.001*
Q3. Where did you have your sleep test?			
Sleep test carried out in hospital	0.69	0.45 - 1.03	0.0803
Sleep test carried out at home	Ref	Ref	Ref
Other	2.04	0.19 - 1.38	0.14
Q4. How did your sleep specialist tell you that you had sleep apnoea?			
F2F (in-person) appointment at the clinic	Ref	Ref	Ref
Remote appointment through a phone call	2.39	1.53 - 3.68	<0.0001*
Remote appointment through a video call	3.94	1.21 - 11.35	0.013*
Q5. How long after your sleep test was it until you received your (CPAP) therapy? (Duration in weeks)			
	1.00	0.99 - 1.01	0.07
Q7. If you have been given training on using your CPAP therapy, how did you receive your training?			
F2F: machine was turned on during training			
F2F: machine was not turned on during training			
Remote training through a phone or a video call			
I did not receive training for my CPAP			
Other			
Logistic regression analysis could not be performed			
Adherence to therapy and utilisation of healthcare services			
Q10. How would you rate your current use of the CPAP therapy?			
Very Good	Ref	Ref	Ref
Good	1.430	0.87 - 2.28	0.14
Neither good nor poor	4.422	2.28 - 8.26	<0.0001*
Poor	22.64	10.42 - 52.35	<0.0001*
Very Poor	27.72	11.58 - 73.81	<0.0001*
Q13. Over the last 12 months, how many times have you contacted your sleep clinic or CPAP provider to seek medical support?			
0	Ref	Ref	Ref
1-2	1.05	0.71 - 1.55	0.80
3-4	3.43	1.84 - 6.23	<0.0001*
5 or more	6.90	2.76 - 17.07	<0.0001*

¹ p-value is derived from unadjusted logistic regression, with the most frequent variable set as the reference value.
 *Statistically significant at (P<0.05). OR: odds ratio of the logistic regression; 95% CI: confidence intervals of the odds ratio;
 CPAP: continuous positive airway pressure; f2f: Face-to-Face.

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6.1.1 Permission for Figure 6.1

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