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1. Title of the project

Novel home-testing devices for diagnosing obstructive sleep apnoea/hypopnea syndrome

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3. Plain English Summary

Obstructive sleep apnoea (OSA) and hypopnoea syndrome (HS) are conditions which affect a person's breathing during sleep, causing it to briefly stop (apnoea) or become shallow (hypopnoea). Many people with OSA also experience HS (hereafter the term 'OSAHS' refers to people with either condition, or people with both). Common symptoms of OSAHS include loud snoring at night and sleepiness during the day. The latter can disrupt a person's ability to work or study, and increase their risk of injury and accidents (e.g. if sleepiness whilst driving leads to a road traffic accident). Left untreated OSAHS can increase the risk of adverse effects on health later on, including heart problems or brain injury.

If someone suspects they have OSAHS they can ask their general practitioner to refer them to a specialist hospital sleep service for further investigation. Tests to diagnose OSAHS are done overnight while the person sleeps and can be performed at home or in a hospital sleep laboratory, depending on the needs of the individual and the availability of hospital facilities. During a sleep study instruments which monitor breathing, heart rate and the amount of oxygen in the blood are attached to the person by wires, belts or nasal tubes. When the test is completed a specialist sleep technician analyses the readings taken while the person was asleep and uses a scientific scoring system to determine whether or not the person has OSAHS. They can also estimate how severe OSAHS is affecting them, for example whether mild, moderate or severe.

For sleep tests to give accurate results they must be carried out correctly. However, this can be challenging for many. For example, some people find they cannot sleep comfortably when wearing multiple attachments attached to recording devices. Consequently, they may not be asleep long enough for all the necessary recordings to be completed. The results of the test therefore may not be correct, and they have to repeat the test, creating delays in receiving appropriate treatment if diagnosed with OSAHS.

Newer portable test devices designed for use in settings such as the home have become available recently. These devices tend to be smaller in design, easier to use, and less intrusive. The attachments may be more comfortable to wear and less likely to interrupt sleep whilst overnight testing takes place. This may reduce test failure rates and the number of times the test needs to be repeated before a valid test result

is available. Another advantage of novel home-testing devices is that the manufacturers can send the device directly to the patient. This could increase the number of patients able to access tests, potentially reducing waiting lists and enabling more timely diagnosis and treatment.

It has been claimed that the accuracy of novel home-test devices for diagnosing OSAHS is at least comparable to in-hospital polysomnography (traditionally regarded as being the 'gold standard' for diagnostic accuracy). However, given the reduced use of in-hospital polysomnography during recent years, an alternative reference standard could be considered, such as respiratory polygraphy in healthcare settings. Importantly, available evidence on diagnostic accuracy, and all other outcomes, requires thorough independent examination to provide assurance of its trustworthiness.

The aim of this research is to review available research studies investigating whether novel home-testing devices for OSAHS are more effective than current home-testing (e.g. in terms of diagnostic accuracy, patient outcomes). We will compare the costs of novel home testing devices available for use in the NHS and, using health economic modelling, estimate whether the benefits to patients represents value for money for the NHS (i.e. are they clinically effective and cost-effective?).

4. Decision problem

4.1. Purpose of the decision to be made

4.1.1. Background to the condition

Obstructive sleep apnoea (OSA) and hypopnoea syndrome (HS) are conditions in which the upper airway is narrowed or closes during sleep when muscles relax, causing shallower or slower breathing than normal (hypopnoea) or stopping breathing (apnoea). The person may awaken or their sleep lighten during such episodes, but they may not necessarily be aware they have the condition. Their symptoms may include loud snoring, sleep disturbance and daytime sleepiness. Many people with OSA experience episodes of both apnoea and hypopnoea, which is referred to as OSAHS.

Approximately 25% of the UK population aged 30–69 years (men and women) have mild to severe obstructive sleep apnoea (OSA).[1] The condition is more prevalent in people with any of the following medical conditions: obesity or overweight, obesity or

overweight in pregnancy, treatment-resistant hypertension, type 2 diabetes, cardiac arrythmia (particularly atrial fibrillation), stroke or transient ischaemic attack, chronic heart failure, moderate or severe asthma, polycystic ovary syndrome, Down's syndrome, non-arteritic anterior ischaemic optic neuropathy (sudden loss of vision in 1 eye due to decreased blood flow to the optic nerve), hypothyroidism and acromegaly.[2] If left untreated, it can increase the risk of cardiovascular and cerebrovascular complications.

The prevalence OSA in children aged 2 to 18 years of age is approximately 2 to 4% and is increasing with the rise in childhood obesity. OSA is more prevalent in children with certain medical conditions including craniofacial anomalies (e.g. Down Syndrome), neurological conditions (e.g. cerebral palsy), other disorders (e.g. sickle cell disease) and a history of premature birth.[3] One of the first symptoms parents often notice in their child is snoring. The resultant sleep deprivation can lead to cognitive and behavioural issues (e.g. difficulty concentrating, hyperactivity in younger children), cardiovascular morbidity, poor growth and weight gain, decreased quality of life, and increased health care utilisation. Currently there are no UK guidelines for the diagnosis and management of paediatric OSAHS.

Signs indicative of possible OSAHS include snoring, unexplained excessive sleepiness, tiredness or fatigue, choking during sleep, sleep fragmentation and insomnia. Rating scales such as the self-administered Epworth Sleepiness Scale (ESS) and the Epworth Sleepiness Scale (ESS) for Children and Adolescents (ESS-CHAD) may be used in the preliminary assessment of OSAHS symptoms. People with suspected OSAHS may be referred from primary care to a specialist sleep service for further assessment and testing.

4.1.2. Diagnostic tests for OSAHS

Tests for diagnosing OSAHS are conducted overnight during sleep and vary in terms of the physiological parameters recorded and the equipment used. The three main test approaches in use are pulse oximetry, respiratory polygraphy and polysomnography.

- **Pulse oximetry** records blood oxygen levels and heart rate during sleep. Commonly, a small monitor called a pulse oximeter is clipped to the person's finger and records oxygen saturation in the blood and heart rate continuously during sleep. This test can be done at home or in hospital. However, when used

as the sole testing medium to diagnose OSAHS it is regarded as less sensitive than other tests.

- **Respiratory polygraphy** records oxygen levels, breathing movements, snoring and body position while a person sleeps. Straps are fastened around the person's torso and chest, an oximetry probe placed on a finger and a nasal cannula attached to a recording monitor with tubes. The test can be used at home or in hospital.
- **Polysomnography** is a type of sleep study done overnight usually in a specially equipped hospital sleep laboratory. The study comprises respiratory polygraphy combined with assessment of quality and duration of sleep quality using brain activity, eye movement, and muscle tone.

Whilst pulse oximetry and/or respiratory polygraphy results can help inform a diagnosis, in certain cases it may be necessary to confirm the results using polysomnography (specifically, hospital sleep laboratory polysomnography supervised by a qualified sleep technician), traditionally regarded as the 'gold standard' to diagnose OSA.

The data recorded by these tests can be scored manually by a sleep physiologist and/or scored electronically using computer automation (available in most test devices) to reach a diagnosis. Scoring is commonly based on the Apnoea Hypopnea Index (AHI) (which measures the number of apnoeas per hour of sleep), and/or the Oxygen Desaturation Index (ODI) (which measures the number of episodes of oxygen desaturation per hour) (3% or 4% desaturation criteria for AHI and ODI). The following criteria are used to assess severity of OSAHS on both the AHI and ODI:

- Mild OSAHS: 5 or more to less than 15 events per hour
- Moderate OSAHS: 15 or more to less than 30 events per hour
- Severe OSAHS: 30 or more events per hour.

The sleep monitors are classified in terms of types I-IV, where polysomnography is a type I device for use in a laboratory setting, and types II-IV are portable sleep monitors for home testing.

The NICE guideline on obstructive sleep apnoea/hypopnoea syndrome and obesity hypoventilation syndrome in over 16s (NG202, 2021)[2] recommends the following approaches for diagnosing OSAHS in people with suspected OSAHS:

- **Home respiratory polygraphy** as the initial testing strategy, where practical.

- If access to home respiratory polygraphy is limited, **home oximetry alone** may be used (with the caveat that this may be inaccurate for differentiating between OSAHS and other causes of hypoxaemia in people with heart failure or chronic lung diseases).
- **Hospital respiratory polygraphy** can be used when home respiratory polygraphy and home oximetry are impractical or where further respiratory polygraphy monitoring is required
- **Polysomnography** can be used if respiratory polygraphy results are negative but symptoms continue.

In addition to NICE NG202,[2] the American Academy of Sleep Medicine (AASM) Clinical Practice Guidelines on diagnostic testing for adult OSA[4] is also used by health professionals in England.

Although both the AASM and NICE guidelines recommend home respiratory polygraphy for diagnosing OSAHS (in uncomplicated cases), this approach is regarded has having limitations. The respiratory polygraphy monitors include multiple wired components attached to the person as they sleep which can be uncomfortable, potentially impeding uninterrupted sleep. If total sleep time is less than the minimum time required to complete the test (usually at least four hours) the results may be inaccurate or inconclusive. Consequently, one or more re-tests may be required, adding to costs and delaying a definitive diagnosis and commencement of treatment, if needed. If a successful home respiratory polygraphy result cannot be achieved, then an in-hospital sleep study (if available) may be required. Expert clinical advice suggests, however, a reduction in hospital testing capacity since the COVID-19 pandemic, creating greater reliance on home-testing and greater inclusiveness in determining suitability for home-testing.

Sufficient training is needed to ensure correct use of testing devices in the home, with cost implications in terms staff time to provide instruction and support to patients. Furthermore, home testing equipment must be collected from, and later returned to, the hospital before diagnosis can be confirmed. This is often the patient's responsibility and requires means of transport and their availability during clinic operating hours. Patients will therefore incur transport costs, and may even need time off work, with consequent loss of earnings for some. Transport costs will inevitably be excessive for patients whose nearest sleep clinic is some distance

away. Some clinics send equipment to patients via the postal service or by courier, accumulating substantial costs to the NHS. Experts consulted during the scoping of this assessment commented that home testing equipment is not always returned, leaving hospitals to cover the cost of replacements.

4.1.3. Novel home-testing devices for diagnosing OSAHS

Recently, a range of newer 'novel' portable devices have become available, designed using advances in technology to improve the performance, convenience, and acceptability of home testing. Novel features of devices include the use of wireless electronic sensors in place of multiple wired connections. These devices may be more comfortable to use whilst sleeping than has previously been the case. Consequently, there may be fewer sleep interruptions and an increase in the number of successfully completed tests, in turn reducing the need for repeat tests and in-hospital testing. A reduction in the number of wired attachments will make it easier for people to put on and operate the device equipment, and less resource-intensive patient training may be sufficient to ensure correct device use. The time saved may release staff capacity for other clinical priorities, potentially increasing the volume of patients a clinic can manage routinely.

Another advantage of these novel devices is that the manufacturers offer delivery services - devices can be sent directly to the patient and, where appropriate, returned to the manufacturer. This contrasts with current home testing devices, which, as described in section 4.1.2, are usually collected and returned to hospital by the patient or delivered and returned using postal or courier services paid for by the NHS. A direct delivery service could improve access to home testing thereby reducing excessive waiting times for home-testing currently seen in practice, particularly since the COVID-19 pandemic. Consequently, this would potentially reduce time to diagnosis, treatment initiation and symptom improvement. Furthermore, a delivery service managed by the manufacturer rather than the NHS would allow NHS staff to focus on other priorities.

Based on the above considerations, the following decision question has been identified for this NICE diagnostic technology assessment: Do novel home-testing devices for OSAHS represent a clinically and cost-effective use of NHS resources?

4.2. Aims and objectives

The aim of this diagnostic assessment is to assess the clinical effectiveness and cost-effectiveness of novel home-testing devices in diagnosing and assessing the severity of obstructive sleep apnoea/hypopnea syndrome (OSAHS). The results will inform NICE diagnostic assessment programme guidance of the technology for use in the NHS.

The objectives of this diagnostic assessment are:

1. To conduct a systematic review of the clinical effectiveness of novel home-testing devices for OSAHS.
2. To conduct systematic reviews to inform an economic evaluation of novel home-testing devices for OSAHS (objective 3, directly below). This will include systematic reviews of cost-effectiveness studies, health-related quality of life (utility) studies, and studies of health care resource use and costs of diagnosing and treating OSAHS.
3. To conduct an economic evaluation using decision-analytic modelling to assess the cost-effectiveness of novel home-testing devices for OSAHS.

4.3. Clear definition of the intervention

The intervention (technology) relevant to this diagnostic assessment is novel home-testing devices for diagnosing OSAHS. Novel devices have been identified as having innovative design features which, in comparison to home-testing devices currently used in the NHS, make them less intrusive, easier to put on and operate and more comfortable to wear during sleep. The following CE marked devices (manufacturer's name in parenthesis) have been identified for inclusion following stakeholder consultation:

- AcuPebble SA100 (Acurable)
- Brizzy (Nomics)
- NightOwl (ResMed)
- Sunrise (Hello Sunrise)
- WatchPAT 300 (Zoll/Itamar)
- WatchPAT ONE (Zoll/Itamar)

These devices have been selected as being novel technologies; however, they may not necessarily share the same novel features. The devices vary in terms of patient suitability (e.g. children and adults; adults only), contraindications for use,

physiological parameters measured (e.g. nasal air flow; respiratory sounds, body movement) single or multi-use, and data transmission functionality. Each device is described briefly in the following subsections.

AcuPebble SA100 (Acurable)

The AcuPebble SA100 is a multi-use device (up to 500 times) for adults only. It consists of a wireless sensor enclosed in a plastic case, which is attached to the person's neck below the Adam's apple using double sided adhesive tape. There is also an option of adding a compatible third-party oximeter. The device records sounds generated by the patient's respiratory and cardiac functions.

A wi-fi connection and a smartphone, tablet or computer with the AcuPebble SA100 app installed is needed for data to be transferred from the device to a secure cloud platform where it is automatically analysed. The company can provide the mobile devices with a pre-installed app if needed. Healthcare professionals can receive an automatically generated report within minutes through the AccuPebble SA100 web application. This report includes the presence and severity of OSA (overall score (rated normal, mild, moderate or severe) based on the Apnoea Hypopnea Index (AHI) or Oxygen Desaturation Index (ODI)). Other outputs include: classification of apnoea events, heart rate, respiratory rate, snoring evaluation, acoustic derived airflow, acoustic derived relative desaturation, and activity.

The web application displays raw data but does not allow manual scoring capability by default. However, manual scoring can be made available upon request. AcuPebble SA100 is not intended to be used for people with pacemakers or other implantable devices, or people with known or suspected arrhythmias. It is not for use in people with significant cardiopulmonary or neurological disorders, or people with a known allergy to acrylate. It may also be unsuitable for patients with sleep bruxism (unconscious grinding of teeth or clenching of jaw during sleep). The company offers a service that posts the device directly to the patient and allows the patient to return the device to the company in the same way after use. Hospitals can also choose to manage delivery and receipt of device if preferred.

Brizzy (Nomics)

The Brizzy is a CE-marked class IIa device and is indicated for use in the screening and diagnostic evaluation of sleep breathing disorders in children and young people

(over 3 years old) and adult patients. The intended use is as a portable sleep recorder for detecting sleep apnoea syndrome and for monitoring its treatment. The technology can be used at home and in sleep clinics.

The Brizzy consists of a recording device hub to which electromagnetic sensors are connected. The sensors are fixed on the chin and forehead and measure jaw activity signal (referred to as “Jawac” by the company): mandibular movement, mouth opening, and nervous gnathic twitch. A pulse oximeter or an electrocardiogram (ECG) with 3 electrodes are optional add-ons. The central device hub is attached to a fastening belt and is worn around the waist during sleep. The company advise having at least 4 hours of recording.

It is currently unclear how the device will be distributed between the user and sleep clinic. Once the device is returned, a physiologist uploads the study to the web portal (CERES software) using a wired USB connection to produce an automated report which can aid in the diagnosis of sleep breathing disorders or be used for further clinical investigation. Raw data from the recorded study can be accessed and manually scored by healthcare professionals if needed.

The Brizzy device measures an output called the ‘respiratory events index JAWAC’ (REI_JAWAC). Other outputs measured by the device are total sleep time (TST), sleep fragmentation, respiratory effort, number and frequency of apnoea events (broken down by type: obstructive, central, or mixed), positional analysis (total sleep time in supine versus non-supine position, REI-JAWAC in supine versus non-supine position), and mandibular activity. If using an add on oximeter or an ECG, the device can also measure heart rate, oxygen saturation (SpO2), ODI, and an ECG graph. The device provides an automated qualitative output of OSAHS severity based on the REI_JAWAC measure using the criteria described earlier in section 4.1.2.

The device has a lithium polymer battery (rechargeable by USB), and the storage capacity and battery life allow for recording several nights if used without oximetry or ECG. The company states that there are no known contraindications, and the technology can be used during pregnancy. However, caution is advised when used by people with restless leg syndrome as the number of apnoea events can be overestimated in this group. Parkinson’s disease and temporomandibular disorders could impact jaw movements and test results should therefore be interpreted

accordingly. The central hub and JAWAC sensors are reusable, made of recyclable Acrylonitrile Butadiene Styrene plastic. The fastening belt may be machine-washed and reused.

NightOwl (ResMed)

NightOwl is suitable for adults and children aged 13 years or over. The company have indicated that the NightOwl device to be commercialised in the UK has a built-in battery that allows for 10 nights of recording. The device is not rechargeable, and after use, it is to be discarded, ideally by any existing recycling programme for electronic waste.

NightOwl consists of a photoplethysmography (PPG) sensor and an accelerometer and is attached to the fingertip or forehead using adhesive. The device measures peripheral arterial tone (PAT), oxygen saturation, actigraphy (body movement), and pulse rate. A probabilistic model determines a respiratory event from the co-occurrence of oxygen desaturation, vasoconstriction manifested as a PAT channel decrease, and a pulse rate increase.

A 3G or 4G smartphone with the NightOwl Companion app installed is needed for data to be automatically uploaded to the analytics platform once the test is concluded. An automated report provides presence and severity of OSA (AHI and AHI severity category). Other outputs include pulse rate, oxygen saturation (SpO_2), ODI, sleep/wake states (TST), presence or absence of a substantial changes in PAT that may be caused by the presence of irregular heart rhythms, information on the location of desaturations and signal artifacts. The raw data can be accessed on the analytics platform and manually scored, if needed. Performance of the device can be adversely impacted if a person has changes in their sympathetic response or has reduced blood flow to the fingers e.g., due to use of drugs that affect the autonomic system (for example, alpha-adrenergic antagonists) or because they have peripheral vascular disease (for example, secondary Raynaud's disease). The device should not be used on patients with known severe ventricular extrasystole (VES) as this is likely to lead to insufficient clean data segments and therefore a failed test. The company offers a service to send the device directly to the patient, though sleep centres can manage delivery if they prefer. In addition, healthcare professionals can specifically request a patient to pick up the device in person, although this is not the preferred method.

Sunrise (Hello Sunrise)

The Sunrise device is a single-use device for adults and children aged at 3 years and above. It consists of wireless sensor that is placed on the chin. The device measures mandibular movements to estimate interruptions and breathing during sleep. An internet connection (wi-fi or 3G/4G) and a smartphone is needed for data to be transferred from the device to a secure cloud platform where it is automatically analysed. An automated report provides OSA severity scoring (non-OSA, mild, moderate, or severe) based on AHI and/or obstructive respiratory disturbance index (ORDI). Other outputs include sleep/wake states (TST), sleep stages, respiratory events (AHI, respiratory disturbance index (RDI), obstructive AHI (OAHI), central AHI (cAHI), obstructive respiratory disturbance index (ORDI), respiratory effort related arousals (RERA) index, respiratory effort), awakenings and arousal index, SpO_2, heart rate, position changes index and sleep bruxism (extent of teeth grinding during sleep). Raw data can be accessed through an online web portal and manually scored, if needed.

The company offers a service to send the device directly to the patient. Alternatively, sleep services can manage delivery or have the patient pick up the device during their consultation appointment. Sunrise provides a prepaid and self-addressed envelope to return the device for disposal in accordance with the European Union's Waste Electrical and Electronic Equipment (WEEE) directive. The device cannot be used for people with conditions affecting the rotation of the condyle (part of the jawbone) in temporo-mandibular joint. The manufacturer advises against using the device in patients with implantable devices e.g. pacemakers.

WatchPAT 300 (Zoll/Itamar)

WatchPAT 300 (WP300) is a multi-use device with some single use components. It is suitable for adults and children aged 12 and above and consists of a wrist worn device, finger probe and chest sensor. It measures a proprietary peripheral arterial tone signal (PAT), heart rate, oximetry, actigraphy (body movement), body position, snoring and chest motion. Snoring and body position safety and effectiveness are validated for an adult population only. After the sleep test, if the device belongs to the NHS trust, it needs to be returned to clinical setting where staff download the data via USB connection and analyse the results using the zzzPAT software. Otherwise, the WatchPAT Direct service provides delivery services directly from and return to the manufacturer, who sends the results to the sleep service.

An automated report provides diagnosis and severity of OSA (no apnoea, mild, moderate or severe apnoea) based on AHI and OHI. Additional outputs include: AHI, cAHI, RDI, ODI, sleep/wake states, sleep stages, body position, snoring, heart rate, chest movement, SpO_2 and actigraphy. The manufacturer states that the WP300 is not indicated for use in people with injuries, deformities or abnormalities that may prevent proper application of the device and should not be used in people on medication including alpha blockers or short acting nitrates (taken less than 3 hours before the study), or for people with a pacemaker, or people with sustained non-sinus cardiac arrythmias. Additional precautions are stated for people aged 12 to 17 years of age, including patients with severe comorbidities such as Down syndrome, neuromuscular disease, underlying lung disease or obesity hypoventilation to be considered for laboratory polysomnograph (PSG) rather than a home sleep testing.

WatchPAT ONE (Zoll/Itamar)

WatchPAT ONE is a single-use version of WatchPAT 300. Unlike WatchPAT 300, an internet connection (wi-fi or 3G/4G) and a smartphone is needed for data to be transferred from the device to a webserver and analysed in an offline procedure using zzzPAT software. Raw data can be accessed and manually scored if needed. The company state they are in the process of setting up a free-of charge recycling service for the device.

4.4. Populations and relevant subgroups

The relevant population for this assessment is people presenting with signs and symptoms suggestive of OSAHS, considered suitable for home-testing. Common presenting symptoms include snoring, unexplained excessive daytime sleepiness, tiredness or fatigue, and choking during sleep. Adults (for the purposes of this assessment defined as 16 years or older) and children/young people (aged 16 and under) as both groups can be affected by OSAHS. It should be noted that none of the named devices included for assessment are indicated for use in children under 2 years of age.

Consideration will be given for evidence, where available, on certain sub-populations with suspected OSAHS of note, including people with neuromuscular disorders, people who have chronic obstructive pulmonary disease (suspected COPD–OSAHS overlap syndrome), people from black, Asian and minority ethnic backgrounds,

pregnant women and pregnant people, and children and young people (between 2-16 years old) with or without comorbidities (see section 5.1).

4.5. Place of the intervention in the treatment pathway(s)

If recommended for use in the NHS it is likely that novel home-testing devices would be used by people with suspected OSAHS who have been assessed by a sleep service as being suitable for at-home respiratory polygraphy. The results of novel home-test devices can be used to inform a diagnosis of OSAHS alongside standard clinical assessment of symptoms and signs, and in certain cases in addition to results of such as respiratory polygraphy done in a healthcare setting or hospital polysomnography (where available).

It is envisaged that, if recommended for use, novel home-testing devices would replace existing home-testing devices as the standard of care.

4.6. Relevant comparators

In people aged 16 years and above, a relevant comparator to novel home testing devices is home respiratory polygraphy (using existing home-based devices), as recommended by NICE guideline NG202.[3] Oximetry is an alternative comparator because it is used where access to respiratory polygraphy is limited. However, for people with suspected COPD–OSAHS overlap syndrome, oximetry alone is not recommended in practice.

For children and young people aged between 2 to 16 years a relevant comparator to novel home testing devices is home respiratory polygraphy (using existing home-based devices), or home oximetry. Additionally, CO_2 monitoring may be used alongside these technologies if required.

4.7. Key factors to be addressed (e.g. clinical and cost outcomes, further considerations, problematic factors)

Definitions of respiratory polygraphy vary in practice, specifically in terms of the number and type of parameters measured. In this diagnostic assessment both the intervention and the comparator can be classified as home respiratory polygraphy. A distinguishing factor is that some parameters measured by novel home-testing devices are surrogates of parameters measured in respiratory polygraphy. The use of surrogate parameters may reflect innovation in the design of a home testing

device, hence its status as a novel technology. For example, a novel device which uses a wireless chest sensor to measure respiratory movement as a surrogate for respiratory flow, a parameter measured by some respiratory polygraphy devices in current practice by wearing a chest belt or band.

4.8. Areas of agreement at the scoping workshop that are outside the scope of the appraisal and therefore do not require any detailed assessment (e.g. key factors for which evidence is already accepted).

This diagnostic assessment will only consider people with suspected OSAHS, and will not include people with other sleep disorders (e.g. central sleep apnoea).

5. Report methods for assessing the outcomes arising from the use of the interventions

The following sub-sections specify the scope (inclusion criteria) and methods for the systematic review of clinical effectiveness.

5.1. Population

People with suspected OSAHS*, who are considered suitable for at-home testing.

*This can include people with suspected:

- OSA or HS
- OSA and HS

The population is stratified by the following age groups:

- People over 16 years old
- Children and young people between 2 and 16 years of age (NB. some technologies included for assessment are not indicated for use in children or young people. None of the technologies are indicated for children aged under 2 years).

Where data permits, the following subgroups will be considered:

- People with COPD
- People who have neuromuscular disorders
- People from black, Asian and minority ethnic backgrounds

- For children and young people aged 2 to 16 years, with and without comorbidities (as defined in the BTS's guidelines for the diagnosis of sleep disordered breathing in paediatrics)
- Pregnant women and pregnant people

5.2. Interventions

The following technologies are eligible for inclusion:

- AcuPebble SA100 (Acurable)
- Brizzy (Nomics)
- NightOwl (ResMed)
- Sunrise (Hello Sunrise)
- WatchPAT 300 (Zoll/Itamar)
- WatchPAT 300 (Zoll/Itamar)

Where appropriate we will consider evidence for earlier, comparable versions of the devices. For children and young people (2-16 years), use of the interventions may be alongside CO_2 monitoring.

5.3. Comparators

For people over 16: Home respiratory polygraphy or home oximetry (can include home test devices currently used in clinical practice but cannot include any of the named novel devices in 5.2 above). For people with COPD, home oximetry alone is not recommended and will therefore not be considered a suitable comparator for this subgroup.

For children and young people aged 2 to 16 years: Home respiratory polygraphy or home oximetry. CO_2 monitoring maybe used alongside these technologies.

Home respiratory polygraphy or home oximetry can include home test devices currently used in clinical practice but cannot include any of the named novel devices in 5.2 above.

The reference standard can include in-hospital polysomnography, polysomnography done outside hospital or respiratory polygraphy done in a healthcare setting (rather than at home).

5.4. Outcomes

The following outcome measures will be included where data are available from primary studies relevant to the systematic review:

5.4.1. Intermediate outcomes

Intermediate outcomes include:

- Measures of performance to detect OSAHS and assess severity
- Measures of concordance or agreement between intervention technologies, or between intervention technologies and comparators
- Impact on clinical decision-making
- Time to interpret device outputs and reach a diagnosis
- Time to diagnosis or starting treatment
- Number of repeat studies done(at home or in hospital)
- Use of healthcare resources (such as number and length of hospital admissions, use of pharmacological and non-pharmacological interventions for management of OSAHS)
- Test failure rate (including incidences where data recorded can't be analysed or a person doesn't sleep long enough to generate enough data for assessment)

5.4.2. Clinical outcomes

Clinical outcomes include:

- Morbidity
- Mortality

5.4.3. Patient reported outcomes

Patient- and carer-reported outcomes include:

- Health-related quality of life
- Ease of use and acceptability for patients and carers
- Patient and carer experience

5.5. Study design

The systematic review clinical effectiveness will not limit inclusion by type of study design, because a range of study designs could potentially be used to assess the clinical effectiveness of novel home testing devices.

If both trial-based and observational evidence is available for any of the comparisons relevant to this review, priority will be given to analysis of the trial-based evidence.

5.6. Search strategy

A search strategy will be developed, tested and refined by an experienced information specialist. The strategy will be comprehensive in order to identify all available relevant studies. The MEDLINE search strategy is provided in Appendix 1 for illustration.

The main sources of evidence to be searched will be:

- Electronic research databases and resources
- Bibliographies of included studies

The electronic resources that will be searched are:

- General health and biomedical databases
    - MEDLINE-ALL including Epub Ahead of Print, In-Process & Other Non-Indexed Citations (via Ovid)
    - Embase (via Ovid)
    - Cochrane Database of Systematic Reviews (CDSR) and the CENTRAL register of controlled trials (via The Cochrane Library, Wiley)
    - Science Citation Index Expanded (SCI-EXPANDED) and the Conference Proceedings Citation Index – Science (CPCI-S) (via Web of Science)
    - International HTA Database (database.inahta.org)
    - Database of Abstracts of Reviews of Effects (DARE) (via the Centre for Reviews and Dissemination website)
    - NHS Economic Evaluations Database (NHS EED) (via the Centre for Reviews and Dissemination website)
    - EconLit (Ebsco)
    - Epistemonikos (epistemonikos.org)
- Grey literature and research in progress
    - OpenGrey
    - PROSPERO register of systematic reviews
    - ClinicalTrials.gov
    - Cochrane CENTRAL, as above
    - BePartOfResearch (formerly the UK Clinical Trials Gateway)

- NIHR Clinical Research Network Portfolio

All databases will be searched from database inception to the present date. Searches will be limited to publications reported in the English language. Any relevant systematic reviews identified will be used as a source of potentially relevant primary studies, and the reference lists of included studies will be searched.

Any relevant studies published as abstracts or conference proceedings will be included only if published in the last three years and only if sufficient details are presented to allow appraisal of the methodology and the assessment of results to be undertaken. Handsearching of relevant sleep and respiratory medicine conferences will not be performed because abstracts from relevant sleep disorders conferences are published in journals that are indexed in at least one of the electronic databases listed above to be searched.

5.7. Study selection and data extraction strategies

Studies will be selected for inclusion using a two-stage screening process. Firstly, the titles and abstracts of bibliographic records retrieved using the above search strategy will be assessed independently by two reviewers against the predefined and explicit inclusion criteria described above. Secondly, the full texts of any potentially relevant records will be obtained and then screened against the inclusion criteria by one reviewer and checked by a second reviewer, before a final decision regarding inclusion is agreed.

Relevant data will be extracted from each included study on its design and methodology, the characteristics of the population, intervention, comparator(s) and outcome measures. Data extraction and critical appraisal will be undertaken by one reviewer using a pre-designed and piloted data extraction form. The extracted data will be checked by a second reviewer. Separate references that refer to the same primary study will be assessed together to avoid double counting of data.

Any disagreements between reviewers during study selection or data extraction will be resolved by discussion, with the involvement of a third reviewer where necessary.

5.8. Critical appraisal strategy

The methodological quality, relevance and risk of bias of the included diagnostic test accuracy studies will be assessed using the QUADAS-2 tool.[5] Additionally, any studies which compare one or more diagnostic tests will be assessed using the QUADAS-C tool.[6] Other types of study (e.g. those reporting intermediate and/or clinical outcomes) will be assessed using standard criteria appropriate to specific study designs e.g. the Cochrane Risk of Bias tool for randomised controlled trials (RCTs) (version 2).[7] Each included study will be critically appraised by one reviewer, and checked by a second reviewer. Any disagreements between reviewers will be resolved through discussion and, if necessary, involvement of a third reviewer.

5.9. Methods of analysis/synthesis

Details of the included studies will be summarised through a structured narrative synthesis, with numerical and statistical data presented in tables and figures/graphs as appropriate. We will assess the appropriateness and feasibility of meta-analysis based on factors including the availability of necessary study data and the degree of clinical and statistical heterogeneity across the included studies. We will consult with specialist health care experts for advice. Based on our scoping work it appears there is variability between the novel home testing devices in their key characteristics. Thus, it may be inappropriate to combine such diverse interventions in a meta-analysis.

If meta-analysis is feasible and appropriate we will use standard statistical methods as recommended by methodological guidelines in evidence synthesis, including the Cochrane Handbook.[8] For test accuracy, we will use methods such as hierarchical bivariate meta-analysis to generate pooled estimates of diagnostic sensitivity and specificity. Statistical software will be used to run the analyses, such as Stata and its specialist plug-in packages for diagnostic meta-analyses. For clinical outcomes we will meta-analyse intervention effects using statistical tests and effect measures appropriate to the type of outcome data (e.g. binary or continuous data). Sensitivity analyses will be performed to test the robustness of results to changes in assumptions such as random effects and fixed effect models. Randomised and non-randomised studies, where available, will be meta-analysed separately, as recommended by methodological guidance.

6. Report methods for synthesising evidence of cost effectiveness

6.1. Systematic review of cost-effectiveness studies

A systematic review will be conducted to identify, critically appraise, and summarise the results of cost-effectiveness studies relevant to the decision problem. The main purpose of this review will be to inform development of our economic model through consideration of alternative model structures, assumptions, and data sources. We will also summarise cost-effectiveness findings that may be applicable to the scope and UK context and which may provide a basis for cross-validation of our model results.

The search for published economic evaluations will be based on the search strategy used for the systematic review of clinical effectiveness (section 5.6 above), with the addition of published filters to identify economic evaluations, estimates of resource use and costs, and health-related quality of life (utility). Targeted searches will also be conducted to identify relevant cost-effectiveness studies reported by health technology assessment bodies (including NICE). Studies that meet the population and intervention/comparator inclusion criteria and report outcomes relevant to the economic evaluation (including resource use and costs, health-related quality of life, life-years and QALYs) will be identified for screening by two health economists.

The cost-effectiveness review will only include ‘full economic evaluations’ that assess both the costs and consequences of novel home testing devices for OSAHS compared to more widely used home-based technologies using a suitable intermediate or final outcome measure (e.g. cases detected, life years and/or QALYs), specifically cost-effectiveness analyses, cost-utility analyses, cost-benefit analyses and cost-consequence analyses. Studies that only report resource use or costs (including comparative cost studies as well as non-comparative budget impact analyses) will be excluded, but considered separately as possible sources of evidence for resource use and cost parameters in our model. Similarly, reports of health-related quality of life assessments with suitable instruments (such as the EQ-5D), will be considered as a source of evidence for utility inputs to our model.

The methods and parameter sources of the included cost-effectiveness studies will be summarised in tables. The relevance and credibility of the included cost-effectiveness studies and their relevance to current UK practice will be assessed using a pre-defined checklist, similar to that in Appendix 2 Relevance and credibility

checklist for full economic evaluationsCost-effectiveness results will be summarised in a table and discussed in a narrative review. Any results that provide a suitable basis for cross-validation with our model will be identified.

6.2. Development of a health economic model

6.2.1. Approach to economic analysis

A decision analytic model will be developed to assess the relative cost-effectiveness of diagnostic strategies using novel, less intrusive, home testing devices compared to more widely used home testing technologies.

The model will be designed to address the decision question specified in the NICE scope and discussed earlier in this protocol (section 4.1). It is anticipated that, as a starting point, we will use the economic model developed to inform the recent NICE guideline on obstructive sleep apnoea/ hypopnoea syndrome and obesity hypoventilation syndrome in over 16s (NG202, 2021).[2] This model was developed in consultation with the committee convened for those specific guidelines.
Where evidence allows, we anticipate adapting the model to estimate the cost-effectiveness of novel, less intrusive, devices compared to more widely used technologies for the diagnosis of OSAHS in adults and children. Due to expected differences in the clinical pathway between adults and children, we anticipate developing one model for adults and one model for children.

The model will also be designed to produce stratified cost-effectiveness results for the patient subgroups as specified in the NICE scope, if data allows.

Analysis will follow the NICE reference case, as specified in Table 4.1 in Section 4 of the NICE process and methods manual for health technology evaluations.[9] Methods for model development and standards of reporting as recommended in the literature will be followed. In particular, the ISPOR (Professional Society for Health Economics and Outcomes Research) Modeling Good Practice reports[10] and CHEERS (Consolidated Health Economic Evaluation Reporting Standards). [11]

6.2.2. Model population and subgroups

The modelled population will be adults and children suspected of having OSAHS considered suitable for home diagnostic testing. Where data are available, we plan to explore subgroups as listed earlier in section 5.1.

6.2.3. Modelled diagnostic strategies

For devices where relevant data are available, the model will be designed to evaluate the diagnostic strategies incorporating the intervention and comparator devices outlined below.

Table 1 Diagnostic tests to be modelled

Population	Interventions	Comparators
Adults (>16 years)	AcuPebble SA100 Brizzy NightOwl Sunrise system WatchPAT ONE WatchPAT 300	Home respiratory polygraphy or, if is limited, home oximetry* *should there be evidence available to model the COPD subgroup, the comparator will not be home oximetry alone
Children (≤16 years)	Sunrise system (≥3 years) Brizzy (>3 years) NightOwl (≥13 years) WatchPAT ONE (≥12 years) WatchPAT 300 (≥12 years)	Home respiratory polygraphy or home oximetry. CO_2 monitoring may be used alongside these technologies

6.2.4. Modelled outcomes

The model will need to reflect evidence on key outcomes associated with the diagnostic technology, as listed in the NICE scope. For each modelled diagnostic strategy this will include:

- Number and severity of diagnoses of OSAHS
- Number of cardiovascular events and road traffic accidents (for adult population)
- Life-years and quality-adjusted life-years (QALYs)
- Costs of the testing devices, any further diagnostic tests and management of OSAHS
- Costs associated with cardiovascular events and road traffic accidents (for the adult population)

The incremental costs and incremental QALYs for each modelled diagnostic strategy using novel, less intrusive, devices compared to strategies incorporating more widely

used technologies will be estimated and reported using the incremental cost-effectiveness ratio and net benefit. If appropriate, a fully incremental comparison of all modelled diagnostic strategies will be undertaken.

6.2.5. Model structure and assumptions

As described above, we intend to develop two models: one for adults and one for children and young people. The expected model structure for the adult population is given below followed by a section describing the likely amendments needed to the adult model to be able to evaluate the novel devices in children, should data allow.

6.2.5.1. Adult population (>16 years old)

It is anticipated that we will follow the general model structure of that used to inform NICE guideline NG202,[2] to capture both the short-term costs and consequences associated with the devices as well as potential longer-term costs and consequences in the adult population. The NG202 model took a linked-evidence approach, consisting of a decision tree followed by a Markov model.

Decision tree

The NG202 model consists of a decision tree capturing short-term diagnosis and treatment decisions. The model distinguishes between individuals who truly have OSAHS (as defined by AHI score ≥ 5) and those who do not have OSAHS (AHI score <5), with further differentiation of those having OSAHS based on severity: mild, moderate and severe. Depending on estimates of sensitivity and specificity for the diagnostic strategies evaluated, individuals are then classified into true positives (correctly identified by the diagnostic as having OSAHS), true negatives (correctly identified by diagnostic as not having OSAHS), false positives (incorrectly identified by the diagnostic as having OSAHS), and false negatives (incorrectly identified by the diagnostic as not having OSAHS).

These classifications are further distinguished by the severity of the true OSAHS condition, as well as the severity result produced by the diagnostic test. For instance, an individual with mild OSAHS may be misdiagnosed as having moderate or severe OSAHS; while an individual with moderate or severe OSAHS may be misdiagnosed as having mild OSAHS. The severity of OSAHS as determined by the diagnostic informs the type of treatment likely received, and subgroups are then defined by true

underlying severity (or absence) of OSAHS and type of treatment received. At this point the subgroups transition into the Markov model.

Within the decision tree, it is assumed that false negatives who truly have moderate or severe OSAHS will go on to have additional sleep study testing, as they are likely to continue to be symptomatic. The costs of any additional testing are accounted for in the NG202[2] model. We aim to capture time to diagnosis associated with the different modelled strategies. Should evidence for this be lacking, we will seek expert opinion to inform exploratory analyses. In the NG202 economic analysis report,[2] different diagnostic cut-offs are assumed to assess the impact on the cost-effectiveness.

Markov model

The NG202[2] Markov model is used to estimate the longer-term costs and outcomes associated with the different diagnostic strategies in an adult population. Two main categories for the potential longer-term impacts from OSAHS are modelled: cardiovascular events and road traffic accidents. The Markov model consists of 12 health states: OSAHS, five acute cardiovascular event states (for stable angina, unstable angina, myocardial infarction, transient ischaemic attack, stroke), five post cardiovascular event states, and death. The risks of a slight, serious or fatal road traffic accident are modelled from any of the alive health states. The cycle length is 12 months, and individuals are assumed to have at most one cardiovascular event.

The structure of the model, the underlying assumptions and input parameters are well-described in an evidence report accompanying the NG202 guideline[2] on the NICE website.

6.2.5.2. Child population (≤16 years old)

To adapt the adult model for children, a number of changes will be required, including:

- Changing the clinical pathway to account for different OSAHS treatment options, e.g. adenotonsillectomy may be considered first line treatment for children
- Updating test accuracy evidence for use in a population of children
- Updating of relevant parameter values to reflect a younger population.

6.2.6. Input parameters

The NG202[2] economic analysis report details the data sources used in the model, including population characteristics, mortality, risk of cardiovascular events and road traffic accidents, treatment adherence and effects, utilities associated with OSAHS and health events, and costs associated with the diagnostic strategies, treatment options and health events.

In adapting the NG202[2] model to evaluate the cost-effectiveness of novel, less intrusive, home testing devices for OSAHS, where possible, the findings of the clinical effectiveness systematic review (see Section 5 above) will be used to inform our model. We aim to update, as far as is possible, any relevant parameter inputs used in the NG202 model by searching for recent evidence, for example from a systematic review of relevant utility values and healthcare resource use and costs.

6.2.7. Process of model adaptation and validation

The key steps in the process of adapting and validating the model for use in this assessment include:

- Replicating the NG202[2] model
- Adapt model for the evaluation of novel, less intrusive, devices, as well as reflecting recommended comparator testing and treatment pathways
- Review and update model parameters:
    - Population characteristics, including prevalence and severity of OSAHS, risk of cardiovascular events
    - Performance of the intervention and comparator technologies for diagnosing OSAHS
    - Utilities
    - Resource use and costs
- Produce draft results
- Model validation:
    - Quality assurance checks by member of the EAG team not involved in model development
    - Expert opinion on face validity of modelled outcomes
    - Cross-validation against results from cost-effectiveness models from published literature or company submissions
    - Validation against internal/external data sources
- Produce final model results

6.2.8. Addressing uncertainty

The following methods will be used to assess uncertainty in model results:

- Deterministic one-way sensitivity analysis for uncertain parameters
- Probabilistic sensitivity analysis for uncertain parameters (the NG202[2] model was built to be probabilistic)
- Scenario analysis to explore alternative assumptions and data sources (including staff time and costs for reviewing the outputs from the home testing technologies).

7. Handling information from the companies

All data submitted by the manufacturers/sponsors will be considered for inclusion if received by the EAG no later than 31st August 2023. Data arriving after this deadline may not necessarily be included. If the data meet the inclusion criteria for the systematic reviews in this protocol they will be extracted and critically appraised in accordance with the procedures described earlier in this protocol.

Any 'commercial in confidence' data provided by a manufacturer and specified as such will be highlighted in blue and underlined in the assessment report (followed by an indication of the relevant company name e.g. in brackets). Any academic-in-confidence data provided will be highlighted in yellow and underlined.

8. Competing interests of authors

The authors declare no competing interests.

9. Timetable/milestones

Milestone	Date to be completed
Final protocol	5/05/2023
Progress report to NIHR ESP	04/08/2023
Draft report submitted to NICE	02/10/2023
Submission of final report to NIHR ESP; NICE	30/10/2023

10. Amendments to the protocol

A minor amendment was made to the protocol ("Final version 10th May 2023") to

include the Brizzy (Nomics) device, as per the amended NICE final scope issued in June 2023.

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11. Appendices

11.1. Appendix 1 Medline search strategy

Database	Clinical effectiveness strategy	Results
Ovid MEDLINE(R) ALL 1946 to May 22, 2023 Date searched: 23/05/2023	1 sleep apnea syndromes/ or sleep apnea, obstructive/ 41054 2 (sleep* adj4 hypopn?ea*).ti,ab,kf. 3948 3 ("obstructive sleep*" adj apn?ea*).ti,ab,kf. 35309 4 (sleep* adj4 disorder* adj4 breath*).ti,ab,kf. 10323 5 (OSA or SDB or OSAS or OSAHS).ti,ab,kf. 27909 6 1 or 2 or 3 or 4 or 5 54992 7 Actigraphy/ 4722 8 (actigraph* or "sleep monitor*" or accelerometer).ti,ab,kf. 22870 9 exp Oximetry/ 16639 10 (oxymet* or oximet*).ti,ab,kf. 18968 11 "oxygen desaturation".ti,ab,kf. 4597 12 (oxi-capnogra* or oxicapnogra* or oxy-capnogra* or oxycapnogra*).ti,ab,kf. 5 13 Capnography/ 1552 14 (capnogra* or ((CO2 or "carbon dioxide") adj1 monitor*)).ti,ab,kf. 3209 15 ("peripheral arterial tone" or "peripheral arterial tonometry" or PAT).ti,ab,kf. 6742 16 Mobile Applications/ 11344 17 ("limited channel*" or limited-channel* or multichannel or multi-channel).ti,ab,kf. 15897 18 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 90429 19 Monitoring, Ambulatory/ and (test* or device* or detect* or identif* or diagnos* or screen*).ti,ab,kf. 5300 20 (home or at-home or home-based or unattended or portable or ambulatory).ti,ab,kf. 402081 21 19 or 20 405379 22 18 and 21 7567 23 Monitoring, Ambulatory/ and (test* or device* or detect* or identif* or diagnos* or screen*).ti,ab,kf. 5300 24 (((home or at-home or home-based or unattended or portable or ambulatory) adj3 (test* or device* or detect* or identif* or diagnos* or screen*)) or HSAT).ti,ab,kf. 20075 25 Wearable Electronic Devices/ and (test* or device* or detect* or identif* or diagnos* or screen*).ti,ab,kf. 6036 26 (((wearable* or nearable*) adj3 (test* or device* or detect* or identif* or diagnos* or screen*)) or WADD).ti,ab,kf. 9435 27 (Acupebble or Acurable).ti,ab,kf. 1 28 (Brizzy or JAWAC or Nomics).ti,ab,kf. 20	1790

	29 (NightOwl or Ectosense or ResMed).ti,ab,kf. 161 30 Sunrise.ti,ab,kf. 1175 31 (WatchPAT or Itamar or Zoll).ti,ab,kf. 275 32 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 43517 33 6 and 32 2133 34 (CPAP or "continuous positive airway pressure").ti. 6249 35 33 not 34 2002 36 letter/ 1217410 37 editorial/ 650049 38 news/ 218952 39 exp historical article/ 409761 40 Anecdotes as Topic/ 4747 41 comment/ 1008163 42 case reports/ 2336495 43 (letter or comment*).ti. 188126 44 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 4921848 45 randomized controlled trial/ or random*.ti,ab. 1546690 46 44 not 45 4889791 47 animals/ not humans/ 5089785 48 exp Animals, Laboratory/ 950048 49 exp Animal Experimentation/ 10320 50 exp Models, Animal/ 639876 51 exp Rodentia/ 3534915 52 (rat or rats or mouse or mice).ti. 1434978 53 46 or 47 or 48 or 49 or 50 or 51 or 52 10874679 54 35 not 53 1921 55 limit 54 to english language 1798 56 remove duplicates from 55 1790	
Database	**Cost-effectiveness, economics strategy**	**Results**
Ovid MEDLINE(R) ALL 1946 to May 23, 2023 Date searched: 24/05/2023	1 sleep apnea syndromes/ or sleep apnea, obstructive/ 41055 2 (sleep* adj4 (apn?ea* or hypopn?ea*)).ti,ab,kf. 47187 3 (sleep* adj4 disorder* adj4 breath*).ti,ab,kf. 10326 4 (OSA or SDB or OSAS or OSAHS).ti,ab,kf. 27918 5 1 or 2 or 3 or 4 59691 6 Monitoring, physiologic/ 58660 7 Actigraphy/ 4722 8 (actigraph* or "sleep monitor*" or accelerometer).ti,ab,kf. 22873 9 exp Oximetry/ 16639 10 (oxymet* or oximet*).ti,ab,kf. 18968 11 "oxygen desaturation".ti,ab,kf. 4600 12 (oxi-capnogra* or oxicapnogra* or oxy-capnogra* or oxycapnogra*).ti,ab,kf. 5 13 Capnography/ 1552 14 (capnogra* or ((CO2 or "carbon dioxide") adj1 monitor*)).ti,ab,kf. 3209 15 Monitoring, Ambulatory/ 8646 16 (home or at-home or home-based or unattended or portable).ti,ab,kf. 318191	192

	17 (((home or at-home or home-based) adj3 (test* or device* or monitor* or detect* or identif* or diagnos* or screen*)) or HSAT).ti,ab,kf. 14406 18 Wearable Electronic Devices/ 7615 19 Mobile Applications/ 11346 20 (((wearable* or nearable* or portable or bed-mounted or ambulatory or unattended) adj3 (device* or technolog* or monitor* or test* or detect* or diagnos* or identif* or sensor* or biosensor* or tracker* or tracking)) or WADD).ti,ab,kf. 43269 21 ("peripheral arterial tone" or "peripheral arterial tonometry" or PAT).ti,ab,kf. 6742 22 ("limited channel*" or limited-channel* or multichannel or multi-channel).ti,ab,kf. 15905 23 (((home or at-home or home-based or unattended) adj3 (polygraph* or polysomnograph*)) or HRP).ti,ab,kf. 16368 24 (Acupebble or Acurable).ti,ab,kf. 1 25 (NightOwl or Ectosense or ResMed).ti,ab,kf. 161 26 Sunrise.ti,ab,kf. 1175 27 (WatchPAT or Itamar or Zoll).ti,ab,kf. 275 28 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 503198 29 5 and 28 8429 30 letter/ 1217557 31 editorial/ 650213 32 news/ 218970 33 exp historical article/ 409767 34 Anecdotes as Topic/ 4747 35 comment/ 1008321 36 case reports/ 2336806 37 (letter or comment*).ti. 188174 38 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 4922558 39 randomized controlled trial/ or random*.ti,ab. 1547094 40 38 not 39 4890493 41 animals/ not humans/ 5090008 42 exp Animals, Laboratory/ 950065 43 exp Animal Experimentation/ 10320 44 exp Models, Animal/ 639903 45 exp Rodentia/ 3535103 46 (rat or rats or mouse or mice).ti. 1435117 47 40 or 41 or 42 or 43 or 44 or 45 or 46 10875730 48 29 not 47 7805 49 limit 48 to english language 7100 50 Economics/ 27500 51 exp "Costs and Cost Analysis"/ 264444 52 Economics, Nursing/ 4013 53 Economics, Medical/ 9246 54 Economics, Pharmaceutical/ 3104 55 exp Economics, Hospital/ 25713 56 Economics, Dental/ 1921 57 exp "Fees and Charges"/ 31356 58 exp Budgets/ 14107 59 budget*.ti,ab,kf. 35762	

	60 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ti,kf. 278926 61 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ab. /freq=2 376767 62 (cost* adj2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)).ab,kf. 207173 63 (value adj2 (money or monetary)).ti,ab,kf. 3010 64 exp models, economic/ 16209 65 economic model*.ab,kf. 4170 66 markov chains/ 15952 67 markov.ti,ab,kf. 28786 68 monte carlo method/ 32136 69 monte carlo.ti,ab,kf. 59686 70 exp Decision Theory/ 13226 71 (decision* adj2 (tree* or analy* or model*)).ti,ab,kf. 37038 72 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 788632 73 49 and 72 300 74 limit 73 to yr="2013 -Current" 192 75 remove duplicates from 74 192	
Database	**HRQoL (utilities) strategy**	**Results**
Ovid MEDLINE(R) ALL 1946 to May 24, 2023 Date searched: 25/05/2023	1 sleep apnea syndromes/ or sleep apnea, obstructive/ 41038 2 (sleep* adj4 hypopn?ea*).ti,ab,kf. 3950 3 ("obstructive sleep*" adj apn?ea*).ti,ab,kf. 35309 4 (sleep* adj4 disorder* adj4 breath*).ti,ab,kf. 10326 5 ((OSA or SDB or OSAS or OSAHS) and sleep).ti,ab,kf. 25189 6 1 or 2 or 3 or 5 50810 7 Quality-Adjusted Life Years/ 15618 8 (quality adjusted or adjusted life year$).ti,ab,kf. 23063 9 (qaly$ or qald$ or qale$ or qtime$).ti,ab,kf. 14409 10 (illness state$1 or health state$1).ti,ab,kf. 8284 11 (hui or hui1 or hui2 or hui3).ti,ab,kf. 1957 12 (multiattribute$ or multi attribute$).ti,ab,kf. 1290 13 (utility adj3 (score$1 or valu$ or health$ or cost$ or measur$ or disease$ or mean or gain or gains or index$)).ti,ab,kf. 19891 14 utilities.ti,ab,kf. 9286 15 (eq-5d or eq5d or eq-5 or eq5 or euro qual or euroqual or euro qual5d or euroqual5d or euro qol or euroqol or euro qol5d or euroqol5d or euro quol or	619

	euroquol or euro quol5d or euroquol5d or eur qolor eurqol or eur qol5d or eur qol5d or eur?qul or eur?qul5d or euro$ quality of life or european qol).ti,ab,kf. 17011 16 (euro$ adj3 (5 d or 5d or 5 dimension$ or 5dimension$ or 5 domain$ or 5domain$)).ti,ab,kf. 5889 17 (sf36$ or sf 36$ or sf thirtysix or sf thirty six).ti,ab,kf. 26379 18 (time trade off$1 or time tradeoff$1 or tto or timetradeoff$1).ti,ab,kf. 2353 19 quality of life/ and ((quality of life or qol) adj (score$1 or measure$1)).ti,ab,kf. 15407 20 quality of life/ and ec.fs. 10875 21 quality of life/ and (health adj3 status).ti,ab,kf. 11626 22 (quality of life or qol).ti,ab,kf. and Cost-Benefit Analysis/ 16752 23 ((qol or hrqol or quality of life).ti,kf. or *quality of life/) and ((qol or hrqol$ or quality of life) adj2 (increas$ or decrease$ or improv$ or declin$ or reduc$ or high$ or low$ or effect or effects or worse or score or scores or change$1 or impact$1 or impacted or deteriorat$)).ab. 52823 24 Cost-Benefit Analysis/ and (cost-effectiveness ratio$ and (perspective$ or life expectanc$)).ti,ab,kf. 5158 25 *quality of life/ and (quality of life or qol).ti. 63923 26 quality of life/ and ((quality of life or qol) adj3 (improv$ or chang$)).ti,ab,kf. 40800 27 quality of life/ and health-related quality of life.ti,ab,kf. 44264 28 models, economic/ 11067 29 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 218682 30 6 and 29 1090 31 letter/ 1217493 32 editorial/ 650118 33 news/ 218962 34 exp historical article/ 409752 35 Anecdotes as Topic/ 4747 36 comment/ 1008383 37 case reports/ 2336813 38 (letter or comment*).ti. 188176 39 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 4922412 40 randomized controlled trial/ or random*.ti,ab. 1546757 41 39 not 40 4890350 42 animals/ not humans/ 5089389 43 exp Animals, Laboratory/ 950016 44 exp Animal Experimentation/ 10319 45 exp Models, Animal/ 639834 46 exp Rodentia/ 3534605 47 (rat or rats or mouse or mice).ti. 1434988 48 41 or 42 or 43 or 44 or 45 or 46 or 47 10874749 49 30 not 48 1056 50 limit 49 to english language 995 51 limit 50 to yr="2013 -Current" 619	

	52	remove duplicates from 51	619

11.2. Appendix 2 Relevance and credibility checklist for full economic evaluations

Questions in this checklist are based on the ISPOR checklist[12] and Philips and colleagues[13] checklist

	Item	Yes/Partly/ No/Unclear/NA	Comments
1. Applicability			
1.1	Is the study population appropriate for the guideline?		
1.2	Are the interventions and services appropriate for the guideline?		
1.3	Is the healthcare system in which the study was conducted sufficiently similar to the current UK NHS context?		
1.4	Are costs measured from the NHS and personal social services (PSS) perspective?		
1.5	Are non-direct health effects on individuals excluded?		
1.6	Are both costs and health effects discounted at an annual rate of 3.5%?		
1.7	Is the value of health effects expressed in terms of quality-adjusted life years (QALYs)?		
1.8	Are changes in health-related quality of life (HRQoL) reported directly from patients and/or carers?		
1.9	Is the valuation of changes in HRQoL (utilities) obtained from a representative sample of the general public?		
1.10	Overall judgement: Directly applicable/Partially applicable/Not applicable		
2. CREDIBILITY			
2.1	Does the model structure adequately reflect the nature of the health condition under evaluation?		

2.2	Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?		
2.3	Are all important and relevant health outcomes included?		
2.4	Are the estimates of baseline health outcomes from the best available source?		
2.5	Are the estimates of relative treatment effects from the best available source?		
2.6	Are all important and relevant costs included?		
2.7	Are the estimates of resource use from the best available source?		
2.8	Are the unit costs of resources from the best available source?		
2.9	Is an appropriate incremental analysis presented or can it be calculated from the data?		
2.10	Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?		
2.11	Is there no potential conflict of interest?		
2.12	Overall assessment: Minor limitations/Potentially serious limitations/Very serious limitations		