TESLA-MICRON
CLINICAL TRIAL

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CLINICAL INVESTIGATION PLAN

Zeus Sleep Technology: A UK-based multi-centre randomised controlled trial using transcutaneous electrical stimulation in patients with obstructive sleep apnoea (TESLA)

Clinical Investigation Plan: ZEUSi4i-10.0-070826
Version Number: 10
Date: 07 August 2026

Administrative Information

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Version and date of CIP	Version 10.0; date: 07/08/2026
Trial Phase	Pivotal stage
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Trial sites	Multi-centre UK trial (6 NHS Trusts, 7 recruitment sites)

Funding and Financial Arrangements

This clinical trial is entirely financed through the National Institute for Health and Care Research (NIHR) Invention for Innovation (i4i) Product Development Awards (PDA). This funding covers all expenses related to the trial, including any unforeseen additional charges that may arise.

As the sponsoring organisation, Zeus Sleep Ltd. offers to the trial sites a range of technical support services. These include expert project management, specialised clinical advisory, quality assurance, guidance on regulatory affairs, and software engineering assistance.

Agreement on the Clinical Investigation Plan

The Chief Investigator (CI) and the trial Sponsor have engaged in discussions regarding this Clinical Investigation Plan (CIP). The investigators hereby affirm their commitment to conducting the trial as outlined in this CIP. While significant care has been taken in the drafting of this CIP, adjustments may be necessary in the future. All amendments will undergo the appropriate approval process prior to implementation.

The investigators commit to carry out the trial in full compliance with the UK ICH Harmonised Guideline For Good Clinical Practice (GCP) guidelines, European Good Clinical Practise, UK Medical Devices Regulations 2002 (UK MDR 2002), the UK Data Protection Act (2018), the Trust Information Governance Policy (or its local equivalent), UK Policy Framework for Health and Social Care Research (UKPF), the Sponsor's Standard Operating Procedures (SOPs), and all relevant regulatory requirements as amended.

The undersigned hereby confirm that the CIP has been reviewed and accepted. The Chief Investigator commits to conducting the study in accordance with the approved CIP and adhering to the principles set forth in the Declaration of Helsinki, the Sponsor's SOPs, and applicable regulatory requirements.

Additionally, the undersigned confirm their intention to disseminate the findings of the study publicly through publication or other means without undue delay, and to provide an honest, accurate, and transparent account of the study's outcomes. Any deviations from the planned CIP will be thoroughly explained.

For, and on behalf of, the Study Sponsor

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List of Abbreviations and Acronyms

AE	Adverse Event
AR	Adverse Reaction
ADE	Adverse Device Effect
AHI	Apnoea-Hypopnoea-Index
CI	Chief Investigator
CPAP	Continuous Positive Airway Pressure
CRF	Case Report Form
CT	Clinical Trial
CTA	Clinical Trials Authorisation
ESS	Epworth Sleepiness Scale
FSN	Field Safety Notice
GCP	Good Clinical Practice
GP	General Practitioner
HRA	Health Research Authority
ICF	Informed Consent Form
IEC	Independent Ethics Committee
IFU	Instructions for Use
MHRA	Medicines and Healthcare products Regulatory Agency
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIH	National Institute of Health
NIHR	National Institute for Health Research
ODI	Oxygen Desaturation Index
OSA	Obstructive Sleep Apnoea
PI	Principal Investigator
PIS	Patient/ Participant Information Sheet
REC	Research Ethics Committee
SAE	Severe Adverse Event
SADE	Serious Adverse Device Effect
SOP	Standard Operating Procedure
SUSAR	Suspected Unexpected Serious Adverse Reaction
TMF	Trial Master File
TSC	Trial Steering Committee
UADE	Unanticipated Adverse Device Effect

1. Overall Synopsis of the Clinical Investigation

Study Title	A UK-based multi-centre randomised controlled trial using transcutaneous electrical stimulation in patients with obstructive sleep apnoea (TESLA)
Study Design	Prospective multi-centre, interventional, randomised-controlled, two parallel arm trial
Outcome Measures	The ***primary outcome*** parameter will be the improvement in OSA severity, as measured by the AHI, at 3-months when comparing intervention with control arm. ***Secondary outcome*** parameters will record symptomatic improvements, as measured by the Epworth Sleepiness Scale (ESS), and change in sleep quality and function, the 4%ODI, adherence to treatment, as measured by the usage of the intervention at night (hours per night; nights used). Subjective comfort and acceptance will be assessed using a visual analogue scale (0 – 10 points), the disease-specific symptoms, as assessed by sleep-related Quality of Life (Functional Outcomes of Sleep Questionnaires, FOSQ), the EQ-5D, as well as snoring (total duration, intensity, partner reporting). Furthermore, health economic data will be collected (with costs and additional contacts). Analysis will focus on differences in the response to treatment between genders (male/female) and socio-economic areas, as well as endotypes. A response to the intervention will be defined as a reduction of more than 50% in the AHI (from baseline), the AHI below 20/hour (SHER20), below 15/hour (SHER15), or a normalisation of the AHI (less than 5/hour).
Eligibility Criteria (overview)	**Inclusion:** Adult patients (≥18 years) who have OSA with an AHI between 5-40 events/hour will be included in this study, if they fail to use CPAP sufficiently with less than 4 hours/night. We will include patients with a body mass index (BMI) of 18.5-32.0 kg/m^2, without significant anatomical obstruction in the upper airway (e.g., tonsil size). **Exclusion:** We will exclude patients with no OSA (AHI <5/h), or with very severe OSA (AHI>40/hour), hypercapnic patients (pCO_2>6.0 kPa) or those with other features of obesity hypoventilation syndrome (elevated bicarbonate, $HCO3^-$ >28mmol/L). Patients should not have significantly enlarged tonsils (size 3-4), polyps or adenoids, hypoglossal nerve palsy, significant heart failure (New York Heart Association, NYHA class III-IV), recent myocardial infarction (within 3 months) or significant cardiac arrhythmias, uncontrolled hypertension, active psychiatric disease, significant metal implants in head/neck, or cardiac/other pacemakers. Patients with long facial hair that interferes with the correct placement of the hydrogel pad who are unwilling to shave or patients with allergy to patches/hydrogel will be excluded. Patients need to be able and willing to provide informed written consent.
Study Methods	Following consenting, patients will undergo baseline assessment with an overnight sleep study at home. They will then be randomised into intervention (ZeusOSA) or usual care (ongoing CPAP) groups. Patients will be assessed at baseline (sleep study after at least 3 nights off CPAP) and at 3-month follow up (on the assigned intervention). The primary

	outcome parameter defined by the apnoea-hypopnoea index (AHI) and secondary parameters (sleepiness, Epworth Sleepiness Scale (ESS) and quality of life) will be assessed at 3-months and compared against baseline between the two groups.
Statistical Methodology and Analysis	Statistical analysis will compare the respective outcome parameters (primary outcome: AHI; secondary outcomes: ESS, ODI, compliance in hours usage/night, comfort) between intervention (active stimulation) and control group (CPAP). Full statistical description will be provided and for each of the variables analysed; univariate descriptive statistics will present an overview of the data. Continuous variables will be presented as median and interquartile range (IQR), unless otherwise stated. For categorical variables, frequency counts and percentages will be presented as summary statistics for the subgroups of interest. To compare study groups, we will use the independent two samples t-test and Mann-Whitney U tests as appropriate for continuous variables, and the χ^2 or Fisher exact test as appropriate for categorical variables. The primary outcome parameter (AHI) will be analysed using the analysis of covariance (ANCOVA) to compare the treatment group (active stimulation) and CPAP at 3 months adjusting for AHI at baseline. Similar analyses will be conducted for secondary outcomes of interest.
Sample Size	n=186 patients (including 20% loss-to-follow-up).
Trial Sites	UK based multi-centre trial (6 NHS Trusts, 7 recruitment sites). Guy's & St Thomas' NHS Foundation Trust, Royal Brompton & Harefield Hospitals, Aintree University Hospital, Imperial College Healthcare NHS Trust, Royal Papworth Hospital NHS Foundation Trust, University Hospitals Birmingham NHS Foundation Trust, Queen Victoria Hospital East Grinstead.
Trial Length per Participant	Three months
Estimated Trial Duration	Three years

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3. Overcoming Treatment Challenges in OSA

3.1 Obstructive Sleep Apnoea Overview

Obstructive Sleep Apnoea (OSA) is a widespread sleep disorder marked by recurrent episodes of upper airway obstruction during sleep, resulting in partial (hypopnoea) or complete (apnoea) obstructions that cause intermittent hypoxemia, frequent arousals, and fragmented, non-restorative sleep (31). OSA is characterised by considerable heterogeneity and is classified into four primary endotypes: Upper Airway Anatomical Compromise, which includes factors such as a narrow airway, excessive soft tissue, and craniofacial structural abnormalities; Unstable Ventilatory Control, defined by high loop gain that leads to unstable breathing patterns; Low Arousal Threshold, where minor breathing disturbances can provoke awakenings; and Impaired Upper Airway Dilator Muscle Responsiveness, exemplified by reduced responsiveness of the genioglossus muscle (31).

The clinical manifestations of OSA typically involve loud snoring, witnessed apnoeas, episodes of choking or gasping during sleep, and excessive daytime sleepiness. However, some patients may exhibit minimal daytime symptoms (33). Diagnosis is most accurately confirmed through polysomnography, which is considered the gold standard, or through validated home sleep apnoea testing. The primary diagnostic measure is the Apnoea–Hypopnoea Index (AHI), classified as follows:

- Mild OSA: AHI ≥ 5–14 events/hour;
- Moderate OSA: AHI of 15–29 events/hour;
- Severe OSA: AHI ≥ 30 events/hour (33-34).

If left untreated, OSA is linked to a range of serious health consequences. These include cardiovascular disorders such as hypertension, arrhythmias, and stroke, as well as metabolic dysfunctions, including insulin resistance and type 2 diabetes. Additionally, OSA can lead to neurocognitive impairments, mood disorders, a reduced quality of life, and a heightened risk of accidents (32, 34).

3.1.1 Standard Care for Patients diagnosed with OSA.

OSA is a highly prevalent condition (1) affecting about 1 billion people worldwide (2). Prevalence has been increasing globally, primary due to increasing rates of obesity and aging populations (2-4, 32). The best treatment for uncomplicated OSA remains Continuous Positive Airway Pressure (CPAP) therapy (5, 6). However, long-term adherence to treatment with CPAP remains limited (7-11) with few alternatives. Mandibular advancement devices (MAD) may be such a non-CPAP therapy which may be better tolerated, but efficacy for MAD is best for mild-moderate cases of OSA and access to dental services is an ongoing issue in the United Kingdom (UK) (6).

The European Respiratory Society (ERS) clinical practice guidelines on non-CPAP therapies have also

reviewed other emerging treatment, such as hypoglossal nerve stimulation (12). Electrical stimulation of the dilator muscles of the upper airway has been shown to reduce nocturnal apnoeas and hypopnoeas significantly (13-19). It can be used effectively by means of an invasive approach with an implantable nerve stimulator (13-15), and by transcutaneous stimulation (16-19). However, the use of electrical stimulation for upper airway muscle contraction may not be as effective as CPAP therapy in patients with OSA (12), but it could be a relevant non-CPAP therapeutic option to treat some of the patients with OSA who fail conventional treatment, or in those whose OSA is not judged sufficiently severe to warrant CPAP (12, 20).

3.1.2 Addressing Current Treatment Limitations

Obstructive sleep apnoea is the most common form of sleep-disordered breathing (1-4). As previously mentioned, prevalence has significantly increased over the last two decades due to the obesity epidemic and OSA affects roughly 10% of the middle-aged men and 3% of middle-aged women (3). This leaves some populations with difficulties to access sleep services within their area (4). Left untreated, OSA leads to adverse long term health outcomes, including cardiovascular risks and stroke (21), as well as excessive daytime sleepiness (22). The best available treatment for patients with OSA remains CPAP therapy (5), as recommended in NICE guidelines (6). However, the need to sleep with a CPAP interface (mask) impacts on long-term compliance with treatment and contributes to the limited long-term uptake of CPAP (7-11) leaving few evidence-based alternatives (12). Mandibular advancement devices have been used in the treatment of patients with mild-moderate OSA (6), however, they are less effective than CPAP for the long-term therapy of severe OSA (12), and, additionally, access to dental services for the fitting of tailored devices remains challenging in the UK.

3.2 Study Rationale

The need to develop other non-CPAP therapies has led to a renaissance of electrical stimulation of the upper airway dilator muscles in patients with OSA (13-19,23,24). The stimulation of upper airway dilator muscles, invasively via hypoglossal nerve stimulation (15-15) and non-invasively via transcutaneous electrical stimulation (16-19) has attracted considerable interest (12). So far, hypoglossal nerve stimulation is not as efficient as CPAP therapy, but in a meta-analysis of published data there was a significant improvement in the AHI (25). In untreated patients with OSA, and in whom CPAP therapy was not tolerated (usage less than 4 hours per night), electrical stimulation may still be sufficient to downstage severe OSA, as defined by an AHI or ODI above 30 events per hour, to a milder category (mild OSA <15 events per hour) (18). The therapeutic effect could improve symptoms, like sleepiness. Although it would require prospective validation, it is also likely that treating OSA may be

associated with a reduced cardiovascular risk profile as well (26, 27).

4. TESLA Technology and ZeusOSA Device

4.1 Identification and Description of Investigational Medical Device

ZeusOSA is a non-implantable transcutaneous electrical nerve stimulation (TENS) medical device designed to be worn under the chin during sleep. The device is intended for use by adult participants in the home environment and is being investigated for the alleviation of symptoms associated with OSA and improvement of sleep-disordered breathing.

The investigational medical device features a lightweight, U-shaped silicone pad incorporating a disposable adhesive hydrogel electrode pad. ZeusOSA delivers low-level transcutaneous electrical stimulation through the skin to the hypoglossal nerve.

Stimulation of the hypoglossal nerve activates the genioglossus muscle, which may help maintain upper airway patency during sleep. Regular application of electrical stimulation promotes genioglossus muscle activity, reducing the risk of throat vibrations and upper airway narrowing or collapse that can lead to snoring or episodes of apnoea and hypopnoea.

Regular application of electrical stimulation may promote genioglossus muscle activity, which might reduce the risk of throat vibrations and upper airway narrowing or collapse that can lead to snoring or episodes of apnoea and hypopnea.

The stimulation output is customisable, allowing users to adjust the intensity through two operational buttons '+' and '-', offering a total of ten different settings to cater to individual preferences. The built-in firmware of the ZeusOSA enables users to select their desired stimulation levels while incorporating a 20-minute delay, allowing sufficient time for users to transition into sleep before stimulation commences.

Activation of the device requires pressing both buttons simultaneously for three seconds. Following activation, users can fine-tune the current intensity using the '+' and '-' buttons to establish a comfortable level. Should the sensation be overly intense for sleep, users have the option to reduce the current. The device is designed to maintain a low-level current throughout the night, ensuring proper neuromuscular tone of the upper airway muscles, such as the genioglossus.

Upon waking, users should carefully remove the device and hydrogel pad, turning the device off by pressing both buttons ('+' and '-') for three seconds before placing it back onto the charger unit for the next usage. For optimal hygiene and maintenance, it is essential to clean the device after each use with

a damp cloth or alcohol-based wipe. Users must refrain from immersing the device in any cleaning fluids or water and allow it to air dry completely before charging.

Figure 1: Investigational Medical Device



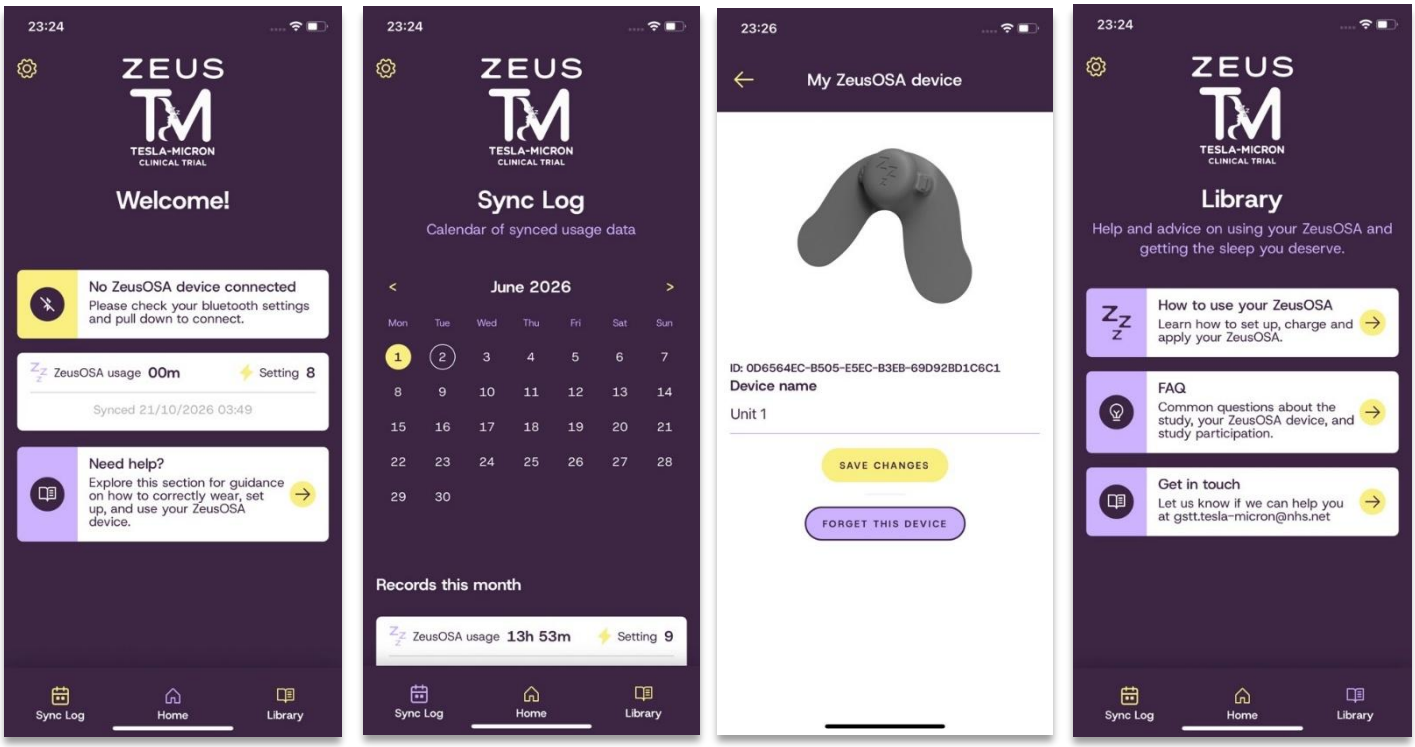
4.2 ZeusOSA System Overview

4.2.1 ZeusOSA Mobile Application

The 'ZeusOSA App' is a custom designed smartphone app that participants will install on their smartphone. Its main features are:

- Guiding the participant on how to wear and use the device
- Link to tutorial video(s) on how to wear and use the device
- Participant can view their usage data
- Relays data from the device to the server
- Provides a source of information about the study
- Contact details page

Figure 2: ZeusOSA Mobile Application Screenshots

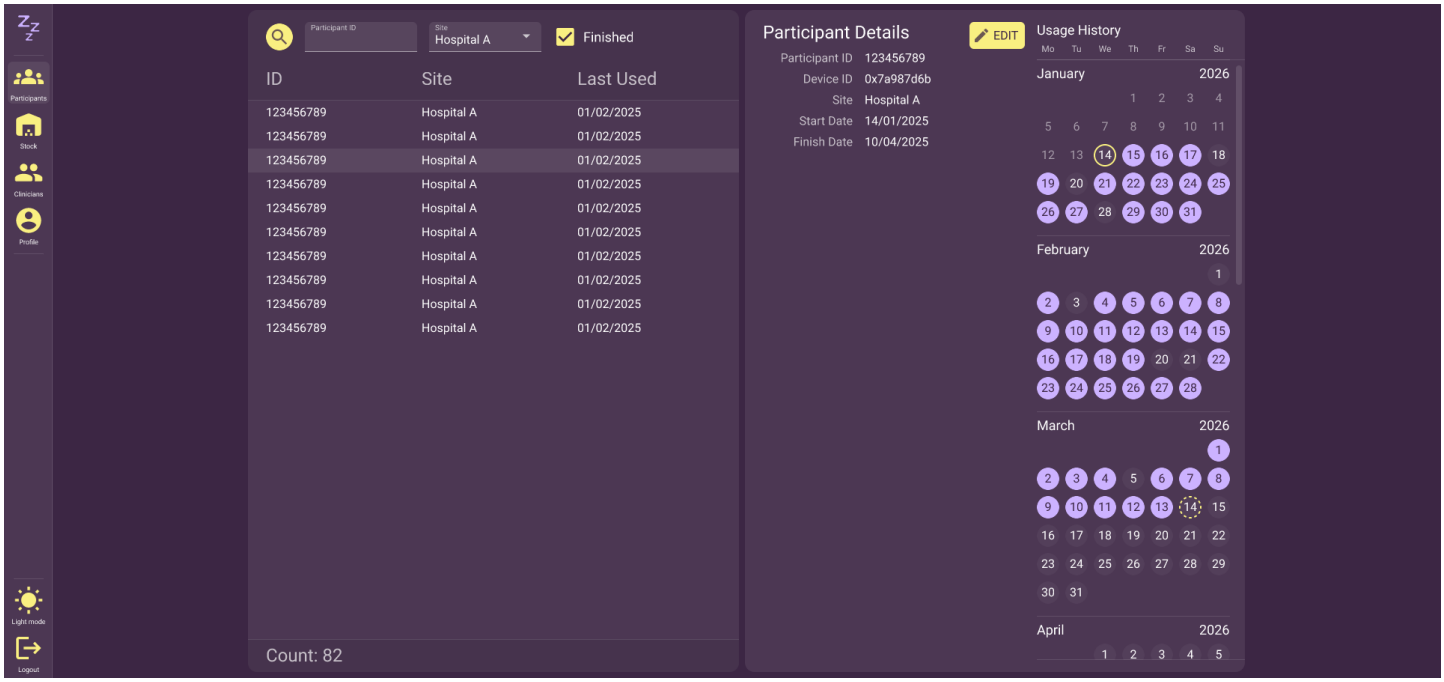


4.2.2 ZeusOSA Clinician Portal

A means of viewing, updating, and extracting data from the ZeusOSA Secure Server. Clinician Portal access is password controlled, with access permissions granted by the Sponsor. The primary functions.

- To facilitate the registering of devices during the recruitment process
    - The Participant PIN & BLE number is entered into the Portal, thereby informing the ZeusOSA Server that this device is activated. This creates an anonymous link between the participant, and data held by The Sponsor.
- To facilitate the control of inventory
- User page to show all active participants at a site
- Participants use data in calendar format to aid compliance checks at follow-up
- To allow low and high-level administrative access to data
    - Low level; Research team access, Operations access. High level; Data controller.

Figure 3: ZeusOSA Clinician Portal Main Screen



4.2.3 ZeusOSA Secure server

A cloud-based server system that utilises the AWS platform. It will be designed by the trial sponsor, and subject to independent security testing at regular intervals. The ZeusOSA Secure Server's primary functions;

- To receive data transmitted from the ZeuOSAs App via Wi-Fi or 4G
- To act as a database of devices, storing information including (but not limited to);
    - Device and charger serial numbers & BLE number.
    - Device inventory and location
    - Information relating to recruitment centres and recruiters

- Store participant device usage data

4.3 Investigational Medical Device Specifications

- Intended Medical Indication: To provide alleviation for patients that are diagnosed with mild to moderate obstructive sleep apnoea.
- Operating Principle: Low current transcutaneous electrical nerve stimulation activates the genioglossus muscles to open the airways when attached underneath the chin with single-use adhesive hydrogel pads.
- Patient Population: People aged 18 or over diagnosed with mild to moderate OSA.
- Mobility of Device: Portable device which attaches under the chin, intended for use when asleep.
- Frequency of Use: Typically, up to 8 hours at night, every night. A fully charged device battery lasts up to 10 hours.
- User Environment: Home use device, indoor spaces.

4.4 Benefits and risks of the Investigational Medical Device

4.4.1 General Benefit

The ZeusOSA medical device will be introduced to participants as a new treatment that they may be able to choose at a later stage following formal approval by regulators. Electrical stimulation with transcutaneous patches, similar to those used in TENS machines, is widely and safely used without significant side effects reported (17, 18, 28). TENS can occasionally cause minimal discomfort or mild muscle twitching; however, these effects are reduced through night-by-night titration of the stimulation current to the highest level comfortably tolerated by the participant. This gradual adjustment according to individual perception will help minimise discomfort, and participants can reduce or stop the stimulation at any time.

It has recently shown in one feasibility study (16) and two randomised controlled trials (17, 18) that the use of TESLA in patients with OSA is well tolerated. There have not been any severe adverse events during research studies spreading about two decades. However, some patients did report minor local skin reactions, and one patient in the above studies was advised to stop the intervention due to mild headaches (18). Overall, we have interviewed many patients with OSA who use CPAP therapy reliably and more than 80% would opt to choose alternatives, preferably less invasive ones (23).

It is acknowledged that the investigational medical device that is proposed in this trial differs from the TENS machine that we used previously in trials. However, it is lighter, with more qualitative materials, hydrogel electrode pad (better electrical conductivity, enhanced safety), and easier to handle than

standard TENS machines, and we are confident that patients will find it easy-to-use. The ZeusOSA device will be used in the intervention arm every night for three months and we have the following procedures in place to avoid any problems:

The intervention arm will receive TESLA treatment with the ZeusOSA device, they will be trained on the use of the device, with settings and usage being recorded. Overnight, the device will be connected to a hydrogel pad which is then placed in the submental area of the neck leaving the mandible free. The device can only be charged when off the body. Ideally, men should shave to guarantee good contact of the hydrogel to promote good transduction of the electrical current. To facilitate best adhesion and contact the hydrogel should be placed on dry skin.

4.4.2 Potential Side Effects

The ZeusOSA device utilises a hydrogel pad, which is applied nightly to deliver mild electrical stimulation to the upper airway dilator muscles. While the device is generally considered safe and well-tolerated, the following potential side effects may occur:

- Skin Irritation or Inflammation: participants may experience localised reactions at the site of the hydrogel pad application, including redness, itching, rash, or discomfort. These reactions may stem from factors such as prolonged skin contact, sweating or adhesive sensitivity.

To minimise the risk of irritation, it is essential to:

- Ensure that the skin is clean and dry prior to application.
- Not apply creams or lotions to the skin in the area where the device will be placed.
- Hydrogel pad to be worn only once.
- Clean the device after each use to remove any hydrogel pad residue.

In most instances, skin irritation is mild and transient. However, any persistent or worsening symptoms should be promptly reported to the study team, as they may advise discontinuation of device use. No systemic adverse effects are anticipated from the use of the ZeusOSA device.

4.4.3 Contraindications

- Not suitable for participants with cardiac pacemakers, defibrillators, or any other implantable medical devices, including, but not limited to hypoglossal nerve stimulators, or cerebral shunts.
- Cannot be worn over or in proximity to cancerous lesions.
- Cannot be worn by participants suffering from arrhythmias, recurrent seizures, epilepsy, alcoholism, leprosy.
- Cannot be worn following surgery where muscle contractions may disrupt the healing process.

- Cannot be worn on scarred areas following surgery for at least 10 months after operation.
- Cannot be worn while connected to high frequency surgical equipment.
- Cannot be worn in conjunction with any other medical devices, including but not limited to: TENS machine, electrical stimulation machine, electrocardiograph (ECG) meter, Magnetic Resonance Imaging (MRI), and electronic diagnosis scanners (e.g. CT scanner).
- Medical advice is required prior to use for participants suffering from severe mental illness, Alzheimer's, dementia, or any other memory impairment.
- Medical advice is required prior to use if suffering from: abnormal blood pressure, skin conditions including broken or damaged skin, loss of feeling in areas of the body, diabetes, and acute disease/fevers.
- Cannot be applied to swollen, infected, inflamed areas or broken skin.
- Cannot be worn whilst driving, operating machinery, or during any activity where involuntary muscle contractions may put participant and others at risk.

5. Study Objectives and Outcomes

5.1 Study Objectives and Hypotheses of the Clinical Investigation

The objective of this trial is to assess efficacy and symptom improvement, compliance and cost-effectiveness of transcutaneous electrical stimulation of the upper airway dilator muscles in patients with obstructive sleep apnoea (TESLA, 16-18) who do not tolerate CPAP therapy (usage <4hours/night) over a period of 3-months in the community when compared against usual care (ongoing CPAP therapy), and to evaluate acceptability, comfort and adverse events, and record outcomes for provision of the health economics analysis.

The proposed study will provide us with data about the efficacy of the domiciliary use of the intervention from a UK-based prospective, multi-centre and randomised controlled trial (Phase III). We will understand whether the primary outcome parameter, the AHI, or the secondary outcomes (e.g., 4%ODI, the ESS, compliance and comfort, FOSQ, EQ-5D) are suitable measures to assess control of OSA using TESLA within reasonable acceptance for the patients to provide the analysis of healthcare resource usage for assessment of cost-efficacy and quality-adjusted life years (QALYs). Responder analysis will provide insights into gender, socio-economic background and endotypes to predict who most suitably benefits from this treatment.

5.1.1 Primary Objective

To determine whether transcutaneous electrical stimulation of the pharyngeal dilator muscles provides a clinically meaningful therapeutic benefit for adults with obstructive sleep apnoea (OSA) in the community when compared with usual care in patients with low adherence to CPAP therapy.

5.1.2 Secondary Objectives

a. To evaluate the feasibility and acceptability of transcutaneous electrical stimulation as a treatment for OSA, with particular reference to patient adherence;

b. To explore the impact of transcutaneous electrical stimulation on symptom control, daytime functioning, and health-related quality of life;

c. To assess the safety and tolerability of the intervention in routine community use;

d. To explore heterogeneity of treatment effect by baseline OSA severity and endotype, BMI, or CPAP history, and to characterise the time course of response and patient acceptability.

e. Evaluate the economic viability of ZeusOSA from an NHS perspective, including healthcare resource use, quality-adjusted life years (QALYs), and potential cost savings from improved clinical outcomes and patient adherence.

f. To assess treatment response by classifying participants as responders or non-responders according to the SHER20 / SHER15 criteria (≥50% reduction in AHI and a residual AHI <20, or AHI<15 events/hour, respectively), or a normalisation of the AHI (<5 events/hour).

5.2 Study Outcomes

5.2.1 Primary Outcome

The primary outcome parameter will be improvement in OSA severity from baseline, as measured by the AHI, at 3-months when comparing intervention with control arm. A response to the intervention will be to demonstrate a statistically significant difference in AHI between the ZeusOSA group and the standard care group (ongoing CPAP therapy).

a. To assess the efficacy of transcutaneous electrical stimulation of the pharyngeal dilator muscles in patients with obstructive sleep apnoea in a community compared to usual care, and follow up for 3 months.

5.2.2 Secondary outcomes

Secondary outcome parameters will record the following parameters:

Symptomatic improvements, as measured by the ESS, and the 4% ODI, adherence to treatment, as measured by the usage of the intervention at night (hours per night; nights used in %). Subjective comfort and acceptance will be assessed using a visual analogue scale (0 – 10 points), disease-specific symptoms, as assessed by sleep-related Quality of Life (Epworth Sleepiness Scale, ESS, Functional

Outcomes of Sleep Questionnaires, FOSQ, European Quality of Life Questionnaire, EQ-5D), as well as snoring (total duration, intensity, partner reporting). Furthermore, health economic data will be collected:

a. To assess compliance of transcutaneous electrical stimulation of the upper airway dilator muscles in patients with obstructive sleep apnoea over time and evaluate the control of symptoms and improvement in quality of life and daytime consequences of sleep disturbance.

b. To assess differences in treatment response to transcutaneous electrical stimulation of the pharyngeal dilator muscles between male and female participants with OSA.

c. To evaluate treatment response according to participants' socioeconomic area, comparing outcomes across different socioeconomic groups.

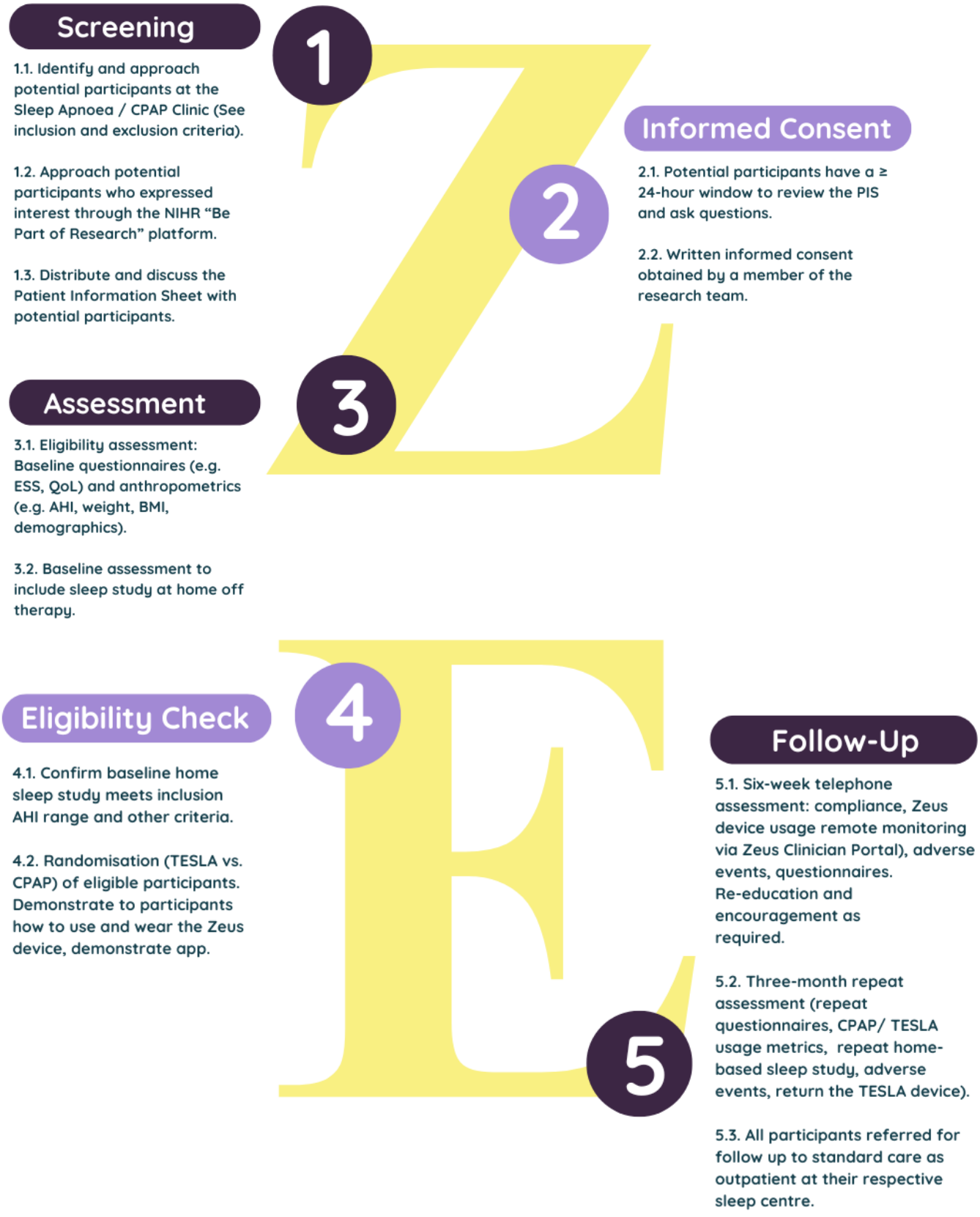
d. To assess the OSA endotypes according to the patients' sleep study characteristics (upper airway collapsibility, arousal threshold, loop gain, and muscle responsiveness).

e. To assess the cost effectiveness of ZeusOSA compared to usual care methods (ongoing CPAP) in patients with low adherence.

f. To assess treatment response by classifying participants as responders or non-responders according to the SHER20 / SHER 15 criteria (≥50% reduction in AHI and a residual AHI <20, or AHI<15 events/hour, respectively), or a normalisation of the AHI (<5/hour).

Note: The secondary outcomes planned for analysis using ANCOVA are fully defined in the **ClinicalTrials.gov registration**. More information can be found at https://clinicaltrials.gov/study/NCT07343362?term=NA (**Study ID: NCT07343362**).

6. Study Schema



6 Data Collection

6.1. Data will be collected at predefined timepoints using clinic records, device usage logs (ZeusOSA mobile app), home sleep studies, and questionnaires.

6.2. Data collected: demographics (age, gender, ethnicity), Anthropometrics: weight, BMI, neck circumference, medical history & comorbidities, medication history, sleep clinic record and ZeusOSA device adherence (from ZeusOSA logs or self-report).

7 Data Storage

7.1. All study data will be pseudonymised and stored securely on NHS-approved, GDPR-compliant servers with encryption at rest and in transit.

7.2. Periodically back-up; Access will be restricted to authorised study staff, with full audit trails maintained to ensure data integrity and GCP compliance.

7.3. The research team will use the ZeusOSA Portal to access and monitor compliance.

7.4 The research team will use an eCRF to collect and report partcipants data.

8 Data Analysis

8.1 Outcomes will be analysed by a group of medical statisticians.

8.2. The anonymised dataset wil be analysed on an intention-to-treat basis, with statistical comparisons between the TESLA and CPAP groups to assess adherence, clinical outcomes, and patient-reported measures.

9 End of Trial

9.1. Ensure that all Study records held by the trial site are archived appropriately when notified by the Sponsor and retained as required by the Protocol.

9.2. Notify local authorities regarding the end of the trial.

9.3 All participants with completed datasets will receive a Zeus device (CE for snoring only) as a thank you for their participation.

9.4 Publication/presentation of findings.

7. Design of Clinical Investigation

7.1 Overview of Clinical Investigation Design

The TESLA-MICRON trial is a prospective UK-based multi-centre trial in a randomised controlled, two-arm, parallel group design testing transcutaneous electrical stimulation in obstructive sleep apnoea for use at home over a 3-month period and compare outcomes of the intervention (TESLA) against ongoing usual care (CPAP). Site initiation visits will take place prior to any site being actively involved in the recruitment.

Patients with previously diagnosed OSA (AHI 5-40/hour) in the participating Sleep Centre will be offered to participate if they have low CPAP adherence at follow up (less than 4 hours/night). Following consenting and a baseline assessment which includes a home-based diagnostic sleep study (watchPAT) off treatment after at least three nights without CPAP therapy participants will be randomised into intervention arm (ZeusOSA) or usual care (ongoing CPAP therapy). All patients will be followed up with a telephone call at 6 weeks, and with a repeat assessment at 3-months which includes a repeat sleep study using the assigned treatment.

7.2 Investigational device and comparators

7.2.1 General Description of Active Treatment

The intervention group will receive TESLA using the ZeusOSA device. They will be trained on the device with settings being recorded throughout the period of use. The device will be connected to a hydrogel pad which is placed in the submental area of the mandible. Once the device is turned on, the current intensity can be increased by pressing the '+' button. Patients are encouraged to increase the current to the highest tolerable level, and decrease with the '-' button if they feel that they may not be able to sleep with this level. Once activated, the ZeusOSA device stimulates with a low current which provides sufficient neuromuscular tone to the upper airway dilator muscles whilst asleep. The device is kept on all night and in the morning taken off together with the hydrogel and disconnected. Once disconnected it should be turned off. The device should then be placed on the provided charger so that it is fully charged again for the next night.

7.2.2 Description of Usual Care

Patients randomised to the usual care group will continue to use their CPAP device on the prescribed pressures, the best available standard treatment according to guidelines (6). In addition, they will be re-educated on the CPAP, their interface will be reviewed; the treatment will be explained again.

Both study groups will receive the same advice on sleep hygiene, posture, weight loss, lifestyle and encouraged to keep a sleep diary for the duration of the trial; both groups will receive a follow up phone call at 6-weeks, and a repeat assessment at 3-months which includes a sleep study on the respectively assigned intervention (ZeusOSA/CPAP) which brings the trial to an end.

7.3 Patient Selection and Withdrawal

Patients with previously confirmed OSA, diagnosed either by respiratory polygraphy (home or sleep centre), or overnight polysomnography will be recruited in this trial; following individual case discussion, overnight pulse oximetries may also be acceptable for inclusion. The OSA syndrome is defined as an AHI of more than 5 events / hour plus symptoms of sleepiness, as measured by the ESS. We will recruit 186 patients with OSA and low CPAP adherence (less than 4 hours/night), following sample size calculation based on data from our previous single centre RCT (18) to detect a difference in the AHI between the treatment arms of at least 10 events / hour (Power of 90% and an alpha of 5%).

7.3.1 Inclusion Criteria

1. Adult participants (≥18 years) who have OSA with an AHI between 5-40 events/hour, as measured by the baseline sleep study (3 nights off CPAP).
2. Participant fails to use CPAP sufficiently, defined as use of CPAP for less than 4 hours/night on fewer than 70% of nights over a minimum period of 3 months prior to enrolment.
3. Adults with a body mass index (BMI) of 18.5-32.0 kg/m^2 (inclusive)
4. Adults without significant anatomical obstruction in the upper airway (e.g., normal sized tonsils).
5. Able and willing to provide informed written consent.
6. Access to a smartphone and internet at home.

7.3.2 Exclusion Criteria

1. Hypercapnic patients (pCO_2>6.0 kPa) or those with other features of obesity hypoventilation syndrome (elevated bicarbonate, HCO_3^- >28mmol/L).
2. Adults with significantly enlarged tonsils (size 3-4)
3. Adults with polyps or adenoids, hypoglossal nerve palsy,
4. Adults with notable medical co-morbidities that could potentially impact participation in or the achievement of the study's objectives (e.g., significant heart failure (New York Heart Association, NYHA class III-IV), recent myocardial infarction (within 3 months) and significant cardiac arrhythmias, uncontrolled hypertension).

5. Participants with an active psychiatric condition that, in the opinion of the Investigator, may affect the participant's capacity to provide informed consent, adhere to study procedures, actively participate in the study, or compromise the integrity of study data.
6. Participants with active implantable medical devices, including but not limited to cardiac pacemakers, implantable cardioverter defibrillators (ICDs), cochlear implants, deep brain stimulation (DBS) systems, vagus nerve stimulation (VNS) devices, neurostimulators, or implanted infusion pumps.
7. Participants with metallic implants in the head or neck region that, in the opinion of the Investigator, may interfere with the safe use of the investigational device.
8. Participants who are physically incapacitated such as to manoeuvre the ZeusOSA device
9. Adults with long facial hair that interferes with the correct placement of the hydrogel pad, and who are unwilling to shave.
10. Participants with an allergy to plasters or similar products.

The above criteria have been developed following experience from previous trials (13-19) and are likely to select responders.

7.3.3 Subject Enrolment

Patients with OSA will be recruited from one of the participating Sleep Centres where they are assessed during follow up appointments in the Sleep Apnoea / CPAP clinics. Each of the participating centres is taking a large and super-regional role, with several centres having more than 10,000 patients with OSA under their care. The direct care team will approach patients after consultation with the medical team and hand out the Patient Information Sheet (HE-P-37) for the TESLA-MICRON trial to discuss the study. Informed written consent will be taken after sufficient time for the patient to consider the information, typically at least a day after the initial consultation to allow for information and questioning. Once consented, patients will be offered a date for the baseline assessment which will also include an overnight sleep study at home without any treatment (at least 3 nights off CPAP). Following the baseline assessment and the sleep study patients will be randomised into the intervention (ZeusOSA) or usual care group (ongoing CPAP therapy). All participants will be followed up with a 6-weeks telephone call and with a 3-month repeat assessment which includes a repeat sleep study using the assigned treatment.

7.3.4 Criteria and Procedures for Subject Withdrawal or Discontinuation

The sample size assumption is that up to 20% of patients may not provide any end of study information. In consideration that the study will aim to recruit 186 allowing for 20% drop out while maintaining an

80% power with 74 participants per arm. The Intention to Treat (ITT) analysis will be adopted and patients will be analysed based on the assigned treatment at randomisation.

A per protocol (PP) analysis will also be performed, including only participants who are adherent to their assigned treatment and who do not have any major protocol deviations. Adherence will be defined as use of the assigned treatment for at least 4 hours per night on at least 70% of nights throughout the study period, for both the ZeusOSA and CPAP treatment arms.

7.3.5 Duration of Study

The study will last three years, 15 months for recruitment, with each participant expected to remain enrolled for a minimum of three months. To support participant retention and compliance, ongoing support and follow-up will be provided.

7.4 Justification for the Design of the Clinical Investigation

Following our initial pilot study using transcutaneous electrical stimulation for 10-minute periods at night (16) we have studied the feasibility of this method for entire nights in a randomised sham-controlled cross-over trial with a prototype device at the bedside in the sleep laboratory (NCT01661712); the data were published in the TESLA trial (17). It revealed that there was a modest improvement in OSA in the entire study cohort, with some patients being identified as responders and some as non-responders. However, 17/36 patients had a clinically relevant improvement, as defined by a more than 25% improvement in the oxygen desaturation index (4%ODI) and/or a 4%ODI of less than 5/hour on treatment (17). In the first domiciliary use of this method, the TESLA-HOME trial, we could show that in patients with low CPAP adherence the intervention improved mechanical indices of OSA, as well as symptoms by a clinically relevant margin following use for 3-months in the community (NCT NCT03160456); the data were published as a single centre RCT (18).

To establish whether TESLA can be used to treat OSA in the responding cohort of patients who have low CPAP adherence, in the domiciliary setting, the ZeusOSA medical device has been developed and will be tested in the intervention arm of the TESLA-MICRON trial, a UK-based multi-centre RCT. We propose to recruit suitable patients with previous diagnosis of obstructive sleep apnoea who have low CPAP adherence (less than 4 hours per night) and provide the intervention for use at home over a three-month period; patients will be asked to use the intervention every night when asleep, for as long as tolerated. The focus of the TESLA-MICRON trial is on the therapeutic efficacy, as assessed by the sleep apnoea severity and symptomatic improvements, patient compliance with the intervention, as measured by usage (total hours / per night; percentage of nights used), and subjective comfort and acceptance, as well as health economics. The results of this study will be used to inform future

application to the MHRA and inclusion in therapeutic guidelines for OSA treatment.

8. Study Procedures

8.1 Screening and Eligibility Assessment

Patients with OSA will be primarily recruited from their respective local Sleep Centre, where they are assessed and managed during routine the Sleep Apnoea / CPAP clinics appointments. About a third of all respiratory referrals to the NHS are related to OSA (30) and patients established on CPAP therapy remain typically under follow up with their local sleep centres. Patients who are compliant with CPAP therapy may be suitable for patient-initiated follow up (PIFU) pathways, but those who have CPAP usage of less than 4 hours/night require further optimisation.

The direct care team will identify and approach adult patients (aged 18 and above) with diagnosed OSA (AHI 5-40/hour) who have insufficient CPAP usage (<4hours/night) following their routine clinical review with a Consultant Sleep Physician.

In addition to recruitment through routine clinical care, the study will utilise the NIHR “Be Part of Research” platform to support participant recruitment. Potential participants who identify the study through this NIHR-supported service and express interest in participation will be able to submit their contact details and will then be contacted by the trial lead recruitment site to discuss the study further, confirm eligibility.

8.2 Participant Recruitment and Screening

Following identification through routine NHS clinical care or approved recruitment pathways, including the NIHR “Be Part of Research” platform, potential participants will be given the patient information sheet (HE-P-37), which explains the purpose of the study, what participation would involve, and the potential benefits.

During the outpatient OSA follow-up appointment, participants will be explained the study and treatment options for OSA again, including CPAP therapy.

The TESLA intervention using the ZeusOSA device will then be explained in detail, and the potential participant will be contacted more than 24h later to be given time to consider participation, discuss the request with friends, family members, GP or the research team, and ask questions before making a decision.

Once the participant agrees to consent, they will be recruited into the trial. At first, they will be invited to provide informed written consent (HE-P-38) following sufficient time to ask further questions. They will then undergo the baseline assessment, which includes an initial home-based sleep study without any treatment (at least 3 nights off CPAP therapy). Following completion of the baseline assessment, participants will be randomised to either: a) the intervention arm (TESLA using the ZeusOSA device), or b) the usual care arm (continuation of standard CPAP therapy).

To improve recruitment and retention rate to the usual care group all participants will be offered a free Zeus anti-snore device and voluntary trial of the intervention following successful completion of the trial and prior to the regular follow up in the clinical sleep service.

8.3 Informed Consent

A member of the direct clinical care team (trained in Good Clinical Practice, GCP) will take informed consent (HE-P-38) once the patients have had the opportunity to read and discuss the Patient Information Sheet (HE-P-37) with sufficient time. It will be clearly stated that the participant is free to withdraw from the study at any time and without this affecting any future care and with no obligation to give any reason for withdrawal. Following sufficient time and the opportunity to question the principal investigator or other independent parties to decide whether they will participate in the study, written informed consent will then be obtained (either electronically or with a hard copy).

8.4 Baseline Assessments

The initial assessment will include an overnight home-based sleep study (watchPAT) and patients will be assessed using the following parameters:

a) Demographics, medical history and clinical parameters

i. Age (years)
ii. Sex at birth
iii. Ethnicity (self-declared according to NHS standards, on electronic patient record)
iv. Height (m), Weight (kg), Body-Mass-Index (BMI, kg/m^2)
v. Neck circumference (cm)
vi. Waist (cm), Hip (cm), W:H ratio
vii. Mallampati and Friedman Score
viii. Blood pressure (mmHg), oxygenation (SpO2, %) and heart rate (bpm)
ix. Medication/comorbidities
x. Snoring assessed by the partner, if available(visual analog scale from 0 to 10 points)
xi. Adherence to treatment (CPAP, hours/night, percentage of nights used)
xii. Smoking history

xiii. Alcohol intake
xiv. Recreational drug use
xv. Index of Multiple Deprivation (Decile)
xvi. Endotype (optional)

b) Sleep study parameters, as measured by respiratory polygraphy (watchPAT)

i. AHI, 3% and 4%ODI, Respiratory Disturbance Index (RDI) (all in events/hour)
ii. Total sleep time (mins)
iii. Sleep efficiency (%)
iv. Posture in bed (%)
v. Different sleep stages (%)
vi. Snoring (total duration (mins), intensity (dB))
vi. Heart Rate Variability (HRV)
vii. Hypoxic burden (for TST per hour)
viii. Arousal Index (events/ hour)

c) Symptom and Quality of Life scores

i. Epworth Sleepiness Scale (ESS, points)
ii. European Quality of Life tool (EQ-5D, points)
iii. Functional Outcome of Sleep Questionnaire (FOSQ-10)

For the home sleep studies, multi-channel wearable sleep technology will be used (watchPAT); the equipment can be couriered out, and data will be downloaded via a cloud-based system. The patient will be provided with a manual on how to use the equipment, the correct fitting will be explained, and instructions on how to wear and use the device will be made accessible online in different formats as well.

8.5 Randomisation

8.5.1 Randomisation and Home Treatment

Following the baseline assessment the severity of OSA will be reviewed and, if eligible (AHI 5-40/h), patients will be randomised into intervention (TESLA) or usual care (CPAP). The active treatment will be domiciliary transcutaneous electrical stimulation at night using the ZeusOSA medical device, while the usual care group will receive ongoing CPAP therapy.

Upon registration in the Medrio EDC System, each participant will be assigned a unique participant identification number (PIN), which includes information about the study site and participant number

(e.g. 01-0001). This PIN will be entered into the randomisation system by the authorised study team member responsible for randomisation. Treatment assignment will be determined according to a computer-generated randomisation list prepared by an individual not directly involved in participant assessments.

The online randomisation platform for the trial will be provided by the King's Clinical Trials Unit (KCTU) at Guy's Campus, London, UK. It will require entry of the following variables for minimisation: age, gender, BMI, and AHI to provide matched groups. Furthermore, recruitment will focus on a balanced ratio of men and women, as women are typically under-represented in studies of OSA and, due to a slim neck/collar size in comparison to men, women are more likely to be responders to the TESLA treatment using the ZeusOSA device.

8.5.2 Subsequent Assessments

Telephone Contact at 6-weeks:

All patients will receive a phone call at 6-weeks post randomisation to encourage usage of the device, according to their assigned treatment arm, and discuss problems with the treatment (ZeusOSA or CPAP). Patients will be asked about their comfort and any adverse events. The following parameters will be assessed:

i. Usage of the assigned treatment (hours/night, nights used)
ii. Epworth Sleepiness Scale (ESS, 0-24 points)
iii. Comfort (visual analogue scale, 0-10 points)
iv. Adverse events and device deficiencies
v. Resource use data for the health economic evaluation

Note: Visual Analogue Scale (VAS) showing patient-reported comfort related to ZeusOSA (intervention) and CPAP (usual care). The scale ranges from 0 ("No Comfort") to 10 ("Highest Comfort"). Comfort Comparison Between Interventions. VAS can be seen in appendix 2 'Comfort Comparison Between Interventions'. At this appointment, the patients will be re-educated on their respective devices, the ZeusOSA device or CPAP, and encouraged to continue with nocturnal usage.

Follow up at 3-months:

At 3-months, the patients will be invited to attend another appointment to have their final assessment. The purpose of this re-assessment is to record the same parameters as at baseline (demographics, sleep study, adherence to intervention device or usual care, questionnaires; ESS, EQ5D & FOSQ). The following parameters will be assessed:

i. Usage of the assigned treatment (hours/night, nights used)
ii. Average pressure of CPAP used (cmH20), Level of Zeus Stimulation used (Average level) per study period on the night of the 2nd sleep study

iii. Epworth Sleepiness Scale (ESS, 0-24 points)

iv. Functional Outcomes of Sleep Questionnaire (FOSQ-10)

v. EQ-5D-5L

vi. Comfort (visual analogue scale, 0-10 points)

vii. Snoring assessment by the bed partner, if available (visual analogue scale, 0-10 points)

viii. Adverse events and device deficiencies

ix. Resource use data for the health economic evaluation.

A repeat home-based sleep study (watchPAT) on the assigned treatment (ZeusOSA or CPAP) will conclude the trial assessments. Patients will then receive a formal debriefing from the study team.

Patient participation concludes with the 3-month follow-up assessment and home sleep study. The patients will then be referred for follow up to standard care in the outpatient setting at their respective sleep centre / at the participating site.

8.6 Participant Discontinuation/ Withdrawal

Each participant has the right to withdraw from the study at any time without providing a reason. In addition, the investigator may discontinue any participant from the study at any time if considered necessary for one of the following reasons:

- Ineligibility (either arising during the study or retrospectively),
- Disease progression, which requires discontinuation of the study, or inability to continue to comply with study procedures,
- Consent withdrawn,
- Lost-to-follow-up.

The reason for withdrawal will be recorded, including 'no reason given', in the case report form (CRF).

9. Data Management

9.1 Source Data and Data to be Collected

Source documents are original documents, data, and records from which the CRF data are obtained. These include, but are not limited to, hospital records (from which medical history, concurrent medication and sleep apnoea treatment may be summarised into the CRF), clinical and office charts and software (e.g., watchPAT and CPAP reports).

CRF entries will be considered source data if the CRF is the site of the original recording (e.g., there is no other written or electronic record of data). In this study, the CRF will be used as the source

document for stable patients recruited into the study. All documents will be stored safely on password-protected systems in locked rooms at the participating NHS site. Only the research team will have access to the data. Rooms are locked and computers are password protected. For all study-specific documents, other than the signed consent, the participant will be referred to by the study participant number/code, not by name. Data are stored for the duration of the study (3 years) and then archived (for at least another 5 years). Direct access will be granted to authorised representatives from the sponsor, host institution and the regulatory authorities to permit trial-related monitoring, audits and inspections.

9.2 Data Handling and Record Keeping

Participants will be identified by a study specific participants number and/or code in any database. The name and any other identifying details will NOT be included in any study data electronic file. The data will be collected by the research team and controlled by the CI/PI on-site, as well as in the quarterly data management meetings with the trial statistician. Records will be maintained for the duration of the trial (3 years) and archived for a minimum of 5 years and a maximum of 15 years following trial completion.

The data controller for the study will be Guy's and St Thomas' NHS Foundation Trust. Study data will be collected, processed, saved and managed using a secure, web-based electronic data capture (EDC) system (Medrio), hosted on secure servers within the EU. Access to study data will be restricted to authorised users via individual, password-protected accounts, with a full audit trail of all data entry and modifications.

The data will be used only for the purposes indicated in the currently-proposed Study. All data collected for the study will be subject to the General Data Protection Regulation and the Data Protection Act 2018. The data collected will be anonymised and stored for a maximum of 15 years. Each participating site will be responsible for archiving its local study records in accordance with local requirements. Guy's and St Thomas' NHS Foundation Trust, as the Chief Investigator site, will be responsible for the archiving of the overall trial records. This is for the purpose of processing the data, protecting intellectual property, and ensuring that regulatory and legal requirements can be demonstrated when obtaining approvals.

Hospital-based data

For the following functions:

1. Signing and storage of Consent Forms

2. Registration of participants
3. Generating participant number/ code, linked to participants' number or code (PIN)
4. Clinical event data
5. Validation and storage of data
6. Receipt and storage of CRFs identified only by participant PIN number or code.
7. Adverse event storage

These can be executed as paper-based hardcopy, with attendant lock-and-key storage of documents, or electronically, on a software module written for the purpose and residing on a hospital-based system, and password controlled by the Investigator. Access to the hospital site is tightly controlled.

9.2.1 Medrio Electronic data capture

A web based electronic data capture (EDC) system will be created in collaboration with the CI and trial analyst(s), using the Medrio system. This will be maintained by the King's Clinical Trials Unit (KCTU) and Medrio for the duration of the project. It will be hosted on secure servers by Medrio in the EU.

Data Entry

No data will be entered onto the EDC unless a participant has signed a consent form to participate in the study. Source data will be entered in the EDC by authorised *site staff / central staff within the coordinating study team,* typically within *7* days of data collection by going to www.ctu.co.uk and clicking the link to Medrio EDCs.

A full audit trail of data entry and any subsequent changes will be automatically date and time stamped, alongside information about the user making the entry/changes. It is the responsibility of the site PI team to ensure all baseline data are collected before a participant is randomised.

EDC Access

The CI or delegate (e.g., Trial Manager) will request email usernames and passwords from KCTU for new staff members joining the study and will request access removal when staff members leave the project. EDC access is strictly restricted through user-specific passwords to the authorised research team members. It is a legal requirement that passwords to the EDC are not shared, and that only those authorised access the EDC.

EDC Troubleshooting

Site staff experiencing issues with the EDC system should contact the CI or delegate (e.g., Trial Manager). Medrio training videos are available at www.ctu.co.uk under 'Resources – Events & Training' tab.

Data Quality Processes

Site staff will respond to data queries within the EDC as required. No data will be amended independently of the study site responsible for entering the data. The KCTU will provide the study team with a Data management plan for Medrio EDC.

Database Lock

At the end of the trial, the site PI will review all the data for each participant to verify that all the data are complete and correct. At this point, all data can be formally locked for analysis.

9.2.2 KCTU Randomisation

A web-based randomisation system will be designed, using the bespoke KCTU randomisation system. The randomisation system will be created in collaboration with the trial analyst/s and the CI and maintained by the King's Clinical Trials Unit for the duration of the project. It will be hosted on a dedicated server within KCL.

Randomisation will be at the level of the individual using the method of block randomisation with randomly varying block sizes, stratified by study site.

Data entry

Randomisation will be undertaken by recruiting site staff, by authorised staff onto the randomisation system by going to www.ctu.co.uk and clicking the link to access the randomisation system. A full audit trail of data entry will be automatically date and time stamped, alongside information about the user making the entry within the system.

Security

The CI or delegate will request usernames and passwords from the KCTU. System access will be strictly restricted through user-specific passwords to the authorised research team members. It is a legal requirement that passwords to the randomisation system are not shared, and that only those authorised to access the system are allowed to do so. If new staff members join the study, a user-specific username and password must be requested via the CI or delegate (e.g., Trial Manager) from the KCTU team and a request for access to be revoked must be requested when staff members leave the project. Study site staff experiencing issues with system access or functionality should contact the CI or delegate (e.g., Trial Manager) in the first instance.

Participant initials and date of birth will be entered on the randomisation system. Whereas NHS number, email addresses, participant names and addresses and full postcodes will not be entered into

the randomisation system. No data will be entered onto the randomisation system unless a participant has signed a consent form to participate in the trial.

Data Quality Processes

The CI team will undertake appropriate reviews of the entered data for the purpose of data cleaning. No data can be amended in the system, however, CI or delegate (e.g., Trial Manager) may request King's Clinical Trials Unit to add notes against individual subject entries to clarify data entry errors.

Database Lock

Upon request, KCTU will provide a copy of the final exported dataset to the CI in .csv format and the CI will onward distribute as appropriate.

9.3 Data Protection: Study Results

- Recruitment will be carried out by a qualified medical professional approved by the chief investigator and principal investigator and trained in Good Clinical Practice and the obligations of Researchers towards protection of the rights of volunteer participants, including personal data protection.
- Candidate participants will be informed that to their results will be matched with certain data from their clinical records. These requirements are noted in the Participant Information Sheet, in the oral recruitment interview, and in the Informed Consent Form which they will be asked to sign.
- Upon giving informed consent, the subject's Consent Form will be registered on the Participant Register by the recruiter and assigned an individual participant number or code. The Register file linking Subject's Identity with participant number or code, either hard-copy or electronic, will be held by the research team. Staff of the Sponsor shall have no access to this linkage.
- These functions will be encoded in an application developed for the purpose by the trial Sponsor. The participant associated with each result will be identified only by their participant number. Data transmitted will be encrypted by the smart-phone's communication protocol(s).
- The security levels and physical redundancy back-up facilities of reputable Cloud-system suppliers are generally much more robust than could realistically be provided by a stand-alone system.

9.4 Data Protection: Clinical Data

- At registration linkage of participant identifiable information to Participant number will be known only to the research team, and will be stored securely by the chief or principal investigator, either in a hard-copy register under lock-and-key or electronically under password protection.
- As set out above, the participant will be well informed prior to their consent of the intention to extract certain clinical information from the records of every participant, and record them in a CRF on conclusion of their participation in the trial. It will be emphasised that the data extraction will be done by a medical professional, and that the participant whose data goes in the CRF will be identified only by participant number/ code number.
- The completed CRF, identified only by participant number or code number, will be generated electronically by clinical staff directly into the electronic case report form database, and matched by participant number or code number with the test results already on file for the subject holding that participant number.

At no point will persons other than the participants' clinicians be aware of the subject's number, or of any clinical information other than that specified in the CRF. The CRF information for a participant pseudonymised by participant attributed number would be meaningless to an unauthorised observer.

9.5 Confidentiality

All data will be handled in accordance with the UK Data Protection Act 2018. The CRFs will not bear the subject's name or other personal identifiable data. The subject's initials, date of birth, and participant identification number (PIN) will be used for identification. Subjects will be assigned a unique PIN by the Medrio EDC System upon registration by the study site following enrolment into the study. The recruitment site will maintain a master Subject Identification Log.

9.6 Patient and Public Involvement and Engagement

Patient and Public Involvement and Engagement (PPIE) is a vital component at every stage of this research, ensuring that the design, development, and deployment of ZeusOSA meet patient's needs and expectations. This approach builds on previous engagements, where patient input during usability testing and feedback sessions significantly shaped the device's fundamental design.

Patients will be actively involved throughout the research process, particularly in guiding recruitment strategies. It will utilise well-defined inclusion and exclusion criteria to ensure diversity and specifically

target underserved groups. An essential part of this process includes reviewing all patient-facing documents, such as consent forms, to ensure that study materials are comprehensible and accessible to participants from various economic and social backgrounds. Hope2Sleep will act as a direct channel for patient feedback and will assist in continuously improving the study methodology. Moreover, patients will co-create informational resources that clarify study procedures and help mitigate potential barriers to participation.

Engagement with participants will focus on capturing user experiences, which will evaluate device usability, comfort, and adherence challenges. This feedback will be instrumental in refining trial execution and informing future deployment strategies, particularly within NHS settings. Real-time insights into usability will be incorporated into product iterations to ensure that ZeusOSA is optimised for practical use.

To enhance inclusion, especially for underserved populations, we will provide flexible participation options, including remote monitoring, to reduce participant burden. This strategy aims to enhance the generalisability of findings and address disparities in treatment response. Ongoing communication, facilitated by Hope2Sleep, will ensure that participants remain informed throughout the study. After the trial concludes, a summary of results will be shared with all participants. This comprehensive strategy guarantees that the research yields patient-centred outcomes, supports adherence strategies, and facilitates the adoption of ZeusOSA within the NHS.

10. Statistical Considerations

10.1 Sample Size Calculation

The sample size estimates were based on the previous trial by Ratneswaran et al. 2023 (18) where the primary outcome was change from baseline in mean AHI at 3-months between the two trial arms. The difference adjusted for the baseline value was -7.0 (95% CI: -15.7;1.8), and the common standard deviation within group was 18. Using these estimates for an analysis of covariance, sample sizes of 74, and 74 are required from each of the 2 trial groups whose means are to be compared. The covariate was assumed to have an R-squared of 0.30. The total sample of 148 subjects achieves 80% power to detect the differences described by Ratneswaran between the two means, with 0.05 significance level. Allowing for 20% dropout the sample required is 186 participants in the two groups.

10.2 Statistical Analysis Plan

All demographic and baseline participants' characteristics will be described overall and by treatment arm. Continuous variables will be presented as mean and standard deviation or median and interquartile range (IQR), as appropriate for these distributions. For categorical variables, frequency counts and percentages will be presented as summary statistics for the subgroups of interest. To compare study groups, we will use the independent two samples t-test or the Mann-Whitney U test as appropriate, for continuous variables of interest, and the $\chi 2$ or Fisher Exact test as appropriate for categorical variables. The primary outcome (AHI) will be analysed using the Analysis of Covariance (ANCOVA) method, with AHI at 3-months as the outcome, adjusting for AHI at baseline to compare the two trial arms, treatment group (active stimulation) and control group (CPAP). Similar analyses will be conducted as appropriate for secondary continuous outcomes. The secondary outcomes planned for analysis using ANCOVA are fully defined in the ClinicalTrials.gov registration. More information can be found at https://clinicaltrials.gov/study/NCT07343362?term=NA (Study ID: NCT07343362). This ensures the SAP aligns with the protocol specifications.

Note that the sample size was calculated specifically to detect a meaningful difference between the treatment arms in the primary outcome only (AHI at 3-months) and thus lacks sufficient statistical power to draw reliable conclusion about any secondary outcomes. The trial follows up each patient for at least 3-months and some patients will inevitably be lost to follow-up. The final follow-up is scheduled at 3 months, but exact timing may vary for practical reasons (e.g., weekends). A window of ±1 week is generally acceptable, with up to ±2 weeks in special circumstances (e.g., patient on leave). Follow-up should not be extended beyond this, and the schedule should be confirmed with the patient at enrolment to minimise dropouts. For patients who withdraw or drop out before the end of the study, the "no change assumption" will be used to impute the missing subsequent values. This may introduce a bias if the main reason for drop-out was deterioration. To examine this possibility, sensitivity analysis will be performed to assess the primary efficacy outcome using different imputation methods including "best-case scenario", and "worst- case scenario" possible scores for the missing data. Additionally, Multiple Imputation (MI) will be used as appropriate following the assessment of missing data mechanisms.

In addition to the intention-to-treat (ITT) analysis, a per-protocol (PP) analysis, including only those subjects with complete follow-up data, will also be performed. Subgroup analysis will examine the responders separately, to understand whether they differ from non-responders. All analyses will be performed using StataTM version 18.0 and R-package. Differences will be considered significant at $p<0.05$.

The senior trial statistician, Dr Salma Ayis, responsible for the primary statistical analysis will remain blinded to treatment allocation until the statistical analysis has been completed and the database has been locked, unless unblinding is required for safety or regulatory reasons.

A separate and full Statistical Analysis Plan (SAP) for the trial will be developed prior to any analysis of the data.

11. Health Economics Analysis

11.1 Overview

The TESLA-MICRON study outcomes will be incorporated into a Health Economics evaluation designed to assess the cost-effectiveness of the ZeusOSA device compared with current standard care pathways for mild to moderate obstructive sleep apnoea (OSA), specifically CPAP therapy in patients with low adherence to treatment (<4 hours/night). The analysis will adopt an NHS perspective, accounting for both costs and health outcomes.

A mixed decision-analytical + Markov health state transition model (illustrated in the figures below) will be constructed to estimate the incremental costs and health effects of the ZeusOSA device relative to CPAP therapy in patients with low adherence. To ensure transparency and simplicity, the model follows a responder/non-responder framework, with two primary treatment pathways:

- ZeusOSA device: responder vs non-responder
- Standard care (CPAP therapy in patients with low adherence): responder vs non-responder

In the model (see figures 2 and 3), each pathway branches according to treatment response. Responders are defined as participants who achieve a clinically meaningful improvement in the Apnoea–Hypopnoea Index (AHI), while non-responders show little or no improvement. Each terminal node represents a health state associated with a corresponding quality of life outcome and cost.

Figure 4: In-Study Decision Tree

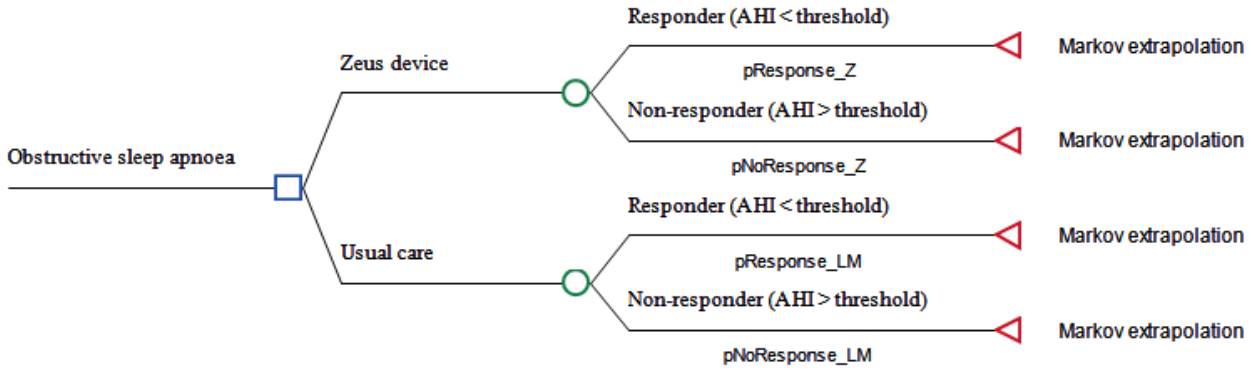
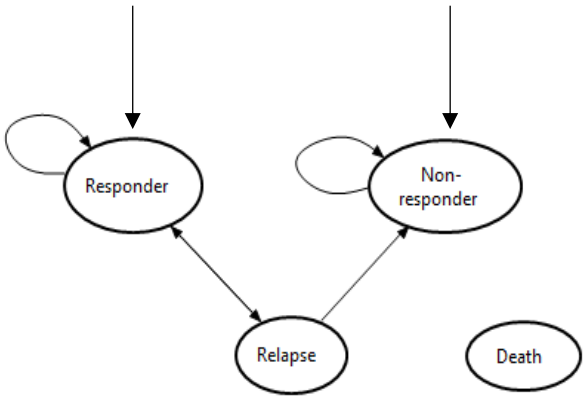


Figure 5: Long-Term Markov Extrapolation



11.2 Model Parameters

The proportion of participants achieving the defined treatment response in each arm will be estimated as part of the primary analysis. If more granular categories of response are used (e.g., complete, partial, or poor response), these will be clearly defined so that each participant is classified consistently within the model structure.

Three core types of parameters will be derived directly from the study and used to underpin the economic model:

- Proportion of Responders: The percentage of participants in each treatment arm achieving a defined clinical response.
- Generic Quality of Life (QoL): Measured using validated instruments (e.g., EQ-5D-5L), mapped to utility estimates and stratified by response status.
- Resource Use and Costs: Direct healthcare resource use associated with each treatment pathway, including intervention delivery, monitoring, and subsequent care needs, mapped to national unit costs.

These three parameter types provide the foundation for the model structure shown in figures 2 and 3, and for extrapolation of results over the longer term, enabling estimation of incremental cost-effectiveness ratios (ICERs) for the ZeusOSA device compared with other standard care options, particularly CPAP therapy in patients with low adherence (<4 hours/night).

11.3 Extrapolation Beyond Study Duration

While the primary data collected during the study will inform short-term outcomes, it is necessary to extrapolate results beyond the trial period to capture the long-term costs and health benefits associated with each intervention. Extrapolation will be performed using modelling techniques consistent with NICE guidance on health technology assessment.

- Maintenance or Decay of Treatment Effect: The proportion of responders and the degree of improvement in AHI and quality of life will be modelled over time.
- Transition to Health States: Patients may move between defined health states (e.g., responder, non-responder, relapse) over time.
- Mortality and Disease Progression: general population mortality rates and any OSA-related risks will be incorporated to ensure realistic projections of survival and quality of life.
- Cost and Utility Accumulation: Costs (e.g., device replacement, healthcare utilisation, ongoing support) and utilities (e.g., quality of life weights for responders *vs* non-responders) will be accumulated over the extrapolated period.

12. Ethical Considerations

12.1 Declaration of Helsinki, National and International Standard and regulations

The clinical investigation will be conducted in accordance with the ethical principles outlined in the Declaration of Helsinki, ISO 14155:2020, and all applicable UK regulations governing medical devices. This includes adherence to the UK Policy Framework for Health and Social Care Research, the Data Protection Act 2018, the Mental Capacity (Amendment) Act 2019, and the Medical Devices Regulations 2002 (UK MDR 2002) and other relevant regulations. Commitment to ethical conduct and regulatory compliance is crucial for maintaining the integrity of the study and protecting participants' rights and safety.

12.2 Vulnerable Population

No vulnerable populations will be selected for recruitment into this trial, in accordance with the ethical principles of the Declaration of Helsinki and relevant UK regulations. Vulnerable individuals require special protections, and this trial prioritises the autonomy and rights of all participants by enrolling only those capable of providing informed consent.

12.3 Premature Termination of the Clinical Investigation

Each participant has the right to withdraw from the study at any time without providing a reason. In addition, the investigator may discontinue patient participation at any time if considered necessary for one of the following reasons:

- Ineligibility (either arising during the study or retrospectively),
- Disease progression which requires discontinuation of the study or inability to continue to comply with study procedures,
- Consent withdrawn,
- Lost to follow up.

The reason for withdrawal will be recorded, including 'no reason given', in the CRF. Premature termination of the clinical investigation will be reported to the relevant authorities.

13 Insurance, Liabilities, and Indemnity

NHS bodies participating in this research are legally liable for the negligent acts and omissions of their employees. Where a patient suffers harm because of negligence on the part of an NHS employee involved in this study, NHS indemnity will apply in the usual way.

The NHS indemnity scheme does not extend to cover non-negligent harm. Participating NHS sites cannot agree in advance to pay compensation in the event of non-negligent harm. In exceptional circumstances, an ex-gratia payment may be offered at the discretion of the organisation concerned. Legislation requires all GMC-registered medical professionals involved in the trial to hold valid professional indemnity or insurance appropriate to their scope of practice.

Zeus Sleep Limited, as Sponsor of the TESLA-MICRON trial, has arranged clinical trial indemnity insurance (Phase III) through Chubb European Group SE, brokered by KnightSure Insurance Brokers (Tony Knight). This insurance is intended to provide cover for liabilities that may arise in relation to the design, management, and conduct of the trial, subject to the terms and conditions of the policy and receipt, review, and acceptance of the relevant Patient Consent documentation and approved

Protocol.

- Insurer: Chubb European Group SE
- Policyholder: Zeus Sleep Limited
- Period of Insurance: 01/11/2025 - 31/10/2027
- Coverage: Clinical Trials Liability
- Territorial Limits: United Kingdom
- Limit of Liability: GBP 5,000,000
- Clinical Investigation Plan Title: Zeus Sleep Technology: A UK-based multi-centre randomised controlled trial using transcutaneous electrical stimulation in patients with obstructive sleep apnoea (TESLA).

Therefore, trial participants are protected through a combination of: Standard NHS indemnity for negligent acts or omissions of NHS staff and Sponsor-arranged clinical trial indemnity insurance to cover other relevant liabilities in connection with the trial.

14 Trial Approval & Amendments

To initiate the TESLA-MICRON medical device clinical trial in England, the trial sponsor and research team must obtain all relevant regulatory and ethical approvals before recruitment can begin.

During the course of the trial, any change to the approved documentation must be categorised and processed in line with UK regulatory requirements.

A substantial amendment is one that significantly affects:

- The safety or physical/mental integrity of trial subjects.
- The scientific value of the study.
- The conduct or management of the study.
- The quality or safety of the device under investigation.

Examples include significant change to the protocol, informed consent, participant information sheets, investigators, chief investigator, or device modifications.

An amendment is considered non-substantial if the modifications do not significantly affect participant safety, scientific value, trial conduct, or investigational device performance. Examples include administrative corrections, updated contact details, or minor wording changes. These amendments must still be recorded, notified through IRAS where required, and communicated to participating sites. All non-substantial amendments should be documented in the Trial Master File and Investigator Site Files to maintain a clear audit trail.

15. Adverse Events and Device Deficiencies

15.1 Definitions

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device. **Note 1:** This definition includes events related to the investigational medical device or the comparator. **Note 2:** This definition includes events related to the procedures involved. **Note 3:** For users or other persons, this definition is restricted to events related to the use of investigational medical devices or comparators.
Adverse Device Effect (ADE)	An adverse event related to the use of an investigational device. **Note 1:** This definition includes AEs resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational device. **Note 2:** This definition includes any event resulting from use error or from intentional misuse of the investigational medical device. **Note 3**: This includes 'comparator' if the comparator is a medical device.
Serious Adverse Event (SAE)	Any adverse event that: • Led to death, • Led to serious deterioration in the health of the subject, users, or other persons as defined by one or more of the following: • a life-threatening illness or injury, or • a permanent impairment of a body structure or a body function, or • in-patient or prolonged hospitalisation, or • medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function, • Led to foetal distress, foetal death or a congenital anomaly or birth defect including physical or mental impairment. **Note 1:** Planned hospitalisation for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health is not considered a SAE.
Serious Adverse Device Effect (SADE)	An adverse effect that has resulted in any of the consequences characteristic of a serious adverse event.

Term	Definition
Unanticipated Serious Adverse Device Effect (USADE)	An SADE which by its nature, incidence, severity or outcome has not been identified in the current risk assessment report.
Device Deficiency (DD)	Inadequacy of the investigational medical device with respect to its identity, quality, durability, reliability, safety or performance. **Note 1:** this includes malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including labelling. **Note 2:** this includes device deficiencies related to the investigational medical device or comparator.

An adverse event does not include:

- Medical or surgical procedures themselves; the underlying condition leading to the procedure is considered the adverse event.
- Pre-existing disease, conditions, or laboratory abnormalities present at the start of the study that do not worsen in frequency or intensity.
- The disease under investigation or its expected signs and symptoms, unless they occur at a greater frequency or severity than expected for the subject's condition.

15.2 Safety Reporting Requirements and Timelines

Term	Reporter	Reported to	Reporting Timeline from awareness of the event
Adverse Event (AE)	Investigator	Sponsor	As agreed with sponsor.
Adverse Device Effect (ADE)	Investigator	Sponsor	As agreed with sponsor.
	Sponsor	MHRA	Summarised in periodic safety updates/progress reports to regulators, if required.
Serious Adverse Event (SAE)/ Serious Adverse Device Effect (SADE)	Investigator	Sponsor	Immediately, no later than 24hrs of becoming aware of the event.
	Investigator/ Sponsor	MHRA[1]	Fatal or life-threatening immediately and no longer than 7 days. Other SADEs within a 15-day reporting window.

[1] SAEs indicating immediate risk of death, serious injury or serious illness and that require prompt remedial action for other patients/subjects, users or other persons or a new finding to it

Term	Reporter	Reported to	Reporting Timeline from awareness of the event
Unanticipated Serious Adverse Device Effect (USADE)	Investigator	Sponsor	Immediately, no more than 24 hours
	CI/Sponsor	MHRA and REC	Fatal or life-threatening Immediately, no later than 7 calendar days. Other USADEs within a 15-day reporting window.
Urgent Safety Measures (USM)	CI/Sponsor	REC and MHRA	(i) Immediately-By telephone (i) Within 7 calendar days -Notice in writing setting out reasons for the USM and plan for further action
Device Deficiency (DD)	Investigator	Sponsor	Immediately, no more than 24 hours of becoming aware of the event
	Sponsor	MHRA	Fatal/ life threatening potential – within 7 calendar days. Serious incident – within 15 calendar days. Only reportable if the event may have led to an SAE if; • suitable action had not taken • intervention had not been made if circumstances had been less fortunate

15.3 Assessments of Adverse Events

Each adverse event will be assessed for the following criteria:

Severity

Category	Definition
Mild	No or minimal interfere with daily activities; no intervention required; causes slight discomfort.
Moderate	Interferes with daily activities or requires intervention; not immediately life-threatening; causes moderate discomfort.
Severe	Results in considerable interference with daily activities, significant alteration, discomfort or clear damage to health. Note: severity ≠ seriousness. An event can be *severe* (e.g., a severe headache) but still not meet SAE criteria, while an event can be *serious* (e.g., hospitalisation for observation) without being rated severe.

Seriousness

Seriousness, as defined for an SAE in section 15.1 'Definitions'.

Causality

The assessment of relationship of adverse events to the study procedure and/ or the investigational medical device will be a clinical judgment made by the investigator, based on all available information

at the time of assessment and recorded in the case report form (HE-P-39). The following categories will be used to define the causality of the adverse event:

Category	Definition
Definitely Related	There is clear evidence to suggest a causal relationship between the adverse event and the investigational medical device and/or study procedure, and the influence of other factors is unlikely.
Probably Related	There is reasonable evidence to suggest a causal relationship between the adverse event and the investigational medical device and/or study procedure. Alternative explanations are possible but less likely.
Possibly Related	There is some evidence to suggest a causal relationship (e.g. the event occurred within a reasonable time after procedure). However, the influence of other factors may have contributed to the event (e.g. the patient's clinical condition, other concomitant events).
Unlikely Related	There is little evidence to suggest a causal relationship between the adverse event and the investigational medical device and/or study procedure. Other factors provide a more likely explanation for the event.
Not related	There is no evidence of any causal relationship between the adverse event and the investigational medical device and/or study procedure.

Expectedness

Category	Definition
Expected	An adverse event that is consistent with the known safety profile of the investigational medical device, as described in the Investigator's Brochure (HE-P-47), the CIP, or other approved reference safety information.
Unexpected	An adverse event that is not consistent with the known safety profile of the investigational medical device in terms of nature, severity, or frequency, based on the Investigator's Brochure (HE-P-47), the CIP, or other approved reference safety information.

The Investigator's Brochure (HE-P-47) will serve as the reference document for assessing the expectedness of adverse events related to the investigational device. The Clinical Investigation Plan will serve as the reference for assessing expectedness of disease-related events and/or events associated with study procedures.

15.4 Procedure for Recording and Reporting of Adverse Events and Device Deficiencies

Investigator responsibilities:

- All AEs and SAEs must be documented in the participant's medical records and in the CRF following participant's consent.
- All SAEs must be reported to the sponsor using the sponsor's SAE report form (HE-P-40) within 24 hours of the investigator becoming aware of the event.
- The Chief or Principal Investigator must complete the sponsor's SAE form (HE-P-40) and email it to the sponsor immediately (or within 24 hours) of they becoming aware of the event. The Chief or Principal Investigator will respond promptly to any sponsor queries.
- Expected SAEs that are anticipated to occur frequently and do not add new safety information may be exempt from expedited reporting to the sponsor, provided this is justified in the CIP. These events must continue to be documented in the source data and CRF.
- For control arm participants, disease-related or procedure-related SAEs may be exempt from expedited reporting to the sponsor, as specified in the CIP. These must still be documented in the CRF and medical records.
- You may choose not to report expected SAEs to the sponsor, for example, if they are expected to occur on a regular basis and offer no further new information to your safety profile. These events must continue to be recorded in the source data and CRF, however you may state that you will not complete an SAE form and forward it to the sponsor.
- All deaths will be reported to the sponsor immediately or within 24hours, irrespective of whether related to disease progression, the investigational device, or other causes.
- The investigator shall maintain detailed records of all adverse events and device deficiencies reported by trial participants and research team; The investigator shall document all relevant information on sponsor provided SAE form (HE-P-40).
- All SAEs, SADEs and USADEs should be reported to the sponsor.
- The sponsor shall maintain detailed records of all adverse events and device deficiencies reported by investigators. The sponsor shall ensure that all reportable events occurring during this clinical trial in United Kingdom are the MHRA, and the relevant RECs, in accordance with applicable requirements and within the timelines specified in section 14.2 'Safety Reporting Requirements and Timelines'. Any follow-up information shall be submitted within the same timeframe as the initial report. The sponsor shall also ensure that relevant information on reportable events with the investigational device arising in any clinical

investigation is communicated promptly to regulatory authorities, ethics committees, and investigators, in accordance with local regulations and REC requirements.

15.5 Progress Quarterly Reports

Quarterly Summary Reports will be submitted to the MHRA and, when necessary, to the REC, alongside expedited reports of individual serious adverse events. These reports will offer a comprehensive overview of all adverse events, device deficiencies, and any emerging safety issues that occurred during the previous quarter. Their purpose is to keep regulatory authorities and ethics committees informed about ongoing safety trends throughout the study.

15.6 Annual Safety Reports

An Annual Safety Report providing an update on the overall safety profile of the investigation, along with Quarterly Summary Reports, will be submitted to the MHRA and to the REC (where required), in addition to the expedited reporting of individual serious adverse events. As the study extends over two years, an Annual Report will be provided each year in accordance with HRA requirements. The following must be included in the report:

- All adverse events and device deficiencies
- Analysis of trends or emerging risks
- Any changes to the risk/benefit assessment

16 Trial Oversight and Governance

16.1 Trial Steering Committee

The Trial Steering Committee (TSC) will oversight of the trial and ensure it is conducted in accordance with the approved CIP, applicable regulations, and the principles of GCP. The TSC will comprise the Chief Investigator, Principal Investigators from each participating site, the Clinical Research Fellow, and a patient representative, as well as a statistician. The Committee will meet at least twice per year, and additionally as required, to review trial progress, safety, data integrity, and adherence to regulatory and ethical requirements.

16.2 Data Monitoring Committee

A Data Monitoring Committee (DMC) will be established to provide independent oversight of the study's conduct, participant safety, and data integrity. The DMC will comprise the CI, Research Fellow, and a Statistician or representative from the Clinical Trials Unit (CTU). The committee will meet on a 6 monthly schedule to review safety and performance data, recruitment progress, and any emerging risks. The DMC will provide recommendations regarding study continuation, modification, or termination as appropriate. All DMC activities and decisions will be documented and reported to the sponsor.

16.3 Site Initiation Visit

All trial sites will have an initiation visit conducted by the sponsor team prior to the start of the trial. During this visit, face-to-face and/or online training will be provided to the research team. The site initiation visit will allow the sponsor to confirm whether the trial sites are ready to commence the trial.

16.4 Trial Site Activation

Before a clinical trial site can be activated, several critical steps must be completed to ensure the site is fully prepared to conduct the study in accordance with the CIP, GCP, and applicable regulatory requirements. Proper site activation is essential to safeguard participant safety, maintain data integrity, and ensure the trial is conducted efficiently and consistently across all sites.

16.5 Monitoring, Audits and Support Activities

Several monitoring and support activities will be implemented to assist the trial sites and ensure high-quality, compliant trial conduct. These include regular site visits, training, CIP and data quality reviews, SAE management, participant recruitment & compliance reviews, and Investigator meetings.

By actively engaging in these activities, the sponsor ensures that trial sites have the necessary guidance and resources to conduct the trial effectively, ethically, and in compliance with regulatory standards.

17 Trial Risk Assessment and Management

17.1 Risk Assessment Statement

Risk management for this clinical investigation has been performed in accordance with ISO 14155:2020 and ISO 14971:2019 (Application of Risk Management to Medical Devices), alongside institutional operating procedures and policies at the lead site (Guy's & St Thomas' NHS Foundation Trust) and participating trial sites.

A risk management file has been established, following ISO 14971 methodology, to systematically identify hazards, estimate and evaluate associated risks, implement control measures, and monitor their effectiveness throughout the study. The risk management file is maintained as a living document and is available for review by investigators, the sponsor, and regulatory authorities. Based on current assessment, no unacceptable risks have been identified that would compromise the safety or well-being of participants or the integrity of the investigation.

17.2 Investigational Device and Clinical Procedure Risks

The investigational device (a transcutaneous electrical nerve stimulation) has been assessed for risks in line with ISO 14971 Identified risks include:

- Local skin reactions at electrode sites (e.g., redness, itching, rash).
- Transient discomfort or intolerance to electrical stimulation, particularly during initial titration.
- Potential interference with sleep onset, if stimulation is perceived as intrusive.
- Device-related operational risks, such as battery depletion, electrode detachment, or user error.

These risks have been mitigated through device design safeguards, written instructions (user's manual and quick start guide), clinical trial support documents and structure, research team was trained on how use the device. Additionally, the IFU (HE-P-33) claim the hydrogel pads are intended for single-use or and participants are instructed to clean the device after each use. All foreseeable risks and their management strategies are explained to participants during the informed consent process.

17.3 Clinical Investigation Process Risks

Risks associated with the clinical investigation process itself include:

- Recruitment and retention risks, which may impact statistical power and study outcomes validity;
- Insufficient staff, which may impact recruitment rate and delay with administrative tasks;
- Non-compliance with device use, potentially affecting data quality and reliability;
- Investigational medical device performance;
- Confidentiality risks, due to the collection and storage of sensitive health data.

Control measures include investigator and research training, ongoing monitoring of adherence, participant support throughout the study, strict compliance with GCP and refreshment training if required, and all data can identify participants will be anonymised.

17.4 Risk-Benefit Statement

Based on the completed risk assessment, all identified risks are considered low and manageable with appropriate control measures. The investigational TENS device is non-invasive, reversible, and user-controlled, and carries a lower safety burden than standard treatment CPAP therapy, which is often associated with adherence challenges.

Potential benefits of participation include:

- Improved control of obstructive sleep apnoea symptoms.
- Reduction in snoring and sleep disruption.
- Enhanced quality of life through improved daytime functioning and sleep quality.

Given the low risk profile of the device and the safeguards in place, the overall anticipated benefits to participants and to future patients outweigh the foreseeable risks of participation in this study.

17.5 Quality Control and Quality Assurance

The study TESLA-MICRON will be conducted in accordance with the principles outlined in the Declaration of Helsinki and in compliance with ISO 14155:2020 – Clinical investigation of medical devices for human subjects – Good Clinical Practice. All trial-related activities will be carried out under the requirements of the UK Medical Devices Regulations 2002 (as amended), the UK Policy Framework for Health and Social Care Research, and all other applicable regulatory guidance for medical device investigations.

Quality control procedures will be implemented at every stage of the study to ensure data integrity, participant safety, and adherence to the CIP. The trial Sponsor is responsible for establishing and

maintaining systems for monitoring, auditing, and quality assurance. This includes routine monitoring visits, data review, and periodic audits to confirm compliance with the protocol, Good Clinical Practice, and regulatory requirements. Any findings will be documented, and corrective or preventive actions will be implemented promptly.

All handling of personal data within the trial will comply with the Data Protection Act 2018 and the UK GDPR, ensuring confidentiality, security, and lawful processing of participant data. Participants' identifiable data will remain at the trial sites and will not be accessible to the Sponsor. In accordance with the Mental Capacity (Amendment) Act 2019, specific provisions will be followed when involving participants who may lack the capacity to provide fully informed consent, ensuring that their rights, dignity, and welfare are protected.

Quality assurance activities will extend to ensuring that trial documentation, investigational device accountability, and reporting processes meet all applicable standards. All deviations, serious breaches, and safety concerns will be reported in line with the CIP, relevant international and national regulations and the regulations mentioned above. This comprehensive framework is designed to maintain the highest scientific, ethical, and regulatory standards throughout the conduct of the TESLA-MICRON trial.

17.6 Protocol Deviations and Serious Breaches

A deviation is defined as any departure from the principles of GCP in connection with the trial, or from the CIP, as amended from time to time. The Investigator shall not deviate from the CIP except where necessary to protect the rights, safety, or well-being of participants, or to preserve the scientific integrity of the investigation. All CIP deviations shall be documented in a site-specific Deviation Log (HE-P-14), maintained throughout the trial and shared with the Sponsor after each cohort. Deviations will be included, as applicable, in the final study report.

The Sponsor must notify relevant parties and regulatory authorities in writing within seven calendar days of becoming aware of any significant deviation that may impact participant or staff safety, or compromise the quality, integrity, or scientific value of the trial data. Serious breaches must be immediately recorded in the Deviation Log and reported without delay to the Sponsor.

Suspected trial-related serious breaches of GCP and/or the CIP must also be promptly reported to the Trials Office. Sites are required to cooperate fully with investigations, providing sufficient information for reporting to the MHRA (where applicable), and implementing any corrective or preventive actions.

Sites demonstrating serious or persistent non-compliance with the CIP, GCP, or inadequate recruitment performance may be suspended from further recruitment. Major issues identified during monitoring

must be reported to the TMG, TSC, the site's R&D department, and the REC. All confirmed serious breaches must also be reported to the REC and the MHRA, with copies of the relevant documentation provided to the Sponsor.

17.7 Premature termination or temporary halt of clinical investigation

In accordance with Regulations 16(11) and 29(10) of the UK MDR 2002, the Sponsor is legally obligated to promptly notify the MHRA if a clinical investigation is suspended or terminated prematurely, providing the reasons for the action. A suspension refers to a temporary pause in participant enrolment or trial activities, with the intention to resume once issues have been resolved. A premature termination (or temporary halt) refers to a formal decision to stop the investigation, either permanently or temporarily, which may or may not be followed by a restart. If suspension or termination is due to participant safety reasons, the Sponsor must notify the MHRA within 7 days; if for other reasons, notification must be made within 15 days. The Sponsor must also inform the REC, HRA, and participating sites, and ensure that appropriate measures are taken to safeguard participants.

18 Definition of End of Study

The end of the study will be defined as the date on which the final participant completes their final study visit, including the three-month follow-up assessment and repeat overnight sleep study, and all required study data have been collected.

Following completion of participant follow-up, study data will be reviewed, cleaned, and analysed in accordance with the statistical analysis plan. The study will then be formally closed in line with the approved protocol, regulatory requirements, and Sponsor procedures.

The MHRA and REC will be notified within 90 days of the end of the study. All study records will be retained and archived in accordance with section 20 of the clinical investigation plan.

19 Publication Policy

The data from the study will be published in national and international, peer-reviewed, high-impact factor journals by the research team. Results will also be presented at relevant conferences (e.g., BTS, ERS, ATS) in poster or spoken form, as agreed. For this purpose, the participating sites' principal

investigators, the chief investigator, and the research fellow, as well as the relevant members of the TPC and DMT (statisticians, patient representatives), will be named as co-authors (on behalf of the TESLA-MICRON investigators). Regardless of the outcome of the trial, the results will be published.

20 Record Retention and Archiving

20.1 Essential Documents

Archiving of essential trial documents will be authorised by the Sponsor following submission of the End of Study Report. The Chief/Principal Investigators, in accordance with their NHS Trust policy, will be responsible for ensuring that all essential documents (e.g., protocol, approvals, monitoring reports, correspondence, Trial Master File, Investigator Site File) are securely archived. These will be retained for a minimum of 15 years after trial completion, in line with ISO 14155, the NHS Records Management Code of Practice, and Sponsor requirements. Essential documents must be stored in a secure physical or validated electronic archive, with controlled access, and remain readily available for inspection by the Sponsor, the MHRA, or other authorised bodies.

20.2 Destruction

No essential documents or data will be destroyed without prior written authorisation from the Sponsor.

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Appendices

1. Schedule of Investigations

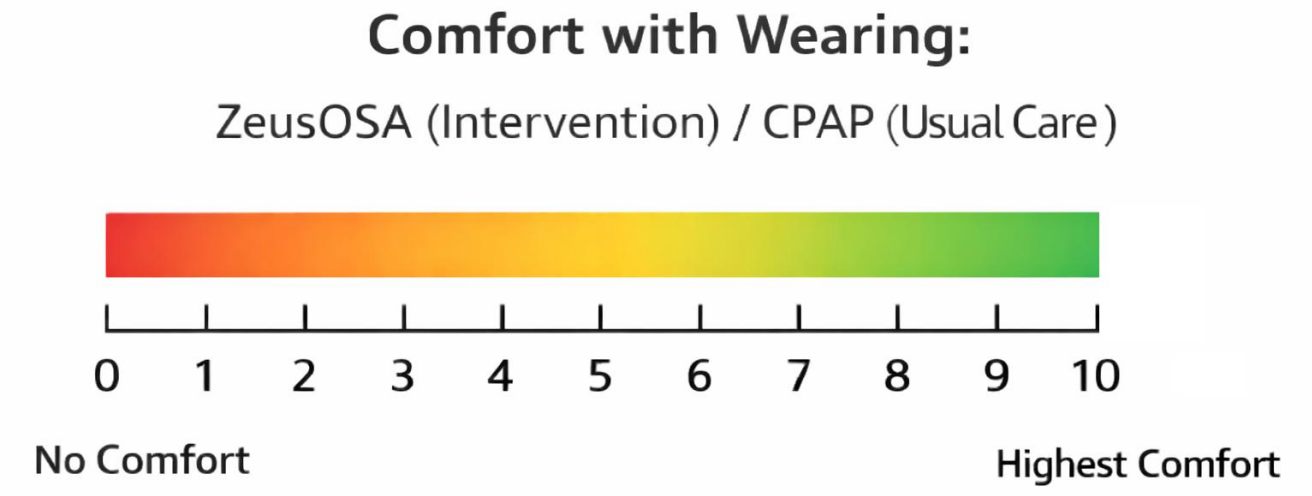
		TIMEPOINT			
		SCREENING	BASELINE (face-to-face)	6-WEEK (telephone call)	3-MONTH (face-to-face)
STUDY PROCEDURE/ ASSESSMENT	Patient Information Sheet	✓	✓		
	Informed Consent		✓		
	Eligibility Check	✓	✓		
	Randomisation		✓		
	Demographics		✓		
	Vitals and anthropometric measurements		✓		✓
	Sleep Study (watchPAT, at home)		✓		✓
	Education / Training (intervention/usual care)		✓		
	Epworth Sleepiness Scale (ESS)		✓	✓	✓
	Functional Outcomes of Sleep Questionnaire (FOSQ-10)		✓		✓
	European Quality of Life Questionnaire (EQ-5D-5L)		✓		✓
	Usage & Compliance (intervention/usual care)			✓	✓
	End of Trial				✓

- **Data Management:** Continuous throughout the study. All data are handled per NHS Information Governance, Good Clinical Practice, General Data Protection Regulation, Data Protection Act 2018 and Sponsor internal policies and procedures. Data used for analysis will be pseudonymised.

- **Adverse Event Monitoring:** At each contact (from consent until end of trial).

2. Comfort Comparison Between Interventions

Visual Analogue Scale assessing patient-reported comfort with **ZeusOSA (intervention)** and **CPAP (usual care)**. The scale ranges from 0 (No Comfort) to 10 (Highest Comfort).



3. Retention Schedule for Essential Documents and Data

Category	Examples	Retention Period	Responsible Party	Notes
Trial Master File (TMF)	Protocol, amendments, approvals, correspondence, monitoring reports	15 years after trial completion	Sponsor	Must be secure and inspection-ready (MHRA, regulatory authorities).
Investigator Site File (ISF)	Delegation logs, local approvals, patient-facing documents, correspondence	15 years after trial completion	Chief Investigator/ NHS Site Trust	Retained locally per Trust archiving policy; Sponsor oversight required.
Case Report Forms (CRFs)	Completed electronic/paper CRFs, query logs	15 years after trial completion	Chief Investigator/ Sponsor	May be electronic or paper; must remain auditable.
Source Data (copies, if held)	Laboratory reports, imaging, clinical notes (if copies retained separately)	15 years after trial completion	Chief Investigator/ NHS Site Trust	Originals remain in NHS medical records (retained as per NHS policy).
Clinical Database	Raw datasets, cleaned datasets, audit trails	15 years after trial completion	Chief Investigator/ Sponsor	Must be retained in secure, validated electronic archive.
Statistical Outputs	Tables, listings, figures, statistical analysis code and reports	15 years after trial completion	Sponsor/ Statistician	Required for regulatory inspection and future submissions.
Final Study Report	End of Study Report, lay summary	15 years after trial completion	Sponsor	Submitted to regulators and NIHR; archived for inspection.
Regulatory Submissions	MHRA/REC submissions, approvals, correspondence	15 years after trial completion	Sponsor	Needed to demonstrate compliance and traceability.
Patient Medical Records (NHS)	Signed consent forms, clinical notes within NHS systems	Per NHS Records Management Code (typically 15 years for CTIMPs)	NHS Site Trust	Governed by NHS retention policy; not controlled by Sponsor.

4. Related Documentation

ID Code	Document Name
HE-P-01	Device Description
HE-P-15	Summary of all clinical experience with the device to date
HE-P-33	User Manual
HE-P-37	Participant Information Sheet
HE-P-38	Participant Consent Form
HE-P-39	Case Report Form
HE-P-40	Adverse Event and Device Deficiency Reporting Form
HE-P-47	Investigator's Brochure

5. Version Control

Version No.	1
Date	03/12/2025
Author(s) (Name/Title)	Joerg Steier - Chief Investigator; Rebecca Quest - Clinical Advisor; Cristina Cacumba - Senior Regulatory Affairs & Quality Manager
Description of Changes	First version
Approved by (Name/Title)	Joerg Steier – Chief Investigator; Nigel Clarke – CEO at Zeus Sleep Ltd.

Version No.	2
Date	19/01/2026
Author(s) (Name/Title)	Cristina Cacumba – Senior Regulatory Affairs & Quality Manager
Description of Changes	ClinicalTrials.gov ID added; reference to ISRCTN removed; Principal Investigators' details added; yellow highlights removed; references to the ZeusOSA app and portal images removed.
Approved by (Name/Title)	Joerg Steier – Chief Investigator

Version No.	3
Date	05/03/2026
Author(s) (Name/Title)	Salma Ayis – Statistician; Joerg Steier – Chief Investigator; Aicha Goubar – Fellow Statistician

Description of Changes	• Section 1: A previously defined primary outcome relating to AHI response thresholds has been reclassified as a secondary outcome: "A response to the intervention will be defined as a reduction of more than 50% in the AHI (from baseline), the AHI below 20/hour (SHER20), below 15/hour (SHER15) or a normalisation of the AHI (less than 5/hour)". • Section 4.2: Added screenshots of the ZeusOSA app and an image of the main screen of the clinician portal. • Section 5.2: Added a note directing readers to the ClinicalTrials.gov registration for detailed information on the secondary outcomes. • Section 8.5.2: Added a reference to the Visual Analogue Scale in the Appendix. • Section 10.2: The statistical analysis plan was revised to strengthen the primary outcome analysis by introducing ANCOVA adjusted for baseline AHI at 3 months and clarifying between-group comparisons, improving methodological robustness and alignment with a parallel-group design. • These changes improve methodological robustness and alignment with a parallel-group study design. • Appendices: Added a Visual Analogue Scale". Comfort Comparison Between Interventions"
Approved by (Name/Title)	Joerg Steier – Chief Investigator; Nigel Clarke – CEO at Zeus Sleep Ltd.

Version No.	4
Date	30/05/2026
Author(s) (Name/Title)	Joerg Steier – Chief Investigator; Cristina Cacumba – Senior Regulatory Affairs & Quality Manager
Description of Changes	The following sections have been reviewed and updated: • Administrative Information: Clarified that six NHS Trusts are participating in the trial, with a total of seven recruitment sites. • Section 1 – Overall Synopsis of the Clinical Investigation: Updated eligibility criteria (overview) and participating trial sites. • Section 4.2.3 – ZeusOSA Secure Server: Updated to reflect current system description and functionality. • Section 6 – Study Schema: Revised to improve clarity and reflect the current study design. • Section 7.3.1 – Inclusion Criteria: Updated for clarity, consistency, and alignment with study objectives. • Section 7.3.2 – Exclusion Criteria: Updated for clarity and to remove duplication with inclusion criteria. • Section 8.4 – Baseline Assessments: Updated to include relevant clinical and anthropometric measurements. • Section 8.5.1 – Randomisation and Home Treatment: Added reference to participant PIN number for device use. • Section 9.2 – Data Handling and Record Keeping: Updated to reflect current data management processes. • Section 10.2 Blinding of Statistical Analysis: new section.

	• Section 11.1 – Health Economics Analysis (Overview): Revised to remove references to lifestyle modifications and focus on the investigational device and standard care (CPAP). • Appendix 1: Schedule of Investigations Table: Demographic data and vital signs were separated into distinct procedures; anthropometric measurements were added. • Appendix 2: Comfort Comparison Between Interventions Graphic: Updated to correct the scale and remove duplication of the value "10". • Appendix 3: Retention Schedule for Essential Documents and Data
Approved by (Name/Title)	Joerg Steier – Chief Investigator

Version No.	5
Date	07/05/2026
Author(s) (Name/Title)	Joerg Steier – Chief Investigator; Cristina Cacumba – Senior Regulatory Affairs & Quality Manager; Jonathan Belsey – Health Economist
Description of Changes	The following sections have been reviewed and updated: • Section 6 – Study Schema: Updated to include the approach of potential participants who are registered in the NIHR Be Part of Research platform. • Section 8 – Study Procedures: Updated to include the approach and inclusion of potential participants who are registered in the NIHR Be Part of Research platform. • Section 11 – Health Economics Analysis: Revised to emphasise that the comparator is CPAP with low adherence vs the intervention device (ZeusOSA).
Approved by (Name/Title)	Joerg Steier – Chief Investigator

Version No.	6
Date	13/05/2026
Author(s) (Name/Title)	Cristina Cacumba – Senior Regulatory Affairs & Quality Manager
Description of Changes	The following sections have been updated and included: • Administrative Information table: Added REC's details. • Section 18 – new section, which covers the definition of the end of study.
Approved by (Name/Title)	Joerg Steier – Chief Investigator

Version No.	7
Date	18/05/2026
Author(s) (Name/Title)	Cristina Cacumba – Senior Regulatory Affairs & Quality Manager
Description of Changes	The following section has been updated:

	• Administrative Information table: Updated REC details following transfer of the application from the previous REC to West of Scotland REC 4.
Approved by (Name/Title)	Joerg Steier – Chief Investigator

Version No.	8
Date	10/06/2026
Author(s) (Name/Title)	Cristina Cacumba – Senior Regulatory Affairs & Quality Manager
Description of Changes	The following sections have been updated: • Sections 1. Overall Synopsis of the Clinical Investigation / Section 8.4 Baseline Assessments / Section 8.5.2 Subsequent Assessments: Clarified collection of resource use data at both the 6-week and 3-month assessments. • Overall Synopsis of the Clinical Investigation / Section 8.4 Baseline Assessments / Section 8.5.2 Subsequent Assessments: Updated terminology from "Spouse" to "Partner" for snoring assessments. • • Section 3.2 Study Rationale: Updated wording relating to cardiovascular risk reduction to ensure consistency with the study objectives and endpoints, clarifying that cardiovascular outcomes are not being assessed in this clinical investigation. • Section 4.1 Identification and Description of Investigational Medical Device: Updated the device description following MHRA feedback to harmonise terminology relating to the mechanism of action and clarify that ZeusOSA is a non-implantable TENS device • Section 4.2.1 ZeusOSA Mobile Application: Updated application screenshots to include the trial logo. • Section 5.1.2 Secondary Objectives: Removed Secondary Objective (d). • Section 7.3.1 Inclusion Criteria: Updated Inclusion Criterion 2 to further define CPAP usage requirements, including duration and frequency of use. • Section 7.3.1 Inclusion Criteria: Corrected numbering of Inclusion Criterion 6. • Section 7.3.1 Inclusion Criteria / Exclusion Criteria: Removed Exclusion Criterion 8 due to duplication with Inclusion Criterion 6. • Section 7.3.4 Criteria and Procedures for Subject Withdrawal or Discontinuation: Added a clear definition of treatment adherence for the per-protocol analysis population. • Section 8.4 Baseline Assessments: Added collection of smoking history, alcohol intake and recreational drug use data. • Section 8.4 Baseline Assessments: Updated terminology from "Gender" to "Sex at Birth". • Section 8.5.1 Randomisation and Home Treatment: Clarified that the participant identification number (PIN) is generated by the EDC system at participant registration and subsequently entered into the randomisation system. • Section 8.5.2 Subsequent Assessments: Clarified that VAS assessments will be conducted at both 6 weeks and 3 months.

	• Section 9.1 Source Data and Data to be Collected: Clarified that only concomitant medications will be collected. • Section 9.2 Data Handling and Record Keeping: Updated data controller and archiving responsibilities. • Section 9.5 Confidentiality: Updated the participant identification process to clarify that participants are assigned a unique Participant Identification Number (PIN) by the Medrio EDC system upon registration by the study site following enrolment. • Section 10.2 Statistical Analysis Plan: Added clarification regarding blinding of the statistician to treatment allocation. • Section 15.3 Assessments of Adverse Events: Updated adverse event relationship categories. • Appendix 3 – Retention Schedule for Essential Documents and Data: Updated the responsible party for the Clinical Database to clarify that the Sponsor and Chief Investigator are responsible for the retention and archiving of raw datasets, cleaned datasets, and audit trails following study close-out.
Approved by (Name/Title)	Joerg Steier – Chief Investigator

Version No.	9
Date	08/07/2026
Author(s) (Name/Title)	Cristina Cacumba – Senior Regulatory Affairs & Quality Manager
Description of Changes	The following sections have been updated: • Section Administrative Information / Section 2 Trial Personnel: Added the details of the Research Fellow. • Section Overall Synopsis of the Clinical Investigation / Section 7.3.2 Exclusion Criteria: Updated terminology from "patches" to "pads" to align with the terminology used by the trial sponsor and ensure consistency across all clinical investigation documents and the protocol. • Section 6 Study Schema: Updated the study schema to include references to the ZeusOSA portal in Actions 6 and 7. • Section 8.4 Baseline Assessments: Updated the respiratory polygraphy (WatchPAT) sleep study parameters to include Hypoxic Burden, with a minimum value of 0, maximum values of 720 (total sleep time) and 120 (per hour), and one decimal place. • Section 8.4 Baseline Assessments: Added Index of Multiple Deprivation (IMD) Decile as a baseline assessment. • Section 8.4 Baseline Assessments: Added Endotype (optional) as a baseline assessment.
Approved by (Name/Title)	Joerg Steier – Chief Investigator

Version No.	10
Date	07/08/2026
Author(s) (Name/Title)	Cristina Cacumba – Senior Regulatory Affairs & Quality Manager

Description of Changes	The following sections have been updated: • Section Administrative Information: Charing Cross Hospital was replaced with Imperial College Healthcare NHS Trust, as requested by the site's Research & Development department. • Section Administrative Information: Queen Elizabeth Hospital Birmingham was replaced with University Hospitals Birmingham NHS Foundation Trust, as requested by the site's Research & Development department. • Section Administrative Information: Updated the title of Professor Salma Ayis, Statistician, to reflect her recent promotion to Professor. • Section Administrative Information: Added the details of the Lead Research Nurse. • Section 1 Overall Synopsis of the Clinical Investigation: Updated two participating trial sites as requested by their Research & Development departments: Charing Cross Hospital was replaced with Imperial College Healthcare NHS Trust, and Queen Elizabeth Hospital Birmingham was replaced with University Hospitals Birmingham NHS Foundation Trust. • Section 2 Trial Personnel: Added the details of the Lead Research Nurse. • Section 2 Trial Personnel: Updated the title of Professor Salma Ayis, Statistician, to reflect her recent promotion to Professor. • Section 8.4 Baseline Assessments: Added Arousal Index (events/hour) as a baseline sleep study parameter. • Section 8.5.2 Subsequent Assessments – Follow-up at 3 Months: Added the following assessment parameters: Average CPAP pressure used (cmH_2O). Average level of Zeus stimulation used over the study period.
Approved by (Name/Title)	Joerg Steier – Chief Investigator