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Mandibular advancement device plus continuous positive airway pressure: does combining two established treatments for obstructive sleep apnoea give added benefits?

Submission date
17/11/2021

Recruitment status
No longer recruiting

Registration date
18/02/2022

Overall study status
Ongoing

Last Edited
27/02/2025

Condition category
Nervous System Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Obstructive sleep apnoea (OSA) is a condition in which the walls of the throat relax and narrow during sleep, interrupting normal breathing. Continuous positive airway pressure (CPAP) machines can be used to treat sleep apnea by delivering a stream of air into the airways through a mask and a tube. A mandibular advancement device (MAD) is a treatment method that works by temporarily moving the jaw and tongue forward, which reduces throat constriction and prevents sleep apnea. This study will test the effectiveness of combining MAD with CPAP therapy, compared with CPAP only therapy, for the treatment of OSA. Some patients have difficulty using CPAP as they require a higher pressure than they can easily tolerate, making CPAP more difficult to sleep with and increasing the risk that they will abandon therapy entirely. Combining MAD with CPAP could potentially open the airway enough to allow CPAP pressure to be reduced, making CPAP therapy more comfortable and increasing the likelihood that patients will continue with their treatment. If the new 'combination therapy' is shown to be effective it could fairly easily be introduced into the NHS as an additional tool for helping patients to use CPAP successfully.

Who can participate?
Patients with moderate to severe OSAS

What does the study involve?
Participants will be given a MAD moulding kit to take home with full instructions including how to send the mould to the manufacturer. Once the MAD device has been produced and returned to Papworth Hospital by the manufacturer research visit 1 will take place. At this visit the participant will be randomly allocated to receive standalone CPAP therapy or CPAP plus MAD and will be switched to auto-CPAP (CPAP that automatically adjusts pressures settings as required). They will also be asked to complete some questionnaires. Participants allocated to the combination treatment will be given their MAD and will start their 10-week treatment after 2 weeks of acclimatisation. They will also be given instructions to complete a sleep diary.

Participants allocated to CPAP only will be asked to initiate auto-CPAP treatment straightaway for 10 weeks. During the treatment period participants will be telephoned to check if there are any issues and to check progress. They will also be sent a Watchpat device to use for a one-night sleep study at home during the final week of treatment. Following completion of the first treatment period, participants will attend research visit 2 (alternatively this can be conducted remotely) when they will be crossed over to the other treatment group. The Watchpat device will be returned (either in person or via post) and study questionnaires will be completed again. Those starting the combination treatment will be given/posted their MAD and asked to initiate their 10-week treatment following 2 weeks of acclimatisation, and to complete the sleep diary. Those starting the standalone CPAP treatment will be asked to return their sleep diary and to immediately stop using the MAD and start 10-week treatment of CPAP only
During the second treatment period the participants will be telephoned again to check if there are any issues and to check progress. As in treatment period 1, participants will be sent a Watchpat device to use for a one-night sleep study at home during the final week of treatment. At the end of the second treatment period the participant will attend research visit 3 - either face to face or remotely. The Watchpat device will be returned and the study questionnaires completed. Participants who were on the combination therapy for the second treatment period will be asked to return their sleep diary for treatment period 2. Clinical review and discussion about continuing with CPAP or combination treatment will then take place.

What are the possible benefits and risks of participating?
There is no guarantee of any benefit by participating in this study, though if the use of combination therapy is found to be successful in the treatment of OSA this could be continued after the patient's participation in the study. It is not anticipated that the risks to the participants will exceed current use from using CPAP or MADS, for example, excessive salivation during sleep and jaw pain

Where is the study run from?
Royal Papworth Hospital (UK)

When is the study starting and how long is it expected to run for?
August 2021 to September 2025

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
Dr Tim Quinnell
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
296163

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 49261, IRAS 296163

Study information

Scientific Title
Positive Airway Pressure plus Mandibular Advancement Therapy (PAPMAT)

Acronym
PAPMAT

Study objectives
Combining mandibular advancement device (MAD) with continuous positive airway pressure (CPAP) therapy improves adherence in patients who require a high pressure on CPAP therapy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 02/08/2021, East of England – Cambridgeshire and Hertfordshire Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 (0)20 7104 8096; cambsandherts.rec@hra.nhs.uk), REC ref: 21/EE/0125

Substantial amendment to add Bristol Royal Infirmary as a study site approved 24/11/2023

Study design
Randomized; Interventional; Design type: Treatment, Device

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Obstructive sleep apnoea

Interventions
Recruitment:
Patients attending a clinical appointment for initiation of CPAP who meet the inclusion criteria will be approached during their appointment. A member of the research team will explain the trial and give the patient the relevant documentation. At the CPAP follow-up clinic appointment (approx. 6 weeks after the first appointment) written informed consent will be obtained (participants will be advised that they are able to withdraw from the study at any point with no impact on their routine NHS care).
Participants will be given a MAD moulding kit to take home with full instructions including how to send the mould to the manufacturer.
The research team will telephone the participant 1 week following consent to check on their progress with the moulding kit.
Once the MAD device has been produced and returned to Papworth Hospital by the

manufacturer, the research team will telephone the participant to check they are still happy to proceed. An appointment will then be made for the participant to return to Royal Papworth Hospital for research visit 1.

Research Visits:

Visit 1
The participant will be randomised to receive standalone CPAP therapy or CPAP plus MAD and will be switched to auto-CPAP. They will also be asked to complete the following questionnaires:
1. Epworth Sleepiness Scale (ESS)
2. Functional Outcomes of Sleep Questionnaire (FOSQ)
3. Pittsburg Sleep Quality Index
4. Short Form 36 Health Survey Questionnaire (SF36)
5. EuroQol-5D (EQ5D)
BP and weight will also be recorded

EITHER
Participants randomised to the combination treatment will be given their MAD and be asked to initiate their 10-week treatment following 2 weeks of acclimatisation. They will be given instructions to complete the sleep diary (electronically or on paper) every day.
OR
Participants randomised to CPAP only will be asked to initiate auto-CPAP treatment straightaway for 10 weeks. No sleep diary is required for this treatment arm.
During their treatment period the participant will be telephoned to check if there are any issues and to check progress. Participants will also be sent a Watchpat device to use for a one-night sleep study at home during the final week of treatment. A pre-paid envelope will be provided to return the device if the patient is unable to attend the next research visit in person.

Visit 2 - cross over to alternative treatment arm
Following completion of the first treatment period, participants will attend a second research visit. It is not essential for this to be a face to face visit as it could be done remotely. BP and weight will be recorded, if possible. The participant will be crossed over to the second treatment arm. Those starting the combination treatment will be given/posted their MAD and asked to initiate their 10-week treatment following 2 weeks of acclimitisation, and to complete the sleep diary. Those starting the standalone CPAP treatment will be asked to immediately stop using the MAD and start 10 week treatment of CPAP only, and return their sleep diary. The Watchpat device will be returned (either in person or via post). The study questionnaires (listed above) will be completed again (via telephone or in-person) by all participants. Automatic download of data from participants' CPAP device will take place.

During the second treatment period the participants will be telephoned again to check if there are any issues and to check progress. As in treatment period 1, participants will be sent a Watchpat device to use for a one-night sleep study at home during the final week of treatment. A pre-paid envelope will be provided to return the device in if the patient is unable to attend the third research visit in person.

Visit 3
At the end of the second treatment period the participant will attend research visit 3 - this can be face to face if it coincides with their routine CPAP follow-up clinic visit, but if not the appointment can be completed remotely. BP and weight will be recorded, if possible. Watchpat device will be returned (either in person or via post). The study questionnaires will be completed and the participants who were on the combination therapy for the second treatment period will

be asked to return their sleep diary for treatment period 2. Final automatic download of data from CPAP devices will take place.

Clinical review and discussion about continuing with CPAP or combination treatment will then take place.

Intervention Type
Device

Pharmaceutical study type(s)
Not Applicable

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Mandibular advancement device

Primary outcome measure
CPAP adherence (means hours of use per night) measured using data downloaded from CPAP device after 10 weeks of treatment

Secondary outcome measures
1. CPAP pressure measured using CPAP data download after 10 weeks
2. Control of obstructive sleep apnoea (OSA) using a peripheral arterial tonometry (PAT) oximeter sleep monitor to determine the apnoea hypopnoea index (AHI) and 4% oxygen desaturation index (4% ODI) in each arm after 10 weeks
3. Diastolic and systolic blood pressure arms measured using office-based automated measurement with patient sitting after 10 weeks
4. Patient-reported outcomes measured after 10 weeks:
4.1. Subjective daytime sleepiness measured using the Epworth Sleepiness Scale
4.2. Quality of life measured using Functional Outcomes of Sleep Questionnaire (FOSQ), EuroQoL, Pittsburgh Sleep Quality Index (PSQI)
4.3. Patient satisfaction measured using visual analogue score

Overall study start date
02/08/2021

Completion date
30/09/2025

Eligibility

Key inclusion criteria
Current inclusion criteria as of 01/05/2024:
1. Adults with moderate to severe OSAS defined by a 4% oxygen desaturation index (4% ODI) or apnoea hypopnoea index (AHI) ≥15/hour
2. An Epworth Sleepiness Scale (ESS) Score >10
3. Auto-titrated CPAP pressure of ≥12 cm water

Previous inclusion criteria:
1. Adults with moderate to severe OSAS defined by a 4% oxygen desaturation index (4% ODI) or apnoea hypopnoea index (AHI) ≥15/hour
2. An Epworth Sleepiness Scale (ESS) Score >10
3. Auto-titrated CPAP pressure of ≥14 cm water

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 64; UK Sample Size: 64

Total final enrolment
94

Key exclusion criteria
1. Inadequate dentition or other contraindication to MAD determined by a clinician or trained CPAP provider
2. Co-morbid sleep disorder that might affect the patient's ability to comply with treatment or benefit from therapy, or confound the interpretation of results
3. Unstable cardio-respiratory disease or other disorder/factor judged by the clinician to preclude trial participation due to safety concerns or significant potential to confound interpretation of results
4. Previous MAD or CPAP use
5. Other reason for an inability to comply with the trial protocol

Date of first enrolment
01/05/2022

Date of final enrolment
26/02/2025

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Royal Papworth Hospital
Papworth Road
Cambridge Biomedical Campus

Cambridge
United Kingdom
CB2 0AY

Study participating centre
University Hospital Bristol
Bristol Royal Infirmary
Marlborough Street
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BS2 8HW

Sponsor information

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Royal Papworth Hospital NHS Foundation Trust

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Sponsor type
Hospital/treatment centre

Funder(s)

Funder type
Government

Funder Name
NIHR Central Commissioning Facility (CCF); Grant Codes: NIHR201124

Results and Publications

Publication and dissemination plan

Publication: the protocol and statistical analysis plan (SAP) will be published early on in the life cycle of the study in an open-access journal. The initial publication of the study results will be published in a high impact peer-reviewed journal based in the UK due to the study's relevance to the NHS (e.g. Thorax). The health economic analyses will be included in the initial article and the intention is for a more detailed paper to follow on the cost-effectiveness model.

Dissemination: findings will be presented at relevant respiratory and sleep disorder conferences and disseminated through Tim Quinnell's links with the British Sleep Society (he is currently its President). Papworth will hold one of its participant feedback events and will produce literature for wider service users via support groups such as the Sleep Apnoea Trust Association.

No other documents will be available at this time.

Intention to publish date

04/04/2026

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be stored in a non-publicly available repository

IPD sharing plan summary

Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 3	29/07/2021	04/02/2022	No	Yes
HRA research summary			28/06/2023	No	No
Protocol article		24/06/2023	25/07/2023	Yes	No