Royal Papworth Hospital
NHS Foundation Trust

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PATIENT INFORMATION SHEET

Study Title: MAD plus CPAP: does combining two established treatments for Obstructive Sleep Apnoea give added benefits?

Short title: Positive Airway Pressure Plus Mandibular Advancement Therapy (PAPMAT)

We would like to invite you to take part in our research study. Before you decide, it is important that you understand why the research is being done and what it will involve. ***One of our team will go through the information sheet with you and answer any questions you have.*** Feel free to discuss it with others if you wish. Ask us if there is anything that is not clear or if you want more information. Please take your time to read the following information carefully and decide if you wish to participate.

1. What is the purpose of the study?

Two recommended treatments for Obstructive Sleep Apnoea (OSA) are Mandibular Advancement Devices (MAD) and Continuous Positive Airway Pressure (CPAP) therapy. CPAP therapy is the main recommended treatment for OSA, but MADs can also be successful in treating milder OSA. This study will test the effectiveness of combining these two treatments compared to just using CPAP on its own. Some patients have difficulty using CPAP as they require a higher CPAP pressure than they can easily tolerate, making CPAP more difficult to sleep with. Combining MAD with CPAP could potentially open the airway enough to allow CPAP pressure to be reduced, making CPAP therapy more comfortable. Patients may use CPAP more, increasing the chance of improving OSA symptoms. 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.

Additionally this study will collect data to examine if combination therapy can improve i) blood pressure, and ii) patient reported outcomes compared to CPAP alone. The data will also be analysed to look at patient use of resources, such as health services.

2. Why have I been invited?

You have been invited to take part in our study because you have OSA and have been referred to the Respiratory Support and Sleep Centre (RSSC) at Royal Papworth Hospital Foundation NHS Trust for CPAP therapy.

3. Do I have to take part?

No. Your participation in this study is entirely voluntary and you are under no pressure to take part.

If your CPAP pressure requirements are high enough for you to be eligible and you decide to take part we will ask you to sign a consent form. If you later change your mind, you are free to withdraw from the study at any time without having to explain why.
If you do not wish to take part in this study, the standard of care that you receive will not be affected.

4. What will happen to me if I agree to take part?
Once the optimum CPAP pressure for you has been identified at your CPAP clinical review clinic (approximately 6 weeks later) you will be consented onto the study, if you are eligible to take part. You will then be given a MAD moulding kit to take away and make an impression of your teeth at home. This is a straightforward process and we will provide packaging for you to post this impression to the company Meditas so they can manufacture your MAD.

One week after you have been given the MAD moulding kit one of the research team may telephone you to check if you have completed the moulding process. See figure 1 at the end of this information sheet for picture of a MAD.

Once the MAD device has been produced and returned to Papworth Hospital by the manufacturer, a member of the research team will telephone you to check you are still happy to proceed. The trial has three visits: for the first research visit you will attend Papworth Hospital; visits 2 and 3 can be conducted either in person or remotely, depending on circumstances

Research Visit 1

We will ask you to come to Papworth Hospital for a research appointment when you will be randomly selected (randomised – like flipping a coin) to either:

- continue with CPAP therapy by itself OR
- start wearing a MAD with CPAP (combination treatment)

We will record your blood pressure and weight.

At this visit we will make sure that you are able to wear your MAD and CPAP mask together. We may change you to a different CPAP mask if we find that it works better for you. We will also change your machine to a slightly different model. The new model (auto-CPAP) automatically adjusts the CPAP pressure throughout the weeks that you use it, so that we can really see what wearing a MAD with CPAP does for your CPAP pressure settings. It will also allow us to monitor your CPAP pressures and usage remotely (i.e. from the hospital when you are at home). The auto-CPAP machine collects therapy data and transfers it via mobile telephone network (using 'Encore Anywhere' to search for the strongest signal to transfer the data). The data collected by your device is stored securely on a remote server that can only be accessed by authorised persons. The data will also be stored on the device and could be manually downloaded by a member of the research team when you attend Papworth for a visit. We will explain more about this at visit 2 if you are eligible for the study. You will be asked to complete some standard quality of life and sleep questionnaires, including the Epworth Sleepiness Scale (ESS) which you may be familiar with from your previous hospital visits. These questionnaires will take about 30 mins.

If you have been randomised to the combination treatment you will be given your MAD and also be given a daily sleep diary to complete. This can be completed on paper or

electronically and we will discuss the options with you. You will be asked to wear the MAD with CPAP for a period of 12 weeks (2 weeks of getting used to it (acclimatisation) and 10 weeks of so-called 'active' treatment).

If you have been randomised to CPAP only, you will be asked to use auto-CPAP treatment for 10 weeks.

The research team telephone you during this period to check your progress and assist with any issues.

Research Visit 2 (remote/in person)

You will then be switched to the other treatment; this process is referred to as cross-over. If you are switching to the combination treatment we will send/give you your MAD. If switching to the standalone CPAP treatment you will be asked to immediately stop using the MAD and start 10 weeks treatment of CPAP only.

If this visit takes place in person we will record your blood pressure and weight.

We will ask you to complete the sleep questionnaires again (if this visit is not completed in person these can be done via telephone with a member of the research team, or you can complete them electronically. Thesleep diary for treatment period 1 will be returned, if applicable. Data from your CPAP device will be downloaded.

You will be telephoned during this period to check your progress and assist with any issues.

Research Visit 3 (remote/in person)

This occurs at the end of the second treatment period. This visit might coincide with your routine CPAP follow-up clinic visit, but if not it can be done remotely.

Study questionnaires will be completed (in person/electronically/via telephone) and the sleep diary for treatment period 2 will be returned, if applicable. Final download of data from your CPAP device will take place. We will record your blood pressure and weight, if possible.

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

Home sleep studies:
At the end of each treatment we would like you to complete a home sleep study. We will send you a 'Watchpat' device to wear for a single night sometime during the last week of the treatment period (as the name implies, this is a home sleep apnoea test device you wear like a wristwatch). If you are returning to Papworth in person then we will ask you to bring back the device with you. If we are due to follow up with you via the telephone we will provide an addressed envelope for the device to be returned to Papworth. Once the device has been returned to Papworth a member of the team will download the date from the device and the results will be saved into your medical records. Please see figure 2 at the end of this information sheet for a picture of a MAD and a Watchpat device.

5. Expenses and payments

You will not be paid for your participation in the study but you will be reimbursed for any travel and parking expenses.

6. What will I have to do?
You will be required to complete a sleep diary for the duration of the combined treatment period, where you will be asked to record how many hours you use the MAD for during the night, how many hours you slept for and if the MAD device fell out during the night.
You will have a choice of either electronic or a paper based version.

7. What are the alternatives for diagnosis and treatment?
You have already undergone a diagnostic sleep study or studies. You do not need any more at the moment but we will sometimes organise for you to undergo repeat sleep studies to check to see if your sleep apnoea is responding to treatment. This is part of your routine care. Your medical team will already have discussed alternative treatment options with you. The reason why you have been invited to take part in this study is because it has already been agreed with you to try CPAP therapy for your sleep apnoea and we have found that your pressure requirements are on the high side (and reach the threshold for eligibility to enter the study). However the medical team may review your treatment options with you at any stage, including at your request.

8. What are the possible disadvantages and risks of taking part?
Patients usually get on quite well with the MAD. Side effects of MAD can be dryness of mouth, excessive salivation, grinding of teeth and gum irritation. Much more rarely there can be damage to teeth but the research team will explain that to you during the consenting process. There are are no other known serious risks/harms involved in this study.

9. What are the possible benefits of taking part?
There is no guarantee of any benefit by participating in this study, though if use of combination therapy is found to be successful in the treatment of your OSA this could be continued after your participation in the study. Results from the completed study may be used to improve treatment of patients with OSA in the future.

10. What happens when the research study stops?
You will continue to receive care as standard practice.

11. What if relevant new information becomes available?
Sometimes we get new information about the treatment being studied. If this happens, your research doctor will tell you and discuss whether you should continue in the study. If you decide not to carry on, your research doctor will make arrangements for your care to continue. If you decide to continue in the study he may ask you to sign an agreement outlining the discussion. If the study is stopped for any other reason, we will tell you and arrange your continuing care.

12. What will happen if I don't want to carry on with the study?
You can withdraw from the study at any time. The questionnaires which you have already completed will be used when the data are analysed. You will continue to receive standard care.

13. What if there is a problem?
If you are concerned about any aspect of this study you should ask to speak to one of the researchers (contact details below) who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the Patient Advice and Liaison Service (PALS) (contact details below*).*

If something goes wrong (including any dental damage when using the MAD) and you are harmed during the study due to someone's negligence then you may have grounds for a legal action for compensation against the hospital involved, but you may have to pay your legal costs. The normal NHS complaints mechanisms will still be available to you.

NHS hospitals are unable to agree in advance to pay compensation for non-negligent harm (situations where no one can be blamed for what happened). However, NHS Trusts are able to consider offering an ex-gratia payment in the case of a claim.

14. Will my taking part in this study be kept confidential?
Royal Papworth Hospital NHS Foundation Trust is the legal representative/sponsor for this study based in the United Kingdom. We will be using information from you and/or your medical records in order to undertake this study and to undertake a health economic analysis. We will act as the data controller for this study; this means we are responsible for looking after your information and using it properly. To safeguard your rights, we will use the minimum personally-identifiable information possible.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained.

Where can you find out more about how your information is used?

- https://royalpapworth.nhs.uk/our-hospital/information-we-publish/privacy-request
- by contacting the Information Governance Manager/Data Protection Officer on 01223 639989 or cathwillcox@nhs.net
- www.hra.nhs.uk/information-about-patients/

Royal Papworth Hospital will use your name, NHS number and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from Royal Papworth Hospital NHS Foundation Trust and regulatory organisations may look at your medical and research records to check the accuracy of the research study. The only people in Royal Papworth Hospital who will have access to information that identifies you will be people who need to contact you to or audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.

Royal Papworth Hospital will collect information about you for this research study from your medical records. This information will include our name/ NHS number/ contact details and

health information, which is regarded as a special category of information. We will use this information for the purposes of the current research study.

Information on paper will be kept in locked filing cabinets and behind security coded, locked doors. Electronic information will be kept on computers that are protected by passwords. To safeguard your rights, we will use the minimum personally-identifiable information possible. The electronic data we store for this study will be kept on a secure, study specific database. This study specific databasewe will notcontain any details of your name or address,but will contain your date of birth linked to your study ID. Some of the study data will be transferred to our collaborating organisations/study partners, but any information about you that leaves the hospital will not be combined with other information in a way that could identify you.

The people who analyse the data collected for the study will not be able to identify you and will not be able to find out your name, or contact details. Royal Papworth Hospital NHS Foundation Trust will keep limited, identifiable information (for example date of birth) about you for up to 5 years after the study has finished. We will not keep this identifiable information about you once the data anaylsis is completed.

. When the study is reported to the funding body, published in medical journals or presented at conferences it will not be possible to identify you personally.

Representatives from regulatory authorities may need to look at your medical records and the data collected in the study to check that the study was carried out correctly. All will have a duty of confidentiality to you.

15. Involvement of the General Practitioner and dentist

Your GP will be notified of your participation. We do not routinely inform a patient's dentist they are trying a MAD; however we will provide you with a letter to give to your dentist in the event that advice is required from your dentist.

16. What will happen to the results of the research study?

Results obtained from this study may be presented in research presentations, posters and publications. When the results of this study are published, your identity will not be disclosed. You have the right to be informed of the results of this study once the entire study is complete. Research data collected from this study may or may not be used in the future.

17. Who is organising and funding the research?

The research is sponsored by Royal Papworth Hospital and funded by the National Institute for Health Research - Research for Patient Benefit programme (NIHR-RfPB).

18. Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. The study was reviewed by the East of England Cambridgeshire and Hertfordshire Research Ethics Committee and the Research and Development Department at Royal Papworth Hospital NHS Foundation Trust.

19. Further information and contact details

For further information, you can speak to the study team Clinical Trial Coordinator:

Hannah Munday
hannahmunday@nhs.net
Direct line: 01223 639716
OR
CPAP Practitioner team
Direct line: 01223 638526

Alternatively, you can speak to an independent contact:
Patient Advice and Liaison Service (PALS)
Papworth Hospital NHS Foundation Trust
Papworth Road
Cambridge Biomedical Campus
Cambridge
CB2 0AY
Phone: 01223 638896
Email papworth.pals@nhs.net

Thank you for considering taking part in this study.

If you decide to participate you will be asked to sign a consent form and will be given a copy of this information sheet and the consent form to keep.

Figure 1: MAD

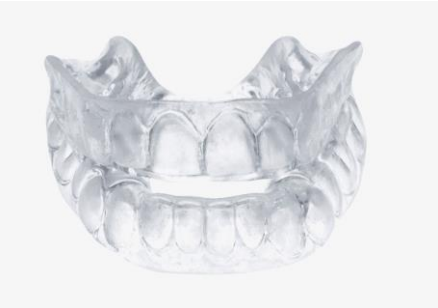

Figure 2: Watchpat Device