Study title: Can Mandibular Advancement Device Treatment For Obstructive Sleep Apnoea Reduce Nocturnal Gastro-Oesophageal Reflux: A Feasibility Study

Chief Investigator: Dr. Saoirse O'Toole, King's College London

Invitation and summary

You are being invited to participate in this research study because you have a diagnosed sleep condition (obstructive sleep apnoea). You may also have a diagnosis of gastro-oesophageal reflux disease (heartburn/reflux) or may be experiencing symptoms. The main treatment for OSA is CPAP (Continuous Positive Airway Pressure), a device which blows air down your throat while you sleep keeping the airway open. This is very effective, but patients often struggle to use it, even when they know it is saving their lives. These patients prefer a dental device called Mandibular Advancement Device (MAD), and wear it for more nights of the week and longer during sleep. Mandibular Advancement Devices have been shown to be effective for mild-moderate obstructive sleep apnoea patients.

The goal of this study is to assess whether management of your sleep condition with a mandibular advancement device affects your gastro-oesophageal reflux disease (heartburn/reflux). As this is the first time that this is being studied, we need to get information about how to best organise the trial before starting a larger clinical trial. We need to see whether this study is feasible to do. This will involve finding out whether patients want to take part, if the study testing procedures are patient-friendly and if there any ways we can improve the trial methods. Before you decide it is important for you to understand why the research is being done and what it will involve.

Please take time to read the following information carefully. Ask us if there is anything that is not clear. Talk to others about the research if you wish and if you would like to ask the research team any further questions please contact Dr Saoirse O'Toole, the chief investigator of this trial, by e-mail Saoirse.otoole@kcl.ac.uk. You can also call the Oral Clinical Research Unit on 0207 848 54128 and the study nurse will be available to answer any questions.

What's involved?

This study is looking to help with two serious problems that patients often suffer from at the same time: Obstructive Sleep Apnoea (OSA) where parts of the airway collapse during sleep, stopping the sufferer from breathing until they wake themselves up, and gastro-oesophageal reflux disease (GORD) where stomach acids backtrack into the mouth causing pain, chronic cough, sore throat and tooth erosion. These conditions are thought to be related which is why about 45% of people with the sleep condition also have reflux. We want to see if managing the sleep condition with a Mandibular Advancement Device (MAD) will this help to reduce the reflux. As nobody has investigated this before, we need to check if the way we recruit participants and test the devices will work. We also need to assess practical things, like if a patient can wear reflux checking devices and sleep devices at the same time. We will see if there will be any problems experienced in the patient journey of the trial and sort through any problems that may come up when multiple teams need to work together.

What would agreeing to take part involve?

The first step is to see if you are suitable to take part in the study. We need to check that you have mild-moderate obstructive sleep apnoea and gastro-oesophageal reflux before accepting you into the trial. Instead of going to separate sleep and reflux checking appointments, these tests will be combined. You will be asked to first attend our gastroenterology (gastric/stomach tract) department at Guy's Hospital. At this appointment we will:

1. Quickly check your teeth with a dental mirror to make sure that wearing a dental device during sleep is a good option for you
2. Do a standard gastric reflux test which you may have had before. This will involve passing a pH testing probe down your nose to rest just above your stomach. This probe will remain in place for 24 hours and will measure how often acid travels into your gullet/mouth
3. We will also ask you to record what you have eaten/drank while the probe is in place as this will impact on your reflux

You will then be given instructions to go to the sleep centre, a 5 minute walk away. Here you will pick up a sleep study testing device. This involves wearing a watch with a device to be worn around your finger and your chest during sleep time. You will be given instructions how to use these and a phone number will be provided to you with 24-hour support in case you have any questions.

The next day you will come back to the gastroenterology department in Guy's Hospital to get the probe taken out and give back the sleep testing device so we can analyse the results.

We will then get in touch to give you the results of both of the tests and tell you whether or not you can participate in the research. You will be asked to consider this study if you have mild-moderate obstructive sleep apnoea and a certain level of acid exposure.

If I am eligible, what would taking part involve?

We plan to recruit up to 44 participants to take part in a randomised controlled trial. "Randomised" means that you will be assigned to a study group at random without knowing in advance which group you will be in, just like flipping a coin. This means you will be randomly placed into one of two groups, 22 people will receive a mandibular advancement device (MAD) and the other 22 will receive CPAP therapy. The choice of which group you will be asked to join will be randomly decided by a computer. Therefore, you might be asked to join the group to be given either a mandibular advancement device (MAD) or continuous positive airway pressure (CPAP) therapy.

If you have been assigned to the MAD group, you will be seen by one of our specialist dentists in Guy's Hospital. They will scan your teeth to take a digital impression of your mouth to make the dental device. This will be fitted three weeks later and you will be given some time to get used to wearing and using the device at night-time.

If you have been assigned to the CPAP group, you will be seen by a specialist sleep technician who will fit you with a CPAP device. You will be given 3 weeks or more if needed to get used to wearing and using the device at night-time.

After you are happy with the device after becoming used to it and we think it is working well for you (a minimum of 3 weeks), we will repeat the gastric reflux study and sleep study. Again, you will attend the gastroenterology department at Guy's Hospital. The pH testing probe will be passed down your nose to rest just above your stomach to remain in place for 24 hours and we will ask you to eat and drink the same things that you did on the day of the first test. We will ask you to walk over to the sleep centre to get your sleep test device again. These tests will then be repeated as you wear your MAD or CPAP during sleep that night.

The next day we will ask you to come in to get the pH probe removed and give back the sleep testing device.

After we have analysed the results, you will be seen by the relevant the sleep and gastroenterology specialists and be told

1. Whether the sleep device has improved your sleep

2. Whether the sleep device has improved your reflux

We will ask you to fill in a questionnaire to tell us how acceptable the trial was and whether your quality of life improved because of the treatment.

This is the end of the study. If, at the end of the study, you would prefer to have the alternative treatment provided (either a MAD or CPAP), we will offer you this at no additional cost. Just your time and the number of appointments needed to get the treatment right for you.

What will happen to me if I decide to take part?

If you agree to participate in this study, you will be asked to read this Research Participant Information Sheet and sign a Consent Form before any study procedures begin. You will be given a copy of this Research Participant Information Sheet and Consent Form to keep.

To complete this study, you will be asked to be screened to see if you can be included in the study. Information will be given to you about the study. You will be given time to ask any questions and decide if you choose to take part. If you are eligible and give consent to take part, you will have additional visits to complete the study.

1. Visit 1: (comprises of two appointments on two consecutive days 90-120 minutes in total) You will attend the gastroenterology department of Guy's Hospital. Following an explanation of the study we will ask you give signed consent to take part in this study. Your gender, date of birth and race will be recorded and a suitably qualified member of staff will take a medical history from you. The dentist will examine your mouth and then ask you a set of standard questions to make sure you can take part in the study. You will then have the pH probe inserted and instructions given to you. You will then go across to our sleep centre (5 mins walk away, wheelchair accessible) where you will be given a home sleep testing study. Instructions will be given and a 24 hour phone number if you have any questions. You will be asked to record everything you eat and drink while the probe is in position and until you return the next day as this impacts on your reflux.

You will return 24 hours later for approximately 50 minutes. You will attend the gastroenterology department where the pH probe will be removed and the sleep testing device returned. We will then analyse the data and be in touch with you over whether your obstructive sleep apnoea and gastric reflux are at the right levels to be included in the study.

2. Visit 2: (approximately 60 minutes) If you are suitable you will be randomised to receive either a dental sleep device (MAD) or CPAP therapy for your sleep condition. All participants will be asked to complete a questionnaire at the beginning of the study and at the end to see how your conditions affect your quality of life. This will take around 10 minutes. For half of the participants (randomly selected) you will be asked to go the dental department to receive a mandibular advancement device. A dentist will take a digital scan of your teeth and bite to make the device. They will give you this device 3-4 weeks later. The other half will be asked to go to a sleep technician who will fit you with a CPAP mask and give you instructions for use.

3. Visit 3 (Adjustment visits of approximately 20 minutes): For both devices (MAD and CPAP), a few adjustment visits may be needed to ensure that the device is comfortable for you to wear as you sleep and that it is effective. This may need a few additional appointments and is a normal part of standard of care.

4. Visit 4 (Three weeks after previous visit for approximately 90-120 minutes): After you and your clinical team are happy that the device is comfortable and working well for you we will ask you to come back to see if it improves your reflux and sleep. All participants will be asked to complete the same questionnaires as at the beginning of the study to see whether anything has changed since the start of the study. You will attend the gastroenterology department of Guy's Hospital. You will then have the pH probe inserted and instructions given to you. You will then go across to our sleep centre (5 mins walk away, wheelchair accessible) where you will be given a home sleep testing study. Instructions will be given and a 24 hour phone number if you have any questions. You will be asked eat and drink the same things that you ate and drank on the first day that you did the test.

5. After 24 hours (60-90 minutes) You will attend the gastroenterology department where the pH probe will be removed and the sleep testing device returned. We will ask you to fill in questionnaires about how you found the trial, if there is anything we could do to improve the experience and whether you would recommend participating in the trial. We will then analyse the data and be in touch with you whether your obstructive sleep apnoea and gastric reflux have improved. You will also be asked if you would like to stick with your assigned treatment (MAD or CPAP), or if you would like to try the alternative. If you would like to try the alternative device this will be arranged for you.

You will receive £50 for each time you undergo the pH probe and sleep testing at the beginning and the end of the study . This is to compensate you for your time and travel costs. We may ask you to partake in an additional 25 minute phone interview to see if we can get any information to further improve the study. For this, the interview will be audio-recorded and transcribed (typed up) by an external company. All audio recordings will be de-identified such that it will be impossible to recognise

you from the recording. Participants who take part in interview will receive an additional £25 to take part. If for any reason you do not complete the study, the sum you receive will be in proportion to the time you have committed to the study.

Is there anything I should or should not do?

You will be given as much time to think about this taking part in the study as needed. Normally this involves at least 24 hours to consider this project before it is started.

Once you have agreed to participate in the study, you will continue your lifestyle without any further interventions.

What are the possible benefits of taking part?

There is no direct, immediate benefit to you from taking part in this research study. However, you will receive your assessment and treatments over a shorter time period, be offered both types of treatment and have increased information over whether your sleep device also helps your reflux. You will also have helped the dental and medical profession gain a better understanding of how sleep treatments impact on gastric reflux.

What are the possible disadvantages and risks of taking part?

We do not know how easy it will be for patients to manage the gastric reflux pH testing, the sleep study and wear their device to treat their sleep condition at the same time. It has been done before but the comfort of this for patients has not been reported on. We think it will be slightly harder for those in the CPAP group as the facemask and pH probe may put pressure on the skin at night-time. However, everything will be done to make it as comfortable as possible for you. There are no lasting side effects and everything we use is standard of care and safe.

Further supporting information

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

You are free to withdraw from the study at any time without it affecting your care. You will be free to keep your sleep device and use it as part of normal standard of care.

Who is organising and funding this study?

The study is being organised by King's College London and Guy's and St-Thomas' Foundation Trust. The study is funded by the National Institute of Health Research (NIHR) as part of their Research for Patient Benefit programme.

What if relevant new information becomes available?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, Dr. Saoirse O'Toole will tell you about it and discuss whether you want to or should continue the study. If you decide to continue in the study you will be

asked to sign an updated consent form. Also, on receiving new information your treating clinician might consider it to be in your best interests to withdraw you from the study and he/she will explain the reasons why. If the study is stopped for any other reason, you will be informed why.

Informing General Practitioner

When the study has finished your participation in the study ends and you return to your own GP and Dentist for continuing care. We will write them a letter at the start and end of the study telling them you have taken part and the results at the end of the trial.

What will happen to the results of this study?

It is possible that the results of the study will be published in an internationally refereed scientific journal. Should this be the case your personal information will not be shared and it will not be possible to identify you or your own results. The protocol summary may be posted on a publicly available protocol register and that a summary of the study results will be posted on a publicly available results register.

Who has reviewed this study?

This study has been reviewed and given favourable ethical approval by a Research Ethics Committee (Nottingham 2, reference 22/EM/0157). The study has also been reviewed by the funding committee.

We have a patient group and a patient member of the research team who have contributed to the study protocol and reviewed all of these documents.

The results of this study will be used to inform whether a full clinical trial with this research question and study lay out is acceptable to patients.

Information on the Use of Data

How will we use information about you?

We will need to use information from you and from your medical records for this research project.

This information will include your initials, NHS number, name, contact details, gender, ethnicity and information about your diagnosis. The research team, consisting of UK academic partners, will use this information to do the research or to check your records to make sure that the research is being done properly. Your contact information will only be used when scheduling appointments.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead. This includes people managing the study and analysing the results.

We will keep all information about you safe and secure in password protected documents, on NHS servers and in locked offices with restricted access.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

What are your choices about how your information is used?

- You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.
- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

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

You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/
- our leaflet available from: www.guysandstthomas.nhs.uk/research/patients/use-of-data.aspx (For GSTT) and www.kcl.ac.uk/research/support/research-ethics/kings-college-london-statement-on-use-of-personal-data-in-research (for KCL)
- by asking one of the research team (contact details included below)
- by contacting the Data Protection Officer: Nick Murphy-O'Kane at DPO@gstt.nhs.uk

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to your research doctor or research nurse who will do their best to answer your questions, or contact the study's Chief Investigator, Dr. Saoirse O'Toole, Saoirse.otoole@kcl.ac.uk.

If you remain unhappy and wish to complain formally, you can do this through the Guy's and St Thomas' Patients Advice and Liaison Service (PALS) on 020 7188 8801, pals@gstt.nhs.uk. The PALS team are based in the main entrance on the ground floor at Guy's Hospital in the Tower Wing.

In the event that something does go wrong and you are harmed during the research you may have grounds for legal action for compensation against Guy's and St Thomas' NHS Foundation Trust and/or King's College London but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

Thank you for your help. If you have any further questions, please do not hesitate to ask.