The **MABEL** study:

A study about the use of morphine for the relief of chronic breathlessness.

Can you help?

(<<INSERT LOCAL TRUST LOGO>>)

We invite you to take part in a study

- Before you decide whether to take part, 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. Talk to others about the study if you wish.
- Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.
- If you have any questions, please contact us.
- Thank you for reading this information sheet.

Contact details
If you require further information about this study, you can contact one of the following:

Principal Investigator:
(<<Insert local PI details>>)

Research Nurse:
(<<Insert RN details>>)

What is the purpose of the MABEL study?

Many people with heart and lung disease have chronic breathlessness. In other illnesses small doses of morphine medication can be safely used to help breathing over a few days. We are not sure whether it helps people with heart or lung disease when used for longer. We want to test whether low dose morphine is better than a placebo (dummy medicine) at relieving breathlessness. We plan to compare morphine with placebo for 8 weeks.

What does "low dose" mean?

The daily study morphine dose is 10mg with the option of going up to 20mg for some. This is less than the dose given by other painkillers such as codeine, commonly used for e.g. arthritis (codeine is converted into morphine by the body): 2 tablets of Co-Codamol strong four times daily will give 24mg of morphine per day.

Why am I being asked to take part?

People with persistent daily breathlessness due to lung or heart disease are being asked if they would like to participate. You will have been asked by a member of your usual medical team if you would like a chance to discuss this with a member of the research team.

Do I have to take part?

No, taking part is entirely voluntary. If you decide not to participate, it will not affect the treatment you receive now or in the future. If you do take part and change your mind once it has started, you can withdraw at any time without having to give a reason. Any data collected up to the point of withdrawal will be used in the final data analysis and data about your safety will continue to be collected until the end of the study for regulatory purposes.

1 What do I have to do if I take part?

The study will last for 8 weeks and you will be required to:

- Attend clinic twice. Other assessments can be done by phone or the research nurse will visit you at home
- Take the study medication* twice a day for 8 weeks
- Complete the study questionnaires when needed (the research nurse will help you)
- Continue with any treatment your medical team advises
- Check with the study team if your GP/specialist intends to start any new medication or makes changes to your regular medication

*NOTE. The study medication contains gelatin which may not be suitable for vegetarians and people of some religious beliefs.

2 What treatment will I get?

You will be allocated to one of two treatment groups by a computer program which will decide which group you are in randomly (by chance), like tossing a coin. You will have an equal chance of being allocated to either group.

Group 1 will be given capsules of 5mg morphine to take every morning and evening. As morphine can cause constipation, this group will also receive capsules of a laxative called Docusate to take one capsule every morning and evening. You may have additional laxatives from your own doctor according to need.

Group 2 will be given capsules identical in appearance to the 5mg morphine medication, and capsules which are identical in appearance to the laxative, but which have no medical effect. Participants should take one dummy "morphine" capsule every morning and evening for the 8 weeks of the study. Participants should also take one dummy "laxative" capsule every morning and evening. You may have additional laxatives from your own doctor according to need.

Neither you nor your doctor will know which treatment you are receiving, nor will you be able to choose which treatment group you are in.

The morphine/ dummy capsules for your breathing will be one colour and the laxative/dummy capsules for your bowels will be another.

Both groups will be assessed at Week 1 to see if there is improvement in breathlessness and if the study drug has acceptable side-effects. If there is no benefit, but the side-effects are acceptable, your dose will be increased to 10mg morphine or "10mg" dummy twice daily from Week 2.

3 What will be measured?

Information about your general health will be collected at the start. The following will be measured:

Breathlessness and other symptoms

A nurse will ask about symptoms of breathlessness, pain and sleepiness 4 times over the first week and then again at weeks 2, 3, 4 and 8. The nurse will also ask you about any other problems since the last check.

If the dose increases to 10mg twice daily, week 1 checks will be repeated during the first week of the increased dose.

Level of exercise

You will be asked to wear an activity monitor around your wrist. It can be taken off and repositioned if needed. This measures the number of steps you take and the time you spend sitting or lying down. It will be worn for **7 days before the study starts** and again during the **last 7 days of the first month**.

Quality of life

You will be asked to complete some questionnaires at the start, at Week 4 and at Week 8 about how your condition affects your life.

Medical tests

If you haven't had a recent blood test to check how well your kidneys are working, this will be done. This is a routine test done as part of your medical care.

4 What will happen after the study?

- If you wish to take morphine (at the lowest study dose) at the end of the study, we can contact your own doctor and ask them to prescribe it for you if they agree. You will not be told whether you were taking dummy treatment or not at the end of the study.
- The research nurse will phone you within the first few days of finishing the study to check that all is well.
- At the end of the 8 weeks, if you agree, you can continue to give us information about how breathless you are. The research nurse will ring you every 3 months to ask until the last participant has completed the study.

5 What are the possible benefits and disadvantages of taking part in the study?

- Laxatives may cause diarrhoea or stomach cramps. If this happens the research nurse will advise you on how best to deal with this.
- Morphine has been used in medical practice for many years. We therefore know what side-effects might occur. Most patients cope very well with the low doses of morphine used in this study.
- Women of childbearing age will need to take contraception for the duration of the trial.
- Although this study may not directly benefit you, it may improve future treatment of breathlessness.
- You may find that coming to the clinic for extra visits for the research study, or completing the study assessments is tiring.
- It is recommended that you do not drink alcohol while you are taking part in the study.
- We will check regularly about the known side effects of morphine that people can get. These include nausea or feeling sick, constipation or sleepiness.
- In some people concentration may be affected until they get used to the steady dose after a few days. We therefore advise you to take special care regarding driving during the first week of taking the medicine and if you are affected, do not drive. -After this time you must still carefully consider whether your concentration is affected before driving – if in doubt, do not drive. If side-effects persist, you would need to inform the DVLA.
- As with any other change in medication, you should inform your motor insurance company to ensure cover is valid. Please note the following about taking morphine and driving:

1. Do not drive after taking your study medicines until you know how they affect you.
2. Do not drive if you feel drowsy, dizzy, unable to concentrate or make decisions, or if you have blurred or double vision.
3. If you are taking your medicine in accordance with the advice of a healthcare professional and your driving is not impaired, then you are not breaking the law.

- As most problems, if any, happen in the first week of use, our research nurse will phone you several times during the first week (and the first week of a dose increase if that applies) to see how you're getting on. You will be able to contact a member of the study team if you are concerned.
- Morphine and morphine-like medications can cause addiction; this is unusual in people who take this type of preparation, and this low dose for health reasons. However, if the body has become accustomed to morphine over time, then it may take a few days to readjust when morphine is stopped. We do not expect this to be an issue in this study but all participants completing the 8 weeks will receive a phone call in the few days after the end of the study to complete a questionnaire to check all is well.
- If you wish to read about the study medication side-effects of morphine in more detail, you may do so in the accompanying list of known side-effects. You can read more detail about the laxative in the accompanying laxative drug information sheet.
- The study has been designed to minimise your risk of exposure to COVID-19 infection by giving you the option to have all your study visits, including study medication delivery, at home, over the phone or video call. This study will follow national guidance on social distancing at all times

6 Carer participation in the study

As part of this study we would like to gather more information from your carer about their experience of living with someone with chronic breathlessness. If you would like to nominate someone who cares for you, we will invite them to give their consent to complete a short questionnaire at the start and at 2,4 and 8 weeks.

If in the unlikely event that you should die whilst on the study, the research nurse may contact your nominated carer a few months later to ask if they would be willing to complete an additional questionnaire about their views on the healthcare you received. We appreciate this will be a difficult time for your carer and they will be totally free to decline if they so wish.

7 More information about taking part

Will taking part in this study cost me anything, and will I be paid?

Participation in this study will not cost you anything and there will not be any payment for taking part. Reasonable expenses will be reimbursed for clinic visits.

What if relevant new information becomes available?

If new information about the study medication becomes available during the study, your research doctor will tell you about it and discuss continuing in the study. If you decide not to carry on, your care will be continued outside of the study. If you decide to continue in the study, you will be asked to sign an updated consent form.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak with the researchers who will do their best to answer all your questions: contact your local research team [INSERT *name / telephone number].*

If you have any concerns or complaints about the way the researcher has carried out this study, or any other aspects of your care, you may contact:
[INSERT *local information, e.g. Patient Advice Liaison Service / contact details]*

In the unlikely event that something does go wrong and you are harmed as a result of the research study the normal NHS complaints mechanism will still be available to you if appropriate.

Will my GP be notified of my participation in this study?
Yes, if you agree to take part in this study we will inform your GP. We will also contact your GP if we have any concerns about your health during the study.

Will my taking part in the study be kept confidential?
Any identifiable information that is collected about you with this study will be kept confidential and secure, disclosed only with your permission, or except as required by law.

Your name will not appear on any materials produced from this study. However access to your medical records may be required by other agencies such as regulatory bodies. This will only occur when necessary and to comply with the law.

A copy of your consent form will be sent to the Hull Health Trials Unit monitoring the study via a secure web-based database. All other personal information collected for this study will be anonymised and entered onto a secure web-based database held at Hull Health Trials Unit or by other relevant third parties for the delivery of the trial.

The research team will need to have access to your medical record to confirm that correct study treatments have been given and that the study has been conducted properly.

What will happen to the data collected in the study?
The results of this study may be published or presented at scientific meetings and in journals so other doctors caring for similar patients can learn from your experience. The costs of treatment will also be explored to see if morphine is a cost-effective treatment for breathlessness. If you would like a copy of the results summary, let your study nurse know.

Anonymised data that you provide may be used by authorised researchers studying other relevant research projects. Please let us know if you do not agree to this. For more detail, see Section 2 at the end of this leaflet.

Who is organising and funding the research?
The Hull University Teaching Hospitals NHS Trust is taking overall responsibility for the study. It is funded by the National Institute for Health Research Health Technology Assessment programme (grant number 17/34/01).

The research team is led by Professor Miriam Johnson, Professor in Palliative Medicine at Hull York Medical School, the University of Hull. The trial is conducted by the Hull Health Trials Unit at the University of Hull.

Who has reviewed the study?
Before any research goes ahead it is looked at by an independent group of people called a Research Ethics Committee, to protect your interests. This study has been reviewed and approved by an NHS Research Ethics Committee and Hull York Medical School Ethics Committee. It has also been reviewed by your local hospital Trust Research and Development Department, as well as by the Funders.

What do I do now?

If you do not wish to take part then there is no need to do anything else. If you would like to take part, or feel you need more information, then please speak to the research nurse, the member of staff who gave you this leaflet or one of the contacts on page one of this leaflet.

Research Nurse [name]
Site [address]
Phone number [contact number]

mabel trial

Section 2 – General Data Protection Regulation (GDPR) 2018

All information collected about you in the course of this study is confidential and will be held in accordance with the General Data Protection Regulation (GDPR 2018).

Hull University Teaching Hospitals NHS Trust is the sponsor for this study. This study is organised and managed by the Hull Health Trials Unit (HHTU), University of Hull. HHTU will be using information from you and / or your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly.

Your local NHS / hospice sites will collect information from you and your medical records for this research study in accordance with our instructions. They will keep your name, NHS number and contact details confidential and will not pass this information to Hull University Teaching Hospitals NHS Trust.

Your local NHS / hospice sites will use this information as needed, to contact you about the research study and make sure that relevant information about the study is recorded for your care. A copy of your consent form with your name on it will be sent via the secure web based database to the HHTU to ensure quality and accuracy. Only designated research team members will see the consent form. This will be the only information sent to the HHTU with identifiable personal data on it.

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. To safeguard your rights, we will use the minimum personally-identifiable information possible.

Research monitors from Hull University Teaching Hospitals NHS Trust, HHTU and regulatory organisations may look at your medical and research records to oversee the quality and accuracy of the research study. All will have a duty of confidentiality to you as a research participant, and nothing that could reveal your identity will be disclosed outside the agreed use of the research data. 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.

Hull University Teaching Hospitals NHS Trust will keep identifiable information about you for 15 years after the closure of the research database. Datasets will be made available for longer periods of time for research purposes as described in other sections of this information sheet.

More information about health care research can be found using the following link:
https://www.hra.nhs.uk/information-about-patients/

You can find out more about how we will use your information by contacting:
hhtuenquiries@hyms.ac.uk or telephone 01482 463444.