

A Feasibility Study Evaluating the Efficacy of Indwelling Pleural Catheters Plus Sclerosant in Persistent Symptomatic Pleural Effusions Secondary to Heart Failure

Patient Information Sheet

You are being invited to take part in a feasibility study called REDUCE 2. Before you decide whether or not to be involved, it is important for you to understand why we are conducting this study and what it will mean for you. Please feel free to discuss this information with someone else, such as your family or GP, if you wish. Please ask any questions if you feel there is something which is not clear, or if you would like to know more.

**Summary**

The study is part of an effort to determine the best way of managing recurrent fluid build-up around the lungs (**a pleural effusion**) caused by problems with the heart that cannot be managed with medications alone.

The current method for managing this fluid build-up is to remove the fluid using a needle and syringe. This procedure is known as a **therapeutic aspiration**. Therapeutic aspirations are generally performed as often as indicated by a patient’s symptoms.

An alternative method is to insert an **Indwelling Pleural Catheter (IPC)** which is a small, soft rubber tube that is placed into the chest wall. This remains in for as long as required and allows the fluid to be drained regularly in patient’s home, without the use of any needles. In REDUCE 2, medical grade talc will be given once only through the IPC to attempt to ‘dry up’ or stop the fluid coming back. This would therefore allow removal of the IPC.

The aim of this study is to compare these two methods and gain some feedback of patient experiences with the use of an IPC to inform future similar trials.

**Contact Details**

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| --- | --- |
| Your local principal investigator is: | *localised details to be added* |
| For routine trial-related questions during working hours, please contact: | *localised details to be added* |
| **For any emergency or non-trial-related issues please contact medical services as per normal.** |
| For further information about research and clinical trials in your local area, please contact: | *localised details to be added* |

Section A – REDUCE 2 Trial Information

1. What is the purpose of the study?

Patients with heart problems can develop fluid around their lungs. The fluid is called a pleural effusion. Fluid build-up around the lung can restrict lung movement and cause breathlessness, but can usually be drained using a needle and syringe in a procedure called a therapeutic aspiration. However, fluid caused by heart problems is likely to return after each therapeutic aspiration, therefore repeated hospital visits are required. As this is the current accepted practice, it is known as standard care.

In patients with pleural effusions related to other health conditions, long term chest drains known as indwelling pleural catheters have been shown to be very effective ways of treating pleural fluid that builds up repeatedly. A recent development has been to administer medicinal talc once only through an IPC with the aim of ‘drying up’ the pleural effusion (a process known as pleurodesis). The IPC can then be removed as the fluid is likely not to return. This technique has been shown to be successful in other groups of patients but has not yet been studied in patients with pleural effusions related to heart failure.

This study aims to find out more information about how this new technique can be used in patients with pleural effusions related to heart failure and to gain more information on the use of both techniques in these patients.



1. What will happen to me during the trial?

Before your doctors consider you for the REDUCE 2 study, you will have been diagnosed with a pleural effusion related to heart problems that is causing you symptoms, and is large enough to allow an IPC to be placed. You and your doctor will have agreed that having an IPC and managing it as an outpatient is both appropriate and practical.

You will be asked to attend your local trial centre for an appointment known as a baseline visit. This will be to check that you are suitable for the study and to discuss it with you. You will usually be given this document at that visit and it may be part of a routine out-patient appointment. You will be given some time to consider whether you would like to be part of the study. If you agree to be considered, you will have a consultation with a trial doctor who will ask questions about your treatment to date, your medical history and your symptoms. You will have an examination and may have blood tests taken. You will also be asked to fill out some health questionnaires and to have a chest x-ray. You may require some further tests to be carried out or arranged at this point, such as additional blood tests or an echocardiogram, if these have not been done already in your previous care. You will then be taken through the consenting process to join the study which will form a record of your agreement to be part of the study. Following this you will be assigned to receive either standard care or the combination of IPC and talc. This process is known as randomisation and is carried out by computer. The trial staff have no influence on which group you are assigned to, and you may not choose. This is to ensure the study is as fair as possible.

To help us understand more about the techniques, we would like you to tell us about chest pain and breathlessness that you are experiencing at specific points in the study. You will be given a booklet to keep a record of your chest pain and breathlessness, IPC drainages if applicable (to be completed by the healthcare professional who drains your IPC) and any healthcare contact. This needs to be competed daily for the first two weeks and then just weekly for the remainder of the study (12 weeks from the date of your IPC insertion or first therapeutic aspiration). Please keep this safe, bring it to every appointment and have it hand when your IPC is drained. It will also contain contact details of your local trial team and a brief summary of the study.

We will ask you to attend for trial visits at 2 weeks, 4 weeks and 12 weeks where you will have a chest x-ray, chest ultrasound and complete questionnaires. Trial visits will normally take place in your local hospital. If you have appointments with other teams you should attend them as normal. Table 1 below details what each trial visit will involve. **Due to the COVID-19 pandemic, it is possible that the appointment schedule may change. Your local trial team will keep you up to date.**

***If you are randomised to continue with the current standard care (Therapeutic Aspiration)*** you will receive an initial therapeutic aspiration to remove as much of the fluid as possible and only have further aspirations as and when needed. You will still be asked to complete the patent booklet and attend all follow up appointments.

***If you are randomised to receive an IPC*** your drain will be inserted at your local trial hospital, and you will have another x-ray immediately afterwards to check its position. The insertion is usually done as a day case procedure so you can be back at home the same evening, but on rare occasions patients are asked to stay in hospital for a short time for monitoring. Following your IPC insertion we will monitor your progress closely for 12 weeks. During this time period your local hospital’s trial team will provide care of your IPC and any associated issues.

After 7 days you will be asked to come back into hospital and have a chest x-ray. This will determine whether your lung has expanded sufficiently to allow you to receive medical talc. If your lung has not expanded (this is known as ‘trapped lung’) then it will not be possible to put talc down the IPC and you will continue with trial follow up without having talc inserted. If your lung has expanded sufficiently you will be able to receive medical talc into your IPC, which will then be administered by a member of the trial team. You will be asked to come back in the following day for a short visit to drain the IPC and check how you are doing.

Arrangements will be made for your fluid to be drained off regularly in between trial visits. This will usually be done by a nurse in your own home, but occasionally you may need to be drained at your local trial hospital. You will have your IPC drained at all outpatient appointments in hospital. Drainage bottles and kits will be provided by your local trial hospital for the duration of your trial involvement.

Table 1. Schedule of Visits

|  |  |  |
| --- | --- | --- |
| **Day** | **Visit** | **What happens during the visit?** |
| **-----** | **Consent, baseline and** **randomisation** | Sign consent formClinical examinationComplete baseline tests:* Chest ultrasound
* Standard blood tests
* Completion of Quality of Life questionnaires
* Chest x-ray (only required if patient has not had a chest x-ray within the last 24 hours)

Randomisation to either IPC or standard care |
| **0** | **IPC insertion/ therapeutic aspiration (Day 0)** | Insertion of an IPC or a therapeutic aspiration |
| **7** | **Talc instillation****(IPC arm only)** | Day case procedure involving the following:* Chest ultrasound
* Chest x-ray
* Instillation of talc into your IPC
* Standard blood tests

Following this appointment you will have your IPC drained daily (or at least 5 times per week) for two weeks. |
| **8** | **Talc instillation + 1 day****(IPC arm only)** | Clinical examinationIPC drainageStandard blood tests |
| **14** | **Week 2 Follow-up Appointment** | Outpatient visits involving the following:* Clinical examination
* Completion of Quality of Life questionnaires
* Chest x-ray
* Chest ultrasound
* Standard blood tests

The frequency of your IPC drainage will be adjusted at these appointments (if applicable). At week 8 you will either be contacted by a research nurse or asked to attend hospital for a short appointment to see how you are getting on. After the week 12 visit, your involvement with the study will end. Your care will continue with your appropriate local team. |
| **28** | **Week 4 Follow-up Appointment** |
| **84** | **Week 12 Follow-up Appointment** |
| **In view of the COVID-19 pandemic, it is possible that this schedule of visits may be subject to change, in order to maximise the safety of all participants. Your local trial staff will update you of any changes at the appropriate time.**  |

The frequency of IPC drainage varies throughout the study period. For the first three weeks after IPC insertion your IPC should be drained daily, or a minimum of five times a week. This is to try to improve the chances of drying the fluid up. After this point, the frequency of drainage will reduce to three times weekly and then twice weekly, unless you require more frequent drainages. If the amount of fluid being drained reduces sufficiently, and you and your doctor feel it is the right thing to do, we may be able to remove your IPC. This is done as a day case procedure in your trial hospital.

After the 12 week initial follow up period your care will be continued by your normal medical team, rather than the trial team.

During the trial we may invite you to participate in an optional interview of your experiences of the study (see Section B).

Once the results of the trial are available we shall be happy to provide you with them if you wish.

1. Blood tests and biological material

You **will be asked to have a number of blood tests during** your time in the study. The number of tests you will be asked to undertake will vary depending on the arm of the study that you are enrolled into. The purpose of the blood tests is to monitor the effect of the different techniques on organ systems such as your kidneys. These tests may be taken at your local study hospital or GP practice.

Participants in the standard care arm will be asked to have up to 4 sets of blood tests throughout the study period.

Participants in the IPC arm will be asked to have up to 8 sets of blood tests in the study period.

These blood tests will be processed in the same way as non-trial blood tests and will **not** be retained for future research purposes. They will be disposed of in a timely fashion in line with local and national practice for clinical blood samples. No other biological samples will be taken or retained as part of REDUCE 2.

1. Information about indwelling pleural catheters (IPCs)

An indwelling pleural catheter is a form of soft rubber chest tube which is designed to be left in place after insertion, sometimes for weeks or months at a time, so that pleural effusions can be drained outside of the hospital environment. They have been used for many years and have been shown to be safe and well tolerated by patients. You should have been given an extra information sheet specifically about your IPC which will hopefully answer any questions you may have, but if not, or if you haven’t received the leaflet, please let us know.

1. Information about medical talc

Talc is a naturally occurring soft powder which has been used in medicine for decades. When inserted into the pleural space it acts as an irritant and has been shown to be the most effective substance for causing pleurodesis, which potentially stops fluid recurring. Medical talc is very carefully selected and is purified and sterilised before use. It has been shown to be safe and well tolerated by patients, but can cause a slight fever and some pain after insertion.

1. What are the potential benefits from taking part?

We hope that every patient will gain benefit from fluid being removed whether it is through an IPC or by therapeutic aspiration. Whichever group you are allocated to, your participation in this trial will contribute to our understanding and development of new and better ways to manage pleural effusions due to heart failure, which will hopefully benefit patients like you in the future.

1. What are the possible disadvantages and risks of taking part?

Therapeutic aspirations are the current standard method for removing fluid build-up around the lung but there is a greater risk of infection as more procedures are carried out. This is one of the reasons for conducting this research to look for an alternative method for managing recurrent fluid build-up. During or at the end of drainage some patients can experience coughing, or mild chest discomfort or pain, but this should settle shortly after the drainage is stopped and is completely normal. With each therapeutic aspiration there is a very small risk of infection entering during the procedure and we reduce the risk of this happening by using sterile techniques.

Neither of the alternative treatments we are proposing to use in this trial are new, with both talc and indwelling pleural catheters having been shown to be safe and well tolerated. Individually they can both cause minor side effects which are detailed below. One of the aims of this study is to determine what side effects, if any, there are from using talc and IPCs together. In order to do this we shall be monitoring you closely throughout the study period.

Talc is generally very safe, but patients can sometimes experience pain in the chest around the time it is inserted. You will usually be given painkillers before the procedure and be given local anaesthetic along with the talc. If you have had a reaction to local anaesthetic before then you should inform a member of the trial team. After talc insertion some people can develop a slight fever, but this is often easily manageable with pain-relieving medications such as paracetamol. All procedures carry a slight risk of infection, including the use of talc, although we shall minimise this risk by using sterile equipment and components.

Indwelling pleural catheters can usually be inserted as a day case procedure, but occasionally we ask patients to stay overnight for further monitoring. After the procedure some people can feel bruised or sore around the insertion site, but we use plenty of local anaesthetic to try and reduce this. Once at home, patients will usually require a number of drainages per week (this can vary from none to daily), but this is often carried out by a district nurse. Similar to a therapeutic aspiration, during or at the end of drainage some patients can experience coughing, or mild chest discomfort or pain, but this should settle shortly after the drainage is stopped and is completely normal. As mentioned earlier, there is a very small risk of infection entering both during the procedure and afterwards, when at home. We shall reduce the risk of this happening by using sterile techniques whenever the drain is used.

Chest x-rays are used for the investigation and monitoring of pleural effusions and will be required whether or not you take part in the study.  The study design requires you to have up to 8 chest x-rays throughout the trial period if you undergo IPC insertion. If you are in the standard care arm, you will have 2 x-rays more than you would require if you were not in the trial. There is a small theoretical risk with the extra radiation that the chest x-rays will expose you to, however chest x-rays are associated with a low level of radiation. Two chest x-rays are equivalent to one and a half weeks of background radiation in the UK. Natural background radiation is the radiation coming from the sun's rays and the earth itself, which we are all exposed to every day.

1. What will we measure?

We will measure breathlessness, pain, quality of life, the number of procedures and hospital admissions required, the cost of treatment, any problems related to the procedures and whether the fluid stops building up. We will measure breathlessness by asking you to mark how breathless you are at the time on a scale. Pain will be measured using the same technique. We will measure quality of life with questionnaires.

1. Why have I been chosen?

You have been invited to take part in this study because you have fluid around the lung caused by problems with your heart. The results of the study will help us decide on the best treatment of patients in your situation in the future. This study will take place in hospitals in different parts of the country.

1. Do I have to take part?

No, it is up to you alone to decide whether you take part. If you do decide to participate then you will be asked to sign a consent form. You will be given a copy of the consent form and this information sheet for your records.

If you decide to take part but later change your mind you are free to withdraw at any time, without giving a reason. A decision to not take part, or to withdraw, will not affect your rights or your future medical care outside of the trial.

1. If I agree to participate, do I get to choose which treatment I have?

No. The study is randomised which means that you will be randomly allocated to either receive one treatment method or the other, without any external influence being possible. This randomisation process is carried out by a computer programme and the trial team has no influence over it.

1. How will we use information about you?

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

This information will include your initials, NHS number, name, date of birth and contact details. People will use this information to do the research or to check your records to make sure that the research is being done properly.

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. We will write our reports in a way that no-one can work out that you took part in the study.

We will keep all information about you safe and secure.

Once we have finished the study, we will keep some of the data so we can check the results. In line with UK law, this data will be kept securely for 5 years after completion of the study.

1. 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.

If you choose to stop taking part in the study, we would like to continue collecting information about your health from central NHS records, your hospital and your GP. If you do not want this to happen, tell us and we will stop.

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.

If you have any queries regarding this, you may contact your local study team, or the local Information Governance lead.

Local Information Governance Lead: Helen Williamson

Helen.E.Williamson@nbt.nhs.uk

1. 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/
* https://www.nbt.nhs.uk/research-innovation/our-research/patient-data-research
* by asking one of your local research team
* by sending an email to researchsponsor@nbt.nhs.uk
* by ringing us on 0117 414 9330.
1. Who is organising and funding the research?

North Bristol NHS Trust is sponsoring the research, which means that the Trust has overall responsibility to ensure that the trial is conducted in a safe and appropriate manner. The study has been funded by a research grant from BD®, a commercial company who manufacture a type of indwelling pleural catheter and its drainage equipment. This company has no input into the planning, running or reporting of the trial, although they are providing the necessary drainage equipment. No payment will be made to the trial doctors or nurses for including you in the study.

1. Travel expenses

You may claim reasonable travel expenses from your local trial team for the cost of travel to your week 4 appointment (as this would be a visit just for the purposes of this research project).

1. Stopping the trial

If the study doctors feel that it is no longer safe or appropriate for you to continue in the trial, they may want to withdraw you from the study. Very occasionally, the sponsor (North Bristol NHS Trust) may also stop the study early. If this happens, the reasons will be explained to you.

1. Who has reviewed and approved the study?

In order to protect your rights, safety and dignity, this study has been reviewed by a Research Ethics Committee, North Bristol NHS Trust Research & Innovation who are sponsoring the research, the Heath Research Authority and the Medicines and Healthcare products Regulatory Agency.

1. What if new information becomes available?

The trial team will continue to review all new research data. If new information that influences the trial becomes available, alterations will be made accordingly. If this changes your involvement in the trial, then you will be contacted with an updated information sheet and asked to sign a further consent form. Your right to withdraw from the trial remains the same with there being no impact on your standard care.

1. What if there is a problem?

If you have a concern, or are displeased about any aspect of this study or your wider care, then we would encourage you to ask to speak to a trial doctor or nurse who will attempt to address any issues you may have. If you remain unhappy and wish to make a formal complaint then you can do this through the NHS complaints procedure. We can provide you with information on how to contact either the Patient Advice and Liaison Service (PALS) or the hospital complaints manager. These details can also be obtained through the hospital switchboard.

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| --- | --- |
| To speak to your local hospital’s Advice and Complaints Team, please contact: | *localised details to be added* |

If there is negligent harm during the REDUCE 2 trial when the NHS body owes a duty of care to the person harmed, NHS indemnity covers NHS staff, medical academic staff with honorary contracts, and those conducting the REDUCE 2 trial. NHS indemnity does not offer no-fault compensation and is unable to agree in advance to pay compensation for non-negligent harm.

1. What will happen to the results of the study?

When the study has finished the results will be analysed. These will then be published in a medical journal so that other doctors can read them and learn from them. No identifiable patient information will be published. If you would like a copy of the medical paper, or would like us to write to you personally to explain the study findings then please indicate this on your consent form.

1. What do I need to do now?

After reading this information sheet you will be invited to ask questions about the trial. If you would like to take part then we shall ask you to sign a consent form, which will also ask if you are happy for your GP to be informed of your involvement. If you would like extra time to consider entry into the trial, perhaps to discuss with your family or GP, then please let us know.

If you decide not to participate, your routine medical care and your legal rights will not be affected in any way.

If you agree to participate in the trial you are free to withdraw at any time without giving a reason.

**Thank you for taking the time to read this information, and for considering taking part in the REDUCE 2 study.**

Section B – Optional Interviews about your experiences in the trial and/or the recruitment process should you decide not to participate

Thank you for considering taking part in the REDUCE 2 study. We would like to invite you take part in a short interview about your experiences of the trial, and how your treatment has impacted on you, or your reasons for not choosing to participate should you decide not to. Please take some time to read this information carefully before deciding whether or not you would like to take part in the interview.  You may also wish to discuss your decision with family, friends or your GP.

1. Why are you conducting interviews with trial participants?

By conducting interviews with patients about their individual experiences, we are hoping to learn more about the treatment methods studied in this trial, and people’s thoughts about these. We would also like to know whether those taking part in the trial are satisfied with the information they receive and reasons that people may chose not to participate. We know very little about the ‘real life’ experience of having a pleural effusion, and the impact it can have on people’s everyday lives. Similarly, we know little of the patient’s perspective of many of the treatments we offer and the impacts they have on people’s everyday lives. Understanding more about these aspects may help us to improve care in the future.

1. Do I have to have an interview?

No. You can still take part in the REDUCE 2 study without having an interview. You can also chose to have an interview without taking part in the trial. If you choose not to participate in the trial or the interview your medical care will not be affected in any way.

1. When and where will the interview take place?

If you agree to take part, we will aim to conduct the interview between 3 and 12 weeks after you first received treatment in the REDUCE 2 study. We will aim to either speak with you over the telephone or with a video call on a computer at a time which is convenient to you. For participants that choose not to enter the study, the interview may be conducted at any convenient time.

1. What will I have to do if I decide to take part?

If you agree in principle to have an interview, you will be contacted by a member of the trial team from Bristol between two and ten weeks after you first received treatment (if you decide not to take part in the main trial but would like to participate in an interview, with your permission we will pass your details to the central trial team to contact you about the interview). They will discuss the interview with you in more detail and answer any questions you have. If you are still willing to help, they will arrange a date and time for the interview that suits you.

On the day of the interview, the researcher will ask you to give your agreement (consent) to speak with them and for us to audio-record the interview. The interview may take up to an hour or for however long you feel comfortable talking. We will be asking the same basic questions to everyone, but we are also interested in anything you feel would be helpful or important to discuss.

With your consent, we may use some anonymised quotations from the interview in the final published results of the study.

1. What are the potential disadvantages of taking part?

The only real disadvantage of taking part is the time we would ask you to give up, to talk with us. You may find talking about personal experiences upsetting. Should you become upset, we will ask you if you want to stop the interview. You are also free to stop the interview or to decide not to answer any questions without giving a reason, at any time.

If you feel that you would like further support with any of the issues that may be raised whilst discussing your condition and involvement in this study, you may find the following resources useful:

British Heart Foundation Support Groups:

<https://www.bhf.org.uk/informationsupport/support/support-groups>

Pumping Marvellous, the UK’s patient-led Heart Failure Charity:

[https://pumpingmarvellous.org](https://pumpingmarvellous.org/)

1. What are the possible benefits of taking part?

Although participating in the interview will not benefit you directly, we hope that the information you share with us and the results of the study will help to improve care for people with pleural effusions in the future.

1. How will you ensure my details are kept confidential?

Ensuring your data is kept safe is an important priority for the research team. Your interview recordings will be stored on a password-protected computer network at the University of Bristol and North Bristol NHS Trust. The interview recording will be sent via a secure link to an approved third party transcription provider to be written down before being anonymised (removing anything that could identify you such as anyone’s names, places, or dates) and analysed by the researcher.

North Bristol NHS Trust is the sponsor for this study. We will be using information from you and your medical records in order to undertake this study and will act as the data controller. This means that we are responsible for looking after your information and using it properly.

North Bristol NHS Trust will keep identifiable information about you (including the audio recording) for 12 months after the study has finished. We will keep the anonymised interview transcripts for 6 years, after which time they will be destroyed.  The University of Bristol, who are assisting with the analysis of interview data, will keep identifiable information about you for 12 months after the study has finished after which time they will be destroyed.

1. Will I be contacted by anyone except the research team?

No. Researchers from the University of Bristol who are working with North Bristol NHS Trust 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.

1. Who should I contact if I have further questions about the interviews?

If you have any questions or concerns about the interview, please speak to a member of your local research team, who will do their best to answer your questions.

You can also contact … TBC – details of researcher conducting the interviews

**Thank you for taking the time to read this information, and for considering taking part in the interview.**