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Comparing methods to manage recurrent fluid build up around the lung caused by problems with the heart - what is the best way to measure this and which method do patients prefer?

Submission date	**Recruitment status**	[X] Prospectively registered
10/08/2021	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
12/08/2021	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
14/05/2025	Respiratory	[_] Record updated in last year

Plain English summary of protocol

Background and study aims

This 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 the patient's home without the use of any needles. In this study 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 on patient experiences with the use of an IPC to inform future similar trials.

Who can participate?

Patients with recurrent fluid build-up around the lungs (a pleural effusion) caused by problems with the heart that cannot be managed with medications alone and who are suitable to have an IPC

What does the study involve?

The study involves five hospital visits:

Visit 1: an initial assessment to discuss the study, check that the patient is suitable and determine which method of managing fluid build up they will receive.

Visit 2: patients would have either an IPC inserted or a therapeutic aspiration depending on which method has been randomly allocated.

Visit 2b: for those with an IPC only - to have medical talc inserted into their IPC 7 days after it has

been inserted and to have a quick check up the following day
Visit 3: Week 2 follow-up appointment
Visit 4: Week 4 follow-up appointment
Visit 5: Week 12 follow-up appointment
At all visits chest x-rays, ultrasounds and blood tests will be performed, similar to a usual hospital follow up. Additional health questionnaires will also be completed. Between visits participants will have fluid drained off regularly if they have an IPC inserted, or only when needed if they have been allocated to the therapeutic aspiration method. Participants will also be asked to keep a diary of any fluid removed and how much breathlessness or chest pain they are experiencing.

What are the possible benefits and risks of participating?
It is hoped that every patient will gain benefit from fluid being removed whether it is through an IPC or by therapeutic aspiration. Participation in this trial will contribute to the understanding and development of new and better ways to manage pleural effusions due to heart failure, which will hopefully benefit patients in the future. 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 the risk is reduced by using sterile techniques.
Neither of the alternative treatments 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 the participants will be monitored closely throughout the study period.
Similar to a therapeutic aspiration, during or at the end of IPC 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. There is a very small risk of infection entering both during the procedure and afterwards, when at home. This risk is reduced by using sterile techniques whenever the drain is used.
Talc is generally very safe, but patients can sometimes experience pain in the chest around the time it is inserted. They will usually be given painkillers before the procedure and be given local anaesthetic along with the talc.

Where is the study run from?
North Bristol NHS Trust (UK)

When is the study starting and how long is it expected to run for?
September 2020 to May 2025

Who is funding the study?
BD (USA)

Who is the main contact?
1. Dr Emma Tucker (emma.tucker2@nbt.nhs.uk) for general queries
2. Dr Hugh Welch (hugh.welch@nbt.nhs.uk) for clinical queries

Contact information

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Scientific

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Additional identifiers

Integrated Research Application System (IRAS)
276051

Central Portfolio Management System (CPMS)
49844

Study information

Scientific Title
A feasibility study evaluating the efficacy of indwelling pleural catheters plus sclerosant in persistent symptomatic pleural effusions secondary to heart failure

Acronym
REDUCE 2

Study objectives
Heart failure is a leading cause of pleural effusions worldwide, with an estimated annual incidence of 500,000 cases per year in the US. Current medical management includes diuresis and optimisation of cardiac function, however, a significant cohort of patients develop effusions that are refractory to medical therapy. These patients are often managed with recurrent pleural aspirations. The REDUCE trial, which has recently completed recruitment, has evaluated the efficacy and acceptability of indwelling pleural catheters (IPCs) for managing these effusions. Given the success of the combination of IPC and talc pleurodesis in the malignant population demonstrated by the IPC-Plus trial, the researchers would like to evaluate whether a similar protocol can be delivered acceptably to patients in this cohort. The efficacy of the protocol could then be evaluated with a full randomised controlled trial in future.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 14/07/2021, London - Riverside Research Ethics Committee (Ground Floor, Temple Quay House, 2 The Square, Bristol, BS1 6PN, UK; +44 (0)207 1048193; riverside.rec@hra.nhs.uk), REC ref: 21/LO/0490

Primary study design
Interventional

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

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Recurrent pleural effusion secondary to heart failure

Interventions
Potential participants will be identified by clinicians and invited to attend an appointment at their local trial centre with a member of the trial team. During this appointment they will be asked to discuss their symptoms and medical history. They will be examined and may have blood tests taken if these have not been done recently. Relevant investigations in their medical records will be reviewed and a thoracic ultrasound and chest x-ray will be performed. Blood tests will be taken. All aspects of the study will be thoroughly explained to them and a patient information sheet (PIS) will be given to them to read and keep.

If they are found to be eligible to enter the study, participants will be invited to join. Should they agree, they will review and sign the relevant consent forms. Following this, participants will be allocated randomly by a computer to either receive the new technique (IPC insertion, daily drainage and talc) or standard care. These groups are known as study 'arms'. The study staff will have no influence over which group participants are allocated to, and participants may not choose.

Consented participants will be asked to complete a selection of questionnaires and measures that assess chest pain, breathlessness, quality of life and impact of their symptoms on daily life.

Participants will be given a booklet to keep a record of chest pain and breathlessness experienced throughout the study. They will be asked to record these initially on a daily basis then less frequently as time goes on. Each arm of the study has a specific booklet to complete.

Within 2 weeks participants will be asked to attend their trial centre for either IPC insertion or therapeutic aspiration depending on which arm they have been allocated to.

IPC arm only:
IPC insertion is usually a day case procedure, using local anaesthetic and occasionally sedation. General anaesthetics are not used. Participants will undergo IPC insertion and drainage of pleural fluid in the same procedure. Following the procedure it is usual to need some simple painkillers such as paracetamol for 2-3 days.
We will ask the local District Nurse team (or equivalent) to attend the participant's home on a daily basis for the next week to drain the IPC. Each drainage usually takes 15-30 minutes. The process of drainage is as follows:
1. The old dressings covering the IPC are removed
2. The IPC is cleaned
3. A disposable vacuum bottle is attached to the IPC which removes the fluid
4. The rate of fluid removal can be controlled by the person undertaking the drainage
5. When either the bottle is full, the flow of fluid stops or the participant wishes the drainage is stopped and the bottle removed from the IPC

6. Dressings are then applied to the IPC and skin
7. Relevant documents are filled in by the healthcare professional carrying out drainage
8. The participant should also complete the relevant sheet in their data collection booklet

Participants will be asked to attend their local trial centre to be given talc 7 days after IPC insertion. This is a daycase procedure that lasts around 3 hours. A chest x-ray will be performed and the participant will be seen by a member of the trial team to make sure that they are suitable to be given talc. Eligible participants will then be given talc through their IPC. Local anaesthetic will also be given through the IPC and oral painkillers will be available if required. Following talc administration a second chest x-ray is performed and the participant will be seen by a member of the trial team, and then discharged.

Participants who are deemed unable to receive talc will be asked to remain in the trial and continue with follow up as planned. The most likely reason for not receiving talc is a condition known as trapped lung, where the lung does not expand following removal of pleural fluid. As a result the edges of the lung are not in contact with the chest wall, which in turn means that the talc will not be able to dry up the fluid.

Participants will be asked to attend their trial hospital the following day for a check-up. For the next 2 weeks they will also undergo daily IPC drainage. The frequency of drainage will reduce after this point, to a minimum of two drainages per week.

Blood tests will be taken four times in the first 2 weeks. Where possible, these tests will be taken on the day of hospital attendance. If the volume of fluid drained from a participant's IPC drops to less than 50 ml on three drainages in a row, they should contact the local trial team who will arrange to see them. They will have a chest x-ray and see a doctor or nurse. If their fluid is confirmed to have dried up, an appointment will be made to remove the IPC. This is a daycase procedure that uses local anaesthetic but no sedation. Once the IPC a further chest x-ray is required and then the participant may go home. They will be asked to continue attending all planned follow up.

Standard care arm only:
Following their screening appointment participants will be invited to attend their local trial hospital to undergo therapeutic aspiration of their pleural fluid. An ultrasound of the chest will be carried out first to ensure the fluid can be safely removed. Fluid is usually removed from the back or side of the chest wall. The clinician performing the procedure will then clean the area and numb it with an injection of local anaesthetic. They will then use a special needle and syringe to remove up to 1.5 litres of fluid. The participant will have a chest x-ray after the procedure and be discharged home.
Further therapeutic aspirations will be carried out as needed – when the participant becomes symptomatic again or if the pleural fluid is found to have built up again by a doctor.

Both arms:
Participants in both arms will be asked to attend their local trial centre for face to face appointments 2, 4 and 12 weeks after their IPC insertion or first pleural aspiration. These appointments will be with members of the trial team. Each appointment will involve drainage of their IPC (if they have one), speaking with a doctor and/or trial nurse, examination by a doctor or trial nurse, a chest x-ray, chest ultrasound and blood tests. Participants will also be asked to fill in some questionnaires and assessments of their symptoms and quality of life. At 8 weeks there will also be a face to face or telephone appointment.
In view of the COVID-19 pandemic, the schedule and arrangements of follow up may be changed in order to avoid unnecessary risk or exposure to participants and trial staff.

The final trial visit occurs at 12 weeks after IPC insertion or initial aspiration. After this appointment the participant will have completed their involvement in the study and their care will be taken over by local services.

Qualitative interviews:
A selection of participants will be invited to take part in interviews to gain a further understanding of their perspectives on their illness, the treatments in the study, the design of the study, and any effects on their symptoms and quality of life caused by the study. The interviews will be conducted by telephone or videoconference and will take up to 1 ½ hours. Participants will be asked to sign a separate consent form for these interviews.

Intervention Type
Procedure/Surgery

Primary outcome(s)
The number of participants recruited from those who meet the eligibility criteria: the study will be deemed successful if the absolute number recruited is at least 32, and ≥50% eligible patients are successfully randomised; Timepoint(s): Randomisation

Key secondary outcome(s)
1. The number of patients with successful pleurodesis at 4 and 12 weeks post intervention. For the purposes of IPC removal, pleurodesis will be defined as the collection of less than, or equal to, 50 ml of pleural fluid on three consecutive occasions, with chest opacification on the side of the IPC less than 25%, as judged by 2 independent clinicians. The x-ray must be taken after the third drainage of 50 ml or less. If a participant (or the district nursing team) feels their fluid volumes have dropped to these levels, they are encouraged to contact the local trial centre for assessment. The local trial team should then see the participant and assess them clinically and with a chest x-ray (see SOP). The appropriate CRF must be completed at this point. If pleurodesis is confirmed the IPC should be removed. Pleurodesis can be identified at any point throughout the study in the IPC/talc arm.
In the control arm, pleurodesis will be defined as chest x-ray opacification of less than 25%, with no further pleural interventions required throughout the duration of the study following the initial aspiration.
2. Self-reported quality of life status measured using the EuroQol-5D (EQ-5D) and Minnesota Living with Heart Failure Questionnaire (MLHFQ) at baseline, 2 weeks, 4 weeks and 12 weeks
3. Breathlessness measured using self-reported VAS scores at baseline and daily for the subsequent 2 weeks then weekly for the remainder of follow up
4. Chest pain measured using self-reported VAS scores at baseline and daily for the subsequent 2 weeks then weekly for the remainder of follow up
5. Heart failure classification based on limitation of physical activity measured using New York Heart Association (NYHA) class at baseline, 2 weeks, 4 weeks, and 12 weeks
6. The number of drainages/procedures per patient per week and total volume of pleural fluid removed, measured by healthcare professionals recording the volume of each drainage, measured at 12 weeks
7. All-cause mortality measured using reported death rates of participants up to 12 weeks post randomisation
8. Degree of loculation of pleural fluid following talc instillation as judged by thoracic ultrasound and septation score at 2, 4 and 12 weeks post randomisation
9. Number and type of episodes of healthcare utilisation in the trial period measured using patient-reported healthcare interactions at 12 weeks
10. Adverse events related to trial intervention measured using reporting rates of adverse

events at 12 weeks
11. Protocol deviation rates measured using reported rates of protocol deviation at 12 weeks
12. Data completion rates measured by analysis of data reporting rates in the central study database at 12 weeks

Completion date
10/05/2025

Eligibility

Key inclusion criteria
1. The presence of a recurrent pleural effusion secondary to heart failure that has not responded to medical therapy
2. Sufficient pleural fluid for IPC insertion
3. Symptomatic breathlessness warranting pleural intervention
4. Pleural infection excluded to satisfaction of treating physician
5. Expected survival >12 weeks
6. Written informed consent to trial participation

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
18

Key exclusion criteria
1. Age <18 years
2. Known pleural malignancy
3. Pregnancy, lactation or intention to become pregnant
4. Absolute contraindication to IPC insertion or therapeutic aspiration of pleural fluid
5. Previous attempts at ipsilateral pleurodesis
6. Evidence of extensive lung entrapment on chest x-ray or CT, or significant fluid loculation on ultrasound scan, to a level which would normally be a contraindication to attempted talc pleurodesis or IPC insertion.
7. Inability to give informed consent
8. Patient has no access to a telephone

Date of first enrolment

19/01/2022

Date of final enrolment
12/07/2024

Locations

Countries of recruitment
United Kingdom

England

Wales

Study participating centre
Southmead Hospital
Clinical Research Centre - Respiratory
North Bristol NHS Trust
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BS10 5NB

Study participating centre
John Radcliffe Hospital
Headley Way
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OX3 9DU

Study participating centre
Manchester Royal Infirmary
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Study participating centre
Royal Stoke University Hospital
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Study participating centre
St Thomas' Hospital
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Study participating centre
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Sponsor information

Organisation
North Bristol NHS Trust

ROR
https://ror.org/036x6gt55

Funder(s)

Funder type
Industry

Funder Name
BD

Alternative Name(s)
Becton, Dickinson and Company, Becton Dickinson & Co

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	version 1.1		11/08/2021	No	Yes
Protocol file	version 1.1		11/08/2021	No	No