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A randomised study to assess the feasibility of pleural biopsy and indwelling pleural catheter insertion as a first procedure versus pleural aspiration in suspected malignant pleural effusion

Submission date 10/10/2023	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 20/10/2023	**Overall study status** Ongoing	
Last Edited 20/10/2023	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims

A malignant pleural effusion (MPE) is a buildup of fluid around the lungs due to any type of cancer that has either started or spread to the lining of the lungs (pleura). This is a very common problem, effecting over 100 people per day in the UK. Typically, people with MPE experience debilitating breathlessness due to fluid buildup. Another challenge for people suffering with MPE is the challenge to reach a diagnosis which can delay treatment with, for example chemotherapy.

At present, in the standard investigation and management pathway for patients with a pleural effusion suspected to be due to cancer, patients have some fluid drawn off and the cells analysed for the presence of cancer cells. This often is not successful and recent data from our site has suggested only 20% of patients receive enough information from fluid alone to treat their cancer. The patient therefore has to come back for a biopsy of the lining of the lung. Once a diagnosis is secured, steps to stop the fluid around the lungs coming back are taken, one of which is to insert a long-term tube in the chest (indwelling pleural catheter, IPC) which is dressed and can be used a few times per week to let fluid out (done by a district nurse or carer at home). Typically, with the current pathway, patients wait 6 weeks for a diagnosis and over 2 months for long term control of breathlessness. Many of these patients have a life expectancy of 3-12 months and as such a large proportion of this is spent breathless and without a diagnosis.

We aim to create a new accelerated pathway (diagnosing and managing fluid build up, which is all part of standard care) for patients suffering with potential MPE, such that at their first visit, patients will be offered a biopsy which give them the highest likelihood (80-95% success rate), of reaching a diagnosis and in the same (first) visit, the patients will have a long term chest tube fitted (indwelling pleural catheter, IPC) so they are not left breathless and needing multiple procedures. This could achieve diagnosis and treatment in one procedure rather than multiple

separate procedures in the standard pathway. As this is a significant change to the way patients with suspected MPE are managed, this study will look at how feasible and acceptable this new pathway is to patients and clinicians.

Who can participate?
Patients with pleural effusion suspected to be caused by cancer that are over 18 years old and meet the inclusion/exclusion criteria

What does the study involve?
Participants assigned to the standard care pathway will have as a first procedure fluid drawn off from around the lung (pleural aspiration). This will be sent for analysis, the pleural team, or the hospitals specialist will then determine if any further procedures are required (including pleural biopsy, chest drainage or IPC). These will be delivered as per the current UK national guidelines at separate visits.
Participants assigned to the accelerated pathway, will have a combined first procedure: pleural biopsy (either via a keyhole local anaesthetic thoracoscopy or biopsy using ultrasound to guide a small biopsy needle). In the same procedure, patients will have a long term chest drain inserted (IPC) which can be drained at home by district nurses, usuall three times per week.

Participants will be asked to fill out a diary with breathlessness scores, quality of life scores and information on healthcare utilisation at home. Follow up visits will occur in person at 2 and 6 weeks post procedure and at 12 weeks either in person or over the phone. During follow up visits participants will have chest x-rays and chest ultrasound scans as part of routine care to check on their clinical progresss and assess if any further procedures are required.

If participants are willing and indicate this on the consent form, they will be contacted to participate in a single interview for the research team to gain insight into participant experience and acceptability in the accelerated pathway and trial as a whole.

What are the possible benefits and risks of participating?
Participants will receive in the standard care pathway, best practice as per national guidelines. In the accelerated pathway, participants may benefit by having the opportunity to receive a diagnosis and definitive treatment for their pleural fluid earlier than current standard care. We will measure this as part of the study.
The main risk of taking part would be the possibility of receiving an IPC in the accelerated pathway may eventually have a diagnosis that is not cancer. This will be mitigated where possible by the use of imaging such as CT scans and ultrasound to identify appropriate patients. In the case that this does occur, the IPC will be removed which is a routine procedure undertaken under local anaesthetic.
One of the risks that we are looking to measure is whether participants in the accelerated pathway have sufficient consideration time before having a long term chest drain inserted.
All of the risks and benefits are detailed further in the patient information leaflet.

Where is the study run from?
The study is co-ordinated by the Oxford Respiratory Trials Unit (University of Oxford, UK)

When is the study starting and how long is it expected to run for?
January 2022 to January 2026

Who is funding the study?
The study is funded via the National Institute for Health and Social Care Research (NIHR, UK), as part of a Doctoral Fellowship award

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
328727

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 58345, NIHR302578, IRAS 328727

Study information

Scientific Title
Smarter therapeutic and diagnostic intervention in malignant pleural effusion - a feasibility randomised study

Acronym
STREAMLINE

Study objectives
Would it be feasible and acceptable to both patients and clinicians to investigate and treat suspected malignant pleural effusion with pleural biopsy and indwelling pleural catheter insertion as a first procedure compared to pleural aspiration alone (current standard care).

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 11/10/2023, London - Brighton & Sussex Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 2071048016; brightonandsussex.rec@hra.nhs.uk), ref: 23/LO/0772

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See additional files

Health condition(s) or problem(s) studied
Malignant pleural effusion (MPE)

Interventions
Eligible patients will be identified from the pleural service in each participating centre. All patients will require initial CT scan as per standard care prior to recruitment, and those with suspected MPE will be randomised to either the standard or accelerated pathway.

Accelerated Pathway group
Patients who are randomised to the accelerated pathway will receive, as their first procedure a pleural biopsy + Indwelling pleural catheter (IPC). The pleural biopsy may be undertaken either via local anaesthetic thoracoscopy (LAT) or ultrasound guided biopsy according to which the local clinical and study team judge to be the most appropriate intervention for the patient. All patients will receive an IPC at their first visit following biopsy.

Standard Pathway Group:
Patients randomised to standard care will receive pleural diagnostics and therapeutic interventions as per current national standards based on the current BTS guidelines. Patients will undergo an initial diagnostic and therapeutic pleural aspiration, with review in clinic with results. Those with a negative pleural fluid result will undergo thoracoscopic or image guided biopsy, and once a diagnosis is achieved, definitive fluid management with either IPC or Talc pleurodesis according to patient choice.

Data Collection and follow-up visits
Demographic data, medical history, relevant clinical data including vital signs (respiratory rate, heart rate, blood pressure and oxygen saturation by pulse oximetry) and measures of breathlessness, pain and quality of life/anxiety will be collected. Recording of breathlessness, pain and quality of life/anxiety will occur via patient diaries 3 times per week over 6 weeks post randomisation. Study follow up visits have been selected to occur in line with usual clinical care - post first procedure at 2 weeks (+/- 3 days), 6 weeks (+/- 3 days) - both in person then either in person over the phone at 12 weeks (+/- 7 days). At the 2 and 6 week visit, completed patient diaries up until the visit will be collected along with a chest radiograph as per standard clinical care.

Participant Interviews
Qualitative interviews will be performed on a proportion of participants. These interviews will be performed by either the study fellow or research nurse. Interviews will be conducted and analysed in collaboration with Oxford Brookes University. In addition, a proportion of those participants, who refused randomisation but consented to be interviewed will also be approached to take part if willing, and, any themes arising from these two groups will be incorporated into the design of the subsequent definitive randomised controlled trial. The interviews will be performed either face to face, over the phone. The interviews will be conducted in a Pseudonymised manner and audio recorded. These recordings will be stored securely, electronically by the Oxford Respiratory Trials Unit. Audio files will be sent securely to a professional transcription company. The transcriptionist will delete the recording when they have completed their work and returned the transcript. The contact details of participants willing to be interviewed will be sent to ORTU by the local sites.

Intervention Type
Other

Phase
Not Specified

Primary outcome measure
Feasibility of recruitment measured using patient records at end of study

Secondary outcome measures
1. Breathlessness as measured by 100mm VAS score weekly for 6 weeks post intervention (trial procedure)
2. Health Related Quality of Life (EQ-5D) weekly for 6 weeks post intervention (trial procedure)
3. Patient Anxiety and Depression (HADS) weekly for 6 weeks post intervention (trial procedure)
4. Time to actionable histopathology/diagnosis measured using patient records throughout the study
5. Healthcare utilisation measured using patient records until end of recruitment

Overall study start date
01/01/2022

Completion date
02/01/2026

Eligibility

Key inclusion criteria
1. Symptomatic unilateral (or bilateral if one side dominates) pleural effusion AND any of the following*
1.1. Suspicion of malignant cause based on imaging features on CT or ultrasound
1.2. Previous proven diagnosis of extrapleural malignancy
1.3. Lack of alternative likely clinical diagnosis such as infection or heart failure (as judged by local PI)
2. Sufficient pleural effusion size as determined on ultrasound to require therapeutic pleural drainage
3. Participant is willing and able to give informed consent for participation in the trial.
4. Male or Female, aged 18 years or above.
*The above features will be assessed by the local recruiting clinician, and judgments on likely clinical diagnosis and the imaging features will be conducted by local recruiting clinicians to remain pragmatic.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 40; UK Sample Size: 40

Key exclusion criteria
1. Technically unable to undergo pleural biopsy and indwelling pleural catheter (e.g. gross respiratory failure, uncorrectable clotting, unable to tolerate position, poor performance status (WHO performance status 3 or worse when accounting for the effusion)).
2. Visual impairment (precluding use of symptom measurement instruments
3. Previous talc pleurodesis within the last 3 months on ipsilateral side.
4. No means of phone contact
5. Age < 18 years
6. Females who are pregnant or lactating

Date of first enrolment
20/11/2023

Date of final enrolment
02/10/2025

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
John Radcliffe Hospital
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
University Hospitals of North Midlands NHS Trust
Newcastle Road
Stoke-on-trent
United Kingdom
ST4 6QG

Study participating centre
Derriford Hospital
Derriford Road
Derriford
Plymouth
United Kingdom
PL6 8DH

Sponsor information

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Sponsor type
University/education

Website
http://www.ox.ac.uk/

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
NIHR Academy

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
31/12/2026

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be 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?
Participant information sheet	version 1.1	27/09/2023	18/10/2023	No	Yes
Protocol file	version 1.0	03/08/2023	18/10/2023	No	No