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Discovering new methods of analysing pleural fluid samples to reach a diagnosis earlier in pleural effusions with an unclear cause

Submission date
21/05/2026

Recruitment status
Recruiting

Registration date
21/05/2026

Overall study status
Ongoing

Last Edited
03/06/2026

Condition category
Respiratory

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
A pleural effusion is a build-up of fluid between the lungs and the chest wall. It can be caused by many different conditions, ranging from temporary infections to serious cancers. To find out the cause, a sample of the fluid is usually collected and examined under a microscope by a specialist. However, in more than one in four cases, this examination cannot identify the cause straight away, and patients may face a long wait before a diagnosis is reached. For some cancers, this delay can be very significant, as treatments work best when started early.

This study aims to find new biological markers ("biomarkers") in pleural fluid samples that could help doctors identify the cause of a pleural effusion more quickly and accurately than current tests. In particular, the study focuses on cases where the standard microscope examination gives an unclear result. By analysing the cells and molecules in pleural fluid using advanced laboratory techniques, the researchers hope to identify patterns that distinguish between different causes of effusion, including cancer, and to develop tests that could one day be used routinely in NHS care.

Who can participate?
Adults aged 18 and over who are attending University Hospitals of Morecambe Bay NHS Foundation Trust (UHMBT) and who are already having a medically necessary pleural fluid sample taken or fluid removed from their chest as part of their NHS care may be invited to take part. The fluid must be suspected or confirmed to be an exudate (a particular type of pleural fluid associated with inflammation or other active disease processes).

People are not eligible to take part if they have or are suspected to have tuberculosis, if they need emergency removal of pleural fluid, if they have previously had a procedure called pleurodesis (where the layers of the pleura are sealed together), or if they are already involved in the public involvement activities for this study.

What does the study involve?
Participants are asked to donate a small amount of their pleural fluid for research. The fluid used

for research is surplus to what is needed for standard NHS tests and would otherwise be discarded.

For participants having fluid removed for symptom relief, the procedure is completely unchanged. A small portion of the fluid already being removed is set aside for research.
For participants having fluid sampled to help reach a diagnosis, the procedure may take one or two minutes longer while a small additional amount of fluid is collected for research.

No extra procedures or hospital visits are required. Participants are also asked to allow researchers to access relevant information from their medical records from up to one year before their sample was taken and up to three years afterwards. This includes information that may be accessed after a participant has passed away. This is necessary so that researchers can match the laboratory findings from the pleural fluid to the eventual clinical diagnosis.

If a participant's pleural effusion returns and further fluid is sampled or removed at a later date, they may be asked to donate a second sample. Participants will always be reminded of their involvement and asked to confirm their consent before any second sample is collected.

Research samples are transferred to Lancaster University, where they are stored securely and analysed in a laboratory using techniques such as genetic sequencing, flow cytometry (which identifies and counts cells), and chemical analysis of the fluid. The results of laboratory analyses will not be shared with participants and will not affect their clinical care.

What are the possible benefits and risks of participating?
There are no direct benefits to participants. However, participation may help future patients by improving the speed and accuracy with which pleural effusions are diagnosed.

The risks of the pleural sampling procedure are the same as those explained by the participant's lung specialist, regardless of whether they take part in the research. For those having a diagnostic sample taken, the procedure may be one or two minutes longer, but this does not introduce any new risks.

Where is the study run from?
The study is run by Lancaster University. Participants are recruited and samples are collected at University Hospitals of Morecambe Bay NHS Foundation Trust (UHMBT). Laboratory analysis is carried out at Lancaster University.

When is the study starting and how long is it expected to run for?
The study is expected to start in 2026. Recruitment will take place over one year, with follow-up of participants for up to three years after their sample is donated.

Who is funding the study?
The study is funded by a Cancer Research UK Predoctoral Bursary Award

Who is the main contact?
Dr Timothy Gatheral, Principal Investigator Email: timothy.gatheral@mbht.nhs.uk

Contact information

Type(s)
Public

Contact name
Dr Oliver Mann

ORCID ID
https://orcid.org/0000-0002-1506-2744

Contact details
Lancaster Medical School, Lancaster University
Lancaster
United Kingdom
LA1 4YW
-
o.mann@lancaster.ac.uk

Type(s)
Scientific

Contact name
Dr Lucy Jackson-Jones

ORCID ID
https://orcid.org/0000-0003-0608-8966

Contact details
B06 Furness College,
Lancaster University
Lancaster
United Kingdom
LA1 4YG
-
l.jackson-jones@lancaster.ac.uk

Type(s)
Principal investigator

Contact name
Dr Timothy Gatheral

Contact details
Respiratory Department, Royal Lancaster Infirmary, Ashton Road
Lancaster
United Kingdom
LA1 4RP
+44 1524591376
timothy.gatheral@mbht.nhs.uk

Additional identifiers

Integrated Research Application System (IRAS)
366402

Central Portfolio Management System (CPMS)
72537

Study information

Scientific Title
PROSPECT-PLEURA: Biomarker Discovery to Refine Diagnosis and Prognosis in Histologically Indeterminate Pleural Effusions

Acronym
PROSPECT-PLEURA

Study objectives
Our research aims to detect molecular and cellular characteristics that can differentiate histologically indeterminate pleural samples into their various causes. Of particular focus for this research are pleural aspirations which are described by histopathologists as ‘atypical mesothelial proliferation’.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 11/05/2026, North West - Greater Manchester West Research Ethics Committee (2 Redman Place Stratford, London, E20 1JQ, United Kingdom; no telephone number provided; gmwest.rec@hra.nhs.uk), ref: 26/NW/0141

Primary study design
Observational

Secondary study design
Cohort study

Study type(s)

Health condition(s) or problem(s) studied
Diagnosis of patients with exudative pleural effusion

Interventions
PROSPECT-PLEURA is a single-site, prospective observational diagnostic test accuracy study. There is no randomisation, no control arm, and no intervention; participants receive standard NHS clinical care throughout.

Participants
Adult NHS patients who are undergoing medically necessary pleural fluid sampling for a suspected or known exudative pleural effusion are eligible for inclusion. Sampling may be via thoracocentesis, intercostal chest drain, or indwelling pleural catheter. Patients with latent, active, or suspected tuberculosis, those requiring emergency pleural drainage, and those who have previously undergone pleurodesis are excluded.

Sample Collection
Pleural fluid is collected at University Hospitals of Morecambe Bay NHS Foundation Trust during clinically indicated procedures. For therapeutic thoracocentesis, intercostal drain, and IPC, up to 200 mL of surplus fluid is collected. For diagnostic thoracocentesis, up to 50 mL of residual fluid beyond clinical requirements is collected. No additional invasive procedures are undertaken as part of the study. The target sample size is 150 participants, with up to 30 participants donating a second sample, yielding up to 180 samples in total.

Sample Processing and Scientific Analysis
Samples are transported on the same day to Lancaster University on ice, in compliance with HTA Code E, T1 traceability requirements. At Lancaster University, samples are centrifuged and separated into supernatant and cell pellet. Supernatants are stored at -80°C; cell pellets are fixed or otherwise preserved for analysis. Some unfixed samples are cultured in containment level 2 facilities for short-term experimental use; no in vitro cell lines are established.

Scientific analyses include:
- Single-cell RNA sequencing of cellular content from pleural fluid, to characterise transcriptional states of immune and mesothelial cells
- Multiplex flow cytometry to assess immune and mesothelial cell populations and their expression of ligands and receptors
- ELISA and multiplex array analysis of pleural fluid supernatant to quantify secreted molecules including hyaluronan, mesothelin, cytokines, chemokines, metabolites, and other tumour-associated factors
- Fluorescence activated cell sorting (FACS) to isolate and culture immune and mesothelial cells for downstream analyses including microscopy, flow cytometry, nucleic acid sequencing, and ELISA
Scientific team members are blinded to clinical outcome during sample analysis.

Clinical Data Collection
Clinical outcomes data are collected by researchers or UHMBT research staff from electronic patient records using a standardised case report form. Data collected include demographic details, relevant blood and imaging results, pleural fluid analysis results (biochemistry, microbiology, cytology), pleural biopsy reports where available, serum circulating tumour DNA results where available, final clinical diagnosis, survival time, treatment, and time from sampling to diagnosis. Clinical outcomes data may be collected on multiple occasions over a follow-up period of up to three years following recruitment.

Biomarker Evaluation
Biomarker results are mapped to clinical outcomes to assess whether candidate biomarkers can predict diagnosis or prognosis with greater accuracy than standard NHS cytological analysis. Sensitivity is the primary accuracy parameter. Diagnostic performance analyses include sensitivity, specificity, positive and negative predictive values, likelihood ratios, and receiver operating characteristic (ROC) curve analysis. Non-inferiority and superiority testing against cytology are performed using McNemar's test for paired binary outcomes and DeLong's test for continuous outputs. Time-to-event analyses and decision curve analysis are also conducted to contextualise clinical utility.

Intervention Type
Not Specified

Primary outcome(s)

1. A final clinical diagnosis, cytology report(s) and biomarker analyses measured using the diagnosis for the formation of a pleural effusion, as determined by the clinical care team. Final diagnosis can be made posthumously. at 3 years

Key secondary outcome(s)

Completion date
31/05/2029

Eligibility

Key inclusion criteria
1. Undergoing medically necessary pleural fluid sampling or removal, via any method
2. The pleural effusion is suspected or known to be exudative
2. Aged 18 years or older and has capacity to consent to participate

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
120 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Latent, active, or suspected tuberculosis, whether pulmonary or extra-pulmonary
2. Clinically unstable patients requiring emergency removal of pleural fluid
3. Previous pleurodesis
4. Participating in ongoing PROSPECT-PLEURA patient and public involvement

Date of first enrolment
01/06/2026

Date of final enrolment
31/05/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Lancaster Infirmary
Ashton Road
Lancaster
England
LA1 4RP

Study participating centre
Furness General Hospital
Dalton Lane
Barrow-in-furness
England
LA14 4LF

Sponsor information

Organisation
Lancaster University

ROR
https://ror.org/04f2nsd36

Funder(s)

Funder type

Funder Name
Cancer Research UK

Alternative Name(s)
CR_UK, Cancer Research UK - London, Cancer Research UK (CRUK), CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.0	20/04/2026	21/05/2026	No	Yes
Protocol file	version 1.0	20/04/2026	21/05/2026	No	No