Smarter Therapeutic and Diagnostic Intervention in Malignant Pleural Effusion (STREAMLINE)

SUMMARY PARTICIPANT INFORMATION SHEET

You have been asked to participate in this trial because you have a build-up of fluid around the lungs (**a pleural effusion**). This study is looking into the best way of both diagnosing and managing fluid build-up. By now, your doctors will have explained that there is a significant concern that the fluid in your chest requires testing to check for cancer as the cause, or that tests already show this is the case.

The current, standard pathway for finding out why the fluid is present (diagnosis) and controlling the fluid over a long term (treatment) is done in a staged way, wherein first the fluid is drawn off the chest to see if we can achieve a diagnosis. Often the fluid alone is not enough to determine the diagnosis with enough information for treatments (studies estimate over 60% of the time, this is the case and in up to 95% of some diagnoses). Patients then need to return for a biopsy of the lining of the lungs (pleura). If the biopsy shows that the fluid is due to cancer or another cause that is likely to cause fluid re-accumulation, we can insert a long term chest drain (indwelling pleural catheter, IPC) which is tunneled under the skin and a district nurse, yourself or family member can attach to a bottle 1-3 times per week at home to drain and control the fluid, along with the symptoms the fluid may be causing (such as breathlessness). Studies before this one have shown that this process can take up to 6-8 weeks in total and patients informed us that the duration of the diagnosis and the need for repeated procedures was a significant burden for them.

We have developed, with patients like yourself, an 'accelerated' pathway that aims to combine standard clinical diagnostic tests and treatment that usually come later as part of the first procedure. This would involve the **first procedure** being a combined **pleural biopsy and IPC.** We would like to compare the standard care pathway with the accelerated pathway to see which one is better overall for patients in terms of breathing control, quality of life and the overall number of procedures.

The objective of this study is not to carry out this comparison, but rather to assess the willingness of people to be randomly allocated to one of the treatment pathways. This will help us decide if a bigger research study actually comparing the two treatment pathways can be done and whether the study can collect the data it needs.

By now, your doctor has already determined that you require some fluid drawing off the chest and investigating for the possibility of cancer causing this. If you agree to take part in the study, a computer will **randomly select** if you are treated with the standard treatment pathway or the accelerated pathway.

If you are assigned to the standard care pathway, your first procedure will be to draw fluid off from around the lung (pleural aspiration). This will be sent for analysis, the pleural team, or your hospital specialist will determine if you require any other procedures (including pleural biopsy, chest drainage or IPC). These will be delivered as per the current UK national guidelines at separate visits.

If you are assigned to the accelerated pathway, your first procedure will be a combined one, wherein you have a pleural biopsy (either via local anaesthetic thoracoscopy which is a keyhole procedure or a

biopsy using ultrasound to target the biopsy needle). In the same procedure, your clinician will insert a long-term chest drain (IPC) and inform the district nurses to drain this 3 times per week at home.

During your hospital visits you will have some blood tests, chest x-rays and chest ultrasound scans as part of routine care to assess which procedures are required and help with finding a diagnosis. A research team member may also visit you to go through some questionnaires if you are well enough, regarding your health, mobility, activities and breathlessness.

You will be required to attend the outpatient clinic as you would normally at roughly 2 weeks, 6 weeks and 12 weeks (the last consultation can be done over the phone) after your first procedure. No additional visits are required for the purposes of the study. At these appointments, you will have similar tests to the ones you had in hospital (such as an ultrasound or chest X Ray).

Once you have completed the trial visits, a member of the research team may contact you, if you consent to, to discuss your views on the treatment you received and your participation in the study through a series of standardised questions.

If there are any problems, your care and wellbeing will be the utmost priority and your hospital doctors will do what has to be done to help you. This will be reported to the study team and acted on accordingly.

This study forms part of a doctoral research fellowship (equivalent to a PhD) undertaken by Dr Addala, and is funded as part of this. Professor Rahman is Dr Addala's supervisor and the supervising researcher (Chief investigator) for the research project as a whole.

PARTICIPANT INFORMATION SHEET

You are being invited to take part in a research study called STREAMLINE. Before you decide to take part it is important for you to understand why the research is being done and what it will involve. Therefore, please take time to read the following information carefully and discuss it with others if you wish. Please feel free to ask us if there is anything that is not clear or if you would like more information.

What is the purpose of the study?

This study is called a feasibility study and it is designed to assess the willingness of patients like you to be randomly allocated to one of two established diagnostic and treatment pathways, which are detailed below, for the diagnosis and treatment of your pleural effusion. None of the procedures are new or experimental. During the study we will gather data on the percentage of participants willing, or not willing, to take part in order for us to run a much larger study in the future.

The accelerated pathway described above has not been directly compared before with the current standard care pathway and this feasibility study is looking to assess whether a direct comparison in a research study is possible.

Why have I been invited?

You have been invited to take part in this trial because you have a pleural effusion and have been referred for a pleural aspiration procedure. Your doctors will have explained by now that there is a possibility that the fluid in your chest has been caused by cancer and this requires investigation.

This study will take place in hospitals across the UK. We are aiming to recruit 40 patients to take part. This study is part of a PhD looking at the best ways to help people with malignant pleural effusions.

Do I have to take part?

It is up to you to decide whether or not to take part. This information sheet is to help you make this decision. If you do decide to take part you will be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect your future medical care outside the study.

If you decide not to take part we may ask for your consent for one of our study doctors to contact you to ask the reasons why you didn't want to take part as your views are very important to us and will be very valuable in adding to our understanding for the purposes of this trial. This will also help us when designing a larger scale study in the future.

What will happen to me if I decide to take part?

You will be seen by one of the study team who will discuss the study with you, answer any questions, and ask you to sign a consent form to enter the study if you are happy to do so. You should have had enough time, in your opinion, to consider participating in the study before consenting. Before the procedure, you will have a consultation with a study doctor who will ask about your symptoms and perform an examination. You will also be asked to complete some questionnaires.

You will be randomly allocated to either receive as your first procedure

a) standard care pathway - pleural aspiration (fluid drawn off only) OR
b) accelerated pathway - a pleural biopsy and indwelling pleural catheter (IPC) Fluid will then be drained through the IPC.

We are not able to influence or predict which procedure you receive. This is so they can be fairly compared. Treatment allocation will happen before your procedure.

If you are allocated to the standard care pathway, after your pleural aspiration, you will be discharged from hospital on the same day (unless it is deemed necessary by your treating team that you are required to stay in hospital after). The fluid will be sent for analysis in the laboratory and your case will likely discussed at a multi-disciplinary team meeting (MDT). From here you will either receive a diagnosis if the fluid is sufficient to provide this, or further diagnostic procedures as necessary (such as a biopsy). Should you need further treatment such as IPC for the condition this can be carried out after a diagnosis is reached.

If you are allocated to the accelerated pathway, you will receive a pleural biopsy for diagnosis. This will be carried out either via a thoracoscopy procedure OR pleural biopsy using ultrasound guidance. A thoracoscopy is a procedure to examine the lining of the lungs with a camera, using a keyhole technique with local anaesthetic and sedation through a drip. The camera is inserted into the chest, between the lung and the chest wall, to allow inspection and biopsies to be taken. Ultrasound guided pleural biopsies use a smaller biopsy needle with ultrasound to direct the needle placement, under local anaesthetic and no sedation. As we are assessing the feasibility of this study, the decision on which way the biopsies are taken will be made taking account of which is technically possible, the judgement of the clinical team and availability of equipment at each site. Immediately after the biopsies have been taken, the team will insert an IPC for long term fluid drainage. Fluid will be drained at the time of insertion for analysis alongside the biopsy and for symptomatic benefit.

It is possible that if one way of biopsy does not achieve a diagnosis, your local medical team may recommend another technique (such as a biopsy using a CT scanner or thoracoscopy if ultrasound guided biopsy was used first).

If you receive an indwelling pleural catheter (IPC), you will go home with the IPC in place. A district nurse will visit and drain any fluid from the IPC for 3 days per week, which is a standard regime. When you are sent home after your procedure, you will be given a supply of drainage bottles to take home with you.

After the first 2 weeks, your local study team will advise how often the IPC should be drained. If you find it more convenient, after the first 2 weeks, a member of your family or carer may perform the drainages at home once they have received appropriate training by a healthcare professional.

We may be able to remove your IPC if the amount of fluid being drained reduces sufficiently. You should contact your local trial team if there is minimal drainage (<50mls) on three consecutive drainages.

All patients in the study will be given a paper diary to complete. This is so we can monitor your progress after your procedure. The diary includes simple questionnaires about how much breathlessness (if any) you are experiencing. This should only take a minute to complete and will be recorded three times per week

You will also be asked to record any appointments or discussions you have with healthcare providers. In addition, there is space for patients who have an IPC to record how much fluid is drained at each district nurse visit. We will collect this information from the diary when you return for follow-up appointments, so you will need to remember to bring it with you.

Following your procedure, we will monitor your progress over the next 12 weeks. Study visits will normally take place in your local hospital.

The table below summarises what the routine visits during the study will involve: It is important to note that whichever pathway you are allocated to, **additional procedures after the first procedure** or reviews to ascertain the diagnosis or for treatment of symptoms **may be required, as decided upon by the local medical team**. The study team will be informed of these visits.

Visit	**What happens at the visit?**	**Is hospital attendance required?**
Before procedure: consent, study enrolment and baseline assessments (can occur anytime between 2 weeks pre-procedure to the day of procedure unless otherwise specified).	Discuss study and sign consent form Randomisation – allocation into a specific arm of the study Clinical assessment, vitals and medical history Complete baseline tests: • Blood tests (routine clinical care for all patients undergoing investigation for pleural effusion) – if these have been done within the previous 4 weeks as part of your clinical care they do not need to be repeated. • Quality of life questionnaires (on the day of procedure, just before the procedure) • Symptom questionnaires (VAS scores) (on the day of procedure, just before procedure) • Chest x-ray (routine for patients with pleural effusion)	Yes
First Procedure: Pleural aspiration	• Chest ultrasound • Procedure as randomly allocated treatment arm	Yes

OR Pleural biopsy + IPC	• Chest x-ray after the procedure (routine clinical care for all patients) • Pleural fluid samples sent for analysis (routine care) • If biopsies conducted, samples sent for analysis (routine care) • Symptom questionnaire (VAS scores) immediately after the procedure.	
Follow up after procedure: appointments at 2 weeks and 6 weeks following procedure.	Outpatient visit involving: • Clinical examination assessment and vitals • Chest x-rays • Blood tests (routine clinical care for all patients undergoing investigation for pleural effusion) • Ultrasound • Quality of life questionnaires • Symptom scores (VAS scores) • Collecting information from patient diary • Semi-structured interview (on or after 6 week)	Yes
Follow up after procedure: appointment 12 weeks following procedure.	Outpatient visit or telephone/ call involving: • Quality of life questionnaires • Collecting information from patient diary	May be done over the phone Quality of life questionnaires and patient diary to be returned by post if not visiting in person.

Your study involvement will finish after the 12-week period, after which you will be looked after by your normal medical team.

What should I consider?

If you agree to take part, your doctor will arrange the study treatment. Once you have completed the study visits, a member of the research team may contact you to discuss your views on the treatment you received and your participation in the study. Even if you decide not to take part in the randomisation process and continue with normal care, your views are still very important to us. Providing you are happy and consented for us to do so, we may also contact you to discuss these.

Interviews will be either performed by telephone or in person, arranged at a convenient time for yourself. All interviews will be audio recorded using a digital audio recorder.

What are the potential benefits of taking part?

All treatments received as part of this study are standard of care, therefore there are no additional benefits to taking part. However, patients who receive a pleural biopsy and IPC in the accelerated pathway may require fewer overall procedures and have their breathlessness definitively managed earlier.

However, these are some of the questions that we will look to answer if we proceed to a larger clinical study and we are not able to influence or predict which treatment you receive. By taking part in this feasibility study, you will be helping to inform medical professionals whether a larger study to fully compare these pathways would be possible in the future.

Are there any possible disadvantages or risks from taking part?

The main study specific risks, beyond the normal investigation and treatment pathway for new pleural effusion is that of 'over treatment'. This means that a small number of patients may have a biopsy wherein the fluid alone would have sufficed to make a diagnosis. Based on published work from our unit we expect the number of patients that the fluid alone would be sufficient to achieve a treatable diagnosis to be 20% or less.

Some patients may receive an IPC who we then discover have a cause of pleural effusion that either drains very little or is not usually treated with an IPC (for example, heart failure).

If you have received an IPC as part of the study and find that there is very little fluid being drained, or we discover that it is not required due to the eventual diagnosis, it can easily be removed if this is the case. If the final diagnosis does not require an IPC, the study team will be informed and your local team can remove the IPC.

If you agree to part of the study, and are in the accelerated pathway your first procedure would include an IPC (long term pleural drainage catheter) that would be drained at home. Having an IPC earlier in your diagnostic journey may have an added psychological impact. It may reduce the uncertainty around further drainage procedures, but could also result in additional burden of home management. One of the purposes of this study is to measure this with questionnaires and interviews. If you are concerned about the psychological impact of the study, please discuss this in further detail with your local trial team.

You may not receive an IPC as part of the study (standard care pathway). However, you will be treated in the same way as any other patient if the fluid does build up again after the pleural aspiration. There is no reason why you cannot have an IPC inserted with a later procedure if your doctor advises this would be helpful.

All medical procedures are associated with certain risks. Your medical team will have advised you about the specific risks involved with a thoracoscopy, talc and IPC insertion and local trust information sheets will be available. The specific risks noted are specific to the procedure and not influenced by

whether you are allocated to the standard or accelerated pathway. All patients taking part in the STREAMLINE study will be carefully monitored during and after their procedure, and any important adverse events reported to the team running the trial. Possible risks of each procedure include:

Procedure	Possible Risk	Frequency
Pleural Aspiration	Pain requiring pain killers after local anaesthetic	Fewer than 1 in 100 Fewer than 1 in 200
	Re-expansion pulmonary oedema (fluid collecting in the lung itself if it expands quickly)	Fewer than 1 in 200
	Damage to local organs	
Pleural Biopsy (Ultrasound guided or thoracoscopy)	Pain during procedure or immediately after	Most patients
	Swelling around the drain site (subcutaneous emphysema)	1 in 25
	Low blood pressure	1 in 50
	Infection	1 in 100
	Re-expansion pulmonary oedema (fluid collecting in the lung itself if it expands quickly	1 in 200
	Unintentional injury to another organ e.g. lung	1 in 200
	Persistent air leak – if this happens the chest drain will need to stay in place until the leak has healed.	Fewer than 1 in 200
	Bleeding	Fewer than 1 in 250 (Fewer than 1 in 500 have serious bleeding requiring an additional procedure)
	Risk of death	Fewer than 1 in 1000
IPC insertion	Pain Some patients experience pain or a pulling sensation when the IPC is being drained. This can be minimised by draining fluid slowly and stopping as soon as you feel any discomfort.	Most patients get some pain after the initial procedure. Persistent pain occurs in fewer than 1 in 100.

	Fluid loculation (development of pockets of fluid – this can limit the amount of fluid drained by the IPC)	Fewer than 1 in 7
	IPC related infection	Fewer than 1 in 20
	Blockage of the IPC by debris	Fewer than 1 in 20
	Cancer growth around the IPC site	Fewer than 1 in 20
	Bleeding during IPC insertion	Fewer than 1 in 100
All procedures	Breathing difficulty	Fewer than 1 in 1000 have serious or life-threatening difficulties.

Radiation dose within the study

If you take part in this study you may have a Chest CT at screening (if no suitable prior imaging available) and further chest x-rays. Some of these may be extra to those that you would have if you did not take part. These procedures use ionising radiation to form images of your body. Ionising radiation can cause cell damage that may, after many years or decades, turn cancerous.

The number of chest X Rays and CT scans in this study have been designed to match what is required clinically and what is typically done for patients in this pathway in the NHS. If you have not had any previous scans, you will have 1 CT scan and 4 chest X Rays during the duration of the study. If your clinical team feel more imaging is required for your medical care, they will discuss this with you.

We are all at risk of developing cancer during our lifetime. The normal risk is that this will happen to about 50% of people at some point in their life. Taking part in this study will increase the chances of this happening to you by approximately 0.04%. The total dose of radiation within the study is equivalent to 3.5 years (8.1mSv) of average natural background radiation in the UK and is typically what we would expect patients with this condition to experience in usual NHS care.

What will happen to the samples taken during the study?

All patients approached to consider participating in STREAMLINE will require pleural fluid to be sent to their local NHS laboratory for analysis on diagnosis regardless of participation in the study.

If you agree to participate in this study and are part of the accelerated pathway, you will have a pleural biopsy earlier than in standard care. These samples will also be sent in line with all biopsy samples in the NHS to your local hospital laboratory to further help diagnose the cause of fluid building up. We will not keep or store any of these samples for research purposes or experimental use.

Optional aspects to the study

Interviews: These will be standardised questions that will be agreed by the study team and asked to all the participants in the same way. They will not include any personal questions or anything of a sensitive nature. The aim of these will be to reflect your experience during the course of treatment you had and your answers will be important of informing the researchers of how the patient experience differs through each of the different treatment pathways for this condition. Your responses will be audio recorded on a digital recorder (Dictaphone) and the data will be transcribed by an external transcription company.

Interviews if you do not wish to consent to the STREAMLINE study

Should you not wish to participate in the STREAMLINE study we would still be interested in your views and reasons for not participating in the study. We will offer you the opportunity to participate in a single interview, audio recorded as above.

If you agree to participate in the interviews, the research team from your local site will pass on your contact details to the interview team based at the University of Oxford so that we can contact you for your interview.

The duration of all interviews will be approximately one hour.

Will my General Practitioner (GP) be informed of my participation?

Your GP will not routinely be informed of your participation in the study but will be kept informed of your treatment via clinical letters from your medical team. Your participation in this study will not affect any other aspect of your clinical care. Your treatment and follow up will be provided in full by your clinicians in hospital or remotely by the study team. Any incidental findings or unexpected events will be handled directly by your treating doctors and the study team, and if any action is required outside the scope of the study or managing your condition, your GP will be informed.

Will my taking part in the study be kept confidential?

All the study information is stored in a secure electronic system and participants will only be identified by a unique code. Responsible members of the University of Oxford, Oxford Brookes University, regulatory authorities, and the relevant NHS Trust(s) may be given access to data for monitoring and/or audit of the study to ensure that the research is complying with applicable regulations.

Will I be reimbursed for taking part?

Travel expenses for any visits additional to normal care will be reimbursed on production of receipts, or a mileage allowance.

What will happen to my data?

Data protection regulation requires that we state the legal basis for processing information about you. In the case of research, this is 'a task in the public interest.' The University of Oxford is the data controller and is responsible for looking after your information and using it properly. We will be using

information from you and your hospital in order to undertake this study and will use the minimum personally-identifiable information possible.

We will store any research documents with personal information, such as consent forms, securely at the University of Oxford for 5 years. We will keep any other identifiable information about you for 3-6 months after the study has finished.

If you agree to participate in the interviews, we will ask your local site to send your consent form to the interview team based at the University of Oxford and share your contact details with us so that we can co-ordinate your interview. These will be held according to the same rules as above.

The interviews that we conduct will be assigned a study code (pseudonymised). The audio recordings of your interview will be stored electronically within the Oxford Respiratory Trials Unit at the University of Oxford and will be sent securely to a professional transcription company. and The transcriptionist will delete the recording when they have completed their work.

The local study team from your hospital will use your name and NHS number 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. A copy of the consent form from this study will be kept in your medical records for as long as those records are retained, in keeping with local policy. They will keep any other identifiable information about you from this study for 6 -12 months after the study has finished.

Data protection regulation provides you with control over your personal data and how it is used. When you agree to your information being used in research, however, some of those rights may be limited in order for the research to be reliable and accurate. Further information about your rights with respect to your personal data is available at https://compliance.web.ox.ac.uk/individual-rightsYou can find out more about how we use your information by contacting ortu@ndm.ox.ac.uk

What will happen if I don't want to carry on with the study?

Participation in the study is completely voluntary and you may change your mind at any stage. You can be completely reassured that your withdrawal from the study will not affect any care you receive from the medical and nursing team looking after you. Standard investigation and treatment of your condition will continue in keeping with current guidelines and you will be followed up after discharge in the usual way. You may also wish to withdraw but keep in contact with us to let us know your progress. Information collected may still be used.

What will happen to the results of this study?

At the end of the study these results will be made available to all doctors, through publication of a medical 'paper', and presentation at medical conferences and as part of fulfilment of an educational requirement.

You can access the results online, and we will post them to:
https://www.expmedndm.ox.ac.uk/research/respiratory-medicine/ORTU/home

What if we find something unexpected or new information becomes available?
As already discussed, this study is looking to evaluate the possibility of comparing two investigation and treatment pathways against each other and there is no new or experimental treatment being used.

The committee monitoring this study will continue to review all new research data. If any new information that influences the study becomes available, alterations will be made accordingly to the study (including patient randomisation, patient information etc. wherever appropriate). Patients will be contacted about new data via their hospital doctors at their local centre.

What if there is a problem?
If there are any problems, your hospital doctors will do what has to be done to help you. They will let the study team know about any problems, and they will act on this information and pass the information on to others in the study as is needed. The University of Oxford, as Sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this study. NHS indemnity operates in respect of the clinical treatment which is provided.

If you wish to complain about any aspect of the way in which you have been approached or treated, or how your information is handled during the course of this study, you should contact <name of investigator><contact details (phone number & email)> or you may contact the University of Oxford Research Governance and Ethical Assurance Team (RGEA) office on 01865 616480, or the head of RGEA, email rgea@admin.ox.ac.uk

The Patient Advisory Liaison Service (PALS) is a confidential NHS service that can provide you with support for any complaints or queries you may have regarding the care you receive as an NHS patient. PALS is unable to provide information about this research study.
If you wish to contact the PALS team please contact ****** or alternatively you can email ******

How have patients and the public been involved in this study?
Patients treated in the Oxford Pleural Unit helped develop the research topic and what research questions should be asked. A focus group of patients and carers were consulted with regard to the design of the study.

If this is something that appeals to you, the following links provide general information about taking part in research:

- www.crn.nihr.ac.uk/can-help/patients-carers-public/how-to-take-part-in-a-study/
- www.nhs.uk/Conditions/Clinical-trials/Pages/Introduction.aspx

Who is organising and funding the study?

The study is run by the Oxford Respiratory Trials Unit. The study is being funded by a grant from the National Institute of Health Research as part of a doctoral training fellowship. Independent experts will regularly monitor the progress of the study in terms of both safety and benefits from the study treatment.

Who has reviewed the study?

The project has been reviewed by the National Institute of Health Research (NIHR) who are funding the research. All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect participants' interests. This study has been reviewed and given favourable opinion by _____Research Ethics Committee.

Oxford Participants Only

Participation in future research:

Provided that you agree for us to do so, your personal details will be kept so that we may contact you regarding similar studies in the future. If you agree to this, we will also retain a copy of your consent form. We will keep the consent form and your details separate from one another and any research data. Agreeing to be contacted does not oblige you in any way to take part in future research and you may ask to be removed at any time.

Thank you very much for reading this information and for considering taking part in the STREAMLINE study