

# TAPPS TRIAL

A randomised, open-label trial to determine the most effective method for the management of malignant pleural effusions in patients with a good performance status.

## 1. Invitation

You are being invited to take part in a research study called the TAPPS trial. 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.

## 2. Trial description

This is a research study which aims to help determine the best way to manage fluid collections around the lungs (pleural effusion) which are caused by cancer (malignancy). It will look to compare two treatment methods which both involve the application of sterile talc powder to the lining of the lung. This aims to 'stick' the lung to the chest wall and so prevent further fluid build-up.

One group of patients will receive a small chest tube to drain away the fluid, before having sterile talc powder (mixed with water to form slurry) inserted through the same tube. The other group of patients will undergo a minor procedure called a thoracoscopy. This involves using a small camera to inspect the lining of the lung and allows the talc to be sprayed evenly over its surface. The main aim of this trial is to see which method is the most effective at preventing the fluid building up again.

This is a 'randomised trial,' which means that you will be randomly allocated to receive one or the other of the treatments described above. We shall not be able to influence or predict which treatment you receive.

### 3. What is the purpose of the trial?

Patients with cancer can develop fluid around the lungs as part of their disease process. This fluid is called a malignant pleural effusion. The pleura are thin layers which normally cover the lungs and help them to move against the chest wall. Fluid which builds up between these layers can restrict lung movement, causing breathlessness, but can usually be drained away to help relieve symptoms. However, fluid caused by cancer will often come back after drainage, sometimes within a few days. To reduce the chances of this happening, doctors can apply an irritant substance to the pleura to try to cause them to stick together, and so prevent any further fluid from building up. This process is called pleurodesis, with the most widely used irritant being sterile talc.

Talc is most commonly given in slurry form, in which a fine powder is mixed with water without it dissolving. Before this can be given, the effusion needs to be drained away using a small chest tube (placed under local anaesthetic) which is then also used to administer the slurry. This method is established and proven, and usually involves a hospital stay of around five to seven days before the drain can be taken out.

An alternative to this involves performing a minor procedure called a thoracoscopy. This technique is also done under local anaesthetic, but often requires a small amount of light sedation as well. During a thoracoscopy, a small camera is inserted through the chest wall and any pleural fluid is drained away before talc powder is sprayed directly onto the pleura, a process known as poudrage. A chest tube is left in place afterwards to allow the lung to re-expand, and can normally be removed after one to two days. Patients who undergo thoracoscopy are normally in hospital for two to three days in total.

**There have been previous studies which have attempted to identify which of these two methods is the best way to apply talc, but none so far have been able to provide doctors and patients with a complete answer. This study therefore looks to definitively establish which method of applying talc, slurry or poudrage, is the most effective at preventing fluid recurrence for patients, and the most cost-effective for healthcare providers such as the NHS. We shall also be collecting information on patients' symptoms and quality of life during the trial to see if one treatment is better than the other from the patient point of view.**

#### **4. Why have I been chosen?**

We have invited you to take part in this trial because you have a pleural effusion caused by your cancer. You are also considered well enough to undergo either a thoracoscopy under local anaesthetic, or a standard chest drain insertion, and to receive sterile talc. The results of this trial will help to inform the future management of patients in your situation. This study will take place in hospitals in different parts of the country. We are going to ask 330 patients in total to participate.

#### **5. 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.

#### **6. If I agree to participate, will I definitely have one of the procedures, and will I definitely receive talc?**

Unfortunately not. In very rare cases, doctors may be unable to safely insert a chest drain, perform a thoracoscopy, or complete a thoracoscopy which has been started. In addition, sometimes these procedures are completed successfully, but it is not possible or safe to give any talc. The risk of something like this happening would be the same for any patient, regardless of whether they are in a trial or not. Even if you are not able to undergo any of the trial procedures as planned, we shall still ask you to participate in trial measurements and follow-up appointments as any information you provide will still go towards our results, which may help people in the future. You will also continue to receive all of your normal medical care throughout the period of your trial involvement, which may include looking for alternative approaches to drain any fluid and manage your symptoms.

#### **7. I am currently receiving chemotherapy/radiotherapy for my cancer. Will being in the trial affect my other treatments?**

No. The treatments in the study do not affect the cancer itself, and neither do they interfere with anti-cancer therapies. The main aim of this trial is to determine the best way to manage pleural effusions, and the symptoms they cause.

## **8. If I take part in the trial, what will happen to me before I enter the trial?**

Before your doctors consider you for the TAPPS trial, you will have been diagnosed with a malignant pleural effusion that is causing you symptoms, and is large enough to allow you to undergo a thoracoscopy if necessary. You and your doctor will have agreed that it is both appropriate and practical for you to have your fluid drained, and for you to have talc applied to try and prevent further fluid build-up. Before you are asked to undergo any trial-related procedures, you will be seen by one of the trial team who will explain the trial to you and give you the opportunity to ask any questions. You will then typically be given an appointment to come to hospital to receive the treatment, unless you are already an inpatient.

## **9. What will happen to me at the beginning of the trial?**

Once you are admitted to hospital, or when it is appropriate if you are already an inpatient, you will be asked to sign a consent form to enter the trial if you are happy to do so. You should have had enough time, in your opinion, to read this information sheet and to fully consider participating in the trial. You will then have a consultation with a trial doctor who will ask questions about your treatment to date, your history and your symptoms. You will have an examination and may have a chest x-ray and blood tests taken. We shall also be asking for your permission to use some of the blood samples we take during the course of your trial involvement for analysis as part of the TAPPS trial, and for future research studies. Trial samples will be stored with a code number so that they are not directly identifiable to you. You will also be asked to fill out some health questionnaires. Following this, you will be randomised to undergo ONE of the two procedures described below, 'a' or 'b'. Your doctors and the trial team have no influence over which treatment you will receive, as this decision is made by a computer.

**a. Chest drain and slurry.** If you are allocated to this group, your doctors will place a small chest tube into your fluid under local anaesthetic. Your tube will be stitched in place and attached to a portable bottle to allow the fluid to drain away. The whole procedure shouldn't take more than half an hour. Once the fluid has drained away, which can take a day or two, a mixture consisting of saline (salt water) and the sterile talc powder will be injected through the tube. During the first 24 hours after the talc is injected, your drainage bottle may be attached to a gentle suction device which is on the wall by your bed. This may restrict the distance you can travel away from the bed, but gives the treatment the best chance of working. Once the amount of fluid draining from the tube has reduced sufficiently, the tube will be removed. On average, patients who undergo this kind of treatment are in hospital for around 5 to 7 days.



**b. Thoracoscopy and poudrage.** If you are allocated to this group, you will undergo a medical thoracoscopy (also known as local anaesthetic thoracoscopy, or LAT). A camera will be inserted through the chest wall under local anaesthetic to inspect the inside of your chest, with most of the fluid being removed through a small incision beforehand. Towards the end of the procedure, sterile talc powder will be sprayed into the chest to coat the lining of the lung. A chest tube will be inserted before being stitched in place and attached to a portable bottle. The whole procedure shouldn't take more than an hour. The bottle may be attached to a gentle suction device, which is on the wall by your bed, for the first 24 hours after the procedure. This may restrict the distance you can travel away from the bed, but gives the treatment the best chance of working. Once the amount of fluid draining from the tube has reduced sufficiently, the tube will be removed, with a small stitch left in place. On average, patients who undergo this kind of treatment are in hospital for around 2 to 3 days, with the stitch coming out about a week later.

We may also ask for your permission to store some of the pleural fluid which will be removed as part of your procedure, so it can be analysed in the same way as your blood samples. On the second day after your talc is given (or sooner if you are due to go home before then), you will have some more blood samples taken, although these ones will not be stored any longer than normal and will be processed quickly.

During your stay in hospital you will also be asked to fill out a simple chart which tells us how breathless you are, and how much pain you are in. This shouldn't take more than a few seconds each day. We shall ask you to complete these scores every day for the first 7 days after your procedure.

Finally, as part of the trial but regardless of which procedure you receive, you will have a chest x-ray about 24 hours after your procedure, and another one performed soon after your drain is removed, usually just before you leave hospital. Alongside these, you may have additional chest x-rays as part of your normal clinical care.

## **10. What will happen to me once I've left hospital?**

Before you go home, you will be given a simple diary to record any contact you have with medical services after discharge. In addition to the diary, you will be asked to record your levels of pain and breathlessness in much the same way as when you were in hospital. We shall provide you with a chart which will only need to be completed once a week.

Following discharge, you will be seen in clinic three times in total, after one month, after 3 months, and after 6 months. These visits will be specifically for the trial and won't necessarily replace any other appointments you may need, although we shall do everything possible to make them coincide with any other appointments you may have. At each of these visits you will be asked to have a chest x-ray, and to fill out some quality of life questionnaires as before. A member of the trial team will also see you to talk about how you are feeling and discuss your chart and your diary.

We may contact you over the telephone to remind you to attend follow-up appointments, or to complete the charts or diary, but only with your permission.

## **11. Information about talc**

Talc is a naturally occurring soft powder which has been used in medicine for decades. It is given on a daily basis in hospitals all over the world, and its use is considered standard care in the UK. 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 completely sterilised before use. It is extremely 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 drugs 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.

## **12. Information about chest drains**

Small chest drains are the mainstay of treatment for removing any substance which builds up around the lungs, including air, fluid and blood. They are regularly used as standard therapy in most hospitals and can be inserted quickly and safely under local anaesthetic, although there are a few minor risks associated with their use. On very rare occasions inserting them can cause damage to underlying structures, or can cause bleeding. These complications are extremely rare and can usually be avoided by guiding the placement of the chest tube with an ultrasound scan. All chest tubes in this trial will be placed using ultrasound. It is also theoretically possible for infection to occur following drain insertion, although this is kept to a minimum by using sterile techniques and equipment. Finally, some patients can experience discomfort with the tube in place. It is difficult to predict who this will affect but all patients will be given painkillers as needed.

### **13. Information about thoracoscopy**

Thoracoscopy is performed in an increasingly large number of hospitals in the UK. All of the centres in this trial perform this procedure as part of their normal routine practice. Thoracoscopy can be used to help diagnose patients with pleural disease, as well as treat them, often at the same time. Medical thoracoscopy is usually done under light sedation and local anaesthetic and, as with any procedure, can carry some minor risks. Whilst performing a thoracoscopy, it is possible to cause damage to the chest or to other structures within it (including the lung). This can usually be avoided by guiding the procedure with an ultrasound scan. All thorascopies in this trial will be performed using ultrasound. It is also possible for infection to be caused by the procedure, although this is kept to a minimum by performing it in a clean environment under sterile conditions. Finally, some patients may feel sore and bruised after the procedure, although this is typically easy to control with painkillers such as paracetamol or codeine, and only lasts for a few days.

### **14. What are the potential benefits from taking part?**

We hope that every patient in the trial will benefit, as normal, from whichever treatment they receive as well as continued follow-up appointments. The main aims of both treatments are to remove pleural fluid and so reduce breathlessness, and to keep people well by preventing any more fluid returning.

Whichever group you are allocated to, your participation in this trial will contribute to our understanding of the best way to manage malignant pleural effusions, which will hopefully benefit patients like you in the future.

### **15. What are the possible disadvantages and risks of taking part?**

You will have at least 6 chest x-rays during your participation in this study, although many of these would need to be done whether you were in the trial or not. There are some theoretical health risks from excessive radiation exposure, but chest x-rays are considered one of the safest tests as the dose from one is only equivalent to around four days' worth of normal background radiation.

We shall be monitoring you closely for the side effects explained in sections 11, 12 and 13.

Apart from these side-effects, and your time commitment, there are no other likely disadvantages to taking part.

Please note that we shall always try to arrange your trial follow-up appointments along your routine clinic appointments to minimise the number of times you need to come to the hospital. If we cannot arrange this, you will be reimbursed for any extra travel expenses you may incur by attending a trial visit.

## **16. Will my medical information be kept confidential?**

Yes, your medical records will be kept confidential but in order for the trial to run smoothly they may need to be looked at by certain groups of people, specifically:

- Key members of the research team, including those based at the trial co-ordinating centre (Oxford Respiratory Trials Unit, ORTU). The research team includes doctors and nurses who would usually be involved in your care, as well as the doctors, nurses and administrators who are co-ordinating the trial.
- Representatives of North Bristol NHS Trust who are sponsoring the trial and who must ensure the trial is run in a proper manner

All of these people have a duty of confidentiality to you as a research participant.

Information about you will be collected for analysis by the Sponsor's trial team at North Bristol NHS Trust, and other collaborators in the study. This will include information about health and other details such as your age and your gender. This information will be stored on a secure database which is accessible only to the research team. Each patient will be allocated a personal study number as an identifier so there will be no record of names or contact details in the study database. With your permission, some identifiable details, such as your name, date of birth, address and NHS number may be transferred to the Sponsor's trial team and/or study co-ordinating centre (ORTU) either on paper or via fax. This will be done for the purpose of follow-up through the Health and Social Care Information Centre which will allow us to keep in touch with you and follow up your health status.

## **17. Stopping your participation in the trial**

The study doctors may withdraw you from the trial at any time, if they feel that it is no longer safe or appropriate for you to continue.

North Bristol NHS Trust may also stop the trial early, although if this happens the reasons will be explained to you.

## **18. 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, or how we handle your samples, 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.

## **19. What if there is a problem?**

If you have any concerns, 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 do not wish to speak to a member of the trial team, or if you remain unhappy and wish to make a formal complaint, then you can do this through your hospital's Advice and Complaints Team, whose contact information can be found below.

If you are harmed as a result of your participation in this study, due to someone's negligence, North Bristol NHS Trust will provide indemnity and / or compensation via the NHS indemnity scheme.

If you are harmed as a result of your participation in this study, but not due to negligence, North Bristol NHS Trust will sympathetically consider any claim for compensation.

## **20. 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 the NIHR Health Technology Assessment (HTA) programme. More information about this can be found online at <http://www.hta.ac.uk>. No payment will be made to the trial doctors or nurses for including you in the study.

## **21. Who has reviewed and approved the trial?**

In order to protect your rights, safety and dignity, this study has been reviewed and approved by the North West (Preston) Research Ethics Committee, as well as by the research department in your local NHS Trust.

## **22. What will happen to the results of the trial?**

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.

## **23. What will happen to the samples taken in the trial?**

Many of the blood tests which are needed for the trial will be done as part of your standard care, but occasionally we may require one or two extra small vials of blood to be taken. We may also need to collect samples of pleural fluid, but these are taken from the drained fluid which would otherwise be thrown away. Some of the blood and pleural fluid samples collected will be kept by the trial team and analysed at a later date. Following this, some samples may be stored and used in future research studies, subject to ethical approval, with the aim of developing diagnostic tools and new treatments to help doctors treating patients like you. Some of these studies may be funded by commercial companies. We are asking you to consider these samples as a gift to the research team to help us with our research in the future.

All samples which need to be stored for trial purposes will be frozen and held securely in a “coded” form, meaning that each sample will be labelled with a number and not your name or date of birth, which protects your confidentiality. The list linking your name to the sample will be securely held separately, meaning that only members of the trial team will be able to link the samples back to you. If samples are used by other researchers, then you will not be identifiable by them.

## **24. Will any genetic tests be performed?**

With your consent, we will perform genetic analysis on your samples which we hope will provide further information on your condition. These tests will look at why some people seem to get fluid around their lungs in association with cancer, and whether genetic differences may be a cause. The results will be used to try to understand this condition further in the future – they are not of direct use to you or your treatment. As the results of these tests do not change how you are looked after, we would not normally let you know the results, and we will not contact members of your family with the results either. The samples will not be tested for chronic diseases or HIV, and will not be used for any genetic manipulation.

## **25. What do I need to do now if I agree to participate?**

If after reading this information sheet you have any questions about the trial, please ask a member of the trial team, whose contact details can be found below.

If you would like to take part then we shall ask you to sign a consent form, which will also ask if you want 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 agree to participate in the trial you are free to withdraw at any time without giving a reason and without affecting your rights or medical care.

## **26. What happens if I decide not to participate?**

If you decide not to participate, your routine medical care and your legal rights will not be affected in any way, and you will not be at any disadvantage over those people who do participate. Any decisions about how to manage your pleural fluid will be made in a normal manner between you and your doctor, who may recommend that you receive one of the above treatments, although not as part of the trial.

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