ESPriT 2

A multi-centre randomised controlled trial to determine the effectiveness of laparoscopic removal of isolated superficial peritoneal endometriosis for the management of chronic pelvic pain in women

PATIENT
INFORMATION SHEET

You have been invited to take part in our research because you are having keyhole surgery (a diagnostic laparoscopy) to find out if you have endometriosis. Before you decide if you wish to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information leaflet carefully and discuss it with friends, relatives or your GP. Ask us if there is anything that is not clear (our contact details are on the back page of this booklet), or if you would like more information. Please take time to decide whether or not you wish to take part.

WHY ARE WE DOING THIS RESEARCH?

Around 50% of women with chronic pelvic pain will have a condition called endometriosis which can only be diagnosed by laparoscopy (a key hole operation). In women with endometriosis, cells similar to those lining the womb are found outside the womb on the lining of the pelvis (called the peritoneum).

There are three types of endometriosis:

- superficial peritoneal endometriosis (disease found on the surface of the lining of the pelvis),
- ovarian endometriosis (cysts found in the ovary, which are called endometriomas or 'chocolate cysts')
- deep endometriosis (sometimes referred to as 'nodules')

If superficial peritoneal endometriosis is found at laparoscopy, gynaecologists usually surgically 'cut out' (excise) or 'burn off' (ablate) the areas of endometriosis. However, many women do not get complete pain relief after the endometriosis has been removed, and some have complications from the surgery. The evidence to support removing the endometriosis is based on small studies (not many women taking part) and where they were not followed up to ask about their ongoing symptoms in the longer term. A recent UK survey of ~1300 women who underwent surgery for endometriosis reported that 90% had a recurrence of their pain within two years. Studies in Scotland of ~18,000 women have shown that of women undergoing surgery for endometriosis, over half will have repeat operations for their endometriosis.

We want to determine whether removing superficial peritoneal endometriosis improves painful symptoms and quality of life, which surgical approach may be best (ablation or excision), or whether surgery is of no benefit, worsens symptoms or may even cause harm. In order for us to prove this we will need 400 women to be entered into our trial.

ESPriT+

In addition to the main ESPriT2 study, you can also decide to take part in an additional sub-study named ESPriT+. In ESPriT+ we want to try and improve how we diagnose endometriosis. At the moment, as we have said above, superficial peritoneal endometriosis can only be diagnosed by having a laparoscopy. We would like to see if we can use a blood test to tell us if a woman has endometriosis.

WHY AM I BEING INVITED TO TAKE PART?

You have been invited to take part because you are having a diagnostic laparoscopy because your doctor thinks that you have endometriosis.

DO I HAVE TO TAKE PART?

No, it is up to you to decide whether or not you wish to take part.

If you decide to take part you can also still withdraw at any time and without giving a reason. Deciding not to take part, or withdrawing from the trial, will not affect the healthcare that you receive, nor your legal rights. You can choose to take part in the main study without taking part in ESPriT+.

WHAT HAPPENS IF I TAKE PART?

If you decide to take part, a member of the research team will ask you to complete a consent form. This may be during a video/telephone call with the research team. You will then be asked some questions about your health, to complete some questionnaires and to tell us about the medications that you are taking. The questionnaires ask about your quality of life, pain symptoms, bowel and bladder function, as well as other factors that endometriosis can affect, such

as sexual relationships. Some of the questionnaires are of a sensitive nature and you can leave these blank if you are not comfortable completing these sections. These questionnaires will be completed online or on paper in private and will not contain any identifying information.

Your laparoscopy will then take place as scheduled by your hospital. Before your laparoscopy a pregnancy test will be carried out by the nursing staff and we will record this result. If you have agreed to take part in ESPriT+, we will also take a blood sample (about 4 to 5 tablespoons) before your operation and/or you may have a transvaginal ultrasound scan (the scan will be in London hospitals only).

This is a randomised controlled trial, which means that once we know if you have superficial peritoneal endometriosis or not, a computer will decide if you should have the endometriosis removed or not. The trial is also "blinded" which means that you will not be told if the endometriosis is removed or not. This is very important because if you know what has happened to you it might affect how you answer some of our questions. In order for us to get a clear result for the trial, it is important that you can answer all of our questions as honestly as possible.

If ovarian or deep endometriosis is found, you will not be randomised into the trial and this may be removed at the time of surgery (or at a later stage) as part of routine clinical care.

If no endometriosis is found, then you will not be randomised and you will not be followed up as part of the trial. You will also not be followed up as part of the trial if you have ovarian/deep endometriosis although we will document the results if any samples of your endometriosis were taken and sent to pathology. All of the information that you give us will be kept in "coded" form so that you cannot be identified. "Coded" means that all information which could identify you, such as your name and contact details are removed and replaced with a number (for example, instead of the patient name "Jane Smith", the information will carry the number "2525"). Only the research team will have the link between your personal information and the coded data. Your data will be kept by us for at least five years. This is so that, if anyone has any questions about the trial, we can answer these fully about all of the women who consented to the trial.

During your laparoscopy, it will be necessary to make a cut in your tummy button (1cm) and another cut (0.5cm) in the lower part of your tummy to insert the ports for the camera and for the instruments used to examine your pelvis. In order to get a better look in your pelvis and to remove the endometriosis, a third cut (0.5cm) is needed to allow another port to be inserted. Whether or not you have your endometriosis removed, this third cut will be made to ensure that all women have the same operation experience. This means that you or anyone examining your tummy will not be able to guess what happened during your operation. The potential risks from the possible addition of this other port include bruising/bleeding, infection and hernia (uncommon; less than 1 in 100) at the port site. These are recognised risks of the surgery that you are having. The three cuts may or may not require stitches. If stitches are required, they usually dissolve and therefore may not require removing later. There should be minimal scarring from these cuts under normal circumstances.

At the time of your laparoscopy photographs will be taken of the inside of your pelvis. The photographs will be coded and shown to experts in endometriosis to ensure they agree with the type, amount and location of endometriosis that was found, and how effectively it was removed, if you were allocated to this arm of the trial. These photographs will have all information about you removed, e.g. it will not have your name on it only the number we will use to identify you in the trial.

Whichever arm of the trial you are randomised into, you will be told whether endometriosis was found after your surgery: the type, amount and location of the endometriosis will be described to you. However, you will not be told if your endometriosis was removed or not. We will also send a letter to your GP telling them about your participation in the trial and your diagnosis but not what happened during your operation.

After your laparoscopy, if required, you will continue to have the option of taking any of the current recommended medical treatment options for endometriosis, such as oral painkillers, hormones, and drugs which work on the nerves in the pelvis as part of your routine hospital care – taking part in the trial will not affect these options. For the first week after your operation, we will ask you to complete a diary giving us information about your pain and any painkillers you may need to take. This can be on paper or online. One month after your laparoscopy, we will contact you to determine if you have had any complications from the procedure. At 3, 6 and 12 months after your surgery, we will ask you to complete the same questionnaires that we asked you to complete at the start of the trial (either online or on paper). We may also look at your medical records (via a system called data linkage) to track outcomes of any future pregnancies and further surgeries related to endometriosis, up to about 5 years after your operation. We may also contact you about 2 and 5 years after your operation to ask you about your health. If you change your mind about continuing in the trial at any time, just contact your research team and they will stop any further contact.

If you wish to know whether you had the endometriosis removed at the end of your participation in the trial, a member of the research team will be able to tell you.

ARE THERE ANY RISKS INVOLVED?

The potential risks from the possible addition of another port are routinely detailed on your NHS hospital consent form and will already have been explained to you by your doctor when you were put on the operation waiting list (or will be discussed on the day of your surgery). However, one of the reasons we are running this trial is to monitor and measure the potential additional risk of complications if you have endometriosis removed, so we will ask you questions about any complications after your operation and keep a record of them for the trial. If you agree to take part in ESPriT+, you may experience bruising at the site that blood is taken.

WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART?

You may or may not get a direct benefit from taking part in this trial. This trial will generate information to allow women with suspected endometriosis and gynaecologists to make an informed choice whether to immediately remove endometriosis when a diagnostic laparoscopy identifies superficial peritoneal endometriosis alone. If the trial shows that removal of superficial peritoneal endometriosis does not help, or makes symptoms worse, this would mean that women could choose to not have it removed or avoid a diagnostic laparoscopy altogether. Women could then opt for early pain management with painkillers, hormones and drugs that work on the nerves in the pelvis.

If you consent to provide a blood sample for the ESPriT+ sub-study, this may enable the discovery of new ways to help diagnose endometriosis.

WHAT WILL HAPPEN IF I DO NOT WANT TO CARRY ON WITH THE TRIAL?

You can withdraw from the trial at any time without having to give a reason. If you decide not to take part in the trial or withdraw at any time, the clinical care that you receive will not be affected and this will continue as normal. With your permission, we will use any information (coded) obtained up to the point of your withdrawal including the blood samples already collected. If you have agreed to be part of the ESPriT+ sub-study the blood samples and data already collected will still be used. If you withdraw, you will be able to find out if you had your endometriosis removed, by asking a member of the research team.

WHAT IF THERE IS A PROBLEM?

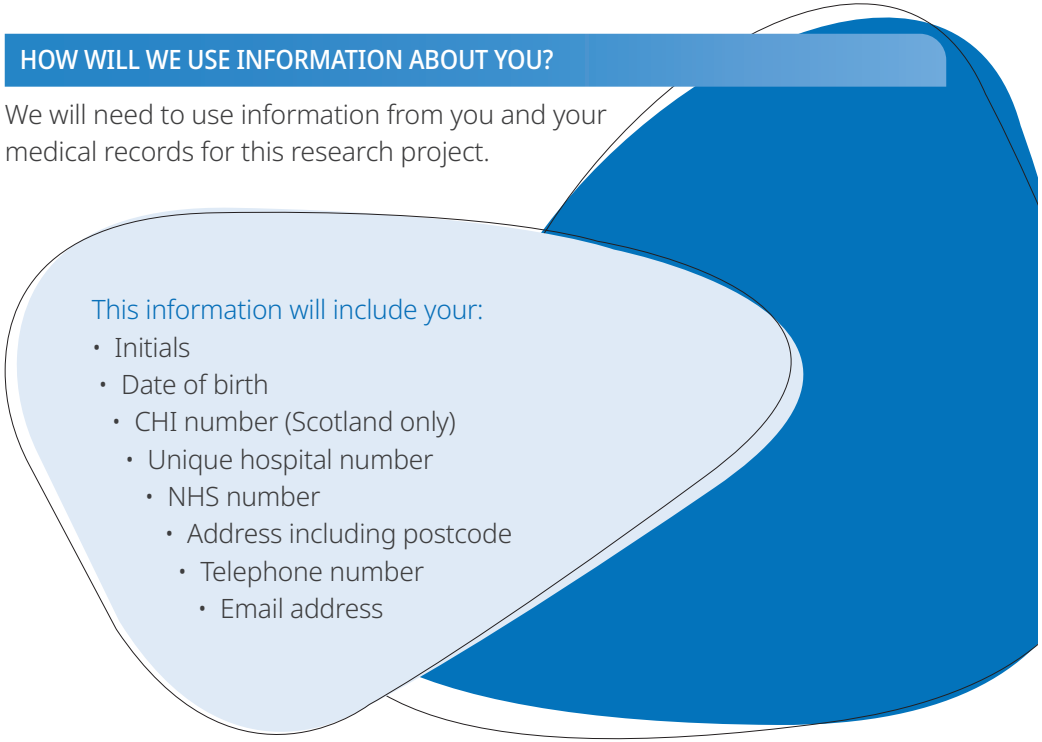
If you have a concern about any aspect of this trial, you should ask to speak with your clinical researchers who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be found at the end of this information leaflet.

WILL MY TAKING PART IN THIS TRIAL BE KEPT CONFIDENTIAL?

All the information we collect during the course of the research will be kept confidential and there are strict laws which safeguard your privacy at every stage.

HOW WILL WE USE INFORMATION ABOUT YOU?

We will need to use information from you and your medical records for this research project.



The University of Edinburgh will use this information to do the research or to check your records to make sure that the research is being done properly.

Any parties who are sent your data who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

We will keep all information about you safe and secure.

We will also ask your consent, to share your contact details with researchers who are carrying out some tests on the fertility of women with endometriosis. They may contact you and send you out kits to test your fertility. These researchers are from Hertility Health and you can find out more information from their website www.hertilityhealth.org.

The images from inside your pelvis taken during your operation may be sent to the USA. These will not contain anything you can be identified from, just a unique number used to identify you. This is so that the images can be looked at by doctors outwith the research team to confirm the trial findings. They must follow our rules about keeping your information safe.

Once we have finished the trial, we will keep some of the data so we can check the results. We will write our reports in a way that no one can work out that you took part in the trial.

WHAT ARE YOUR CHOICES ABOUT HOW YOUR INFORMATION IS USED?

You can stop being part of the trial at any time, without giving a reason, but we will keep information about you that we already have.

ESPriT+

If you agree to take part in ESPriT+, part of the blood sample will be kept by the University of Edinburgh in the Queen's Medical Research Institute. This will be used to identify a biomarker to help with the diagnosis of endometriosis. If any part of the sample is not used, this will be kept by the University and used in other related women's health research. You cannot be identified from this sample as it will only contain your unique trial number.

Part of your blood sample and some data collected from the trial will be shared with Roche Diagnostics and its affiliates in a coded form that you cannot be identified from, also to be used to identify a biomarker to help with the diagnosis of endometriosis. Only the research team and not Roche will have the link between your personal information and the coded data. The results of this study may be published (e.g., in a study report, scientific presentation or on a webpage). Such publications will not include information that can be used to identify you. You will not be notified when publications are available but you can find out about these on the trial website www.ed.ac.uk/esprit2.

The sample and data will be shared with Roche Diagnostics for use in future research and product development in the field of endometriosis and other areas of women's health. Roche cannot specify at the moment the specific research objectives and projects but the projects will always be designed to learn about medical science and improvement of health of humans, for example aiming at helping to understand diseases, their detection and prediction, developing new uses for existing products or developing new medical products, or learning from past studies and past research. This can include your disease or another.

Roche can share your coded data and samples with its research partners, service providers (like scientific research partners, clinical research organizations or laboratories) including other Roche companies. Roche may also transfer the coded data and samples to other countries for the above mentioned purposes. Depending on where you live, this may mean that your data will be sent to

countries that have different standards for privacy than your own. If these recipients are outside the European Economic Area (EEA), Roche will ensure that safeguards are in place so that your coded data and sample will be adequately protected like in the EU. To ensure that level of protection for such transfer, in most cases, Roche uses standard contractual clauses provided by the EU Commission.

You can make use of your rights under data protection laws. You have the possibility to withdraw your consent for the further research at any time without providing any reason. If you do change your mind and choose to withdraw, please notify your research team at the contact details found at the end of this information sheet and explicitly state that you want to withdraw your consent for the further research. Your decision to withdraw your consent for further research, however, will not affect any processing, testing, or research already done on your personal information, coded data and samples acquired prior to that time. This is to guarantee that study results are valid and comply with regulatory requirements. Withdrawal from the further research will have no effect on your participation in the study.

Coded data and samples will be stored for a minimum of five years. Roche reserves the right to delete your coded data and destroy your samples for any reason at any time without further notice.

IF FOLLOW UP DATA WILL BE COLLECTED AFTER WITHDRAWAL

If you choose to stop taking part in the trial, we would like to continue collecting information about your health from central NHS records. If you do not want this to happen, tell us and we will stop.

We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

IF FOLLOW UP DATA WILL BE USED FOR FUTURE RESEARCH

If you agree to take part in the main trial, you will have the option to take part in future research using your data saved from this trial.

WHERE CAN YOU FIND OUT MORE ABOUT HOW YOUR INFORMATION IS USED?

You can find out more about how we use your information

- at **www.hra.nhs.uk/information-about-patients/**
- our leaflet available from **www.hra.nhs.uk/patientdataandresearch**
- by asking one of the research team
- by sending an email to, or
- by ringing us on **contact details are on the back of this information sheet**.
- Data Protection Officer contact information:

University of Edinburgh
Data Protection Officer
Governance and Strategic Planning
University of Edinburgh
Old College
Edinburgh
EH8 9YL
Tel: 0131 651 4114
dpo@ed.ac.uk

NHS Lothian
Data Protection Officer
NHS Lothian
Waverley Gate
2-4 Waterloo Place
Edinburgh
EH1 3EG
Tel: 0131 465 5444
Lothian.DPO@nhs.net

WHAT WILL HAPPEN TO THE RESULTS OF THE CURRENT RESEARCH TRIAL?

The results of this trial will be published e.g. in medical journals, reports, textbooks and conference presentations. You will not be identifiable in any publication or report. You will be able to see the published results of the trial on our website www.exppectedinburgh.co.uk or www.ed.ac.uk/esprit2, on Endometriosis UK's website and on Endometriosis.org. We anticipate that the results of this trial will be available in 2026.

WHO IS ORGANISING AND FUNDING THE RESEARCH?

The trial has been organised by Professor Andrew Horne (Consultant Gynaecologist) and Dr Lucy Whitaker (Clinical Lecturer in Gynaecology). The trial is co-sponsored by the University of Edinburgh and NHS Lothian. The trial is funded by the NIHR (National Institute for Health Research) and ESPriT+ has been funded by Roche Diagnostics.

WHO HAS REVIEWED THE TRIAL?

All research within the NHS is reviewed by an independent group of people called a Research Ethics Committee. A favourable opinion has been obtained from the East of Scotland Research Ethics Service REC 1, which has responsibility for scrutinising all proposals for medical research on humans, has examined the proposal and has raised no objections from the point of view of research ethics. It is a requirement that your records in this research, together with any relevant medical records, be made available for scrutiny by monitors from the University of Edinburgh and NHS Lothian, whose role is to check that research is properly conducted and the interests of those taking part are adequately protected. The trial proposal has been peer-reviewed by researchers at University of Edinburgh. NHS management approval has also been given.

WHAT IF SOMETHING GOES WRONG?

In the event that something does go wrong and results in you being harmed during the research and this is due to someone's negligence, then you may have grounds for legal action for compensation against local NHS Boards but you may have to pay your legal costs. The standard National Health Service complaints mechanisms will still be available to you (if appropriate).

DETAILS OF VISITS

CONSENT VISIT

This visit might be in the hospital at a clinic appointment or can be over a telephone/video call. During this visit, the trial will be explained to you, and if you agree to take part, you will be asked to give consent. Once you have given consent, we will ask you a few questions about yourself and your past medical history. We will also make sure that you have contact details for the research team. We will record contact details which will include an email address so that, if you choose, you can complete all of the trial questionnaires online.

BEFORE YOUR OPERATION DATE

We will contact you just before your operation to allow you to complete the trial questionnaires.
London hospitals only – you may have an ultrasound scan if you have consented to this.

ON THE DAY OF YOUR OPERATION

Before your operation, we will ask you to sign your consent form in person if you completed the telephone consent process. We will also make sure that you have completed the questionnaires. We will ask you some questions about your painkillers and other medicines that you might have taken, visits to your GP, hospital, etc. We will also give you a diary so that you can record your pain scores and use of painkillers in the week after your operation. We will take a blood sample if you have consented to ESPriT+. The diary will also have a reminder of what information we will collect each time we speak to you and a space to note these down. This diary information can also be completed online if you prefer at the end of that first week.

During your operation, you will be randomised to either surgical removal of endometriosis or no removal, and the surgeons will take some photographs of inside your tummy.

FOR THE SEVEN DAYS AFTER YOUR OPERATION

We will ask you to complete the diary detailed above with information on your pain and any painkillers that you take for this. This can then either be entered online or posted back to the research team.

THIRTY DAYS AFTER YOUR OPERATION

We will give you a call to ask you how you are and if you have had any complications following your operation. The call will take about 5 minutes.

THREE MONTHS AFTER YOUR OPERATION

We will call you and ask you to complete the same questionnaires that you filled in just before your operation. Again, these can be completed online. We will also ask you questions about your pain, painkillers, hormone use, employment and visits to any doctors, nurses, etc for your pelvic pain. The call will take about 10 minutes.

SIX MONTHS AFTER YOUR OPERATION

We will call you and ask you to complete the same questionnaires that you filled in just before your operation. Again, these can be completed online. We will also ask you questions about your pain, painkillers, hormone use, employment and visits to any doctors, nurses, etc for your pelvic pain. The call will take about 10 minutes.

If you consented for the ESPriT + study and were randomised into the trial, we will ask you to return in person to the clinic, if possible, for the follow up visit so a blood sample can be taken.

TWELVE MONTHS AFTER YOUR OPERATION

We will call you and ask you to complete the same questionnaires that you filled in just before your operation. Again, these can be completed online. We will also ask you questions about your pain, painkillers, hormone use, fertility, employment and visits to any doctors, nurses, etc for your pelvic pain. We will ask you if you think that you had your endometriosis removed or not and we can tell you that information at this time, if you would like to know. The call will take about 15 minutes.

TWO AND FIVE YEARS AFTER YOUR OPERATION

We may contact you to complete some of the questionnaires that you completed during the trial so that we can look at longer term symptoms.

Contact details

You may contact the clinical research team directly – details below. If you require any further information from a doctor who is not involved in this trial you can contact Prof Colin Duncan on 0131 242 1000.

FOR MORE INFORMATION CONTACT:

Local Contact Details

PI:
Research nurse:
Tel:

Local Complaints procedure:

Tel:
Email:

Thank you for reading this information sheet.