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Participant Information Leaflet

The PRE-EMPT Trial: Preventing Recurrence of Endometriosis by Means of long acting Progestogen Therapy

Invitation to take part in the PRE-EMPT Trial
You are invited to take part in a research study to compare treatments to prevent recurrence after surgical removal of endometriosis. The study is comparing options you will be offered anyway, it is not offering new or experimental drugs. The study is entirely voluntary – you do not have to take part, nor do you have to give a reason if you decide not to participate. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it would involve. Please take your time to read this information sheet carefully and talk to others if you wish. If there is anything that is not clear, or if you would like more information, you should ask your gynaecologist or the research nurse for further advice.

Part 1 tells you the purpose of this study and what will happen to you if you take part.

Part 2 gives you more detailed information about the conduct of the study

Contact details for information can be found on the last page.
The PRE-EMPT Trial: Preventing Recurrence of Endometriosis by Means of long acting Progestogen Therapy

Why have I been asked to take part?
Your doctor has referred you to a specialist clinic for symptoms related to endometriosis. You are going to have a laparoscopy, which may find that you have endometriosis. Endometriosis is a common condition where the cells that line the uterus (or womb) are found elsewhere in the body: on the outside of the uterus, on the ovaries or on the outer surface of the bowel. Many women have endometriosis without knowing it and do not need treatment. However, endometriosis can cause pelvic pain, painful periods, fertility problems, tiredness and other symptoms. There is no strong evidence which suggests the extent of endometriosis is related to the amount of pain women with little visible endometriosis can experience intense pain. Doctors describe endometriosis as grade I (mild) to IV (severe) depending on the amount and location of endometriosis patches and the extent of adhesions (scar tissue) between the internal organs. Many women also have pelvic pain without endometriosis if no endometriosis is found at laparoscopy, you will not be eligible for PRE-EMPT.

What are the treatments for endometriosis?
The standard surgical treatment is to remove visible patches of endometriosis during the laparoscopy, either with a scapel or a laser. This will usually improve pain in most women. However, symptoms recur in about 40% of women and 25% women have another operation within 5 years of her first laparoscopy.

To prevent recurrence, there are a number of medical options.
Long-acting progesterone treatment. This class of treatment are reversible contraceptives and reduce the monthly growth and shedding of the uterus lining. There are two options:
Who is funding and organising the research?
The PRE-EMPT study researchers are receiving a grant from the National Institute for Health Research’s Health Technology Assessment programme to enable them to carry out this study. The central study organisers are based at the Universities of Aberdeen and Birmingham, who are collaborating with colleagues around the UK. The discussion groups and interviews will be led by researchers from Birmingham City University and the University of Sheffield. The Clinical Trials Unit at the University of Birmingham will collect and analyse the data. The doctors involved are not being paid for recruiting women into the study. Patients are not paid to take part either, but their help in finding out more about how best to treat endometriosis is much appreciated. The study is sponsored by the University of Aberdeen.

Who has reviewed the study?
All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This study has been reviewed and given a favourable opinion by the North of Scotland Research Ethics Committee 1 13/NS/0103 and the R&D Department for each hospital involved. All of the medical treatments are widely used as contraceptives and endometriosis and their use in PRE-EMPT has been approved by the Medicines and Healthcare products Agency. Please keep this copy of this PRE-EMPT Participant Information Sheet. You will also be given a copy of your signed consent form to keep if you decided to participate in the PRE-EMPT trial.

Do you have any further questions?
Having read this leaflet, it is hoped that you will choose to take part in the PRE-EMPT trial. If you have any questions about the study now or later feel free to ask your gynaecologist or clinic nurse. Their names and telephone numbers are given on the back of this leaflet. Please take the time before your appointment to decide whether you wish to take part in the PRE-EMPT trial. You may like to discuss your decision with friends or relatives.

- the levonorgestrel releasing coil (Mirena®). This is an effective but reversible contraceptive. It is a 2cm T-shaped plastic rod that it inserted into the uterus by a doctor and can remain there for up to 5 years. You cannot feel it inside you. This can stop menstrual periods, but many women find their periods become irregular, or get spotting, during the first six months.

- a progesterone injection (Depo-provera®) This is another effective reversible Contraceptive and is given as an injection every 3 months by your GP or practice nurse. Again, many women experience irregular periods and spotting.

- the contraceptive pill The oral contraceptive pill is another option, although not advised for women over 35 who smoke. This can be taken every day for three weeks and then stopped for one week, during which you have a menstrual period. Alternatively the pill can be taken every day without a break. This will stop your periods almost completely. Either option is allowable in PRE-EMPT.

- no immediate hormonal treatment Most women will find their pain improves after surgery. If long acting hormonal contraception is not required or acceptable, the endometriosis can be managed without hormonal treatment.
Will information about me be kept confidential?
Yes, all information collected in the study will remain strictly confidential in the same way as your other medical records. If you agree to take part, your doctor will send basic information about you and your condition to the study’s central organisers at the University of Birmingham Clinical Trials Unit. This information will be put into a computer and analysed by the PRE-EMPT trial office staff. The questionnaires will not contain your name and will be identified using a code number and will not be seen by your GP or gynaecologist. For women participating in the optional discussion groups or interviews, the conversations will be recorded but will not be played back to your GP or gynaecologist. All information will be held securely and in strict confidence. No named information about you will be published in the study report. Information held by the NHS may be used to keep in touch with participants and follow up their health status. Occasionally, inspections of clinical study data are undertaken to ensure that, for example, all participants have given consent to take part, so a copy of the consent form will be sent to the PRE-EMPT study office. Responsible members of the University of Aberdeen or the NHS Trusts may also be given access to data to ensure we are complying with regulations. But, apart from this, only the study organisers will have access to the data.

Involvement of the General Practitioner / Family Doctor (GP)
With your consent we will inform your GP of your participation in the PRE-EMPT Trial. We may seek to confirm treatment details with your GP.

What will happen to the results of the research study?
The results will be reported in a medical journal. It is expected that the first results will be published about two years after the study finishes recruiting women. Everyone who takes part will then be told the results in a newsletter that will be posted directly to them.

What is the purpose of the study?
The coil, the injection and the pill are safe, effective drugs, they are reliable contraceptives if used properly but do not affect the ability to get pregnant once stopped. However, they all have advantages and disadvantages. These drugs all reduce pain, but doctors do not know which women will benefit most and for how long. Surgical treatment is also known to effectively reduce pain, and may be the best option for women not needing contraception or wanting to avoid hormonal treatments. Since the options are so different, to compare the four options against each other.

Do I have to take part?
You do not have to take part. It is up to you to decide. If you do not wish to take part, you do not have to give a reason and your decision will not affect the standard of care you will receive. Similarly, if you do decide to take part, you are entitled to withdraw from the study at any time, without having to give a reason, and this will not affect the standard of your medical care in any way. Participation in this study would not affect any private health insurance.

What will happen to me if I take part?
If you decide to take part in the trial, you will be asked to sign a consent form to say that you understand the trial and that you are willing to take part. In the PRE-EMPT trial, all four options are available. Neither you nor your doctor can choose exactly which treatment you receive. You can say which option or options you definitely do not want to receive. However, you must be prepared to have either the coil or injection, and to have either the pill or no medical treatment after the initial surgery. Once you have decided which options you are prepared to potentially receive, the decision as to which actual treatment is made randomly by computer at the PRE-EMPT trial office. This is essential so that a fair comparison can be made between the various treatment groups. Dividing people into groups in this way is called a ‘randomised clinical trial’ and it is the standard and most reliable way of comparing different treatments. The table opposite summarises the options available depending on your preferences.
<table>
<thead>
<tr>
<th>My preferences</th>
<th>You will have either</th>
<th>Or</th>
<th>Or</th>
<th>Or</th>
</tr>
</thead>
<tbody>
<tr>
<td>I am happy to have any of the 4 options</td>
<td>Coil</td>
<td>Injection</td>
<td>Pill</td>
<td>Surgery, no medical treatment</td>
</tr>
<tr>
<td>I want a medical treatment, but am happy to have any</td>
<td>Coil</td>
<td>Injection</td>
<td>Pill</td>
<td></td>
</tr>
<tr>
<td>I want a medical treatment, but don’t want the coil</td>
<td>Injection</td>
<td>Pill</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I want a medical treatment, but don’t want the injection</td>
<td>Coil</td>
<td>Pill</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I don’t want the coil but am happy to accept no medical treatment</td>
<td>Injection</td>
<td>Pill</td>
<td>Surgery, no medical treatment</td>
<td></td>
</tr>
<tr>
<td>I don’t want injections, but am happy to accept no medical treatment</td>
<td>Coil</td>
<td>Pill</td>
<td>Surgery, no medical treatment</td>
<td></td>
</tr>
<tr>
<td>I am happy with either the coil or injection, but don’t want the pill</td>
<td>Coil</td>
<td>Injection</td>
<td>Surgery, no medical treatment</td>
<td></td>
</tr>
<tr>
<td>I am happy with the coil, but don’t want the injection or pill</td>
<td>Coil</td>
<td>Surgery, no medical treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I am happy with the injection, but don’t want the coil or pill</td>
<td>Injection</td>
<td>Surgery, no medical treatment</td>
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</tr>
</tbody>
</table>

Not all combinations are allowed in PRE-EMPT, for example, if you would only accept the coil or injection, you would not be able to participate. You will have an equal chance of being allocated each option. You do not have to stay on the allocated treatment forever – see page 7.

Part 2 If the information in Part 1 has interested you and you are considering participation, please read the additional information in this section before making any decisions

What will happen if I don’t want to continue with the study?
If you do decide to take part, you are entitled to withdraw from the study at any time, without having to give a reason, and this will not affect the standard of your medical care in any way. We would like to use the data collected about you up to your withdrawal. Even if you no longer wish to complete the questionnaires, we would like to continue to collect a few important details from your GP, such as repeat surgeries, if you get pregnant or when your baby is born. In the unlikely event of you losing the ability to give continued consent during the study we would like to keep data that we have already collected about you for research purposes.

What if there is a problem?
You have the same legal rights whether or not you take part in this study. If you are harmed by taking part in this study, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. The University of Aberdeen has arrangements in place to provide for harm arising from participation in the study for which the University is the research sponsor. NHS indemnity operates in respect of the clinical treatment with which you are provided.

If you wish to complain about any aspect of the way in which you have been approached or treated during the course of this study, you should contact the lead investigator named on the back page or you may contact your local Patient Advice and Liaison Services (PALS) group or local equivalent group (insert name where applicable) {contact details here}
You can also find out more from the National Centre for Health and Clinical Excellence (NICE). There are clinical guidelines regarding the coil and injection, known as long-acting reversible contraceptives (reference CG30). You can download this from NICE’s website www.nice.org.uk or you can request them by email publications@nice.org.uk or by phone 0845 003 7783.

If I take part in the PRE-EMPT study, what else will happen?
The same questionnaire you completed at the beginning will be sent to you at home at 6 months, then 1, 2 and 3 years after treatment. We may wish to send a questionnaire to you again at 5 and 10 years to ask questions about your general health. The questions are designed to find out if there are any improvements or changes in your symptoms following treatment. It is important for the reliability of the study to find out how all women are progressing and what treatment, if any, they are taking. The study organisers may, therefore, phone, text or email you to remind you to complete the questionnaires. Should you get pregnant at any time after the procedure, we would like you to contact the Trial Office. We would like to collect a few details about the outcome of the pregnancy, which we will do by telephone or through your GP.

What are the risks and discomforts?
The three trial drugs are all widely used as contraceptives, so the risks and side effects are well known. Please ask your doctor or nurse about side effects of the treatments you would consider having.

Are there any benefits for me from taking part in the study?
Participants may not gain any individual benefit. The trial will provide valuable information for future patients suffering from endometriosis.

What if there is a problem?
Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. Detailed information is given in Part 2.

Will my taking part in the study be kept confidential?
Yes. The study will follow ethical and legal practice and all information about you will be handled in confidence.

The details are included in Part 2.

If you are allocated to no medical treatment and do not want to get pregnant, you will need to use barrier methods. You will be able to obtain free condoms from your doctor or practice nurse.

You will be asked to complete a questionnaire before the procedure. There are several parts to the questionnaire – your assessment of your pain and symptoms, what additional symptoms you are having, some questions on how the symptoms affect your quality of life and your sexual relationships, and some questions about visits to doctors, time off work and expenses incurred.

How long will I have to take the medical treatments? What if I want to change?
PRE-EMPT wants to reflect real life, so you are not committed to taking the treatments forever if they are not helping or if you want to get pregnant. We would like you to take the medical treatments for as long as possible, provided they are suiting you. We would like to keep in touch with you for at least 3 years, regardless of whether you remain in your original group.

We anticipate that some women allocated to the coil or injection may experience irregular bleeding to begin with, but it is worth continuing for a few months as this normally settles down. If you remain unhappy, your hospital doctor or GP can discuss alternatives. The coil has to be removed by a trained doctor. If you are in the no medical treatment group, and want to use hormonal contraceptives, you will be able to choose any available option.

As the medical treatments are all contraceptives, you will not get pregnant whilst taking them properly. If you decide you want to get pregnant, you should discuss how to stop treatment with your GP. It is usually best to wait for one regular menstrual period before trying, in order to accurately date the pregnancy.

If your endometriosis symptoms recur and you want to change treatments, you should discuss these with your hospital doctor.

Your doctor or the research nurse will also give you a hospital leaflet about each treatment.