
# Premature Ovarian Insufficiency Study of Effectiveness of hormonal therapy (the POISE study)

## Participant Information Sheet

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## 1. You are invited to take part in our research study

- The POISE study aims to find out what is the most effective hormone treatment for women with premature ovarian insufficiency (POI), in both the short and long-term.
- The cause of POI is often unknown, but in some women it may be caused by genetic conditions such as Turner's syndrome, as well as immune disorders, treatments for cancer, or surgery involving the ovaries.
- This information sheet is to help you understand why the research is being carried out and what it will involve for you if you decide to take part.
- Please take time to read this information and ask us if there is anything that is not clear to you or you would like more information.
- It is entirely your decision whether to take part in this study. If you agree to take part, you are free to withdraw at any time without giving a reason. If you choose not to take part, your care will not be affected.

## 2. A summary of the study

- Women with POI are treated with either the combined oral contraceptive pill (COC) or hormone replacement therapy (HRT). Both are recommended treatments.
- Women with POI need to take treatment until at least the average age of menopause, which is around the age of 51. This is because in women with POI, the body stops producing normal levels of certain hormones that need to be replaced to protect from long term health risks.
- We want to find out which treatment is best for relief of symptoms and reducing the long-term health risks of POI.
- If you are able to take part in the study, you will receive either HRT or COC (we will call this your study treatment). Neither you nor your doctor will be able to choose which treatment you receive.
- We would like you to continue to take part in the study for up to 5 years, a minimum duration of 2 years. However, you will be free to withdraw at any time if you wish.
- During the study you will be asked to complete questionnaires on your symptoms, sexual activity, lifestyle and working life.
- You will have your bone density measured and checks of your blood pressure and weight. You may need to make extra clinic visits for this.
- The patient support groups the Daisy Network and the Turner's Syndrome Society UK are actively supporting this study.
- All information collected during the course of the study will be kept safe and confidential.

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

When menopause occurs in women under the age of 40, it is termed POI. Your doctor will have discussed the diagnosis with you and the possible reasons why it has happened.

The main symptom of POI is absent or very irregular periods. Many women get other menopause symptoms, such as hot flushes and sweats, loss of libido (sexual drive), painful intercourse, mood changes and tiredness. The ability to get pregnant naturally is greatly reduced. The impact of symptoms and infertility can be distressing.

In the long-term, women with POI are at higher risk of bone thinning (osteoporosis), fractures, heart disease and memory problems compared with women who experience menopause at the typical age, around 51 years

Treatments involve taking hormones, either in the form of HRT or COC. There are benefits and risks of each treatment and healthcare professionals are uncertain which is the best for relief of symptoms, and which is more effective in protecting against long term health risks, such as reduced bone density (bone thinning).

The aim of this study is to find out what is the best treatment for women with POI in the short and long term.

## 4. Why have I been invited to take part?

You have been invited to take part in this study as you have been diagnosed with POI, and are aged between 18 and 40 years. We are looking for a total of 380 women to take part from throughout the United Kingdom. If you are planning to become pregnant within the next 12 months, you will not be able to take part.

## 5. Do I have to take part?

It is up to you whether or not you take part in the study. We will talk to you about the study and answer any questions you may have. If you agree to take part, we will ask you to sign a consent form (this may be provided online or by email). If you decide to take part, you will be free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive.

## 6. What would taking part involve?

If you are already taking treatment for your POI, you will be asked to stop taking this for 4 weeks. This is so that we can assess how you are without any treatment.

You will need to have some tests to assess your health before you start the study treatment. You will have your blood pressure, height, weight and bone density measured. The bone density measurement may be at a different time and/or location to the other tests. These initial tests will need to be completed at your treating clinic. During the bone density scan, you will need to lie still on your back on a flat, open x-ray table. This usually takes 10-20 minutes. The results will be discussed with you at your next clinic appointment.

You will also be asked to complete questionnaires about your treatment, symptoms, lifestyle, pregnancy status as well as the impact POI has on your sexual activity and your working life.

In a few clinics, women are also being invited to provide blood and urine samples to look at their bone and heart health in more detail. In these clinics, women with an unknown cause of their POI who have not had their chromosomes analysed will also be offered the opportunity to be tested. Results of the test will be provided to you at your next follow-up appointment.

Providing blood and urine samples is optional and your doctor will advise you if this is happening at your clinic. If you are happy to give blood samples, we will take about 30 ml of blood for each sample, which is the equivalent of about 6 teaspoons. You can still take part in the study even if you do not want to provide blood and/or urine samples. You will be asked to fast prior to the blood test being performed. This means that you should have nothing to eat or drink (except plain water) for 12 hours before the blood test. However, you can continue to take any prescribed medication with water only. Your appointment will be made as early in the morning as possible where fasting is required.

**What treatment would I have?**

Once you have completed these initial tests, you will be told which study treatment you will receive (HRT or the COC). This will be selected randomly by a computer and you will have an equal chance of being in either of the two groups.

HRT can be prescribed as a tablet which is taken once daily, a gel applied to the skin daily or as a skin patch which is

changed twice weekly, without any breaks. Most HRT treatment is a combination of oestrogen and progesterone, but it is also possible to take the oestrogen and progesterone separately (oestrogen as a tablet, patch, or gel applied to skin daily, and progesterone as a tablet or contraceptive coil inside the womb). If you have had a hysterectomy, you may only need oestrogen treatment. Your doctor will discuss the best option with you and

If you are in the COC group, this will involve taking one tablet a day for 9 weeks followed by a 4-7 day break. In certain cases where this is not suitable, e.g. if you have had a hysterectomy or feel like this way of taking COC is not working for you, please discuss other options with your study doctor. The COC contains oestrogen and progesterone hormones together.

We know that some women will need to change their study treatment. It is possible to try different formulations or forms of administration (e.g. tablet or patch) of your study treatment if you feel what you were first prescribed is not working for you. If this is the case please speak to your study doctor, who will discuss your options with you.

We will ask you to take your allocated study treatment for at least 2 years and up to 5 years. You will be notified by the clinic when your study participation comes to an end. However, we know that some women may want to change or stop their treatment. We ask that you speak to your study doctor first if this becomes the case, who will discuss it with you and inform your GP what to prescribe for you.

If you wish to become pregnant, please speak to your study doctor. If you are taking COC, you will need to stop taking your study treatment. HRT is not necessarily a contraceptive.

When you start the study, your study treatment will be prescribed by your study doctor. We will inform your GP that you are taking part in this study, and your GP will give you further prescriptions; you will need to contact your GP when you are running low on medication to request more. If you are in England and pay for your prescriptions, you will have to pay for HRT treatment (unfortunately, POI is not a medical condition that is exempt from prescription charges and the study cannot pay directly for HRT prescription charges (often charged as two prescriptions)). However, you can apply for a pre-payment certificate for HRT (**https://www.gov.uk/get-a-ppc/hrt-ppc**). COC does not have prescription charges as contraceptives are exempt from payment

**What else will I be asked to do?**

While you are taking your treatment, we will need to repeat some of the initial tests that were performed. This is so we can see if there are any changes over time. The tests will be performed as part of your routine clinic appointments as much as possible. For example, it is routine to check your blood pressure and weight while on treatment for POI. This will be done after 3 months, 6 months and one year on the study treatment, then annually. If you are unable to get to your clinic appointment and if your GP or local pharmacy has agreed to take your blood pressure and weight, then you can use these services.

You will be asked to complete questionnaires about your treatment, symptoms, lifestyle, pregnancy status, as well as the impact POI has on your sexual activity and your working life. You may receive the questionnaires by email if you prefer. All information collected during the study will be kept safe and confidential.

In addition to the initial tests to assess your health before you start your study treatment (baseline assessments), the study will require you to have a bone density measurement after 1 year and 2 years on the study treatment and possibly again at 5 years. Bone density measurements are not always offered as part of routine medical care for women with POI, so you may need to make extra visits for the purpose of the study.

If you have agreed to provide blood and/or urine samples, these will be taken at your baseline clinic appointment and then again at 3 months and 1 year, then annually for blood only

If you become pregnant or wish to become pregnant whilst taking part in the study please contact your study doctor.

## 7. What are the possible benefits of taking part?

You will be offered recommended treatments for POI whether or not you decide to take part in the study. However, if you choose to take part, the monitoring of your health, including any changes to your bone density, may be increased compared to routine treatment. In addition, you will have access to your study doctor throughout the duration of the study. The information we collect from this study may help us to understand more about the best way to treat women with POI in the future.

There is no monetary benefit for taking part in the study and travel costs will not be reimbursed. However, you will receive a voucher of total £110 (£20 at 3- and 6-months clinic visits, and £35 at 1 and 2 years clinic visits) to partially compensate towards the travel costs and HRT prescriptions. All participants that were enrolled in on the previous incentive system will receive vouchers retrospectively.

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

**Study treatment:**
Both HRT and COC are routine treatments for POI. As with all medications, there is a small risk of side-effects. Common side effects of both HRT and COC include headaches, breast pain and irregular bleeding; however, these side effects are not specific to the study and could also occur with standard care. Your doctor or nurse will discuss any possible effects of the potential treatments with you when talking about the options and your preferences. They will check that any treatment will not interact with any other medication you might take. HRT is not necessarily a contraceptive, and the use of non-hormonal contraception is advised.

**Bone density measurements:**
Bone density is measured using low dose radiation (x-rays). Everyone is exposed to radiation sources every day, for example from the sun. The amount of radiation from a bone density measurement is less than 2 days' exposure to natural radiation and much lower than that of a standard x-ray. However, you must not have a bone density scan if you are or think you could be pregnant.

**Blood samples:**
If you are having blood samples taken, this is a standard procedure which is unlikely to cause any problems but can sometimes cause discomfort. There is a risk of bruising, reddening and swelling of the vein, but this normally clears up with no further trouble.

## 9. What if there is a problem?

If you have concerns or questions about any aspect of this study, you should ask to speak to the local researchers. Their contact details are at the end of this information sheet.

If any questions remain, you can contact the study coordinating centre:
Email: **poise@nottingham.ac.uk**

Every care will be taken in the course of this study. However, in the unlikely event that you are injured by taking part, compensation may be available. If you suspect that the injury is the result of the Sponsor's (University College London) or the hospital's negligence, then you may be able to claim compensation. After discussing with your study doctor, please make the claim in writing to Dr Melanie Davies (Department of Women's Health, University College London Hospitals NHS Foundation Trust, London NW1 2PG) who is the Chief Investigator for the clinical trial. The Chief Investigator will then pass the claim to the Sponsor and on to Sponsor's Insurers. If you have a claim then it

might be helpful to consult a lawyer. Participants may also be able to claim compensation for injury caused by participation in this study without the need to prove negligence on the part of University College London or another party. You should discuss this possibility with your study doctor in the same way as above.

Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated by members of staff or about any side effects (adverse events) you may have experienced due to your participation in the study, the normal National Health Service complaints mechanisms are available to you. Please ask your study doctor if you would like more information on this. Details can be obtained from the NHS website.

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

You can change or stop treatments at any time, without having to withdraw from the study. It is still very important for us to know about your symptoms, heart and bone health, even if you are not taking the treatment, you were first given. You can stop providing information about your symptoms, heart and bone health at any time, without giving any reason, and without your care and legal rights being affected. If you withdraw, the information already collected will not be erased and this information may still be used in the study analysis.

If you have been asked to provide blood and urine samples, you can decide to stop providing samples at any time. However, any samples taken before this will be retained and used.

If you become pregnant, you do not need to withdraw from the study, but please contact your study doctor as you may need to stop taking your assigned treatment. You cannot have bone density measurements whilst pregnant and we will not ask you to continue completing the questionnaires. We would also like to know the outcome of your pregnancy and will ask your doctor to provide us with this information. After your pregnancy, you can resume your hormonal treatment. We would like to resume the tests and questionnaires, if you are OK to continue.

## 11. How will information about me be used?

Researchers at the Nottingham Clinical Trials Unit (part of the University of Nottingham) will need to use information from you and your medical records for this study. This information will include your initials, NHS number (CHI number if you are living in Scotland), name and contact details. The researchers will use this information to do the research or to check your records to make sure that the research is being done properly.

People 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. All information about you will be kept safe and secure.

Once the study has finished, some of the information will be kept so the results can be checked and you can be told what happened in the study (unless you tell us you do not want to know). Reports will be written in a way that no-one can work out that you took part in the study.

Your personal contact details will be available to the Nottingham Clinical Trials Unit (NCTU) so they can contact you during the study and send you the questionnaires. Your name and telephone number will be shared with Esendex, our text messaging provider and their subprocessors, and will be used to send you text message reminders about the study and study questionnaires whilst you are participating in the study.

## 12. What are your choices about how your information is used?

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

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 you give us your permission, we may keep your contact details so we can get in touch if there is any future research to do with your condition that you may be interested in taking part in. You will also have the option to take part in future research using your data saved from this study.

If you do not wish your contact details to be kept for a copy of the study results to be sent to you or to be contacted about future research, these will be disposed of securely at the end of the study. After 25 years, your data collected during the study will be disposed of securely.

## 13. Where can you find about more about how your information is used?

You can find out more about how we use your information:

- at **www.hra.nhs.uk/patientdataandresearch**
- at **https://www.ucl.ac.uk/legal-services/privacy/participants-health-and-care-research-privacy-notice**
- at **http://www.nctu.ac.uk/data-protection/data-protection.aspx**
- by asking one of the research team
- by sending an email to **poise@nottingham.ac.uk**

## 14. Who is organising and funding this study? How has it been approved?

The study is being organised by University College London (the Sponsor) and co-ordinated by the Nottingham Clinical Trials Unit (NCTU). The funding for the study is provided by the research arm of the NHS, the National Institute for Health and Care Research Health Technology Assessment (NIHR HTA) Programme. All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given approval by a Research Ethics Committee.

The Daisy Network, the charity for women with POI in the UK, and the Turner's Syndrome Society UK are active partners in our study. Patients who have been treated for POI have helped us plan and design this study. Patient representatives are also involved in the teams that oversee the running of the study.

The study has also been approved by the Medicines and Healthcare products Regulatory Agency (MHRA) who are responsible for regulating medicines in the UK and ensuring they meet applicable standards of safety, quality and effectiveness.

## 15. What if relevant new information becomes available?

Sometimes we get new information about your treatment during the study. This is unlikely, as both COC and HRT have been used for many years, but if this happens your research doctor will tell you about this new information and discuss whether you should continue with your treatment. If you decide not to carry on with the treatment you were taking, your research doctor will make arrangements for a different treatment. If you decide to continue with the study treatment, he/she may ask you to sign a new Informed Consent Form.

## 16. What will happen to any samples I give?

If you have been asked to provide blood and/or urine samples and are willing to do so (this is optional), they will be used to look at the health of your bones and heart. Your blood and urine samples will be labelled with your study

identification number, initials and date of birth.

Blood samples looking at the health of your heart will be analysed by the hospital routine laboratory service. If any of the results are abnormal, your doctor will discuss these with you.

Blood and urine samples looking at the health of your bones will be stored and analysed at the end of the study. Samples will be stored and analysed in a secure laboratory in the UK.

If you agree, any remaining blood will be stored for 5 years and used for future research into the cause and treatment of POI. This may include looking at changes in genes thought to be important in POI. All future research will have to be reviewed and approved by a Research Ethics Committee before-hand . You will not be identified in any way if your samples are used, and neither you nor your doctor will receive the results of any tests. If you choose not to allow this, then any remaining samples will be disposed of in accordance with the laboratory guidelines. You can still provide blood samples for testing within this study, even if you don't want your blood stored afterwards; just indicate this on the consent form.

## 17. What happens at the end of the study?

This is a very long study. We will look at the results two years after the last woman has agreed to take part, and again after 5 years. At each timepoint, the results will be published in scientific medical journals and presented at conferences. You will not be identified in any publication. We will send you a newsletter with a summary of the study findings, unless you ask us not to.

Study results (when available) will also be published here:
**https://www.isrctn.com/ISRCTN91141124?q=91141124&filters=&sort=&offset=1&totalResults=1&page=1&pageSize=10**

It is recommended that women with POI take hormonal treatment until the average age of menopause, which is about 51 years. How long you will take hormonal treatment will depend on your age at diagnosis. When the study ends, you will return to standard care and be treated for your POI as usual.

## 18. How to contact us

Contact details of your local care team;

Women's Health Research Team
Email: kch-tr.womenshealthresearch@nhs.net
Telephone: 07890 251 949

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