Clinical and cost-effectiveness of **DE**sogestrel versus the combined oral contraceptive pill for problem **B**leeding on the etonogestrel **I**mplant (The **DEBI** Trial)

IRAS ID: 1007190

Participant Information Sheet

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1. You are invited to take part in our research trial

We'd like to ask you to take part in the DEBI trial, which is looking at people aged 16-45 years with problem bleeding whilst using the etonogestrel implant (implant) for contraception. We are interested in understanding whether desogestrel (a progestogen only pill) is as good as the combined oral contraceptive pill (combined pill which contains estrogen and progesterone) in treating people with problem bleeding whilst using the implant.

Before you decide whether to take part, it is important 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 trial. 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 continue in the normal way.

2. A summary of the trial

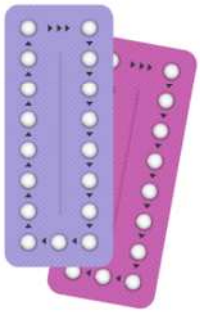
Nearly a quarter (24%) of implant users experience some form of problem bleeding once the implant has been inserted. Problem bleeding can include any bleeding pattern that a person considers problematic e.g. heavy bleeding, continuous bleeding or irregular bleeding. The most common treatment for problem bleeding on the implant is the combined pill, however not everyone can take it. Desogestrel, a progestogen only contraceptive pill, is also used by doctors to treat problem bleeding. This is often prescribed to people who can't take the combined pill or when the combined pill has not improved bleeding. However, we don't know if it works as well as the combined pill to treat problem bleeding in implant users.

The DEBI trial is needed to find out if taking a daily desogestrel contraceptive pill is as good as taking a daily combined pill at improving problem bleeding in implant users. We plan to recruit 690 participants from sexual health clinics and doctor's surgeries in the UK. Half of participants will be given the combined pill and the other half will be given desogestrel. Participants will have an equal chance of being given either treatment (using a process called randomisation) and neither the participant nor the research team will know which pill has been given until the end of the trial. Participants will be asked to take a pill once a day for 90 days. We follow up participants over 90 days to see if there are any changes in their bleeding patterns and to check that they are taking their trial treatment.

DEBI
DESOGESTREL FOR PROBLEM BLEEDING ON THE IMPLANT

If you visit clinic with problem bleeding you might be given information about the DEBI trial.

If you are eligible you will be asked to complete a consent form. You will also be asked a few questions about you and your problem bleeding.



You will then be randomised to one of our study treatments and be given the medication in clinic.

You will be asked to complete a daily bleeding diary to record your currently bleeding status via an app.

We will also send you a questionnaire to complete at day 30, 60 and 90 after you start treatment. These can be completed online or via post.

3. What is the purpose of the trial?

The purpose of the trial is to find out whether desogestrel is as good as the combined pill in treating problem bleeding in implant users.

4. Why have you been invited to take part?

You have been invited to take part in this trial because you are an implant user who is seeking treatment for problem bleeding. Your suitability to take part in the trial will be determined by a doctor to ensure that participation is safe.

5. Do you have to take part?

No, it is up to you whether or not you take part in the trial. Even if you agree now, you are free to withdraw at a later date if you wish. We will talk to you about the trial and answer any questions you may have. If you agree to take part, we will ask you to sign a consent form electronically or on paper.

If you decide that participating in the trial isn't for you, then that is OK. This will not affect the quality of care you receive.

6. What would taking part involve?

If you agree to take part, your involvement in the trial will last 90 days from starting your treatment to finishing your treatment and answering your last questionnaire (3 questionnaires in total).

Seeing the doctor or nurse in clinic:
As part of your clinic appointment today, your doctor or nurse will have talked to you about your problem bleeding, taken a pregnancy and Sexually Transmitted Infection ('STI') test and examined you to rule out other possible causes of your bleeding to make sure that you will be given suitable treatment. One of the treatment options is taking part in the DEBI trial. If you choose to take part, you will be asked to sign a consent form and provide some information including your contact details, so that the trial questionnaires can be sent to you. The results of tests and examinations will be used to decide if you are eligible to take part in the trial.

Your Medicine
You will be given either the combined pill or desogestrel to take once per day. Which medication you receive will be allocated in a process called randomisation. This means you will have an equal chance of receiving the combined pill or desogestrel. Randomisation is used as it creates groups of patients that are similar except for the medication received. This means we can fairly compare the two medicines to understand whether desogestrel is as good as the combined pill at the end of the trial. Neither you, the doctors or the research team can choose which group you will go in, as this could result in the groups being unequal and the findings unreliable. Whichever medication you receive, you'll be asked to take it orally, once a day, at the same time each day for 90 days. Neither you or your doctor will know which treatment you have been randomised to.

Following your progress
After today, there are no more in-person trial visits. As part of your usual care, you will be asked to revisit your sexual health service or GP in about 3 months time to understand whether your medication has worked. During this visit you will be told which of the two medications you took as part of the trial (this may be in-person or a telephone call). You will be asked to complete a daily bleeding diary at home, recording your daily bleeding status, using a mobile phone app or a paper diary during the 90 days that you are taking the

medication.

At 30, 60 and 90 days after your enrolment in the trial you will be asked to complete a questionnaire asking about your bleeding, medication and side effects. Some of the topics or questions may feel sensitive, embarrassing or upsetting but they are important for us to understand how the trial treatment is impacting your bleeding and daily life. It may be necessary for your local care team or a member of the trial co-ordinating team to contact you to provide support with your daily bleeding diary and questionnaires.

With your permission, we will inform your General Practitioner (GP) about your participation in this trial. We will also ask for your optional consent to use your routinely collected data for a separately funded long-term follow-up. This will look at whether you have continued with your prescription of COCP, desogestrel or other treatments for problem bleeding, and whether you have had a change or removal of implant.

7. What are the possible benefits of taking part?

Taking part in the trial may not directly benefit you, but the information we collect may help us to treat people with problem bleeding while using the implant in the future.

You will receive a £15 'thank you' voucher when you complete each of the questionnaires (30, 60 and 90 days), a total of £45 for all 3 questionnaires as a thank you for your time.

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

Although desogestrel is used to treat problem bleeding in patients on the implant, we don't know if it works as well as the combined pill. With all medications there is a small chance you may experience some side effects. The most common side effects for the two trial medications are listed below and in the DEBI medicine information leaflet:

Medicine	Side effects
Combined pill	Nausea, abdominal pain, increased weight, headache, depressed mood, altered mood, breast pain/tenderness.
Desogestrel	Irregular bleeding, acne, mood changes, breast pain, nausea and weight increase.

Both study medications are licenced for and regularly prescribed in clinical practice in this age group. Both desogestrel and the COCP have marketing authorisation in the UK for oral contraception, but for this trial they will be used outside of their licensed indications. More information can be found in the medicine information leaflet.

Please inform your doctor if you have (or think you may have) an allergy to lactose or soybean oil as the trial medications may contain these ingredients.

There are some medicines that you cannot take whilst on the trial and some medicines that we will ask you to let us know about in your questionnaires at days 30, 60 and 90- please refer to the DEBI medicine information leaflet which lists these medicines and what you should do if you start to take them.

9. What if there is a problem?

If you have concerns or questions about any aspect of this trial, 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 trial coordinating centre:
Tel: +44 (0) 115 8231595 , Email: DEBI@nottingham.ac.uk

If you remain unhappy and wish to complain formally, you can do this through the National Health Service (NHS) Complaints Procedure via your local Patient Advisory and Liaison Service (PALS) <insert Local PALS details>.

The University has in force relevant insurance policies which apply to this trial. In the event that something does go wrong and you are harmed during the trial, there are no special compensation arrangements. If you are harmed and this is due to someone's negligence then you have grounds for a legal action for compensation but you may have to pay your legal costs. The normal NHS complaints mechanism will still be available to you.

10. What will happen if you don't want to carry on with the trial?

You are free to withdraw at any time, without giving any reason, and without your legal rights being affected. If you would like to withdraw, contact your local researchers / NCTU Trial team and they can organise this for you. Their contact details are at the end of this information sheet. If you withdraw, or are withdrawn from the study for any reason, the information collected will not be erased and this information may still be used in the project analysis.

11. How will information about you be used?

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

This information will include your initials, NHS number, Community Health Index (CHI) number (if registered in Scotland), name, contact details and your consent form which will be held by the University of Nottingham and the site People 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.

The University of Nottingham is the sponsor of this research and is responsible for looking after your information. "We" (meaning the sponsor) will keep all information about you safe and secure by:

- Following and adhering to the laws relating to General Data Protection Regulation (GDPR)
- Having strict access controls on our electronic systems
- Deleting your personal data (as outlined in this information sheet) when it is no longer required
- Keeping the details we have to contact you separate from the trial data

Your data will not be shared outside the UK.

Your name and telephone number may be shared with Esendex, our text messaging provider and their subprocessors, and be used to send you text message reminders about the trial and trial questionnaires

whilst you are participating in the trial should that be necessary.

All information about you will be kept safe and secure.

Once the trial has finished, 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.

We will keep your trial data for a maximum of 7 years.

The trial data will then be fully anonymized and securely archived or destroyed.

12. 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. Any data we collected will be kept and used in the analysis.

You have the right to ask us to remove, change or delete data we hold about you for the purposes of this trial. We might not always be able to do this if it means we cannot use your data to do the research. If so, we will tell you why we can't do this.

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

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.nottingham.ac.uk/utilities/privacy/privacy-information-for-research-participants.aspx
- http://www.nctu.ac.uk/data-protection/data-protection.aspx
- by asking one of the research team
- by sending an email to DEBI@nottingham.ac.uk
- by calling the Nottingham Clinical Trials Unit on +44 (0) 115 8231595
- by sending an email to our Data protection officer at dpo@nottingham.ac.uk

14. Who is organising and funding this trial? How has it been reviewed and approved?

The trial is being organised by the University of Nottingham (the Sponsor) and coordinated by the Nottingham Clinical Trials Unit (NCTU). The funding for the trial is provided by the National Institute for Health and Care Research. All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This trial has been reviewed and given favourable opinion by a Research Ethics Committee.

Patients who have experienced problem bleeding on the implant have helped us plan and design this trial. Patients' representatives are also involved in the teams that oversee the running of the trial.

15.What if relevant new information becomes available?

We may get new information about the trial medicines or problem bleeding whilst using the implant during the trial. If this happens whilst you are still taking part, your research doctor will tell you about this new information and discuss whether you should continue in the trial. If you decide not to carry on, your research doctor will make arrangements for your care to continue as normal. If you decide to continue in the trial they may ask you to sign a new Informed Consent Form.

16.What will happen to any samples I give?

Any samples provided to assess eligibility are part of standard care, these will be processed following local standard operating procedures and will not be collected or stored for the purpose of this trial.

17.What happens at the end of the trial?

When your participation in the trial ends, you will be told which medication you received (either as part of your 3-month standard care visit or via telephone call). The information will be sent to the recruiting centre to support your ongoing care. The clinician will discuss the most appropriate treatment with you at the end of the trial. If you withdraw from the trial, we will need to keep and use the data collected up to your withdrawal. At the end of the trial 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 trial findings, unless you ask us not to.

18.How to contact us

Contact details of your local care team who will be your main point of contact for the duration of the trial;

- <insert contact details here>

- DEBI@nottingham.ac.uk