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DEsogestrel for Bleeding on the Implant (DEBI)

Submission date 27/03/2025	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 28/05/2025	**Overall study status** Ongoing	
Last Edited 02/01/2026	**Condition category** Other	

Plain English summary of protocol

Background and study aims
The contraceptive implant (68mg etonogestrel) is a hormone-containing rod that is placed under the skin of the arm and is more than 99% effective at preventing pregnancy. Unfortunately, 24% of users have the implant removed early due to frustrating and unpredictable changes in their periods. Bad experiences with the implant deter people from using other effective contraceptive methods and may increase the risk of unintended pregnancy.
The current first-line treatment that is recommended is to take the combined oral contraceptive pill (COCP). This research aims to see whether desogestrel is as good as COCP in reducing problematic bleeding while using the implant. Desogestrel is slightly safer and cheaper than the combined pill, can be used in people who cannot take the combined pill and can be bought without a prescription. Using desogestrel means that people are only exposed to one type of hormone rather than two in the combined oral contraceptive pill. People taking the combined pill require annual blood pressure and weight monitoring, which is not required with desogestrel. If desogestrel is found to be as good as the combined pill, it will mean a safer, cheaper, more accessible treatment for problematic bleeding on the implant.

Who can participate?
The trial will recruit 690 menstruating people aged 16-45 with self-reported problem bleeding whilst using the etonogestrel implant. Problem bleeding is defined as bleeding of any type (e.g. spotting/heavy) considered problematic by the person.They must be willing to complete a daily bleeding diary for the trial duration.

What does the study involve?
The research aims to see whether desogestrel is as good as the combined oral contraceptive pill in settling problem bleeding during 90 days for people with problem bleeding whilst using the etonogestrel implant.Resolution of problem bleeding is defined as people self-reporting a significant improvement in the bleeding pattern during the 90-day reference period.Daily bleeding diary and adherence questions have been combined to reduce the time burden on participants. There are no follow-up visits required in addition to usual care, and follow-up questionnaires have been designed to only ask what is needed to answer the trial outcomes.

What are the possible benefits and risks of participating?
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 marketed purpose. Desogestrel is an

unevidenced treatment used in clinical practice. Risks related to trial treatment (common side effects) are described in the patient information sheet and medicine information leaflet (for both COCP and desogestrel), and they will be advised by the clinician on treatment in accordance with their local policies. Full details of side effects are available in the individual SmPC patient information sheet. Safety monitoring will be conducted as per the Monitoring Plan.

Where is the study run from?
University of Nottingham, UK

When is the study starting and how long is it expected to run for?
April 2024 to July 2027

Who is funding the study?
NIHR Health Technology Assessment Programme, HTA

Who is the main contact?
debi@nottingham.ac.uk

Contact information

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Scientific, Principal investigator

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Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1007190

Protocol serial number
24045

Study information

Scientific Title
Clinical and cost-effectiveness of desogestrel versus the combined oral contraceptive pill for problematic bleeding on the etonogestrel implant: DEBI trial

Acronym
DEBI

Study objectives
To establish whether desogestrel is non-inferior to the combined oral contraceptive pill (COCP) in settling problem bleeding during a 90-day reference period for people with problem bleeding whilst using the etonogestrel implant. Resolution of problem bleeding is defined as people self-reporting significant improvement in the bleeding pattern during the 90-day reference period.

To establish if the proportion of participants reporting problem bleeding is not worse in participants treated with desogestrel compared to COCP.
To determine the effect of desogestrel compared with COCP on total number of non-bleeding, spotting and bleeding days during the 90-day treatment period.

To determine the effect of desogestrel compared with COCP on the number and duration of bleeding episodes (one or more consecutive days of bleeding, bounded by bleed-free days) within the 90 days .
To determine the effect of desogestrel compared with COCP on the time to the longest consecutive non-bleeding days.
To determine the acceptability with trial treatment.
To establish participant adherence to treatment.
To determine the effect of desogestrel and COCP on participant Quality of life.
To determine the cost of treating implant user problem bleeding with desogestrel or the COCP.
To determine the proportion of participants who intend to continue their allocated treatment.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 07/05/2025, North West - Greater Manchester Central Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8084; gmcentral.rec@hra.nhs.uk), ref: 25/NW/0110

Study design
Multicentre clinician- and participant-blinded randomized non-inferiority trial with economic evaluation

Primary study design
Interventional

Study type(s)
Efficacy

Health condition(s) or problem(s) studied
Self-reported problem bleeding on the contraceptive implant

Interventions
Intervention: desogestrel 75 micrograms, once daily by mouth.
Active comparator: 30 microgram ethinylestradiol and 150 microgram levonorgestrel COCP, 1 tablet daily by mouth (without a hormone-free interval). Both COCP and desogestrel tablets will be similar oval, unmarked, white tablets to mask the allocation.
This is a phase IV, multicentre, clinician and participant-blinded, randomised non-inferiority trial, with economic evaluation. Equal allocation (1:1) to receive either desogestrel (intervention) or COCP (usual care). Recruitment of 690 participants is required to achieve 90% power and conclude non-inferiority with respect to the resolution of problem bleeding.
Randomisation will be provided by REDCap, a secure online randomisation system at the NCTU. Unique log-in usernames and passwords will be provided to those who have been delegated the role of randomising participants into the trial as detailed on the DEBI Delegation Log. The online randomisation system will be available 24 hours a day, 7 days a week, apart from short periods of scheduled maintenance.
After participant eligibility has been confirmed, informed consent has been received, baseline data items have been provided, the participant can be randomised into the trial and a trial number allocated. Following randomisation, a confirmatory email will be sent to the randomising clinician, local Principal Investigator, and the local pharmacy. A randomisation notification will be sent to the Chief Investigator and NCTU.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Feanolla (Desogestrel) 75 mcg film coated tablets (Lupin Healthcare ltd, PL 35507/0195). [desogestrel] , Levest (Levonorgestrel 150mcg and Ethinylestradiol 30mcg) coated tablets [150 micrograms levonorgestrel, 30 micrograms ethinylestradiol]

Primary outcome(s)
Participant-reported resolution of problem bleeding, with resolution defined as self-reported significant improvement in the bleeding pattern during the 90-day reference period. Improvement in problem bleeding will be measured by participants' self-determination that their bleeding pattern has improved using a 5-point Likert scale, 90 days after the participants start their study medicine

Key secondary outcome(s))
Clinical effectiveness
1. Longest duration of consecutive non-bleeding (no bleeding or spotting) whole days within the 90 days measured using a 5-point Likert scale at Days 30 and 60
2. Total number of non-bleeding, spotting and bleeding days measured using a Daily bleeding diary during the 90-day treatment period
3. Number and duration of bleeding episodes (one or more consecutive days of bleeding, bounded by bleed-free days) measured using a Daily bleeding diary within the 90 days
4. Time to the longest consecutive non-bleeding days measured using a Daily bleeding diary within the 90 days

Treatment acceptability and adherence
1. Acceptability of treatment (global and progestogenic side effects) measured using a Participant Questionnaire on days 30, 60 and 90
2. Adherence to treatment measured using a Daily bleeding diary

Safety
Discontinuation of allocated treatment and of implant measured using participant-reported discontinuation/removal of their implant in a Participant Questionnaire on days 30, 60 and 90

Cost-effectiveness
1. Quality of life (EQ-5D-5L and ICECAP-A) measured using participant-reported EQ-5D-5L and ICECAP-A on days 30, 60 and 90
2. Primary care, sexual health, and secondary care health resource use measured using a Participant Questionnaire on days 30, 60 and 90
3. Personal and out-of-pocket expenses arising from problem bleeding measured using a Participant Questionnaire on days 30, 60 and 90
4. Intention to continue the trial drug at 3 months measured using a Participant Questionnaire on days 30, 60 and 90

Completion date
31/07/2027

Eligibility

Key inclusion criteria
1. Female, or trans-male and non-binary people with a uterus, ovary/ovaries and vagina not using hormones other than etonogestrel implant
2. 16 – 45 years old
3 Etonogestrel implant user, with current implant in situ for at least 3 but no more than 24 months
4. Self-reported problem bleeding
5. Willing to complete daily bleeding diary for the trial duration
6. Able to provide Informed Consent
7. Sexually transmitted infection screening undertaken and high sensitivity pregnancy test negative at time of recruitment

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
16 years

Upper age limit
45 years

Sex
Female

Total final enrolment
0

Key exclusion criteria
1. Current routine use of oral NSAIDs
2. Current use or use within the last 3 months of hormones or medications known to affect menstrual bleeding, including progestogens, estrogens, androgens, tranexamic acid, selective progestogen receptor modulators
3. Current use or use within the last 6 weeks of liver enzyme inducing medicines which induce the cytochrome CYP3A4
4. Postpartum < 6 weeks (UKMEC 3 or 4)
5. Current use or use within the last 6 months of gonadotrophin-releasing hormone analogues
6. Current use or use within the last 9 months of DMPA
7. Surgery to genital tract altering bleeding, including hysterectomy, bilateral-oophorectomy or endometrial ablation
8. Contraindication (UKMEC Category 3 or 4) or allergy to desogestrel or excipients (including soya bean oil)
9. Contraindication (UKMEC Category 3 or 4) or allergy to COCP containing levonorgestrel and

ethinylestradiol or excipients
10. Established pathological reasons for abnormal uterine bleeding, including malignancy or endometrial hyperplasia, fibroids, cervical polyps or lesions (seen on speculum examination), endometrial polyp(s), adenomyosis, coagulopathy, ovulation disorder (e.g. polycystic ovary syndrome)
11. Current known sexually transmitted infection (If STI screening comes back positive then the participant will remain in the trial)
12. Currently pregnant (positive urinary pregnancy test)
13. Previous participation in this trial
14. Declines screening for sexually transmitted infection dual nucleic amplification test (NAAT) for Neisseria Gonorrhoeae and Chlamydia Trachomatis at the time of presentation
15. Declines a speculum examination to assess the cervix for abnormality or other cause for problem bleeding at the time of presentation
16. Declines examination of the implant insertion site to ensure palpable and present at the time of presentation

Date of first enrolment
30/09/2025

Date of final enrolment
31/10/2026

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Study participating centre
Nottingham University Hospitals NHS Trust
Trust Headquarters
Queens Medical Centre
Derby Road
Nottingham
England
NG7 2UH

Study participating centre
Leeds Community Healthcare NHS Trust
3 White Rose Office Park
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LS11 0DL

Study participating centre
Cambridgeshire Community Services NHS Trust
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Study participating centre
University Hospitals Sussex NHS Foundation Trust
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BN11 2DH

Study participating centre
Hampshire and Isle of Wight Healthcare NHS Foundation Trust
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SO40 2RZ

Study participating centre
University of Nottingham Health Service
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University Park
Nottingham
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NG7 2QW

Study participating centre
Kingston and Richmond NHS Foundation Trust
Galsworthy Road

Kingston upon Thames
England
KT2 7QB

Study participating centre
Northamptonshire Healthcare NHS Foundation Trust
St Marys Hospital
77 London Road
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NN15 7PW

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
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Study participating centre
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Sponsor information

Organisation
University of Nottingham

ROR
https://ror.org/01ee9ar58

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from debi@nottingham.ac.uk. Anonymised participant data may be shared with researchers external to the trial research team in accordance with the NCTU's data sharing procedure and the National Institute for Health Care Research (NIHR) policy on the sharing of research data. All requests for data should be sent to the Nottingham Clinical Trials Unit. Participants consent to their anonymised information being used to support other research in the future and that it may be shared with other researchers.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 2.0	06/06/2025	03/09/2025	No	Yes
Protocol file	version 2.0	06/06/2025	03/09/2025	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes