

A large, multi-clinic study to evaluate contraceptive efficacy and safety of depot medroxyprogesterone acetate (150 mg/ml) injected under the skin every 6 months

Submission date 22/03/2022	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 26/05/2022	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 16/07/2024	Condition category Pregnancy and Childbirth	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

The study is being done to find out if the existing 3-month depot medroxyprogesterone acetate (DMPA) contraceptive injection is as effective and safe when injected every 6 months under the skin instead of into the muscle. The product being tested is called '6-month DMPA SC'. A previous study of 21 women showed that injecting DMPA under the skin stopped 21 women from ovulating (i.e., producing eggs) for at least 6 months when it was given under the skin. This study will test if it prevents actual pregnancy and is safe among a larger number of women.

Who can participate?

Healthy, sexually active women aged 18 to 35 years who are willing to use 6-month DMPA SC as their only means of contraception for 12 months (i.e., receive two injections 6 months apart).

What does the study involve?

Participants in the study will receive two shots of 6-month DMPA SC (at enrollment and 6 months after the first injection) under the skin of either their abdomen or thigh. Participants will be asked to return for follow up visits at Months 3, 6 and 9, and a final visit at Month 12, and complete monthly pregnancy tests either at home or at the clinic during the study. Additional tests after the Month 12 visit to provide information on return to ovulation may be scheduled if a participant consents to participate.

What are the possible benefits and risks of participating?

There is no direct benefit from taking part in this study, however, participants may help to develop a new, longer-acting contraceptive method.

Pregnancy: Risk of pregnancy is low but unknown. Participants will be tested for pregnancy before and during the study to make sure they are not pregnant. Any positive tests will be confirmed by a blood test and/or ultrasound. The researchers will refer participants for medical care at NHS in the unlikely scenario that they become pregnant. Many studies have found that babies who are exposed to DMPA while in the womb do not have a higher risk of birth defects or

health problems.

Future fertility: Participants' typical ability to get pregnant will return when the last injection wears off. It may take as long as a year after getting the last shot of 6-month DMPA SC for this to happen.

Skin reactions: There is a chance that participants will have skin reactions where they receive the shots. No skin reactions were reported to be severe or serious during previous studies.

Irregular bleeding: Most women have irregular bleeding, spotting or no bleeding at all while using DMPA. Regular bleeding is expected to return when most of MPA is cleared from the body.

Weight gain: Some women gain weight while using DMPA (about 3-5 pounds in a year).

Sexually transmitted infections: According to WHO, it is safe for women who are at high risk of sexually transmitted infections (STIs) including human immunodeficiency virus (HIV), to use DMPA. DMPA does not protect against STIs, including HIV.

Bone mineral density: Use of DMPA for more than 2 years may weaken bones (the condition known as osteopenia which may increase the risk of broken bones). It is not expected that getting two injections of 6-month DMPA SC in this study will have any effect on bones due to the short duration of the study (12 months).

Cancer: Some studies found a slightly increased risk of breast cancer among women using 3-month DMPA for 12 months or longer. It is unlikely that getting two injections of 6-month DMPA SC in this study will lead to breast cancer.

Allergic reaction: Severe allergic reaction to DMPA, also known as anaphylactic reaction, is rare. Such reactions usually happen right after the injection. The researchers will ask participants to remain in the clinic for observation for at least 30 minutes after each injection where we have drugs to treat severe allergic reactions and easy access to emergency care in the unlikely event of such a reaction.

Additional potential side effects: acne, headache, tiredness, decreased sexual desire, breast pain, depression.

Blood draw: It is possible that participants may feel some pressure or discomfort while their blood is being drawn and they may have a small bruise where the blood was drawn. There is also a small risk of infection with a blood draw.

Ultrasound: A transvaginal ultrasound may be done to confirm a positive urine pregnancy test. This procedure is usually not painful but may cause discomfort, anxiety or embarrassment.

Gynaecological examination: This examination usually does not hurt but may cause slight discomfort, anxiety or embarrassment.

Non-medical: Potential non-medical risks in this study include a breach of confidentiality, potentially missing work to come to study visits, and answering questions about sensitive subjects like sexual history and keeping a bleeding diary. The researchers will do their best to prevent anyone outside the study from knowing about participants in this study. All attempts will be made to accommodate the participants' availability when scheduling clinic visits.

If participants have a side effect after an injection, the drug cannot be removed immediately to stop the reaction. Most of the side effects do not pose a serious risk to health and go away with time without clinical care. Participants will be provided with study team contact details and emergency contacts for the study in case they experience any of the above risks. The site team will make every attempt to resolve the issue by providing appropriate medical care and ensuring the safety of their patients.

Where is the study run from?
FHI 360 (USA)

When is the study starting and how long is it expected to run for?
March 2022 to January 2026

Who is funding the study?
FHI 360 (USA)

Who is the main contact?
Sarah Cordes
SCordes@fhi360.org

Contact information

Type(s)

Principal Investigator

Contact name

Dr Vera Halpern

Contact details

359 Blackwell Street
Suite 200
Durham
United States of America
27701
+1 (0)919 321 3331
vhalpern@fhi360.org

Type(s)

Scientific

Contact name

Dr Vera Halpern

Contact details

359 Blackwell Street
Suite 200
Durham
United States of America
27701
+1 (0)919 321 3331
vhalpern@fhi360.org

Type(s)

Principal Investigator

Contact name

Prof Sharon Cameron

Contact details

2a Chalmers Street
Edinburgh
United Kingdom
EH3 9ES

+44 (0)131 5362091
sharon.cameron@ed.ac.uk

Type(s)

Public

Contact name

Dr Sarah Cordes

Contact details

359 Blackwell Street
Suite 200
Durham
United States of America
27701
+1 (0)919 321 3809
scordes@fhi360.org

Additional identifiers

EudraCT/CTIS number

2021-004106-22

IRAS number

1005048

ClinicalTrials.gov number

Nil known

Secondary identifying numbers

1706176, IRAS 1005048

Study information

Scientific Title

A Phase III, open-label, multicenter study to evaluate contraceptive efficacy and safety of depot medroxyprogesterone acetate (150 mg/ml) injected subcutaneously every 6 months

Acronym

DMPA-XT

Study objectives

The main objective is to evaluate the contraceptive efficacy of 6-month depot medroxyprogesterone acetate (DMPA) subcutaneously (SC) injected every 6 months for 12 months in the abdomen or thigh. The primary study endpoint is the occurrence of pregnancy, as defined by a positive urine pregnancy test and confirmed by a valid method (i.e., ultrasound and /or serum human chorionic gonadotropin (hCG)). The primary efficacy endpoint will be assessed by reporting the Pearl Index (pregnancies per 100 women-years of treatment) and an associated 95% confidence interval for the Pearl Index.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 20/05/2022, South Central - Oxford B Research Ethics Committee (Ground Floor, Temple Quay House, 2 The Square, Bristol, BS1 6PN, UK; +44 (0)207 104 8360; oxfordb.rec@hra.nhs.uk), ref: 22/SC/0104

Study design

Randomized parallel trial

Primary study design

Interventional

Secondary study design

Randomised parallel trial

Study setting(s)

Other

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied

Contraception for up to 6 months

Interventions

Current intervention as of 22/12/2023:

Subjects will be randomly assigned using a 1:1 allocation ratio to receive both of their subcutaneous injections of 6-month DMPA SC in either the abdomen or upper thigh. 6-month DMPA SC will be administered by a trained staff member as a single subcutaneous injection in either the abdomen or thigh at a dose of 150 mg in 1 ml using a 26-gauge 3/8-inch needle.

All subjects will receive two injections of 6-month DMPA SC: the first injection during the enrollment visit which will be scheduled during the first five days of the menstrual cycle, or at the time of switching from the previous form of highly effective contraception (e.g., contraceptive patch, ring, implant, pills, copper or hormonal IUD), and the second injection during the scheduled follow-up visit at month 6 (reinjection). There will be a plus 7-day grace period for reinjection at month 6 but women may receive re-injection up to 28 days late. Subjects who are more than 28 days late for reinjection will be discontinued from the study. All subjects will have scheduled follow up visits 3, 6 (reinjection) 9, and 12 months after the first injection.

Randomization will be done using paper envelopes once eligibility is confirmed.

Previous intervention:

Subjects will be randomly assigned using a 1:1 allocation ratio to receive both of their subcutaneous injections of 6-month DMPA SC in either the abdomen or upper thigh. 6-month DMPA SC will be administered by a trained staff member as a single subcutaneous injection in either the abdomen or thigh at a dose of 150 mg in 1 ml using a 26-gauge 3/8-inch needle.

All subjects will receive two injections of 6-month DMPA SC: the first injection during the enrollment visit which will be scheduled during the first five days of the menstrual cycle, or at the time of switching from the previous form of highly effective contraception (e.g., contraceptive patch, ring, implant, pills, copper or hormonal IUD), and the second injection during the scheduled follow-up visit at month 6 (reinjection). There will be a plus 7-day grace period for reinjection at month 6 but women may receive re-injection up to 28 days late. Subjects who are more than 28 days late for reinjection will be discontinued from the study. All subjects will have scheduled follow up visits 3, 6 (reinjection) 9, and 12 months after the first injection.

Randomization will be done electronically through the electronic data capture (EDC) system once eligibility is confirmed. Paper envelopes are provided to the clinical sites as a backup randomization method in the event that the EDC cannot be used.

Intervention Type

Drug

Phase

Phase III

Drug/device/biological/vaccine name(s)

Depot medroxyprogesterone acetate (DMPA)

Primary outcome measure

The occurrence of pregnancy, defined as a positive urine pregnancy test and confirmed by a valid method (i.e., ultrasound and/or serum human chorionic gonadotropin [hCG]) at months 3, 6, 7, 9, and 12

Secondary outcome measures

1. Trough MPA levels, MPA accumulation, and the impact of injection site on these PK parameters. Serum MPA concentrations will be measured in the safety subset of 100 subjects on days 0 and 7 and months 1, 3, 4, 5, 6, 9, 10, 11, and 12
2. The safety of 6-month DMPA SC injected every 6 months for 12 months in the abdomen or thigh. The safety measures are:
 - 2.1. Occurrence of adverse events (AEs) throughout the study
 - 2.2. Use of concomitant medications throughout the study
 - 2.3. Vital signs (blood pressure and pulse) and body weight at day 0 and months 3, 6, 9 and 12
 - 2.4. Bleeding and spotting recorded in daily diaries throughout the study
 - 2.5. Hemoglobin and hematocrit at screening and month 12 visits
 - 2.6. Estradiol (E2) at day 0, months 6 and 12
 - 2.7. Safety laboratory tests at screening and month 12 visits (in the Safety Subset of 100 subjects)
 - 2.8. Progesterone (P) and E2 levels at day 0, months 3, 6, 9 and 12 (in the Safety Subset of 100 subjects)
 - 2.9. Bone mineral density (BMD) prior to enrollment and at the end of study participation (in all

subjects at the SA investigational center and in the Safety Subset of 100 subjects at the DR investigational center)

3. Satisfaction among users with 6-month DMPA SC injected every 6 months for 12 months in the abdomen or thigh. Satisfaction will be measured using the subject's responses to the patient satisfaction questionnaire (PSQ) at enrollment, months 6 and 12 and the subject's responses to questions about the acceptability of the bleeding pattern at months 3, 6, 9 and 12.

Overall study start date

17/03/2022

Completion date

15/01/2026

Eligibility

Key inclusion criteria

Current inclusion criteria as of 22/12/2023:

Women may be included in the study if they meet all of the following criteria:

1. In good general health as determined by medical history, physical and gynecological exams
2. Aged 18-35 years at treatment initiation, inclusive
3. Willing to provide informed consent, follow all study requirements and rely on 6-month DMPA SC as the only means of contraception for 12 months (i.e., two injections 6 months apart)
4. At risk of pregnancy (in a heterosexual relationship, no diagnosis of infertility, no history of tubal ligation or hysterectomy, primary partner is not vasectomized or otherwise sterile, and an average of one or more acts of vaginal intercourse per month)
5. Not pregnant and has no desire to become pregnant for at least the next 12 months
6. Regular (21-35 days) menstrual cycle (when not using hormonal contraceptives)
7. At least two normal menses since the last injection of any injectable contraceptive (if not using other hormonal contraceptives)
8. Hemoglobin ≥ 9.5 g/dl

Previous inclusion criteria:

Women may be included in the study if they meet all of the following criteria:

1. In good general health as determined by medical history, physical and gynecological exams
2. Aged 18-35 years at treatment initiation, inclusive
3. Willing to provide informed consent, follow all study requirements and rely on 6-month DMPA SC as the only means of contraception for 12 months (i.e., two injections 6 months apart)
4. At risk of pregnancy (in a heterosexual relationship, no diagnosis of infertility, no history of tubal ligation or hysterectomy, primary partner is not vasectomized or otherwise sterile, and an average of one or more acts of vaginal intercourse per month)
5. Not pregnant and has no desire to become pregnant for at least the next 12 months
6. Regular (21-35 days) menstrual cycle (when not using hormonal contraceptives)
7. At least two normal menses since the last injection of any injectable contraceptive (if not using other hormonal contraceptives)
8. Hemoglobin ≥ 11.0 g/dl

Participant type(s)

Healthy volunteer

Age group

Adult

Lower age limit

18 Years

Upper age limit

35 Years

Sex

Female

Target number of participants

750

Key exclusion criteria

Current exclusion criteria as of 22/12/2023:

Women will be excluded from participating in this study if they meet or have one or more of the following criteria:

1. Lactating
2. Hypertension with systolic BP ≥ 160 mm Hg or diastolic BP ≥ 100 mm Hg
3. Multiple risk factors for cardiovascular disease (eg, smoking, obesity, diabetes, hypertension and known dyslipidemias)
4. Current and/or history of deep venous thrombosis (DVT)/pulmonary embolism (PE)
5. Current and/or history of arterial thrombotic or thromboembolic events (ATE) (ie, myocardial infarction, ischaemic heart disease, stroke, or peripheral arterial disease)
6. Systemic lupus erythematosus
7. Migraine with aura
8. Unexplained vaginal bleeding
9. Undiagnosed mass in the breast
10. Current and/or history of breast cancer
11. Diabetes:
 - 11.1. Of >20 years' duration
 - 11.2. Complicated by nephropathy/retinopathy/neuropathy or other vascular disease
12. Cirrhosis
13. Current or history of liver tumors, benign or malignant, or active liver disease
14. Active renal disease
15. Known cervical cancer
16. History of suicide attempt
17. At high risk of sexually transmitted infections (STIs), including any of the following:
 - 17.1. Use condoms consistently for STI prevention
 - 17.2. Known to be HIV-positive (self or partner)
 - 17.3. Use IV drugs (self or partner)
 - 17.4. Diagnosis and/or treatment for an STI in the past month (self or partner), excluding recurrent herpes or condyloma
 - 17.5. Not in a mutually monogamous relationship having lasted at least 3 months (SA investigational center only)
 - 17.6. Tested positive for HIV, gonorrhea, chlamydia, trichomoniasis at screening (SA investigational center only)
18. Received an injection of DMPA in the past 9 months
19. Received an injection of a combined injectable contraceptive or norethisterone enanthate in the past 4 months

20. Currently uses or plans (in the next 12 months) to use a protocol-prohibited drug, another experimental drug, or any other drug that in the opinion of the center PI could complicate interpretation of study findings
 21. Plans to relocate outside of study area in the next 12 months
 22. Participates in another clinical study which in the opinion of the center PI would make study participation unsafe, would interfere with adherence to study requirements, or complicate data interpretation
 23. Has already participated in this study
 24. History of chronic alcoholism, drug dependence or abuse, psychotic states or severe neurosis or any other condition that, by the judgment of the center PI, might impair the subject's ability to cooperate
 25. Current, confirmed diagnosis of COVID-19 unless they have recovered from the disease and have completed their quarantine period per local guidelines
 26. Any condition (social or medical) which in the opinion of the center PI would make study participation unsafe, would interfere with adherence to study requirements, or complicate data interpretation
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Previous exclusion criteria:

Women will be excluded from participating in this study if they meet or have one or more of the following criteria:

1. Lactating
2. Hypertension with systolic BP ≥ 160 mm Hg or diastolic BP ≥ 100 mm Hg
3. Multiple risk factors for cardiovascular disease (eg, smoking, obesity, hypertension, known low high-density lipoprotein (HDL), high low-density lipoprotein (LDL), or high triglyceride levels)
4. Current and/or history of deep venous thrombosis (DVT)/pulmonary embolism (PE)
5. Current and/or history of arterial thrombotic or thromboembolic events (ATE) (ie, myocardial infarction, ischaemic heart disease, stroke, or peripheral arterial disease)
6. Hereditary or acquired predisposition for venous or arterial thrombosis
7. Systemic lupus erythematosus
8. Migraine with aura
9. Unexplained vaginal bleeding
10. Undiagnosed mass in the breast
11. Current and/or history of breast cancer
12. Diabetes:
 - 12.1. Of >20 years' duration
 - 12.2. Complicated by nephropathy/retinopathy/neuropathy or other vascular disease
13. Cirrhosis
14. Current or history of liver tumors, benign or malignant, or active liver disease
15. Known cervical cancer
16. Hospitalization for clinical depression or bipolar disorder in the last three years, with or without suicidal ideation
17. History of suicide attempt
18. At high risk of sexually transmitted infections (STIs), including any of the following:
 - 18.1. Use condoms consistently for STI prevention
 - 18.2. Known to be HIV-positive (self or partner)
 - 18.3. Use IV drugs (self or partner)
 - 18.4. Diagnosis and/or treatment for an STI in the past month (self or partner), excluding recurrent herpes or condyloma
 - 18.5. Not in a mutually monogamous relationship having lasted at least 3 months (SA investigational center only)
 - 18.6. Tested positive for HIV, gonorrhea, chlamydia, trichomoniasis at screening (SA

investigational center only)

19. Received an injection of DMPA in the past 9 months

20. Received an injection of a combined injectable contraceptive or norethisterone enanthate in the past 4 months

21. Plans (in the next 12 months) to use a protocol prohibited drug, another experimental drug, or any other drug that in the opinion of the center PI could complicate interpretation of study findings

22. Plans to relocate outside of study area in the next 12 months

23. Participates in another clinical study which in the opinion of the center PI would make study participation unsafe, would interfere with adherence to study requirements, or complicate data interpretation

24. Has already participated in this study

25. History of chronic alcoholism, drug dependence or abuse, psychotic states or severe neurosis or any other condition that, by the judgment of the center PI, might impair the subject's ability to cooperate

26. Current, confirmed diagnosis of COVID-19 unless they have recovered from the disease and have completed their quarantine period per local guidelines

27. Any condition (social or medical) which in the opinion of the center PI would make study participation unsafe, would interfere with adherence to study requirements, or complicate data interpretation

Date of first enrolment

07/07/2022

Date of final enrolment

31/12/2024

Locations

Countries of recruitment

Chile

Dominican Republic

Scotland

South Africa

United Kingdom

Study participating centre

Chalmers Sexual Health Centre

2a Chalmers Street

Edinburgh

Lothian

United Kingdom

EH3 9ES

Study participating centre**The Gatehouse**

Ayrshire Central Hospital
Irvine
United Kingdom
KA12 8SS

Study participating centre**Profamilia**

Calle Socorro Sánchez 160
Santo Domingo
Dominican Republic

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Study participating centre**ICMER**

José Victorino Lastarria 29
Depto 101
Santiago
Chile
8320165

Study participating centre**MatCH Research Unit**

40 Dr AB Xuma Street
11th Floor
Suite 1108-9
Commercial City
Durban
South Africa
4001

Study participating centre**IDIMI**

Av. Sta. Rosa 1234
2do piso
Santiago
Chile

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Sponsor information

Organisation

Family Health International 360

Sponsor details

359 Blackwell Street
Suite 200
Durham
United States of America
27701
+1 (0)919 544 7040
scordes@fhi360.org

Sponsor type

Charity

Website

<https://www.fhi360.org>

ROR

<https://ror.org/007kp6q87>

Funder(s)**Funder type**

Charity

Funder Name

FHI 360

Alternative Name(s)

Family Health International

Funding Body Type

Private sector organisation

Funding Body Subtype

Trusts, charities, foundations (both public and private)

Location

United States of America

Results and Publications

Publication and dissemination plan

1. Peer-reviewed scientific journals
2. Internal report
3. Conference presentation
4. Publication on website
5. Submission to regulatory authorities
6. Access to raw data and right to publish freely by all investigators in study or by Independent Steering Committee on behalf of all investigators
7. After the study is completed, the de-identified data will be posted in a public data repository for use by other researchers including those outside of the study per the Open Data Management Plan. A statement regarding the data repository will be included in the Participant Information Sheet.

Intention to publish date

17/03/2027

Individual participant data (IPD) sharing plan

IPD will be registered in USAID's Data Development Library (DDL) (<https://data.usaid.gov>) for use by other researchers including those outside of the study within 30 days of the primary peer-reviewed publication. A statement regarding the data repository is included in the informed consent. Data shared includes all quantitative data collected for the conduct of the trial, data from approved patient questionnaires, and laboratory data. Data will be archived in 21 CFR Part 11, GCP-compliant clinical database management systems once the final analysis and all publications of data are complete.

IPD sharing plan summary

Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No