ISRCTN78792722 https://doi.org/10.1186/ISRCTN78792722

Preventing miscarriage through platform testing of multiple novel interventions

Submission date
04/11/2025

Recruitment status
Recruiting

Registration date
24/02/2026

Overall study status
Ongoing

Last Edited
05/10/2026

Condition category
Pregnancy and Childbirth

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Omega-3 fatty acids play a crucial role in modulating factors linked to the origin and development of recurrent miscarriage, including immune cell dysregulation, oxidative stress, and inflammation. Long-chain polyunsaturated fatty acids (LCPUFAs), specifically docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), play a vital role in gestational health, particularly in influencing gestational length in singleton pregnancies. Studies have shown that adequate intake of these fatty acids during pregnancy is associated with a reduced risk of preterm birth and may promote longer gestation periods.

Miscarriage and preterm birth share several common causes, including inflammation, which can adversely affect pregnancy outcomes. Given these shared causes, interventions designed to prevent preterm birth—such as nutritional supplementation, lifestyle modifications, and pharmacological therapies—could also prove beneficial in reducing the risk of miscarriage.

It remains unknown whether DHA deficiency or insufficiency reduces the risk of miscarriage. At the moment, there are no strategies in the NHS in the UK to increase DHA levels and potentially reduce the risk of miscarriage. The study's definitive primary objective is to test the hypothesis that DHA supplementation at two different doses, used alone, increases the rate of live birth ≥ 34 weeks of gestation by at least 8% in women who have experienced two or more miscarriages. The intermediate primary objective is to test the hypothesis that DHA supplementation at two different doses, used alone, increases the rate of ongoing pregnancy, at 11-14 weeks, by at least 10% in women who have experienced two or more miscarriages.

Who can participate?
Females aged 16 years or over who have experienced two or more previous miscarriages, actively trying to become pregnant, and have confirmation of positive pregnancy test

What does the study involve?
Participants will be randomly assigned to one of three groups:

Control group: no DHA (omega 3)
Low dose group: 750 mg of (omega 3) DHA per day
High dose group: 1125 mg of (omega 3) DHA per day

The low dose will be taken as two capsules daily, and the high dose as three capsules daily, both taken by mouth until 24 weeks of pregnancy.
These doses were chosen based on a thorough review of existing research and the known safety of the supplement. Because there is variation in the evidence about the best amount of DHA to take during pregnancy, the study will test both the low and high dose options.

What are the possible benefits and risks of participating?
Despite the benefits, many pregnant individuals do not consume sufficient levels of DHA and EPA, highlighting the need for increased awareness and potential dietary interventions to optimise pregnancy outcomes. The participants randomised to receive the omega-3 supplements will be provided with omega-3 supplements at no cost and as part of the care pathway.

There are no known risks to taking DHA (omega-3) supplements. However, any queries that arise may be discussed with the participants local care team.

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

When is the study starting and how long is it expected to run for?
August 2026 to May 2030

Who is funding the study?
Tommy's Charity, UK

Who is the main contact?
Mr Lee Priest, Research Fellow/Team Leader, l.priest.1@bham.ac.uk, premis@trials.bham.ac.uk

Contact information

Type(s)
Scientific, Public

Contact name
Mr Lee Priest

Contact details
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Type(s)
Principal investigator

Contact name
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Additional identifiers

Integrated Research Application System (IRAS)
1011519

Protocol serial number
RG_25-038

Study information

Scientific Title
PREMIS: Preventing miscarriage through platform testing of multiple (novel) interventions. Intervention 1: DHA trial: Docosahexaenoic acid (DHA) (omega-3) to improve live birth rate in women with previous miscarriage

Acronym
PREMIS

Study objectives
Definitive primary objective:
To test the hypothesis that docosahexaenoic acid (DHA) (omega-3) supplementation increases the rate of live birth ≥ 34 weeks of gestation by at least 8% in women with a history of two or more previous miscarriages.

Intermediate primary objective:
To test the hypothesis that docosahexaenoic acid (DHA) (omega-3) supplementation increases the rate of ongoing pregnancy at 11-14 weeks by at least 10% in women a history of two or more previous miscarriages.

To assess the effect of DHA supplementation on additional clinical and safety outcomes.

Ethics approval required

Ethics approval required

Ethics approval(s)
Approved 13/02/2026, West Midlands – Edgbaston Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8155; edgbaston.rec@hra.nhs.uk), ref: 25/WM/0241

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Open (masking not used)

Control
Placebo

Assignment
Parallel

Purpose
Treatment

Study type(s)
Efficacy

Health condition(s) or problem(s) studied
Medical condition: Miscarriage
Medical condition in lay language: Miscarriage
Therapeutic areas: Diseases [C] - Female diseases of the urinary and reproductive systems and pregancy complications [C13]

Interventions
Randomisation will be conducted by a computer algorithm in a 1:1:1 (control:intervention: intervention) ratio to either the control arm, omega-3 intervention low-dose arm (750mg) or the high-dose arm (1125mg).

The choice of 750 mg (two capsules) and 1125 mg (three capsules) daily was made after a) careful review of the existing literature and b) the safety profile of the supplement. Due to variation in the evidence base regarding the optimal level of DHA to consume, two intervention arms will be investigated:

1. 750mg docosahexaenoic acid (2 capsules) daily, taken orally until 24 weeks of gestation.
2. 1125mg docosahexaenoic acid (3 capsules) daily, taken orally until 24 weeks of gestation.

Intervention Type
Supplement

Primary outcome(s)

1. Definitive (D) primary outcome: Live births ≥ 34 weeks of gestation as a proportion of all women randomised measured using data collected from medical records at one timepoint at the pregnancy end

2. Intermediate (I) primary outcome: Ongoing pregnancies at 11 – 14 weeks of gestation as a proportion of all women randomised measured using data collected from medical records at one timepoint at the end of the study

Key secondary outcome(s)

The following secondary outcome measures will be collected using a questionnaire at one timepoint:
1. Miscarriage rate (defined as delivery before 24 weeks of gestation)
2. Live birth <34 weeks
3. Ectopic pregnancy
4. Termination
5. Stillbirth
6. Molar pregnancy
7. Multiple pregnancy
8. Gestational age at miscarriage
9. Gestational age at live birth
10. First-trimester miscarriage, defined as loss of pregnancy up to 13 weeks and 6 days
11. Early first-trimester miscarriage, defined as loss of pregnancy up to 7 weeks and 6 days
12. Late first-trimester miscarriage, defined as loss of pregnancy between 8 weeks and 0 days and up to 13 weeks and 6 days
13. Second-trimester miscarriage, defined as loss of pregnancy between 14 weeks and 0 days and up to 23 weeks and 6 days
14. Where live birth ≥24 weeks: gestational age <28/<32/<37 weeks
15. Mode of delivery (unassisted vaginal, instrumental vaginal, elective caesarean section, emergency caesarean section, vaginal breech delivery, other)
16. Birth weight
17. Antenatal complications: antepartum haemorrhage, pregnancy-induced hypertension, pre-eclampsia, obstetric cholestasis, cervical cerclage, preterm (<37 weeks) pre-labour rupture of membranes, gestational diabetes, fetal growth restriction, small for gestational age, macrosomia. Other complications will be tabulated but not formally analysed.
18. Post-partum complications: haemorrhage (other complications will be tabulated but not formally analysed)
19. Maternal complications: admission to high dependency unit (HDU) or intensive therapy unit (ITU) (other complications will be tabulated but not formally analysed)
20. Maternal mental health: confirmed diagnosis or sought medical support for a psychological disorder related to miscarriage
21. Neonatal complications: admission to neonatal care unit (neonatal intensive care unit [NICU] or Special Care Baby Unit [SCBU]) (other complications will be tabulated but not formally analysed); congenital and chromosomal abnormalities
22. Survival at 28 days of neonatal life
23. Compliance: Compliance with the intervention
24. Maternal adverse events (tabulated but not formally analysed)
25. Serious adverse events

Completion date

31/07/2030

Eligibility

Key inclusion criteria
1. Written informed consent to receive DHA (omega-3) supplements
2. Patient confirmation of positive pregnancy test
3. Fish consumption - 0, 1 or 2 portions per week (1 portion defined as 140g or 4.9oz when cooked)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
16 Years

Upper age limit
50 Years

Sex
Female

Total final enrolment
0

Key exclusion criteria
1. Currently taking omega-3 supplementation with DHA concentration >300mg and unwilling to stop
2. Sensitive or allergic to fish or seafood

Date of first enrolment
01/11/2026

Date of final enrolment
31/01/2030

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Wales

Study participating centre
Aberdeen Royal Infirmary
Foresterhill Road
Aberdeen
Scotland
AB25 2ZN

Study participating centre
Leicester Royal Infirmary
Infirmary Square
Leicester
England
LE1 5WW

Study participating centre
Arrow Park Hospital
Arrowe Park Hospital
Arrowe Park Road
Wirral
England
CH49 5PE

Study participating centre
Birmingham Women's Hospital
Mindelsohn Way
Edgbaston
Birmingham
England
B15 2TG

Study participating centre
University Hospital Coventry
Clifford Bridge Road
Coventry
England
CV2 2DX

Study participating centre
St Peters Hospital
Guildford Road
Chertsey
England
KT16 0PZ

Study participating centre
Burnley General Hospital
Casterton Avenue
Burnley
England
BB10 2PQ

Study participating centre
Ipswich Hospital
Heath Road
Ipswich
England
IP4 5PD

Study participating centre
Worthing Hospital
Lyndhurst Road
Worthing
England
BN11 2DH

Study participating centre
Princess Royal Hospital
Sussex Mri Centre
Lewes Road
Haywards Heath
England
RH16 4EX

Study participating centre
Royal Sussex County Hospital
Eastern Road

Brighton
England
BN2 5BE

Study participating centre
St Richards Hospital
Spitalfield Lane
Chichester
England
PO19 6SE

Study participating centre
St Mary's Hospital
Praed Street
London
England
W2 1NY

Study participating centre
Princess Royal Hospital
Lewes Road
Haywards Heath
England
RH16 4EX

Study participating centre
St Michaels Hospital
Southwell Street
Bristol
England
BS2 8EG

Study participating centre
University Hospital of North Tees
Hardwick Road
Stockton-on-tees
England
TS19 8PE

Study participating centre
Royal Victoria Infirmary
Queen Victoria Road
Newcastle upon Tyne
England
NE1 4LP

Study participating centre
Stoke Mandeville Hospital
Mandeville Road
Aylesbury
England
HP21 8AL

Study participating centre
Maidstone Hospital
Hermitage Lane
Maidstone
England
ME16 9QQ

Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Charity

Funder Name
Tommy's

Alternative Name(s)

Funding Body Type

Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Requests for the final dataset can be made through the chief investigator, Dr Rima Dhillon-Smith, r.k.smith@bham.ac.uk, in accordance with the data-sharing policies of Birmingham Clinical Trials Unit, Tommy's National Centre for Miscarriage, University of Birmingham. Only scientifically sound proposals from appropriately qualified research groups will be considered for data sharing. The request will be reviewed by the trial management group, or where appropriate (in absence of the chief investigator) any of the following: the Trial Sponsor, and independent trial steering committee.

IPD sharing plan summary
Available on request