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Prevention of anaemia with oral iron supplementation

Submission date	Recruitment status	[X] Prospectively registered
18/10/2023	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
20/11/2023	Ongoing	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
01/08/2025	Circulatory System	[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Iron tablets are the main form of treatment for anaemia, but it is not known whether the routine taking of iron, started early in pregnancy, to prevent anaemia, has clinical benefits for the mother and baby. Currently, there is no recommendation for taking iron tablets and given the high burden of anaemia during later pregnancy, it is likely that many women develop low iron levels during pregnancy. The aim of this study is to find out whether iron tablet taking using a low dose given from early pregnancy (first booking clinic) will improve mother and baby outcomes, compared to a placebo (dummy table).

Who can participate?
Healthy non-anaemic pregnant women aged 18 years and above

What does the study involve?
Participants are randomly allocated to take iron tablets once daily or a matched placebo. The estimated duration of treatment is 34 weeks, from about 12 weeks gestation to 6+ weeks post-delivery.

What are the possible benefits and risks of participating?
There are possible side effects from taking iron supplements. Some side effects include abdominal pain, nausea and vomiting, constipation, diarrhoea, dark stools, lack of appetite and mouth ulcers. Instructions will be provided to participants on how to take the iron tablet in a way which will reduce the possibility of side effects occurring.

Where is the study run from?
NHS Blood and Transplant (UK)

When is the study starting and how long is it expected to run for?
October 2023 to May 2027

Who is funding the study?
National Institute for Health and Care Research (UK)

Who is the main contact?
Catherine Bain, catherine.bain@nhsbt.nhs.uk

Contact information

Type(s)
Scientific

Contact name
Dr Catherine Bain

Contact details
Long Road
Cambridge
United Kingdom
CB2 0PT
+44 (0)1223 588182
Catherine.bain@nhsbt.nhs.uk

Type(s)
Principal investigator

Contact name
Dr Simon Stanworth

Contact details
John Radcliffe Hospital
Oxford
United Kingdom
OX3 9BQ
+44 (0)1865 381037
simon.stanworth@nhsbt.nhs.uk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1008549

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
23AS0003, IRAS 1008549, CPMS 58186

Study information

Scientific Title
A Phase III, multi-centre, randomized placebo-controlled trial of oral iron supplementation for the prevention of maternal anaemia

Acronym
PANDA

Study objectives
Primary objectives:
To evaluate the clinical- and cost-effectiveness of a primary prevention strategy for iron deficiency anaemia in pregnancy with an optimised low-dose oral iron supplementation intervention.

Secondary objectives:
To conduct a process evaluation to assess the fidelity, feasibility, and acceptability of iron supplementation and the adherence intervention. This will inform the interpretation of the clinical trial results, intervention refinement and subsequent scalability and implementation.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 17/11/2023, North of Scotland Research Ethics Committee 1 (Summerfield House, 2 Eday Road, Aberdeen, AB15 6RE, United Kingdom; +44 (0)1224 558458; gram.nosres@nhs.scot), ref: 23/NS/0123

Study design
Double-blind randomized placebo-controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Iron deficiency anaemia in pregnancy

Interventions
Two-arm parallel group, with 11,020 women being allocated in a 1:1 ratio to 200 mg ferrous sulphate once daily vs a matched placebo. The estimated duration of treatment is 34 weeks, from approximately 12 weeks gestation to 6+ weeks post-delivery. Participating sites will be supplied with sealed individually numbered kits. Kits containing active ferrous sulphate or matched placebo will be indistinguishable. Women will be randomised by the allocation of the next numbered kit once consent and eligibility are established.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Ferrous sulfate

Primary outcome(s)
A composite outcome of the proportion of pregnancies with pre-term birth (<37 completed weeks gestation), stillbirth (at 24 weeks gestation or above), neonatal death (up to 28 days) and small for gestational age (SGA) (<10th centile sex-specific weight for age, defined by UK growth charts)

Key secondary outcome(s))
Secondary outcomes relating to the mother are as follows:
1. Components of the composite primary outcome measured using case report form (CRF):
1.1. Pre-term birth (<37 completed weeks gestation)
1.2. Small for gestational age (<10th centile sex-specific weight for age)
1.3. Stillbirth (at 24 weeks gestation or above)
1.4. Neonatal death (up to 28 days)
2. Proportion of women developing anaemia during pregnancy measured using CRF
3. Mean transitions in haemoglobin measured using CRF from recruitment to 28 weeks & birth
4. Proportion of women with primary postpartum haemorrhage (PPH) measured using CRF
5. Proportion of women requiring red cell transfusions measured using CRF prior to discharge but not more than 48 hours post-birth
6. Proportion of women receiving an iron infusion measured using CRF prior to discharge and up to 6 weeks after birth
7. Proportion of women with an infection and or sepsis measured using CRF before discharge and up to 6 weeks after birth
8. Proportion of women breastfeeding or providing breast milk for pre-term infant or baby measured using CRF at discharge from maternity care and at 6 weeks
9. Proportion of women with postpartum depression/psychosis measured using CRF at 6 weeks post-birth
10. Mean adherence to medication measured using the MGL-4 score at 28 weeks
11. Health-related quality of life (HRQoL) measured using EQ-5D-5L at baseline, 28 weeks and at 6 weeks post-birth
12. Healthcare utilisation measured using CRF over the trial period

Secondary outcomes relating to the infant are as follows:
1. Mean birthweight measured using CRF
2. Mean gestation at birth measured using CRF
3. Apgar score at 5 minutes post-birth
4. Proportion of infants treated for possible neonatal early-onset infection, measured using CRF up to 6 weeks post-birth
5. Proportion of infants with culture-positive neonatal early-onset infection, measured using CRF up to 6 weeks post-birth
6. Proportion of infants admitted to neonatal/transitional care, measured using CRF up to 6 weeks post-birth
7. Healthcare utilisation including initial hospital stay, subsequent hospital readmissions, measured using CRF up to 6 weeks post-birth

Secondary outcomes relating to the process evaluation (WS4):
1. Intervention fidelity (i.e. whether intervention delivered and engaged with as planned) over the trial period, measured using website analytics, surveys, interviews, Medication Adherence

Report Scale (MARS-5)
2. Intervention acceptability via survey and interviews at 28 weeks and +6 weeks delivery
3. Intervention feasibility via survey and interviews at 28 weeks and +6 weeks delivery

Completion date
31/05/2027

Eligibility

Key inclusion criteria
1. Healthy non-anaemic pregnant women of all parities (haemoglobin concentration [Hb] ≥110 g/l measured by the first-trimester blood profile) at booking or screening
2. A live fetus on a first-trimester ultrasound scan carried out for viability or dating.
3. 15 weeks + 6 days gestation or less
4. Aged 18 years and above
5. Able to give informed consent and willing to fulfil trial requirements

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Female

Key exclusion criteria
1. Known haemoglobinopathies (women with haemoglobinopathy trait are still eligible)
2. Anaemia of any type, defined by British Society for Haematology guidelines
3. Severe gastrointestinal disease requiring ongoing treatment and potentially affecting tolerability of oral iron
4. Allergies to iron
5. Multiple pregnancies, given the higher iron demands
6. Known haemochromatosis
7. Recent red cell transfusion, within 30 days

Date of first enrolment
01/03/2024

Date of final enrolment
01/08/2025

Locations

Countries of recruitment
United Kingdom

Study participating centre
Not provided at time of registration
United Kingdom
-

Sponsor information

Organisation
NHS Blood and Transplant

ROR
https://ror.org/0227qpa16

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

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 trial will be available upon request from the NHSBT Clinical Trials Unit after de-identification (text, tables, figures and appendices) 9 months after publication and ending 5 years following article publication. Data will be shared with investigators whose use of the data has been assessed and approved by the PANDA Steering Committee, and if appropriate an ethics committee, as a methodologically sound proposal.

IPD sharing plan summary

Available on request