



PANDA: INFORMATION FOR PROFESSIONALS

This is a protocol summary of the PANDA prevention research trial, it will provide:

- Information about the trial processes.
- the rationale behind the trial; and
- answers to common questions from professionals.

Why Are We Studying Iron Deficiency Anaemia (IDA) in Pregnancy?

Iron deficiency anaemia (IDA) affects around one-third of expectant mothers in the UK.

Mothers with low iron experience symptoms of extreme fatigue, weakness and poor concentration, and are exposed to the risk of poor outcomes such as:

- infection
- preterm labour.
- postpartum haemorrhage.
- delivering babies that are smaller than expected.
- And increased neonatal and maternal morbidity and mortality.

Iron deficiency anaemia during pregnancy can also negatively impact mothers and their babies long after birth. Mothers may develop postnatal depression and their babies may have developmental problems in childhood.

Evidently, IDA is a significant health concern for pregnant women and their babies, and we want to find out if we can prevent maternal anaemia and these poor outcomes.

What will the trial entail?

Non-anaemic women early into pregnancy will be started on low-dose iron supplements (Ferrous Sulphate 200mg) or a placebo as part of a randomised double-blind trial to see if iron prophylaxis:

- Will impact on the rates of pre-term birth, stillbirth, neonatal death, and the delivery of small for gestational age (SGA) babies.
- Will improve long term maternal and neonatal outcomes.
- And is possible to be implemented as a universal preventative treatment for maternal anaemia.

The use of oral iron will be compared against placebos to determine both its clinical and cost effectiveness and safety.

We are also testing against clinical outcomes (shown above) that matter to women and their babies. This means not solely looking at increased haemoglobin levels as an indicator of improvement.

Throughout the duration of the trial, we will consider the following factors:

1. Diagnosing Anaemia in Pregnancy Can Be Challenging

Currently, women are routinely screened for IDA at booking and at 28 weeks. This is done by blood tests which check for:

- Haemoglobin (Hb): the protein contained in red blood cells.
- Sometimes supplemented by Ferritin: a blood protein that contains iron.

However, there is sometimes confusion. Some women will have a normal haemoglobin and a low ferritin and others vice versa.

Ferritin, can be an unreliable indicator of iron status in pregnancy because:

- There are differing opinions on the thresholds for ferritin in pregnant women.
- Ferritin can be raised when there is infection or inflammation as is often the case in pregnancy.
- Ferritin represents iron stores and is not necessarily indicative of functional iron capacity.

Diagnosis can also be challenging due to the natural physiological changes that occur during pregnancy, that lower haemoglobin levels because of haemodilution.

2. Iron Can Interact with Other Medications

Medications like antacids, certain antibiotics, and mineral supplements can affect iron absorption.

Iron itself can affect the absorption of some drugs. One such drug is Methyl dopa, which is sometimes used to treat hypertension during pregnancy and Levothyroxine used to treat hypothyroidism.

To minimise these effects, advise women to:

- take iron on an empty stomach, at least 30 minutes before eating.
- Take iron with orange juice but to avoid tea or coffee as they reduce iron absorption.
- If other medications are being taken, leave a 2-hour gap between iron and the other drugs to avoid interactions.

3. Iron Treatment When Not Needed Might Cause Harm

- Non-anaemic pregnant women on iron supplements may experience the side effects. These can range from gastrointestinal issues such as constipation or diarrhoea, heartburn, indigestion and nausea. Some work has suggested that iron during pregnancy might predispose to infections, or gestational diabetes or gestational hypertension.
- The trial is designed to monitor for these problems, and we will be able to not only judge the effectiveness of iron but also its safety profile.

4. However, it should be remembered Not All Symptoms Are Attributable to Iron

Some women may report symptoms of nausea, constipation, vomiting, heartburn and indigestion while on iron. From previous research, we know that these symptoms occur frequently in otherwise normal pregnancies and are not attributable to iron.

If women develop these symptoms and express concern, we advise:

- Check that there is no other evidence of an underlying medical condition, e.g. inflammation of the gut. If there are no other clinical indicators of disease:
- Reassure them that these symptoms are experienced by many normal pregnant women.
- Advise them to try simple remedies for these symptoms:
 - Indigestion and Heartburn: Eat smaller, more frequent meals, avoid spicy and fatty foods, and stay upright after eating.
 - Nausea: Ginger tea, eating crackers, or small, frequent meals can help.
 - Constipation: Increase fibre intake, drink plenty of water, and stay active.

If their symptoms persist, consider changing from daily to alternate daily iron supplements for 1-2 weeks, then resume daily tablets.

5. Some Women May Develop Anaemia at Some Point in the Trial

If a trial participant develops anaemia, clinicians should:

- Adhere to guidelines such as those provided by the British Society for Haematology (BSH).
- Refrain from unblinding. Anaemia development is a secondary outcome and maintaining trial fidelity is crucial.
- Stop the trial medications
- Manage anaemia according to local unit guidelines, as if the participant were not in the trial.
- Assure Participants who develop anaemia that they:
 - will not be withdrawn from the PANDA prevention study, unless they specifically request it.
 - will continue to receive standard care as per local guidelines and policies.
 - will still contribute to all primary and secondary outcomes and follow-up, including for their baby.



We believe that this trial will produce the robust evidence required to decide whether all women should be offered a tablet of iron during pregnancy to prevent anaemia and thus reduce the associated adverse outcomes. Thank you for considering the trial and for more information please visit the PANDA website at: PANDA@nhsbt.nhs.uk