Treatments for iron-deficiency anaemia in pregnancy (Review)

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ABSTRACT

Background
Iron deficiency, the most common cause of anaemia in pregnancy worldwide, can be mild, moderate or severe. Severe anaemia can have very serious consequences for mothers and babies, but there is controversy about whether treating mild or moderate anaemia provides more benefit than harm.

Objectives
To assess the effects of different treatments for iron-deficiency anaemia in pregnancy (defined as haemoglobin less than 11 g/dl) on maternal and neonatal morbidity and mortality.

Search strategy
We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (January 2007), the Cochrane Central Register of Controlled Trials (*The Cochrane Library* 2005, Issue 4), MEDLINE (1966 to December 2005), EMBASE (1976 to December 2005), LILACS (1982 to 40 edition), BIOSIS Previews (1980 to June 2002) and ongoing clinical trial registers.

Selection criteria
Randomised controlled trials comparing treatments for iron-deficiency anaemia in pregnancy.

Data collection and analysis
We identified 17 trials, involving 2578 women. We assessed trial quality.

Main results
The trials were small and generally methodologically poor. They covered a very wide range of differing drugs, doses and routes of administration, making it difficult to pool data. Oral iron in pregnancy showed a reduction in the incidence of anaemia (one trial, 125 women; relative risk 0.38; 95% confidence interval 0.26 to 0.55). It was not possible to assess the effects of treatment by severity of anaemia. A trend was found between dose and reported adverse effects. We found that most trials had no assessments on relevant clinical outcomes and a paucity of data on adverse effects, including some that are known to be associated with iron administration. Although the intramuscular and intravenous routes produced better haematological indices in women than the oral route, no clinical outcomes were assessed and there were insufficient data on adverse effects, for example, on venous thrombosis and severe allergic reactions.

Authors' conclusions
Despite the high incidence and burden of disease associated with this condition, there is a paucity of good quality trials assessing clinical maternal and neonatal effects of iron administration in women with anaemia. Daily oral iron treatment improves haematological indices but causes frequent gastrointestinal adverse effects. Parenteral (intramuscular and intravenous) iron enhances haematological response, compared with oral iron, but there are concerns about possible important adverse effects. Large, good quality trials, assessing clinical outcomes (including adverse effects) are required.

PLAIN LANGUAGE SUMMARY

Insufficient evidence to say when or how iron-deficiency anaemia in pregnancy needs to or should be treated

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Anaemia happens when the blood has insufficient red cells, or when red cells carry insufficient haemoglobin to deliver adequate oxygen to the tissues. Haemoglobin levels change in pregnancy with a normal reduction at the beginning of pregnancy and a slight rise towards the end of pregnancy. Anaemia in pregnancy can be mild, moderate or severe, and women are offered different treatments according to their level of anaemia and the possible cause. Anaemia can be caused by a range of factors including certain diseases or a shortage of iron, folic acid or vitamin B12. The most common cause of anaemia in pregnancy is due to iron shortage. Iron treatment can be given by mouth, or an injection into the muscle (intramuscular) or into the vein (intravenous), or by giving a blood transfusion. In this review we identified 17 randomised controlled trials involving over 2500 women. However, many treatment variations were studied leaving rather small study populations for each treatment and, therefore, imprecise estimates that make it difficult to draw conclusions on the effects of treatment on women with different degrees of anaemia. Amongst the complications of iron treatments, we found that intravenous treatment may cause venous thrombosis (blockages in the veins) and the intramuscular treatment caused important pain and discolouration at the injection site; but it is unclear if women and babies are healthier when women are given iron for anaemia during pregnancy. It also remains unclear what the effects of treatments given by different routes and in different populations are; therefore, it is not possible to draw a well-informed balance of benefits and harms for the differing levels of severity of anaemia. This would be better addressed if a few frequently-used treatments were compared in a multicenter randomised controlled trial involving women from different backgrounds and settings, and this study was big enough to respond to these questions in a valid way.

BACKGROUND

Worldwide, iron deficiency is the most common cause of anaemia in pregnancy. Anaemia is a reduction in the normal number of circulating red blood cells and in the quantity of haemoglobin in the blood. More than half a million maternal deaths occur each year, approximately 90% of which are in developing countries, making evident a large discrepancy between developed and developing countries. The diverse main preventable factors relating to maternal mortality have been described, and include chronic anaemia, infections, bleeding, hypertensive disorders, obstructed labour and unsafe abortions (WHO 2000).

Anaemia in pregnancy is defined by the World Health Organization as a haemoglobin value below 11 g/dl (WHO 1992; WHO 2001). Although anaemia is frequently graded as "mild", "moderate", or "severe", the haemoglobin values at which the division into these three categories is made vary and are arbitrary. Standardised cut-off values are difficult to define because populations, geographic settings and needs are different according to specific areas. Some authors suggest that haemoglobin values at sea level should be categorised as follows (WHO 1989): (1) mild anaemia (Hb 10 to 10.9 g/dl); (2) moderate anaemia (Hb 7 to 9.9 g/dl); (3) severe anaemia (Hb less than 7 g/dl). However, other criteria have been widely used in the literature to define anemia cut-off values: (1) mild (Hb 9 to 10.9 g/dl), (2) moderate (Hb 7 to 8.9 g/dl) and (3) severe (Hb below 7 g/dl) (Adam 2005); and (1) mild anaemia (Hb 7 to 11 g/dl), moderate anaemia (5 to 7 g/dl) and severe anaemia (below 5 g/dl) (Brabin 2001). Haemoglobin is the protein in the red blood cell which carries oxygen to the tissues. However, the estimation of the haemoglobin concentration in the blood is not a particularly sensitive indicator of anaemia because the delivery of oxygen to the tissues depends on the concentration of haemoglobin in the blood, the capacity of haemoglobin to bind oxygen and the blood flow through the tissue. A high haemoglobin concentration causes increased blood viscosity, which decreases the blood flow through the tissues. In some cases, for example in pre-eclampsia, increased haemoglobin concentration is caused by poor increase in plasma volume which is under independent control from the red cell mass (Letsky 1991).

The common causes of anaemia include iron deficiency, folate deficiency, vitamin B12 deficiency, bone marrow suppression, haemolytic diseases (sickle cell disease and malaria), chronic blood loss (for example, hook worm infestation) and underlying malignancies (WHO 1992), with iron-deficiency anaemia being the most common cause of anaemia in pregnant women worldwide (Goroll 1997; Lops 1995; Williams 1992). However, neither blood haemoglobin concentration nor serum iron are thought to be good indicators of anaemia because there can be depletion of body iron stores in the presence of normal haemoglobin levels and serum iron fluctuates depending on recent iron intake. Serum ferritin may be a better indicator of iron status as the examination of iron stores in the bone marrow is impractical. However, historically, blood haemoglobin levels have been used, the test being simple and inexpensive to undertake.

During pregnancy, there is an increase in both red cell mass and plasma volume to accommodate the needs of the growing uterus and fetus. However, plasma volume increases more than the red cell mass leading to a fall in the concentration of haemoglobin in the blood, despite the increase in the total number of red cells (Letsky 1991). This drop in haemoglobin concentration decreases the blood viscosity and it is thought this enhances the placental perfusion providing a better maternal-fetal gas and nutrient exchange (Mani 1995). There is controversy around the significance for women and their babies of this physiological haemodilution of pregnancy and at what level of haemoglobin women and babies would benefit from iron treatment. As discussed below, some studies suggest that the physiological decrease in haemoglobin is

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associated with improved outcomes for the baby (Mahomed 1989; Steer 1995), whilst others have identified adverse long-term outcomes for the baby (Walter 1994).

Anaemia has been associated with general weakness, tiredness and dizziness but the level of haemoglobin associated with these symptoms in pregnancy is unknown. It is suggested that the iron stores of the woman's body become reduced during pregnancy (as a result of the increased red cell mass and the demands of the fetus exceeding iron intake), and that this can take place in the presence of normal blood haemoglobin levels. Some will argue that this is a well-designed mechanism to continue to deliver oxygen to the tissues in the presence of lowered iron stores. An observational study undertaken in London, UK, found that low levels of haemoglobin, commonly considered as mild anaemia, were associated with a better prognosis for the fetus, although figures did not appear to be corrected for women with pre-eclampsia (Steer 1995). However, others argue that reduced iron stores are a health problem for pregnant women and their babies (Letsky 2001). Several studies considered anaemia (haemoglobin levels between 7 g/dl and 10 g/dl) as a risk factor for fetal death, premature delivery, low birthweight and other adverse outcomes (Williams 1992). Some suggest a link between maternal anaemia in pregnancy on the later developmental problems of the children (Letsky 2001; Williams 1992). There is evidence indicating that maternal haemoglobin levels under 7 g/dl are associated with a higher risk in the mother of developing cardiac heart failure, which has adverse consequences on the mother and fetus (Lops 1995; WHO 1992; Williams 1992). A cohort study done in Pakistan found that the risk of low birthweight and preterm delivery among the anaemic women (haemoglobin under 11 g/dl) was 1.9 and 4 times higher, respectively, than the non-anaemic women. In addition, the neonates of anaemic women had a 3.7 greater risk of intrauterine fetal death and 1.8 times increased risk having low Apgar scores at one minute when compared to non-anaemic women (Lone 2004).

The suggestion that low iron stores in the mother during pregnancy may affect the child's later development, means that long-term outcomes on the baby should be outcome measures in any study on the treatment of anaemia in pregnancy. There is also a strong case for studying separately physiological anaemia, mild anaemia and severe anaemia in pregnancy.

In developing countries, anaemia in pregnancy is frequent and has been attributed to poor nutrition and a high incidence of concurrent diseases, and can potentially complicate conditions such as postpartum haemorrhage which is a major contributor to maternal mortality in many developing countries (WHO 1992). However, anaemia may only be a marker of various social and nutritional conditions, and raising haemoglobin levels could have little, if any, effect on morbidity or mortality if other conditions are not improved (Goroll 1997).

There are various possible forms of treatment for iron-deficiency anaemia. Iron can be given by mouth, by intramuscular (IM) injection or intravenous (IV) injection. It is also possible to deliver iron by giving a blood transfusion, and recombinant erythropoietin in conjunction with iron is a further possibility. Anecdotal evidence suggests that oral iron given to anaemic pregnant and non-pregnant women is associated with gastrointestinal side-effects such as nausea and constipation. IM or IV iron is thought to be associated with allergic reactions and anaphylactic shock, as well as venous thrombosis and occasionally cardiac arrest and death. Blood transfusion carries the risk of transmitting parasitic or viral infections including HIV, hepatitis, and Chagas disease (trypanosomiasis), despite preventive blood screening. There is also the possibility of bovine spongiform encephalitis, and as yet unknown viral infections. Oral iron is often the preferred route of administration for mild anaemia, while IM and IV routes are more frequently used in people with extreme anaemia when the risks of cardiac failure due to severe anaemia are perceived to outweigh the risks of potential adverse effects. Recommendations for the treatment of anaemia are frequently based on the expectation that they may be benevolent but are seldom supported by reproducible robust studies, especially randomised controlled trials. Furthermore, they may not take into account important adverse effects such as allergic reactions, viral or parasitic transmission from blood transfusions, gastrointestinal complications, and discomfort generated by common side-effects of iron. Therefore, it is difficult to balance the benefits and harms of treatments, let alone determine if there is a case to recommend a particular anaemia treatment for all women with anaemia in pregnancy.

The aim of this review was to use a systematic approach to identify and synthesise the evidence of randomised controlled trials evaluating the effects of treatments for iron-deficiency anaemia in pregnancy, and provide robust valid and useful evidence to inform clinical practice.

OBJECTIVES

The principal objective was to determine the overall effects of iron therapy given to women diagnosed with iron-deficiency anaemia in pregnancy, measuring neonatal and maternal morbidity and mortality, haematological parameters and side-effects, especially adverse effects of treatment. The review also compared different forms of iron therapy for iron-deficiency anaemia on neonatal and maternal morbidity and mortality, haematological parameters and adverse effects on women and their offspring. The review aimed to assess the effects of iron treatments when delivered to women categorised in three groups (mild, moderate or severe, as defined by trialists) at inception into the randomised controlled trial.

The review did not address the need for iron supplementation of non-anaemic women; this question has been addressed in several other reviews and evidence summaries. Similarly, it did not focus on vitamin A, vitamin B12, micronutrients, folate deficiency, infectious or genetic anaemia, which will be covered in other re-

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views. Another Cochrane systematic review focuses on the effects of routine oral iron supplementation with or without folic acid for women during pregnancy (Pena-Rosas 2006).

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

This review considered randomised controlled trials assessing the effects of treatments for iron-deficiency anaemia in pregnancy. When information in the abstract was unclear or incomplete, we reviewed the 'materials and methods' of the reports. Quasi-random studies were not eligible for this review.

Iron-deficiency anaemia definitions may be problematic due to the controversy about which diagnostic tests are sufficient and reliable enough to rule out other causes of anaemia, and that anaemia causes are frequently combined. Therefore, for this review we accepted the diagnosis of iron-deficiency anaemia defined by the authors of the studies.

Types of participants

Pregnant women with a diagnosis of anaemia (haemoglobin levels under 11 g/dl) attributed to iron deficiency.

Types of intervention

(1) All types of iron preparations versus placebo or no treatment.
(2) Different forms of oral iron preparations used for the treatment of anaemia.
(3) Oral iron in combination with other haematinics versus regular oral iron.
(4) Oral iron in combination with substances that could increase its absorption versus regular oral iron.
(5) Slow-release preparations versus regular oral iron.
(6) Intramuscular (IM) iron versus regular oral iron.
(7) Intravenous (IV) iron versus regular oral iron.
(8) IV versus IM iron therapies.
(9) Different dosages of the above combinations.
(10) Blood transfusion versus oral iron therapy.
(11) Blood transfusion versus parenteral iron.
(12) Recombinant erythropoietin versus oral iron therapy.
(13) Recombinant erythropoietin versus parenteral iron therapy.
(14) Parenteral iron versus oral iron.

* For the purpose of this review, regular oral iron will include preparations different from controlled-release oral iron.

Types of outcome measures

(1) Women

1.1 Clinical outcomes
1.1.1 Mortality
1.1.2 Morbidity
1.1.2.1 Preterm labour
1.1.2.2 Premature delivery
1.1.2.3 Puerperal sepsis
1.1.2.4 Systemic bacterial infection after delivery
1.1.2.5 Fever
1.1.2.6 Pneumonia
1.1.2.7 Postpartum haemorrhage (equal to or more than 500 ml)
1.1.2.8 Heart failure
1.1.2.9 Incapacity to work due to disease
1.1.2.10 Days in intensive care unit
1.1.2.11 Days hospitalised during pregnancy
1.1.2.12 Hypertensive disorders of pregnancy
1.1.2.13 Malaria
1.1.2.14 Urinary tract infection

1.2 Haematological outcomes
1.2.1 Maternal serum ferritin
1.2.2 Maternal serum iron
1.2.3 Haemoglobin levels

1.3 Long-term haematological outcomes (not prespecified in original protocol)

(2) Newborn

2.1 Clinical outcomes
2.1.1 Mortality
2.1.2 Morbidity
2.1.2.1 Low birthweight (less than 2500 g)
2.1.2.2 Jaundice requiring hospital admission or plasmapheresis
2.1.2.3 Respiratory disease requiring ventilation
2.1.2.4 Admission to neonatal intensive care unit
2.1.2.5 Five minute Apgar score under seven
2.1.2.6 Days hospitalised
2.1.2.7 Small-for-gestational age
2.1.3 Haematological outcomes
2.1.3.1 Cord serum ferritin
2.1.3.2 Cord haemoglobin
2.1.4 Long-term outcomes (not prespecified in original protocol)
2.1.4.1 Haemoglobin levels at one year (not prespecified in original protocol)
2.1.4.2 Serum ferritin at one year (not prespecified in original protocol)
2.1.4.3 Neurological development at one year (not prespecified in original protocol)

(3) Maternal side-effects

3.1 Gastrointestinal effects
3.1.1 Nausea
3.1.2 Vomiting
3.1.3 Diarrhoea
3.1.4 Epigastric pain
3.1.5 Constipation

3.2 Local symptoms
3.2.1 Pain or tenderness
3.2.2 Discolouration

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3.2.3 Pigmentation or staining of injection site
3.2.4 Erythema

3.3 Systemic symptoms
3.3.1 Myalgia
3.3.2 Arthralgia
3.3.3 Abscess formation at injection site
3.3.4 Fever following treatment (more than 37.5°C)
3.3.5 Allergic reactions
3.3.6 Anaphylactic shock

3.4 Incapacity to work due to an adverse effect of medication

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: methods used in reviews.

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting the Trials Search Co-ordinator (January 2007).

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:
(1) quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
(2) monthly searches of MEDLINE;
(3) handsearches of 30 journals and the proceedings of major conferences;
(4) weekly current awareness search of a further 36 journals plus BioMed Central email alerts.

Details of the search strategies for CENTRAL and MEDLINE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Search strategies for identification of studies' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are given a code (or codes) depending on the topic. The codes are linked to review topics. The Trials Search Co-ordinator searches the register for each review using these codes rather than keywords

In addition, we searched the Cochrane Central Register of Controlled Trials (*The Cochrane Library* 2005, Issue 4), MEDLINE (1966 to December 2005), EMBASE (1976 to December 2005), LILACS (1982 to 40 edition), and BIOSIS Previews (from 1980 to June 2002) using the following strategy (adapted for each database):

(Randomized-controlled-trial:PT OR Randomized-clinical-trials:PT)
AND
(Pregnancy in Mesh OR Prenatal care in Mesh)

(Anemia, Hypochromic/drug therapy in MESH OR
Anemia, Hypochromic/prevention and control in MESH OR
Anemia, Hypochromic/therapy in MESH OR
Anemia, Iron deficiency/drug therapy in MESH OR
Anemia, Iron deficiency/prevention and control in MESH OR
Anemia, Iron deficiency/therapy in MESH)
Iron/therapeutic use
Pregnancy complications/prevention and control

Haematinics/adverse effects.

We also searched trials registers such as www.controlled-trials.com, www.clinicaltrials.gov, NHS Trusts Clinical Trials Register, National Health Service Research and Development Health Technology Assessment Programme (HTA), Action Medical Research, King's College London (UK), Medical Research Council (UK), The Wellcome Trust, in January 2006.

We searched the bibliographies of all papers identified by these strategies and relevant articles obtained. We did not apply any language restrictions and eligible randomised controlled trials have been included regardless of the language of publication of their report.

METHODS OF THE REVIEW

(1) Study selection
Two review authors (L Reveiz (LR) and LG Cuervo (LGC)) checked the titles and abstracts identified from the searches. If it was clear that the study did not refer to a randomised controlled trial on iron-deficiency anaemia in pregnancy, it was excluded. If it was unclear, then we obtained the full text of the study for independent assessment by LR and G Gyte (GG). LR and GG assessed each trial for inclusion and resolved any disagreements through discussion, with referral to a third author (LGC) when necessary. Excluded studies and reasons for exclusion are described in the 'Characteristics of excluded studies' table.

(2) Assessment of methodological quality
We assessed trials under consideration for methodological quality and for appropriateness for inclusion without consideration of their results. We processed data from included trials as described in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2005). We undertook quality assessment by evaluating the following components for each included study, since there was some evidence that these are associated with biased estimates of treatment effect:
(a) the method of generation of the randomisation sequence; if it delivered a known chance allocation to each given group but individual allocation could not be anticipated;
(b) the method of allocation concealment, which was considered 'adequate' when the assignment could not be foreseen;

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(c) who was blinded or not blinded (participants, clinicians, outcome assessors);
(d) participants lost to follow up in each arm of the study (split into postrandomisation exclusions and later losses if possible), and whether participants were analysed in the groups to which they were originally randomised (intention to treat).

The information was recorded in a table of quality criteria and a description of the quality of each study was given based on a summary of these components.

(3) Data extraction
Data extraction was carried out independently by one author (LR) using a data extraction form. Data were extracted for all outcomes for all relevant drugs, paying particular attention to the dosage and periodicity of treatment. GG checked the data extraction. We resolved disagreements by discussion until we reached consensus. We obtained missing data from the trial authors, when possible.

(4) Analysis
To estimate differences between treatments, we pooled the results of randomised controlled trials (RCTs) that evaluated similar interventions (and controls), and calculated a weighted treatment effect across RCTs using a fixed-effect model. The results were expressed as relative risk, and 95% confidence intervals (CI)) for dichotomous outcomes, and weighted mean difference (and 95% CI) for continuous outcomes. Results were expressed as number needed to treat where appropriate. We summarised the information we found available. Quasi-randomised and non-randomised controlled studies were identified and listed, but were not further discussed. A qualitative description was provided for adverse effects when this was available.

DESCRIPTION OF STUDIES

The search identified 111 references: two unpublished trials, five congress abstracts, and 104 published trials. An initial trawl through this list (LR) excluded 55 references of non-randomised controlled trials (RCTs). This left 56 trials for a more detailed evaluation. Two authors (Ludovic Reveiz (LR) and Gill Gyte (GG)) independently checked the trials against the inclusion criteria, and a third author (Luis Gabriel Cuervo (LGC)) acted as the arbiter. Thirty-eight studies were further excluded after first review because they were not RCTs; included mostly non-anaemic women; evaluated postpartum iron treatments; focused on non iron-deficiency anaemia; or had methodological flaws that seriously compromised their validity or resulted in insufficient useful reliable information. We actively tried to contact the authors using contact information provided in their articles and on the internet. We contacted the authors listed in the articles by Singh (Singh 1998), Visca (Visca 1996), Suharno (Suharno 1993), Mumtaz (Mumtaz 2000), Siega-Riz (Siega-Riz 2001), De Souza (De Souza 2004) and Breymann (Breymann 2001). We received responses from the authors of the Visca, Suharno, Mumtaz, De Souza and Breymann articles. We did not receive a response to our communications, including faxes, from the authors of the article listed as Al Momen 1996. We were unable to contact the authors for the articles by Stein 1991 and Wu 1998.

We included 17 RCTs in the review (Al 2005; Bayoumeu 2002; Breymann 2001; Dawson 1965; De Souza 2004; Kaisi 1988; Komolafe 2003; Kumar 2005; Mumtaz 2000; Ogunbode 1980; Oluboyede 1980; Singh 1998; Sood 1979; Suharno 1993; Symonds 1969; Wali 2002; Zutschi 2004). Most focused on laboratory results rather than clinical outcomes. Clinical outcomes were assessed in six RCTs (Al 2005; Bayoumeu 2002; Breymann 2001; Oluboyede 1980; Singh 1998; Zutschi 2004) although Breymann and Singh's data were unpublished; these data were provided by the main author of Singh 1998 and have been incorporated into the review. LR and GG independently extracted data from the articles. LGC was expected to act as arbiter if differences arose in the data extraction, but this did not happen. LR did data entries, and GG double checked data entries for accuracy.

Seven groups of RCTs were described according to the type of intervention. However, groups were further divided according to co-interventions, dose, regimen, route, or type of chemical components of the intervention (i.e. iron sucrose, dextran), as follows.

(1) Oral iron

- Oral iron versus placebo (Suharno 1993; Symonds 1969)
- Oral iron plus vitamin A versus placebo (Suharno 1993)
- Oral iron plus vitamin A versus oral iron (Suharno 1993)

(2) Different regimens of oral iron treatment

- Daily oral iron versus twice weekly (De Souza 2004; Mumtaz 2000)
- Daily oral iron versus once a week (De Souza 2004)
- Twice-weekly iron versus once weekly iron (De Souza 2004)
- 600 mg oral iron versus 1200 mg oral iron (Ogunbode 1980)
- Controlled-release oral iron versus regular oral iron (Symonds 1969)

(3) Intramuscular (IM) iron

- IM iron sorbitol versus IM dextran (Dawson 1965)
- IM iron sorbitol versus intravenous (IV) iron dextran (Oluboyede 1980)

(4) IV iron

- IV route versus placebo (Symonds 1969)

(5) Parenteral route (IM or IV) versus oral route

- IM versus oral iron treatment (Komolafe 2003; Kumar 2005; Ogunbode 1980; Zutschi 2004)

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- IV versus oral iron treatment (Al 2005; Bayoumeu 2002; Singh 1998; Sood 1979; Symonds 1969)

(6) IV iron versus IM iron with different regimens of parenteral iron treatment

- IV iron versus IM iron (Oluboyede 1980)
- Different IM preparations (Dawson 1965)
- IV iron versus IM iron (Dawson 1965)
- IV iron with hydrocortisone versus IV iron (Dawson 1965)
- Two differing IV doses (Kaisi 1988)
- IV iron versus IM iron (Wali 2002)

(7) IV administered iron sucrose with and without adjuvant recombinant human erythropoietin (Breymann 2001)

For details of included and excluded studies, *see* the 'Characteristics of included studies' and the 'Characteristics of excluded studies' tables.

METHODOLOGICAL QUALITY

Ludovic Reveiz and Gill Gyte assessed the methodological quality of the included studies independently as described in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2005). Differences in interpretations were sorted by consensus among all three authors, after checking the criteria agreed in the original review protocol. When RCTs had potential validity or interpretation problems and just part of the data were deemed useful, we would only use such data. For example, when RCTs had a high withdrawal rates and therefore incomplete data on outcomes at the end of follow up, but still offered complete data at a given time that fulfilled our predefined inclusion criteria, the later data were used.

The quality assessment included an evaluation of the following components for each included study, since there is some evidence that these are associated with biased estimates of treatment effect (Juni 2001):
(a) the method of generation of the randomisation sequence;
(b) the method of allocation concealment, which was considered adequate if the assignment could not be foreseen;
(c) parties masked to the intervention (i.e. blinding of participants, clinicians, outcome evaluators);
(d) how many participants were lost to follow up in each arm and whether participants were analysed in the groups to which they were originally randomised (intention to treat).

Allocation generation and concealment
Six out of 17 randomised controlled trials (RCTs) reported on how the randomisation sequence was generated (Al 2005; Bayoumeu 2002; Breymann 2001; Mumtaz 2000; Singh 1998; Suharno 1993) whilst no information was available for the remaining 11 RCTs. The randomisation list generation strategy was considered inadequate for the trial by Dawson 1965.

Five out of 17 studies reported adequate allocation concealment (Al 2005; Breymann 2001; Mumtaz 2000; Singh 1998; Suharno 1993). Published details of the randomisation were insufficient in the Singh 1998 and Breymann 2001 articles, but additional details were provided by the authors upon request.

The allocation strategy and concealment were considered adequate in 3 of the 17 studies (Al 2005; Breymann 2001; Mumtaz 2000).

Blinding
In most RCTs, blinding was not used; these were open RCTs. Two RCTs described blinding (masking) but it is unclear whether they were blinding the participants or healthcare providers to the interventions (Mumtaz 2000; Suharno 1993); both RCTs assessed oral administration. None of the RCTs masked the interventions to people assessing outcomes.

Loss to follow up
Withdrawal rates (drop outs and losses to follow up) were reported in seven RCTs. (Al 2005; Breymann 2001; Komolafe 2003; Ogunbode 1980; Singh 1998; Symonds 1969; Zutschi 2004).

- Less than 5%: withdrawal rates were lower than 5% in two RCTs (Oluboyede 1980; Sood 1979).
- 5% to 9.9%: an RCT from Pakistan (Wali 2002) had five withdrawals (8.3%) due to intolerance in the intramuscular (IM) iron group. An RCT from France had three withdrawals (6%) (Bayoumeu 2002).
- 10% to 19.9%: the West Java RCT (Suharno 1993) had complete data available on 251 (83%) women: reasons for withdrawals are further described in the article.
- More than 20%: an RCT from Pakistan (Mumtaz 2000) recruited 191 women; of these, 160 were successfully followed for at least four weeks and supplemented for an average of 10.9 weeks. Fifty-five per cent completed the entire duration of follow up; 15% of the women recruited did not return for a single visit and were excluded from the analysis. The remaining 30% did not complete the entire 12 weeks of planned follow up. No significant differences were found for population characteristics (age, socioeconomic status score, parity, time since last pregnancy, body mass index, initial haemoglobin, dependants or family and the duration of follow up) between women who withdrew and those who completed the study. The Brazilian RCT (De Souza 2004) had 41 (21.5%) women who withdrew or were lost to follow up; the reasons were described in the article. The analysis was done using data at 16 weeks of treatment. The UK RCT (Dawson 1965) had high rates of losses to follow up. The RCT was focused on assessing adverse effects. The RCT from Tasmania (Kaisi 1988) had high withdrawal rates for most outcomes (loss to follow up for haemoglobin result was 47%) and only data on adverse effects were used for this

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review. The Indian RCT (Kumar 2005) recruited 220 women of whom 150 (68%) completed the study. No significant differences were found on data of initial hematological parameters, gestation, parity or literacy between women who completed the study and women who withdrew. However, withdrawals were different for women receiving oral treatment (13.5%) and those receiving IM treatment (38.5%).

Intention-to-treat analysis

One RCT seemed to have a proper intention-to-treat analysis (Mumtaz 2000).

RESULTS

Seventeen randomised controlled trials (RCTs), involving 2578 women, met the inclusion criteria. Overall, we found insufficient assessment of the outcomes relevant to the focus of this review, especially of clinical outcomes. Most results were provided by one or two small RCTs with methodological limitations. The effect size for these are represented in this review using the relative risk (RR) and weighted mean difference (WMD). Uncertainty levels are quantified using 95% confidence intervals (CI).

(1) Oral iron

Oral iron versus placebo (comparison 01)

We found two RCTs involving 176 women (Suharno 1993; Symonds 1969). Data from the first RCT showed that women receiving iron (ferrous sulphate) had a lower risk of being anaemic during the second trimester (one RCT, 125 women; RR 0.38; 95% CI 0.26 to 0.55; graph 01.01). In the group receiving iron, the mean haemoglobin level was higher (one RCT, 125 women; 11.3 g/dl versus 10.5 g/dl; WMD 0.80; 95% CI 0.62 to 0.98; graph 01.02). Similarly, the mean serum ferritin was higher for women receiving iron (one RCT, 125 women; WMD 0.70; 95% CI 0.52 to 0.88; graph 01.03). A trend towards increased adverse effects (for example, nausea, vomiting, constipation and abdominal cramps) was also noticed in the second RCT (Ferrous gluconate), but figures were small to allow worthy comparisons (11/51 women with adverse effects). No other assessments were found for clinical outcomes. Hence, it is difficult to establish the clinical effects of treatments in women and newborns. Conclusions need to be approached with care because they are drawn from a small sample of participants (125 women). Furthermore, one RCT assessed outcomes at the second trimester (Suharno 1993) and it is unclear if those women sustained similar haemoglobin levels during the rest of their pregnancy, and no assessment of haematological results was done at delivery.

Oral iron plus vitamin A versus placebo (comparison 02)

We found one RCT involving 125 women (Suharno 1993). It included anaemic women with a high risk of suffering vitamin A deficiency. Adding vitamin A to regular iron (ferrous sulphate), resulted in improved haemoglobin level. Anaemia during the second trimester was lower with oral iron plus vitamin A, compared with placebo (one RCT, 125 women; RR 0.04; 95% CI 0.01 to 0.15; graph 02.01). The difference was not as big when the comparator was iron therapy only (*see* below). The applicability of these results may be limited to women in populations with vitamin A deficiency.

Oral iron plus vitamin A versus oral iron (comparison 03)

One RCT involving 126 women (Suharno 1993) found a reduction in anaemia during the second trimester with oral iron plus vitamin A, compared with oral iron alone (RR 0.10; 95% CI 0.02 to 0.41; graph 03.01). This study was carried out amongst women living in areas of Indonesia where vitamin A deficiency is prevalent.

(2) Different regimens of oral iron treatment (comparisons 17, 18, 19 and 23)

Daily oral iron versus twice weekly (comparison 17)

An RCT from Pakistan (Mumtaz 2000) found that daily oral iron (ferrous sulphate) significant increased haemoglobin levels at 4 weeks, 8 weeks, and 12 weeks, compared with twice-weekly oral iron. At 12 weeks, the mean haemoglobin level was 11.36 g/dl compared with 10.09 g/dl, respectively (one RCT, 105 women; WMD 1.27; 95% CI 0.68 to 1.86; graph 17.03). In women receiving daily versus twice-weekly oral iron therapy (ferrous sulphate), an RCT from Brazil (De Souza 2004) found no significant difference in haemoglobin levels (one RCT, 102 women; WMD 0.30; CI -0.01 to 0.61; graph 17.04) or anaemia (one RCT, 102 women; RR 1.38; 95% CI 0.86 to 2.23; graph 17.05) at 16 weeks of treatment. A trend was found between higher doses of iron and reported adverse effects (19/48 (40%) for 1/week, 24/53 (45%) for twice/week and 35/49 (71%) for daily treatment). No further description of adverse effects was provided.

Daily oral iron versus once a week (comparison 18)

One RCT done in Brazil (De Souza 2004) found that daily oral treatment (ferrous sulphate) increased haemoglobin level after 16 weeks of treatment, compared with weekly oral iron (one RCT, 97 women; WMD 0.70; 95% CI 0.36 to 1.04; graph 18.01), the proportion of women non-anaemic at the end of follow up (one RCT, 97 women; RR 1.73; 95% CI 1.00 to 3.01; graph 18.02) and reduced treatment failure (one RCT, 97 women; RR 0.05; 95% CI 0.01 to 0.35; graph 18.03).

Twice-weekly iron versus once weekly iron (comparison 19)

One RCT done in Brazil (De Souza 2004) found that a twice-weekly regimen of ferrous sulphate resulted in a modest increase in haemoglobin levels, compared with a weekly iron regimen (one RCT, 101 women; WMD 0.40; 95% CI 0.03 to 0.77; graph 19.01) and reduced treatment failure (one RCT, 101 women; RR 0.32; 95% CI 0.15 to 0.68; graph 19.03). However, no significant differences were found in the proportion of women non anaemic at 16 weeks of treatment (one RCT, 101 women; RR 1.25; 95% CI 0.69 to 2.28; graph 19.02).

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600 mg oral iron versus 1200 mg oral iron (comparison 23)
An RCT done in Nigeria (Ogunbode 1980) found no significant differences in haemoglobin levels at four weeks (one RCT, 56 women; WMD 0.37; 95% CI -0.77 to 1.51; graph 23.01) and eight weeks (one RCT, 56 women; WMD 0.02; 95% CI -1.03 to 1.07; graph 23.02) of treatment between women receiving 600 mg versus 1200 mg of oral ferrous sulphate. All women received daily 5 mg of folic acid and 25 mg of pyrimethamine daily, in addition to ferrous sulphate.

Controlled-release oral iron versus regular oral iron (comparison 04)
One RCT done in Australia (Symonds 1969) compared controlled-release oral iron versus other iron preparations. It provided information on adverse effects, but data on effectiveness were not included because it had a very high withdrawal rate. It found no differences in nausea and vomiting, constipation and abdominal cramps at one month between controlled-release iron and regular oral iron. The small sample size and broad confidence intervals illustrate that the sample size is clearly insufficient to rule out any difference (graphs 04.01 to 04).

(3) Intramuscular (IM) iron
We found no RCTs comparing IM iron versus placebo.

IM iron sorbitolversus IM dextran (comparison 05)
We found one RCT that recruited 74 women (Dawson 1965). It did not provide effectiveness figures and had high withdrawal rates. It found that iron sorbitol produced less skin discolouration (one RCT, 48 women; RR 0.21; 95% CI 0.07 to 0.65; graph 05.02) and fewer headaches (one RCT, 48 women; RR 0.13; 95% CI 0.02 to 0.99; graph 05.05) than IM dextran. These findings are inconclusive given the limitations of this single study.

IM iron sorbitol versus intravenous (IV) iron dextran (comparison 25)
We found one RCT involving 63 women conducted in Nigeria (Oluboyede 1980). It found that IM iron sorbitol increased hematocrit after four weeks of treatment (one RCT, 59 women; WMD 2.18; 95% CI 0.77 to 3.59; graph 25.01) and after eight weeks of treatment (one RCT, 43 women; WMD 1.48; 95% CI 0.15 to 2.81; graph 25.02), compared with IV iron dextran.

(4) IV iron

IV route versus placebo (comparison 08)
We found one small RCT involving 54 women and conducted in Australia (Symonds 1969). The RCT provided data on adverse effects. Data on effectiveness were not included. It found no significant differences between IV iron and placebo for: nausea and vomiting (one RCT, 54 women; RR 0.33; 95% CI 0.01 to 7.84), abdominal cramps (not estimable), and constipation (one RCT, 54 women; RR 0.25; 95% CI 0.03 to 2.09). However, the small sample size and broad confidence intervals illustrate that the sample size is clearly insufficient to rule out any such adverse effects.

(5) Parenteral route (IM or IV) versus oral route

IM versus oral irontreatment (comparisons 14, 15 and 16)
We found four RCTs (571 women) comparing IM and oral administration of iron (Komolafe 2003; Ogunbode 1980; Kumar 2005; Zutschi 2004).

The first RCT, from India, (Zutschi 2004) evaluated 150 mg IM iron sorbitol (via three injections a day) at four-weekly intervals versus 100 mg of elemental oral iron for at least 100 days. IM iron significantly increased haemoglobin (one RCT, 200 women; WMD 0.54; 95% CI 0.30 to 0.78; graph 14.02), and haematocrit levels (one RCT, 200 women; WMD 1.40; 95% CI 0.67 to 2.13; graph 14.03), compared with oral iron. A higher proportion of women were found to be non-anaemic at labour (one RCT, 200 women; RR 1.23; 95% CI 1.01 to 1.48; graph 14.01). Adverse effects were not included in the reports of the article.

The second RCT, from India, compared IM sorbitol citric acid dose versus oral ferrous sulphate (100 mg of elemental iron) plus 5 mg of folic acid at 36 weeks of pregnancy (Kumar 2005). Women receiving oral iron plus folic acid had a higher haemoglobin level (one RCT, 150 women; WMD 0.26; 95% CI 0.04 to 0.48; graph 16.01). No significant differences were found for caesarean section rates or mean birthweight. Adverse effects were reported by 40 women receiving IM treatment versus 16 receiving oral treatment at 36 weeks of treatment (graphs 16.03 to 16.15). Gastrointestinal side-effects (dyspepsia, constipation, diarrhea, vomiting) were observed predominately in oral group, while systemic reactions (local pain, staining, fever, systemic ache, arthralgia, itching and rash, immediate headache, malaise and vaso-vagal due to apprehension (it is unclear what the authors meant by this and what diagnostic criteria they used) were more frequently found in women receiving IM iron. No anaphylactic reaction or abscess formation were observed, but too few women participated in the RCT to assess these and other important adverse effects.

The third RCT, from Nigeria, (Ogunbode 1980) was a three-arm RCT comparing iron sorbitol versus 600 mg oral ferrous sulphate versus 1200 mg oral ferrous sulphate. All women received a daily supplement of 5 mg of folic acid and 25 mg of pyrimethamine. After eight weeks, IM iron sorbitol had significantly improved haematocrit levels compared to 600 mg of oral iron (one RCT, 59 women; WMD 2.62; 95% CI 1.26 to 3.98; graph 14.06), and compared with 1200 mg of oral iron (one RCT, 59 women; WMD 2.60; 95% CI 1.02 to 4.18; graph 14.08). Adverse effects were not assessed.

The fourth RCT, conducted in Nigeria, compared IM iron dextran (250 mg iron dextran thrice-weekly until total calculated dose was given) versus 600 mg of oral ferrous sulphate plus vitamin C and folic acid (Komolafe 2003). It found that iron dextran significantly improved haematocrit levels after six weeks (one RCT, 60 women; WMD 4.47; 95% CI 3.67 to 5.27; graph 15.01) and the proportion of non-anaemic women after six weeks (one RCT, 60 women; RR 11.00; 95% CI 1.51 to 79.96; graph 15.02).

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IV versus oral iron treatment (comparisons 09 and 10)

Pooled estimates (Al 2005; Bayoumeu 2002) for haemoglobin levels at four weeks favoured IV iron (two RCTs, 137 women; WMD 0.60; 95% CI 0.33 to 0.87; X^2 = 2.03; P = 0.15; graph 09.12). Diarrhoea was less frequent in women receiving IV iron (three RCTs, 237 women; RR 0.16; 95% CI 0.03 to 0.86; graph 09.05).

A French RCT compared IV iron sucrose given in six slow IV injections on days 1, 4, 8, 12, 15 and 21 according to a formula described in the article, with 240 mg of elemental iron sulphate tablets (Bayoumeu 2002); all women received folic acid 15 mg of folic acid in addition to iron. No significant differences were found in maternal haemoglobin levels at four weeks of treatment, haemoglobin levels in excess of 12 g/dl, neonatal haemoglobin, ferritin levels, and birthweight. Similarly, no significant differences were found in the incidence of diarrhea, postpartum haemorrhage, blood transfusion required, or neonatal mortality. The RCTs were underpowered to assess these outcomes properly.

An RCT conducted in Turkey (Al 2005) compared IV iron sucrose calculated according to a formula described in the article (total dose was administered over five days and maximum daily dose administered was 400 mg elemental iron) versus 300 mg of elemental iron (polymaltose complex); all women were given 5 mg of folic acid daily. It found that IV iron significantly increased maternal haemoglobin at four weeks (one RCT, 90 women; WMD 0.68; 95% CI 0.39 to 0.97; graph 09.12) and at birth (one RCT, 90 women; WMD 0.75; 95% CI 0.34 to 1.16; graph 09.09) and increased the proportion of non-anaemic women - those with haemoglobin level equal or greater than 11 g/dl (90 women; RR 1.54; 95% CI 1.21 to 1.94; graph 09.26). No significant differences were found for caesarean section rates, neonatal birthweight, gestational hypertension, gestational diabetes and arthralgias (graphs 9.2; 5; 15; 17; 24; 25; 28).

A comparison of oral ferrous fumarate 200 mg three times a day versus IV iron dextrin (calculated according to described formula) found that oral treatments increased constipation, compared with IV treatments (Singh 1998) (one RCT, 100 women; RR 0.04; 95% CI 0.00 to 0.61; graph 09.03). No significant differences were found for constipation when IV iron was compared to controlled-release iron. However, only one small RCT (Symonds 1969) assessed this and it seemed to be underpowered to rule out clinically important effects (one RCT, 51 women; RR 0.22; 95% CI 0.03 to 1.85; graph 09.03). One RCT, recruiting mostly Malayan and Chinese women, found that higher haemoglobin levels were found at the end of gestation with IV versus oral treatments (Singh 1998). However, the standard deviations are 50 to 100 times narrower than those found in other studies, raising questions about their validity (Al 2005; Suharno 1993). We exclude data from the analysis pending a response from the trial's authors. No maternal or neonatal deaths were recorded in this RCT, which was the only one specifically assessing these outcomes in women receiving oral or IV treatments.

Three RCTs (Al 2005; Singh 1998; Symonds 1969), including one that assessed controlled-release iron (Symonds 1969), found that oral iron was more frequently associated with complaints of nausea than IV preparations, and the magnitude of the effects was consistent across all three RCTs (three trial, 244 women; RR 0.33; 95% CI 0.15 to 0.74; graph 09.02).

Two women were reported as suffering severe allergic reactions with IV dextran in an RCT comparing the latter with oral ferrous sulphate (Sood 1979). Data on other relevant outcomes were not available for comparison.

(6) IV iron versus IM iron with different regimens of parenteral iron treatment (comparisons 05, 06, 07, 11, 20, 22 and 25)

IV iron versus IM iron (comparison 25)

An RCT from Nigeria (Oluboyede 1980) found that IM sorbitol increased haematocrit levels compared with IV dextran group at four weeks (one RCT, 59 women; WMD 2.18; 95% CI 0.77 to 3.59, one RCT; graph 25.01) and eight weeks (one RCT, 43 women; WMD 1.48; 95% CI 0.15 to 2.81; graph 25.02). One women receiving IV iron suffered a severe allergic reaction whereas one participant of the IM group had viral hepatitis three months later. Authors reported that no significant differences in newborn weight and Apgar score at birth were found between groups (no data were provided). Neonates were assessed for any complication at birth and within the first week of life; one neonate in each treatment group developed neonatal jaundice. Maternal outcomes were not reported for each group of treatment.

Different IM preparations(comparison 05)

One RCT compared two IM preparations (Dawson 1965). It found that women receiving IM iron-sorbitol complex had lower incidence of skin discoloration at injection sites at eight weeks (one RCT, 48 women; RR 0.21; 95% CI 0.07 to 0.65; graph 05.02) and fewer headaches (one RCT, 48 women; RR 0.13; 95% CI 0.02 to 0.99; graph 05.05) compared with IM iron dextran. Results should be interpreted with care as they come from a single, small RCT. However, this particular RCT had a robust randomisation and concealment strategy.

IV iron versus IM iron (comparison 06)

One factorial RCT conducted in the UK compared IM treatments with IV treatment (Dawson 1965). It found that IM iron was more frequently associated with pain in the injection site. This factorial design had some problems that were not addressed during the analysis: active treatments were compared with a single control group and no adjustments for multiple comparisons were done. This increases the possibilities of finding spurious associations. The RCT found a higher risk of skin discoloration in women receiving IM iron dextran compared to IV iron. Findings suggested a trend towards a higher risk of venous thrombosis with IV iron versus IM iron, but no statistical differences were found (one RCT,

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49 women; 4/26 with IV iron dextran (15%) versus 0/23 with IM iron; RR 0.13; 95% CI 0.01 to 2.20, graph 06.03). However, this raises concern and an association can not be ruled out; the RCTs were underpowered to assess these outcomes properly, and these are very serious adverse effects.

The RCT found that IM iron dextran was not associated with higher complaints of headaches, compared with IV infusion of iron dextran (one RCT, 49 women; RR 3.96; 95% CI 0.91 to 17.17; graph 06.05). The RCT was too small to rule out important clinical differences in measured adverse effects outcomes such as shivering, itching, metallic taste in mouth, severe delayed allergic reaction (graphs 06.04 to 06.09).

IV iron with hydrocortisone versus IV iron (comparison 11)

An RCT conducted in the UK compared iron-dextran infusion plus hydrocortisone versus iron-dextran infusion without hydrocortisone (Dawson 1965). It found a non-significant but nevertheless conspicuous reduction of venous thrombosis with hydrocortisone (one RCT, 30 women; 0/15 with hydrocortisone versus 5/15 (33%) without hydrocortisone; RR 0.09; 95% CI 0.01 to 1.51; graph 11.02).

Two differing IV doses

An RCT conducted in Tanzania compared two doses of IV iron dextran by total dose infusion (Kaisi 1988). All participants were given the full dose recommended by the manufacturer; group A received an additional 10 ml whereas group B was given two-thirds of that total dose. It found that allergic reactions after the infusion had finished were reduced with the lower dose (one RCT, 623 women; RR 0.62; 95% CI 0.45 to 0.86; graph 12.02). No significant differences were found for life threatening allergic reactions. This RCT was not used to assess effectiveness as it failed to fulfil our quality criteria.

IV iron versus IM iron (comparisons 21 and 22)

An RCT conducted in Pakistan (Wali 2002) evaluated two doses of IV iron sucrose (500 mg versus 200 mg) and IM iron sorbitol. The participants were divided into three groups. In group A (n = 15), IV iron sucrose was administered intravenously according to the following formula: total iron deficit = body weight x (target haemoglobin - actual haemoglobin) x 0.24 + 500; in group B (n = 20) IV iron sucrose was administered using the same formula but 200 mg of iron being given for storage instead of 500; in group C, iron was administered IM daily or alternate days; after parenteral administration, oral iron therapy (ferrous gluconate 250 mg) was continued till the time of giving birth. No significant differences were found regarding haemoglobin level and the proportion of non-anaemic women (with haemoglobin levels greater than 11 g/dl at delivery) when the two different doses of IV iron were compared. Abdominal pain was reported by one woman in each group. Administration of IV iron sucrose (500 mg) significantly increased haemoglobin levels (one RCT, 40 women; WMD 1.60; 95% CI 0.87 to 2.33, graph 21.01) and the proportion of women with haemoglobin greater than 11 g/dl at delivery (one RCT, 40 women; RR 2.86; 95% CI 1.45 to 5.63; graph 21.02) compared with IM iron sorbitol. Similarly, significant results favoring IV treatment were found when comparing IV iron sucrose (200 mg) and IM iron sorbitol for the same outcomes (one RCT, 45 women; WMD 1.10; 95% CI 0.49 to 1.71; graph 22.01), and (one RCT, 45 women; RR 2.50; 95% CI 1.25 to 4.99; graph 22.02). In the IV groups 2/35 (5.7%) women had shivering and feeling of weakness within a few hours, and 3/35 (8.6%) had phlebitis at the site where IV canula was retained. In the IM group, 5/25 (20%) withdrew from the study due to intolerance (no further description was provided) and the majority complained of pain at the injection site.

(7) IV administered iron sucrose with and without adjuvant recombinant human erythropoietin (comparison 13)

One small size study evaluated adjuvant recombinant human erythropoietin when iron sucrose was administered intravenously (Breymann 2001). No statistically significant differences were found in the number of women with a rise of haemoglobin greater than 11 g/dl or caesarean delivery. The author provided unpublished data concerning birthweight and mean maternal blood pressure at the end of therapy; no significant differences were found (comparison 13.06 and 08) for these outcomes. None of the women required additional antepartum or postpartum blood transfusion.

DISCUSSION

The objective of this review was to address the effects of iron anaemia treatments on maternal and neonatal morbidity and mortality. The review included 17 randomised controlled trials (RCTs), most of which were small and with significant methodological flaws. These RCTs assessed many different questions and a broad range of treatments resulting in very limited opportunities to pool useful data. The paucity of robust studies assessing clinical effects of treatments makes it impossible to balance the benefits and harms of differing treatments for different levels of anaemia in pregnancy, in a meaningful and useful way. Many questions remain open. We cannot determine if women with mild anaemia, but otherwise healthy, will benefit from anaemia treatment; adverse effects can potentially outweigh benefits. It also remains unclear which treatments are safer and more effective in women with moderate or severe anaemia with and without associated illness.

Although iron treatments consistently increase maternal haematological indices in women diagnosed with iron-deficiency anaemia in pregnancy, we found no evidence that these laboratory improvements reflected in clinical improvements such as reduced preterm delivery, reduced infant low birthweight, lower rates of pre-eclampsia, sepsis or postpartum haemorrhage and its complications (Scholl 1992; Scholl 2000). We found very few RCTs assessing clinical outcomes, and these RCTs were too small to estimate important clinical effects. Moreover, the studied populations

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turned out to be too small to deliver clear-cut answers to this review's questions.

The findings suggest that gastrointestinal adverse effects are more frequent with oral iron treatments, compared with other routes of iron administration. The results of one RCT suggest that daily iron treatment is better than intermittent iron supplementation in increasing haemoglobin at delivery in pregnant women based in developing countries. Higher doses of iron were not associated with improved haematological values. The assessment of the effects of controlled versus regular oral iron were mostly inconclusive; there seems to be a reduced incidence of constipation. Most oral iron studies were marred by high withdrawal rates, highlighting the importance of assessing adverse effects and compliance issues with these frequently-prescribed treatments.

The findings of this review suggest that adding vitamin A to regular iron (ferrous sulphate) resulted in improved haemoglobin levels. Another Cochrane review that focused on vitamin A supplementation during pregnancy suggested beneficial effects for women in areas of poor nutritional intake (Van den Broek 2002).

Compared with oral iron, intramuscular (IM) iron sorbitol and iron dextran improved haematological values, reduced the proportion of women without anaemia, and resulted in lower gastrointestinal side-effects. But these preparations were associated with higher rates of systemic reactions especially with IM iron.

The findings of this review also suggest that intravenous (IV) iron sucrose is effective, but there is uncertainty whether it may increase the incidence of serious adverse effects such as thrombosis, which was frequent (9/41; 22%). Similarly, there are worrying trends towards an increased risk of severe allergic reaction with IV dextran iron, but data were few. One study suggests that the risk of venous thrombosis may be lowered by adding hydrocortisone to the infusion, but it is unclear what the real impact of this might be and whether it has any other effects. Evidence of a relationship between doses of IV iron and risk of adverse allergic reactions is inconclusive. No effectiveness assessments were done for the compared doses of IV drugs. Compared with IM iron sucrose, IV iron sucrose significantly increased haematological indices but it is unclear what the effects are on maternal and neonatal morbidity.

RCTs were insufficient to determine the clinical effects of treatments in women with iron-deficiency anaemia during pregnancy.

AUTHORS' CONCLUSIONS

Implications for practice

Avoidable limitations in the included randomised controlled trials (RCTs) resulted in these failing to provide sound evidence that currently available treatments for iron-deficiency anaemia in pregnant women are beneficial for women or their children. We found no scientific basis to suggest that in otherwise healthy women, the benefits of treatments for mild anaemia in pregnancy will outweigh the adverse effects associated with them. We found no evidence that in women with iron-deficiency anaemia in pregnancy, improvement in women's haematological indices translate into clinical improvements for them or their children. However, treatments are associated with frequent adverse effects such as gastrointestinal disturbances and poor compliance. Compared with oral iron, intramuscular (IM) iron improves haematological indices. But again, the support from clinical research seems to be missing and adverse effects remain poorly evaluated despite indications that treatments can result in important adverse outcomes. Intravenous iron sorbitol improves haematological values compared to IM or oral iron, but serious adverse effects are possible and remain poorly studied; knowledge of their magnitude and mitigation strategies is missing. Potential adverse effects may include venous thrombosis and severe allergic reactions. Treatment of mild anaemia in pregnancy remains controversial and unsupported by scientific proof. It is also unclear what treatments work better for severe anaemia in pregnancy.

Iron-deficiency anaemia in pregnancy is frequently diagnosed and treated, but the effects of these treatments remain largely unknown. Severe iron-deficiency anaemia affects many pregnant women in developing countries and may have considerable impact on maternal and neonatal health.

Implications for research

Considerable resources are being used globally to diagnose and treat anaemia in pregnant women, but it remains unclear if these efforts are worthy and beneficial to individuals or populations. Also, it is unclear if there is a positive return for this investment, and if it improves people's lives. This review is an invitation for researchers, especially those working towards the improvement of health of communities in under-resourced settings, to implement high quality RCTs addressing knowledge gaps (such as those flagged up by this review), for this common condition. In particular, determining when treatments are worthwhile, and providing sufficient information to allow better balancing of the benefits and harms of treatments. The authors of this systematic review consider that a solution to this would be to conduct a large multicenter RCT assessing the clinical effects of a selection of commonly used treatments in different regions of the world. The sample and duration of the follow up in such an RCT should be estimated to allow the identification of important, frequent, and long-term effects in women and babies. Large RCTs such as the MAGPIE trial or the CRASH trial illustrate how gaps in knowledge can be effectively addressed through research, and how this can reduce harmful practices and inappropriate use of resources. We found a compelling case for a similar approach to be taken on iron-deficiency anaemia in pregnancy.

Some important considerations for future research are as follows.

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(1) There is an urgent need to determine what treatments improve maternal and neonatal prognosis in women with severe and moderate anaemia in poorly-resourced settings.
(2) The effects of different doses, regimens and routes of administrations for commonly-used treatments remain to be determined. The suitability of the route of administration may be influenced by the setting or cultural background.
(3) Stratification according to anaemia severity can help address questions of the effects in different populations, and balance differently the benefits and harms.
(4) Women with additional factors contributing to their anaemia, such as vitamin A deficiency, need to be studied as a different population.
(5) Clinical outcomes, including adverse effects and quality of life, need to be better addressed and considered for study sample size calculations.
(6) Offspring outcomes are particularly important given the possibility that iron has been associated with adverse effects in some observational studies.
(7) RCTs need to have sample sizes big enough to allow assessing adverse effects such as venous thrombosis, allergic reactions, infections, and rare but serious adverse effects, as well as long-term outcomes.
(8) For women with mild iron-deficiency anaemia, it would be helpful to assess whether oral iron is overall beneficial compared with placebo or no treatment. Researchers need to remain aware about the clinical effects of high iron on haemoglobin levels, and possible overdosing.
(9) We found no studies on oral erythropoietin or transfusions; these need to be evaluated in populations where they remain likely to be used. But providing scientific support for commonly used treatments seems to be the priority; we do not know if more harm then good is being done and yet these interventions remain widely prescribed and used.
(10) Studies are needed to determine the effects in specific populations such as pregnant women who are anaemic and also infected with human immunodeficiency virus.
(11) To use the CONSORT statement to improve the quality of reports of randomised trials (http://www.consort-statement.org/).

POTENTIAL CONFLICT OF INTEREST

None known.

Luis Gabriel Cuervo has contributed to this systematic review in a personal capacity and during his spare time. Most of his contributions were made before joining the Pan American Health Organization. The Pan American Health Organization does not assume responsibility for the statements contained therein.

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* *Indicates the major publication for the study*

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TABLES

Characteristics of included studies

Study	Al 2005
Methods	Group allocation was predetermined by one of the authors who was not involved with women's care. Authors used opaque envelopes that were consecutively-numbered by means of a computer-generated randomisation table. As each woman gave consent for the study, the next envelope was opened to assign the participant to either of the 2 groups. A sample-size analysis was performed before initiation of the study. The analysis was based on the intention-to-treat principle. No participants were lost to follow up, and there were no dropouts.
Participants	90 pregnant women, between the 26th and 34th weeks of gestation, with established iron-deficiency anemia who had hemoglobin levels between 8 and 10.5 g/dL and ferritin levels less than 13 g/ L. Women were excluded when serum folate and vitamin B12 levels were found to be less than 4 pg/mL and 100 pg/mL respectively. Anaemia from causes other than iron-deficiency, multiple pregnancy, previous blood transfusion, history of hematological disease, risk of preterm labour, intolerance to iron derivatives, recent administration of iron for the treatment of iron-deficiency anaemia, or current usage of iron supplement were the reasons for other exclusions.
Interventions	Experimental group: the dose for total iron sucrose was calculated from the following formula: weight x (target hemoglobin – actual hemoglobin)x 0.24 + 500 mg. In each infusion, the maximum total dose administered was 200 mg elemental iron in 100 mL 0.9% NaCl, infused in 20–30 minutes. Total dose was administered over 5 days and maximum daily dose administered was 400 mg elemental iron. Most of the women received iron sucrose at the rate of 200 mg every other day. Control group: 3 100 mg iron polymaltose complex (300 mg elemental iron per day) tablets per day orally administered iron were given throughout pregnancy. Both groups were supplemented by 0.5 mg folic acid treatment per day.
Outcomes	The primary outcome measure was hemoglobin concentration on day 28 and at birth. Secondary outcome measures included ferritin levels, the recorded adverse effects, and fetal birthweight.
Notes	
Allocation concealment	A – Adequate

Study	Bayoumeu 2002
Methods	Women were assigned to the group treatment by a randomisation table. Sample size and power calculation was described. Neither the women nor caregivers were blinded to the interventions. It is unclear if the outcome assessor was blinded to the interventions. The trialists reported that 3 (6%) women were excluded from the study and that 2 others where lost to follow up.
Participants	50 pregnant women. Inclusion criteria: pregnant women at 6 months of pregnancy > 18 years, with Hb 8-10 g/dl at 6 months; MCV < 100 fl; ferritin < 50 ug/l (corresponds to iron store of < 500 mg). Exclusion criteria: anaemia not linked to iron deficiency; asthma; cirrhosis; viral hepatitis; multiple pregnancy; risk of premature birth; suspected acute infection; parenteral iron treatment before inclusion; intolerance to iron. Also transport problems etc.

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Characteristics of included studies (*Continued*)

Interventions	Experiment group: IV iron sucrose. Total dose calculated from weight before pregnancy in kg x (target Hb - actual Hb) x 0.24 + 500 mg rounded up to nearest 100 mg. Target Hb set at 120 g/l because of physiological hemodilution during pregnancy. Given in 6 slow IV injections (days 1, 4, 8, 12, 15 and 21). Control group: oral iron. 3 x 80 mg iron sulphate tablets (Tardyferon) per day for 4 weeks (i.e. 240 mg elemental iron a day for 4 weeks). Women asked to note compliance in calendar. "Women were also given 15 mg folic acid per day to prevent an eventual folic-acid deficiency and to eliminate the influence of such a deficiency on the results." "After 4 weeks, physician or midwife decided duration and dose of any continuing iron treatment."
Outcomes	The trial measured haematological response, transferrin level and saturation coefficient, erythrocytic folates, ferritin level, baby's ferritin level and full blood cell count and adverse reactions.
Notes	
Allocation concealment	B – Unclear

Study	**Breymann 2001**
Methods	Women randomly assigned to 2 treatment groups by means of a computer-generated list. It is unclear whether participants, clinicians and outcome assessor were blinded to the interventions. Trial had no withdrawals. No description of the sample size or power calculation was recorded.
Participants	40 pregnant women. Inclusion criteria: pregnant women with Hb < 10 g/dl in 2nd trimester and < 11 g/dl in 3rd trimester; ferritin < 15 ug/l. Exclusion criteria: women with anaemia not caused by iron deficiency, e.g. B12 or folate deficiency; chronic bleeding; renal failure.
Interventions	Women were randomised to receive IV administered iron sucrose (200 mg IV administered twice weekly 72 to 96 hours apart) with vs without adjuvant recombinant human erythropoietin (300 U/kg body weight). All women received orally administered iron sulfate (80 mg twice daily) for = 2 weeks before starting. Random assignment was initiated when the haemoglobin dropped to < 10.0 g/dL despite orally administered iron supplementation. Median durations of therapy were 18 days in group 1 and 25 days in group 2.
Outcomes	Blood index values, maternal outcomes (which cannot be obtained separately for both groups of treatment) and safety were reported.
Notes	
Allocation concealment	B – Unclear

Study	**Dawson 1965**
Methods	Method of allocation was a random-number table. It is not clearly stated how allocation was concealed. Loss to follow up: at 2 weeks: loss: A = 24%; B = 9%; C = 27%. At 4 weeks: loss: A = 48%; B = 39%; C = 38%. At 8 weeks: loss: A = 88%; B = 70%; C = 85%.
Participants	74 pregnant women in the 3rd trimester with haemoglobin with less than 10 g/dl, MCHC under 30% and a marrow aspiration indicating iron deficiency. Women with toxemia, infection or antepartum haemorrhage were excluded. All women received prophylactic folate and oral iron was stopped prior to randomisation. Women were followed for 8 weeks and outcomes assessed at admission, 2, 4 and 8 weeks. Side-effects were assessed during the treatment period.
Interventions	Iron sorbitol-citric acid complex (Jectofer) IM 25 women. Iron dextran (Imferon) IM 23 women. Iron dextran (Imferon) IV 26 women. Dosages of all preparations were calculated to replace iron stores.
Outcomes	Side-effects: 1. pain at injection site; 2. skin discoloration;

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	3. venous thrombosis; 4. nausea or vomiting; 5. headaches; 6. shivering; 7. itching; 8. metallic taste in mouth.
Notes	Other outcomes were not considered due to a high dropout rate. Haemoglobin level data are not included due to 81% dropouts at predelivery. The authors made an additional trial of iron dextran IV vs iron dextran + 50 mg of hydrocortisone in the infusion to assess if this had any effect on the rate of side-effects.
Allocation concealment	B – Unclear

Study	**De Souza 2004**
Methods	Method of allocation generation and concealment are unclear. Neither the women nor treating physicians were blinded to the interventions. Trialists reported that the laboratory was blind to the interventions. 41 (21.5%) women were reported to drop the trial or were lost to follow up and the reasons described. Intention-to-treat analysis was not used. Sample size and power calculation were described.
Participants	150 pregnant women at 16-20 weeks of gestation, with an initial haemoglobin of < 11 g/dL and > 8 g/dL.
Interventions	Women were randomly distributed into 3 groups, 1 receiving daily (300 mg of ferrous sulphate), the 2nd twice-weekly and the 3rd one-weekly iron supplementation for 16 weeks.
Outcomes	The trial measured haemoglobin concentration, MCV and ferritin before and after the treatment.
Notes	
Allocation concealment	B – Unclear

Study	**Kaisi 1988**
Methods	A randomisation list was used to generate the randomisation sequence.
Participants	630 pregnant women. The study was done in a population of indigenous women. Inclusion criteria were: 1. diagnosis of iron-deficiency anaemia defined as haemoglobin under 10 g/dl; MCHC under 32%; hypochromia; poikilocytosis and anisocytosis; 2. age 16 years and above; 3. gestational age under 36 weeks. Exclusion criteria were: 1. history of reaction to parenteral iron; 2. hypersensitivity to iron dextran; 3. asthma history; 4. allergic conditions; 5. hepatic impairment; 6. renal impairment; 7. rheumatoid arthritis; 8. fever. 314 women received the full dose while 309 women received the 2/3 dose. Age, gravidity, parity, duration of pregnancy and basal haemoglobin levels were similar for the groups. Nearly one forth of the women had haemoglobin levels under 7.0 g/dl in both groups.
Interventions	The dose of the 2 studied treatments was determined according to the recommendations of providers. In the intervention group, women received 2/3 of the total dose calculated of iron dextran 'Imferon' while in the control group they received the total dose of iron dextran plus 10 additional ml as suggested for pregnant women. The iron dextran was diluted in 500 ml of 5% dextrose and infused at a steady rate of 40 drops

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	per minute. A test dose was given at the start of each infusion. This test dose was administered at a rate of 5 drops per minute over 10 minutes.
Outcomes	Women were followed up regularly throughout the remaining part of their pregnancy, during delivery and for 16 weeks postpartum. Infants were examined at the time of birth. Maternal haemoglobin levels were assessed at each visit to the antenatal clinic and 6 and 16 weeks after delivery. Cord haemoglobin was measured as well.
Notes	Women were analysed by intention to treat. Loss to follow up for haemoglobin result was 47% so these results were not included in this review. For other clinical outcomes, loss to follow up was 18% and 20% so they were included.
Allocation concealment	B – Unclear

Study	**Komolafe 2003**
Methods	The women were assigned randomly by offering them a choice from sealed envelopes containing computer-generated random numbers. No description of the sample size or power calculation was described and neither the participants nor treating physicians were blinded to the interventions. This trial had no withdrawals.
Participants	60 women at 14-32 weeks of pregnancy were included. Inclusion criteria: PCV 22-26% due to iron-deficiency anaemia. Fe def anaemia defined as: Hb genotype AA; MCV < 75 pg; MCHC < 32 g/dl; blood film - picture of Fe def. Exclusion criteria: symptomatic anaemia; acute malaria; acute urinary tract infection; history of allergy to parenteral Fe; multiple pregnancy atopic individual and haemoglobinopathy.
Interventions	Experiment group: 30 women. IM iron dextran. 50 mg iron dextran into buttock preceded by 25 mg promethazine tablet 30 minutes before. If no untoward reaction after 48 hours, 250 mg (5 ml) iron dextran thrice weekly I = until total dose given. Total dose = Fe (mg) = weight (kg) x Hb deficit (g/dl) x 4.4 + 500. Control group: 30 women Oral Fe: 200 mg ferrous sulphate 3 times daily between meals, with vitamin C 100 mg 3 times daily and 5 mg folic acid. Both groups were treated for 6 weeks.
Outcomes	The trial measured the mean PCV, corrected anaemia at the end of the follow period, the cost of the treatment and the side-effects.
Notes	Results given in % and not specific numbers.
Allocation concealment	B – Unclear

Study	**Kumar 2005**
Methods	Participants were randomly allocated to 2 groups. Method of allocation generation and allocation concealment were unclear. Both the participants and treating physicians were not blinded to the interventions. Sample size considerations were not provided. 47 women in parenteral iron group and 23 women in oral iron group were lost to follow up.
Participants	220 pregnant women were including according to the following criteria. Inclusion criteria: women with gestation period of 16-24 weeks, were selected according to the following inclusion criteria: singleton pregnancy, moderate anemia (Hb 8-11 g%) by cyanmethaemoglobin method, microcytic hypochromic blood smear and willingness for enrollment to the study. Exclusion criteria: the women with anemia due to hemoglobinopathies, chronic bleeding, parasitosis, diseases of liver, cardiovascular system and kidney; medical disorders like tuberculosis, diabetes mellitus; women who had any form of parenteral iron therapy for anemia during pregnancy; women with antepartum hemorrhage and intolerance to test dose (0.5 ml) of IM administration of iron were excluded from the study.

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Characteristics of included studies (*Continued*)

Interventions	Experiment group: IM iron: parenteral iron group were given 2 IM injections of 250 mg elemental iron as iron sorbitol citric acid in a injection volume of 5 ml at an interval of 4-6 weeks in the antenatal clinic. An initial test dose of 0.5 ml was given. If there was no adverse reaction to the test dose, then a full 250 mg dose was given deeply in the outer quadrant of the buttock using Z-tract technique. Control group: oral iron: tablets of 100 mg elemental iron (ferrous sulphate) and 500 Ag of folic acid daily.
Outcomes	The trial measured values of blood indices at 36 weeks as well as mean birthweight, mode of delivery and side-effects.
Notes	
Allocation concealment	B – Unclear

Study	**Mumtaz 2000**
Methods	Randomisation was performed using a random-number generator, and each women was assigned a unique identifier. The women and the investigator were blinded to the allocation of treatment group (daily vs twice weekly) at initial recruitment and the 3 follow-up visits. The appearance of the capsules and the blister packs of the 2 groups were identical. The randomisation code was opened only after the follow up for all participants had been completed. Sample size considerations were provided. This trial had 86 participants, (45%) that did not complete the entire duration of follow up (i.e., 4 follow-up visits). However data on 83.8% of the participants were available for 4 weeks of follow up. Analysis by intention to treat.
Participants	191 pregnant women between the age of 17-35 years, with an initial haemoglobin of < 110 g/L were included. Uneventful obstetric history. All given health education materials on importance of diet in pregnancy.
Interventions	Experiment group: daily iron - plus daily folate. 200 mg iron sulphate (60 mg elemental Fe) each day and 1 mg folate. Control group: twice weekly iron - plus daily folate. 200 mg iron sulphate (60 mg elemental) twice weekly and 1 mg folate. Placebo was given for the rest of the days.
Outcomes	Venous blood samples were taken for complete blood count at each visit and for serum ferritin at the 1st, 3rd and 4th visits. A peripheral film was made to rule out congenital disorders such as thalassemia minor. No information about maternal and fetal outcomes and side-effects was provided.
Notes	There was no difference between the women who dropped out compared with those who continued in the trial in terms of age, initial haemoglobin, parity and in the 2 treatment groups (41 versus 45).
Allocation concealment	A – Adequate

Study	**Ogunbode 1980**
Methods	There was no information on methods of randomisation. No description of the sample size or power calculation was described and both the participants and treating physicians were blinded to the interventions. No participants were reported to have dropped out or were lost to follow up.
Participants	91 women in the first or second trimester of pregnancy with a PCV of 33% or less were randomly allocated to 3 treatment groups.
Interventions	In group A, 32 participants received 200 mg of oral ferrous sulphate thrice daily; in group B 28 participants received 400 mg of oral ferrous sulphate 3 times daily; in group C, 31 women received IM iron poly (sorbitol gluconic acid) complex rerastral (500 mg Fe) on alternate days until completion of the required dose (between 1250 to 2500 mg of iron). No formal formula to calculate the dose was described. All participants received 5 mg of folic acid and 25 mg of pyrimethamine once weekly.
Outcomes	The trial measured the reticulocyte response and haematocrit level.
Notes	
Allocation concealment	B – Unclear

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Characteristics of included studies (*Continued*)

Study	**Oluboyede 1980**
Methods	Participants were allocated by restricted random allocation. There was no further information on methods of randomisation. No description of the sample size or power calculation was described and neither the participants nor treating physicians were blinded to the interventions. One participant from the imferon group was reported to have dropped out due to a severe reaction.
Participants	63 pregnant women with established iron-deficiency anaemia defined as a PCV of 30% or less were included. Hb AA genotype only. Exclusion criteria: if had previously had iron therapy.
Interventions	Experiment group: 32 women. IM ferastral (sorbitol gluconic acid). 500 mg ferestral (5 ml in each buttock) IM on alternate days until completion of required dose. Control group: 31 women. IV imferon (iron dextran). Calculated dose given in 540 ml normal saline and 50 ml promethazine hydrochloride (phenegran) was given IM before infusion. Drip ran slowly for first 30 minutes then 60 drops a minute until completion. Discharged home though 10 kept in. All women received anti-malarial of 25 mg pyrimethamine and 5 mg of folic acid throughout pregnancy.
Outcomes	Weekly or 2-weekly PCV estimations were done on all participants, after 4 weeks of treatment liver function tests were repeated and after 6 weeks bone marrow aspirations were repeated on 21 women. The trial also measured the reticulocyte response in 10 women randomly selected from each group and babies birthweights and any complication within the first week of life.
Notes	
Allocation concealment	B – Unclear

Study	**Singh 1998**
Methods	Women were allocated using sealed envelopes with consecutive numbers.
Participants	First 100 women with diagnosed iron-deficiency anaemia while attending for antenatal care at the National University Hospital, Singapore. Data provided by one of the authors reveals that compared groups had similar age distribution, parity, mean total income, weight, height, history of anaemia in previous pregnancies, history of intrauterine growth retardation in previous pregnancies and similar time-gap between pregnancies. Races were distributed as follows: Chinese (10% parenteral and 6% of oral iron therapy), Malayan (46% and 78% in the same order), Indian (16 and 8%). History of preterm delivery was seen in 16% of the parenteral treatment group and 12% of oral iron group.
Interventions	Total dose iron polymaltose complex - iron dextrin (ferrum hausmann) infusion vs oral therapy with 3 x 200 mg/day iron fumarate. The dose was determined according to the body weight and estimated iron deficiency.
Outcomes	This paper provided data at 36 weeks, delivery and 6 weeks postpartum. The paper provided haematological outcomes. In addition, the publication mentioned some side-effects and similar clinical outcomes in both groups. The authors were contacted and provided precise data on clinical outcomes and side-effects that were included too.
Notes	Dr Kuldip Singh at the National University Hospital - University of Singapore was the contacted author. Contact was established through a search on internet. Further contact is being undertaken to check the units used for serum iron and ferritin estimations, then further comparison tables can be added to this review.
Allocation concealment	A – Adequate

Study	**Sood 1979**
Methods	There was no information on methods of randomisation. No description of the sample size or power calculation was described and researchers kept unmasked the 5 groups. 2 women were reported to have dropped in the group receiving IV Fe due to severe delayed adverse allergic reaction.
Participants	151 pregnant women. Inclusion criteria: pregnant women, 26 + 2 weeks' gestation. Divided into 3 strata according to their Hb concentration: 50-79; 80-109; 110 or above.

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Characteristics of included studies (*Continued*)

	Exclusion criteria: women with chronic illness; with Hb < 50 g/l; who had received haematinics during the last months.
Interventions	Within each stratum they were randomised to one of the following groups. 1. Oral ferrous sulphate providing 120 mg of 120 mg elemental Fe, given once per day 6 weeks. 2. Fe dextran complex providing 100 mg Fe given IM twice per week. 3. Fe as in group 1 + pteroylmonoglutamic acid (5 mg, 6 day/week) + cyanocobalamin (100 µg IM once per 14 day). 4. Fe IM as in group 2 + pteroylmonoglutamic acid + cyanocobalamin as in group 3. 5. Fe dextran complex given IV as a single total dose infusion according to the formula (15 - women's haemoglobin (g/dl)) x (body-weight (kg) x 3) + pteroylmonoglutamic acid + cyanocobalamin as in group 3. Treatment was continued for 10-12 weeks.
Outcomes	Haemoglobin, PCV was estimated 48 before the treatment was started and at least 48 hours after the last injection or tablet was given.
Notes	
Allocation concealment	D – Not used

Study	**Suharno 1993**
Methods	Allocation was done using a random-number list from 1 to 305 and allocating women sequentially in the list. The manufacturers of the active treatments provided placebos. An independent researcher randomly labelled the active and placebo preparations. Coding colours were given to the preparations and these codes were opened once the data for all analyses had been entered in the computer and cleaned.
Participants	305 pregnant women. The study was conducted from April to September 1992 in 20 rural villages in 3 subdistricts of Bogor, West Java. Participants came from middle and low socio-economic groups. They were aged between 17 and 35 years, with parity in the ranges of 0 to 4 and gestational age of 16 to 25 weeks. 572 women met inclusion criteria. 305 participated in the study. Haemoglobin levels of participants were in the range of 8.0 to 10.9 g/dl. Women receiving iron or vitamin A treatments or supplements in the 6 months prior to study were excluded. Outcomes were assessed 2 and 7 days after the last dose of treatment was given (24 to 33 weeks). Participants had similar age, height, weight, pregnancies, parity and gestational age at admission.
Interventions	4 different groups received 2 active treatments at most (factorial design). All preparations were given daily for 8 weeks. 1. 60 mg elemental oral iron (as ferrous sulphate) + vitamin A (2.4 mg of retinol as retinyl palmitate). 2. 60 mg elemental oral iron (as ferrous sulphate) + placebo of vitamin A. 3. Placebo of oral iron + vitamin A (2.4 mg of retinol as retinyl palmitate). 4. Placebo or oral iron + placebo or vitamin A.
Outcomes	Haemoglobin, ferritin and serum iron mean values and standard deviations were extracted for this review from the published paper. Percentage of women that became non-anaemic (Hb > 10.9 g/dl) was counted as a dichotomic variable. Numbers needed to treat were calculated by the authors of this review.
Notes	Results for vitamin A + placebo were not considered since this is part of a different review. Vitamin A combined with iron was included in this review. Serum iron levels were given in umol/l and converted to mg/l by the authors (umol/l x 0.056 = mg/l). Loss to follow up accounted for 17% of the women. Analysis was done by intention to treat.
Allocation concealment	A – Adequate

Study	**Symonds 1969**
Methods	Women were assigned randomly although the method is not clearly specified. Baseline data for the 4 groups compared are very similar.
Participants	103 women attending the Queen Elizabeth Hospital in Woodville, Australia. Inclusion criteria were a gestational age of 32 weeks or less and a haemoglobin level of 10.8 g/dl or less.

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Characteristics of included studies (*Continued*)

Interventions	4 treatment groups were assembled. 1. Ferrous gluconate 108 mg of elemental iron daily divided in 3 doses given orally throughout pregnancy. 2. Ferrogradumet tablets (controlled release) iron tablets with 105 mg elemental iron given once daily throughout pregnancy. 3. Placebo for the controlled release iron tablets provided by the same pharmaceutical laboratory. 4. IV iron-dextran 2% solution. Initial test dose of 2 ml IV followed by 5 injections of 5 ml (100 mg). Participants received controlled-release iron or placebo for the first month. After that time side-effects were evaluated, and then all participants were given a daily dose of active controlled-release oral iron. The trial was masked only the first 2 months and only for these 2 groups.
Outcomes	For this review, side-effects were considered. The other data were incomplete, without reported standard deviations of mean values and irrelevant due to important flaws in the design of the study.
Notes	Haemoglobin results were presented as increases in haemoglobin. Since standard deviations for the values cannot be added to baseline data, the data were not included.
Allocation concealment	B – Unclear

Study	**Wali 2002**
Methods	There was no information on methods of randomisation described and neither the participants nor treating physicians were blinded to the interventions. No description of the sample size or power calculation was provided.
Participants	60 pregnant women with anaemia were included in the study. Inclusion criteria: pregnant women; 12-34 weeks; Fe def anaemia; Hb 5-10 g/dl; PCV < 30%; MCV < 80 fl; MCH < 28 pg. Women with Hb < 7 g/dl (n = 2) were given IV iron sucrose (venofer) as an alternative to blood transfusion; those with Hb 7-10 g/dl were randomised for IV iron or IM iron. Exclusion criteria: chronic diseases; anaemic failure.
Interventions	Experiment group A: 15 women. IV iron sucrose 500 mg for iron storage. Experiment group B: 20 women. IV iron sucrose 200 mg iron. Experiment group C: 25 women IM iron sorbitol with varying doses depending on Hb level; 5 g/dl - 24 injections; 6 g/dl - 22 injections; 7 g/dl - 20 injections; 8 g/dl - 17 injections; 9 g/dl - 14 injections; 10 g/dl - 12 injections; 11 g/dl - 10 injections. After parenteral iron, oral iron given till birth of baby.
Outcomes	The trial outcomes focused on laboratory values (haemoglobin) and side-effects.
Notes	
Allocation concealment	B – Unclear

Study	**Zutschi 2004**
Methods	There was no information on methods of randomisation. No women were reported to have dropped out or were lost to follow up. Neither the women nor treating physicians were blinded to the interventions. No description of the sample size or power calculation was described.
Participants	200 women with uncomplicated pregnancy enrolled at 24-26 weeks of gestation with a haemoglobin of > 8 gm% but < 11 gm% were included. Women dropped out of study if Hb fell below 8 g/l or if severe problems arose.

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Interventions	Group A (100 women) received injectable iron-sorbitol-citrate in 3 IM doses of 150 mg each at 4 weekly intervals and group B (100 women) were given oral iron having 100 mg elemental iron daily for at least 100 days.
Outcomes	The trial measured haemoglobin levels at the time of inclusion into the study, 4 weekly thereafter and at delivery as well as the proportion of caesarean delivery.
Notes	
Allocation concealment	B – Unclear

Hb: haemoglobin
IM: intramuscular
IV: intravenous
MCHC: mean corpuscular haemoglobin concentration
MCV: mean corpuscular volume
PCV: packed cell volume
vs: versus

Characteristics of excluded studies

Study	Reason for exclusion
Al Momen 1996	Not a randomised controlled trial. Sequential allocation.
Allaire 1961	Loss to follow up of 56%. Used quasi-random allocation.
Amir 1983	Excluded: inclusion criteria < 12 gr. No baseline characteristics that lead to infer levels of Hg at the beginning of the study.
Bare 1960	They allocated participants using alternate order. This is not considered random.
Barrada 1991	Insufficient information for critical appraisal was provided. There are no explicit inclusion or exclusion criteria.
Basu 1973	Randomisation method not posed. No information is provided regarding blinding or number of women that completed the trial or that were accounted for each result.
Breymann 1998	Randomised open-label trial.
Breymann 2002	Not an RCT.
Buglanov 1984	No mention of randomisation.
Chanarin 1965	This study addressed megaloblastic anaemia.
Christiansen 1961	Alternate participants; not Hg < 11.0 d/L.
Coelho 2000	No mention that women were anaemic.
Dede 2005	Postpartum iron-deficiency anemia.
Dommisse 1982	Folic acid trial.
Ekstrom 2002	Centers were randomly assign (not women) and only some women had Hb < 11.5 g/dl.
Finzi 1972	No random allocation.
Fochi 1985	Randomisation is not well balanced. The paper does not explain unbalanced groups.
Halksworth 2003	No randomisation method. Evaluate the absorption of iron.
Hamilton 1973	Allocation was done using a haphazard strategy, not a random one.
Hampel 1974	Used a haphazard allocation method (day of diagnosis).
Hawkins 1970	The study evaluates the use of medication in women with hemoglobin levels over 10.5 g/dl and uses non-random strategy for allocation.
Holly 1955	The study is in women with haemoglobin levels over 10 g/dl. Treatment allocation was not random.

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Characteristics of excluded studies (*Continued*)

Izak 1973	Although the authors state that allocation was random, the groups are very different (184, 76 and 22). The authors used an inappropriate control group of healthy women. They do not explain the randomisation method.
Jackson 1982	More than 50% of their women were lost to follow up.
Jaud 1979	Used open-randomisation list. We tried to contact to verify data but it was impossible. Open-randomisation lists are considered inadequate since there is no concealment and it is prone to bias.
Juarez-Vazquez 2002	The trial evaluated folic acid + iron versus iron.
Mahale 1993	This study has dropouts that surpasses the limit established for this review.
Mathan 1979	The trial evaluated group 1 Fe + pteroylmonoglutamic acid and cyanocobalamin versus group 1 + ascorbic acid versus group 1 + calcium caseinate.
Minganti 1995	Sample size: 15 participants. Data not available.
Mukhopadhyay 2004	The trial excludes women with haemoglobin level < 10 g/dL. The mean baseline haemoglobin was 11.3 and 11.6 g/dL in both groups of treatment.
Mukhopadhyay 2004a	Double publication.
Ogunbode 1984	Folic acid trial.
Preziosi 1997	No fundamental data to assess validity.
Reddy 2000	No comparison group.
Ridwan 1996	Health centers were randomised, rather than individuals.
Sharma 2004	No randomisation.
Sood 1975	This study has a high proportion of women lost to follow up exceeding the cut-off point established for this review.
Stein 1991	No fundamental data to assess validity.
Steiner 1977	No information regarding random allocation or allocation concealment. Insufficient baseline data provided.
Szarfarc 2001	Non-anaemic women.
Valli Rani 1995	They used sequential strategy for allocation and not a random one.
Visca 1996	No fundamental data to assess validity.
Von Peiker 1986	The differences between the groups was not iron, but vitamins.
Wu 1998	The numbers of participants in the 3 groups are not similar (93 for maternal, 50 for ferrous sulphate and 35 for ferroids) and is higher at follow up than at the beginning of the trial. It is unclear how they were allocated to the groups and whether therefore they are similar at baseline.
Young 2000	A weekly iron/folate supplement was compared with a standard daily iron/folate supplement in pregnant women living in rural Malawi. Acid folic trial.

ADDITIONAL TABLES

Table 01. FDA iron adverse effects description

Drug Substance	Adverse Effect
Iron	Oral preparations: produces gastrointestinal irritation and abdominal pain with nausea and vomiting, when administered orally. The effect is usually dose related to the amount of elemental iron, rather than the preparation. Diarrhoea and constipation. Better to administer with foods, and to increase doses gradually.

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Table 01. FDA iron adverse effects description (*Continued*)

Drug Substance	Adverse Effect
	Oral liquid preparations may stain teeth. Oral preparations should not be given concomitantly with parenteral preparations. Parenteral preparations: anaphylactoid reactions, peripheral vascular flushing with intravenous administration, tachycardia, hypotension and syncope, thrombophlebitis (higher if given with glucose 5% versus sodium chloride 0.9%), nausea, vomiting, taste disturbance. Delayed reactions may include arthralgia, myalgia, regional lymphadenopathy, chills, fever, paresthesia, dizziness, malaise, headache, nausea, vomiting and haematuria. Intramuscular use in animals has resulted in the development of sarcomas at the injection site. It interacts with enalapril (potentiates adverse systemic reactions) and chloramphenicol.
Iron sulphate (oral)	
Ferrous gluconate (oral)	
Iron fumarate (oral)	
Iron aucrose (intravenous)	In addition to the adverse effects for parenteral preparations: bronchospasm, dyspnoea, myalgia, pruritus, urticaria, rash, reactions in the injection site.
Iron sorbitol	In addition to the adverse effects for parenteral preparations: severe systemic reactions with potentially fatal cardiac complications. Dark urine. Do not administer intravenously.
Iron dextran (intramuscular)	
Iron polymaltose complex -iron dextrin-	
Adjuvant recombinant human erythropoietin	Epoetin: recombinant human erythropoietin. Darbepoetin: derivative of epoetin. Headache, hypertension and seizures, specially in people with poor renal function. Thrombosis at vascular access sites, flu-like symptoms, hyperkalaemia, skin rashes, and rare reports of anaphylactoid reactions.
Iron polymaltose complex (oral)	

†Martindale, The Complete Drug reference. Pharmaceutical Press. 32 ed. London 1999. ‡British National Formulary. Royal Pharmaceutical Society. 49 ed. London, March 2005
‡British National Formulary. Royal Pharmaceutical Society. 49 ed. London, March 2005
†Martindale, The Complete Drug reference. Pharmaceutical Press. 32 ed. London 1999.

ANALYSES

Comparison 01. Oral iron versus placebo

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Anaemic during 2nd trimester	1	125	Relative Risk (Fixed) 95% CI	0.38 [0.26, 0.55]
02 Haemoglobin levels (g/dl)	1	125	Weighted Mean Difference (Fixed) 95% CI	0.80 [0.62, 0.98]
03 Ferritin levels (ug/l)	1	125	Weighted Mean Difference (Fixed) 95% CI	0.70 [0.52, 0.88]
04 Serum iron (mg/l)	1	125	Weighted Mean Difference (Fixed) 95% CI	0.04 [0.03, 0.05]
05 Side-effects	1	51	Relative Risk (Fixed) 95% CI	1.97 [0.66, 5.91]
06 Nausea and vomiting	1	51	Relative Risk (Fixed) 95% CI	4.50 [0.54, 37.54]
07 Constipation	1	51	Relative Risk (Fixed) 95% CI	1.13 [0.32, 4.01]

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08 Abdominal cramps	1	51	Relative Risk (Fixed) 95% CI	5.60 [0.28, 111.15]

Comparison 02. Oral iron + vitamin A versus placebo

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Anaemic during 2nd trimester	1	125	Relative Risk (Fixed) 95% CI	0.04 [0.01, 0.15]
02 Haemoglobin levels (g/dl)	1	125	Weighted Mean Difference (Fixed) 95% CI	1.30 [1.11, 1.49]
03 Ferritin levels (ug/l)	1	125	Weighted Mean Difference (Fixed) 95% CI	0.70 [0.52, 0.88]
04 Serum iron (mg/l)	1	125	Weighted Mean Difference (Fixed) 95% CI	0.08 [0.07, 0.09]

Comparison 03. Oral iron + vitamin A versus oral iron

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Anaemia during second trimester	1	126	Relative Risk (Fixed) 95% CI	0.10 [0.02, 0.41]
02 Haemoglobin levels (g/dl)	1	126	Weighted Mean Difference (Fixed) 95% CI	0.50 [0.31, 0.69]
03 Ferritin (ug/l)	1	126	Weighted Mean Difference (Fixed) 95% CI	0.00 [-0.17, 0.17]
04 Serum iron (mg/l)	1	126	Weighted Mean Difference (Fixed) 95% CI	0.04 [0.03, 0.05]

Comparison 04. Controlled release oral iron versus regular oral iron

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Side-effects	1	49	Relative Risk (Fixed) 95% CI	0.96 [0.40, 2.33]
02 Nausea and vomiting	1	49	Relative Risk (Fixed) 95% CI	0.96 [0.27, 3.41]
03 Constipation	1	49	Relative Risk (Fixed) 95% CI	0.24 [0.03, 2.00]
04 Abdominal cramps	1	49	Relative Risk (Fixed) 95% CI	0.48 [0.05, 4.95]

Comparison 05. Intramuscular iron sorbito-citric acid versus intramuscular dextran

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Pain at injection site	1	48	Relative Risk (Fixed) 95% CI	1.00 [0.58, 1.72]
02 Skin discolouration at injection site	1	48	Relative Risk (Fixed) 95% CI	0.21 [0.07, 0.65]
03 Venous thrombosis	1	48	Relative Risk (Fixed) 95% CI	Not estimable
04 Nausea or vomiting	1	48	Relative Risk (Fixed) 95% CI	0.92 [0.06, 13.87]
05 Headaches	1	48	Relative Risk (Fixed) 95% CI	0.13 [0.02, 0.99]
06 Shivering	1	48	Relative Risk (Fixed) 95% CI	0.31 [0.01, 7.20]
07 Itching	1	48	Relative Risk (Fixed) 95% CI	0.92 [0.26, 3.26]
08 Metallic taste in mouth	1	48	Relative Risk (Fixed) 95% CI	3.68 [0.44, 30.56]

Comparison 06. Intramuscular iron dextran versus intravenous iron dextran

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Pain at injection site	1	49	Relative Risk (Fixed) 95% CI	4.52 [1.45, 14.05]
02 Skin discolouration at injection site	1	49	Relative Risk (Fixed) 95% CI	14.70 [2.08, 103.81]
03 Venous thrombosis	1	49	Relative Risk (Fixed) 95% CI	0.13 [0.01, 2.20]
04 Nausea or vomiting	1	49	Relative Risk (Fixed) 95% CI	0.57 [0.05, 5.83]

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05 Headaches	1	49	Relative Risk (Fixed) 95% CI	3.96 [0.91, 17.17]
06 Shivering	1	49	Relative Risk (Fixed) 95% CI	0.57 [0.05, 5.83]
07 Itching	1	49	Relative Risk (Fixed) 95% CI	1.51 [0.38, 6.04]
08 Metallic taste in mouth	1	49	Relative Risk (Fixed) 95% CI	1.13 [0.07, 17.07]
09 Severe delayed allergic reaction	1	62	Relative Risk (Fixed) 95% CI	0.21 [0.01, 4.26]

Comparison 07. Intramuscular iron sorbitol citric acid versus intravenous iron dextran

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Pain at injection site	1	51	Relative Risk (Fixed) 95% CI	4.51 [1.46, 13.94]
02 Skin discolouration at injection site	1	51	Relative Risk (Fixed) 95% CI	3.12 [0.35, 28.03]
03 Venous thrombosis	1	51	Relative Risk (Fixed) 95% CI	0.12 [0.01, 2.04]
04 Nausea or vomiting	1	51	Relative Risk (Fixed) 95% CI	0.52 [0.05, 5.38]
05 Headaches	1	51	Relative Risk (Fixed) 95% CI	0.52 [0.05, 5.38]
06 Shivering	1	51	Relative Risk (Fixed) 95% CI	0.21 [0.01, 4.12]
07 Itching	1	51	Relative Risk (Fixed) 95% CI	1.39 [0.34, 5.58]
08 Metallic taste in mouth	1	51	Relative Risk (Fixed) 95% CI	4.16 [0.50, 34.71]

Comparison 08. Intravenous iron versus placebo

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Side-effects	1	54	Relative Risk (Fixed) 95% CI	0.75 [0.19, 3.04]
02 Nausea or vomiting	1	54	Relative Risk (Fixed) 95% CI	0.33 [0.01, 7.84]
03 Constipation	1	54	Relative Risk (Fixed) 95% CI	0.25 [0.03, 2.09]
04 Abdominal cramps	1	54	Relative Risk (Fixed) 95% CI	Not estimable

Comparison 09. Intravenous iron versus regular oral iron

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Side-effects	1	51	Relative Risk (Fixed) 95% CI	0.38 [0.11, 1.31]
02 Nausea or vomiting or epigastric discomfort	3	244	Relative Risk (Fixed) 95% CI	0.33 [0.15, 0.74]
03 Constipation	2	151	Relative Risk (Fixed) 95% CI	0.08 [0.02, 0.43]
04 Abdominal cramps	1	51	Relative Risk (Fixed) 95% CI	0.18 [0.01, 3.54]
05 Diarrhoea	3	237	Relative Risk (Fixed) 95% CI	0.16 [0.03, 0.86]
06 Haemoglobin at 36 weeks	0	0	Weighted Mean Difference (Fixed) 95% CI	Not estimable
07 Blood transfusion required	2	137	Relative Risk (Fixed) 95% CI	0.33 [0.03, 3.06]
08 Neonates mean hemoglobin	1	47	Weighted Mean Difference (Fixed) 95% CI	-0.15 [-1.37, 1.07]
09 Maternal haemoglobin at birth	1	90	Weighted Mean Difference (Fixed) 95% CI	0.75 [0.34, 1.16]
10 Maternal haemoglobin at 6 weeks	0	0	Weighted Mean Difference (Fixed) 95% CI	Not estimable
11 Neonates ferritin level	1	47	Weighted Mean Difference (Fixed) 95% CI	-2.00 [-62.36, 58.36]
12 Maternal haemoglobin at 4 weeks	2	137	Weighted Mean Difference (Fixed) 95% CI	0.60 [0.33, 0.87]
13 Maternal mortality	1	100	Relative Risk (Fixed) 95% CI	Not estimable
14 Preterm labour	1	100	Relative Risk (Fixed) 95% CI	Not estimable
15 Caesarean section	2	190	Relative Risk (Fixed) 95% CI	0.88 [0.46, 1.67]
16 Operative vaginal birth	1	100	Relative Risk (Fixed) 95% CI	1.50 [0.26, 8.60]

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17 Postpartum haemorrhage	2	147	Relative Risk (Fixed) 95% CI	0.87 [0.34, 2.26]
18 Low birthweight (under 2500 g)	1	100	Relative Risk (Fixed) 95% CI	Not estimable
19 Neonatal birthweight	3	237	Weighted Mean Difference (Fixed) 95% CI	15.09 [-111.73, 141.91]
20 Small-for-gestational age	1	100	Relative Risk (Fixed) 95% CI	1.60 [0.56, 4.56]
21 Five minute Apgar score under seven	1	100	Relative Risk (Fixed) 95% CI	1.00 [0.06, 15.55]
22 Neonatal mortality	2	147	Relative Risk (Fixed) 95% CI	Not estimable
23 Haemoglobin level > 12 g/dL at 30 days	1	47	Relative Risk (Fixed) 95% CI	0.72 [0.18, 2.87]
24 Gestational hypertension	1	90	Relative Risk (Fixed) 95% CI	5.00 [0.25, 101.31]
25 Gestational diabetes	1	90	Relative Risk (Fixed) 95% CI	0.20 [0.01, 4.05]
26 Haemoglobin level > 11 g/dL at birth	1	90	Relative Risk (Fixed) 95% CI	1.54 [1.21, 1.94]
27 Severe delayed allergic reaction	1	67	Relative Risk (Fixed) 95% CI	5.45 [0.27, 109.49]
28 Arthralgia	1	90	Relative Risk (Fixed) 95% CI	1.00 [0.06, 15.50]

Comparison 10. Intravenous iron versus controlled release oral iron

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Side-effects	1	52	Relative Risk (Fixed) 95% CI	0.40 [0.12, 1.37]
02 Nausea or vomiting	1	52	Relative Risk (Fixed) 95% CI	0.10 [0.01, 1.82]
03 Constipation	1	52	Relative Risk (Fixed) 95% CI	0.93 [0.06, 14.03]
04 Abdominal cramps	1	52	Relative Risk (Fixed) 95% CI	0.31 [0.01, 7.26]

Comparison 11. Intravenous iron + hydrocortisone versus intravenous iron

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Tenderness or erythema	1	30	Relative Risk (Fixed) 95% CI	5.00 [0.26, 96.13]
02 Venous thrombosis	1	30	Relative Risk (Fixed) 95% CI	0.09 [0.01, 1.51]

Comparison 12. 2/3 dose intravenous iron versus full dose intravenous iron

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Allergic reaction during infusion	1	623	Relative Risk (Fixed) 95% CI	0.66 [0.35, 1.25]
02 Allergic reaction after infusion	1	623	Relative Risk (Fixed) 95% CI	0.62 [0.45, 0.86]
03 Life-threatening allergic reaction during infusion	1	623	Relative Risk (Fixed) 95% CI	2.54 [0.50, 13.00]
04 Discomfort needing analgesics after infusion	1	623	Relative Risk (Fixed) 95% CI	0.49 [0.27, 0.89]
05 Immobilised by painful joints	1	623	Relative Risk (Fixed) 95% CI	0.79 [0.30, 2.10]
06 Non-live births	1	507	Relative Risk (Fixed) 95% CI	0.85 [0.36, 2.03]
07 Neonatal death	1	507	Relative Risk (Fixed) 95% CI	0.52 [0.13, 2.07]
08 Stillbirth	1	507	Relative Risk (Fixed) 95% CI	0.70 [0.25, 1.93]
09 Spontaneous abortion	1	507	Relative Risk (Fixed) 95% CI	3.13 [0.33, 29.92]

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Comparison 13. Intravenous iron sucrose with adjuvant recombinant human erythropoietin versus intravenous iron sucrose

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Hb < 11 g/dl at 4 weeks	1	40	Relative Risk (Fixed) 95% CI	0.20 [0.03, 1.56]
02 Mean corpuscular volume	1	40	Weighted Mean Difference (Fixed) 95% CI	6.30 [2.96, 9.64]
03 Caesarean section	1	40	Relative Risk (Fixed) 95% CI	1.00 [0.39, 2.58]
04 Metallic taste	1	40	Relative Risk (Fixed) 95% CI	0.50 [0.05, 5.08]
05 Warm feeling	1	40	Relative Risk (Fixed) 95% CI	1.00 [0.07, 14.90]
06 Birthweight	1	40	Weighted Mean Difference (Fixed) 95% CI	-130.00 [-380.44, 120.44]
07 Birth < 37 weeks	1	40	Relative Risk (Fixed) 95% CI	0.33 [0.01, 7.72]
08 Maternal mean blood pressure	1	40	Weighted Mean Difference (Fixed) 95% CI	-0.20 [-5.02, 4.62]
09 Need transfusion	1	40	Relative Risk (Fixed) 95% CI	Not estimable

Comparison 14. Intramuscular iron sorbitol citric acid versus oral iron

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Not anaemic at term	1	200	Relative Risk (Fixed) 95% CI	1.23 [1.01, 1.48]
02 Mean maternal haemoglobin at birth	1	200	Weighted Mean Difference (Fixed) 95% CI	0.54 [0.30, 0.78]
03 Mean maternal hematocrit level at birth	1	200	Weighted Mean Difference (Fixed) 95% CI	1.40 [0.67, 2.13]
04 Caesarean section	1	200	Relative Risk (Fixed) 95% CI	1.09 [0.66, 1.81]
05 Haematocrit (%) at 4 weeks of treatment	1	56	Weighted Mean Difference (Fixed) 95% CI	1.25 [-0.03, 2.53]
06 Haematocrit (%) at 8 weeks of treatment	1	59	Weighted Mean Difference (Fixed) 95% CI	2.62 [1.26, 3.98]
07 Haematocrit (%) at 4 weeks of treatment	1	56	Weighted Mean Difference (Fixed) 95% CI	1.25 [-0.03, 2.53]
08 Haematocrit (%) at 8 weeks of treatment	1	59	Weighted Mean Difference (Fixed) 95% CI	2.60 [1.02, 4.18]

Comparison 15. Intramuscular iron dextran versus oral iron + vitamin C + folic acid

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Haematocrit	1	60	Weighted Mean Difference (Fixed) 95% CI	4.47 [3.67, 5.27]
02 Not anaemic at 6 weeks (packed cell volume > 33%)	1	60	Relative Risk (Fixed) 95% CI	11.00 [1.51, 79.96]

Comparison 16. Intramuscular iron sorbitol citric acid versus oral iron + folic acid

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Mean haemoglobin at 36 weeks	1	150	Weighted Mean Difference (Fixed) 95% CI	-0.26 [-0.48, -0.04]
02 Haemoglobin > 11 g/dL at 36 weeks	1	150	Relative Risk (Fixed) 95% CI	0.82 [0.64, 1.06]
03 Caesarean section	1	150	Relative Risk (Fixed) 95% CI	1.67 [0.41, 6.73]
04 Mean birthweight (kg)	1	150	Weighted Mean Difference (Fixed) 95% CI	-20.00 [-164.35, 124.35]

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05 Diarrhoea	1	150	Relative Risk (Fixed) 95% CI	0.09 [0.01, 1.62]
06 Constipation	1	150	Relative Risk (Fixed) 95% CI	0.06 [0.00, 1.00]
07 Dyspepsia	1	150	Relative Risk (Fixed) 95% CI	0.05 [0.00, 0.89]
08 Local site mainly pain	1	150	Relative Risk (Fixed) 95% CI	125.00 [7.87, 1984.19]
09 Staining	1	150	Relative Risk (Fixed) 95% CI	113.00 [7.11, 1795.82]
10 Arthralgia	1	150	Relative Risk (Fixed) 95% CI	13.00 [0.75, 226.73]
11 Itching and rash	1	150	Relative Risk (Fixed) 95% CI	29.00 [1.76, 477.47]
12 Fever	1	150	Relative Risk (Fixed) 95% CI	17.00 [1.00, 289.34]
13 Malaise	1	150	Relative Risk (Fixed) 95% CI	15.00 [0.87, 258.02]
14 Vaso-vagal due to apprehension	1	150	Relative Risk (Fixed) 95% CI	9.00 [0.49, 164.29]
15 Systemic ache	1	150	Relative Risk (Fixed) 95% CI	23.00 [1.38, 383.37]
16 Haemoglobin > 12 g/dL at 36 weeks	1	150	Relative Risk (Fixed) 95% CI	0.52 [0.27, 1.01]

Comparison 17. Oral iron daily versus oral iron twice weekly

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Haemoglobin level at 4 weeks	1	160	Weighted Mean Difference (Fixed) 95% CI	0.54 [0.14, 0.94]
02 Haemoglobin level at 8 weeks	1	129	Weighted Mean Difference (Fixed) 95% CI	1.17 [0.67, 1.67]
03 Haemoglobin level at 12 weeks	1	105	Weighted Mean Difference (Fixed) 95% CI	1.27 [0.68, 1.86]
04 Haemoglobin level at 16 weeks	1	102	Weighted Mean Difference (Fixed) 95% CI	0.30 [-0.01, 0.61]
05 Haemoglobin level > 11 g/dL at 16 weeks of treatment	1	102	Relative Risk (Fixed) 95% CI	1.38 [0.86, 2.23]
06 Treatment failure (haemoglobin < 10 g/dL) at 16 weeks	1	102	Relative Risk (Fixed) 95% CI	0.15 [0.02, 1.21]

Comparison 18. Oral iron daily versus oral iron once week

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Haemoglobin level at 16 weeks	1	97	Weighted Mean Difference (Fixed) 95% CI	0.70 [0.36, 1.04]
02 Haemoglobin level > 11 g/dL at 16 weeks of treatment	1	97	Relative Risk (Fixed) 95% CI	1.73 [1.00, 3.01]
03 Treatment failure (haemoglobin < 10 g/dL) at 16 weeks	1	97	Relative Risk (Fixed) 95% CI	0.05 [0.01, 0.35]

Comparison 19. Oral iron twice week versus oral iron once week

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Haemoglobin level at 16 weeks	1	101	Weighted Mean Difference (Fixed) 95% CI	0.40 [0.03, 0.77]
02 Haemoglobin level > 11 g/dL at 16 weeks of treatment	1	101	Relative Risk (Fixed) 95% CI	1.25 [0.69, 2.28]
03 Treatment Failure (haemoglobin < 10 g/dL) at 16 weeks	1	101	Relative Risk (Fixed) 95% CI	0.32 [0.15, 0.68]

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Comparison 20. Intravenous iron sucrose 500 mg versus intravenous iron sucrose 200 mg

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Haemoglobin level at delivery	1	35	Weighted Mean Difference (Fixed) 95% CI	0.50 [-0.18, 1.18]
02 Haemoglobin level > 11g/dL at delivery	1	35	Relative Risk (Fixed) 95% CI	1.14 [0.78, 1.68]
03 Moderate abdominal pain	1	35	Relative Risk (Fixed) 95% CI	1.33 [0.09, 19.64]

Comparison 21. Intravenous iron sucrose 500 mg versus intramuscular iron sorbitol

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Maternal haemoglobin level at birth	1	40	Weighted Mean Difference (Fixed) 95% CI	1.60 [0.87, 2.33]
02 Haemoglobin level > 11g/dL at delivery	1	40	Relative Risk (Fixed) 95% CI	2.86 [1.45, 5.63]

Comparison 22. Intravenous iron sucrose 200 mg versus intramuscular iron sorbitol

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Haemoglobin level at delivery	1	45	Weighted Mean Difference (Fixed) 95% CI	1.10 [0.49, 1.71]
02 Haemoglobin level > 11 g/dL at delivery	1	45	Relative Risk (Fixed) 95% CI	2.50 [1.25, 4.99]

Comparison 23. Oral ferrous sulphate iron 1200 mg/day versus 600 mg/day

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Haematocrit (%) at 4 weeks of treatment	1	56	Weighted Mean Difference (Fixed) 95% CI	0.37 [-0.77, 1.51]
02 Haematocrit (%) at 8 weeks of treatment	1	56	Weighted Mean Difference (Fixed) 95% CI	0.02 [-1.03, 1.07]

Comparison 24. Oral ferrous sulphate (300 mg) versus ferroids (525 mg)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Haemoglobin level at birth	0	0	Weighted Mean Difference (Fixed) 95% CI	Not estimable

Comparison 25. Intramuscular iron sorbitol-glu acid versus intravenous iron dextran

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Haematocrit (%) at 4 weeks of treatment	1	59	Weighted Mean Difference (Fixed) 95% CI	2.18 [0.77, 3.59]
02 Haematocrit (%) at 8 weeks of treatment	1	43	Weighted Mean Difference (Fixed) 95% CI	1.48 [0.15, 2.81]
03 Neonatal jaundice	1	62	Relative Risk (Fixed) 95% CI	0.94 [0.06, 14.33]
04 Viral hepatitis	1	62	Relative Risk (Fixed) 95% CI	2.82 [0.12, 66.62]
05 Severe allergic reaction	1	62	Relative Risk (Fixed) 95% CI	0.31 [0.01, 7.40]

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INDEX TERMS

Medical Subject Headings (MeSH)

Anemia, Iron-Deficiency [*therapy]; Injections, Intramuscular; Injections, Intravenous; Iron Compounds [*administration & dosage; adverse effects]; Pregnancy Complications, Hematologic [*therapy]; Randomized Controlled Trials

MeSH check words

Female; Humans; Pregnancy

COVER SHEET

Title	Treatments for iron-deficiency anaemia in pregnancy
Authors	Reveiz L, Gyte GML, Cuervo LG
Contribution of author(s)	For the 2006 update, Ludovic Reveiz and Gill Gyte appraised the papers independently. Ludovic Reveiz took the lead on writing the review, with Gill Gyte and Luis Gabriel Cuervo providing comments on the various drafts, and revised the review in response to the editorial feedback. The first published review was prepared by Luis Gabriel Cuervo and Kassam Mahomed, and cited as: Cuervo LG, Mahomed K. Treatments for iron deficiency anaemia in pregnancy. Cochrane Database of Systematic Reviews 2001, Issue 2. Art. No.: CD003094. DOI: 10.1002/14651858.CD003094.
Issue protocol first published	1999/4
Review first published	2001/2
Date of most recent amendment	19 February 2007
Date of most recent SUBSTANTIVE amendment	13 February 2007
What's New	February 2007 This update is based on a search run in December 2005, which identified twelve new trials (Al 2005; Bayoumeu 2002; Breymann 2001; De Souza 2004; Komolafe 2003; Kumar 2005; Mumtaz 2000; Ogunbode 1980; Oluboyede 1980; Sood 1979; Wali 2002; Zutschi 2004). There are now a total of 17 trials included in the review. The inclusion of these trials have generally not changed the conclusions although there are now concerns about possible important adverse effects. . An updated search of the Pregnancy and Childbirth Group's Trials Register on 31 January 2007 identified seven new trial reports which have been added to the awaiting assessment section for assessment in the next update. Ludovic Reveiz is now the guarantor of the review.
Date new studies sought but none found	Information not supplied by author
Date new studies found but not yet included/excluded	31 January 2007
Date new studies found and included/excluded	Information not supplied by author
Date authors' conclusions section amended	Information not supplied by author
Contact address	Dr Ludovic Reveiz Coordinator Project Research Unit

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GRAPHS AND OTHER TABLES

Analysis 01.01. Comparison 01 Oral iron versus placebo, Outcome 01 Anaemic during 2nd trimester

Review: Treatments for iron-deficiency anaemia in pregnancy
Comparison: 01 Oral iron versus placebo
Outcome: 01 Anaemic during 2nd trimester

Study	Oral iron n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Suharno 1993	20/63	52/62		100.0	0.38 [0.26, 0.55]
Total (95% CI)	63	62		100.0	0.38 [0.26, 0.55]
Total events: 20 (Oral iron), 52 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=5.04 p<0.00001					

Analysis 01.02. Comparison 01 Oral iron versus placebo, Outcome 02 Haemoglobin levels (g/dl)

Review: Treatments for iron-deficiency anaemia in pregnancy
Comparison: 01 Oral iron versus placebo
Outcome: 02 Haemoglobin levels (g/dl)

Study	Oral iron N	Mean(SD)	Placebo N	Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Suharno 1993	63	11.30 (0.52)	62	10.50 (0.51)		100.0	0.80 [0.62, 0.98]
Total (95% CI)	63		62			100.0	0.80 [0.62, 0.98]
Test for heterogeneity: not applicable							
Test for overall effect z=8.68 p<0.00001							

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Analysis 01.03. Comparison 01 Oral iron versus placebo, Outcome 03 Ferritin levels (ug/l)

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 01 Oral iron versus placebo

Outcome: 03 Ferritin levels (ug/l)

Study	Oral iron N	Oral iron Mean(SD)	Placebo N	Placebo Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Suharno 1993	63	3.30 (0.50)	62	2.60 (0.50)		100.0	0.70 [0.52, 0.88]
Total (95% CI)	63		62			100.0	0.70 [0.52, 0.88]

Test for heterogeneity: not applicable

Test for overall effect z=7.83 p<0.00001

Analysis 01.04. Comparison 01 Oral iron versus placebo, Outcome 04 Serum iron (mg/l)

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 01 Oral iron versus placebo

Outcome: 04 Serum iron (mg/l)

Study	Oral iron N	Oral iron Mean(SD)	Placebo N	Placebo Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Suharno 1993	63	0.43 (0.04)	62	0.39 (0.02)		100.0	0.04 [0.03, 0.05]
Total (95% CI)	63		62			100.0	0.04 [0.03, 0.05]

Test for heterogeneity: not applicable

Test for overall effect z=7.09 p<0.00001

Analysis 01.05. Comparison 01 Oral iron versus placebo, Outcome 05 Side-effects

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 01 Oral iron versus placebo

Outcome: 05 Side-effects

Study	Oral iron n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Symonds 1969	7/24	4/27		100.0	1.97 [0.66, 5.91]
Total (95% CI)	24	27		100.0	1.97 [0.66, 5.91]

Total events: 7 (Oral iron), 4 (Placebo)

Test for heterogeneity: not applicable

Test for overall effect z=1.21 p=0.2

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Analysis 01.06. Comparison 01 Oral iron versus placebo, Outcome 06 Nausea and vomiting

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 01 Oral iron versus placebo

Outcome: 06 Nausea and vomiting

Study	Oral iron n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Symonds 1969	4/24	1/27		100.0	4.50 [0.54, 37.54]
Total (95% CI)	24	27		100.0	4.50 [0.54, 37.54]
Total events: 4 (Oral iron), 1 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.39 p=0.2					

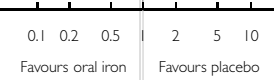
Analysis 01.07. Comparison 01 Oral iron versus placebo, Outcome 07 Constipation

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 01 Oral iron versus placebo

Outcome: 07 Constipation

Study	Oral iron n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Symonds 1969	4/24	4/27		100.0	1.13 [0.32, 4.01]
Total (95% CI)	24	27		100.0	1.13 [0.32, 4.01]
Total events: 4 (Oral iron), 4 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.18 p=0.9					



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Analysis 01.08. Comparison 01 Oral iron versus placebo, Outcome 08 Abdominal cramps

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 01 Oral iron versus placebo

Outcome: 08 Abdominal cramps

Study	Oral iron n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Symonds 1969	2/24	0/27		100.0	5.60 [0.28, 111.15]
Total (95% CI)	24	27		100.0	5.60 [0.28, 111.15]
Total events: 2 (Oral iron), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.13 p=0.3					

Analysis 02.01. Comparison 02 Oral iron + vitamin A versus placebo, Outcome 01 Anaemic during 2nd trimester

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 02 Oral iron + vitamin A versus placebo

Outcome: 01 Anaemic during 2nd trimester

Study	Oral iron + vit A n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Suharno 1993	2/63	52/62		100.0	0.04 [0.01, 0.15]
Total (95% CI)	63	62		100.0	0.04 [0.01, 0.15]
Total events: 2 (Oral iron + vit A), 52 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=4.69 p<0.00001					

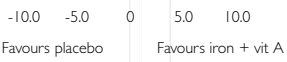
Analysis 02.02. Comparison 02 Oral iron + vitamin A versus placebo, Outcome 02 Haemoglobin levels (g/dl)

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 02 Oral iron + vitamin A versus placebo

Outcome: 02 Haemoglobin levels (g/dl)

Study	Oral iron + vit A N	Mean(SD)	Placebo N	Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Suharno 1993	63	11.80 (0.55)	62	10.50 (0.51)		100.0	1.30 [1.11, 1.49]
Total (95% CI)	63		62			100.0	1.30 [1.11, 1.49]
Test for heterogeneity: not applicable							
Test for overall effect z=13.71 p<0.00001							



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Analysis 02.03. Comparison 02 Oral iron + vitamin A versus placebo, Outcome 03 Ferritin levels (ug/l)

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 02 Oral iron + vitamin A versus placebo

Outcome: 03 Ferritin levels (ug/l)

Study	Oral iron + vit A N	Oral iron + vit A Mean(SD)	Placebo N	Placebo Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Suharno 1993	63	3.30 (0.50)	62	2.60 (0.50)		100.0	0.70 [0.52, 0.88]
Total (95% CI)	63		62			100.0	0.70 [0.52, 0.88]

Test for heterogeneity: not applicable

Test for overall effect z=7.83 p<0.00001

Analysis 02.04. Comparison 02 Oral iron + vitamin A versus placebo, Outcome 04 Serum iron (mg/l)

Review: Treatments for iron-deficiency anaemia in pregnancy

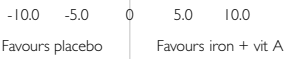
Comparison: 02 Oral iron + vitamin A versus placebo

Outcome: 04 Serum iron (mg/l)

Study	Oral iron + vit A N	Oral iron + vit A Mean(SD)	Placebo N	Placebo Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Suharno 1993	63	0.47 (0.04)	62	0.39 (0.02)		100.0	0.08 [0.07, 0.09]
Total (95% CI)	63		62			100.0	0.08 [0.07, 0.09]

Test for heterogeneity: not applicable

Test for overall effect z=14.18 p<0.00001



Analysis 03.01. Comparison 03 Oral iron + vitamin A versus oral iron, Outcome 01 Anaemia during second trimester

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 03 Oral iron + vitamin A versus oral iron

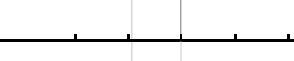
Outcome: 01 Anaemia during second trimester

Study	Oral iron + vit A n/N	Oral iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Suharno 1993	2/63	20/63		100.0	0.10 [0.02, 0.41]
Total (95% CI)	63	63		100.0	0.10 [0.02, 0.41]

Total events: 2 (Oral iron + vit A), 20 (Oral iron)

Test for heterogeneity: not applicable

Test for overall effect z=3.20 p=0.001



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Analysis 03.02. Comparison 03 Oral iron + vitamin A versus oral iron, Outcome 02 Haemoglobin levels (g/dl)

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 03 Oral iron + vitamin A versus oral iron

Outcome: 02 Haemoglobin levels (g/dl)

Study	Oral iron + vit A		Oral iron		Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	(%)	95% CI
Suharno 1993	63	11.80 (0.55)	63	11.30 (0.52)		100.0	0.50 [0.31, 0.69]
Total (95% CI)	63		63			100.0	0.50 [0.31, 0.69]
Test for heterogeneity: not applicable							
Test for overall effect z=5.24 p<0.00001							

Analysis 03.03. Comparison 03 Oral iron + vitamin A versus oral iron, Outcome 03 Ferritin (ug/l)

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 03 Oral iron + vitamin A versus oral iron

Outcome: 03 Ferritin (ug/l)

Study	Oral iron + vit A		Oral iron		Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	(%)	95% CI
Suharno 1993	63	3.30 (0.50)	63	3.30 (0.50)		100.0	0.00 [-0.17, 0.17]
Total (95% CI)	63		63			100.0	0.00 [-0.17, 0.17]
Test for heterogeneity: not applicable							
Test for overall effect z=0.00 p=1							

Analysis 03.04. Comparison 03 Oral iron + vitamin A versus oral iron, Outcome 04 Serum iron (mg/l)

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 03 Oral iron + vitamin A versus oral iron

Outcome: 04 Serum iron (mg/l)

Study	Oral iron + vit A		Oral iron		Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	(%)	95% CI
Suharno 1993	63	0.47 (0.04)	63	0.43 (0.04)		100.0	0.04 [0.03, 0.05]
Total (95% CI)	63		63			100.0	0.04 [0.03, 0.05]
Test for heterogeneity: not applicable							
Test for overall effect z=5.61 p<0.00001							

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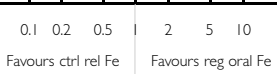
Analysis 04.01. Comparison 04 Controlled release oral iron versus regular oral iron, Outcome 01 Side-effects

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 04 Controlled release oral iron versus regular oral iron

Outcome: 01 Side-effects

Study	Ctrl release iron n/N	Regular oral iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Symonds 1969	7/25	7/24		100.0	0.96 [0.40, 2.33]
Total (95% CI)	25	24		100.0	0.96 [0.40, 2.33]
Total events: 7 (Ctrl release iron), 7 (Regular oral iron)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.09 p=0.9					



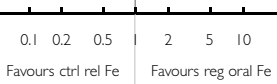
Analysis 04.02. Comparison 04 Controlled release oral iron versus regular oral iron, Outcome 02 Nausea and vomiting

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 04 Controlled release oral iron versus regular oral iron

Outcome: 02 Nausea and vomiting

Study	Ctrl release iron n/N	Regular oral iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Symonds 1969	4/25	4/24		100.0	0.96 [0.27, 3.41]
Total (95% CI)	25	24		100.0	0.96 [0.27, 3.41]
Total events: 4 (Ctrl release iron), 4 (Regular oral iron)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.06 p=0.9					



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Analysis 04.03. Comparison 04 Controlled release oral iron versus regular oral iron, Outcome 03 Constipation

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 04 Controlled release oral iron versus regular oral iron

Outcome: 03 Constipation

Study	Ctrl release iron n/N	Regular oral iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Symonds 1969	1/25	4/24		100.0	0.24 [0.03, 2.00]
Total (95% CI)	25	24		100.0	0.24 [0.03, 2.00]
Total events: 1 (Ctrl release iron), 4 (Regular oral iron)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.32 p=0.2					

Analysis 04.04. Comparison 04 Controlled release oral iron versus regular oral iron, Outcome 04 Abdominal cramps

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 04 Controlled release oral iron versus regular oral iron

Outcome: 04 Abdominal cramps

Study	Ctrl release iron n/N	Regular oral iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Symonds 1969	1/25	2/24		100.0	0.48 [0.05, 4.95]
Total (95% CI)	25	24		100.0	0.48 [0.05, 4.95]
Total events: 1 (Ctrl release iron), 2 (Regular oral iron)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.62 p=0.5					

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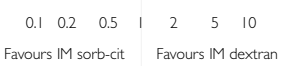
Analysis 05.01. Comparison 05 Intramuscular iron sorbito-citric acid versus intramuscular dextran, Outcome 01 Pain at injection site

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 05 Intramuscular iron sorbito-citric acid versus intramuscular dextran

Outcome: 01 Pain at injection site

Study	IM iron sorb-cit n/N	IM iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dawson 1965	13/25	12/23		100.0	1.00 [0.58, 1.72]
Total (95% CI)	25	23		100.0	1.00 [0.58, 1.72]
Total events: 13 (IM iron sorb-cit), 12 (IM iron dextran)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.01 p=1					



Analysis 05.02. Comparison 05 Intramuscular iron sorbito-citric acid versus intramuscular dextran, Outcome 02 Skin discolouration at injection site

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 05 Intramuscular iron sorbito-citric acid versus intramuscular dextran

Outcome: 02 Skin discolouration at injection site

Study	IM iron sorb-cit n/N	IM iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dawson 1965	3/25	13/23		100.0	0.21 [0.07, 0.65]
Total (95% CI)	25	23		100.0	0.21 [0.07, 0.65]
Total events: 3 (IM iron sorb-cit), 13 (IM iron dextran)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.71 p=0.007					

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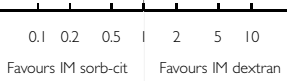
Analysis 05.03. Comparison 05 Intramuscular iron sorbito-citric acid versus intramuscular dextran, Outcome 03 Venous thrombosis

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 05 Intramuscular iron sorbito-citric acid versus intramuscular dextran

Outcome: 03 Venous thrombosis

Study	IM iron sorb-cit n/N	IM iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× Dawson 1965	0/25	0/23		0.0	Not estimable
Total (95% CI)	25	23		0.0	Not estimable
Total events: 0 (IM iron sorb-cit), 0 (IM iron dextran)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



Analysis 05.04. Comparison 05 Intramuscular iron sorbito-citric acid versus intramuscular dextran, Outcome 04 Nausea or vomiting

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 05 Intramuscular iron sorbito-citric acid versus intramuscular dextran

Outcome: 04 Nausea or vomiting

Study	IM iron sorb-cit n/N	IM iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dawson 1965	1/25	1/23		100.0	0.92 [0.06, 13.87]
Total (95% CI)	25	23		100.0	0.92 [0.06, 13.87]
Total events: 1 (IM iron sorb-cit), 1 (IM iron dextran)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.06 p=1					

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Analysis 05.05. Comparison 05 Intramuscular iron sorbito-citric acid versus intramuscular dextran, Outcome 05 Headaches

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 05 Intramuscular iron sorbito-citric acid versus intramuscular dextran

Outcome: 05 Headaches

Study	IM iron sorb-cit n/N	IM iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dawson 1965	1/25	7/23		100.0	0.13 [0.02, 0.99]
Total (95% CI)	25	23		100.0	0.13 [0.02, 0.99]
Total events: 1 (IM iron sorb-cit), 7 (IM iron dextran)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.97 p=0.05					

Analysis 05.06. Comparison 05 Intramuscular iron sorbito-citric acid versus intramuscular dextran, Outcome 06 Shivering

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 05 Intramuscular iron sorbito-citric acid versus intramuscular dextran

Outcome: 06 Shivering

Study	IM iron sorb-cit n/N	IM iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dawson 1965	0/25	1/23		100.0	0.31 [0.01, 7.20]
Total (95% CI)	25	23		100.0	0.31 [0.01, 7.20]
Total events: 0 (IM iron sorb-cit), 1 (IM iron dextran)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.73 p=0.5					

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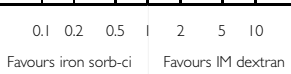
Analysis 05.07. Comparison 05 Intramuscular iron sorbito-citric acid versus intramuscular dextran, Outcome 07 Itching

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 05 Intramuscular iron sorbito-citric acid versus intramuscular dextran

Outcome: 07 Itching

Study	IM iron sorb-cit n/N	IM iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dawson 1965	4/25	4/23		100.0	0.92 [0.26, 3.26]
Total (95% CI)	25	23		100.0	0.92 [0.26, 3.26]
Total events: 4 (IM iron sorb-cit), 4 (IM iron dextran)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.13 p=0.9					



Analysis 05.08. Comparison 05 Intramuscular iron sorbito-citric acid versus intramuscular dextran, Outcome 08 Metallic taste in mouth

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 05 Intramuscular iron sorbito-citric acid versus intramuscular dextran

Outcome: 08 Metallic taste in mouth

Study	IM iron sorb-cit n/N	IM iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dawson 1965	4/25	1/23		100.0	3.68 [0.44, 30.56]
Total (95% CI)	25	23		100.0	3.68 [0.44, 30.56]
Total events: 4 (IM iron sorb-cit), 1 (IM iron dextran)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.21 p=0.2					

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Analysis 06.01. Comparison 06 Intramuscular iron dextran versus intravenous iron dextran, Outcome 01 Pain at injection site

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 06 Intramuscular iron dextran versus intravenous iron dextran

Outcome: 01 Pain at injection site

Study	IM iron dextran n/N	IV iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dawson 1965	12/23	3/26		100.0	4.52 [1.45, 14.05]
Total (95% CI)	23	26		100.0	4.52 [1.45, 14.05]
Total events: 12 (IM iron dextran), 3 (IV iron dextran)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.61 p=0.009					

Analysis 06.02. Comparison 06 Intramuscular iron dextran versus intravenous iron dextran, Outcome 02 Skin discolouration at injection site

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 06 Intramuscular iron dextran versus intravenous iron dextran

Outcome: 02 Skin discolouration at injection site

Study	IM iron dextran n/N	IV iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dawson 1965	13/23	1/26		100.0	14.70 [2.08, 103.81]
Total (95% CI)	23	26		100.0	14.70 [2.08, 103.81]
Total events: 13 (IM iron dextran), 1 (IV iron dextran)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.69 p=0.007					

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Analysis 06.03. Comparison 06 Intramuscular iron dextran versus intravenous iron dextran, Outcome 03 Venous thrombosis

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 06 Intramuscular iron dextran versus intravenous iron dextran

Outcome: 03 Venous thrombosis

Study	IM iron dextran n/N	IV iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dawson 1965	0/23	4/26		100.0	0.13 [0.01, 2.20]
Total (95% CI)	23	26		100.0	0.13 [0.01, 2.20]
Total events: 0 (IM iron dextran), 4 (IV iron dextran)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.42 p=0.2					

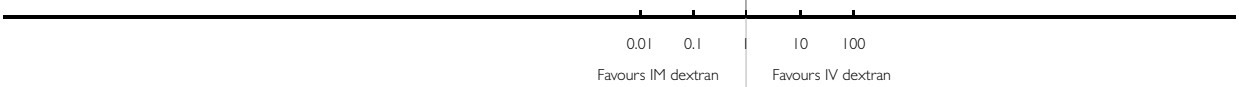
Analysis 06.04. Comparison 06 Intramuscular iron dextran versus intravenous iron dextran, Outcome 04 Nausea or vomiting

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 06 Intramuscular iron dextran versus intravenous iron dextran

Outcome: 04 Nausea or vomiting

Study	IM iron dextran n/N	IV iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dawson 1965	1/23	2/26		100.0	0.57 [0.05, 5.83]
Total (95% CI)	23	26		100.0	0.57 [0.05, 5.83]
Total events: 1 (IM iron dextran), 2 (IV iron dextran)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.48 p=0.6					



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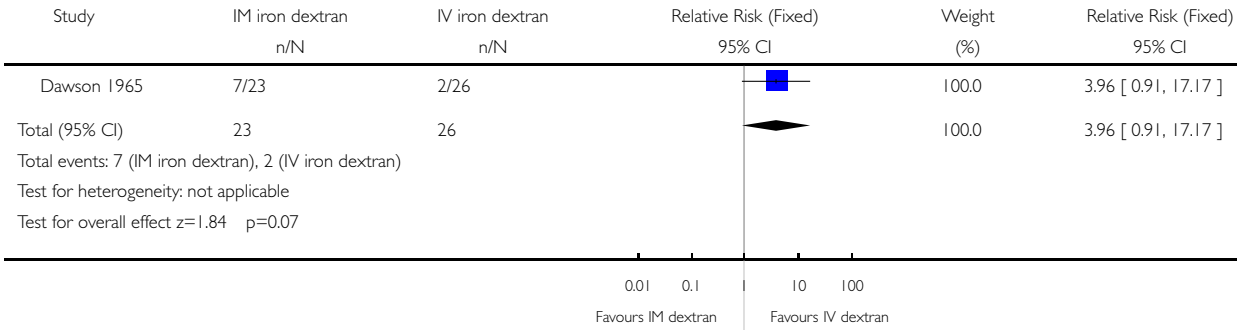
Analysis 06.05. Comparison 06 Intramuscular iron dextran versus intravenous iron dextran, Outcome 05 Headaches

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 06 Intramuscular iron dextran versus intravenous iron dextran

Outcome: 05 Headaches

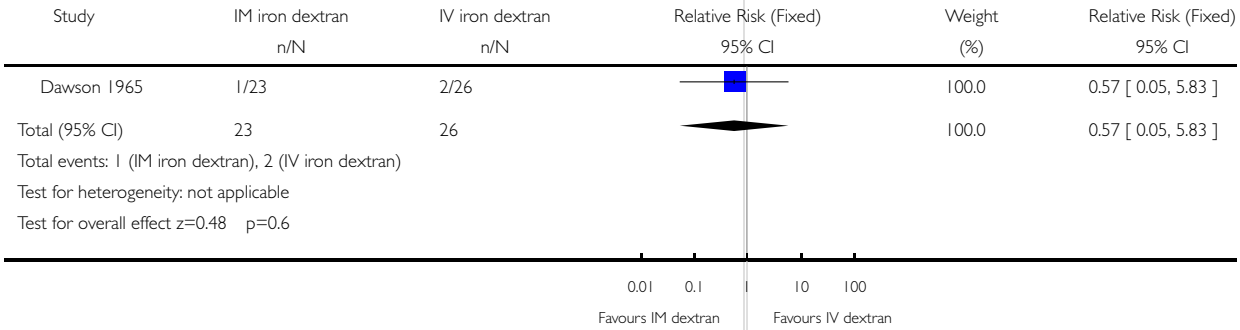


Analysis 06.06. Comparison 06 Intramuscular iron dextran versus intravenous iron dextran, Outcome 06 Shivering

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 06 Intramuscular iron dextran versus intravenous iron dextran

Outcome: 06 Shivering



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Analysis 06.07. Comparison 06 Intramuscular iron dextran versus intravenous iron dextran, Outcome 07 Itching

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 06 Intramuscular iron dextran versus intravenous iron dextran

Outcome: 07 Itching

Study	IM iron dextran n/N	IV iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dawson 1965	4/23	3/26		100.0	1.51 [0.38, 6.04]
Total (95% CI)	23	26		100.0	1.51 [0.38, 6.04]

Total events: 4 (IM iron dextran), 3 (IV iron dextran)

Test for heterogeneity: not applicable

Test for overall effect z=0.58 p=0.6

Analysis 06.08. Comparison 06 Intramuscular iron dextran versus intravenous iron dextran, Outcome 08 Metallic taste in mouth

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 06 Intramuscular iron dextran versus intravenous iron dextran

Outcome: 08 Metallic taste in mouth

Study	IM iron dextran n/N	IV iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dawson 1965	1/23	1/26		100.0	1.13 [0.07, 17.07]
Total (95% CI)	23	26		100.0	1.13 [0.07, 17.07]

Total events: 1 (IM iron dextran), 1 (IV iron dextran)

Test for heterogeneity: not applicable

Test for overall effect z=0.09 p=0.9

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Analysis 06.09. Comparison 06 Intramuscular iron dextran versus intravenous iron dextran, Outcome 09 Severe delayed allergic reaction

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 06 Intramuscular iron dextran versus intravenous iron dextran

Outcome: 09 Severe delayed allergic reaction

Study	IM iron dextran n/N	IV iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Sood 1979	0/30	2/32		100.0	0.21 [0.01, 4.26]
Total (95% CI)	30	32		100.0	0.21 [0.01, 4.26]

Total events: 0 (IM iron dextran), 2 (IV iron dextran)

Test for heterogeneity: not applicable

Test for overall effect z=1.01 p=0.3

Analysis 07.01. Comparison 07 Intramuscular iron sorbitol citric acid versus intravenous iron dextran, Outcome 01 Pain at injection site

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 07 Intramuscular iron sorbitol citric acid versus intravenous iron dextran

Outcome: 01 Pain at injection site

Study	IM iron sorb-cit n/N	IV iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dawson 1965	13/25	3/26		100.0	4.51 [1.46, 13.94]
Total (95% CI)	25	26		100.0	4.51 [1.46, 13.94]

Total events: 13 (IM iron sorb-cit), 3 (IV iron dextran)

Test for heterogeneity: not applicable

Test for overall effect z=2.61 p=0.009

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Analysis 07.02. Comparison 07 Intramuscular iron sorbitol citric acid versus intravenous iron dextran, Outcome 02 Skin discolouration at injection site

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 07 Intramuscular iron sorbitol citric acid versus intravenous iron dextran

Outcome: 02 Skin discolouration at injection site

Study	IM iron sorb-cit n/N	IV iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dawson 1965	3/25	1/26		100.0	3.12 [0.35, 28.03]
Total (95% CI)	25	26		100.0	3.12 [0.35, 28.03]
Total events: 3 (IM iron sorb-cit), 1 (IV iron dextran)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.02 p=0.3					

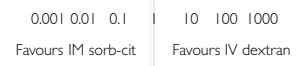
Analysis 07.03. Comparison 07 Intramuscular iron sorbitol citric acid versus intravenous iron dextran, Outcome 03 Venous thrombosis

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 07 Intramuscular iron sorbitol citric acid versus intravenous iron dextran

Outcome: 03 Venous thrombosis

Study	IM iron sorb-cit n/N	IV iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dawson 1965	0/25	4/26		100.0	0.12 [0.01, 2.04]
Total (95% CI)	25	26		100.0	0.12 [0.01, 2.04]
Total events: 0 (IM iron sorb-cit), 4 (IV iron dextran)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.47 p=0.1					



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Analysis 07.04. Comparison 07 Intramuscular iron sorbitol citric acid versus intravenous iron dextran, Outcome 04 Nausea or vomiting

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 07 Intramuscular iron sorbitol citric acid versus intravenous iron dextran

Outcome: 04 Nausea or vomiting

Study	IM iron sorb-cit n/N	IV iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dawson 1965	1/25	2/26		100.0	0.52 [0.05, 5.38]
Total (95% CI)	25	26		100.0	0.52 [0.05, 5.38]
Total events: 1 (IM iron sorb-cit), 2 (IV iron dextran)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.55 p=0.6					

Analysis 07.05. Comparison 07 Intramuscular iron sorbitol citric acid versus intravenous iron dextran, Outcome 05 Headaches

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 07 Intramuscular iron sorbitol citric acid versus intravenous iron dextran

Outcome: 05 Headaches

Study	IM iron sorb-cit n/N	IV iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dawson 1965	1/25	2/26		100.0	0.52 [0.05, 5.38]
Total (95% CI)	25	26		100.0	0.52 [0.05, 5.38]
Total events: 1 (IM iron sorb-cit), 2 (IV iron dextran)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.55 p=0.6					

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Analysis 07.06. Comparison 07 Intramuscular iron sorbitol citric acid versus intravenous iron dextran, Outcome 06 Shivering

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 07 Intramuscular iron sorbitol citric acid versus intravenous iron dextran

Outcome: 06 Shivering

Study	IM iron sorb-cit n/N	IV iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dawson 1965	0/25	2/26		100.0	0.21 [0.01, 4.12]
Total (95% CI)	25	26		100.0	0.21 [0.01, 4.12]
Total events: 0 (IM iron sorb-cit), 2 (IV iron dextran)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.03 p=0.3					

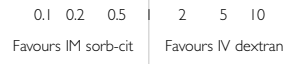
Analysis 07.07. Comparison 07 Intramuscular iron sorbitol citric acid versus intravenous iron dextran, Outcome 07 Itching

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 07 Intramuscular iron sorbitol citric acid versus intravenous iron dextran

Outcome: 07 Itching

Study	IM iron sorb-cit n/N	IV iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dawson 1965	4/25	3/26		100.0	1.39 [0.34, 5.58]
Total (95% CI)	25	26		100.0	1.39 [0.34, 5.58]
Total events: 4 (IM iron sorb-cit), 3 (IV iron dextran)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.46 p=0.6					



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Analysis 07.08. Comparison 07 Intramuscular iron sorbitol citric acid versus intravenous iron dextran, Outcome 08 Metallic taste in mouth

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 07 Intramuscular iron sorbitol citric acid versus intravenous iron dextran

Outcome: 08 Metallic taste in mouth

Study	IM iron sorb-cit n/N	IV iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dawson 1965	4/25	1/26		100.0	4.16 [0.50, 34.71]
Total (95% CI)	25	26		100.0	4.16 [0.50, 34.71]
Total events: 4 (IM iron sorb-cit), 1 (IV iron dextran)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.32 p=0.2					

Analysis 08.01. Comparison 08 Intravenous iron versus placebo, Outcome 01 Side-effects

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 08 Intravenous iron versus placebo

Outcome: 01 Side-effects

Study	IV iron n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Symonds 1969	3/27	4/27		100.0	0.75 [0.19, 3.04]
Total (95% CI)	27	27		100.0	0.75 [0.19, 3.04]
Total events: 3 (IV iron), 4 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.40 p=0.7					

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Analysis 08.02. Comparison 08 Intravenous iron versus placebo, Outcome 02 Nausea or vomiting

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 08 Intravenous iron versus placebo

Outcome: 02 Nausea or vomiting

Study	IV iron n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Symonds 1969	0/27	1/27		100.0	0.33 [0.01, 7.84]
Total (95% CI)	27	27		100.0	0.33 [0.01, 7.84]
Total events: 0 (IV iron), 1 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.68 p=0.5					

Analysis 08.03. Comparison 08 Intravenous iron versus placebo, Outcome 03 Constipation

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 08 Intravenous iron versus placebo

Outcome: 03 Constipation

Study	IV iron n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Symonds 1969	1/27	4/27		100.0	0.25 [0.03, 2.09]
Total (95% CI)	27	27		100.0	0.25 [0.03, 2.09]
Total events: 1 (IV iron), 4 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.28 p=0.2					

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Analysis 08.04. Comparison 08 Intravenous iron versus placebo, Outcome 04 Abdominal cramps

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 08 Intravenous iron versus placebo

Outcome: 04 Abdominal cramps

Study	IV iron n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× Symonds 1969	0/27	0/27		0.0	Not estimable
Total (95% CI)	27	27		0.0	Not estimable
Total events: 0 (IV iron), 0 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					

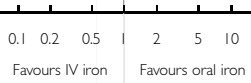
Analysis 09.01. Comparison 09 Intravenous iron versus regular oral iron, Outcome 01 Side-effects

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 01 Side-effects

Study	IV iron n/N	Oral regular iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Symonds 1969	3/27	7/24		100.0	0.38 [0.11, 1.31]
Total (95% CI)	27	24		100.0	0.38 [0.11, 1.31]
Total events: 3 (IV iron), 7 (Oral regular iron)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.53 p=0.1					



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Analysis 09.02. Comparison 09 Intravenous iron versus regular oral iron, Outcome 02 Nausea or vomiting or epigastric discomfort

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 02 Nausea or vomiting or epigastric discomfort

Study	IV iron n/N	Oral regular iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Al 2005	6/45	13/45		61.9	0.46 [0.19, 1.11]
Singh 1998	0/50	3/50		16.7	0.14 [0.01, 2.70]
Symonds 1969	0/27	4/27		21.4	0.11 [0.01, 1.97]
Total (95% CI)	122	122		100.0	0.33 [0.15, 0.74]

Total events: 6 (IV iron), 20 (Oral regular iron)

Test for heterogeneity chi-square=1.41 df=2 p=0.49 I^2 =0.0%

Test for overall effect z=2.70 p=0.007

Analysis 09.03. Comparison 09 Intravenous iron versus regular oral iron, Outcome 03 Constipation

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 03 Constipation

Study	IV iron n/N	Oral regular iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Singh 1998	0/50	13/50		76.1	0.04 [0.00, 0.61]
Symonds 1969	1/27	4/24		23.9	0.22 [0.03, 1.85]
Total (95% CI)	77	74		100.0	0.08 [0.02, 0.43]

Total events: 1 (IV iron), 17 (Oral regular iron)

Test for heterogeneity chi-square=1.17 df=1 p=0.28 I^2 =14.3%

Test for overall effect z=2.96 p=0.003

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Analysis 09.04. Comparison 09 Intravenous iron versus regular oral iron, Outcome 04 Abdominal cramps

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 04 Abdominal cramps

Study	IV iron n/N	Oral regular iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Symonds 1969	0/27	2/24		100.0	0.18 [0.01, 3.54]
Total (95% CI)	27	24		100.0	0.18 [0.01, 3.54]
Total events: 0 (IV iron), 2 (Oral regular iron)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.13 p=0.3					

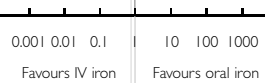
Analysis 09.05. Comparison 09 Intravenous iron versus regular oral iron, Outcome 05 Diarrhoea

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 05 Diarrhoea

Study	IV iron n/N	Oral regular iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Al 2005	0/45	4/45		47.2	0.11 [0.01, 2.01]
Bayoumeu 2002	0/24	1/23		16.1	0.32 [0.01, 7.48]
Singh 1998	0/50	3/50		36.7	0.14 [0.01, 2.70]
Total (95% CI)	119	118		100.0	0.16 [0.03, 0.86]
Total events: 0 (IV iron), 8 (Oral regular iron)					
Test for heterogeneity chi-square=0.26 df=2 p=0.88 I^2 =0.0%					
Test for overall effect z=2.13 p=0.03					



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Analysis 09.06. Comparison 09 Intravenous iron versus regular oral iron, Outcome 06 Haemoglobin at 36 weeks

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 06 Haemoglobin at 36 weeks

Study	IV iron N Mean(SD)	Oral regular iron N Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Total (95% CI)	0	0		0.0	Not estimable
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					

Analysis 09.07. Comparison 09 Intravenous iron versus regular oral iron, Outcome 07 Blood transfusion required

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 07 Blood transfusion required

Study	IV iron n/N	Oral regular iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Al 2005	0/45	1/45		49.5	0.33 [0.01, 7.97]
Bayoumeu 2002	0/24	1/23		50.5	0.32 [0.01, 7.48]
Total (95% CI)	69	68		100.0	0.33 [0.03, 3.06]
Total events: 0 (IV iron), 2 (Oral regular iron)					
Test for heterogeneity chi-square=0.00 df=1 p=0.99 I^2 =0.0%					
Test for overall effect z=0.98 p=0.3					

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Analysis 09.08. Comparison 09 Intravenous iron versus regular oral iron, Outcome 08 Neonates mean hemoglobin

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 08 Neonates mean hemoglobin

Study	IV iron N	IV iron Mean(SD)	Oral regular Iron N	Oral regular Iron Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Bayoumeu 2002	24	15.15 (2.10)	23	15.30 (2.17)		100.0	-0.15 [-1.37, 1.07]
Total (95% CI)	24		23			100.0	-0.15 [-1.37, 1.07]
Test for heterogeneity: not applicable							
Test for overall effect z=0.24 p=0.8							

Analysis 09.09. Comparison 09 Intravenous iron versus regular oral iron, Outcome 09 Maternal haemoglobin at birth

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 09 Maternal haemoglobin at birth

Study	IV iron N	IV iron Mean(SD)	Oral regular iron N	Oral regular iron Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Al 2005	45	12.01 (0.88)	45	11.26 (1.10)		100.0	0.75 [0.34, 1.16]
Total (95% CI)	45		45			100.0	0.75 [0.34, 1.16]
Test for heterogeneity: not applicable							
Test for overall effect z=3.57 p=0.0004							

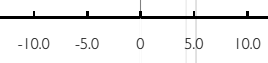
Analysis 09.10. Comparison 09 Intravenous iron versus regular oral iron, Outcome 10 Maternal haemoglobin at 6 weeks

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 10 Maternal haemoglobin at 6 weeks

Study	IV iron N Mean(SD)	Oral regular iron N Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Total (95% CI)	0	0		0.0	Not estimable
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



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Analysis 09.11. Comparison 09 Intravenous iron versus regular oral iron, Outcome 11 Neonates ferritin level

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 11 Neonates ferritin level

Study	IV iron N	IV iron Mean(SD)	Oral regular Iron N	Oral regular Iron Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Bayoumeu 2002	24	132.00 (104.00)	23	134.00 (107.00)		100.0	-2.00 [-62.36, 58.36]
Total (95% CI)	24		23			100.0	-2.00 [-62.36, 58.36]

Test for heterogeneity: not applicable

Test for overall effect z=0.06 p=0.9

Analysis 09.12. Comparison 09 Intravenous iron versus regular oral iron, Outcome 12 Maternal haemoglobin at 4 weeks

Review: Treatments for iron-deficiency anaemia in pregnancy

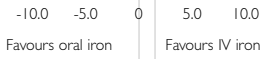
Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 12 Maternal haemoglobin at 4 weeks

Study	IV iron N	IV iron Mean(SD)	Oral regular iron N	Oral regular iron Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Al 2005	45	11.08 (0.72)	45	10.40 (0.68)		86.4	0.68 [0.39, 0.97]
Bayoumeu 2002	24	11.11 (1.30)	23	11.00 (1.25)		13.6	0.11 [-0.62, 0.84]
Total (95% CI)	69		68			100.0	0.60 [0.33, 0.87]

Test for heterogeneity chi-square=2.03 df=1 p=0.15 I^2 =50.7%

Test for overall effect z=4.39 p=0.00001



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Analysis 09.13. Comparison 09 Intravenous iron versus regular oral iron, Outcome 13 Maternal mortality

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 13 Maternal mortality

Study	IV iron n/N	Oral regular iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× Singh 1998	0/50	0/50		0.0	Not estimable
Total (95% CI)	50	50		0.0	Not estimable
Total events: 0 (IV iron), 0 (Oral regular iron)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					

Analysis 09.14. Comparison 09 Intravenous iron versus regular oral iron, Outcome 14 Preterm labour

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 14 Preterm labour

Study	IV iron n/N	Oral regular iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× Singh 1998	0/50	0/50		0.0	Not estimable
Total (95% CI)	50	50		0.0	Not estimable
Total events: 0 (IV iron), 0 (Oral regular iron)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					

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Analysis 09.15. Comparison 09 Intravenous iron versus regular oral iron, Outcome 15 Caesarean section

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

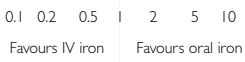
Outcome: 15 Caesarean section

Study	IV iron n/N	Oral regular iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Al 2005	9/45	12/45		75.0	0.75 [0.35, 1.60]
Singh 1998	5/50	4/50		25.0	1.25 [0.36, 4.38]
Total (95% CI)	95	95		100.0	0.88 [0.46, 1.67]

Total events: 14 (IV iron), 16 (Oral regular iron)

Test for heterogeneity chi-square=0.47 df=1 p=0.49 I^2 =0.0%

Test for overall effect z=0.40 p=0.7



Analysis 09.16. Comparison 09 Intravenous iron versus regular oral iron, Outcome 16 Operative vaginal birth

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 16 Operative vaginal birth

Study	IV iron n/N	Oral regular iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Singh 1998	3/50	2/50		100.0	1.50 [0.26, 8.60]
Total (95% CI)	50	50		100.0	1.50 [0.26, 8.60]

Total events: 3 (IV iron), 2 (Oral regular iron)

Test for heterogeneity: not applicable

Test for overall effect z=0.46 p=0.6

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Analysis 09.17. Comparison 09 Intravenous iron versus regular oral iron, Outcome 17 Postpartum haemorrhage

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 17 Postpartum haemorrhage

Study	IV iron n/N	Oral regular iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Bayoumeu 2002	1/24	1/23		12.7	0.96 [0.06, 14.43]
Singh 1998	6/50	7/50		87.3	0.86 [0.31, 2.37]
Total (95% CI)	74	73		100.0	0.87 [0.34, 2.26]

Total events: 7 (IV iron), 8 (Oral regular iron)

Test for heterogeneity chi-square=0.01 df=1 p=0.94 I^2 =0.0%

Test for overall effect z=0.29 p=0.8

Analysis 09.18. Comparison 09 Intravenous iron versus regular oral iron, Outcome 18 Low birthweight (under 2500 g)

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 18 Low birthweight (under 2500 g)

Study	IV iron n/N	Oral regular iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× Singh 1998	0/50	0/50		0.0	Not estimable
Total (95% CI)	50	50		0.0	Not estimable

Total events: 0 (IV iron), 0 (Oral regular iron)

Test for heterogeneity: not applicable

Test for overall effect: not applicable

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Analysis 09.19. Comparison 09 Intravenous iron versus regular oral iron, Outcome 19 Neonatal birthweight

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 19 Neonatal birthweight

Study	IV iron N	IV iron Mean(SD)	Oral regular iron N	Oral regular iron Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Al 2005	45	3498.00 (452.00)	45	3439.00 (451.00)		46.2	59.00 [-127.56, 245.56]
Bayoumeu 2002	24	3595.00 (785.00)	23	3220.00 (570.00)		10.5	375.00 [-16.02, 766.02]
Singh 1998	50	2966.70 (540.90)	50	3086.00 (437.30)		43.3	-119.30 [-312.10, 73.50]
Total (95% CI)	119		118			100.0	15.09 [-111.73, 141.91]

Test for heterogeneity chi-square=5.33 df=2 p=0.07 I^2 =62.5%

Test for overall effect z=0.23 p=0.8

Analysis 09.20. Comparison 09 Intravenous iron versus regular oral iron, Outcome 20 Small-for-gestational age

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 20 Small-for-gestational age

Study	IV iron n/N	Oral regular iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Singh 1998	8/50	5/50		100.0	1.60 [0.56, 4.56]
Total (95% CI)	50	50		100.0	1.60 [0.56, 4.56]

Total events: 8 (IV iron), 5 (Oral regular iron)

Test for heterogeneity: not applicable

Test for overall effect z=0.88 p=0.4

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Analysis 09.21. Comparison 09 Intravenous iron versus regular oral iron, Outcome 21 Five minute Apgar score under seven

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 21 Five minute Apgar score under seven

Study	IV iron n/N	Oral regular iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Singh 1998	1/50	1/50		100.0	1.00 [0.06, 15.55]
Total (95% CI)	50	50		100.0	1.00 [0.06, 15.55]
Total events: 1 (IV iron), 1 (Oral regular iron)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.00 p=1					

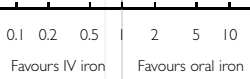
Analysis 09.22. Comparison 09 Intravenous iron versus regular oral iron, Outcome 22 Neonatal mortality

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 22 Neonatal mortality

Study	IV iron n/N	Oral regular iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× Bayoumeu 2002	0/24	0/23		0.0	Not estimable
× Singh 1998	0/50	0/50		0.0	Not estimable
Total (95% CI)	74	73		0.0	Not estimable
Total events: 0 (IV iron), 0 (Oral regular iron)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



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Analysis 09.23. Comparison 09 Intravenous iron versus regular oral iron, Outcome 23 Haemoglobin level > 12 g/dL at 30 days

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 23 Haemoglobin level > 12 g/dL at 30 days

Study	IV iron n/N	Oral regular iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Bayoumeu 2002	3/24	4/23		100.0	0.72 [0.18, 2.87]
Total (95% CI)	24	23		100.0	0.72 [0.18, 2.87]
Total events: 3 (IV iron), 4 (Oral regular iron)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.47 p=0.6					

Analysis 09.24. Comparison 09 Intravenous iron versus regular oral iron, Outcome 24 Gestational hypertension

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 24 Gestational hypertension

Study	IV iron n/N	Oral regular iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Al 2005	2/45	0/45		100.0	5.00 [0.25, 101.31]
Total (95% CI)	45	45		100.0	5.00 [0.25, 101.31]
Total events: 2 (IV iron), 0 (Oral regular iron)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.05 p=0.3					

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Analysis 09.25. Comparison 09 Intravenous iron versus regular oral iron, Outcome 25 Gestational diabetes

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 25 Gestational diabetes

Study	IV iron n/N	Oral regular iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Al 2005	0/45	2/45		100.0	0.20 [0.01, 4.05]
Total (95% CI)	45	45		100.0	0.20 [0.01, 4.05]
Total events: 0 (IV iron), 2 (Oral regular iron)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.05 p=0.3					

Analysis 09.26. Comparison 09 Intravenous iron versus regular oral iron, Outcome 26 Haemoglobin level > 11 g/dL at birth

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 26 Haemoglobin level > 11 g/dL at birth

Study	IV iron n/N	Oral regular iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Al 2005	43/45	28/45		100.0	1.54 [1.21, 1.94]
Total (95% CI)	45	45		100.0	1.54 [1.21, 1.94]
Total events: 43 (IV iron), 28 (Oral regular iron)					
Test for heterogeneity: not applicable					
Test for overall effect z=3.56 p=0.0004					

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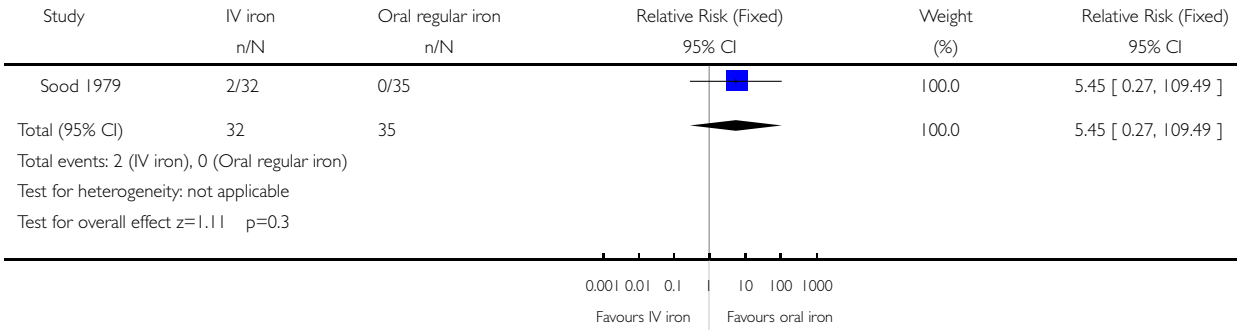
Analysis 09.27. Comparison 09 Intravenous iron versus regular oral iron, Outcome 27 Severe delayed allergic reaction

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 27 Severe delayed allergic reaction

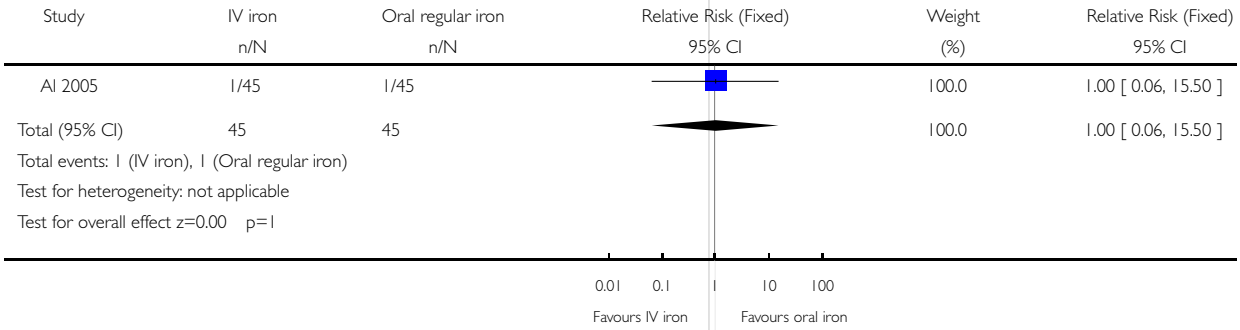


Analysis 09.28. Comparison 09 Intravenous iron versus regular oral iron, Outcome 28 Arthralgia

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 09 Intravenous iron versus regular oral iron

Outcome: 28 Arthralgia



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Analysis 10.01. Comparison 10 Intravenous iron versus controlled release oral iron, Outcome 01 Side-effects

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 10 Intravenous iron versus controlled release oral iron

Outcome: 01 Side-effects

Study	IV iron n/N	Control release iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Symonds 1969	3/27	7/25		100.0	0.40 [0.12, 1.37]
Total (95% CI)	27	25		100.0	0.40 [0.12, 1.37]
Total events: 3 (IV iron), 7 (Control release iron)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.46 p=0.1					

Analysis 10.02. Comparison 10 Intravenous iron versus controlled release oral iron, Outcome 02 Nausea or vomiting

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 10 Intravenous iron versus controlled release oral iron

Outcome: 02 Nausea or vomiting

Study	IV iron n/N	Control release iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Symonds 1969	0/27	4/25		100.0	0.10 [0.01, 1.82]
Total (95% CI)	27	25		100.0	0.10 [0.01, 1.82]
Total events: 0 (IV iron), 4 (Control release iron)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.55 p=0.1					

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Analysis 10.03. Comparison 10 Intravenous iron versus controlled release oral iron, Outcome 03 Constipation

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 10 Intravenous iron versus controlled release oral iron

Outcome: 03 Constipation

Study	IV iron n/N	Control release iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Symonds 1969	1/27	1/25		100.0	0.93 [0.06, 14.03]
Total (95% CI)	27	25		100.0	0.93 [0.06, 14.03]
Total events: 1 (IV iron), 1 (Control release iron)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.06 p=1					

Analysis 10.04. Comparison 10 Intravenous iron versus controlled release oral iron, Outcome 04 Abdominal cramps

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 10 Intravenous iron versus controlled release oral iron

Outcome: 04 Abdominal cramps

Study	IV iron n/N	Control release iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Symonds 1969	0/27	1/25		100.0	0.31 [0.01, 7.26]
Total (95% CI)	27	25		100.0	0.31 [0.01, 7.26]
Total events: 0 (IV iron), 1 (Control release iron)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.73 p=0.5					

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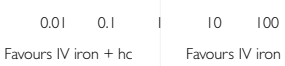
Analysis 11.01. Comparison 11 Intravenous iron + hydrocortisone versus intravenous iron, Outcome 01 Tenderness or erythema

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 11 Intravenous iron + hydrocortisone versus intravenous iron

Outcome: 01 Tenderness or erythema

Study	IV iron + hydrocort n/N	IV iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dawson 1965	2/15	0/15		100.0	5.00 [0.26, 96.13]
Total (95% CI)	15	15		100.0	5.00 [0.26, 96.13]
Total events: 2 (IV iron + hydrocort), 0 (IV iron)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.07 p=0.3					



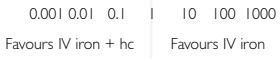
Analysis 11.02. Comparison 11 Intravenous iron + hydrocortisone versus intravenous iron, Outcome 02 Venous thrombosis

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 11 Intravenous iron + hydrocortisone versus intravenous iron

Outcome: 02 Venous thrombosis

Study	IV iron + hydrocort n/N	IV iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Dawson 1965	0/15	5/15		100.0	0.09 [0.01, 1.51]
Total (95% CI)	15	15		100.0	0.09 [0.01, 1.51]
Total events: 0 (IV iron + hydrocort), 5 (IV iron)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.67 p=0.09					



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Analysis 12.01. Comparison 12 2/3 dose intravenous iron versus full dose intravenous iron, Outcome 01 Allergic reaction during infusion

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 12 2/3 dose intravenous iron versus full dose intravenous iron

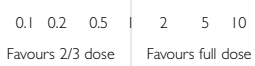
Outcome: 01 Allergic reaction during infusion

Study	2/3 dose IV iron n/N	Full dose IV iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Kaisi 1988	15/309	23/314		100.0	0.66 [0.35, 1.25]
Total (95% CI)	309	314		100.0	0.66 [0.35, 1.25]

Total events: 15 (2/3 dose IV iron), 23 (Full dose IV iron)

Test for heterogeneity: not applicable

Test for overall effect z=1.28 p=0.2



Analysis 12.02. Comparison 12 2/3 dose intravenous iron versus full dose intravenous iron, Outcome 02 Allergic reaction after infusion

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 12 2/3 dose intravenous iron versus full dose intravenous iron

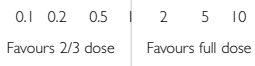
Outcome: 02 Allergic reaction after infusion

Study	2/3 dose IV iron n/N	Full dose IV iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Kaisi 1988	47/309	77/314		100.0	0.62 [0.45, 0.86]
Total (95% CI)	309	314		100.0	0.62 [0.45, 0.86]

Total events: 47 (2/3 dose IV iron), 77 (Full dose IV iron)

Test for heterogeneity: not applicable

Test for overall effect z=2.86 p=0.004



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Analysis 12.03. Comparison 12 2/3 dose intravenous iron versus full dose intravenous iron, Outcome 03 Life-threatening allergic reaction during infusion

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 12 2/3 dose intravenous iron versus full dose intravenous iron

Outcome: 03 Life-threatening allergic reaction during infusion

Study	2/3 dose IV iron n/N	Full dose IV iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Kaisi 1988	5/309	2/314		100.0	2.54 [0.50, 13.00]
Total (95% CI)	309	314		100.0	2.54 [0.50, 13.00]

Total events: 5 (2/3 dose IV iron), 2 (Full dose IV iron)

Test for heterogeneity: not applicable

Test for overall effect z=1.12 p=0.3

Analysis 12.04. Comparison 12 2/3 dose intravenous iron versus full dose intravenous iron, Outcome 04 Discomfort needing analgesics after infusion

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 12 2/3 dose intravenous iron versus full dose intravenous iron

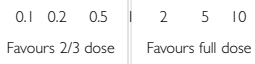
Outcome: 04 Discomfort needing analgesics after infusion

Study	2/3 dose IV iron n/N	Full dose IV iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Kaisi 1988	15/309	31/314		100.0	0.49 [0.27, 0.89]
Total (95% CI)	309	314		100.0	0.49 [0.27, 0.89]

Total events: 15 (2/3 dose IV iron), 31 (Full dose IV iron)

Test for heterogeneity: not applicable

Test for overall effect z=2.33 p=0.02



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Analysis 12.05. Comparison 12 2/3 dose intravenous iron versus full dose intravenous iron, Outcome 05 Immobilised by painful joints

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 12 2/3 dose intravenous iron versus full dose intravenous iron

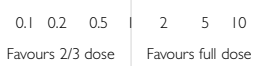
Outcome: 05 Immobilised by painful joints

Study	2/3 dose IV iron n/N	Full dose IV iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Kaisi 1988	7/309	9/314		100.0	0.79 [0.30, 2.10]
Total (95% CI)	309	314		100.0	0.79 [0.30, 2.10]

Total events: 7 (2/3 dose IV iron), 9 (Full dose IV iron)

Test for heterogeneity: not applicable

Test for overall effect z=0.47 p=0.6



Analysis 12.06. Comparison 12 2/3 dose intravenous iron versus full dose intravenous iron, Outcome 06 Non-live births

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 12 2/3 dose intravenous iron versus full dose intravenous iron

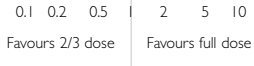
Outcome: 06 Non-live births

Study	2/3 dose IV iron n/N	Full dose IV iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Kaisi 1988	9/248	11/259		100.0	0.85 [0.36, 2.03]
Total (95% CI)	248	259		100.0	0.85 [0.36, 2.03]

Total events: 9 (2/3 dose IV iron), 11 (Full dose IV iron)

Test for heterogeneity: not applicable

Test for overall effect z=0.36 p=0.7



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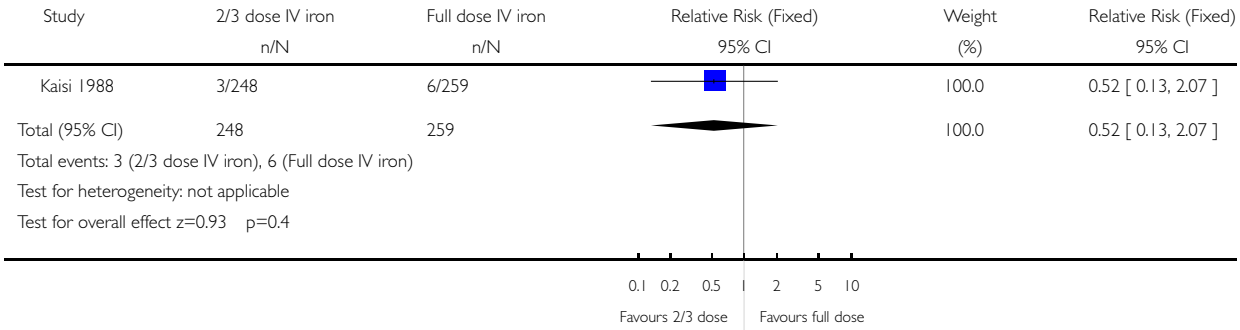
Analysis 12.07. Comparison 12 2/3 dose intravenous iron versus full dose intravenous iron, Outcome 07 Neonatal death

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 12 2/3 dose intravenous iron versus full dose intravenous iron

Outcome: 07 Neonatal death

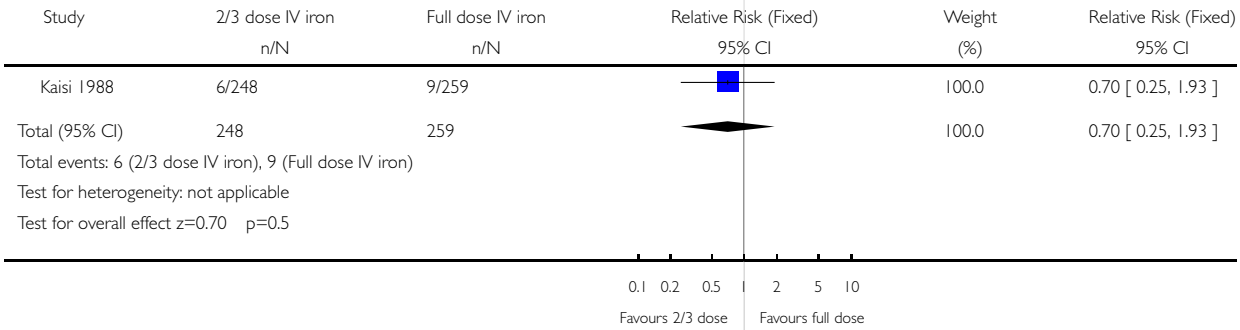


Analysis 12.08. Comparison 12 2/3 dose intravenous iron versus full dose intravenous iron, Outcome 08 Stillbirth

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 12 2/3 dose intravenous iron versus full dose intravenous iron

Outcome: 08 Stillbirth



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Analysis 12.09. Comparison 12 2/3 dose intravenous iron versus full dose intravenous iron, Outcome 09 Spontaneous abortion

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 12 2/3 dose intravenous iron versus full dose intravenous iron

Outcome: 09 Spontaneous abortion

Study	2/3 dose IV iron n/N	Full dose IV iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Kaisi 1988	3/248	1/259		100.0	3.13 [0.33, 29.92]
Total (95% CI)	248	259		100.0	3.13 [0.33, 29.92]

Total events: 3 (2/3 dose IV iron), 1 (Full dose IV iron)

Test for heterogeneity: not applicable

Test for overall effect z=0.99 p=0.3

Analysis 13.01. Comparison 13 Intravenous iron sucrose with adjuvant recombinant human erythropoietin versus intravenous iron sucrose, Outcome 01 Hb < 11 g/dl at 4 weeks

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 13 Intravenous iron sucrose with adjuvant recombinant human erythropoietin versus intravenous iron sucrose

Outcome: 01 Hb < 11 g/dl at 4 weeks

Study	rhEPO +IV Fe sucrose n/N	IV Fe sucrose n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Breymann 2001	1/20	5/20		100.0	0.20 [0.03, 1.56]
Total (95% CI)	20	20		100.0	0.20 [0.03, 1.56]

Total events: 1 (rhEPO +IV Fe sucrose), 5 (IV Fe sucrose)

Test for heterogeneity: not applicable

Test for overall effect z=1.53 p=0.1

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Analysis 13.02. Comparison 13 Intravenous iron sucrose with adjuvant recombinant human erythropoietin versus intravenous iron sucrose, Outcome 02 Mean corpuscular volume

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 13 Intravenous iron sucrose with adjuvant recombinant human erythropoietin versus intravenous iron sucrose

Outcome: 02 Mean corpuscular volume

Study	rhEPO +IV Fe sucrose		IV Fe sucrose		Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	(%)	95% CI
Breymann 2001	20	91.10 (4.30)	20	84.80 (6.30)		100.0	6.30 [2.96, 9.64]
Total (95% CI)	20		20			100.0	6.30 [2.96, 9.64]
Test for heterogeneity: not applicable							
Test for overall effect z=3.69 p=0.0002							

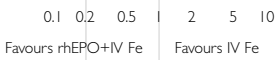
Analysis 13.03. Comparison 13 Intravenous iron sucrose with adjuvant recombinant human erythropoietin versus intravenous iron sucrose, Outcome 03 Caesarean section

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 13 Intravenous iron sucrose with adjuvant recombinant human erythropoietin versus intravenous iron sucrose

Outcome: 03 Caesarean section

Study	rhEPO +IV Fe sucrose	IV Fe sucrose	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
Breymann 2001	6/20	6/20		100.0	1.00 [0.39, 2.58]
Total (95% CI)	20	20		100.0	1.00 [0.39, 2.58]
Total events: 6 (rhEPO +IV Fe sucrose), 6 (IV Fe sucrose)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.00 p=1					



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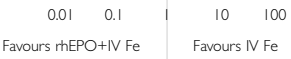
Analysis 13.04. Comparison 13 Intravenous iron sucrose with adjuvant recombinant human erythropoietin versus intravenous iron sucrose, Outcome 04 Metallic taste

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 13 Intravenous iron sucrose with adjuvant recombinant human erythropoietin versus intravenous iron sucrose

Outcome: 04 Metallic taste

Study	rhEPO +IV Fe sucrose n/N	IV Fe sucrose n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Breymann 2001	1/20	2/20		100.0	0.50 [0.05, 5.08]
Total (95% CI)	20	20		100.0	0.50 [0.05, 5.08]
Total events: 1 (rhEPO +IV Fe sucrose), 2 (IV Fe sucrose)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.59 p=0.6					



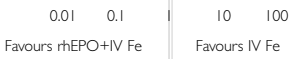
Analysis 13.05. Comparison 13 Intravenous iron sucrose with adjuvant recombinant human erythropoietin versus intravenous iron sucrose, Outcome 05 Warm feeling

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 13 Intravenous iron sucrose with adjuvant recombinant human erythropoietin versus intravenous iron sucrose

Outcome: 05 Warm feeling

Study	rhEPO +IV Fe sucrose n/N	IV Fe sucrose n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Breymann 2001	1/20	1/20		100.0	1.00 [0.07, 14.90]
Total (95% CI)	20	20		100.0	1.00 [0.07, 14.90]
Total events: 1 (rhEPO +IV Fe sucrose), 1 (IV Fe sucrose)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.00 p=1					



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Analysis 13.06. Comparison 13 Intravenous iron sucrose with adjuvant recombinant human erythropoietin versus intravenous iron sucrose, Outcome 06 Birthweight

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 13 Intravenous iron sucrose with adjuvant recombinant human erythropoietin versus intravenous iron sucrose

Outcome: 06 Birthweight

Study	Iron + EPO N	Iron + EPO Mean(SD)	Iron N	Iron Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Breymann 2001	20	3332.00 (282.00)	20	3462.00 (497.00)		100.0	-130.00 [-380.44, 120.44]
Total (95% CI)	20		20			100.0	-130.00 [-380.44, 120.44]
Test for heterogeneity: not applicable							
Test for overall effect z=1.02 p=0.3							

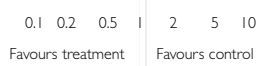
Analysis 13.07. Comparison 13 Intravenous iron sucrose with adjuvant recombinant human erythropoietin versus intravenous iron sucrose, Outcome 07 Birth < 37 weeks

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 13 Intravenous iron sucrose with adjuvant recombinant human erythropoietin versus intravenous iron sucrose

Outcome: 07 Birth < 37 weeks

Study	Iron + EPO n/N	Iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Breymann 2001	0/20	1/20		100.0	0.33 [0.01, 7.72]
Total (95% CI)	20	20		100.0	0.33 [0.01, 7.72]
Total events: 0 (Iron + EPO), 1 (Iron)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.69 p=0.5					



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Analysis 13.08. Comparison 13 Intravenous iron sucrose with adjuvant recombinant human erythropoietin versus intravenous iron sucrose, Outcome 08 Maternal mean blood pressure

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 13 Intravenous iron sucrose with adjuvant recombinant human erythropoietin versus intravenous iron sucrose

Outcome: 08 Maternal mean blood pressure

Study	Iron + EPO		Iron		Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	(%)	95% CI
Breymann 2001	20	75.80 (8.30)	20	76.00 (7.20)		100.0	-0.20 [-5.02, 4.62]
Total (95% CI)	20		20			100.0	-0.20 [-5.02, 4.62]
Test for heterogeneity: not applicable							
Test for overall effect z=0.08 p=0.9							

Analysis 13.09. Comparison 13 Intravenous iron sucrose with adjuvant recombinant human erythropoietin versus intravenous iron sucrose, Outcome 09 Need transfusion

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 13 Intravenous iron sucrose with adjuvant recombinant human erythropoietin versus intravenous iron sucrose

Outcome: 09 Need transfusion

Study	Iron + EPO	Iron	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
× Breymann 2001	0/20	0/20		0.0	Not estimable
Total (95% CI)	20	20		0.0	Not estimable
Total events: 0 (Iron + EPO), 0 (Iron)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					

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Analysis 14.01. Comparison 14 Intramuscular iron sorbitol citric acid versus oral iron, Outcome 01 Not anaemic at term

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 14 Intramuscular iron sorbitol citric acid versus oral iron

Outcome: 01 Not anaemic at term

Study	IM iron n/N	Oral iron n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Zutschi 2004	76/100	62/100		100.0	1.23 [1.01, 1.48]
Total (95% CI)	100	100		100.0	1.23 [1.01, 1.48]
Total events: 76 (IM iron), 62 (Oral iron)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.11 p=0.03					

Analysis 14.02. Comparison 14 Intramuscular iron sorbitol citric acid versus oral iron, Outcome 02 Mean maternal haemoglobin at birth

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 14 Intramuscular iron sorbitol citric acid versus oral iron

Outcome: 02 Mean maternal haemoglobin at birth

Study	IM iron N	IM iron Mean(SD)	Oral iron N	Oral iron Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Zutschi 2004	100	10.50 (0.84)	100	9.96 (0.89)		100.0	0.54 [0.30, 0.78]
Total (95% CI)	100		100			100.0	0.54 [0.30, 0.78]
Test for heterogeneity: not applicable							
Test for overall effect z=4.41 p=0.00001							

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Analysis 14.03. Comparison 14 Intramuscular iron sorbitol citric acid versus oral iron, Outcome 03 Mean maternal hematocrit level at birth

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 14 Intramuscular iron sorbitol citric acid versus oral iron

Outcome: 03 Mean maternal hematocrit level at birth

Study	IM iron		Oral iron		Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	(%)	95% CI
Zutschi 2004	100	31.20 (2.60)	100	29.80 (2.70)		100.0	1.40 [0.67, 2.13]
Total (95% CI)	100		100			100.0	1.40 [0.67, 2.13]
Test for heterogeneity: not applicable							
Test for overall effect z=3.73 p=0.0002							

Analysis 14.04. Comparison 14 Intramuscular iron sorbitol citric acid versus oral iron, Outcome 04 Caesarean section

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 14 Intramuscular iron sorbitol citric acid versus oral iron

Outcome: 04 Caesarean section

Study	IM iron	Oral iron	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
Zutschi 2004	24/100	22/100		100.0	1.09 [0.66, 1.81]
Total (95% CI)	100	100		100.0	1.09 [0.66, 1.81]
Total events: 24 (IM iron), 22 (Oral iron)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.34 p=0.7					

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Analysis 14.05. Comparison 14 Intramuscular iron sorbitol citric acid versus oral iron, Outcome 05 Haematocrit (%) at 4 weeks of treatment

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 14 Intramuscular iron sorbitol citric acid versus oral iron

Outcome: 05 Haematocrit (%) at 4 weeks of treatment

Study	IM iron N	IM iron Mean(SD)	Oral iron (600 mg) N	Oral iron (600 mg) Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Ogunbode 1980	28	32.50 (2.65)	28	31.25 (2.22)		100.0	1.25 [-0.03, 2.53]
Total (95% CI)	28		28			100.0	1.25 [-0.03, 2.53]
Test for heterogeneity: not applicable							
Test for overall effect z=1.91 p=0.06							

Analysis 14.06. Comparison 14 Intramuscular iron sorbitol citric acid versus oral iron, Outcome 06 Haematocrit (%) at 8 weeks of treatment

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 14 Intramuscular iron sorbitol citric acid versus oral iron

Outcome: 06 Haematocrit (%) at 8 weeks of treatment

Study	IM iron N	IM iron Mean(SD)	Oral iron (600 mg) N	Oral iron (600 mg) Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Ogunbode 1980	31	35.29 (3.60)	28	32.67 (1.30)		100.0	2.62 [1.26, 3.98]
Total (95% CI)	31		28			100.0	2.62 [1.26, 3.98]
Test for heterogeneity: not applicable							
Test for overall effect z=3.79 p=0.0002							

Analysis 14.07. Comparison 14 Intramuscular iron sorbitol citric acid versus oral iron, Outcome 07 Haematocrit (%) at 4 weeks of treatment

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 14 Intramuscular iron sorbitol citric acid versus oral iron

Outcome: 07 Haematocrit (%) at 4 weeks of treatment

Study	IM iron N	IM iron Mean(SD)	Oral iron (1200 mg) N	Oral iron (1200 mg) Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Ogunbode 1980	28	32.50 (2.65)	28	31.25 (2.22)		100.0	1.25 [-0.03, 2.53]
Total (95% CI)	28		28			100.0	1.25 [-0.03, 2.53]
Test for heterogeneity: not applicable							
Test for overall effect z=1.91 p=0.06							

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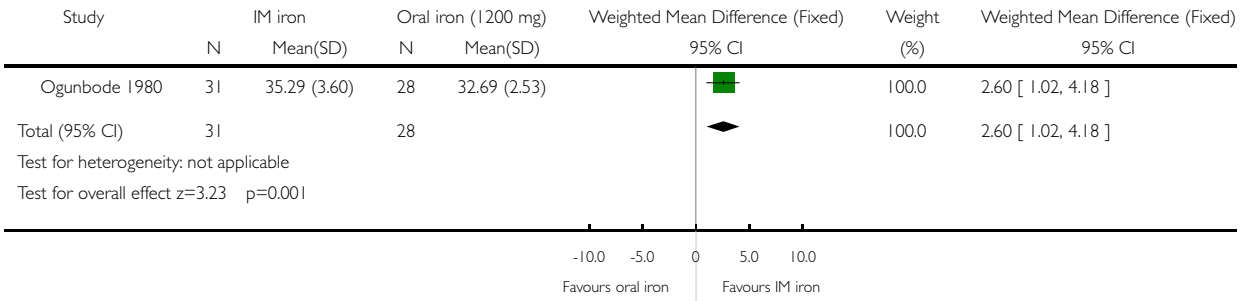
Analysis 14.08. Comparison 14 Intramuscular iron sorbitol citric acid versus oral iron, Outcome 08 Haematocrit (%) at 8 weeks of treatment

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 14 Intramuscular iron sorbitol citric acid versus oral iron

Outcome: 08 Haematocrit (%) at 8 weeks of treatment

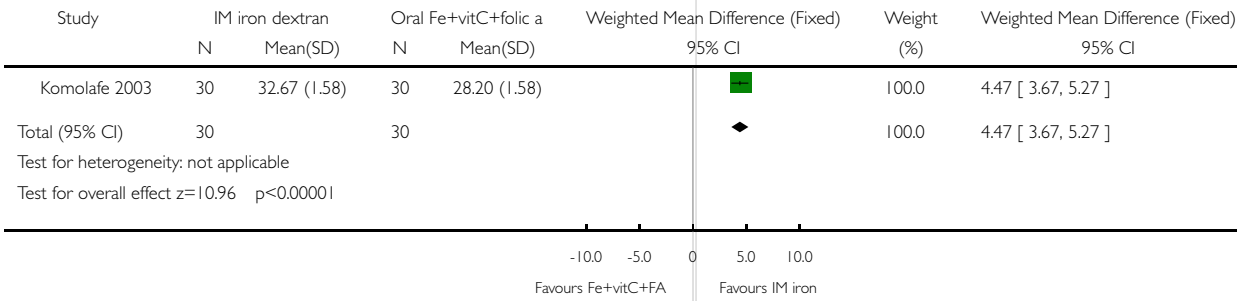


Analysis 15.01. Comparison 15 Intramuscular iron dextran versus oral iron + vitamin C + folic acid, Outcome 01 Haematocrit

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 15 Intramuscular iron dextran versus oral iron + vitamin C + folic acid

Outcome: 01 Haematocrit



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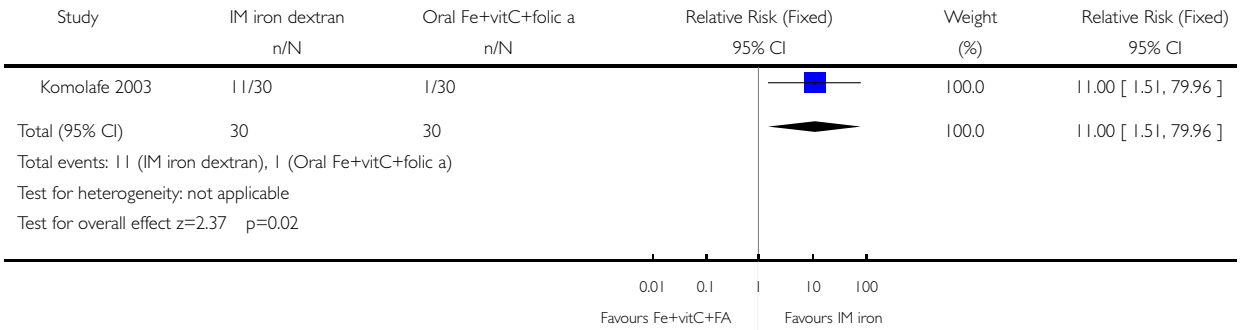
Analysis 15.02. Comparison 15 Intramuscular iron dextran versus oral iron + vitamin C + folic acid, Outcome 02 Not anaemic at 6 weeks (packed cell volume > 33%)

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 15 Intramuscular iron dextran versus oral iron + vitamin C + folic acid

Outcome: 02 Not anaemic at 6 weeks (packed cell volume > 33%)

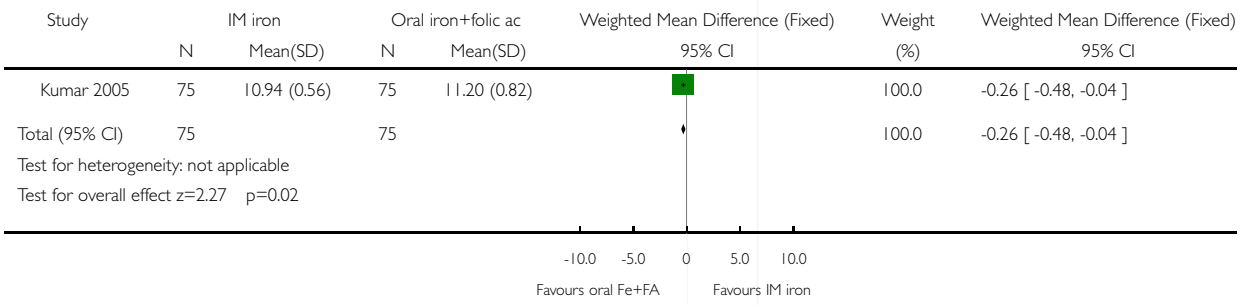


Analysis 16.01. Comparison 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid, Outcome 01 Mean haemoglobin at 36 weeks

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid

Outcome: 01 Mean haemoglobin at 36 weeks



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Analysis 16.02. Comparison 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid, Outcome 02 Haemoglobin > 11 g/dL at 36 weeks

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid

Outcome: 02 Haemoglobin > 11 g/dL at 36 weeks

Study	IM iron n/N	Oral iron+folic acid n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Kumar 2005	42/75	51/75		100.0	0.82 [0.64, 1.06]
Total (95% CI)	75	75		100.0	0.82 [0.64, 1.06]
Total events: 42 (IM iron), 51 (Oral iron+folic acid)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.50 p=0.1					

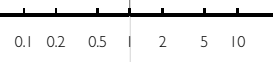
Analysis 16.03. Comparison 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid, Outcome 03 Caesarean section

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid

Outcome: 03 Caesarean section

Study	IM iron n/N	Oral iron+folic acid n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Kumar 2005	5/75	3/75		100.0	1.67 [0.41, 6.73]
Total (95% CI)	75	75		100.0	1.67 [0.41, 6.73]
Total events: 5 (IM iron), 3 (Oral iron+folic acid)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.72 p=0.5					



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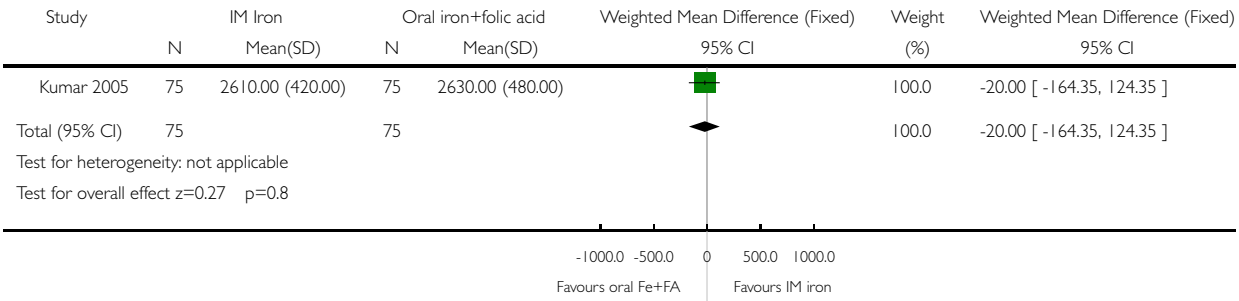
Analysis 16.04. Comparison 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid, Outcome 04 Mean birthweight (kg)

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid

Outcome: 04 Mean birthweight (kg)

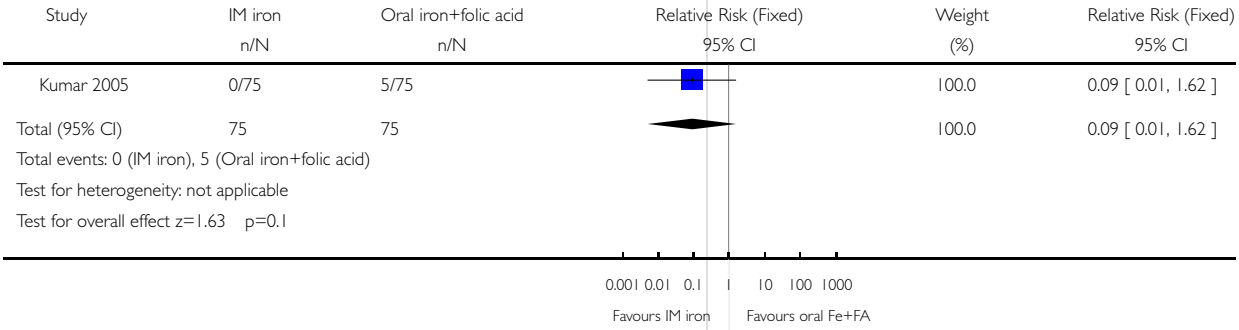


Analysis 16.05. Comparison 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid, Outcome 05 Diarrhoea

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid

Outcome: 05 Diarrhoea



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Analysis 16.06. Comparison 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid, Outcome 06 Constipation

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid

Outcome: 06 Constipation

Study	IM iron n/N	Oral iron+folic acid n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Kumar 2005	0/75	8/75		100.0	0.06 [0.00, 1.00]
Total (95% CI)	75	75		100.0	0.06 [0.00, 1.00]
Total events: 0 (IM iron), 8 (Oral iron+folic acid)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.96 p=0.05					

Analysis 16.07. Comparison 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid, Outcome 07 Dyspepsia

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid

Outcome: 07 Dyspepsia

Study	IM iron n/N	Oral iron+folic acid n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Kumar 2005	0/75	9/75		100.0	0.05 [0.00, 0.89]
Total (95% CI)	75	75		100.0	0.05 [0.00, 0.89]
Total events: 0 (IM iron), 9 (Oral iron+folic acid)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.04 p=0.04					

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Analysis 16.08. Comparison 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid, Outcome 08 Local site mainly pain

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid

Outcome: 08 Local site mainly pain

Study	IM iron n/N	Oral iron+folic acid n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Kumar 2005	62/75	0/75		100.0	125.00 [7.87, 1984.19]
Total (95% CI)	75	75		100.0	125.00 [7.87, 1984.19]
Total events: 62 (IM iron), 0 (Oral iron+folic acid)					
Test for heterogeneity: not applicable					
Test for overall effect z=3.42 p=0.0006					

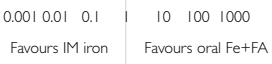
Analysis 16.09. Comparison 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid, Outcome 09 Staining

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid

Outcome: 09 Staining

Study	IM iron n/N	Oral iron+folic acid n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Kumar 2005	56/75	0/75		100.0	113.00 [7.11, 1795.82]
Total (95% CI)	75	75		100.0	113.00 [7.11, 1795.82]
Total events: 56 (IM iron), 0 (Oral iron+folic acid)					
Test for heterogeneity: not applicable					
Test for overall effect z=3.35 p=0.0008					



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Analysis 16.10. Comparison 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid, Outcome 10 Arthralgia

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid

Outcome: 10 Arthralgia

Study	IM iron n/N	Oral iron+folic acid n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Kumar 2005	6/75	0/75		100.0	13.00 [0.75, 226.73]
Total (95% CI)	75	75		100.0	13.00 [0.75, 226.73]
Total events: 6 (IM iron), 0 (Oral iron+folic acid)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.76 p=0.08					

Analysis 16.11. Comparison 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid, Outcome 11 Itching and rash

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid

Outcome: 11 Itching and rash

Study	IM iron n/N	Oral iron+folic acid n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Kumar 2005	14/75	0/75		100.0	29.00 [1.76, 477.47]
Total (95% CI)	75	75		100.0	29.00 [1.76, 477.47]
Total events: 14 (IM iron), 0 (Oral iron+folic acid)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.36 p=0.02					

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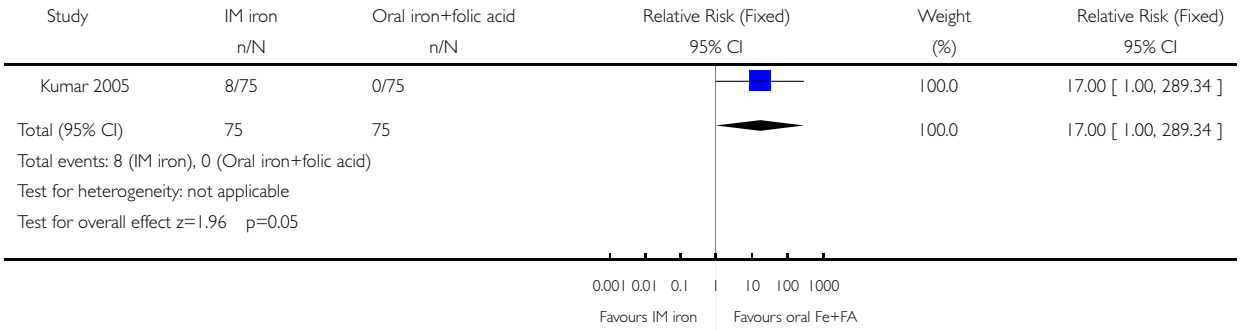
Analysis 16.12. Comparison 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid, Outcome 12 Fever

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid

Outcome: 12 Fever

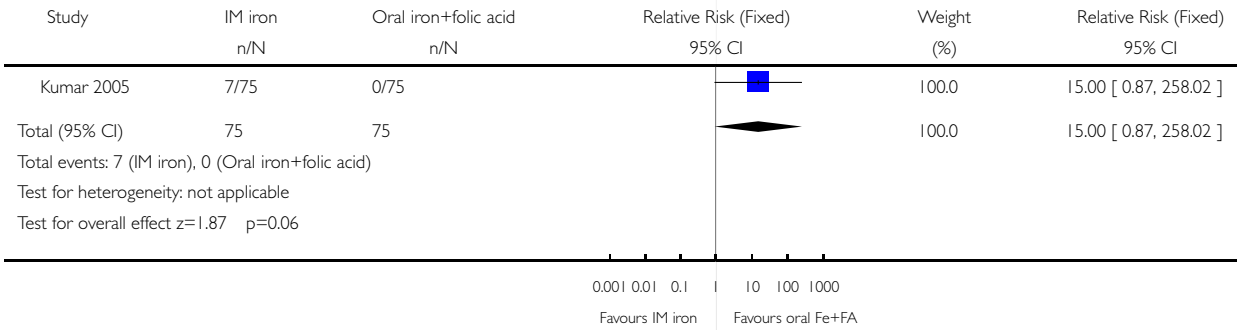


Analysis 16.13. Comparison 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid, Outcome 13 Malaise

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid

Outcome: 13 Malaise



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Analysis 16.14. Comparison 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid, Outcome 14 Vaso-vagal due to apprehension

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid

Outcome: 14 Vaso-vagal due to apprehension

Study	IM iron n/N	Oral iron+folic acid n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Kumar 2005	4/75	0/75		100.0	9.00 [0.49, 164.29]
Total (95% CI)	75	75		100.0	9.00 [0.49, 164.29]
Total events: 4 (IM iron), 0 (Oral iron+folic acid)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.48 p=0.1					

Analysis 16.15. Comparison 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid, Outcome 15 Systemic ache

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid

Outcome: 15 Systemic ache

Study	IM iron n/N	Oral iron+folic acid n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Kumar 2005	11/75	0/75		100.0	23.00 [1.38, 383.37]
Total (95% CI)	75	75		100.0	23.00 [1.38, 383.37]
Total events: 11 (IM iron), 0 (Oral iron+folic acid)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.18 p=0.03					

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Analysis 16.16. Comparison 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid, Outcome 16 Haemoglobin > 12 g/dL at 36 weeks

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 16 Intramuscular iron sorbitol citric acid versus oral iron + folic acid

Outcome: 16 Haemoglobin > 12 g/dL at 36 weeks

Study	IMiron n/N	Oral iron+folic acid n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Kumar 2005	11/75	21/75		100.0	0.52 [0.27, 1.01]
Total (95% CI)	75	75		100.0	0.52 [0.27, 1.01]

Total events: 11 (IMiron), 21 (Oral iron+folic acid)

Test for heterogeneity: not applicable

Test for overall effect z=1.93 p=0.05

Analysis 17.01. Comparison 17 Oral iron daily versus oral iron twice weekly, Outcome 01 Haemoglobin level at 4 weeks

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 17 Oral iron daily versus oral iron twice weekly

Outcome: 01 Haemoglobin level at 4 weeks

Study	Oral iron daily N	Oral iron daily Mean(SD)	Oral iron twice week N	Oral iron twice week Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Mumtaz 2000	84	10.16 (1.52)	76	9.62 (1.05)		100.0	0.54 [0.14, 0.94]
Total (95% CI)	84		76			100.0	0.54 [0.14, 0.94]

Test for heterogeneity: not applicable

Test for overall effect z=2.63 p=0.008

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Analysis 17.02. Comparison 17 Oral iron daily versus oral iron twice weekly, Outcome 02 Haemoglobin level at 8 weeks

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 17 Oral iron daily versus oral iron twice weekly

Outcome: 02 Haemoglobin level at 8 weeks

Study	Oral iron daily		Oral iron twice week		Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	(%)	95% CI
Mumtaz 2000	68	10.87 (1.72)	61	9.70 (1.14)		100.0	1.17 [0.67, 1.67]
Total (95% CI)	68		61			100.0	1.17 [0.67, 1.67]
Test for heterogeneity: not applicable							
Test for overall effect z=4.60 p<0.00001							

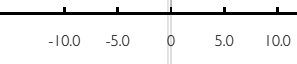
Analysis 17.03. Comparison 17 Oral iron daily versus oral iron twice weekly, Outcome 03 Haemoglobin level at 12 weeks

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 17 Oral iron daily versus oral iron twice weekly

Outcome: 03 Haemoglobin level at 12 weeks

Study	Oral iron daily		Oral iron twice week		Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	(%)	95% CI
Mumtaz 2000	55	11.36 (1.83)	50	10.09 (1.23)		100.0	1.27 [0.68, 1.86]
Total (95% CI)	55		50			100.0	1.27 [0.68, 1.86]
Test for heterogeneity: not applicable							
Test for overall effect z=4.21 p=0.00003							



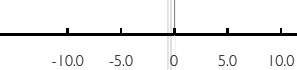
Analysis 17.04. Comparison 17 Oral iron daily versus oral iron twice weekly, Outcome 04 Haemoglobin level at 16 weeks

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 17 Oral iron daily versus oral iron twice weekly

Outcome: 04 Haemoglobin level at 16 weeks

Study	Oral iron daily		Oral iron twice week		Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	(%)	95% CI
De Souza 2004	49	11.00 (0.70)	53	10.70 (0.90)		100.0	0.30 [-0.01, 0.61]
Total (95% CI)	49		53			100.0	0.30 [-0.01, 0.61]
Test for heterogeneity: not applicable							
Test for overall effect z=1.89 p=0.06							



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Analysis 17.05. Comparison 17 Oral iron daily versus oral iron twice weekly, Outcome 05 Haemoglobin level > 11 g/dL at 16 weeks of treatment

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 17 Oral iron daily versus oral iron twice weekly

Outcome: 05 Haemoglobin level > 11 g/dL at 16 weeks of treatment

Study	Oral iron daily n/N	Oral iron twice week n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Souza 2004	23/49	18/53		100.0	1.38 [0.86, 2.23]
Total (95% CI)	49	53		100.0	1.38 [0.86, 2.23]
Total events: 23 (Oral iron daily), 18 (Oral iron twice week)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.32 p=0.2					

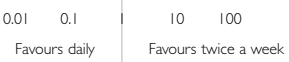
Analysis 17.06. Comparison 17 Oral iron daily versus oral iron twice weekly, Outcome 06 Treatment failure (haemoglobin < 10 g/dL) at 16 weeks

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 17 Oral iron daily versus oral iron twice weekly

Outcome: 06 Treatment failure (haemoglobin < 10 g/dL) at 16 weeks

Study	Oral iron daily n/N	Oral iron twice week n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Souza 2004	1/49	7/53		100.0	0.15 [0.02, 1.21]
Total (95% CI)	49	53		100.0	0.15 [0.02, 1.21]
Total events: 1 (Oral iron daily), 7 (Oral iron twice week)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.78 p=0.08					



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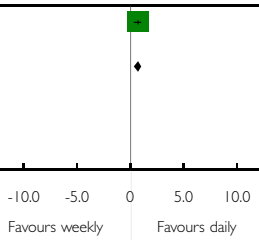
Analysis 18.01. Comparison 18 Oral iron daily versus oral iron once week, Outcome 01 Haemoglobin level at 16 weeks

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 18 Oral iron daily versus oral iron once week

Outcome: 01 Haemoglobin level at 16 weeks

Study	Oral iron daily		Oral iron once week		Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	(%)	95% CI
De Souza 2004	49	11.00 (0.70)	48	10.30 (1.00)		100.0	0.70 [0.36, 1.04]
Total (95% CI)	49		48			100.0	0.70 [0.36, 1.04]
Test for heterogeneity: not applicable							
Test for overall effect z=3.99 p=0.00007							



Analysis 18.02. Comparison 18 Oral iron daily versus oral iron once week, Outcome 02 Haemoglobin level > 11 g/dL at 16 weeks of treatment

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 18 Oral iron daily versus oral iron once week

Outcome: 02 Haemoglobin level > 11 g/dL at 16 weeks of treatment

Study	Oral iron daily	Oral iron once week	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
De Souza 2004	23/49	13/48		100.0	1.73 [1.00, 3.01]
Total (95% CI)	49	48		100.0	1.73 [1.00, 3.01]
Total events: 23 (Oral iron daily), 13 (Oral iron once week)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.95 p=0.05					

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Analysis 18.03. Comparison 18 Oral iron daily versus oral iron once week, Outcome 03 Treatment failure (haemoglobin < 10 g/dL) at 16 weeks

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 18 Oral iron daily versus oral iron once week

Outcome: 03 Treatment failure (haemoglobin < 10 g/dL) at 16 weeks

Study	Oral iron daily n/N	Oral iron once week n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Souza 2004	1/49	20/48		100.0	0.05 [0.01, 0.35]
Total (95% CI)	49	48		100.0	0.05 [0.01, 0.35]
Total events: 1 (Oral iron daily), 20 (Oral iron once week)					
Test for heterogeneity: not applicable					
Test for overall effect z=3.00 p=0.003					

Analysis 19.01. Comparison 19 Oral iron twice week versus oral iron once week, Outcome 01 Haemoglobin level at 16 weeks

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 19 Oral iron twice week versus oral iron once week

Outcome: 01 Haemoglobin level at 16 weeks

Study	Oral iron twice week N	Mean(SD)	Oral iron once week N	Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
De Souza 2004	53	10.70 (0.90)	48	10.30 (1.00)		100.0	0.40 [0.03, 0.77]
Total (95% CI)	53		48			100.0	0.40 [0.03, 0.77]
Test for heterogeneity: not applicable							
Test for overall effect z=2.10 p=0.04							

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Analysis 19.02. Comparison 19 Oral iron twice week versus oral iron once week, Outcome 02 Haemoglobin level > 11 g/dL at 16 weeks of treatment

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 19 Oral iron twice week versus oral iron once week

Outcome: 02 Haemoglobin level > 11 g/dL at 16 weeks of treatment

Study	Oral iron twice week n/N	Oral iron once week n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Souza 2004	18/53	13/48		100.0	1.25 [0.69, 2.28]
Total (95% CI)	53	48		100.0	1.25 [0.69, 2.28]

Total events: 18 (Oral iron twice week), 13 (Oral iron once week)

Test for heterogeneity: not applicable

Test for overall effect z=0.74 p=0.5

Analysis 19.03. Comparison 19 Oral iron twice week versus oral iron once week, Outcome 03 Treatment Failure (haemoglobin < 10 g/dL) at 16 weeks

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 19 Oral iron twice week versus oral iron once week

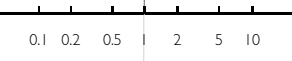
Outcome: 03 Treatment Failure (haemoglobin < 10 g/dL) at 16 weeks

Study	Oral iron twice week n/N	Oral iron once week n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
De Souza 2004	7/53	20/48		100.0	0.32 [0.15, 0.68]
Total (95% CI)	53	48		100.0	0.32 [0.15, 0.68]

Total events: 7 (Oral iron twice week), 20 (Oral iron once week)

Test for heterogeneity: not applicable

Test for overall effect z=2.94 p=0.003



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Analysis 20.01. Comparison 20 Intravenous iron sucrose 500 mg versus intravenous iron sucrose 200 mg, Outcome 01 Haemoglobin level at delivery

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 20 Intravenous iron sucrose 500 mg versus intravenous iron sucrose 200 mg

Outcome: 01 Haemoglobin level at delivery

Study	IV iron sucrose 500		IV iron sucrose 200		Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	(%)	95% CI
Wali 2002	15	11.80 (1.10)	20	11.30 (0.90)		100.0	0.50 [-0.18, 1.18]
Total (95% CI)	15		20			100.0	0.50 [-0.18, 1.18]

Test for heterogeneity: not applicable

Test for overall effect z=1.44 p=0.2

Analysis 20.02. Comparison 20 Intravenous iron sucrose 500 mg versus intravenous iron sucrose 200 mg, Outcome 02 Haemoglobin level > 11g/dL at delivery

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 20 Intravenous iron sucrose 500 mg versus intravenous iron sucrose 200 mg

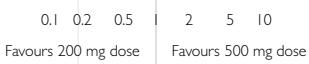
Outcome: 02 Haemoglobin level > 11g/dL at delivery

Study	IV iron sucrose 500	IV iron sucrose 200	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
Wali 2002	12/15	14/20		100.0	1.14 [0.78, 1.68]
Total (95% CI)	15	20		100.0	1.14 [0.78, 1.68]

Total events: 12 (IV iron sucrose 500), 14 (IV iron sucrose 200)

Test for heterogeneity: not applicable

Test for overall effect z=0.68 p=0.5



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Analysis 20.03. Comparison 20 Intravenous iron sucrose 500 mg versus intravenous iron sucrose 200 mg, Outcome 03 Moderate abdominal pain

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 20 Intravenous iron sucrose 500 mg versus intravenous iron sucrose 200 mg

Outcome: 03 Moderate abdominal pain

Study	IV iron sucrose 500 n/N	IV iron sucrose 200 n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Wali 2002	1/15	1/20		100.0	1.33 [0.09, 19.64]
Total (95% CI)	15	20		100.0	1.33 [0.09, 19.64]

Total events: 1 (IV iron sucrose 500), 1 (IV iron sucrose 200)

Test for heterogeneity: not applicable

Test for overall effect z=0.21 p=0.8

Analysis 21.01. Comparison 21 Intravenous iron sucrose 500 mg versus intramuscular iron sorbitol, Outcome 01 Maternal haemoglobin level at birth

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 21 Intravenous iron sucrose 500 mg versus intramuscular iron sorbitol

Outcome: 01 Maternal haemoglobin level at birth

Study	IV iron sucrose 500 N	Mean(SD)	IM iron sorbitol N	Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Wali 2002	15	11.80 (1.10)	25	10.20 (1.20)		100.0	1.60 [0.87, 2.33]
Total (95% CI)	15		25			100.0	1.60 [0.87, 2.33]

Test for heterogeneity: not applicable

Test for overall effect z=4.30 p=0.00002

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Analysis 21.02. Comparison 21 Intravenous iron sucrose 500 mg versus intramuscular iron sorbitol, Outcome 02 Haemoglobin level > 11g/dL at delivery

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 21 Intravenous iron sucrose 500 mg versus intramuscular iron sorbitol

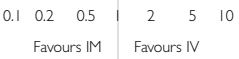
Outcome: 02 Haemoglobin level > 11g/dL at delivery

Study	IV iron sucrose 500 n/N	IM iron sorbitol n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Wali 2002	12/15	7/25		100.0	2.86 [1.45, 5.63]
Total (95% CI)	15	25		100.0	2.86 [1.45, 5.63]

Total events: 12 (IV iron sucrose 500), 7 (IM iron sorbitol)

Test for heterogeneity: not applicable

Test for overall effect z=3.04 p=0.002



Analysis 22.01. Comparison 22 Intravenous iron sucrose 200 mg versus intramuscular iron sorbitol, Outcome 01 Haemoglobin level at delivery

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 22 Intravenous iron sucrose 200 mg versus intramuscular iron sorbitol

Outcome: 01 Haemoglobin level at delivery

Study	IV iron sucrose 200 N	Mean(SD)	IM iron sorbitol N	Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Wali 2002	20	11.30 (0.90)	25	10.20 (1.20)		100.0	1.10 [0.49, 1.71]
Total (95% CI)	20		25			100.0	1.10 [0.49, 1.71]

Test for heterogeneity: not applicable

Test for overall effect z=3.51 p=0.0004

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Analysis 22.02. Comparison 22 Intravenous iron sucrose 200 mg versus intramuscular iron sorbitol, Outcome 02 Haemoglobin level > 11 g/dL at delivery

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 22 Intravenous iron sucrose 200 mg versus intramuscular iron sorbitol

Outcome: 02 Haemoglobin level > 11 g/dL at delivery

Study	IV iron sucrose 200 n/N	IM iron sorbitol n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Wali 2002	14/20	7/25		100.0	2.50 [1.25, 4.99]
Total (95% CI)	20	25		100.0	2.50 [1.25, 4.99]
Total events: 14 (IV iron sucrose 200), 7 (IM iron sorbitol)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.60 p=0.009					

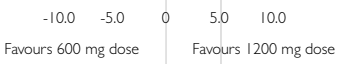
Analysis 23.01. Comparison 23 Oral ferrous sulphate iron 1200 mg/day versus 600 mg/day, Outcome 01 Haematocrit (%) at 4 weeks of treatment

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 23 Oral ferrous sulphate iron 1200 mg/day versus 600 mg/day

Outcome: 01 Haematocrit (%) at 4 weeks of treatment

Study	Oral iron 1200 mg N	Mean(SD)	Oral iron 600 mg N	Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Ogunbode 1980	28	31.62 (2.14)	28	31.25 (2.22)		100.0	0.37 [-0.77, 1.51]
Total (95% CI)	28		28			100.0	0.37 [-0.77, 1.51]
Test for heterogeneity: not applicable							
Test for overall effect z=0.63 p=0.5							



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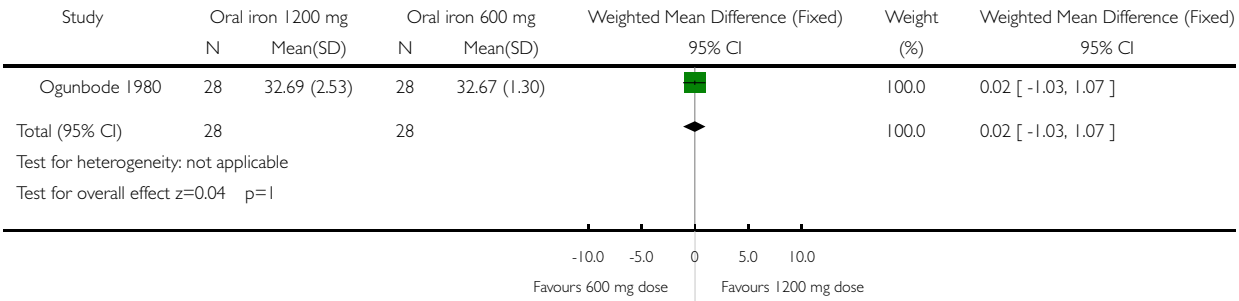
Analysis 23.02. Comparison 23 Oral ferrous sulphate iron 1200 mg/day versus 600 mg/day, Outcome 02 Haematocrit (%) at 8 weeks of treatment

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 23 Oral ferrous sulphate iron 1200 mg/day versus 600 mg/day

Outcome: 02 Haematocrit (%) at 8 weeks of treatment

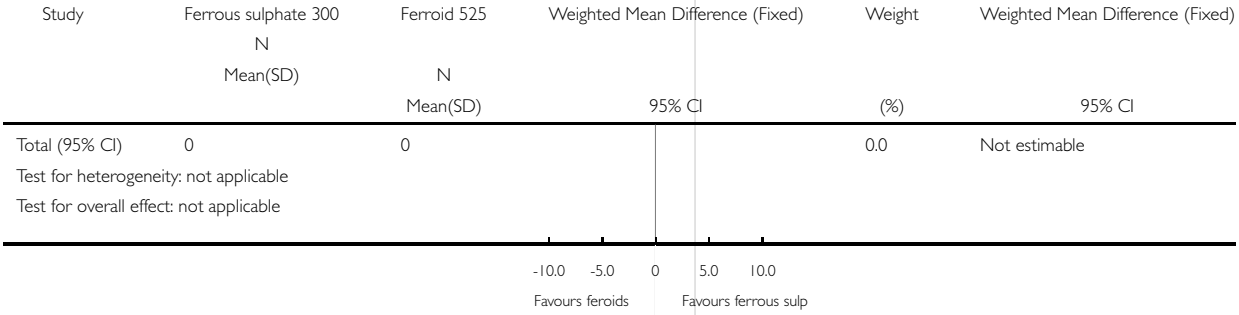


Analysis 24.01. Comparison 24 Oral ferrous sulphate (300 mg) versus ferroids (525 mg), Outcome 01 Haemoglobin level at birth

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 24 Oral ferrous sulphate (300 mg) versus ferroids (525 mg)

Outcome: 01 Haemoglobin level at birth



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Analysis 25.01. Comparison 25 Intramuscular iron sorbitol-glu acid versus intravenous iron dextran, Outcome 01 Haematocrit (%) at 4 weeks of treatment

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 25 Intramuscular iron sorbitol-glu acid versus intravenous iron dextran

Outcome: 01 Haematocrit (%) at 4 weeks of treatment

Study	IM iron sorb-gluc		IV iron dextran		Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	(%)	95% CI
Oluboyede 1980	31	32.39 (2.16)	28	30.21 (3.19)		100.0	2.18 [0.77, 3.59]
Total (95% CI)	31		28			100.0	2.18 [0.77, 3.59]
Test for heterogeneity: not applicable							
Test for overall effect z=3.04 p=0.002							

Analysis 25.02. Comparison 25 Intramuscular iron sorbitol-glu acid versus intravenous iron dextran, Outcome 02 Haematocrit (%) at 8 weeks of treatment

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 25 Intramuscular iron sorbitol-glu acid versus intravenous iron dextran

Outcome: 02 Haematocrit (%) at 8 weeks of treatment

Study	IM iron sorb-gluc		IV iron dextran		Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	N	Mean(SD)	N	Mean(SD)	95% CI	(%)	95% CI
Oluboyede 1980	21	34.43 (2.31)	22	32.95 (2.13)		100.0	1.48 [0.15, 2.81]
Total (95% CI)	21		22			100.0	1.48 [0.15, 2.81]
Test for heterogeneity: not applicable							
Test for overall effect z=2.18 p=0.03							

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Analysis 25.03. Comparison 25 Intramuscular iron sorbitol-glu acid versus intravenous iron dextran, Outcome 03 Neonatal jaundice

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 25 Intramuscular iron sorbitol-glu acid versus intravenous iron dextran

Outcome: 03 Neonatal jaundice

Study	IM iron sorb-gluc n/N	IV iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Oluboyede 1980	1/32	1/30		100.0	0.94 [0.06, 14.33]
Total (95% CI)	32	30		100.0	0.94 [0.06, 14.33]
Total events: 1 (IM iron sorb-gluc), 1 (IV iron dextran)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.05 p=1					

Analysis 25.04. Comparison 25 Intramuscular iron sorbitol-glu acid versus intravenous iron dextran, Outcome 04 Viral hepatitis

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 25 Intramuscular iron sorbitol-glu acid versus intravenous iron dextran

Outcome: 04 Viral hepatitis

Study	IM iron sorb-gluc n/N	IV iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Oluboyede 1980	1/32	0/30		100.0	2.82 [0.12, 66.62]
Total (95% CI)	32	30		100.0	2.82 [0.12, 66.62]
Total events: 1 (IM iron sorb-gluc), 0 (IV iron dextran)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.64 p=0.5					

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Analysis 25.05. Comparison 25 Intramuscular iron sorbitol-glu acid versus intravenous iron dextran, Outcome 05 Severe allergic reaction

Review: Treatments for iron-deficiency anaemia in pregnancy

Comparison: 25 Intramuscular iron sorbitol-glu acid versus intravenous iron dextran

Outcome: 05 Severe allergic reaction

Study	IM iron sorb-gluc n/N	IV iron dextran n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Oluboyede 1980	0/32	1/30		100.0	0.31 [0.01, 7.40]
Total (95% CI)	32	30		100.0	0.31 [0.01, 7.40]
Total events: 0 (IM iron sorb-gluc), 1 (IV iron dextran)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.72 p=0.5					

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