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Daily iron supplementation for improving anaemia, iron status and health in menstruating women (Review)

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[Intervention Review]

Daily iron supplementation for improving anaemia, iron status and health in menstruating women

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ABSTRACT

Background

Iron-deficiency anaemia is highly prevalent among non-pregnant women of reproductive age (menstruating women) worldwide, although the prevalence is highest in lower-income settings. Iron-deficiency anaemia has been associated with a range of adverse health outcomes, which restitution of iron stores using iron supplementation has been considered likely to resolve. Although there have been many trials reporting effects of iron in non-pregnant women, these trials have never been synthesised in a systematic review.

Objectives

To establish the evidence for effects of daily supplementation with iron on anaemia and iron status, as well as on physical, psychological and neurocognitive health, in menstruating women.

Search methods

In November 2015 we searched CENTRAL, Ovid MEDLINE, EMBASE, and nine other databases, as well as four digital thesis repositories. In addition, we searched the World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) and reference lists of relevant reviews.

Selection criteria

We included randomised controlled trials (RCTs) and quasi-RCTs comparing daily oral iron supplementation with or without a cointervention (folic acid or vitamin C), for at least five days per week at any dose, to control or placebo using either individual- or cluster-randomisation. Inclusion criteria were menstruating women (or women aged 12 to 50 years) reporting on predefined primary (anaemia, haemoglobin concentration, iron deficiency, iron-deficiency anaemia, all-cause mortality, adverse effects, and cognitive function) or secondary (iron status measured by iron indices, physical exercise performance, psychological health, adherence, anthropometric measures, serum/plasma zinc levels, vitamin A status, and red cell folate) outcomes.

Data collection and analysis

We used the standard methodological procedures of Cochrane.

Main results

The search strategy identified 31,767 records; after screening, 90 full-text reports were assessed for eligibility. We included 67 trials (from 76 reports), recruiting 8506 women; the number of women included in analyses varied greatly between outcomes, with endpoint haemoglobin concentration being the outcome with the largest number of participants analysed (6861 women). Only 10 studies were considered at low overall risk of bias, with most studies presenting insufficient details about trial quality.

Women receiving iron were significantly less likely to be anaemic at the end of intervention compared to women receiving control (risk ratio (RR) 0.39 (95% confidence interval (CI) 0.25 to 0.60, 10 studies, 3273 women, moderate quality evidence). Women receiving iron had a higher haemoglobin concentration at the end of intervention compared to women receiving control (mean difference (MD) 5.30, 95% CI 4.14 to 6.45, 51 studies, 6861 women, high quality evidence). Women receiving iron had a reduced risk of iron deficiency compared to women receiving control (RR 0.62, 95% CI 0.50 to 0.76, 7 studies, 1088 women, moderate quality evidence). Only one study (55 women) specifically reported iron-deficiency anaemia and no studies reported mortality. Seven trials recruiting 901 women reported on 'any side effect' and did not identify an overall increased prevalence of side effects from iron supplements (RR 2.14, 95% CI 0.94 to 4.86, low quality evidence). Five studies recruiting 521 women identified an increased prevalence of gastrointestinal side effects in women taking iron (RR 1.99, 95% CI 1.26 to 3.12, low quality evidence). Six studies recruiting 604 women identified an increased prevalence of loose stools/diarrhoea (RR 2.13, 95% CI 1.10, 4.11, high quality evidence); eight studies recruiting 1036 women identified an increased prevalence of hard stools/constipation (RR 2.07, 95% CI 1.35 to 3.17, high quality evidence). Seven studies recruiting 1190 women identified evidence of an increased prevalence of abdominal pain among women randomised to iron (RR 1.55, 95% CI 0.99 to 2.41, low quality evidence). Eight studies recruiting 1214 women did not find any evidence of an increased prevalence of nausea among women randomised to iron (RR 1.19, 95% CI 0.78 to 1.82). Evidence that iron supplementation improves cognitive performance in women is uncertain, as studies could not be meta-analysed and individual studies reported conflicting results. Iron supplementation improved maximal and submaximal exercise performance, and appears to reduce symptomatic fatigue. Although adherence could not be formally meta-analysed due to differences in reporting, there was no evident difference in adherence between women randomised to iron and control.

Authors' conclusions

Daily iron supplementation effectively reduces the prevalence of anaemia and iron deficiency, raises haemoglobin and iron stores, improves exercise performance and reduces symptomatic fatigue. These benefits come at the expense of increased gastrointestinal symptomatic side effects.

PLAIN LANGUAGE SUMMARY

Iron supplementation taken daily for improving health in menstruating women

Review question

What are the effects of iron, taken orally for at least five days a week, on health outcomes in menstruating women (compared with not giving iron)?

Background

Iron deficiency (a shortage of iron stored in the body) and anaemia (low levels of haemoglobin - healthy red blood cells - in the blood) are common problems globally, especially in women. Low levels of iron can eventually cause anaemia (iron-deficiency anaemia). Among non-pregnant women, around one third are anaemic worldwide. The problem is seen most commonly in low-income countries, but iron deficiency and anaemia are more common in women in all contexts. Iron-deficiency anaemia is considered to impair health and well-being in women, and iron supplements - tablets, capsules, syrup or drops containing iron - are a commonly used intervention to prevent and treat this condition. We sought to review the evidence of iron, taken orally for at least five days per week, for improving health outcomes in non-pregnant women of reproductive age (menstruating women).

Search data

The review is current to November 2015.

Study characteristics

We included studies comparing the effects of iron compared with no iron when given at least five days per week to menstruating women. We identified 67 trials recruiting 8506 women eligible for inclusion in the review. Most trials lasted between one and three months. The most commonly used iron form was ferrous sulphate.

Key results

We found evidence that iron supplements reduce the prevalence of anaemia and iron deficiency, and raise levels of haemoglobin in the blood and in iron stores. Iron supplementation clearly increases the risk of side effects, for example, constipation and abdominal pain.

Quality of the evidence

We found high quality evidence that iron improves haemoglobin and produces changes in bowel function, but moderate quality evidence that iron reduces the prevalence of anaemia and iron deficiency. Evidence of the effects of iron on other outcomes, such as abdominal pain, is of low quality. There are no data on the effects of iron on mortality in this population group.

Further definitive studies are needed to identify whether taking iron supplements orally for at least five days a week has an impact on key, health-related outcomes.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Daily oral iron supplementation

Patient or population: menstruating women (non-pregnant women of reproductive age)
Settings: all settings
Intervention: daily oral iron supplementation
Comparison: no daily iron supplementation

Outcomes	Relative effect (95% CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
Anaemia at end of therapy (total), as defined by trial authors	**RR 0.39** (0.25 to 0.60)	3273 (10)	⊕⊕⊕◯ **Moderate**[1]	Large effect, but downgraded 1 level for risk of bias and 1 level for inconsistency
Haemoglobin at end of therapy (total), g/L	**MD 5.30** (4.14 to 6.45)	6861 (51)	⊕⊕⊕⊕ **High**	-
Iron deficiency at end of therapy (total), as defined by trial authors	**RR 0.62** (0.50 to 0.76)	1088 (7)	⊕⊕⊕◯ **Moderate**[1]	Downgraded 1 level for risk of bias
Iron-deficiency anaemia at end of therapy, as defined by trial authors	-	55 (1)	-	Meta-analysis not possible
All-cause mortality, over the course of the study	-	-	-	Not measured
Any adverse side effects (total), as defined and reported by trial authors	**RR 2.14** (0.94 to 4.86)	901 (7)	⊕⊕◯◯ **Low**[2]	Downgraded 1 level for imprecision, and 1 level for risk of bias
GI side effects (total), events during study, as defined and reported by trial authors	**RR 1.99** (1.26 to 3.12)	521 (5)	⊕⊕◯◯ **Low**[2]	Downgraded 1 level for risk of bias, and 1 level for imprecision
Loose stools/diarrhoea (total), events during study, as defined and reported by trial authors	**RR 2.13**, (1.10 to 4.11)	604 (6)	⊕⊕⊕⊕ **High**[2]	-

Hard stools/constipation (total), events during study, as defined and reported by trial authors	**RR 2.07** (1.35 to 3.17)	1036 (8)	⊕⊕⊕⊕ **High**[2]	-
Abdominal pain (total), events during study, as defined and reported by trial authors	**RR 1.55** (0.99 to 2.41)	1190 (7)	⊕⊕◯◯ **Low**[2]	Downgraded 1 level for risk of bias, and 1 level for imprecision
Cognitive function, as measured by trial authors	-	-	-	Unable to combine the data in a meta-analysis

CI: confidence interval; **GI:** gastrointestinal; **GRADE:** Grades of Recommendation, Assessment, Development, and Evaluation; **MD:** mean difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]Anaemia and iron deficiency are rated as moderate as, although iron benefits both outcomes, further studies are needed to more accurately quantify benefit.
[2]The quality of evidence for several adverse outcomes (any adverse effect, GI side effects and abdominal pain) were deemed low due to insufficient numbers to determine the true effect of intervention with wide CIs. Diarrhoea and constipation had similar participant numbers, however, the magnitude of the difference between intervention and control arms were larger.

BACKGROUND

Description of the condition

Over 1.6 billion people worldwide have anaemia, a condition in which haemoglobin production is diminished. Women of menstruating age account for approximately a third of all cases of anaemia across the globe (WHO/CDC 2008). The most recent estimates suggest that 29% of non-pregnant women worldwide are anaemic (Stevens 2013). Iron deficiency is believed to contribute to at least half the global burden of anaemia, especially in non-malaria-endemic countries (Stoltzfus 2001). Iron deficiency is thus considered the most prevalent nutritional deficiency in the world.

Iron deficiency occurs following negative iron balance. As body iron stores are exhausted, the production of red blood cells is impaired, and finally iron-deficiency anaemia results (Suominen 1998). The major causes of negative iron balance include inadequate dietary iron intake (due to consumption of a diet with a low overall or bioavailable iron content); increased losses of iron due to chronic blood loss (in women, due to menstruation and exacerbated in cases of heavier menstrual bleeding, and by intestinal hookworm infection in individuals living in endemic settings (Hotez 2005)); and increased iron requirements (e.g. during growth or pregnancy). Low dietary iron intake and bioavailability are considered key contributors to the burden of iron deficiency. This is especially so in populations consuming diets that are low in meat sources and high in cereals such as wheat, rice, maize and

millet, which are rich in phytates, compounds that bind to iron in the meal preventing its absorption (Sharpe 1950). Other dietary components such as tannins (found in tea) and calcium (contained in milk products) also inhibit iron absorption.

Women beyond menarche and prior to menopause are at especially high risk of iron deficiency due to menstrual blood losses. The onset of menstrual blood losses accompanied by rapid growth, with an associated expansion of red cell mass and tissue iron requirements, means adolescent girls have a particularly high iron need compared with their male counterparts. If this is compounded by inadequate dietary iron intake, they may be at especially high risk of iron deficiency (Dallman 1992). Other important causes of iron deficiency in women include intestinal malabsorptive conditions such as coeliac disease, chronic blood losses due to menorrhagia from uterine pathologies (such as fibroids), frequent blood donation, and benign and malignant gastrointestinal lesions (Goddard 2011). Iron deficiency, with and without anaemia, has also been noted to be prevalent among female athletes and is thought to be due to diets deficient in iron, increased losses due to gastrointestinal tract bleeding, and reduced iron absorption due to subclinical inflammation (Peeling 2008). The risk of iron deficiency may be modified by genetic factors such as inheritance of genes associated with haemochromatosis and polymorphisms in the TMPRSS6 gene (Chambers 2009).

As well as being critical to the production of haemoglobin, iron has a critical role in many other aspects of human physiology as it is involved in a range of oxidation-reduction enzymatic reactions in the muscle and nervous tissue (Andrews 1999), as well as other organs. Iron deficiency and iron-deficiency anaemia have been associated with a range of adverse physical, psychological, and cognitive effects. Animal models suggest a role for iron in brain development and function, with iron depletion being associated with dysregulated neurotransmitter levels (Lozoff 2007), and some, but not all, clinical studies have shown associations between iron supplementation and improvement in cognitive performance (Murray-Kolb 2007) and mood and well being, with a reduction in fatigue (Verdon 2003). Observational studies have suggested that iron deficiency in the absence of anaemia impairs exercise performance in women (Scholz 1997), while some, but not all, interventional studies of iron supplementation among the same population have shown variable improvements in maximal and submaximal exercise performance (Brownlie 2002; LaManca 1993), endurance (Brownlie 2004; Hinton 2000), and muscle fatigue (Brutsaert 2003). There may also be associations between iron status and haemoglobin concentrations and work productivity (Li 1994: Scholz 1997; Wolgemuth 1982). When anaemia is severe, it may cause lethargy, fatigue, irritability, pallor, breathlessness and reduced tolerance for exertion.

Alleviation of iron-deficiency anaemia among menstruating women is thus considered a major public health priority, both to improve their existing health status and to enhance their health in preparation for future pregnancies (WHO 2009).

Other causes of anaemia important to distinguish from iron deficiency include anaemia of chronic disease (associated with inflammation, which causes iron to be withheld from erythropoiesis (the process by which red blood cells are produced)), functional iron deficiency (associated with renal impairment), genetic conditions of the red cell (haemoglobin, enzymes and membrane), and infectious diseases (including malaria).

Description of the intervention

Strategies to improve iron intake and alleviate iron-deficiency anaemia include mass and point-of-use fortification of foods with iron; dietary diversification to increase iron intake, absorption and utilisation; iron supplementation; and antihelminthic treatment. Supplementation is probably the most widespread intervention practiced clinically and in public health.

Oral iron supplementation, administered once a day or more frequently, is the standard clinical practice of many physicians in the treatment of iron deficiency in women (Goddard 2011). Daily iron and folic acid supplementation for three months should be considered for the prophylaxis of iron deficiency in populations where the prevalence of anaemia exceeds 40% (WHO/UNICEF/UNU 2001). In addition to its haematological effects, the use of folic acid during the periconceptional period helps prevent the risk of neural tube defects in babies (WHO/UNICEF/UNU 2001).

Iron is generally administered as a salt compound in a tablet, capsule, liquid or dispersible formulation. The most commonly prescribed salts are ferrous sulphate, fumarate, and gluconate (Pasricha 2010). Ferrous sulphate is perhaps the most commonly used of these interventions. Iron formulations are commonly combined with vitamin C to improve absorption, or folic acid to improve child outcomes when used before or during pregnancy. Commonly reported side effects of iron supplements include gastrointestinal disturbances (especially constipation and nausea) and dark stools. In those using liquid formulations, tooth staining can occur. Slow or sustained-release formulations in which iron is surrounded by a coating, aim to alleviate gastrointestinal side effects by delaying delivery of iron to a more distal point in the gastrointestinal tract, but their efficacy has been questioned. Thus, compliance to daily oral iron interventions due to adverse events can be a critical limiting factor to their effectiveness.

How the intervention might work

Iron is absorbed by intestinal cell luminal and basal transporters, bound to proteins and transported to the bone marrow, muscle and other tissue, where it is taken up by specific receptors and used for biological functions or stored (Andrews 1999). Textbooks advise that in an iron-deficient anaemic individual, haemoglobin concentrations should rise by 1 g/dL per week, with early evidence

of red blood cell formation discernible in the peripheral blood after 72 hours of supplementation (Mahoney 2011).

There is an inverse relationship between iron status and the ability to absorb iron. Iron deficiency induces changes in intestinal iron transport that can double absorption of iron from the diet (Thankachan 2008). Thus, as with dietary sources of iron, absorption from supplements depends on the baseline iron status of the individual and the co-consumption of iron absorption enhancers (such as vitamin C, other acidic foods, and meat) and inhibitors (calcium, phytates and tannins) (Hurrell 2010; Sharpe 1950).

As mentioned above, the ubiquitous presence of iron in the human body is such that its deficiency impairs a number of physiological functions and iron supplementation may thus benefit physical, psychological and cognitive health. Improvements in haemoglobin and myoglobin concentrations may ensure adequate tissue oxygenation and performance (Umbreit 2005). Iron is also present in the brain in relatively large amounts and is involved in neurotransmitter function (Burhans 2005); an adequate supply may contribute to maintaining normal cognitive and psychological health, although the mechanisms are not completely elucidated as yet.

An additional consideration when providing supplements at population level is the endemicity of malaria in a given region. Approximately 40% of the world's population is exposed to the malaria parasite and it is endemic in over 100 countries, causing more than a million deaths per year (WHO 2010). Provision of iron in malaria-endemic areas, particularly to children, has been controversial due to concerns that iron therapy may exacerbate infections, in particular malaria (Okebe 2011; Oppenheimer 2001). It is still not completely clear whether iron produces the same effects among older populations or whether subclinical malaria alters the response to iron supplementation.

Why it is important to do this review

Daily oral supplementation in women has been a longstanding intervention in both public health and clinical fields. Many patients and clinicians ascribe adverse health outcomes (including fatigue and lethargy, impaired cognitive performance and psychological dysfunction) to iron deficiency, even in the absence of anaemia, and attribute improvement in these symptoms to iron supplementation. In addition, many sporting authorities (including the International Olympic Committee (IOC 2009)) recommend screening of female athletes for iron deficiency in order to target the use of iron supplementation, with a view to improving performance. Daily iron and folic acid supplementation for three months should be considered for the prophylaxis of iron deficiency in populations where the prevalence of anaemia exceeds 40%. Iron supplementation has been recommended for preventing anaemia in women of childbearing age, and to optimise pre-conception iron status (WHO 2011).

Several intervention trials have evaluated improvements in haemoglobin and iron status, as well as non-haematologic outcomes such as physical, cognitive and psychological health, in menstruating women receiving iron supplementation. However, evaluation of this intervention has not been subject to systematic review and thus it is difficult to estimate the benefits and risks associated with the daily use of iron supplements in menstruating women.

This review will complement the findings of other Cochrane systematic reviews assessing the use of iron supplements alone, or in combination with other vitamins and minerals, in different female populations: intermittent supplementation in children (De-Regil 2011), iron supplementation among children in malaria-endemic areas (Okebe 2011), intermittent iron supplementation in menstruating women (Fernández-Gaxiola 2011), daily and intermittent iron and folic acid supplementation in pregnant women (Peña-Rosas 2009), multiple micronutrient supplementation in pregnancy (Haider 2006), and iron supplementation during the postpartum period (Dodd 2004).

OBJECTIVES

To establish the evidence for effects of daily supplementation with iron on anaemia and iron status, as well as on physical, psychological and neurocognitive health, in menstruating women.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) and quasi-RCTs with either individual- or cluster-randomisation. Quasi-RCTs are trials that use non-random systematic methods to allocate participants to treatment groups such as alternation, or assignment based on date of birth or case record number (Higgins 2011a).

We did not include observational study designs (e.g. cohort or case-control studies) in the meta-analysis but, where relevant, considered such evidence in the discussion.

Types of participants

Inclusion criteria

1. Menstruating women, that is, women beyond menarche and prior to menopause who were not pregnant or lactating or had any condition that impeded the presence of menstrual

periods, regardless of their baseline iron or anaemia status (or both), ethnicity, country of residence or level of endurance.

2. We included studies for which results for females between 12 years and 50 years of age (plausible age range for menstruation) could be extracted separately, or in which more than half of the participants fulfilled this criterion.

Exclusion criteria

1. Studies targeting populations with conditions affecting iron metabolism, intestinal malabsorption conditions, ongoing excessive blood loss (including ongoing blood donations), inflammatory bowel disease, cancer, chronic congestive cardiac failure, chronic renal failure, chronic liver failure or chronic infectious disease.

2. Studies that were purely evaluating kinetics of erythropoiesis or pharmacology of iron supplements or absorption.

3. Studies in hospitalised or ill people.

Types of interventions

We considered iron supplements to comprise iron formulations that may or may not have also contained folic acid or vitamin C, since these are commonly included in iron preparations. Doses needed to be given no less than five days a week, regardless of dose and duration of the intervention.

We included, in an overall comparison, effects of daily oral supplementation with iron alone, or in combination with folic acid or vitamin C, versus receiving no supplemental iron. In this review, 'iron supplement' refers to compounds containing iron salts such as ferrous sulphate, ferrous fumarate, ferrous gluconate, carbonyl or colloidal iron. Iron may have been delivered as a tablet (including dispersible forms), capsule, or liquid.

We included (and noted) studies in which iron supplements were given along with cointerventions such as other nutrients (e.g. zinc, vitamin A), deworming, education or other approaches but only if the cointerventions were the same in both the intervention and comparison groups. We did not include studies where additional haemopoietic agents were administered such as exogenous erythropoietin.

We undertook a simple overall comparison (iron versus control) and considered use of cointerventions as subgroups. This enabled us to appraise the overall evidence for intervening with iron supplementation, but differed from what we had proposed in our original protocol (Differences between protocol and review).

Interventions excluded from this review include point-of-use fortification with micronutrient powders or lipid-based foods, mass fortification of staple foods such as wheat or maize flours or condiments, and intermittent iron supplementation, which are evaluated in previous or ongoing Cochrane reviews (see Fernández-Gaxiola 2011; Pasrischa 2012; Peña-Rosas 2014; Self 2012).

Types of outcome measures

Primary outcomes

1. Anaemia (haemoglobin concentrations below a cut-off defined by trial authors).*

2. Haemoglobin (g/L).*

3. Iron deficiency (as measured by trial authors using indicators of iron status such as ferritin or transferrin).*

4. Iron-deficiency anaemia (defined by the presence of anaemia plus iron deficiency, diagnosed with an indicator of iron status selected by trialists).*

5. All-cause mortality.*

6. Adverse side effects (as measured by trial authors such as abdominal pain, vomiting, nausea, heartburn, diarrhoea, constipation).*

7. Cognitive function (as defined by trial authors. For example, for adolescents, school grades, test performance, intelligence testing; for adults not in school, formal tests addressing intelligence, memory, attention, and other cognitive domains). We accepted any measure of cognitive function that has been previously validated as an appropriate test in this domain.*

Outcomes marked with an asterisk (*) are included in Summary of findings for the main comparison.

Secondary outcomes

1. Iron status (as reported: ferritin, transferrin saturation, soluble transferrin receptor, soluble transferrin receptor-ferritin index, total iron binding capacity, serum iron).

2. Physical exercise performance (as defined by trial authors, in particular peak exercise performance (VO_2 max/peak - absolute and relative), submaximal exercise performance (heart rate, percentage VO_2 max, energy consumption), and endurance (time)).

3. Psychological health (e.g. depression as defined by the Center for Epidemiological Studies - Depression (CES-D) scale (Radloff 1977) or visual analogue scales; fatigue as defined by the trial authors, anxiety as defined by trial authors.

4. Adherence (percentage of women who consumed more than 70% of the expected doses).

5. Anthropometric measures (Z scores for height and weight by age for adolescents, and body mass index for adults).

6. Serum/plasma zinc (μmol/L).

7. Vitamin A status (serum/plasma retinol (mmol/L) or retinol binding protein (mmol/L)).

8. Red cell folate (mmol/L).

For populations in malaria-endemic areas, we reported two additional outcomes.

1. Malaria incidence.

2. Malaria severity.

If two outcomes evaluated the same construct (e.g. iron status evaluated with either ferritin or soluble transferrin receptors), we treated them separately.

Search methods for identification of studies

Electronic searches

We searched the following databases in March 2012, November 2014 and again on 12 November 2015.

1. Cochrane Central Register of Controlled Trials (CENTRAL, 2015, Issue 10, part of *The Cochrane Library*), and which includes the specialised register of the Cochrane Developmental, Psychosocial and Learning Problems Group.
2. Ovid MEDLINE (1946 to November Week 1 2015).
3. Embase (1980 to 2015 Week 45; Ovid).
4. CINAHL (1937 to current; EBSCOHost).
5. Conference Proceedings Citation Index - Science (CPCI-S; 1937 to current; Web of Science).
6. Science Citation Index (SCI; 1970 to 10 November 2015; Web of Science).
7. POPLINE (popline.org; all available years).

We searched the following regional indexes from the World Health Organization (WHO) Global Health Library on 28 May 2015, and again on 8 December 2015.

1. Literature in the Health Sciences in Latin America and the Caribbean (LILACS; all available years).
2. African Index Medicus (AIM; all available years).
3. Western Pacific Region Index Medicus (WPRIM; all available years).
4. Index Medicus for the Eastern Mediterranean Region (IMEMR; all available years).
5. Index Medicus for South-East Asia Region (IMSEAR; all available years).

We used the following sources to search for theses on 28 May 2015, and again on 8 December 2015.

1. WorldCat (worldcat.org; all available years).
2. DART-Europe E-theses Portal (dart-europe.eu; all available years).
3. Australasian Digital Theses Program (trove.nla.gov.au; all available years).
4. Proquest Dissertations and Theses Global (all available years).

The search strategies for each database are reported in Appendix 1. We did not apply any date or language restrictions.

Searching other resources

We searched all available years of the WHO International Clinical Trials Registry Platform (ICTRP) on 25 May 2015, and again on 8 December 2015 (apps.who.int/trialsearch). We also screened previously published reviews in order to identify other possible studies.

Data collection and analysis

Selection of studies

We stored all studies identified by our search strategy in Endnote 2015 reference manager software prior to evaluation. Titles and abstracts of obtained studies were screened by two authors (MSYL and SRP) independently. For those studies that were selected as potentially eligible for inclusion, two of the review authors (from CES, JS, MSYL or SRP) assessed whether they met the review's inclusion criteria. We kept records of all eligibility decisions using a digital eligibility form for each study. If study reports contained insufficient information on methods, participants or interventions, we attempted to contact the authors for further information. Disagreements were resolved through discussion between the coauthors.

Data extraction and management

We extracted data from studies using a digital extraction form designed for this review. We first piloted the form on a small number of study reports and modified it as necessary. For eligible studies, two review authors (two from JS, MSYL, CS or SRP) independently extracted data using the form. One author (MSYL) then entered data into Review Manager (RevMan) software (RevMan 2014) and a second author (SRP) checked data entry for accuracy. We resolved discrepancies through discussion between all review authors.

For each study, we collected data on the following domains.

1. Trial methods:
   i) study design;
   ii) unit and method of allocation;
   iii) masking of participants and outcomes; and
   iv) exclusion of participants after randomisation and proportion of losses at follow-up.
2. Participants:
   i) location of the study;
   ii) sample size;
   iii) age;
   iv) baseline status of anaemia;
   v) baseline status of iron deficiency; and
   vi) inclusion and exclusion criteria, as described in Criteria for considering studies for this review.
3. Intervention:
   i) dose of iron;
   ii) type of iron compound;
   iii) duration of the intervention; and
   iv) cointerventions.

4. Comparison group:
    i) use of placebo or no intervention.ppe
5. Outcomes:
    i) primary and secondary outcomes, as outlined in Types of outcome measures.

We recorded outcomes that were both prespecified and not prespecified, although we did not use the latter to underpin the conclusions of the review.

Assessment of risk of bias in included studies

For each study, two of the four review authors (CES, JS, MSYL, SRP) used the standard Cochrane 'Risk of bias' tool to assess the risk of bias of each included study across the following eight domains: sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, other biases, and overall risk of bias (Higgins 2011b). They applied the following criteria. Disagreements were resolved through discussion between review authors.

1. Random sequence generation (checking for possible selection bias)

We assessed whether the method used to generate the allocation sequence was described in sufficient detail to allow an assessment of whether it produced comparable groups and rated it as follows.

1. Low risk of bias: any truly random process (e.g. random number table, computer random number generator).
2. High risk of bias: any non-random process (e.g. odd or even date of birth, hospital or clinic record number).
3. Unclear risk of bias: random sequence generation not stated or insufficient information to deem whether study was at low or high risk of bias.

2. Allocation concealment (checking for possible selection bias)

We assessed whether the method used to conceal the allocation sequence was described in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment and rated it as follows.

1. Low risk of bias: telephone or central randomisation, consecutively numbered sealed opaque envelopes used to conceal the allocation sequence.
2. High risk of bias: open random allocation, unsealed or non-opaque envelopes used to conceal the allocation sequence.
3. Unclear risk of bias: not stated or insufficient information to deem whether study was at low or high risk of bias.

3. Blinding of participants and personnel (checking for possible performance bias)

We assessed all measures used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We rated the risk of performance bias associated with blinding as follows.

1. Low risk of bias: participants and personnel were reported to be blinded in such a manner that they could not determine the groups to which participants belonged.
2. High risk of bias: participant or personnel were not blinded or blinding was performed in such a manner that it was possible to determine the groups to which participants belonged.
3. Unclear risk of bias: insufficient information to permit a judgement of low or high risk of bias.

Whilst assessed separately, we combined these assessments into a single evaluation of risk of bias associated with blinding (Higgins 2011b).

4. Blinding of outcome assessment (checking for possible detection bias)

We assessed all measures used, if any, to blind outcome assessors from knowledge as to which intervention a participant received and rated it as follows.

1. Low risk of bias: blinding of outcome assessment or no blinding of outcome assessment but measurement is unlikely to be influenced by lack of blinding.
2. High risk of bias: no blinding of outcome assessment, where measurement is likely to be influenced by lack of blinding, or where blinding could have been broken.
3. Unclear risk of bias: insufficient information to permit a judgement of low or high risk of bias.

5. Incomplete outcome data (checking for possible attrition bias through withdrawals, dropouts, protocol deviations)

We assessed whether incomplete outcome data were adequately addressed and rated it as follows.

1. Low risk of bias: either there were no missing outcome data, or the missing outcome data were unlikely to bias the results because the study authors provided transparent documentation of participant flow throughout the study, or the proportion of missing data was similar in the intervention and control groups, the reasons for missing data were provided and balanced across intervention and control groups, or the reasons for missing data were not likely to bias the results (e.g. moving house).
2. High risk of bias: missing outcome data were likely to bias the results. Studies were also considered at high risk of bias if more than 30% of randomised participants were lost to follow-up and unavailable for final assessment.
3. Unclear risk of bias: insufficient information was available to permit a judgement of low or high risk of bias.

6. Selective outcome reporting (checking for possible reporting bias)

We evaluated whether reports of the study were free from selective outcome reporting and rated it as follows.

1. Low risk of bias: where it was clear that all of the study's pre-specified outcomes and all expected outcomes of interest to the review were reported.
2. High risk of bias: where not all of the study's pre-specified outcomes were reported, one or more reported primary outcomes were not prespecified, outcomes of interest were reported incompletely and so could not be used, or the study failed to include results of a key outcome that was expected to have been reported.
3. Unclear risk of bias: insufficient information to deem whether the study was at low or high risk of bias.

7. Other sources of bias

We assessed whether the study was free from other problems that could put it at risk of bias as follows.

1. Low risk of bias: no other sources of bias appeared relevant to the trial that were not covered in previous categories of bias.
2. High risk of bias: another source of bias was uncovered.
3. Unclear risk of bias: insufficient evidence was available to permit a judgement of high or low risk of bias.

8. Overall risk of bias

We summarised the risk of bias at two levels: within studies (across domains) and across studies (for each primary outcome).

For the first, we assessed the likely magnitude and direction of the bias in each of the above mentioned domains and whether we considered them likely to impact on the findings. We considered studies to be at low overall risk of bias if they were not at high risk of bias for any category, and were assessed as having low risk of bias for random sequence generation OR low risk of bias for allocation concealment (selection bias), and were also rated at low risk of bias for either blinding (performance or detection bias) or incomplete outcome data (attrition bias). Studies which failed to provide sufficient information (i.e. unclear risk of bias) to enable categorisation of risk of bias were excluded from categorisation as being at low risk of bias. We explored the impact of including only studies at low risk of bias on primary outcomes through a Sensitivity analysis.

For the assessment across studies, we set out the main findings of the review in Summary of findings for the main comparison. The primary outcomes for each comparison were listed with estimates of relative effects along with the number of participants and studies contributing data for those outcomes. For each primary outcome, we assessed the quality of the evidence across all trials contributing data using the GRADE (Grades of Recommendation, Assessment, Development, and Evaluation) approach (Balshem 2011), which involves consideration of within-study risk of bias (methodological quality), directness of evidence, heterogeneity, precision of effect estimates, and risk of publication bias. The results were expressed as one out of four levels of quality (high, moderate, low or very low). This assessment was limited to the trials included in this review only. We produced the tables using GRADEpro GDT 2015.

Measures of treatment effect

We did not combine dichotomous and continuous data for analysis, and instead considered them separately.

Dichotomous data

We presented the results as average risk ratios (RRs) with 95% confidence intervals (CI).

Continuous data

We used the mean difference (MD) with 95% CI if outcomes were measured in the same way between trials. Where some studies reported endpoint data and others reported change from baseline data (with errors), we combined these in the meta-analysis using the MD providing the outcomes were reported using the same scale.

We used the standardised mean difference (SMD) with 95% CI to combine trials that measured the same outcome but used different methods of measurement.

Unit of analysis issues

Cluster-randomised trials

We combined the results from both cluster-randomised and individually-randomised studies if there was little heterogeneity between these study designs and the interaction between the effect of intervention and the choice of randomisation unit was considered as unlikely.

If the results from cluster trials were not adjusted by trial authors, we calculated the trials' effective sample size to account for the effect of clustering in the data. We used the intracluster correlation coefficient (ICC) derived from the trial (if available), or from another source (e.g. used the ICCs derived from other, similar trials), and then calculated the design effect with the formula provided in the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2011).

Studies with multiple intervention groups

For studies with more than two intervention groups (multi-arm studies), we included the directly relevant arms only. Where we identified studies with various relevant arms, we combined the

groups into a single pair-wise comparison (Deeks 2011) and included the disaggregated data in the corresponding subgroup category. If the control group was shared by two or more study arms, we divided the control group (events and total population) over the number of relevant subgroup categories to avoid double counting the participants.

Cross-over trials

We only included the first period of any randomised cross-over trial prior to the wash-out period or to a change in the sequence of treatments, and treated them as parallel trials.

Dealing with missing data

Missing individuals

We noted the dropout rate for each included study, which can be seen in Characteristics of included studies tables. We reported rates of attrition in the 'Risk of bias' tables (beneath the Characteristics of included studies tables) and included them in the 'Risk of bias' summary graph. We conducted analysis on an available case-analysis basis: data were included from those participants whose results were known. We considered variation in the degree of missing data as a potential source of heterogeneity.

Missing data

Where key data (e.g. standard deviations) were missing from the report, we attempted to contact corresponding authors (or other authors if necessary) of included studies to request unreported data. Two authors were contacted for further information (Pereira 2014; Waldvogel 2012). If we were not able to obtain this information, we used methods recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011c), to attempt to calculate it (performed in one study Zavaleta 2000). If this could not be achieved, we did not impute it and noted that the study did not provide data for that particular outcome.

Assessment of heterogeneity

We assessed methodological heterogeneity by examining the methodological characteristics and risk of bias of the studies, and clinical heterogeneity by examining the similarity between the types of participants, interventions and outcomes (Deeks 2011).
For statistical heterogeneity, we examined the forest plots from meta-analyses for heterogeneity among studies and used the I^2 statistic (Higgins 2003), Tau^2, and Chi^2 test for heterogeneity to quantify the level of heterogeneity among the trials in each meta-analysis.

Assessment of reporting biases

Where more than 10 trials contributed data to the primary outcomes, we presented a funnel plot to evaluate asymmetry - a possible indicator of publication bias. Where funnel plot asymmetry was evident, this was formally assessed using Egger's regression test (continuous outcomes) or Peter's or Harbord's test (Sterne 2011); see Differences between protocol and review for more information. This was undertaken using the metan and metabias user-written modules in Stata 13 (Harbord 2009).

Data synthesis

We conducted a meta-analysis to obtain an overall estimate of the effect of treatment when more than one study examined similar interventions using similar methods, was conducted in similar populations, and measured similar (comparable) outcomes. We carried out statistical analysis using RevMan 2014.
We used a random-effects meta-analysis for combining data, as we anticipated that there was natural heterogeneity between studies attributable to the different doses, durations, populations and implementation/delivery strategies.
Where different studies reported the same outcomes using both continuous and dichotomous measures, we re-expressed RRs as SMDs or vice versa, and combined the results using the generic inverse-variance method, as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2011).
We performed meta-analyses of dichotomous outcomes using the Mantel-Haenszel method.

Subgroup analysis and investigation of heterogeneity

We performed the following subgroup analyses on the primary outcomes only.

1. Age: adolescents (12 to 18 years), older adults (50 to 55 years).
2. Nutrient: iron alone or iron + other intervention versus intervention alone, iron plus vitamin C versus vitamin C alone, iron + any cointervention versus that same cointervention alone.
3. Baseline anaemia status (as defined by trial authors): anaemic, non-anaemic, mixed or unknown.
4. Baseline iron status (as defined by trial authors): iron deficient, non-iron deficient, mixed or unknown.
5. Baseline iron-deficiency anaemia status (as defined by trial authors): iron deficient with anaemia, iron deficient without anaemia, non-iron deficient/unknown status of deficiency.
6. Daily dose of elemental iron supplementation: less than 30 mg, 30 mg to 60 mg, 61 mg to 100 mg, 101 mg or more elemental iron.
7. Duration of iron supplementation: 30 days (one month) or less, more than one month to three months inclusive, more than three months.
8. Malaria endemicity of the setting in which the study was performed: endemic, not endemic, not reported/unknown.

We added a further subgroup analysis post-hoc: types of iron (ferrous sulphate, ferrous fumarate and others). In addition, we decided to undertake subgroup analysis on the following secondary outcome: ferritin (see Differences between protocol and review).
For meta-analysis including both endpoint and change scores data, we also conducted a subgroup analysis to separate the effects of the two outcome measures.
We did not conduct subgroup analyses in those outcomes with three or less trials. We explored the forest plots visually and identified where CIs did not overlap to assess differences between subgroup categories. We also formally investigated differences between two or more subgroups (Borenstein 2008).

Sensitivity analysis

We conducted sensitivity analyses examining effects of removing studies at high risk of bias (studies with poor or unclear allocation concealment and either inadequate blinding or high/imbalanced loss to follow-up) from the analysis. Likewise, for cluster studies reporting outcomes where reliable ICCs could not be obtained, we examined the effects of removing these studies from the analysis.
For additional sensitivity analyses archived for future updates of this review, please see our protocol (Pasricha 2012) and Appendix 2.

RESULTS

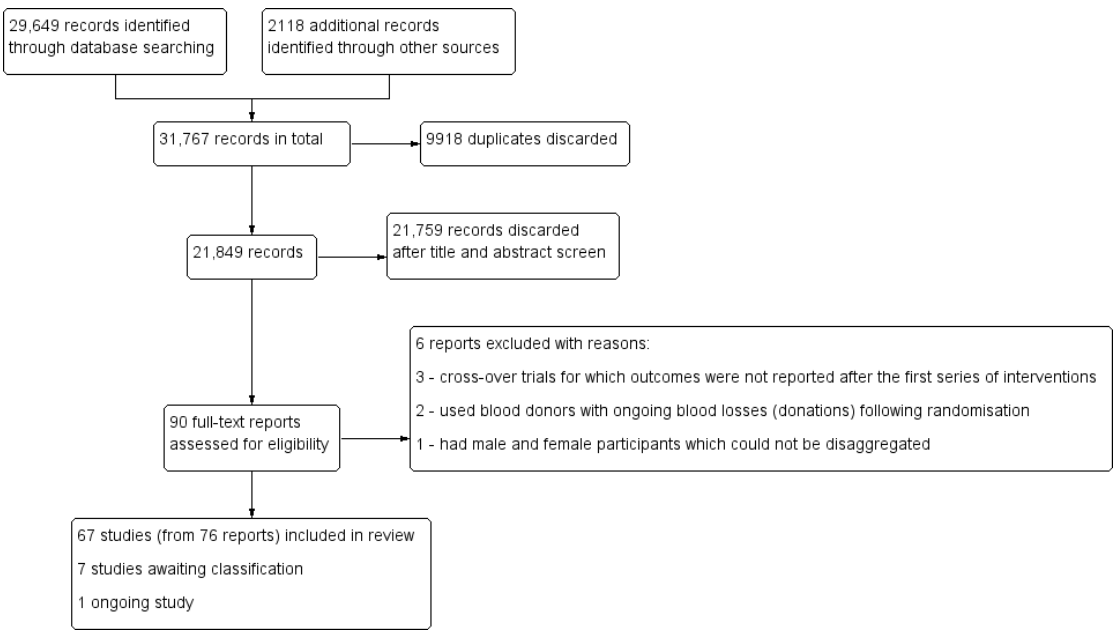
Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of studies awaiting classification; Characteristics of ongoing studies.

Results of the search

The search strategy identified 31,767 records for possible inclusion, 9918 of which were duplicates. Three studies were published in languages other than English (Machado 2011; Radjen 2011; Wang 2012) - these were translated to English for extraction. After screening, we assessed 90 full-text reports for eligibility. We included 67 studies (from 76 reports and one personal communication (see DellaValle 2012)), excluded six studies and classified seven studies as awaiting assessment either because we were unable to access the full text for the trials, despite assistance from an academic library, or determine if they were eligible for inclusion. Our search of WHO ICTRP identified one ongoing study, which may be eligible for inclusion when the results become available, although the findings are unlikely to alter the conclusions of this analysis (IRCT201409082365N9).
Figure 1 depicts the process by which we assessed and selected studies.

Figure 1. Study flow diagram.



Included studies

Overall, we included 67 trials that recruited a total of 8506 women. The sample size ranged between 10 and 1390 participants but overall tended to be small: 96% of the studies included fewer than 400 women.

Settings

Studies were conducted in numerous countries of differing cultural and economic background. Included studies in this review were conducted in USA (Binkoski 2004; Bruner 1996; Cooter 1978; DellaValle 2012; Gordeuk 1987; Gordeuk 1990; Hinton 2000; Hinton 2007; Jensen 1991; Kiss 2015; Klingshirn 1992; LaManca 1993; Lyle 1992; McClung 2009; Murray-Kolb 2007; Rajaram 1995; Rowland 1988; Swain 2007; Viteri 1999; Yadrick 1989; Zhu 1998), Australia (Booth 2014; Leonard 2014; Marks 2014; Walsh 1989; Zaman 2013), United Kingdom (Bryson 1968; Elwood 1966; Elwood 1970; Pereira 2014), Iran (Eftekhari 2006; Kianfar 2000; Maghsudlu 2008), Sri Lanka (Edgerton 1979; Jayatissa 1999; Lanerolle 2000), Sweden (Flink 2006; Hoppe 2013; Rybo 1985), Canada (Larocque 2006; Newhouse 1989), China (Li 1994; Wang 2012), Finland (Fogelholm 1992; Fogelholm 1994), India (Agarwal 2003; Kanani 2000), Israel (Ballin 1992; Magazanik 1991), Japan (Taniguchi 1991; Yoshida 1990), New Zealand (Heath 2001; Prosser 2010), Switzerland (Verdon 2003; Waldvogel 2012), Bolivia (Berger 1997), Brazil (Machado 2011), Chile (Mujica-Coopman 2015), Korea (Kang 2004), Mexico (Brutsaert 2003), Nepal (Shah 2002), Norway (Røsvik 2010), Peru (Zavaleta 2000), Phillipines (Florencio 1981), Serbia (Radjen 2011), Tanzania (Gunaratna 2015) and Thailand (Charoenlarp 1988).

Only two studies specifically stated being conducted in low socioeconomic settings (Kanani 2000; Zavaleta 2000); however it is likely that other studies were also performed in situations that would include low socioeconomic participants. One study specifically targeted middle-class participants (as defined by the trial authors) (Agarwal 2003).

Nine studies were performed specifically in an urban setting (Agarwal 2003; Ballin 1992; Bruner 1996; Florencio 1981; Heath 2001; Rybo 1985; Shah 2002; Wang 2012; Zavaleta 2000), four in a rural setting (Berger 1997; Charoenlarp 1988; Edgerton 1979; Gunaratna 2015). One study reports specifically recruiting from both rural and urban settings (Lanerolle 2000). The majority of studies did not specifically state whether the trials were performed in rural or urban settings (Binkoski 2004; Booth 2014; Brutsaert 2003; Bryson 1968; Cooter 1978; DellaValle 2012; Eftekhari 2006; Elwood 1966; Elwood 1970; Flink 2006; Fogelholm 1992; Fogelholm 1994; Gordeuk 1987; Gordeuk 1990; Hinton 2000; Hinton 2007; Jayatissa 1999; Jensen 1991; Hoppe 2013; Kanani 2000; Kang 2004; Kianfar 2000; Kiss 2015; Klingshirn 1992; LaManca 1993; Larocque 2006; Leonard 2014; Li 1994; Lyle 1992; Machado 2011; Magazanik 1991; Maghsudlu 2008; Marks 2014; McClung 2009; Mujica-Coopman 2015, Murray-Kolb 2007; Newhouse 1989; Pereira 2014; Prosser 2010; Radjen 2011; Rajaram 1995; Rowland 1988; Røsvik 2010; Swain 2007; Taniguchi 1991; Verdon 2003; Viteri 1999; Waldvogel 2012; Walsh 1989; Yadrick 1989; Yoshida 1990; Zaman 2013; Zhu 1998).

Only two studies specifically reported being performed in a malaria-endemic area (Charoenlarp 1988; Gunaratna 2015), with the majority not reporting malaria endemicity at the site of the trial.

Participants

Across the included studies a total of 8508 women were included; 4444 in the intervention arm, 4,064 in the control arm. The majority of studies recruited women between the ages of 13 years and 45 years. Three studies included women below 13 years of age: Agarwal 2003: range 10 years to 17 years (mean age not stated); Shah 2002: age range 11 years to 18 years (mean age 15 years); Zavaleta 2000: age range 12 years to 18 years (mean age 15 years). Six studies recruited females older than 45 years (Edgerton 1979: age range 20 years to 60 years (mean age: 35 years); Kiss 2015: age range not reported (mean age: 45.7 years); Machado 2011: age range 20 years to 49 years (mean age: not reported); Røsvik 2010: age range 18 years to 69 years (mean age: 43 years); Swain 2007: age range 21 years to 51 years (mean age: 40 years); Verdon 2003: age range 18 years to 55 years (mean age: 35 years). In these trials, data for participants aged within the target age range could not be extracted separately, although they met our inclusion criteria of comprising more than half of participants within the eligible age range.

Twenty-six studies recruited women in an educational setting with 12 in secondary education (Agarwal 2003; Ballin 1992; Bruner 1996; Eftekhari 2006; Jayatissa 1999; Kanani 2000; Kianfar 2000; Lanerolle 2000; Larocque 2006; Rowland 1988; Shah 2002; Zavaleta 2000) and 14 in tertiary education (Cooter 1978; DellaValle 2012; Hoppe 2013; Jensen 1991; Klingshirn 1992; Lyle 1992; Murray-Kolb 2007; Pereira 2014; Rajaram 1995; Taniguchi 1991; Viteri 1999; Yoshida 1990; Zaman 2013; Zhu 1998).

Four studies recruited women through a specific workplace: factory workers (Bryson 1968; Florencio 1981), tea pickers (Edgerton 1979; Li 1994). Ten studies recruited women through sports teams (Cooter 1978; DellaValle 2012; Fogelholm 1992; Kang 2004; Klingshirn 1992; LaManca 1993; Radjen 2011; Rowland 1988; Walsh 1989; Yoshida 1990). Seven studies recruited women through blood donation centres (Gordeuk 1987; Gordeuk 1990; Kiss 2015; Maghsudlu 2008; Marks 2014; Røsvik 2010; Waldvogel 2012); in these studies, women did not undergo further blood donations between enrolment and outcome measurement.

Dose and type of iron interventions

A variety of oral iron formulations were included in this review. The most frequently used was ferrous sulphate (33 studies; Binkoski 2004; Bruner 1996; Brutsaert 2003; DellaValle 2012; Edgerton 1979; Eftekhari 2006; Florencio 1981; Fogelholm 1992; Hinton 2000; Hinton 2007; Jensen 1991; Kianfar 2000; Klingshirn 1992; Lanerolle 2000; Leonard 2014; Li 1994; Lyle 1992; Machado 2011; Magazanik 1991; Maghsudlu 2008; McClung 2009; Mujica-Coopman 2015; Murray-Kolb 2007; Newhouse 1989; Pereira 2014; Radjen 2011; Rajaram 1995; Shah 2002; Verdon 2003; Viteri 1999; Waldvogel 2012; Zavaleta 2000; Zhu 1998). One study included two arms: ferrous sulphate and carbonyl iron (Gordeuk 1987). Two studies used carbonyl iron (Gordeuk 1990; Marks 2014). Five studies used ferrous fumarate (Bryson 1968; Cooter 1978; Flink 2006; Fogelholm 1994; Hoppe 2013), and one study used ferric pyrophosphate and ferrous fumarate together (Wang 2012).

Other iron formulations that were used included ferrous carbonate (Elwood 1966; Elwood 1970), ferrous gluconate (Booth 2014; Kiss 2015; Larocque 2006; Zaman 2013), ferric ammonium citrate (Taniguchi 1991), ferrous succinate (Rybo 1985), Niferex ferrous glycine sulphate (Røsvik 2010), amino acid chelate (Heath 2001; Prosser 2010), ferrous sodium citrate (Yoshida 1990), LiquiFer® (Iron polystyrene sulfonate) (Ballin 1992). Twelve studies did not state the specific iron formulation used (Agarwal 2003; Berger 1997; Charoenlarp 1988; Gunaratna 2015; Jayatissa 1999; Kanani 2000; Kang 2004; LaManca 1993; Rowland 1988; Swain 2007; Walsh 1989; Yadrick 1989). Doses of elemental iron varied from 1 mg of elemental iron to approximately 300 mg of elemental iron a day. Duration of iron supplement also varied significantly, ranging from 1 week to 24 weeks.

Excluded studies

We excluded six studies because they did not meet eligibility criteria. Three studies were cross-over trials that did not report on outcomes at the end of the first parallel intervention period (Brigham 1993; Powell 1991; Schoene 1983). Two studies were undertaken in blood donors in whom further donations during the trial indicated ongoing blood losses (Cable 1988; Simon 1984). In one trial, data from male and female participants could not be disaggregated (Powers 1988).

Risk of bias in included studies

Study methods were generally not well described in many of the studies and thus 'Risk of bias' assessment was difficult (see Figure 2 and Figure 3). Using the criteria defined above, only 11 studies were assessed as being at low risk of bias (Bruner 1996; DellaValle 2012; Flink 2006; Fogelholm 1992; Gunaratna 2015; Machado 2011; Marks 2014; Pereira 2014; Verdon 2003; Waldvogel 2012; Zaman 2013). The remaining studies were either assessed as being at high risk of bias or the methods were unclear and thus could not be rated as being at low risk of bias.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

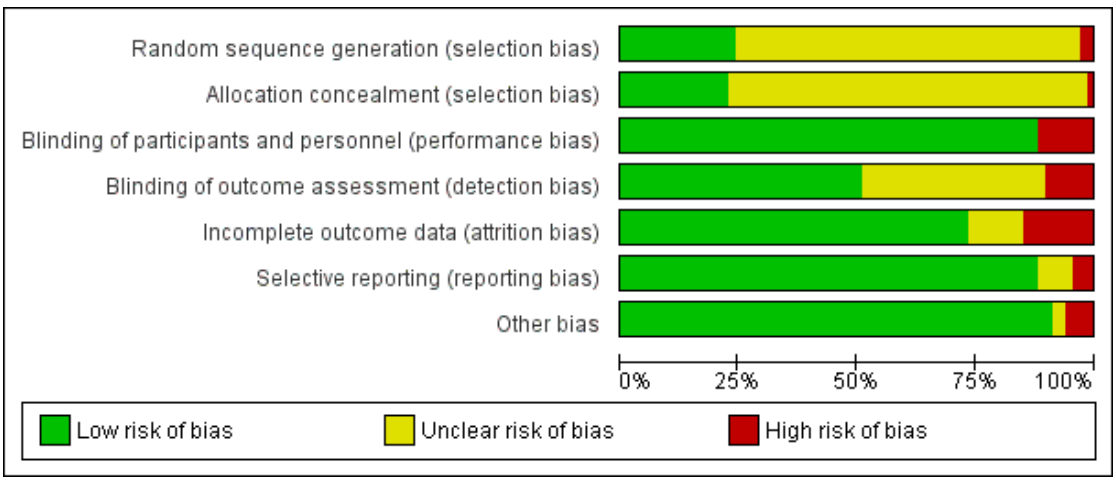
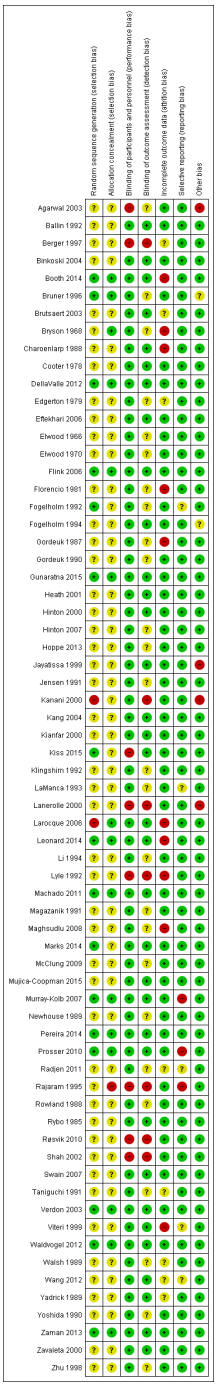


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

Sixteen studies were considered to have generated the random sequence using a method considered to be at low risk of bias (Booth 2014; Bruner 1996; DellaValle 2012; Flink 2006; Fogelholm 1992; Gunaratna 2015; Kiss 2015; Leonard 2014; Machado 2011; Marks 2014; Murray-Kolb 2007; Pereira 2014; Prosser 2010; Verdon 2003; Waldvogel 2012; Zaman 2013. Sequence generation was considered at high risk of bias in two studies (Kanani 2000; Larocque 2006). In 49 of the included trials, it was unclear how the randomisation sequence had been generated.

Fifteen of the included studies used methods of concealing group allocation that we judged to be at low risk of bias (Booth 2014; Bruner 1996; Bryson 1968; DellaValle 2012; Flink 2006; Gunaratna 2015; Larocque 2006; Leonard 2014; Machado 2011; Murray-Kolb 2007; Pereira 2014; Prosser 2010; Verdon 2003; Waldvogel 2012; Zaman 2013). In one trial, methods were considered at high risk of bias (Rajaram 1995). In the remaining 51 trials, methods were either not described or were unclear.

Blinding

Most trials administered the placebo to blinded participants and relatively few trials reported on methods for blinding outcome assessors. Overall, 59 studies reported blinding of participants and were deemed at low risk of performance bias (Ballin 1992; Binkoski 2004; Booth 2014; Bruner 1996; Brutsaert 2003; Bryson 1968; Charoenlarp 1988; Cooter 1978; DellaValle 2012; Edgerton 1979; Eftekhari 2006; Elwood 1966; Elwood 1970; Flink 2006; Florencio 1981; Fogelholm 1992; Fogelholm 1994; Gordeuk 1987; Gordeuk 1990; Gunaratna 2015; Heath 2001; Hinton 2000; Hinton 2007; Hoppe 2013; Jayatissa 1999; Jensen 1991; Kanani 2000; Kang 2004; Kianfar 2000; Klingshirn 1992; LaManca 1993; Larocque 2006; Leonard 2014; Li 1994; Machado 2011; Magazanik 1991; Marks 2014; Maghsudlu 2008; McClung 2009; Mujica-Coopman 2015; Murray-Kolb 2007; Newhouse 1989; Pereira 2014; Prosser 2010; Radjen 2011; Rowland 1988; Rybo 1985; Swain 2007; Taniguchi 1991; Verdon 2003; Viteri 1999; Waldvogel 2012; Walsh 1989; Wang 2012; Yadrick 1989; Yoshida 1990; Zaman 2013; Zavaleta 2000; Zhu 1998). Eight studies were deemed to be at high risk of performance bias: seven as placebo was not used (Agarwal 2003; Berger 1997; Kiss 2015; Lanerolle 2000; Rajaram 1995; Røsvik 2010; Shah 2002), one as diet intervention was not blinded and would have revealed placebo group from intervention group (Lyle 1992).

Thirty-four studies were deemed to be at low risk of detection bias (Ballin 1992; Binkoski 2004; Booth 2014; Brutsaert 2003; Charoenlarp 1988; Cooter 1978; DellaValle 2012; Eftekhari 2006; Flink 2006; Fogelholm 1994; Gunaratna 2015; Heath 2001; Hinton 2000; Jayatissa 1999; Kang 2004; Kianfar 2000; Kiss 2015; Larocque 2006; Leonard 2014; Machado 2011; Marks 2014; Mujica-Coopman 2015; Murray-Kolb 2007; Pereira 2014; Prosser 2010; Rybo 1985; Swain 2007; Verdon 2003; Viteri 1999; Waldvogel 2012; Wang 2012; Yadrick 1989; Zaman 2013; Zavaleta 2000). Twenty-six studies were deemed unclear for detection bias as the study failed to state whether personnel were blinded or it remained unclear if outcomes would be affected by lack of blinding (Agarwal 2003; Bruner 1996; Bryson 1968; Edgerton 1979; Elwood 1966; Elwood 1970; Florencio 1981; Fogelholm 1992; Gordeuk 1987; Gordeuk 1990; Hinton 2007; Hoppe 2013; Jensen 1991; Klingshirn 1992; LaManca 1993; Li 1994; Magazanik 1991; Maghsudlu 2008; McClung 2009; Newhouse 1989; Radjen 2011; Rowland 1988; Taniguchi 1991; Walsh 1989; Yoshida 1990; Zhu 1998). Seven studies were deemed at high risk of detection bias as assessors may have known which participants belonged to which group due to a lack of placebo or unblinded personnel, with outcomes that may have been influenced by this lack of blinding (Berger 1997; Kanani 2000; Lanerolle 2000; Lyle 1992; Rajaram 1995; Røsvik 2010; Shah 2002).

Incomplete outcome data

While we assessed that the majority of the included trials had acceptable levels of attrition (with loss to follow-up and missing data being less than 30% and balanced across groups), in nine trials the levels of attrition were high or not balanced across groups (Booth 2014; Bryson 1968; Charoenlarp 1988; Florencio 1981; Gordeuk 1987; Larocque 2006; Leonard 2014; Lyle 1992; Viteri 1999), while attrition was not reported in a further eight trials (Berger 1997, Brutsaert 2003, Edgerton 1979, Radjen 2011, Taniguchi 1991, Walsh 1989; Wang 2012; Yadrick 1989).

Selective reporting

We were not able to fully assess outcome reporting bias as we only had access to published study reports. We assessed publication bias using funnel plots for haemoglobin, anaemia, iron deficiency, ferritin and adverse effects (any effects, any gastrointestinal effects, constipation, loose stools/diarrhoea, and abdominal pain). While we detected no funnel plot asymmetry for haemoglobin or ferritin, we observed evidence of asymmetry for anaemia and ferritin (both indicating the possibility of missing studies reporting a smaller than observed effect on anaemia prevalence from iron). However, there were few studies reporting these outcomes precluding more detailed statistical analysis of these funnel plots. Nevertheless, the possibility of publication bias exists for these key outcomes. Five studies were deemed to be at an unclear risk of selective reporting (Fogelholm 1992; LaManca 1993; Radjen 2011; Viteri 1999;

Wang 2012) and three studies were deemed to be at high risk of selective reporting due to outcomes mentioned being analysed but not presented (Murray-Kolb 2007; Prosser 2010; Rajaram 1995).

Other potential sources of bias

The majority of trials had no clear other sources of bias. Only four studies used a cluster design but did not report the ICC or other relevant data in the manuscript and were thus deemed to be at high risk of other bias (Agarwal 2003; Jayatissa 1999; Kanani 2000; Lanerolle 2000). These papers reported on the following outcomes: haemoglobin and anaemia (Agarwal 2003); haemoglobin, anaemia and ferritin (Jayatissa 1999); haemoglobin, weight and body mass index (Kanani 2000); haemoglobin, ferritin, iron deficiency, transferrin saturation (Lanerolle 2000). We obtained the ICC from external sources (Gulliford 1999): the ICC for haemoglobin was 0.00059, which is low; for example, for a cluster comprising 30 individuals, the design effect would be only 1.017, which implies adjustment of the sample size would only be minor. Likewise, the ICC for ferritin from this source was only 0.00004, which again is unlikely to result in a large design effect and obviates the need for an adjustment of the sample size (Ukoumunne 1999). For weight and body mass index, reported in Kanani 2000, we undertook a sensitivity analysis to evaluate effects of excluding this study (which can be seen in Analysis 9.5).

Of the remaining studies, two were deemed at unclear risk of other bias (Bruner 1996; Fogelholm 1994) as data was only presented in a table making other sources of bias unable to be excluded, and 61 studies (from 71 reports) had no other identifiable potential source of bias and were therefore deemed at low risk (Ballin 1992; Berger 1997; Binkoski 2004; Booth 2014; Brutsaert 2003; Bryson 1968; Charoenlarp 1988; Cooter 1978; DellaValle 2012; Edgerton 1979; Eftekhari 2006; Elwood 1966; Elwood 1970; Flink 2006; Florencio 1981; Fogelholm 1992; Gordeuk 1987; Gordeuk 1990; Gunaratna 2015; Heath 2001; Hinton 2000; Hinton 2007; Hoppe 2013; Jensen 1991; Kang 2004; Kianfar 2000; Kiss 2015; Klingshirn 1992; LaManca 1993; Larocque 2006; Leonard 2014; Li 1994; Lyle 1992; Machado 2011; Magazanik 1991; Maghsudlu 2008; Marks 2014; McClung 2009; Mujica-Coopman 2015; Murray-Kolb 2007; Newhouse 1989; Pereira 2014; Prosser 2010; Radjen 2011; Rajaram 1995; Rowland 1988; Rybo 1985; Røsvik 2010; Shah 2002; Swain 2007; Taniguchi 1991; Verdon 2003; Viteri 1999; Waldvogel 2012; Walsh 1989; Wang 2012; Yadrick 1989; Yoshida 1990; Zaman 2013; Zavaleta 2000; Zhu 1998.

Effects of interventions

See: **Summary of findings for the main comparison**

All included trials contributed data to the review but some studies randomised participants to intervention arms that were not relevant to the comparisons we assessed. For these studies we did not include data from all groups in the analyses. Furthermore, some studies did not contain data in an extractable form, or did not contain data in a way in which they could be combined in meta-analyses. For these studies, we provided a narrative description of the results.

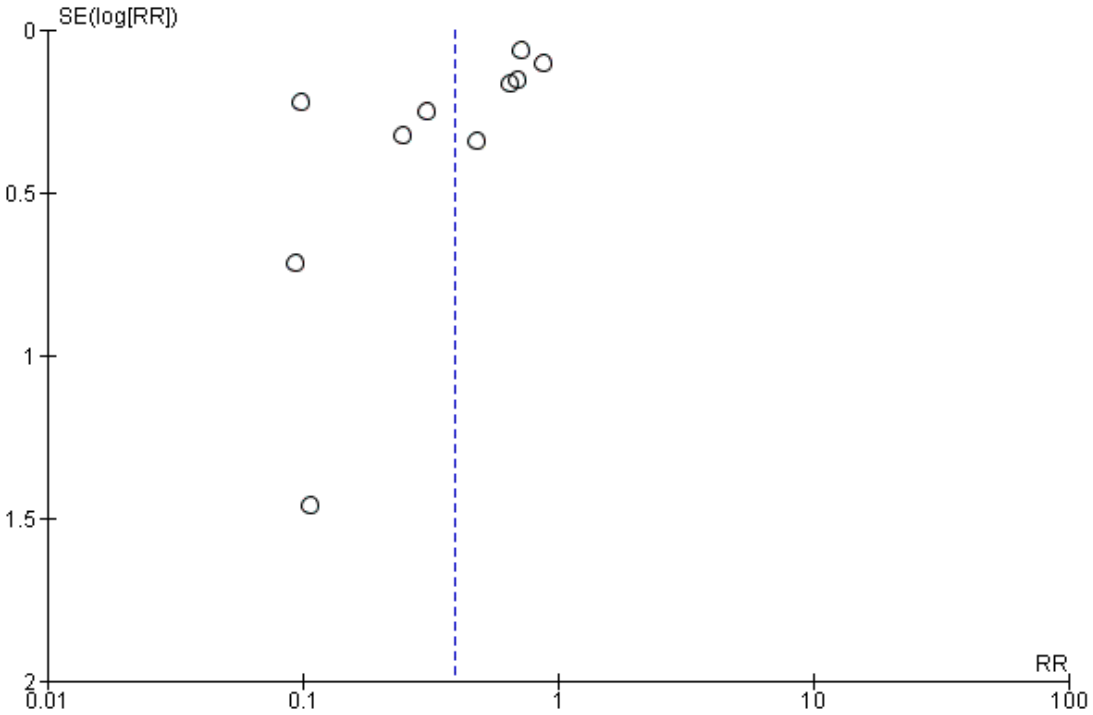
For cluster-randomised trials we extracted the estimated effective sample size by adjusting the data to account for the clustering effect.

Primary Outcomes

Anaemia

Ten studies, comprising 3273 women, measured anaemia prevalence at the end of intervention (Agarwal 2003; Charoenlarp 1988; Florencio 1981; Gordeuk 1990; Gunaratna 2015; Jayatissa 1999; Shah 2002; Viteri 1999; Wang 2012; Zavaleta 2000). Women receiving iron were significantly less likely to be anaemic at the end of intervention compared to women receiving control (RR 0.39, 95% CI 0.25 to 0.60, moderate quality evidence; Analysis 1.1; Summary of findings for the main comparison). There was variation among trials in terms of the size of the treatment effect ($Tau^2 = 0.37$; $Chi^2 = 124.24$, $df = 9$, ($P < 0.00001$); $I^2 = 93\%$). Although visual inspection of the funnel plot indicated asymmetry, broadly suggesting missing studies reported smaller effect sizes on anaemia, which may be in keeping with a reporting bias, formal statistical testing using the Harbord and Peters tests did not demonstrate evidence of publication bias (Sterne 2011); see Figure 4.

Figure 4. Funnel plot of comparison: 1 Anaemia, outcome: 1.1 Anaemia at end of therapy (total).



Only one study reporting this outcome was considered at low overall risk of bias (Gunaratna 2015). Analysis of this study did not show a difference between iron and control (Analysis 1.2).

Subgroup analysis

There was evidence of differences between subgroups. Specifically, women in studies comparing iron alone with control experienced a smaller reduction in the prevalence of anaemia (RR 0.57, 95% CI 0.45 to 0.74, 8 studies, 2775 women) compared with women randomised to iron + vitamin C versus vitamin C alone (RR 0.10, 95% CI 0.06 to 0.15, 2 studies, 498 women; test for subgroup differences: Chi^2 = 51.2, df = 1 (P < 0.00001), I^2 = 98%; Analysis 1.3). There were no differences observed in effect sizes based on age of participants (Analysis 1.4). Although subgroup differences were observed based on baseline anaemia status (Analysis 1.5), iron status (Analysis 1.6), and iron-deficiency anaemia status (Analysis 1.7), most studies fell into the 'unclassified' subgroup and thus subgroup analyses were not constructive. Significant differences in effect size on risk of anaemia were seen for different doses and durations of iron supplementation, however these were non-linear with increasing dose (Analysis 1.8) or duration (Analysis 1.9). No studies in malaria-endemic settings were included. Limited data indicated that ferrous sulphate is more effective than other formulations in reducing prevalence of anaemia (ferrous sulphate: RR 0.20, 95% CI 0.09 to 0.48, 4 studies, 838 women; ferrous fumarate: RR 0.65, 95% CI 0.47 to 0.90, 1 study, 69 women; other formulations: RR 0.66, 95% CI 0.50 to 0.87, 4 studies, 2285 women; test for subgroup differences: Chi^2 = 6.85, df = 2 (P value = 0.03), I^2 = 70.8%; Analysis 1.10).

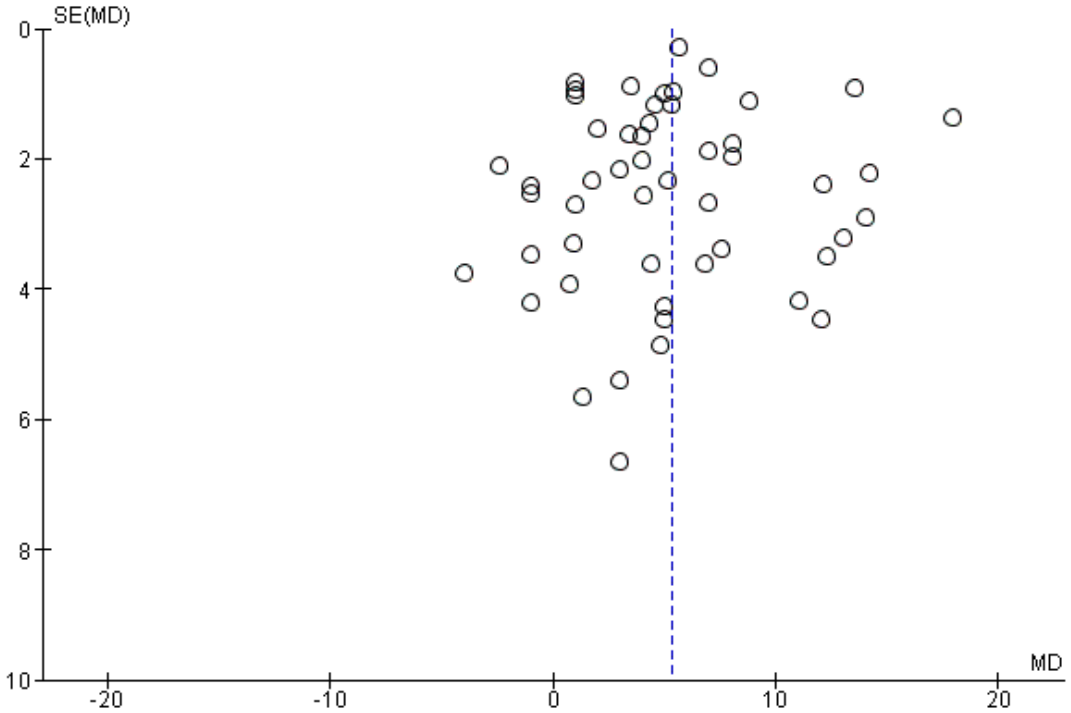
High levels of heterogeneity may be explained by variation in the clinical matrix of study designs (i.e. more than one factor could account for heterogeneity, which cannot be adequately captured by each subgroup analysis. For example, studies used different doses and durations, and recruited participants with different underlying iron status.

Haemoglobin

Fifty-one trials recruiting 6861 women measured haemoglobin concentrations at the end of intervention (Agarwal 2003; Berger 1997; Binkoski 2004; Booth 2014; Bruner 1996; Brutsaert 2003; Charoenlarp 1988; Cooter 1978; DellaValle 2012; Edgerton 1979; Eftekhari 2006; Elwood 1966; Florencio 1981; Fogelholm 1992; Fogelholm 1994; Gordeuk 1987; Gordeuk 1990; Hinton 2000; Hinton 2007; Hoppe 2013; Jayatissa 1999; Jensen 1991; Kanani 2000; Kang 2004; Kianfar 2000; Klingshirn 1992; LaManca 1993; Lanerolle 2000; Larocque 2006; Leonard 2014;

Li 1994; Maghsudlu 2008; Marks 2014; McClung 2009; Mujica-Coopman 2015; Murray-Kolb 2007; Newhouse 1989; Radjen 2011; Rowland 1988; Rybo 1985; Røsvik 2010; Taniguchi 1991; Viteri 1999; Waldvogel 2012; Walsh 1989; Wang 2012; Yadrick 1989; Yoshida 1990; Zaman 2013; Zavaleta 2000; Zhu 1998). Women receiving iron had a higher haemoglobin concentration at the end of intervention compared with women receiving control (MD 5.30, 95% CI 4.14 to 6.45; heterogeneity: $Tau^2 = 11.74$; $Chi^2 = 356.76$, df = 50 ($P < 0.00001$); $I^2 = 86\%$; high quality evidence; Analysis 2.1; Summary of findings for the main comparison). There was no obvious funnel plot asymmetry (Figure 5).

Figure 5. Funnel plot of comparison: 2 Haemoglobin, outcome: 2.1 Haemoglobin (total).



When only studies considered at low overall risk of bias were included in the analysis (six studies; 581 women: Bruner 1996; DellaValle 2012; Fogelholm 1992; Marks 2014; Waldvogel 2012; Zaman 2013), the effect size was similar (MD 5.08, 95% CI 2.99 to 7.17; Analysis 2.2).

Subgroup analysis

Subgroup analyses may explain the observed heterogeneity. The large number of studies and participants for this outcome provide a rich data set for evaluation of subgroup differences. There was no evidence of a difference in MD between women receiving iron alone or iron with vitamin C or another cointervention (Analysis 2.3). There was no subgroup difference based on age of women (Analysis 2.4). There was a greater increase in haemoglobin in studies among women with baseline anaemia (MD 8.67, 95%

CI 5.16 to 12.18, 8 studies, 558 women) or in whom baseline anaemia status was not defined (MD 6.30, 95% CI 4.52 to 8.08, 25 studies, 4207 women) compared with those who were non-anaemic at baseline (MD 3.11, 95% CI 1.67 to 4.54, 25 studies, 2120 women; test for subgroup differences: Chi^2 = 12.73, df = 2 (P value = 0.002), I^2 = 84.3%; Analysis 2.5). Similarly, iron did not improve haemoglobin in iron replete women (MD 0.84, 95% CI -2.26 to 3.95, 5 studies, 421 women), but did increase haemoglobin concentration in women who were either iron deficient (as defined by the trial authors) (MD 6.92, 95% CI 4.76 to 9.09, 21 studies, 1124 women) or in whom iron status had not been defined at baseline (MD 4.92, 95% CI 3.49 to 6.35, 28 studies, 5296 women; test for subgroup differences: Chi^2 = 9.90, df = 2 (P value = 0.007), I^2 = 79.8%); see Analysis 2.6. There was no subgroup difference in the effect of iron on haemoglobin between women who were iron-deficient anaemic, non-anaemic iron deficient, non-anaemic non-iron deficient, and undefined (Analysis 2.7). There was no difference in effect from iron on haemoglobin according to dose of iron given (Analysis 2.8). Haemoglobin levels increased more when iron was given for one to three months (MD 6.14, 95% CI 4.70 to 7.58, 37 studies, 4171 women) when compared to less than one month (MD 2.60, 95% CI 0.28 to 4.91, 6 studies, 765 women) or greater than three months (MD 3.84, 95% CI 0.94 to 6.75, 8 studies, 1925 women; test for subgroup differences: Chi^2 = 7.15, df = 2 (P value = 0.03), I^2 = 72%; Analysis 2.9). Only one study had been undertaken in a malaria-endemic area limiting subgroup analyses by malaria endemicity. There was no evidence of subgroup difference between trials using different formulations of iron (ferrous sulphate, ferrous fumarate, and others) (Analysis 2.10).

Iron deficiency

Seven studies recruiting 1088 women measured iron deficiency at the end of the intervention (Ballin 1992; Lanerolle 2000; Leonard 2014; Marks 2014; Mujica-Coopman 2015; Viteri 1999; Wang 2012). Women receiving iron had a reduced risk of iron deficiency compared with women receiving control (RR 00.62, 95% CI 0.50 to 0.76; heterogeneity: Tau^2 = 0.02; Chi^2 = 8.37, df = 6 (P value = 0.21); I^2 = 28%; moderate quality evidence; Analysis 3.1). When only the single study (257 women) at low risk of bias was included (Marks 2014), the effect size was similar (RR 0.65, 95% CI 0.54 to 0.78; Analysis 3.2).

Subgroup analysis

There were too few studies to enable subgroup analysis.

Iron-deficiency anaemia

Only one study (Mujica-Coopman 2015), involving 55 women, specifically reported iron-deficiency anaemia, with no events in either the iron or control groups (Analysis 4.1). One other study (Gunaratna 2015) reported microcytic anaemia and showed a significant reduction with iron therapy compared to controls (RR 0.51, 95% CI 0.33 to 0.77, 378 women; Analysis 4.2).

All-cause mortality

No studies reported data on all-cause mortality.

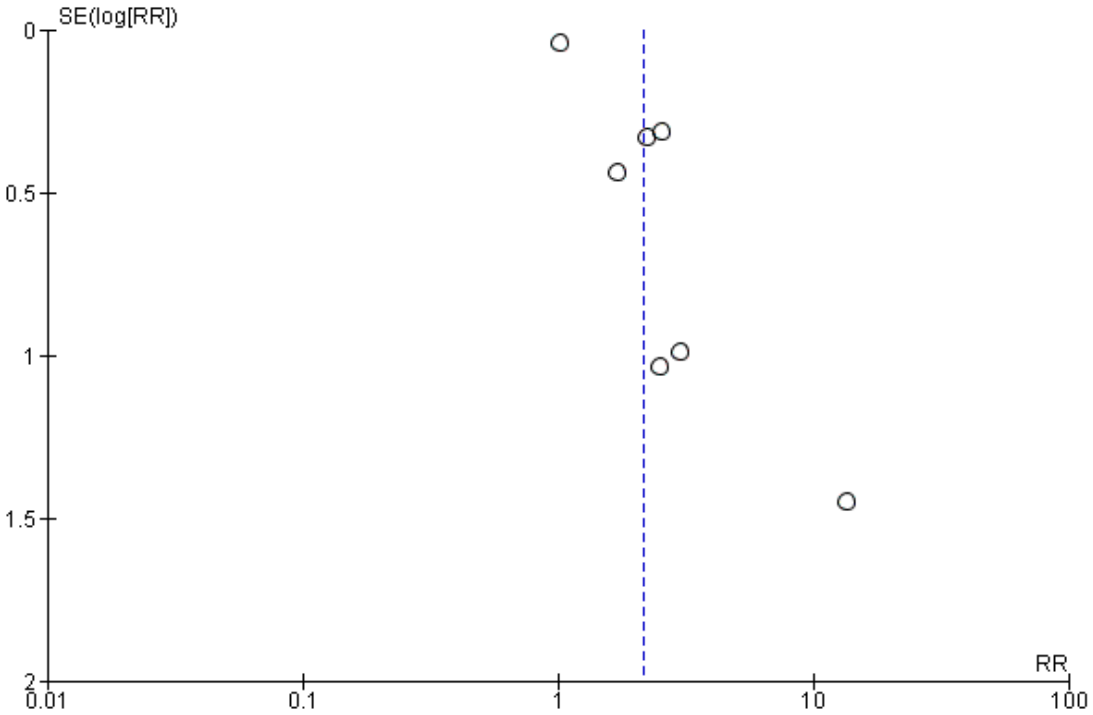
Adverse side effects

Data on adverse effects were generally reported as proportions of populations experiencing side effects. Data were amalgamated using terms defined by the trial authors: 'any side effect' (Ballin 1992; Hoppe 2013; Leonard 2014; Maghsudlu 2008; Marks 2014; Pereira 2014; Waldvogel 2012), 'any gastrointestinal side effect' (Gordeuk 1987; Hoppe 2013; Marks 2014; Pereira 2014; Waldvogel 2012), 'loose stools/diarrhoea' (Gordeuk 1987; Leonard 2014; Marks 2014; Pereira 2014; Rybo 1985; Waldvogel 2012), 'hard stools/constipation' (Bruner 1996; Gordeuk 1990; Leonard 2014; Maghsudlu 2008; Marks 2014; Pereira 2014; Rybo 1985; Waldvogel 2012), 'abdominal pain' (Bryson 1968; Gordeuk 1990; Maghsudlu 2008; Marks 2014; Pereira 2014; Rybo 1985; Waldvogel 2012), 'nausea' (Bryson 1968; Gordeuk 1990; Leonard 2014; Maghsudlu 2008; Marks 2014; Pereira 2014; Rybo 1985; Waldvogel 2012), 'change in stool colour' (Bruner 1996; Leonard 2014; Marks 2014; Pereira 2014), 'reflux/heartburn' (Pereira 2014), and 'headache' (Gordeuk 1987; Gordeuk 1990; Maghsudlu 2008; Pereira 2014).

Any side effects

Seven trials recruiting 901 women reported on 'any side effect' and did not identify an overall increased prevalence of side effects from iron supplements (RR 2.14, 95% CI 0.94 to 4.86, P value = 0.07; heterogeneity: Tau^2 = 0.84; Chi^2 = 49.95, df = 6 (P < 0.00001); I^2 = 88%, low quality evidence; Analysis 5.1; Summary of findings for the main comparison). The funnel plot of this outcome indicates asymmetry (Figure 6), raising the possibility of missing studies with fewer adverse effects. When only the three trials (415 women) considered at low overall risk of bias were included in the analysis (Marks 2014; Pereira 2014; Waldvogel 2012), the effect of iron on 'any adverse effect' was similar (RR 1.59, 95% CI 0.66 to 3.81; Analysis 5.2).

Figure 6. Funnel plot of comparison: 7 Side effects, outcome: 7.1 Any Side effect (Total).



Subgroup analysis

There were too few studies in different subgroup categories to enable subgroup analyses by cointervention, age, baseline anaemia/iron deficiency/iron-deficiency anaemia status, duration of intervention, malaria endemicity, or type of iron utilised. However, there was evidence of a trend towards an increase in risk of any adverse effects as dose of elemental iron was increased, from 30 mg to 60 mg (RR 1.01, 95% CI 0.93 to 1.10, 3 studies, 305 women), to 61 mg to 100 mg (RR 2.61, 95% 1.44 to 4.75, 2 studies, 157 women), to more than 100 mg (2.15, 95% CI 1.24 to 3.73, 3 studies, 439 women; test for subgroup differences: Chi^2 = 16.30, df = 2 (P value = 0.0003), I^2 = 87.7%; Analysis 5.3).

Any gastrointestinal side effects

Five studies recruiting 521 women identified an increased prevalence of gastrointestinal side effects in women taking iron (RR 1.99, 95% CI 1.26 to 3.12; heterogeneity: Tau^2 = 0.11; Chi^2 = 7.33, df = 4 (P value = 0.12); I^2 = 45%; low quality evidence; Analysis 5.4). When three studies (415 women) considered at low overall risk of bias were included in the analysis (Marks 2014; Pereira 2014; Waldvogel 2012), the magnitude of effect was similar (RR 1.91, 95% CI 0.96 to 3.80; heterogeneity: Tau^2 = 0.23; Chi^2 = 5.56, df = 2 (P value = 0.06); I^2 = 64%; Analysis 5.5).

Subgroup analysis

There were too few studies in different subgroup categories to enable subgroup analyses by cointervention, age, baseline anaemia/iron deficiency/iron-deficiency anaemia status, duration of intervention, malaria endemicity, or type of iron utilised. However, there was evidence of a trend towards an increase in risk of gastrointestinal adverse effects as dose of elemental iron was increased: from 31 mg to 60 mg (RR 1.23, 95% CI 0.84 to 1.81, 2 studies, 293 women), to 61 mg to 100 mg (RR 3.00, 95% CI 1.45 to 6.20, 1 study, 145 women), to more than 100 mg (RR 2.42, 95% CI 1.45 to 4.05, 2 studies, 83 women; test for subgroup differences: Chi^2 = 6.80, df = 2 (P value = 0.03), I^2 = 70.6%; Analysis 5.6).

Loose stools/diarrhoea

Six studies recruiting 604 women identified an increased prevalence of loose stools/diarrhoea (defined by the trial authors): RR 2.13, 95% CI 1.10 to 4.11; heterogeneity: Tau^2 = 0.11; Chi^2 =

5.99, df = 5 (P value = 0.31); I^2 = 17%; high quality evidence; Analysis 5.7; Summary of findings for the main comparison.

Subgroup analysis

Data were inadequate for subgroup analyses for this outcome given the small number of trials in each subgroup category.

Hard stools/constipation

Eight studies recruiting 1036 women demonstrated an increased prevalence of hard stools/constipation (as defined by the authors): RR 2.07, 95% CI 1.35 to 3.17; heterogeneity: Tau^2 = 0.00; Chi^2 = 4.10, df = 7 (P value = 0.77); I^2 = 0%; high quality evidence; Analysis 5.8. When only the four studies (480 women) considered at low overall risk of bias were included (Bruner 1996; Marks 2014; Pereira 2014; Waldvogel 2012), an increased risk for this outcome was still observed (RR 2.14, 95% CI 1.04 to 4.38; Analysis 5.9).

Subgroup analysis

Data were inadequate for subgroup analyses given the small number of trials in each subgroup category.

Abdominal pain

Seven studies recruiting 1190 women showed no definitive increase in abdominal pain (RR 1.55, 95% CI 0.99 to 2.41; heterogeneity: Tau^2 = 0.00; Chi^2 = 4.04, df = 6 (P value = 0.67); I^2 = 0%; low quality evidence; Analysis 5.10).

Subgroup analysis

Data were inadequate for subgroup analyses given the small number of trials in each subgroup category.

Nausea

Eight studies recruiting 1214 women did not find any evidence of an increased prevalence of nausea among women randomised to iron (RR 1.19, 95% CI 0.78 to 1.82; heterogeneity: Tau^2 = 0.00; Chi^2 = 6.30, df = 7 (P value = 0.51); I^2 = 0%; Analysis 5.11).

Subgroup analysis

Data were inadequate for subgroup analyses given the small number of trials in each subgroup category.

Change in stool colour

Four studies (359 women) reported a markedly elevated increase in prevalence reporting a change in stool colour among women receiving iron (RR 6.92, 95% CI 3.83 to 12.52; heterogeneity: Tau^2 = 0.00; Chi^2 = 0.08, df = 3 (P value = 0.99); I^2 = 0%; Analysis 5.12).

Subgroup analysis

Data were inadequate for subgroup analyses given the small number of trials in each subgroup category.

Reflux/Heartburn

Only one study reported rates of reflux/heartburn (Pereira 2014). Four patients in the iron intervention group reported reflux/heartburn compared to none in the control group.

Headache

Four studies involving 526 women reported on prevalence of headache and found no evidence of an effect on this outcome from iron (RR 0.98, 95% CI 0.58 to 1.66; heterogeneity: Tau^2 = 0.00; Chi^2 = 1.11, df = 3 (P value = 0.78); I^2 = 0%; Analysis 5.13).

Subgroup analysis

Data were inadequate for subgroup analyses given the small number of trials in each subgroup category.

Cognitive function

Five studies reported on cognitive function but reported outcomes using different tools or domains, and thus results could not be meta-analysed. We present the data from the five studies below.

Bruner 1996 randomised 81 adolescent girls with non-anaemic iron deficiency to iron supplementation versus placebo and found that girls taking iron had a significant improvement over baseline and end of treatment, compared to those taking placebo, in the total recall score in a test of verbal learning (Hopkins Verbal Learning Test) (P < 0.02), with no differences in any other domains of this test. There were no differences attributable to iron on the Symbol Digit Modalities Test, the Visual Search and Attention Test, or the Brief Test of Attention.

Elwood 1970 randomised women, aged 20 years or older, with anaemia (Hb < 10.5 g/dL) to daily iron supplementation or placebo for eight weeks, and administered several cognitive tests. Data were not reported to directly compare intervention and control, and thus groups (haematologic responders and non-responders) were merged. Women randomised to iron demonstrated a reduction in the number of errors made while completing a maze

(MD -9.73, 95% CI -17.22 to -2.24). However, no effects from iron were seen on other cognitive tests (Serial 7s, E-test, Card Sorter test, Peg board time).

Larocque 2006 randomised schoolgirls, aged 14 years to 16 years, to iron or placebo and measured a series of cognitive outcomes. There was no effect from iron on the results of any of the cognitive tests performed (Trail Making Test Part A and Part B, Motor-Free Visual Perception Test, Digit Span, Covert Orienting of Visual Attention Task).

Leonard 2014 randomised 24 women, aged 18 years to 35 years, who were not iron deficient and not currently taking iron, to ferrous sulphate at two doses (60 mg and 80 mg) and compared them to placebo. Participants underwent testing at baseline and the end of intervention with the IntegNeuro Battery of Cognitive Tests (Brainclinics 2015). Women treated with iron (at either dose) had a significant reduction in impulsivity (P value = 0.047), but no difference in memory, response speed, attention, information processing, executive function or emotion identification.

Murray-Kolb 2007 randomised women, aged 18 to 35 years, of differing iron status (iron replete, non-anaemic iron deficient, iron-deficient anaemic) to daily iron supplementation or placebo. Unfortunately, effect sizes for cognitive scores at end of intervention or change from baseline were not reported and hence could not be extracted.

Secondary outcomes

Iron status

Ferritin

Forty-two studies (3881 women) reported on ferritin concentrations at the end of intervention; iron increased ferritin levels (MD 10.27, 95% CI 8.90 to 11.65; heterogeneity: $Tau^2 = 9.96$; $Chi^2 = 475.21$, df = 41 (P < 0.00001); $I^2 = 91\%$; Analysis 6.1).

Subgroup analysis

We further explored potential sources of heterogeneity with subgroup analyses (even though these were not prespecified), as it offered an opportunity to evaluate subgroup effects on effects of iron status changes induced by iron supplementation (see Differences between protocol and review). Subgroup analyses indicated that iron interventions had a lesser effect when coadministered with vitamin C (Analysis 6.2), but had no effect on difference of effect on different age groups (Analysis 6.3). The effect of iron on ferritin was not affected by baseline anaemia status (Analysis 6.4), but women who were iron deficient had a smaller increase in ferritin (MD 8.40, 95% CI 6.31 to 10.49, 20 studies, 1065 women) compared with women who were iron replete (MD 13.38, 95% CI 6.74 to 20.01, 5 studies, 297 women) or in whom iron status had not been characterised (MD 12.88, 95% CI 9.99 to 15.78, 20 studies, 2499 women; test for subgroup differences: $Chi^2 = 7.02$, df = 2 (P value = 0.03), $I^2 = 71.5\%$; Analysis 6.5). No difference in effect was observed by iron-deficiency anaemia status (Analysis 6.6). Ferritin levels rose less among women given 30 mg or less elemental iron compared with women given higher doses; test for subgroup differences: $Chi^2 = 8.59$, df = 3 (P value = 0.04), $I^2 = 65.1\%$; Analysis 6.7). Giving iron for one to three months (MD 12.17, 95% CI 9.81 to 14.53, 31 studies, 2829 women) showed a larger increase in ferritin than giving iron for less than one month (MD 7.60, 95% CI 4.64 to 10.57, 7 studies, 794 women) or more than three months (MD 7.85, 95% CI 1.31 to 14.38, 4 studies, 258 women; test for subgroup differences: $Chi^2 = 6.12$, df = 2 (P value = 0.05), $I^2 = 67.3\%$; Analysis 6.8). There was no evidence of an effect from different iron formulations (Analysis 6.9). Although examination of the funnel plot suggested asymmetry, Egger's regression test did not indicate evidence of publication bias (P value = 0.644).

Transferrin saturation

Twenty-three studies recruiting 1637 women identified an effect from iron supplementation on transferrin saturation (5.98, 95% CI 3.93 to 8.02; heterogeneity: $Tau^2 = 13.38$; $Chi^2 = 142.46$, df = 22 (P < 0.00001); $I^2 = 85\%$; Analysis 6.10).

Soluble transferrin receptor

Eleven studies recruiting 579 women identified an effect from iron supplementation on soluble transferrin receptor (as many assays are available, each with a different scale, we estimated the SMD (-0.32, 95% CI -0.49 to -0.16; heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 9.34$, df = 10 (P value = 0.50); $I^2 = 0\%$; Analysis 6.11).

Total iron binding capacity

Nineteen studies recruiting 960 women identified no effect from iron supplementation on total iron binding capacity at the end of the intervention (SMD -0.64, 95% CI -1.38 to 0.09; heterogeneity: $Tau^2 = 2.49$; $Chi^2 = 390.10$, df = 18 (P < 0.00001); $I^2 = 95\%$; Analysis 6.12).

Serum iron

Seventeen studies recruiting 902 women identified an increase from iron supplementation on serum iron concentrations (SMD 0.47, 95% CI 0.19 to 0.74; heterogeneity: $Tau^2 = 0.19$; $Chi^2 = 48.20$, df = 16 (P < 0.00001); $I^2 = 67\%$; Analysis 6.13).

Erythrocyte protoporphyrin

Only a single study reported on erythrocyte protoporphyrin (Berger 1997), finding that iron supplementation did not significantly affect erythrocyte protoporphyrin. (For illustrative purposes, see Analysis 6.14).

Physical exercise performance

Exercise performance was reported in terms of both peak (maximal) and submaximal performance.

Peak (maximal) exercise performance

A meta-analysis found that women receiving iron had increased absolute VO_2 max score (MD 0.11 L/min, 95% CI 0.02 to 0.20, 8 studies, 276 women ; heterogeneity: Tau^2 = 0.00; Chi^2 = 4.96, df = 7 (P value = 0.66); I^2 = 0%; Analysis 7.1) and relative VO_2 max (MD 2.36 mL/kg/min, 95% CI 0.55 to 4.17, 15 studies, 407 women; heterogeneity: Tau^2 = 8.39; Chi^2 = 58.26, df = 14 (P < 0.00001), I^2 = 0.76; Analysis 7.2), indicating that iron supplementation increases peak exercise performance in women. No effects on peak respiratory exchange ratio (RER; Analysis 7.3), heart rate (Analysis 7.4), or lactate at longest point of exercise (Analysis 7.5) were observed from iron. There was no evidence of funnel plot asymmetry.

Submaximal exercise performance

Five studies recruiting 126 women found that women randomised to iron required a lower proportion of their VO_2 max to achieve a defined submaximal exercise task (MD -3.34%, 95% CI -6.17 to -0.51; heterogeneity: Tau^2 = 4.45; Chi^2 = 7.33, df = 4 (P value = 0.12); I^2 = 45%; Analysis 8.1). Similarly, six studies recruiting 212 women found that women randomised to iron required a lower heart rate to achieve the same exercise task (MD -4.72 beats per minute, 95% CI -8.64 to -0.80; heterogeneity: Tau^2 = 0.00; Chi^2 = 2.27, df = 5 (P value = 0.81); I^2 = 0%; Analysis 8.2). No effects from iron on energy consumption during exercise (Analysis 8.3), submaximal RER (Analysis 8.4), achieved workload (Analysis 8.5) or time to exhaustion (Analysis 8.6) were observed. There was no evidence of funnel plot asymmetry.

Psychological health

Waldvogel 2012 compared four weeks of iron supplementation with placebo following blood donation in females, and observed an improvement in self-reported physical condition (as assessed by the Short Form 12 (SF-12) health survey (Gandek 1998)) at the end of intervention, but found no differences in self-reported fatigue, vitality or mental health scores.

Zaman 2013 compared 12 weeks of iron supplementation as ferrous gluconate with vitamin C to placebo in females recruited through advertisements at the Univeristy of Sydney. Using the Short Form 36 Health Survey (SF-36) (Ware 1992), participants receiving iron self-reported improvement in vitality but no difference in other scores.

Adherence

Adherence was not reported in any form in 34 of the studies; other studies reported adherence in heterogenous ways, and hence we could not include data in a meta-analysis. We have described data in the 'Notes' section of the Characteristics of included studies tables. Participants randomised to iron did not appear to have poorer adherence compared with those randomised to placebo.

Anthropometric measures

Height

Four studies recruiting 302 women did not identify an effect of iron on height (MD -0.32, 95% CI -2.25 to 1.61; heterogeneity: Tau^2 = 1.84; Chi^2 = 5.87, df = 3 (P value = 0.12); I^2 = 49%; Analysis 9.1).

Weight

Eight studies recruiting 593 women did not identify evidence of an effect from iron supplementation on weight (MD 0.76 kg, 95% CI -0.41 to 1.92; heterogeneity: Tau^2 = 0.00; Chi^2 = 3.19, df = 7 (P value = 0.87); I^2 = 0%; Analysis 9.2). A sensitivity analysis excluding the single cluster randomised trial (Kanani 2000) did not meaningfully affect this finding (MD 0.24 kg, 95% CI -1.13 to 1.60; Analysis 9.3).

Body mass index

Six studies recruiting 520 women found that iron supplementation increased body mass index in women (MD 0.53, 95% CI 0.10 to 0.96; heterogeneity: Tau^2 = 0.00; Chi^2 = 1.33, df = 5 (P value = 0.93); I^2 = 0%; Analysis 9.4). A sensitivity analysis excluding the single cluster randomised trial (Kanani 2000) resulted in a similar effect size although the statistical significance of this finding was no longer observed (MD 0.52, 95% CI -0.04 to 1.07; Analysis 9.5).

Serum/plasma zinc (μmol/L)

Four studies recruiting 151 women did not identify evidence of an effect from iron supplementation on zinc concentrations (MD -0.65, 95% CI -2.70 to 1.40; Analysis 10.1).

No studies reported data on the following secondary outcomes: vitamin A status and red cell folate.

Other outcomes

Productivity

Although not a pre-specified outcome, productivity is an important clinical and economic outcome linked with iron interventions and thus we extracted these data where available (see Differences between protocol and review). We identified three studies (446 women), which reported effects of iron supplementation on productivity, defined as a particular work-related output per unit time (Edgerton 1979; Florencio 1981; Li 1994). Meta-analysis of these studies revealed that iron supplementation did not increase productivity (SMD 0.07, 95% CI -0.12 to 0.26; Analysis 11.1).

Malaria prevalence

Only one study (378 women) reported malaria prevalence (Gunaratna 2015), with no difference between iron and control groups (P value = 0.66; Analysis 12.1).

Fatigue

Although not a pre-specified outcome, fatigue is considered an important clinical outcome from iron deficiency and anaemia, and thus we extracted data from studies reporting on effects of daily iron supplementation on fatigue.

Ballin 1992 reported that a larger number of adolescent girls randomised to iron (n = 29) compared to placebo (n = 30) experienced an improvement in 'lassitude' (about 25% iron, about 4% control, data reported on graphs).

Booth 2014 recruited 49 women undertaking cadet training in the Australian army and reported no difference in fatigue scores (P > 0.9) with daily oral iron (mean 12.9) compared to controls (mean 15.7).

Bruner 1996 reported that 35.3% (n = 37) of adolescent girls randomised to iron compared with 22.6% (n = 36) randomised to placebo reported an improvement in 'energy' levels after intervention.

Elwood 1966 reported that 40 women with a Hb > 10 g/dL randomised to iron experienced a mean increase in fatigue scores of 0.15 ± 0.78 points (graded along a 16-point scale), whereas 49 women randomised to placebo experienced a mean increase in fatigue scores of 0.39 ± 0.73 points.

Elwood 1970 randomised anaemic (Hb < 10.5 g/dL), community-living women to iron (n = 26) or placebo (n = 21) and reported that women receiving iron experienced a mean -1.32 point (standard deviation (SD) 1.78) change in fatigue scores, compared with a -0.7 point (SD 1.83) change in women receiving placebo.

McClung 2009 randomised female soldiers at the onset of their rigorous basic combat training to iron (n = 86) versus placebo (n = 85), and did not find evidence that iron benefited fatigue (mean: 9.8 ± 7.0 iron, 9.3 ± 6.4 placebo), as measured by the Profile of Mood States (McNair 1971), although there was an increase (P < 0.05 for group interaction) in reported 'vigour' (mean: 13.1 ± 6.3 iron, 11.6 ± 6.5 placebo).

Verdon 2003 specifically recruited women presenting with fatigue for which no other cause (including anaemia) could be identified, and randomised them to iron (n = 75) versus placebo (n = 69): women receiving iron experienced a greater reduction in fatigue scores along a 10-point scale (mean -1.82, SD 1.7) compared with control (mean 0.85, SD 2.1) (difference 0.97, P value = 0.004); interestingly, a benefit was identified exclusively in women with a baseline ferritin < 50 ug/L.

Waldvogel 2012 recruited 154 non-anaemic iron-deficient female blood donors and randomised them to iron or placebo; women receiving iron experienced similar endpoint fatigue scores (mean: 3.4 iron, 3.5 control) and fatigue severity scores (mean: 2.5 iron, 2.6 control), as assessed by the Fatigue Severity Scale (Krupp 1989).

The variation in outcome measures and proportion/change from baseline/endpoint data reported precludes meta-analysis. However, these data appear to indicate that iron may improve symptoms among women who are fatigued, although the effects on asymptomatic women appear less evident.

DISCUSSION

Summary of main results

The findings, together with an assessment of the quality of the evidence for the primary outcomes, are summarised in Summary of findings for the main comparison. Overall, 67 studies involving 8506 women were included in the review.

Findings suggest that women receiving iron were less likely to be anaemic and iron deficient at the end of intervention, and more likely to experience an increase in haemoglobin concentrations and iron stores (as measured by indices such as ferritin and soluble transferrin receptor). Effects of iron supplementation on haemoglobin did not appear dose related, although increases in ferritin concentration were greater at higher doses. Also, providing iron for one to three months achieved greater increases in haemoglobin and ferritin than either shorter or more prolonged durations.

Although only limited data reported on functional health outcomes associated with iron supplementation, our meta-analyses indicate that iron supplementation improves maximal and submaximal exercise performance in women, and reduces symptomatic fatigue. No effects on cognitive function or self-reported psychological health were evident.

Iron supplementation was associated with an increase in gastrointestinal adverse effects, among women receiving doses exceeding 30 mg elemental iron.

Vitamin C appeared to augment the beneficial effect of iron on anaemia prevalence (but not on haemoglobin or ferritin concen-

tration), although only limited data were available for these subgroup analyses.

Overall completeness and applicability of evidence

Despite the overall large number of trials assessing the effects of daily iron supplementation in menstruating women, most of these collected basic haematologic and iron indices data, with surprisingly few studies reporting on key outcomes - anaemia, iron deficiency, iron-deficiency anaemia; functional outcomes such as cognitive performance and psychological health (e.g. depression, fatigue); and only a very small proportion of the overall number of studies collected data on adverse effects experienced by the participants. This indicates that trials included in this review frequently did not address these clinically relevant endpoints. In particular, even though haemoglobin measurements are commonly performed, the field is limited by the lack of reporting of the effects of iron on anaemia in these key trials. Ultimately, however, the trials which do report on anaemia collectively provide moderate quality evidence to support a substantial benefit from iron on this outcome (RR 0.39, 95% CI 0.25 to 0.60). Likewise, reporting of effects of iron supplementation on iron deficiency and iron-deficiency anaemia was uncommon (even though ferritin levels were frequently reported). A similar pattern of reporting the continuous rather than dichotomous outcomes has been observed in systematic reviews of daily iron supplementation in children (Low 2013; Pasricha 2013).

We did not undertake a formal subgroup analysis to compare trials undertaken in low- and middle-income countries and those undertaken in high-income countries. Many trials in high-income countries were undertaken in participants who were iron deficient at baseline, and thus, such a subgroup comparison would not have been appropriate. However, the effects of iron in anaemic and iron-deficient populations, reminiscent of the burden of these conditions in low-income settings, can be inferred from the subgroup analyses we did perform.

The design of this review could not account for differences in efficacy between iron alone or iron in addition to common cointerventions such as folic acid or vitamin C (compared to no intervention).

Quality of the evidence

Although there have been many RCTs addressing the issue of daily iron supplementation in menstruating women, we considered only few at overall low risk of bias. In particular, only 14 studies reported using a low risk of bias method of random sequence generation (with two being at high risk of bias, and the remainder not reporting on sequence generation), and 15 reported using a low risk method of allocation concealment. Eight studies did not attempt to blind participants; while this is unlikely to affect laboratory-measured outcomes, such as haemoglobin and iron indices, outcomes relying on more subjective tools (e.g. patient reports of adverse effects, fatigue, exercise performance and self-reported quality of life) may have been at risk of bias. Attrition was a problem in nine trials. Overall, only 10 studies were assessed as being at low overall risk of bias.

The quality of evidence for haematologic and iron status-related outcomes was generally moderate or high, but was poor for other outcomes, including the pre-specified primary outcome of cognitive function. Adherence was frequently not reported, and where it was reported, it was described heterogeneously, preventing detailed analysis of the effects of adherence on outcomes.

Potential biases in the review process

The systematic review encompassed a broad and sensitive search strategy across multiple international databases, and at least two authors independently screened and extracted data. We did not apply language restrictions. We sought to identify published data and data published in the grey literature.

One potential bias in the review, however, is that it is possible that historic studies may have been undertaken that are no longer indexed or available on accessible databases, and hence for which data were not identified. Also, our classification of risk of bias may have been excessively stringent, as many trials were undertaken many years ago, before formal recommendations for trial reporting were released, and thus for which methods used to reduce risk of bias were not included in the manuscript.

Agreements and disagreements with other studies or reviews

The effects of daily iron supplementation on women's health have not been previously subject to a systematic review and meta-analysis. A systematic review evaluating intermittent iron supplementation in menstruating women found that it was a feasible intervention for reducing anaemia compared with no iron intervention, although in comparison with daily supplementation, intermittent iron was less effective in controlling anaemia (Fernández-Gaxiola 2011).

AUTHORS' CONCLUSIONS

Implications for practice

Daily iron supplementation appears to be an effective clinical and public health strategy for alleviating anaemia and iron deficiency,

and for increasing haemoglobin and iron stores. Daily iron supplementation also improves exercise performance (maximal and submaximal) in women. There is evidence, moreover, that iron supplementation improves fatigue scores, particularly among women with baseline fatigue. However, these benefits come at the risk of adverse effects, especially abdominal side effects. Providing iron at lower doses (e.g. up to 30 mg elemental iron) for one to three months may have an optimal benefit and adverse effect profile. There is no evidence of difference in efficacy between different iron salts.

Implications for research

Studies reporting on haemoglobin and ferritin alone are no longer required. Only limited data exist for a range of key outcomes (both primary and secondary) relating to iron supplementation - for example, effects of iron on cognitive function, psychological health, well-being, and economic productivity. Lack of these data preclude precise economic and risk-benefit analyses of this intervention. Further studies are needed to identify whether iron has effects on these outcomes. In the public health setting, further research is needed to understand the benefits of oral iron interventions in the preconception context on future pregnancy outcomes, and again whether iron interventions ultimately have functional benefits on well-being and health. In low- and middle-income countries, where iron may interact with infection and iron supplementation may coexist with other micronutrient deficiencies, the risk benefit of iron interventions must be more clearly understood.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Agarwal 2003

Methods	**Design:** cluster randomised controlled trial **Randomisation:** by school class **Trial:** daily iron versus weekly iron versus control. Weekly iron arm not extracted for this review **Date of study:** not stated
Participants	**Setting:** middle class area of New Delhi, North India **Malaria endemicity:** not stated **Included:** adolescent high-school girls aged 10 years to 17 years (mean age not reported) , attending government high schools **Excluded:** children with haemoglobin < 7 g/dL **Dropouts:** 7 girls from daily iron group failed to complete trial. No reports in other groups **Sample size:** total: 1390; intervention: 699, control: 691
Interventions	**Intervention:** daily iron (100 mg) + folic acid (500 mcg) daily **Control:** no intervention **Duration:** 100 days
Outcomes	Haemoglobin, anaemia, iron status*
Notes	**ICC:** not provided **Compliance:** not reported **Conflicts of interest:** not reported **Funded by:** UNICEF *Not included in our analyses as ferritin was not measured at study endpoint in daily iron arm

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported. Class randomisation
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported. Only biochemical measures were reported

Agarwal 2003 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	7 girls dropped out
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	High risk	No intracluster correlation coefficient included

Ballin 1992

Methods	**Design:** randomised, double-blind, placebo-controlled trial **Randomisation:** individual **Trial:** daily iron versus placebo **Date of study:** not stated
Participants	**Setting:** high school in a middle socioeconomic-level community in urban Israel **Malaria endemicity:** not stated **Included:** adolescent girls aged 16 years to 17 years attending high school (mean age not reported) **Excluded:** if they had a prior gastrointestinal or haematologic illness **Dropouts:** not reported **Sample size:** total: 59; intervention: 29, control: 30
Interventions	**Intervention:** LiquiFer® liquid iron solution (105 mg elemental iron) daily **Control:** placebo **Duration:** 2 months
Outcomes	Haematology, subjective reports of health, physical fitness, side effects
Notes	**Compliance:** not reported **Conflicts of interest:** not stated **Funded by:** not stated **Other notes:** physical fitness not reported in extractable manner, subjective reports of health data derived from bar charts

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method for sequence generation not described
Allocation concealment (selection bias)	Unclear risk	Method for allocation concealment not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo liquid administered to control group

Ballin 1992 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not reported in paper, outcomes unlikely to be affected.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts or loss to follow-up
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	No evidence of other bias

Berger 1997

Methods	**Design:** randomised, double-blind, controlled trial **Randomisation:** individual **Trial:** daily oral iron versus control **Date of study:** not stated
Participants	**Setting:** two rural populations of the Bolivian Altiplano in the region of Potosi: Atocha (3600 m) and Santa Barbara (4800 m) **Malaria endemicity:** not stated **Included:** women aged 15 years to 40 years (mean age 28 years), non-pregnant, well-nourished, not suffering from chronic illness and/or acute infection, residing in the study region for at least the two previous years **Excluded:** not meeting above criteria or planning to leave the study region during the following 6 months **Dropouts:** not reported **Sample size:** total: 130; intervention: 65, control: 65
Interventions	**Intervention:** 3 mg elemental iron/d (6 days a week) + 20 ug folic acid **Control:** no intervention **Duration:** 3 months
Outcomes	Haemoglobin, height, weight, erythrocyte protoporphyrin
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** not stated

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated

Berger 1997 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	High risk	No placebo
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not stated
Selective reporting (reporting bias)	Low risk	No evidence
Other bias	Low risk	No evidence

Binkoski 2004

Methods	**Design:** randomised, cross-over study **Randomisation:** individual **Trial:** daily iron versus placebo **Date of study:** not stated
Participants	**Setting:** USA, no further information regarding location **Malaria endemicity:** not stated **Included:** healthy women aged 19 years to 47 years (mean age 26 years) **Excluded:** did not have serum low-density lipoprotein (LDL) cholesterol between the 50th and 90th percentiles and high-density lipoprotein (HDL) cholesterol and triglycerides between the 5th and 95th percentiles. Must also have had low normal baseline haemoglobin (120 to 140 g/L) and low ferritin (15 to 40 ng/mL) **Dropouts:** not stated **Sample size:** total: 26; intervention: 14, control: 12
Interventions	**Intervention:** 320 mg of ferrous sulphate daily administered as 160 mg ferrous sulphate (50 mg elemental iron) twice a day **Control:** placebo **Duration:** 10 weeks
Outcomes	Haematology, iron status
Notes	**Compliance:** not reported **Conflicts of interest:** reported that no conflict of interest **Funded by:** donation from "Intelligent Cuisine products"

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Binkoski 2004 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Method for sequence generation not described
Allocation concealment (selection bias)	Unclear risk	Method for allocation concealment not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered to control group
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not reported. Only biochemical outcomes were evaluated
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	No evidence of other bias

Booth 2014

Methods	**Design:** randomised, double-blind controlled study **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** initial recruitment started February 2003 (completion not stated)
Participants	**Setting:** Australian defence force academy, Canberra, Australia **Malaria endemicity:** not stated **Included:** first and second year female officer cadets; age range not reported (mean age 20 years) **Excluded:** current medical problems, recent blood donation, pregnancy in the previous 12 months, breast-feeding, anaemia (haemoglobin < 120 g/L), iron overload (serum ferritin > 300 μg/L), or a positive *Helicobacter pylori* antibody test **Dropouts:** 49 participants completed from 71 initially recruited (69%) **Sample size:** total: 49, Iron: 25, placebo: 24
Interventions	**Intervention:** ferrous gluconate containing 18 mg of elemental iron + 0.5 mg of folate daily **Control:** 0.5 mg of folate daily **Duration:** 13 weeks
Outcomes	Haemaglobin, iron status, general fatigue scores
Notes	**Compliance:** 85% compliance in both groups (equivalent to 6 tablets a week) **Conflicts of interest:** not declared **Funded by:** Defence Science & Technology Organisation's annual tasking

Booth 2014 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	On-line random number generator
Allocation concealment (selection bias)	Low risk	Reported allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Reported double blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not evident
Incomplete outcome data (attrition bias) All outcomes	High risk	31% dropout rate
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Bruner 1996

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** iron daily versus placebo **Date of study:** August to September 1993
Participants	**Setting:** two public high schools and two private Catholic high schools in Baltimore, Maryland, USA **Malaria endemicity:** not stated **Included:** girls in grades 9 to 12, aged 13 years to 18 years (mean age 16 years) **Excluded:** if did not have non-anaemic iron deficiency (i.e. haemoglobin > 120g/L (> 115g/L for African American girls)); ferritin < 12mg/L) **Dropouts:** 8 in total. 5 became anaemic and were excluded (3 in intervention, 2 in control group). 3 were lost to follow-up **Sample size:** total: 73; intervention: 37, control: 36
Interventions	**Intervention:** ferrous sulphate 1300 mg daily (420 mg elemental iron daily) **Control:** placebo **Duration:** 8 weeks
Outcomes	Haematology, cognitive function, iron status, side effects

Bruner 1996 (*Continued*)

Notes	**Compliance:** not reported **Conflicts of interest:** authors report no conflict of interest **Funded by:** SmithKline Beecham Consumer Brand Pharmaceuticals **Other notes:** results of most cognitive tests were presented only in figures (without error bars), not tables, and thus could not be used for meta-analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random number lists
Allocation concealment (selection bias)	Low risk	**Quote:** "Participants and investigators were unaware of group assignment"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	3 dropouts, 5 withdrawn from study. Not stated from which arm losses occurred
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Unclear risk	Outcomes only reported in figures, not in tables or in the text

Brutsaert 2003

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** not stated
Participants	**Setting:** Mexico. No further details **Malaria endemicity:** not stated **Included:** untrained* women, aged 18 years to 45 years (mean age 29 years), screened and found to have iron depletion (ferritin < 20 ng/mL) and be non-anaemic (haemoglobin > 120 g/L) **Excluded:** current pregnancy or pregnancy within the previous year, recent infectious illness or fever, haemolytic anaemia, asthma, musculoskeletal problems, recent history of eating disorders, smoking, excess alcohol consumption, recent use of recreational drugs, or consumption of prescription medications that would interfere with dietary

	iron absorption **Dropouts:** unclear. Reports that 20 women were selected for final study from 92 eligible women. Unclear as to how women were selected **Sample size:** total: 20; intervention: 10, control: 10
Interventions	**Intervention:** elemental iron 10 mg as ferrous sulphate **Control:** placebo **Duration:** 6 weeks
Outcomes	Haematology, iron indices, exercise performance
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** not stated *The authors did not further define the term "untrained"

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not reported in paper, outcomes unlikely to be affected.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Reports that 20 women were selected for final study from 92 eligible women. Unclear as to how women were selected (i.e. if drop outs affected numbers)
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Bryson 1968

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily iron with vitamin C versus vitamin C alone **Date of study:** not stated
Participants	**Setting:** semi-skilled female factory workers in Stevenston, Scotland **Malaria endemicity:** not stated **Included:** aged 15 years to 19 years (mean age not reported) **Excluded:** receiving therapy from General Practioner (GP), haemoglobin < 9 g/dL, GP started iron therapy during the trial, those who reported ill effects due to the tablet **Dropouts:** 94 of 269 failed to take more than 2 months supply (total 34%) **Sample size:** total: 254; intervention: 134, control: 120
Interventions	**Intervention:** elemental iron (40 mg/d) as ferrous fumarate + vitamin C **Control:** vitamin C alone **Duration:** 3 months
Outcomes	Haemoglobin, side effects
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** not stated, however Lederle Laboratories provided drugs **Other notes:** errors not reported for haemoglobin, therefore haemoglobin data not extracted

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Low risk	Manufacturer maintained allocation code
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported. Side effects being measured, thus blinding of outcome assessment would be important
Incomplete outcome data (attrition bias) All outcomes	High risk	269 enrolled, 175 completed study
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Charoenlarp 1988

Methods	**Design:** two randomised controlled trials **Randomisation:** individual **Trial:** Trial 1: daily iron at 2 different doses with and without supervision versus placebo. Trial 2: daily iron at two different doses with and without folic acid versus placebo **Date of study:** Trial 1: 1977 to 1979, Trial 2: 1978 to 1980 **TWO STUDIES:** 1. Study A: Non-pregnant women and men; data for women presented separately. Participants with haemoglobin E or B thalassaemia trait were excluded. Study performed between March 1977 and March 1979 2. Study C: Study performed between September 1978 and August 1980
Participants	**Setting:** Trial 1: Rural area of Central Thailand 80 km north of Bangkok near Ayudhya. Trial 2: Northern Thailand; two villages 50 km south and 100 km south west of Chiang Mai **Malaria endemicity:** malaria is endemic to both trials **Included:** women of fertile age Trial 1: age range 15 years to 45 years (mean age not stated) Trial 2: age range 16 years to 45 years (mean age not stated) **Excluded:** Haemoglobin < 80, thalassaemia trait or disease, uncooperative **Dropouts:** Trial 1: 16% across all groups (reported as similar), Trial 2: reported at 36%, group status unclear **Sample size:** total: 863; intervention: 690, control: 173
Interventions	**Intervention:** 1. Trial 1: 5 groups: placebo, daily iron 120 mg supervised, daily iron 240 mg supervised, daily iron 240 mg + 5 mg folic acid supervised, daily iron 120 mg unsupervised 2. Trial 2: 4 groups: placebo, daily iron 120 mg, daily iron 240 mg, daily iron 240 mg plus 5 mg of folic acid **Control:** placebo **Duration:** 3 months
Outcomes	Anaemia, haemoglobin, iron status
Notes	**Compliance:** not stated **Conflicts of interest:** not stated. **Funded by:** World Health Organization (WHO), Belgian administration of co-operation to development, Danish International Development Authority, and Swedish International Development Authority

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated

Charoenlarp 1988 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo used
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Placebo used
Incomplete outcome data (attrition bias) All outcomes	High risk	Loss to follow-up: 16% in trial 1 and 36. 6% in trial 2
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Cooter 1978

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily vitamins including iron versus daily vitamins without iron **Date of study:** not stated
Participants	**Setting:** university at Georgetown University (USA) **Malaria endemicity:** not stated **Included:** female varsity basketball players aged 18 years to 24 years (mean age not reported) **Excluded:** not stated **Dropouts:** not stated **Sample size:** total: 10; intervention: 5, control: 5
Interventions	**Intervention:** vitamin including iron (18 mg) as ferrous fumarate daily **Control:** vitamin without iron daily **Duration:** 4 months
Outcomes	Haemoglobin, iron indices
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** not stated

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported

Cooter 1978 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not reported. Biochemical indices unlikely to be influenced by assessors' knowledge of allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	No apparent attrition
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

DellaValle 2012

Methods	**Design:** randomised placebo-controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** 2008 to 2009
Participants	**Setting:** university in USA, no further details given **Malaria endemicity:** not stated **Included:** female college rowers (varsity and second year novice) > 18 years of age (age range not reported, mean age not reported) **Excluded:** smokers or anaemic **Dropouts:** 9; 6 in intervention, 3 in control **Sample size:** total: 40; intervention: 21, control: 19
Interventions	**Intervention:** 50 mg ferrous sulphate per capsule twice a day (i.e. 100 mg FeSO4, approximately 30 mg elemental iron daily) **Control:** placebo **Duration:** 6 weeks
Outcomes	Haemoglobin, iron indices, peak exercise performance, perceived exercise quality
Notes	**Compliance:** 60.3% of tablets taken iron arm, 75.6% in control arm (mean intake iron arm 64 tablets, control arm 80 tablets) **Conflicts of interest:** authors report no conflict of interest **Funded by:** authors report no financial disclosures **Other notes:** provided both endpoint and change from baseline data for all outcomes. Endpoint data included in meta-analysis

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

DellaValle 2012 (*Continued*)

Random sequence generation (selection bias)	Low risk	Randomisation was done by assigning each participant a random number, with even and odd numbers being assigned to either treatment group
Allocation concealment (selection bias)	Low risk	Each participant was randomly assigned to a treatment group by a research assistant who was not involved in data collection or contact with participants
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Each participant was randomly assigned to a treatment group by a research assistant who was not involved in data collection or contact with participants
Incomplete outcome data (attrition bias) All outcomes	Low risk	31 of 40 rowers finished the entire study protocol; 22% loss to follow-up: 6 in iron group, 3 in placebo group
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Edgerton 1979

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** not stated
Participants	**Setting:** female tea workers of Kandy area, Sri Lanka **Malaria endemicity:** not stated **Included:** age range 20 years to 60 years (mean age 35 years). Allocation stratified by economic area and matched by economic productivity and haemoglobin **Excluded:** not stated **Dropouts:** not stated **Sample size:** total: 199; intervention: 103, control: 96
Interventions	**Intervention:** ferrous sulphate 200 mg/d (elemental iron 67 mg) **Control:** placebo (calcium lactate) **Duration:** 7 weeks
Outcomes	Haematology, productivity, voluntary physical activity

Edgerton 1979 (*Continued*)

Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** B Williams Co., New York **Other notes:** physical activity only reported in figures without errors: not useable. Change in productivity data not reported with SE, therefore not extractable

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported. Measurement of productivity may be influenced by knowledge of allocation arm
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Eftekhari 2006

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** two comparisons: daily iron with iodine versus iodine alone, daily iron versus no intervention **Date of study:** 2002 to 2003
Participants	**Setting:** Province of Lar in Iran **Malaria endemicity:** not stated **Included:** adolescent, grades 1 to 4 in high school; age within the range of 14 years to 18 years (mean age 16 years), who were non-anaemic iron-deficient (ferritin < 12 ng/mL & transferrin saturation < 16%, haemoglobin > 120 g/L) **Excluded:** any systemic disease, abnormal serum albumin (normal range: 3.5 g/dl to 5.5 g/dl), urinary iodine < 4100 mg/L or BMI < 19 kg/m² **Dropouts:** 9 of 103 girls failed on complete study (groups not described) **Sample size:** total: 94; iron + iodine 24, iron 23, iodine 25, control 22

Eftekhari 2006 (*Continued*)

Interventions	**Intervention:** 300 mg of ferrous sulphate (60 mg/day elemental iron) daily (5 days/week), with or without single oral dose of 190 mg of iodine **Control:** single oral dose of 190 mg of iodine or no intervention **Duration:** 12 weeks
Outcomes	Haemoglobin, iron status, weight, height, albumin, TFT (not extracted)
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** Tehran University of Medical Science

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not reported. However, only biochemical indices unlikely to be affected by knowledge of allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	103 individuals at baseline, on completion of study 9 were excluded (< 9%). No indication as to which arms excluded participants belonged
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Elwood 1966

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** not stated
Participants	**Setting:** women living in a community near a clinic in Wales **Malaria endemicity:** not stated **Included:** women attended for a general checkup: recruited if haemoglobin 100 g/L to 135 g/L, along with a 1:2 ratio of women with haemoglobin > 135 g/L. Age range 15

Elwood 1966 (*Continued*)

	years to 65 years (mean age not reported) **Excluded:** not stated **Dropouts:** 22 of 111 failed to complete study (group not stated) **Sample size:** total: 89; intervention: 40, control: 49
Interventions	**Intervention:** ferrous carbonate 200 mg daily **Control:** placebo **Duration:** 8 weeks
Outcomes	Haemoglobin, physical health, symptoms of anaemia (e.g. fatigue, concentration etc.)
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** trial drugs provided by Allen and Hanburys **Other notes:** not stated whether SD or SE used for error. Assumed to be SD

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported.Recording of symptoms could be influenced by knowledge of allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	111 enrolled, final data from 89
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Elwood 1970

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** not stated

Elwood 1970 (*Continued*)

Participants	**Setting:** outpatient women living in a Welsh mining community **Malaria endemicity:** not stated **Included:** haemoglobin < 105 g/L; non-macrocytic anaemia (age range not reported, mean age not reported) **Excluded:** not stated **Dropouts:** 2 of 49 women enrolled failed to complete trial (group unstated) **Sample size:** total: 47; intervention: 26, control: 21
Interventions	**Intervention:** 150 mg ferrous carbonate daily **Control:** placebo **Duration:** 8 weeks
Outcomes	Haemoglobin, symptoms, cognitive outcomes
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** not stated **Other notes:** errors presented as SEs (not SDs)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated. However, knowledge of allocation could influence subjective outcomes
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Flink 2006

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** not stated
Participants	**Setting:** patients attending public dental clinic in Sala, Sweden **Malaria endemicity:** not stated. **Included:** unstimulated salivary flow rate of < 0.2 ml/min; ferritin > 10 ng/mL and < 30 mg/mL (females), < 50 mg/mL (males). Of 50 participants recruited, 46 were female. Age range 16 years to 46 years (mean age 34 years) **Excluded:** not stated **Dropouts:** 3 of 50 participants failed to complete trial (group unstated) **Sample size:** total: 47; intervention: 24, control: 23
Interventions	**Intervention:** elemental iron (approximately 40 mg) as ferrous fumarate daily **Control:** placebo **Duration:** 3 months
Outcomes	Iron status
Notes	**Compliance:** mean compliance during the intervention period was 82% (95% CI 76 to 90) for the placebo group and 71% (95% CI 61 to 82) for the iron group (i.e. resulting in an average daily dose of 85 mg of iron). There was no significant difference in compliance between intervention compared to control groups **Conflicts of interest:** not stated **Funded by:** grants from Vastmanland County, Sweden, the Swedish Patent Revenue Research Fund and the Swedish Dental Society

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer random number generator
Allocation concealment (selection bias)	Low risk	Identical containers, identity in numbered envelopes and not revealed until end of study
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not reported. However, biochemical measures unlikely to be affected by knowledge of allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	Loss to follow-up: 1 in iron arm, 2 in placebo arm

Flink 2006 (*Continued*)

Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Florencio 1981

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron with vitamin C versus placebo **Date of study:** not stated
Participants	**Setting:** Manilla, Phillipines **Malaria endemicity:** not stated **Included:** garment workers working in a single factory. Minimum age 16 years (age range not reported, mean age not reported) **Excluded:** not stated **Dropouts:** 78 of 196 participants failed to complete trial (groups unstated) **Sample size:** total: 122; intervention: 81, control: 41
Interventions	**Intervention:** 525 mg ferrous sulphate with vitamin C **Control:** placebo **Duration:** 3 months
Outcomes	Haemoglobin, hematocrit, anaemia, work productivity
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** not stated

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo given
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported. Productivity could be affected by knowledge of allocation
Incomplete outcome data (attrition bias) All outcomes	High risk	Of 196 participants recruited, 78 dropped out

Florencio 1981 (*Continued*)

Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not reported

Fogelholm 1992

Methods	**Design:** randomised controlled trial **Randomisation:** individual. Randomisation stratified by menstrual status (regular/irregular) **Trial:** daily oral iron versus placebo **Date of study:** not stated
Participants	**Setting:** sports teams in Finland (athletics, basketball, handball) **Malaria endemicity:** not stated **Included:** women from sport teams aged 17 years to 31 years (mean age not reported, median age 24 years), with subclinical iron depletion (ferritin < 25 mg/mL, haemoglobin > 120 g/L) **Excluded:** not stated **Dropouts:** 2 from intervention group, none from control group **Sample size:** total: 31; intervention: 14, control: 17
Interventions	**Intervention:** 100 mg elemental iron as ferrous sulphate **Control:** placebo **Duration:** 8 weeks
Outcomes	Haemoglobin, iron status, VO_2 max
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** grant from the Ministry of Education (presumed of Finland)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random permutated blocks
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported. Exercise outcomes could be influenced by knowledge of allocation

Fogelholm 1992 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	No attrition
Selective reporting (reporting bias)	Unclear risk	HR and oxygen consumption data stated to be non significantly different between arms but data not shown. Lactate only shown in a figure
Other bias	Low risk	Not evident

Fogelholm 1994

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron at two doses (9 mg/27 mg per day) versus placebo **Date of study:** not stated
Participants	**Setting:** Helsinki, Finland **Malaria endemicity:** not stated **Included:** premenopausal women who were non-anaemic, iron depleted (haemoglobin > 120 g/L, ferritin < 20 mg/L). Age range not reported (mean age 38 years) **Excluded:** not stated **Dropouts:** 7 in placebo group, 6 in two iron groups **Sample size:** total: 72; intervention: 37, control: 35
Interventions	**Intervention:** two iron doses: one and three tablets as 8 mg iron fumarate with 1 mg porcine heme iron (3 mg elemental iron per capsule) **Control:** placebo **Duration:** 6 months
Outcomes	Haemoglobin, iron status
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** Cederroth International

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method for sequence generation not stated
Allocation concealment (selection bias)	Unclear risk	Method for allocation concealment not stated

Fogelholm 1994 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not reported. Biochemical measures only
Incomplete outcome data (attrition bias) All outcomes	Low risk	13 (16.7%) loss to follow-up: 7 placebo group, 2 Fe-9 group, and 4 Fe-27 group
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Unclear risk	Outcomes only reported in figures, not in tables or in the text

Gordeuk 1987

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral carbonyl iron versus ferrous sulphate versus placebo **Date of study:** not stated
Participants	**Setting:** Ohio red cross blood service (USA) **Malaria endemicity:** not stated **Included:** Female, non-anaemic (haemoglobin > 125 g/L) blood donors aged 18 years to 40 years (mean age not reported); donated at least once previously **Excluded:** any other medical condition **Dropouts:** 24 of 75 lost to follow-up with incomplete results (groups unstated). Partial data available for 70 of 75 enrolled participants **Sample size:** total: 70; intervention: 47, control: 23
Interventions	**Intervention:** two intervention arms, extracted separately: carbonyl iron 600 mg three times daily; ferrous sulphate 300 mg three times daily **Control:** placebo **Duration:** 2 months
Outcomes	Haemoglobin, iron status, iron deficiency, side effects
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** Food and Drug Administration orphan drugs development grant **Other notes:** haematologic outcomes measured 7 weeks following cessation of therapy. Carbonyl iron and ferrous sulphate reported separately: placebo group divided into two because odd number in placebo arm (23) - assumed 11 for carbonyl iron, 12 for ferrous sulphate
Risk of bias	

Gordeuk 1987 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported. As side effects were recorded, blinding of outcome assessors is important
Incomplete outcome data (attrition bias) All outcomes	High risk	Of 75 at baseline, 24 lost to follow-up. Partial data available for 70 of 75 enrolled participants
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Gordeuk 1990

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** not stated
Participants	**Setting:** Ohio red cross blood service (USA) **Malaria endemicity:** not stated **Included:** female, non-anaemic (haemoglobin > 125 g/L) blood donors aged 18 years to 40 years (mean age not reported); donated at least once previously **Excluded:** any other medical condition **Dropouts:** 18 **Sample size:** total: 76; intervention: 40, control: 36
Interventions	**Intervention:** carbonyl iron daily (equivalent to 100 mg elemental iron) **Control:** placebo **Duration:** 56 days
Outcomes	Haemoglobin, iron status, side effects, anaemia
Notes	**Compliance:** 35% of iron arm consumed all tablets; 44% of placebo arm consumed all tablets **Conflicts of interest:** not stated **Funded by:** Food and Drug Administration orphan drugs development grant

Gordeuk 1990 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported. As side effects were recorded, blinding of outcome assessors is important
Incomplete outcome data (attrition bias) All outcomes	Low risk	24% loss to follow-up
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Gunaratna 2015

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron with folate versus folate alone versus multivitamin containing iron and folate (multivitamin group not extracted) **Date of study:** October 2010 to June 2011
Participants	**Setting:** conducted in Ikwiriri and Kibiti, two rural wards in Rufiji District, Pwani Region, Tanzania **Malaria endemicity:** endemic **Included:** women between 15 years and 29 years of age (mean age 21 years), not pregnant, planning to remain in the study area for six months, and willing to provide written informed consent themselves or through a guardian if under 18 years of age **Excluded:** amenorrhoea, had given birth within the past six months, were already on vitamin supplements, or had any severe illness requiring hospitalisation during screening or enrolment **Dropouts:** 561 completed of 802 enrolled (70%) **Sample size:** total: 378, iron: 184, control: 194 (multivitamin and iron: 183 - not included)
Interventions	**Intervention:** 30 mg of elemental iron + 0.4 mg of folate **Control:** 0.4 mg of folate **Duration:** 6 months

Gunaratna 2015 (*Continued*)

Outcomes	Anaemia, malaria infection and microcytosis
Notes	**Compliance:** median compliance were 82% in control arm and 84% in iron arm **Conflicts of interest:** trial authors declare no conflict of interest **Funded by:** Harvard School of Public Health

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation sequence using blocks of size 15 created by a scientist
Allocation concealment (selection bias)	Low risk	States concealed
Blinding of participants and personnel (performance bias) All outcomes	Low risk	States double blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not evident
Incomplete outcome data (attrition bias) All outcomes	Low risk	561 completed of 802 enrolled (70%)
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Heath 2001

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus dietary treatment versus placebo. Dietary group not extracted **Date of study:** not stated
Participants	**Setting:** Dunedin area of New Zealand **Malaria endemicity:** not stated **Included:** women aged 18 years to 40 years (mean age 26 years) with mild iron deficiency (ferritin < 20 ng/mL) but haemoglobin > 120 g/L **Excluded:** pregnancy or lactation, irregular menstruation, health problems likely to influence iron status (for instance, gastrointestinal disease), medication likely to affect iron status, anorexia nervosa or bulimia, and veganism **Dropouts:** 8 failed to complete trial (groups reported but unclear). 10 excluded for other reasons **Sample size:** total: 35; intervention: 16, control: 19

Heath 2001 (*Continued*)

Interventions	**Intervention:** amino acid chelate (bis-glycino iron II) providing 50 mg of elemental iron with no change to diet **Control:** maltodextrin with no change in diet **Duration:** 16 weeks
Outcomes	Haemoglobin, ferritin (not extractable)
Notes	**Compliance:** 97% of tablets taken in iron group; not reported for placebo group **Conflicts of interest:** not stated **Funded by:** Health Research Council of New Zealand. Tablets provided by Albion Laboratories, Inc. (Clearfield, Utah) **Other notes:** no data extractable as no SDs given

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo provided
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not reported. Measurement of biochemical outcomes not influenced by knowledge of allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	Of 75 at baseline, 8 patients excluded during study, further 10 patients withdrew from study (24% attrition), balanced between arms
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Hinton 2000

Methods	**Design:** randomised placebo controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** not stated

Hinton 2000 (*Continued*)

Participants	**Setting:** local community in USA. No further details given **Malaria endemicity:** not stated **Included:** physically active, untrained* women aged between 18 years and 33 years (mean age 21 years) with non-anaemic iron deficiency (i.e. haemoglobin > 120 g/L and ferritin < 16 mg/L) **Excluded:** current pregnancy or pregnancy within the previous year, recent infectious illness or fever, haemolytic anaemia, asthma, musculoskeletal problems, recent history of eating disorders, smoking, excess alcohol consumption, recent use of recreational drugs, consumption of prescription medications that may interfere with dietary iron absorption, or participation in competitive athletics **Dropouts:** 16% groups not stated **Sample size:** total: 42; intervention: 22, control: 20
Interventions	**Intervention:** 50 mg ferrous sulphate (8 mg elemental iron) capsules **Control:** placebo **Duration:** 6 weeks
Outcomes	Haemoglobin, iron status, exercise performance, fat mass, height, weight
Notes	**Compliance:** 88.6% of all tablets taken in placebo group versus 91.4% in iron group **Conflicts of interest:** cost of publication defrayed in part of pay charges, thereby marked as advertisement **Funded by:** in part by Mead Johnson Research Fund and National Institute of Child Health and Human Development Training Grant HD-07331 *Women were eligible if they were identified as physically active but untrained; further details were not provided by the author

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of sequence allocation not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Investigators blinded to allocation of participants
Incomplete outcome data (attrition bias) All outcomes	Low risk	16% dropped out
Selective reporting (reporting bias)	Low risk	Not evident

Hinton 2000 (*Continued*)

Other bias	Low risk	No evidence of other bias

Hinton 2007

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** not stated
Participants	**Setting:** recruited from University of Missouri Colombia (USA) and surrounding community via fliers and newspaper advertisements **Malaria endemicity:** not stated **Included:** 17 women and 3 men, aged 18 years to 41 years (mean age 28 years). Participants were iron deficient (serum ferritin < 16 mg/L; serum transferrin receptor > 48.0 mg/L; or transferrin receptor/log ferritin index > 44.5) and non-anaemic (haemoglobin > 120 g/L for women; > 130 g/L for men) **Excluded:** current pregnancy or pregnancy within the previous year, recent infectious illness or fever, chronic inflammatory diseases, haemolytic anaemia, musculoskeletal problems, history of eating disorders, smoking, or consumption of iron supplements or medications that may interfere with dietary iron absorption or that have anticoagulant properties **Dropouts:** no reported dropouts **Sample size:** total: 20; intervention: 10, control: 10
Interventions	**Intervention:** ferrous sulphate equivalent to 30 mg elemental iron **Control:** placebo **Duration:** 6 weeks
Outcomes	Haemoglobin, iron status, exercise performance, fat mass, height, weight
Notes	**Compliance:** on average, participants in the iron group ingested 98 (±8.2)% and the placebo group 99 (±5.4)% of their supplements. There was no significant difference in compliance between the two groups **Conflicts of interest:** trial authors report no conflict of interest **Funded by:** no funding reported

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method for sequence generation not stated
Allocation concealment (selection bias)	Unclear risk	Method for allocation concealment not stated

Hinton 2007 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported. Measurement of exercise performance may be influenced by knowledge of allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	No attrition
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	The study appears free of other sources of bias

Hoppe 2013

Methods	**Design:** randomised controlled study **Randomisation:** individual **Trial:** two doses of oral iron versus folate **Date of study:** 2010 and 2011 (two stages)
Participants	**Setting:** Swedish universities **Malaria endemicity:** not stated **Included:** women of childbearing age who were healthy, non-smoking without anaemia (haemoglobin < 120 g/L). Not pregnant/lactating and not exercising heavily or had donated blood less than 2 months prior. Age range not reported (mean age 24 years) **Excluded:** if any medication being taken or dietary supplements or underlying malabsorption or serious illness **Dropouts:** 3 dropped out (1 in intervention, 2 in control). 3 excluded due to infection **Sample size:** total: 36; intervention: 24, control: 12
Interventions	**Intervention:** two doses of iron: 35 mg of elemental iron and 60 mg of elemental iron (ferrous fumarate) **Control:** folate **Duration:** 12 weeks
Outcomes	Haemoglobin, iron status, BMI and side effects
Notes	**Compliance:** > 99% of tablets taken in all groups **Conflicts of interest:** not stated **Funded by:** Local Research and Development Council of Gothenburg and Southern Bohuslän, Sweden

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Hoppe 2013 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo/folate
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated. Side effects reported and could be influenced.
Incomplete outcome data (attrition bias) All outcomes	Low risk	20% loss to follow-up (combining exclusion and dropout rates)
Selective reporting (reporting bias)	Low risk	No evidence
Other bias	Low risk	Not evident

Jayatissa 1999

Methods	**Design:** cluster randomised controlled trial **Randomisation:** by classroom **Trial:** daily iron with folic acid with vitamin C plus deworming versus weekly iron with folic acid with vitamin C plus deworming versus placebo plus deworming alone (weekly arm not extracted) **Date of study:** not stated
Participants	**Setting:** randomly selected schools in Columbo, Sri Lanka **Malaria endemicity:** not stated **Included:** adolescent girls aged 10 years to 17 years (mean age 13 years), in 3 parallel classes in each school **Excluded:** chronic infectious diseases or cardiopathies, taken supplements or medications containing iron during the previous month, or had a haemoglobin level less than 10 g/dL with a blood picture showing any other kind of anaemia **Dropouts:** 4.5% across all groups **Sample size:** total: 439; intervention: 222, control: 217
Interventions	**Intervention:** 60 mg elemental iron with 250 mcg folic acid, administered Monday to Friday, plus deworming **Control:** placebo plus deworming **Duration:** 8 weeks
Outcomes	Haemoglobin, iron status, anaemia

Jayatissa 1999 (*Continued*)

Notes	**ICC:** not reported **Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** World Health Organization

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not reported. Biochemical indices unlikely to be influenced by assessor's knowledge of allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	690 enrolled, 659 completed
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	High risk	ICC not reported

Jensen 1991

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** not stated
Participants	**Setting:** Purdue University, Indiana, USA **Malaria endemicity:** not stated **Included:** women aged 18 years to 25 years (mean age 21 years) who were sedentary participants who did not regularly participate in an exercise programme. Willing to participate in an intensive 12-week exercise programme **Excluded:** not stated **Dropouts:** not stated **Sample size:** total: 13; intervention: 7, control: 6
Interventions	**Intervention:** 50 mg elemental iron in the form of ferrous sulphate **Control:** placebo **Duration:** 12 weeks

Jensen 1991 (*Continued*)

Outcomes	Haemoglobin, iron status, exercise performance, fat mass, height, weight
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** medication provided by SmithKline Consumer Products, Philadelphia, PA

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported. Knowledge of allocation could influence outcome assessment regarding exercise performance
Incomplete outcome data (attrition bias) All outcomes	Low risk	No attrition reported
Selective reporting (reporting bias)	Low risk	Not reported
Other bias	Low risk	Not evident

Kanani 2000

Methods	**Design:** cluster randomised controlled trial **Randomisation:** by community **Trial:** daily oral iron versus placebo **Date of study:** not stated
Participants	**Setting:** India (Vadodora) **Malaria endemicity:** not stated **Included:** high school students aged 10 years to 18 years (mean age 12.4 years) in 3 low-income communities **Excluded:** not stated **Dropouts:** not reported **Sample size:** total: 203; intervention: 101, control: 102
Interventions	**Intervention:** elemental iron (60 mg) + folic acid (0.5 mg) daily **Control:** placebo **Duration:** 3 months

Kanani 2000 (*Continued*)

Outcomes	Haemoglobin, BMI, weight, hunger score
Notes	**ICC:** not provided **Compliance:** 90% of the girls consumed > 85 of the 90 tablets provided; not divided by iron/placebo **Conflicts of interest:** not stated **Funded by:** Office of Health and Nutrition, USAID, under terms of contract number HRN-C-00-93-00038-00, and the MotherCare Project, John Snow, Incorporated (JSI)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	Appears to be a cluster randomised trial, randomisation by community **Quote:** "For feasibility reasons and to ensure similar sample sizes, the two smaller communities were combined with respect to the intervention. Through random allocation, the larger community became the iron group and the two smaller ones became the control group." Sequence generation not presented in paper
Allocation concealment (selection bias)	Unclear risk	Allocation concealment method not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	High risk	Assessors may have known which group was intervention and which was control
Incomplete outcome data (attrition bias) All outcomes	Low risk	Baseline 210; follow-up 180 (loss to follow-up 14.3%)
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	High risk	ICC not reported

Kang 2004

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** not stated
Participants	**Setting:** Korean national women's soccer team **Malaria endemicity:** not stated **Included:** members aged 20 years to 28 years (mean age 23 years) **Excluded:** not stated **Dropouts:** not stated **Sample size:** total: 25; intervention: 11, control: 14
Interventions	**Intervention:** 40 mg elemental iron in liquid daily **Control:** placebo **Duration:** 1 month
Outcomes	Haemoglobin, iron status, antioxidants (not extracted)
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** not stated

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Sequence generation method not described
Allocation concealment (selection bias)	Unclear risk	Allocation concealment method not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not reported. Biochemical indices unlikely to be influenced by knowledge of allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	No attrition
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	The study appears free of other sources of bias

Kianfar 2000

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus weekly iron (in two forms) versus control. Weekly iron arm not extracted **Date of study:** 1996 to 1997
Participants	**Setting:** Iran **Malaria endemicity:** not stated **Included:** high school female students. Age range not reported (mean age 16 years) **Excluded:** cases with suspected thalassaemia (based on red cell indices) **Dropouts:** no apparent dropouts **Sample size:** total: 240; intervention: 92, control: 148
Interventions	**Intervention:** ferrous sulphate: 150 mg (50 mg elemental iron) daily **Control:** placebo **Duration:** 3 months
Outcomes	Haemoglobin, ferritin, anaemia
Notes	**Compliance:** "among anaemic and non-anaemic subjects was 70 to 90% on average" **Conflicts of interest:** not stated **Funded by:** not stated

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method for sequence generation not stated
Allocation concealment (selection bias)	Unclear risk	Method for allocation concealment not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not reported. Biochemical indices unlikely to be influenced by knowledge of allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	Not reported. Apparently no loss to follow-up
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	The study appears free of other sources of bias

Kiss 2015

Methods	**Design:** randomised control trial **Randomisation:** individual **Trial:** daily oral iron versus no intervention **Date of study:** April to December 2012
Participants	**Setting:** 4 USA blood centres participating in the National Heart, Lung and Blood Institute (NHLBI) Recipient Epidemiology and Donor Evaluation Study-III (REDS-III) programme: American Red Cross Blood Services, Farmington, Connecticut; Blood Center of Wisconsin, Milwaukee; Blood Centers of the Pacific, San Francisco, California; and Institute for Transfusion Medicine, Pittsburgh, Pennsylvania **Malaria endemicity:** not reported **Included:** successful donation of a full (500 mL) whole blood unit on the day of enrolment and a history of 1 or more previous whole blood donations but no donations in the previous 4 months. Age range not reported (mean age 46 years) **Excluded:** baseline ferritin level exceeding 300 ng/mL **Dropouts:** 215 enrolled, 193 included in final analysis. 22 dropouts (10%) **Sample size:** total: 136, iron: 71, control: 65
Interventions	**Intervention:** 325 mg of ferrous gluconate (37.5 mg of elemental iron) daily **Control:** no intervention **Duration:** 24 weeks
Outcomes	Time to normalisation of haemoglobin (no extractable data)
Notes	**Compliance:** not reported **Conflicts of interest:** Dr Mask received a grant from Novo Nordisk and honoraria from Siemens. Reports no other conflicts of interests **Funded by:** National Heart, Lung and Blood Institute (of USA) **Other notes:** men also included. Female data presented separately

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Stratified randomisation to increase those with high risk of iron deficiency in iron group
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not evident

Kiss 2015 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	215 enrolled, 193 included in final analysis
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Klingshirn 1992

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** not stated
Participants	**Setting:** Columbia, South Carolina (USA) **Malaria endemicity:** not stated **Included:** female endurance runners training at least 3 x per week, attending road races. Age range 22 years to 39 years (mean age 29 years) **Excluded:** not stated **Dropouts:** no apparent dropouts **Sample size:** total: 18; intervention: 9, control: 9
Interventions	**Intervention:** elemental iron (50 mg) as ferrous sulphate (160 mg) daily **Control:** placebo **Duration:** 8 weeks
Outcomes	Haemoglobin, iron status, exercise performance
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** Society of Sigma Xi and CIBA Pharmaceuticals

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported. Assessment of exercise outcomes may be influenced by knowledge of allocation

Klingshirn 1992 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	One participant dropped out of study
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

LaManca 1993

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** not stated
Participants	**Setting:** athletics clubs in Florida, USA **Malaria endemicity:** not stated **Included:** healthy women aged 18 years to 35 years (mean age 28 years) with ferritin < 20 ng/mL **Excluded:** not stated **Dropouts:** none reported **Sample size:** total: 20; intervention: 10, control: 10
Interventions	**Intervention:** 100 mg elemental iron daily **Control:** placebo **Duration:** 8 weeks
Outcomes	Iron indices, haemoglobin, hematocrit, exercise performance
Notes	**Compliance:** iron 82% of tablets taken, placebo 85% of tablets taken **Conflicts of interest:** not stated **Funded by:** FSU President's Club fund and Sigma Xi. Tablets provided by SmithKline Laboratories

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered

LaManca 1993 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported. Assessment of exercise outcomes may be influenced by knowledge of allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Unclear risk	Not evident
Other bias	Low risk	Not evident

Lanerolle 2000

Methods	**Design:** cluster randomised controlled trial **Randomisation:** by school **Trial:** daily oral iron plus education versus education alone **Date of study:** not stated
Participants	**Setting:** rural and urban schools in Sri Lanka with low socioeconomic status **Malaria endemicity:** not stated **Included:** adolescent girls. Age range not reported (mean age 16 years) **Excluded:** not stated **Dropouts:** 15.3%, matched between arms **Sample size:** total: 565; intervention: 281, control: 284
Interventions	**Intervention:** elemental iron 60 mg (as ferrous sulphate) plus education **Control:** education alone **Duration:** 10 weeks
Outcomes	Haemoglobin, iron status, iron deficiency
Notes	**ICC:** not provided **Compliance:** in the urban area, 71% of participants in the iron-supplemented group and 77% of girls in the placebo group took more than 50% of the tablets provided; in the rural area, the percentages were 90% and 93%, respectively **Conflicts of interest:** not stated **Funded by:** financial support from UNICEF for the study in the urban area and from the OMNI (Opportunities for Micronutrient Interventions) project of the US Agency for International Development for the study in the rural area

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported

Lanerolle 2000 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo given (education alone)
Blinding of outcome assessment (detection bias) All outcomes	High risk	No placebo given. It would be possible for assessors to know which intervention arm participants belong to (although measurement of biochemical indices unlikely to be influenced)
Incomplete outcome data (attrition bias) All outcomes	Low risk	15.3% loss to follow-up, matched between arms
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	High risk	No ICC's reported

Larocque 2006

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** not stated
Participants	**Setting:** Thunder Bay area, Canada **Malaria endemicity:** not stated **Included:** grade 10 schoolgirls aged 14 years to 16 years (mean age not reported). Iron depleted (i.e. ferritin < 20 ng/mL), non-anaemic (i.e. haemoglobin > 120g/L) **Excluded:** not stated **Dropouts:** 10 out of 31 (32.2%) **Sample size:** total: 21; intervention: 12, control: 9
Interventions	**Intervention:** ferrous gluconate 100 mg daily (approximately 12 mg elemental iron) **Control:** placebo **Duration:** 8 weeks
Outcomes	Haemoglobin, ferritin, cognitive scales (Motor Free Visual Perception Test, Digit span, Covert Orienting of Visual Attention Task: Facilitation and Inhibition, Trail Making Test Parts A and B)
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** intervention provided by Jamieson Pharmaceuticals

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Larocque 2006 (*Continued*)

Random sequence generation (selection bias)	High risk	Participants lined up in random order and were allocated to therapy/placebo according to order in queue
Allocation concealment (selection bias)	Low risk	Code to numbered bottles kept in sealed envelopes, unknown until conclusion of study
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Low risk	No knowledge of allocation due to allocation being kept in sealed envelope until conclusion of study
Incomplete outcome data (attrition bias) All outcomes	High risk	31 enrolled, 21 at final analysis. 32.2 % attrition
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	The study appears free of other sources of bias

Leonard 2014

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron (two doses) versus placebo **Date of study:** 2010 to 2013
Participants	**Setting:** women recruited via flyer through the Hunter Medical Research Institute (Australia) **Malaria endemicity:** not stated **Included:** women aged 18 years to 35 years (mean age 26 years) with BMI between 18 kg/m² and 30 kg/m² and English speaking **Excluded:** iron deficient in last 12 months, taking iron, chronic medical condition or pregnant **Dropouts:** 12 out of 36 lost to follow-up **Sample size:** total: 24; intervention: 16, control: 8
Interventions	**Intervention:** 60 mg or 80 mg elemental iron as ferrous sulphate **Control:** placebo **Duration:** 16 weeks
Outcomes	Haemoglobin, iron status, side effects and cognitive outcomes

Leonard 2014 (*Continued*)

Notes	**Compliance:** on average 90.4% of capsules taken **Conflicts of interest:** authors declare no conflict of interest **Funded by:** Australian Post-Graduate Award, Meat and Livestock Australia and the School of Health Sciences at the University of Newcastle

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number generator
Allocation concealment (selection bias)	Low risk	Reports concealment
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	No evidence
Incomplete outcome data (attrition bias) All outcomes	High risk	> 30% loss in many groups
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Li 1994

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** 1989 to 1991
Participants	**Setting:** cotton workers in Beijing, China **Malaria endemicity:** not stated **Included:** women aged 19 years to 44 years (mean age 30 years) with iron deficiency (haemoglobin > 120 g/L, ferritin < 12 ng/mL, FEP > 0.62), or iron-deficiency anaemia (haemoglobin 120 g/L + iron deficiency) **Excluded:** not stated **Dropouts:** 3 of 83 participants failed to complete study **Sample size:** total: 80; intervention: 40, control: 40
Interventions	**Intervention:** variable dosage of iron depending on anaemia status. Used pills containing 60 mg ferrous sulphate. Mild Iron-deficiency anaemia or iron deficiency without anaemia given one pill per day; moderate iron-deficiency anaemia given 2 pills per day (i.e. 60

Li 1994 (*Continued*)

	mg and 120 mg doses, i.e. elemental iron 20 mg and 40 mg respectively) **Control:** placebo **Duration:** 12 weeks
Outcomes	Haematology, iron indices, productivity/production efficiency, exercise performance
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** Nestlé foundation, Laussanne, Switzerland

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo given
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported. Blinding of outcome assessment could influence evaluation of work productivity
Incomplete outcome data (attrition bias) All outcomes	Low risk	3 lost to follow-up
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Lyle 1992

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron (two groups) plus exercise programme versus placebo plus exercise programme versus no intervention versus low fat muscle plus exercise programme. Only iron and placebo groups extracted **Date of study:** not stated
Participants	**Setting:** Purdue University College students (USA) **Malaria endemicity:** not stated **Included:** Caucasian females who had not participated in exercise programme. Age range not reported (mean age 19 years) **Excluded:** smokers, on oral contraceptive pill, taking iron supplements or who had

Lyle 1992 (*Continued*)

	irregular menstrual periods **Dropouts:** 28% dropout rate (groups unstated) **Sample size:** total: 34; intervention: 20, control: 14
Interventions	**Intervention:** two doses: 50 mg elemental iron as ferrous sulphate or 10 mg elemental iron as ferrous sulphate. Also received low iron diet and exercise programme **Control:** exercise alone **Duration:** 4 weeks
Outcomes	Exercise performance
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** iron supplements donated by SmithKline Beecham, Parsippany, NJ

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	Diets not blinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	Diets not blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	72% completed protocol but not stated from which group dropouts occurred
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Machado 2011

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** 2005 to 2006
Participants	**Setting:** clinic in Brazil **Malaria endemicity:** not stated

Machado 2011 (*Continued*)

	Included: non-pregnant women, aged between 20 years and 49 years (mean age not reported), attending a clinic (Centro Integrado de Saúde Amaury de Medeiros; CISAM) . Must have had a telephone for follow-up contact **Excluded:** excluded if had gastrointestinal disorders or haemoglobin > 15 g/dL or < 11 g/dL **Dropouts:** 26% dropout rate **Sample size:** total: 539; intervention: unclear, control: unclear
Interventions	**Intervention:** 60 mg of elemental iron as ferrous sulphate **Control:** placebo **Duration:** 8 weeks
Outcomes	Side effects
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** not stated **Other notes:** unable to extract data as also had iron tablets twice a week group and results were combined

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random numbers handed out
Allocation concealment (selection bias)	Low risk	Reports concealment
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not evident
Incomplete outcome data (attrition bias) All outcomes	Low risk	26% loss to follow-up
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Magazanik 1991

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** not stated
Participants	**Setting:** Israel physical training programme **Malaria endemicity:** not stated **Included:** women aged 19 years who were non-smokers, menstruating regularly. Age range not reported (mean age 19 years) **Excluded:** not stated **Dropouts:** no loss to follow-up reported **Sample size:** total: 28; intervention: 13, control: 15
Interventions	**Intervention:** ferrous sulphate 160 mg (elemental iron about 50 mg) daily **Control:** placebo **Duration:** 7 weeks
Outcomes	Haematology, iron indices, VO_2 max
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** Israeli Sports Authority

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo given
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported. Evaluation of exercise performance could be influenced by knowledge of allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Maghsudlu 2008

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** oral iron three times a day versus placebo **Date of study:** not stated
Participants	**Setting:** Kermanshah and Golestan blood transfusion services, Iran **Malaria endemicity:** not stated **Included:** women attending blood donation. Age range not reported (mean age 28.7 years) **Excluded:** pregnancy, medical condition such as hereditary haemochromatosis chronic gastrointestinal disorder or intestinal cancer or polyps **Dropouts:** 207 out of 417 (50%) failed to return for follow-up visit **Sample size:** total: 367, iron: 185, control: 182
Interventions	**Intervention:** 150 mg of ferrous sulphate three times a day **Control:** placebo **Duration:** 1 week
Outcomes	Haemoglobin, iron status, side effects
Notes	**Compliance:** 75.2% of tablets taken across all groups **Conflicts of interest:** not stated **Funded by:** Iranian blood transfusion organisation

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Unclear if double blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear if double blinded. Side effects reported and may be influenced
Incomplete outcome data (attrition bias) All outcomes	High risk	50% dropout rate
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	No other source of bias identified

Marks 2014

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** study performed between March 2009 and October 2010
Participants	**Setting:** Australian Red Cross Blood Service **Malaria endemicity:** not stated **Included:** premenopausal female blood donors with one successful whole blood donation in the past 2 years, eligibility to donate in accordance with Australian Red Cross Blood Service guidelines (including haemoglobin ≥ 120 g/L), willingness to use an agreed method of contraception for the duration of the study, ability to attend a second visit at 12 weeks, ability to provide written informed consent and a successful whole blood donation on the day of enrolment. Age range not reported (mean age 30 years) **Excluded:** participants with red blood cell abnormalities or potential allergies to constituents of the placebo or carbonyl iron. Participants with medications that potentially interact with iron or mask or exacerbate gastrointestinal abnormalities by iron supplementation **Dropouts:** 12/141 in intervention group, 13/141 in control group (8.8% total) **Sample size:** total: 257; intervention: 129, control: 128
Interventions	**Intervention:** carbonyl iron containing 45 mg elemental iron **Control:** placebo **Duration:** 12 weeks
Outcomes	Haemoglobin, ferritin, side effects and eligibility to donate blood
Notes	**Compliance:** in the carbonyl iron group, 84.4% of the participants were treatment compliant compared to 88.7% of the participants in the placebo group (compliance as per authors) **Conflicts of interest:** authors report no conflict of interest **Funded by:** authors report no funding sources **Other notes:** trial authors contacted regarding breakdown of side effects and responded

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number generator, block randomisation with fixed block lengths
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo given
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Placebo given

Marks 2014 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	8% loss to follow-up, balanced between arms
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

McClung 2009

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** 2007
Participants	**Setting:** military recruits in the USA, undergoing 8 to 9 weeks of basic combat training **Malaria endemicity:** not stated **Included:** female, age range not reported (mean age 20 years) **Excluded:** iron-deficiency anaemia **Dropouts:** 22% loss of follow-up (groups unstated) **Sample size:** total: 171; intervention: 86, control: 85
Interventions	**Intervention:** 100 mg ferrous sulphate, found to have a mean elemental iron content of 15 mg **Control:** placebo **Duration:** 8 weeks
Outcomes	Haemoglobin, iron status, fatigue, exercise performance, mood
Notes	**Compliance:** overall compliance in the placebo group was 94% (4378 of 4675 total capsules); compliance in the iron-treated group was 93% (4391 of 4730 total capsules) **Conflicts of interest:** authors declare no conflict of interest **Funded by:** United States Army Medical Research and Materiel Command

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method for sequence generation not stated
Allocation concealment (selection bias)	Unclear risk	Method for allocation concealment not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo given

McClung 2009 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported. Assessments of mood and exercise performance could be influenced by knowledge of allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	22% loss of follow-up; from 219 participants at baseline to 171 participants at follow-up
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	The study appears free of other sources of bias

Mujica-Coopman 2015

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo versus daily oral iron with zinc. (Zinc arm not extracted) **Date of study:** not stated
Participants	**Setting:** Chile, no further details **Malaria endemicity:** not stated **Included:** healthy women aged 18 years to 45 years (mean age 32 years) **Excluded:** consumed vitamin or mineral supplements for 6 months, or were pregnant or breast feeding at time **Dropouts:** 7 women dropped out from a total of 87 across all groups. 1 control, 0 iron, 6 iron and zinc arm **Sample size:** total: 55; iron: 28, control: 27
Interventions	**Intervention:** 30 mg of elemental iron daily as ferrous sulphate **Control:** placebo **Duration:** 88 days
Outcomes	Haemoglogin, iron status and zinc status, anaemia, zinc deficiency
Notes	**Compliance:** reports no difference in compliance across groups (no further details) **Conflicts of interest:** not stated **Funded by:** Fondo Nacional de Desarrollo Cientifico y Tecnologico Chile Grant number 1130075

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not stated

Mujica-Coopman 2015 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Reports being double blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not evident
Incomplete outcome data (attrition bias) All outcomes	Low risk	7 out of 87 dropped out
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	No other source of bias identified

Murray-Kolb 2007

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** 1999 to 2002
Participants	**Setting:** communities around University Park campus of The Pennsylvania State University in State College in the USA **Malaria endemicity:** not stated **Included:** women aged 18 years to 35 years (mean age 21 years) **Excluded:** chronic illnesses or serious health problems, not speaking English as the primary language at home **Dropouts:** 39 out of 152 (26% total loss to follow-up) **Sample size:** total: 113; intervention: 56, control: 57
Interventions	**Intervention:** 160 mg ferrous sulphate containing 60 mg elemental iron **Control:** placebo **Duration:** 16 weeks
Outcomes	Haemoglobin, iron status, anxiety and psychological scores
Notes	**Compliance:** 95% (determine by pill count) not divided by iron/placebo group **Conflicts of interest:** authors declare no conflict of interest **Funded by:** USDA NRICGP 99-35200-7610 and GCRC MO1RR10732 **Other notes:** cognitive endpoint data reported in figures and without errors, not extractable

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Murray-Kolb 2007 (*Continued*)

Random sequence generation (selection bias)	Low risk	Stratified randomisation performed by using random permuted blocks
Allocation concealment (selection bias)	Low risk	Bottles coded preventing disclosure of allocated arm
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded as intervention and control could not be discerned; bottles coded
Incomplete outcome data (attrition bias) All outcomes	Low risk	26% loss to follow-up; 152 enrolled, 113 completed study
Selective reporting (reporting bias)	High risk	Endpoint data for several key cognitive outcomes not reported in study. Only shown on figures without SE/SD/CIs to enable extraction
Other bias	Low risk	The study appears free of other sources of bias

Newhouse 1989

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** not stated
Participants	**Setting:** Canada **Malaria endemicity:** not stated **Included:** recreational runners undertaking at least 120 minutes (and at least three times per week) of exercise. Participants had latent iron deficiency: ferritin < 20 ng/mL, haemoglobin > 120 g/L. Age range 15 years to 40 years (mean age not reported) **Excluded:** Aspirin, PR blood loss, blood donation, urinary blood loss, recent fever, use of oral contraceptive pill **Dropouts:** 10 out of 47 failed to complete study (groups unstated) **Sample size:** total: 37; intervention: 19, control: 18
Interventions	**Intervention:** 200 mg elemental iron daily as ferrous sulphate **Control:** placebo **Duration:** 8 weeks
Outcomes	Haemoglobin, iron status, exercise performance

Newhouse 1989 (*Continued*)

Notes	**Compliance:** authors state "same in both groups and over 75% as obtained by pill counts" **Conflicts of interest:** not stated **Funded by:** Ciga-Geigy Pharmaceuticals of Canada **Other notes:** reports 40 completed study but only data for 37 available

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo given
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported. Knowledge of allocation could influence assessment of exercise performance
Incomplete outcome data (attrition bias) All outcomes	Low risk	47 enrolled. 37 completed study
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Pereira 2014

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** not stated
Participants	**Setting:** King's College, London, United Kingdom. **Malaria endemicity:** not stated **Included:** 20 healthy participants, 7 men and 13 women aged 18 to 65 years (mean age 32 years) **Excluded:** chronic disease, pregnancy or lactation **Dropouts:** reports no loss to follow-up **Sample size:** total: 13; intervention: 7, control: 6
Interventions	**Intervention:** ferrous sulphate 200 mg (65 mg of elemental iron), twice a day **Control:** placebo **Duration:** 7 days

Pereira 2014 (*Continued*)

Outcomes	Side effects
Notes	**Compliance:** not stated **Conflicts of interest:** authors declare no conflict of interest **Funded by:** United Kingdom Medical Research Council **Other notes:** data for women only, provided by authors via email

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random sequence generation
Allocation concealment (selection bias)	Low risk	Reported allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo
Blinding of outcome assessment (detection bias) All outcomes	Low risk	SEs unlikely to be affected
Incomplete outcome data (attrition bias) All outcomes	Low risk	No losses to follow-up
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Prosser 2010

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo versus dietary advice. Dietary advice group not extracted **Date of study:** 1997 to 1998
Participants	**Setting:** Greater Dunedin area, New Zealand **Malaria endemicity:** not stated **Included:** women aged 18 years to 40 years (mean age not reported) with mild iron deficiency (serum ferritin < 20 mg/L; haemoglobin > 120 g/L in the absence of infection) and consumption of a non-vegan Western-style diet **Excluded:** anaemia, pregnancy or lactation, and health problems (for example, eating disorders) or medication **Dropouts:** 30.6% attrition reported (6/23 iron group, 9/26 control) **Sample size:** total: 34; intervention: 17, control: 17

Prosser 2010 (*Continued*)

Interventions	**Intervention:** 50 mg elemental iron in the form of an amino acid chelate ('FerroChel') **Control:** placebo **Duration:** 16 weeks
Outcomes	Zinc levels
Notes	**Compliance:** 97% in iron group, 94% in placebo group **Conflicts of interest:** authors report no conflict of interest **Funded by:** not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Throwing dice
Allocation concealment (selection bias)	Low risk	Sequentially numbered, sealed envelopes containing allocation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Low risk	**Quote:** "Blinding of all the other research staff was maintained until completion of the study"
Incomplete outcome data (attrition bias) All outcomes	Low risk	20.4% attrition reported
Selective reporting (reporting bias)	High risk	Data only provided in tables
Other bias	Low risk	The study appears to be free of other sources of bias

Radjen 2011

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** not stated
Participants	**Setting:** Belgrade (Serbia) **Malaria endemicity:** not stated **Included:** female elite volleyball players aged 16 years to 25 years (mean age not reported) , otherwise healthy, normal menstrual periods **Excluded:** not stated

Radjen 2011 (*Continued*)

	Dropouts: dropout rates not reported **Sample size:** total: 37; intervention: 19, control: 18
Interventions	**Intervention:** ferrous sulphate 200 mg daily (approximately 50 mg elemental iron) **Control:** placebo **Duration:** 8 weeks
Outcomes	Haemoglobin, iron status, exercise performance, height, body fat, weight
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported. Knowledge of allocation could influence assessment of exercise performance
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Unclear risk	Not reported
Other bias	Low risk	Not evident

Rajaram 1995

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo versus meat and exercise versus control. Only iron and placebo extracted **Date of study:** not stated
Participants	**Setting:** Purdue University, Indiana (USA) **Malaria endemicity:** not stated **Included:** female college students with sedentary life style, not smoking, not on contra-

Rajaram 1995 (*Continued*)

	ceptive pill or iron tablets. Age range not reported (mean age 19 years) **Excluded:** not stated **Dropouts:** 62 of 78 completed trial (20% total loss to follow-up - groups not stated) **Sample size:** total: 29; intervention: 16, control: 13
Interventions	**Intervention:** ferrous sulphate 50 mg plus low iron diet plus exercise **Control:** placebo plus exercise and normal diet **Duration:** 24 weeks
Outcomes	Exercise performance
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** National Livestock and Meat Board

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not reported. Based on haemoglobin
Allocation concealment (selection bias)	High risk	Inadequate
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo
Blinding of outcome assessment (detection bias) All outcomes	High risk	No placebo
Incomplete outcome data (attrition bias) All outcomes	Low risk	20% loss to follow-up; 78 enrolled, 62 at follow-up
Selective reporting (reporting bias)	High risk	Haemoglobin and transferrin saturation reported in text but not table. No data provided for these outcomes
Other bias	Low risk	Not evident

Rowland 1988

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** not stated
Participants	**Setting:** high school cross country teams (USA) **Malaria endemicity:** not stated **Included:** female, adolescent, iron deficient (ferritin < 20 ng/mL), non-anaemic (haemoglobin > 120 g/L). Age range not reported (mean age not reported) **Excluded:** not stated **Dropouts:** reports no dropouts **Sample size:** total: 14; intervention: 7, control: 7
Interventions	**Intervention:** 325 mg elemental iron plus 4 weeks' exercise training **Control:** placebo plus exercise training **Duration:** 4 weeks
Outcomes	Haematology, iron indices, exercise performance
Notes	**Compliance:** 75% of iron and 83% of control pills taken **Conflicts of interest:** not stated **Funded by:** grant from Sports Therapy for Athletic Rehabilitation and Treatment, Springfield, Mass

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported. Knowledge of allocation could influence assessment of exercise performance
Incomplete outcome data (attrition bias) All outcomes	Low risk	No attrition
Selective reporting (reporting bias)	Low risk	Not reported
Other bias	Low risk	Not evident

Rybo 1985

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** 1968 to 1969
Participants	**Setting:** Gothenberg, Sweden **Malaria endemicity:** not stated **Included:** 38-year-old women identified on a previous cross-sectional study. Must have had iron deficiency based on absence of stainable iron on sternal bone marrow aspirate. All participants aged 38 years **Excluded:** not stated **Dropouts:** 24 of 113 failed to complete trial (21% total loss to follow-up - groups unstated) **Sample size:** total: 89; intervention: 45, control: 44
Interventions	**Intervention:** ferrous succinate, 37 mg three times daily for a median of 68 days **Control:** placebo three times daily **Duration:** variable
Outcomes	Haemoglobin, iron status, side effects
Notes	**Compliance:** median intake was 155 tablets in 68 days **Conflicts of interest:** not stated **Funded by:** not stated **Other notes:** variable follow-up and duration of treatment

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not reported. Measurement of biochemical indices unlikely to be influenced by knowledge of allocation by assessor
Incomplete outcome data (attrition bias) All outcomes	Low risk	89 of 113 women completed study; 21.4% attrition
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Røsvik 2010

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus no intervention **Date of study:** not stated
Participants	**Setting:** blood donors in Norway **Malaria endemicity:** not stated **Included:** at least one previous blood donation, haemoglobin > 12.5 g/dl (women), serum ferritin > 20mg L. Age range 18 years to 69 years (mean age 43 years) **Excluded:** not stated **Dropouts:** 20% in intervention group, 18% in control group **Sample size:** total: 161; intervention: 82, control: 79
Interventions	**Intervention:** 100 mg standard Niferex ferroglycin sulphate complex tablet daily, following donation **Control:** no intervention **Duration:** 8 days
Outcomes	Haemoglobin, iron status
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** grant from Western Norway Regional Health Authority **Other notes:** both males and females recruited, analysis presented separately for each sex. Male data not extracted

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Sequence generation not described in study
Allocation concealment (selection bias)	Unclear risk	Allocation concealment not described in study
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo given to control participants
Blinding of outcome assessment (detection bias) All outcomes	High risk	No placebo given to control participants
Incomplete outcome data (attrition bias) All outcomes	Low risk	20% loss to follow-up among female participants
Selective reporting (reporting bias)	Low risk	Not evident

Other bias	Low risk	The study appears to be free of other source of bias

Shah 2002

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus weekly iron versus control. Weekly iron group not extracted **Date of study:** 1998 to 1999
Participants	**Setting:** government girls' school in Dharan, Nepal, an urban foothill town 305 m above sea level **Malaria endemicity:** not stated **Included:** healthy adolescent girls attending a girls' school, matched for age, anthropometry and demography. Age range 11 years to 18 years (mean age 15 years) **Excluded:** any chronic illnesses (e.g. asthma, rheumatic heart disease), receiving any long-term allopathic or indigenous drug treatments, those with recent hospitalisation **Dropouts:** 6 of 148; 4 iron, 2 control **Sample size:** total: 142; intervention: 70, control: 72
Interventions	**Intervention:** 350 mg of ferrous sulphate and 1.5 mg of folic acid once a day for 90 to 100 days **Control:** no intervention **Duration:** 14 weeks
Outcomes	Haematocrit, anaemia
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** the Research Committee of B.P. Koirala Institute of Health Sciences, Dharan

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Sequence generation not described in study
Allocation concealment (selection bias)	Unclear risk	Allocation concealment method not described in study
Blinding of participants and personnel (performance bias) All outcomes	High risk	No placebo in control arm
Blinding of outcome assessment (detection bias) All outcomes	High risk	No placebo in control arm

Shah 2002 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition: 4 iron, 2 control
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	The study appears to be free of other source of bias

Swain 2007

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus electrolytic iron versus reduced iron versus bakery-grade ferrous sulphate versus placebo. Only daily oral iron and placebo groups extracted **Date of study:** not stated
Participants	**Setting:** USA community. No further details given **Malaria endemicity:** not stated **Included:** healthy women of child-bearing age. All women were healthy, menstruating, neither pregnant nor breast-feeding, and were not using medication (except possibly hormonal contraceptives used for > 6 months). Age range 21 years to 51 years (mean 40 years) **Excluded:** any other medication **Dropouts:** 3 of 24; 3 intervention, 0 control **Sample size:** total: 21; intervention: 9, control: 12
Interventions	**Intervention:** 5 mg iron as heme iron supplement **Control:** placebo **Duration:** 12 weeks
Outcomes	Iron status
Notes	**Compliance:** 97% of capsules consumed **Conflicts of interest:** not stated **Funded by:** Sharing Science and Technology to aid in the improvement of Nutrition, Washington DC

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Sequence generation not described in study
Allocation concealment (selection bias)	Unclear risk	Allocation concealment not described in study

Swain 2007 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not reported. Outcomes unlikely to be influenced
Incomplete outcome data (attrition bias) All outcomes	Low risk	4 participants dropped out from study, not clear from which arm
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	The study appears to be free of other sources of bias

Taniguchi 1991

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron with vitamin C plus exercise versus placebo with vitamin C and exercise versus daily oral iron with vitamin C (no exercise) versus vitamin C (no exercise) **Date of study:** not stated	
Participants	**Setting:** colleges in Japan **Malaria endemicity:** not stated **Included:** female college students aged 18 years to 22 years (mean age not reported). Iron deficiency (ferritin < 6 ng/mL) not anaemic (haemoglobin > 120 g/L) **Excluded:** not stated **Dropouts:** not stated **Sample size:** total: 54; intervention: 27, control: 27	
Interventions	**Intervention:** ferric ammonium citrate: 6 mg (approximately 1 mg of elemental iron) + vitamin C ± exercise **Control:** vitamin C ± exercise **Duration:** 9 weeks	
Outcomes	Haemoglobin, iron status, exercise performance	
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** not stated	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Taniguchi 1991 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo (iron-free vitamin C) administered to control participants
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported. May have influenced measurement of exercise outcomes
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not indicated in report
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Verdon 2003

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** 1997 to 2000
Participants	**Setting:** primary care practices in Switzerland **Malaria endemicity:** not stated **Included:** women aged 18 years to 55 years (mean age 35 years) presenting with fatigue without anaemia (haemoglobin > 117) or other obvious physical or psychiatric cause for fatigue or chronic fatigue syndrome **Excluded:** not stated **Dropouts:** 4 in each arm **Sample size:** total: 144; intervention: 75, control: 69
Interventions	**Intervention:** ferrous sulphate (80 mg/day of elemental iron) **Control:** placebo **Duration:** one month
Outcomes	Iron status, fatigue, anxiety, depression
Notes	**Compliance:** 95% iron arm versus 98% placebo arm, P value = 0.25 **Conflicts of interest:** FV and BF received financial support from Robapharm for producing a preliminary report of the study **Funded by:** Robapharm. The sponsor was not involved in the analysis of the results or in writing or correcting the manuscript

Verdon 2003 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomisation took place at an independent pharmacy, according to a pre-established list
Allocation concealment (selection bias)	Low risk	Drug package was coded with a unique number according to the randomisation schedule
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Codes were held by the pharmacist and remained unbroken until the analyses were completed
Incomplete outcome data (attrition bias) All outcomes	Low risk	Loss to follow-up: 4 in each arm
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	The study appears to be free of other source of bias

Viteri 1999

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus weekly iron versus placebo. Weekly arm not extracted **Date of study:** not stated
Participants	**Setting:** University of California, Berkeley USA **Malaria endemicity:** not stated **Included:** healthy, menstruating women > 18 years of age who responded to public notices. Age range 18 years to 44 years (mean age 22 years) **Excluded:** blood donation during the previous 6 months, pregnancy, pregnancy terminated during the previous year, lactation, menorrhagia, having a chronic condition interfering with normal iron metabolism, currently taking or having taken therapeutic iron in the previous 6 months, and predicted impossibility to comply with the iron protocol **Dropouts:** 39% dropout across all groups with losses equal across all groups **Sample size:** Total: 81; intervention: 37, control: 44

Viteri 1999 (*Continued*)

Interventions	**Intervention:** iron (60 mg as ferrous sulphate; 20 mg elemental iron) + folate (250 mcg) **Control:** folate alone **Duration:** 3 months
Outcomes	Iron status, haemoglobin, anaemia
Notes	**Compliance:** 88% or more ingested over 90% of all tablets; not reported by intervention group **Conflicts of interest:** not stated **Funded by:** partially supported by a grant from the International Nutrition Foundation for Developing Countries (INFDC) and by a Research Grant from the Agricultural Research Station, University of California

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Sequence generation not described in the study
Allocation concealment (selection bias)	Unclear risk	Allocation concealment not described in the study
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebos administered
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not reported. Biochemical indices unlikely to be influenced by assessor knowledge of allocation
Incomplete outcome data (attrition bias) All outcomes	High risk	39% attrition
Selective reporting (reporting bias)	Unclear risk	No evidence of selective reporting bias
Other bias	Low risk	The study appears free of other bias

Waldvogel 2012

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** November 2008 to September 2011
Participants	**Setting:** Switzerland Red Cross Blood Service **Malaria endemicity:** not stated **Included:** female blood donors aged 18 years to 50 years (mean age 31 years), 1 week

	post-donation, with haemoglobin > 120 g/L, ferritin < 30ng/mL **Excluded:** psychiatric conditions or diseases that rendered the participant unable to give consent; thyroid, hepatic, rheumatic, kidney, cardiopulmonary, or intestinal disease; acute or chronic inflammation; diabetes; haemochromatosis; pregnancy; medical treatment that could alter iron absorption and any iron supplementation **Dropouts:** 4 in each group **Sample size:** total: 145; intervention: 74, control: 71
Interventions	**Intervention:** iron 80 mg/day as ferrous sulphate (FeSO4; Tardyferon, Robapharm, Boulogne, France) **Control:** placebo **Duration:** 4 weeks
Outcomes	Haemoglobin, iron status, quality of life, exercise performance, side effects
Notes	**Compliance:** intervention arm took tablets for a mean 26.3 (of 28) days; control arm took tablets for a mean 26.5 (of 28) days **Conflicts of interest:** one author (BF) gave lectures to both Pierre Fabre Medicament and Vifor Pharma companies that may have interest in work. All other authors had no conflict of interest **Funded by:** not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Simple random allocation sequence without restriction was generated by an independent pharmacy according to a pre-established computer-generated list
Allocation concealment (selection bias)	Low risk	Each drug package was identified with a unique number according to the randomisation schedule and given to the nurse in charge of the participant
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The code was held by the pharmacist and remained unbroken until the end of the trial
Incomplete outcome data (attrition bias) All outcomes	Low risk	< 20% attrition, similar in both arms
Selective reporting (reporting bias)	Low risk	Not evident

Waldvogel 2012 (*Continued*)

Other bias	Low risk	Not evident

Walsh 1989

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** not stated
Participants	**Setting:** unclear although researchers from Launceston, Tasmania **Malaria endemicity:** not stated **Included:** female competitive swimmers. Age range not reported (mean age 15 years) **Excluded:** not stated **Dropouts:** no apparent loss to follow-up **Sample size:** total: 20; intervention: 10, control: 10
Interventions	**Intervention:** iron supplementation (150 mg) daily **Control:** placebo (gelatin) **Duration:** 12 weeks
Outcomes	Haemoglobin, iron status, exercise performance
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** not stated **Other notes:** VO_2 max recorded but not reported in the paper for the iron arm (i.e. placebo arm reported, iron arm not reported). Thus, VO_2 max data not extractable. Author not contactable

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported. Exercise performance may have been influenced
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported

Walsh 1989 (*Continued*)

Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	Not evident

Wang 2012

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** not stated
Participants	**Setting:** Shanghai **Malaria endemicity:** not stated **Included:** women of childbearing age, aged 21 years to 45 years (mean age not reported) with anaemia **Excluded:** pregnancy **Dropouts:** dropout rates not stated **Sample size:** total: 69; intervention: 34, control: 35
Interventions	**Intervention:** ferric pyrophosphate and ferrous fumarate (8 mg elemental iron) daily **Control:** placebo **Duration:** 6 months
Outcomes	Haemoglobin, iron status, anaemia
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** not stated **Other notes:** written In Mandarin

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo used
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not stated. Unlikely that biochemical outcomes affected

Wang 2012 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not stated
Selective reporting (reporting bias)	Unclear risk	Not stated
Other bias	Low risk	Not stated

Yadrick 1989

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** not stated
Participants	**Setting:** Oklahoma (USA) **Malaria endemicity:** not stated **Included:** female volunteers aged 25 years to 40 years (mean age not reported). Participants in good health, not using medications, including the oral contraceptive pill **Excluded:** not stated **Dropouts:** dropout rates not stated **Sample size:** total: 18; intervention: 9, control: 9
Interventions	**Intervention:** 25 mg iron + 25 mg zinc **Control:** 25 mg zinc alone **Duration:** 10 weeks
Outcomes	Haemoglobin, iron status, zinc, ceruloplasmin
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** not stated **Other notes:** sample sizes for each arm not specifically provided: stated that half the participants allocated to each arm; assume 9 participants per arm

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Allocation matched by baseline ferritin and erythrocyte superoxide dismutase. Random sequence generation not described in study
Allocation concealment (selection bias)	Unclear risk	Allocation concealment not described in study

Yadrick 1989 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo (zinc alone) provided
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not reported. Should not influence biochemical outcomes
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not stated
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	The study appears free of other bias

Yoshida 1990

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** not stated
Participants	**Setting:** Japanese institution **Malaria endemicity:** not stated **Included:** female endurance (distance) athletes, undergoing a training programme. Age range not stated (mean age 19 years) **Excluded:** not stated **Dropouts:** study reports no dropouts **Sample size:** total: 12; intervention: 6, control: 6
Interventions	**Intervention:** ferrous sodium citrate 200 mg + multivitamin (containing vitamin C, B6 and folic acid) thrice daily **Control:** multivitamin alone without iron **Duration:** 8 weeks
Outcomes	Haemoglobin, iron status, exercise performance
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** not stated **Other notes:** data not presented in a table - data extracted from hand-drawn bar graphs (including SDs)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Yoshida 1990 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo given
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported. Detection bias could influence measurement of exercise performance
Incomplete outcome data (attrition bias) All outcomes	Low risk	No losses to follow-up
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Zaman 2013

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus diet versus placebo. Diet group not extracted **Date of study:** not stated
Participants	**Setting:** women recruited through advertisements at the Univeristy of Sydney, Australia **Malaria endemicity:** not stated **Included:** women aged 18 years to 35 years (mean age 25 years) and not vegetarian, pregnant, lactating, long-term illness, hypertension, diabetes, or who consumed nutritional supplements **Excluded:** not stated **Dropouts:** 10 of 54 withdrew (4 intervention, 6 in control) **Sample size:** total: 44; intervention: 22, control: 22
Interventions	**Intervention:** ferrous gluconate containing 37.4 mg of elemental iron and vitamin C **Control:** cellulose placebo **Duration:** 12 weeks
Outcomes	Iron status, haemoglobin, quality of life scores, zinc, B12 levels
Notes	**Compliance:** not stated **Conflicts of interest:** not stated **Funded by:** a grant-in-aid from the Pork CRC and University of Sydney internal research funds
Risk of bias	

Zaman 2013 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random number generation
Allocation concealment (selection bias)	Low risk	Reports blinded
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Reports blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Describes losses as 6 in control and 4 in treatment group
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

Zavaleta 2000

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus weekly iron versus placebo **Date of study:** August to December 1996
Participants	**Setting:** school located in a shanty town of Lima, Peru **Malaria endemicity:** not stated **Included:** high school students aged 12 years to 18 years (mean age 15 years), living in community for 6 months before the study, healthy, nulliparous, menstruating regularly in the last 3 months, had not taken any multivitamin-mineral supplement in the last 6 months and a haemoglobin > 80 g/L **Excluded:** not stated **Dropouts:** 16 out of 312 lost to follow-up **Sample size:** total: 198; intervention: 101, control: 97
Interventions	**Intervention:** ferrous sulphate 60 mg/d (20 mg elemental iron) administered Monday to Friday (i.e. 5 days per week) **Control:** placebo **Duration:** 17 weeks
Outcomes	Haemoglobin, anaemia

Notes	**Compliance:** girls took 94% of the expected dose of 85 pills, and the median consumption was 80 tablets in the three groups **Conflicts of interest:** not stated **Funded by:** partially by Office of Health and Nutrition, USAID, under the terms of contract number (HRN-C-00-93-00038-00), and the MotherCare Project, John Snow, Incorporated (JSI) **Other notes:** change in prevalence reported as % (thus actual n/N calculated from sample sizes). No SDs provided for follow-up haemoglobin: imputed based on SDs of overall haemoglobin

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Sequence generation not described in study
Allocation concealment (selection bias)	Unclear risk	Allocation concealment not described in study
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not reported. Unlikely to affect laboratory outcomes
Incomplete outcome data (attrition bias) All outcomes	Low risk	312 participants at baseline. 16 dropped out of study
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting bias
Other bias	Low risk	The study appears free of other bias

Zhu 1998

Methods	**Design:** randomised controlled trial **Randomisation:** individual **Trial:** daily oral iron versus placebo **Date of study:** not stated
Participants	**Setting:** Ithaca (Cornell University, USA) **Malaria endemicity:** not stated **Included:** women aged 19 years to 36 years (mean age 36 years) with haemoglobin > 120 g/L and ferritin < 16 ng/mL **Excluded:** current pregnancy or pregnancy within the past year, infectious illness in the past month, fever in the past week, haemolytic anaemia, asthma, musculoskeletal

Zhu 1998 (*Continued*)

	problems, smoking, excess alcohol consumption (more than seven glasses of an alcoholic beverage per week), recent history of eating disorders, and use of prescription medications that potentially interfere with dietary iron absorption **Dropouts:** 2 of 39 (1 in each arm) **Sample Size:** total: 37; intervention: 20, control: 17
Interventions	**Intervention:** 135 mg elemental iron daily (45 mg thrice daily) as ferrous sulphate **Control:** placebo **Duration:** 8 weeks
Outcomes	Haemoglobin, iron status, exercise performance, fat mass, weight, lactate
Notes	**Compliance:** on average, the placebo group consumed 144 ± 23 capsules (87.3 ± 9.5% of the total prescription) and the iron-supplemented group consumed 145 ± 29 capsules (87.5 ± 16.5% of the total prescription); no significant difference between these arms **Conflicts of interest:** not stated **Funded by:** United States Department of Agriculture Grant (9500850) and by a Graduate Research Grant from the Division of Nutritional Sciences, Cornell University

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo administered
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported. Unlikely to affect biochemical/laboratory indices but could affect assessor's measurement of exercise performance
Incomplete outcome data (attrition bias) All outcomes	Low risk	39 enrolled. 2 lost to follow-up, 1 in each arm
Selective reporting (reporting bias)	Low risk	Not evident
Other bias	Low risk	Not evident

BMI - body mass index
CI(s) - confidence interval(s)
GP - general practitioner
Fe - iron

FEP - free erythrocyte protoporphyrin
HR - heart rate
ICC - intraclass correlation coefficient
PR blood loss - bleeding in any part of the gastrointestinal tract
SD - standard deviation
SE - standard error
TFT - thyroid function test
UNICEF - United Nations International Children's Emergency Fund

VO_2 max - maximal oxygen consumption

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Brigham 1993	Randomised controlled cross-over trial; data not presented for outcomes at the end of the first parallel comparison
Cable 1988	Study in blood donors; ongoing donations (blood losses) during study
Powell 1991	Randomised controlled cross-over trial; data not presented for outcomes at the end of the first parallel comparison
Powers 1988	Data for men and women not disaggregated
Schoene 1983	Randomised controlled cross-over trial; data not presented for outcomes at the end of the first parallel comparison
Simon 1984	Study in blood donors; ongoing donations (blood losses) during study

Characteristics of studies awaiting assessment *[ordered by study ID]*

Blot 1980

Methods	Randomised controlled trial
Participants	Blood donors
Interventions	Iron supplementation - women and men
Outcomes	Unclear
Notes	Unable to obtain text

Böttiger 1971

Methods	No abstract, no details available
Participants	
Interventions	
Outcomes	
Notes	

Charoenlarp 1981

Methods	No abstract, no details available
Participants	
Interventions	
Outcomes	
Notes	

Greene 1995

Methods	Apparently a randomised controlled trial
Participants	Male and female adolescents aged 11 years to 16 years
Interventions	Iron versus placebo
Outcomes	Raven's Progressive Matrices (RPM): iron supplementation did not significantly improve RPM compared with placebo in females. IQ measured and not reported
Notes	

Isager 1974

Methods	No abstract, no details available
Participants	
Interventions	
Outcomes	
Notes	

Izak 1973

Methods	No abstract, no details available
Participants	
Interventions	
Outcomes	
Notes	

Parkinson 1981

Methods	No abstract, no details available
Participants	
Interventions	
Outcomes	
Notes	

IQ - intelligence quotient.

Characteristics of ongoing studies *[ordered by study ID]*

IRCT201409082365N9

Trial name or title	The effects of vitamin D or iron-vitamin supplementation on bone metabolism and inflammation in 18-year to 40-year women
Methods	**Randomisation:** randomised **Blinding**: double blinded **Placebo:** used **Assignment:** parallel **Purpose:** prevention
Participants	**Sample size:** 90 **Inclusion criteria:** 1. Healthy 2. Non-smoker 3. Non-pregnant 4. Non-lactating 5. Body mass index 18.5 to 29.9 kg/m² 6. Ferritin less than 30 ng/ml 7. Haemoglobin less than 12 g/dl

	8. 25-hydroxyvitamin D less than 30 ng/ml **Exclusion criteria:** 1. Amenorrhea 2. Menopause 3. Minor thalassaemia 4. Haemochromatosis 5. Inflammatory bowel diseases 6. Crohn's disease 7. Gastric ulcer 8. Coeliac disease 9. Gastrointestinal bleeding diseases 10. Renal diseases 11. Blood donation during past three months 12. Iron or vitamin D supplement use during past three months
Interventions	**Intervention 1:** 1. Intervention group participants will be prescribed two tablets (one 1000 international unit vitamin D plus one 27 mg elemental iron every day). They will be instructed to take the tablets separately **Intervention 2:** 1. Control group participants will be prescribed two tablets (one 1000 international unit vitamin D plus one placebo every day). They will be instructed to take the tablets separately
Outcomes	Haemoglobin, ferritin, serum iron
Starting date	2011
Contact information	Dr Mohammadreza Vafa Nutrition and Health Group, Faculty of Health, Iran University of Medical Sciences, Hemmat highway, Tehran, Iran
Notes	Recruitment closed late 2014. Data not published or publicly available at time of closing of data extraction for this review. Pre-specified outcomes listed do not include any of the primary outcomes of this review for which few data are presently available. Author not contacted as given haematologic and iron outcomes only and relatively small sample size compared with sample size in the meta-analyses. This study was judged unlikely to produce major alterations to the findings

IRCT: Iranian Registry of Clinical Trials.

DATA AND ANALYSES

Comparison 1. Anaemia

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Anaemia at end of therapy (total)	10	3273	Risk Ratio (M-H, Random, 95% CI)	0.39 [0.25, 0.60]
2 Anaemia at end of therapy (sensitivity analysis)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3 Anaemia at end of therapy (cointervention)	10	3273	Risk Ratio (M-H, Random, 95% CI)	0.39 [0.25, 0.60]
3.1 Iron alone	8	2775	Risk Ratio (M-H, Random, 95% CI)	0.57 [0.45, 0.74]
3.2 Iron + vitamin C versus vitamin C	2	498	Risk Ratio (M-H, Random, 95% CI)	0.10 [0.06, 0.15]
3.3 Iron + cointervention versus cointervention	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
4 Anaemia at end of therapy (age)	10	3273	Risk Ratio (M-H, Random, 95% CI)	0.39 [0.25, 0.60]
4.1 12 to 18 years of age	4	2169	Risk Ratio (M-H, Random, 95% CI)	0.32 [0.11, 0.93]
4.2 50 to 55 years of age	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
4.3 Mixed/unstated	6	1104	Risk Ratio (M-H, Random, 95% CI)	0.51 [0.33, 0.78]
5 Anaemia at end of therapy (baseline Hb)	10	3273	Risk Ratio (M-H, Random, 95% CI)	0.39 [0.25, 0.60]
5.1 Anaemic	1	69	Risk Ratio (M-H, Random, 95% CI)	0.65 [0.47, 0.90]
5.2 Non-anaemic	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
5.3 Mixed/unstated	9	3204	Risk Ratio (M-H, Random, 95% CI)	0.36 [0.22, 0.59]
6 Anaemia at end of therapy (iron status)	10	3273	Risk Ratio (M-H, Random, 95% CI)	0.39 [0.25, 0.60]
6.1 Iron deficient	1	69	Risk Ratio (M-H, Random, 95% CI)	0.65 [0.47, 0.90]
6.2 Not iron deficient	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.3 Mixed/unstated	9	3204	Risk Ratio (M-H, Random, 95% CI)	0.36 [0.22, 0.59]
7 Anaemia at end of therapy (iron-deficiency anaemia)	10	3273	Risk Ratio (M-H, Random, 95% CI)	0.39 [0.25, 0.60]
7.1 Iron-deficiency anaemia	1	69	Risk Ratio (M-H, Random, 95% CI)	0.65 [0.47, 0.90]
7.2 Iron deficient, not anaemic	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.3 Not iron deficient, not anaemic	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.4 Mixed/unstated	9	3204	Risk Ratio (M-H, Random, 95% CI)	0.36 [0.22, 0.59]
8 Anaemia at end of therapy (dose)	10	3273	Risk Ratio (M-H, Random, 95% CI)	0.39 [0.25, 0.60]
8.1 < 30 mg	3	348	Risk Ratio (M-H, Random, 95% CI)	0.57 [0.37, 0.88]
8.2 31 mg to 60 mg	2	807	Risk Ratio (M-H, Random, 95% CI)	0.30 [0.03, 3.45]
8.3 61 mg to 100 mg	2	1466	Risk Ratio (M-H, Random, 95% CI)	0.44 [0.16, 1.25]
8.4 > 100 mg	3	652	Risk Ratio (M-H, Random, 95% CI)	0.34 [0.14, 0.82]
9 Anaemia at end of therapy (duration)	10	3273	Risk Ratio (M-H, Random, 95% CI)	0.39 [0.25, 0.60]
9.1 < 30 days (1 month)	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
9.2 1 to 3 months	5	1106	Risk Ratio (M-H, Random, 95% CI)	0.20 [0.06, 0.64]
9.3 > 3 months	5	2167	Risk Ratio (M-H, Random, 95% CI)	0.63 [0.48, 0.82]

10 Anaemia at end of therapy (type of iron)	9	3192	Risk Ratio (M-H, Random, 95% CI)	0.40 [0.26, 0.62]
10.1 Ferrous sulphate	4	838	Risk Ratio (M-H, Random, 95% CI)	0.20 [0.09, 0.48]
10.2 Ferrous fumurate	1	69	Risk Ratio (M-H, Random, 95% CI)	0.65 [0.47, 0.90]
10.3 Other	4	2285	Risk Ratio (M-H, Random, 95% CI)	0.66 [0.50, 0.87]

Comparison 2. Haemoglobin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Haemoglobin (total)	51	6861	Mean Difference (IV, Random, 95% CI)	5.30 [4.14, 6.45]
2 Haemoglobin (sensitivity analysis)	6	581	Mean Difference (IV, Random, 95% CI)	5.08 [2.99, 7.17]
3 Haemoglobin (cointervention)	51	6861	Mean Difference (IV, Random, 95% CI)	5.49 [4.35, 6.63]
3.1 Iron alone	44	6117	Mean Difference (IV, Random, 95% CI)	5.39 [4.22, 6.55]
3.2 Iron + vitamin C versus vitamin C	4	655	Mean Difference (IV, Random, 95% CI)	6.59 [1.36, 11.82]
3.3 Iron + cointervention versus cointervention	4	89	Mean Difference (IV, Random, 95% CI)	3.80 [-6.41, 14.01]
4 Haemoglobin (age)	51	6861	Mean Difference (IV, Random, 95% CI)	5.30 [4.14, 6.45]
4.1 12 to 18 years of age	10	3220	Mean Difference (IV, Random, 95% CI)	6.99 [3.85, 10.13]
4.2 50 to 55 years of age	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.3 Mixed/unstated	41	3641	Mean Difference (IV, Random, 95% CI)	4.69 [3.55, 5.83]
5 Haemoglobin (baseline Hb)	51	6885	Mean Difference (IV, Random, 95% CI)	5.30 [4.11, 6.48]
5.1 Anaemic	8	558	Mean Difference (IV, Random, 95% CI)	8.67 [5.16, 12.18]
5.2 Non-anaemic	25	2120	Mean Difference (IV, Random, 95% CI)	3.11 [1.67, 4.54]
5.3 Mixed/unstated	25	4207	Mean Difference (IV, Random, 95% CI)	6.30 [4.52, 8.08]
6 Haemoglobin (iron status)	51	6841	Mean Difference (IV, Random, 95% CI)	5.15 [4.00, 6.30]
6.1 Iron deficient	21	1124	Mean Difference (IV, Random, 95% CI)	6.92 [4.76, 9.09]
6.2 Not iron deficient	5	421	Mean Difference (IV, Random, 95% CI)	0.84 [-2.26, 3.95]
6.3 Mixed/unstated	28	5296	Mean Difference (IV, Random, 95% CI)	4.92 [3.49, 6.35]
7 Haemoglobin (iron-deficiency anaemia)	51	6811	Mean Difference (IV, Random, 95% CI)	5.44 [4.31, 6.56]
7.1 Iron-deficiency anaemia	4	154	Mean Difference (IV, Random, 95% CI)	9.01 [4.64, 13.37]
7.2 Iron deficient, not anaemic	15	586	Mean Difference (IV, Random, 95% CI)	5.15 [3.30, 6.99]
7.3 Not iron deficient, not anaemic	3	278	Mean Difference (IV, Random, 95% CI)	2.10 [-1.77, 5.97]
7.4 Mixed/unstated	33	5793	Mean Difference (IV, Random, 95% CI)	5.59 [4.15, 7.03]
8 Haemoglobin (dose)	51	6861	Mean Difference (IV, Random, 95% CI)	5.26 [4.12, 6.41]
8.1 < 30 mg	14	872	Mean Difference (IV, Random, 95% CI)	4.56 [2.50, 6.63]
8.2 31 to 60 mg	19	2600	Mean Difference (IV, Random, 95% CI)	4.93 [2.20, 7.66]
8.3 61 mg to 100 mg	9	1897	Mean Difference (IV, Random, 95% CI)	6.87 [4.24, 9.49]
8.4 > 100 mg	10	1492	Mean Difference (IV, Random, 95% CI)	4.85 [3.03, 6.67]
9 Haemoglobin (duration)	51	6861	Mean Difference (IV, Random, 95% CI)	5.30 [4.14, 6.45]
9.1 < 30 days (1 month)	6	765	Mean Difference (IV, Random, 95% CI)	2.60 [0.28, 4.91]
9.2 1 to 3 months	37	4171	Mean Difference (IV, Random, 95% CI)	6.14 [4.70, 7.58]
9.3 > 3 months	8	1925	Mean Difference (IV, Random, 95% CI)	3.84 [0.94, 6.75]
10 Haemoglobin (type of iron)	47	6542	Mean Difference (IV, Random, 95% CI)	5.63 [4.44, 6.82]

10.1 Ferrous sulphate	27	3167	Mean Difference (IV, Random, 95% CI)	5.56 [3.74, 7.38]
10.2 Ferrous fumurate	2	79	Mean Difference (IV, Random, 95% CI)	6.66 [-4.66, 17.97]
10.3 Other/not stated	19	3296	Mean Difference (IV, Random, 95% CI)	5.71 [3.93, 7.49]

Comparison 3. Iron deficiency

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Iron deficiency at end of therapy (total)	7	1088	Risk Ratio (M-H, Random, 95% CI)	0.62 [0.50, 0.76]
2 Iron deficiency at end of therapy (sensitivity analysis)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Comparison 4. Iron-deficiency anaemia

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Iron-deficiency anaemia (total)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2 Microcytic anaemia (Total)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Comparison 5. Side effects

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Any side effect (total)	7	901	Risk Ratio (M-H, Random, 95% CI)	2.14 [0.94, 4.86]
2 Any side effect (sensitivity analysis)	3	415	Risk Ratio (M-H, Random, 95% CI)	1.59 [0.66, 3.81]
3 Any side effect (dose)	7	901	Risk Ratio (M-H, Random, 95% CI)	2.04 [0.93, 4.48]
3.1 < 30 mg	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3.2 31 mg to 60 mg	3	305	Risk Ratio (M-H, Random, 95% CI)	1.01 [0.93, 1.10]
3.3 61 mg to 100 mg	2	157	Risk Ratio (M-H, Random, 95% CI)	2.61 [1.44, 4.75]
3.4 > 100 mg	3	439	Risk Ratio (M-H, Random, 95% CI)	2.15 [1.24, 3.73]
4 Gastrointestinal side effects (total)	5	521	Risk Ratio (M-H, Random, 95% CI)	1.99 [1.26, 3.12]
5 Gastrointestinal side effects (sensitivity analysis)	3	415	Risk Ratio (M-H, Random, 95% CI)	1.91 [0.96, 3.80]
6 Gastrointestinal side effects (dose)	5	521	Risk Ratio (M-H, Random, 95% CI)	1.99 [1.26, 3.12]
6.1 < 30 mg	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
6.2 31 mg to 60 mg	2	293	Risk Ratio (M-H, Random, 95% CI)	1.23 [0.84, 1.81]
6.3 61 mg to 100 mg	1	145	Risk Ratio (M-H, Random, 95% CI)	3.00 [1.45, 6.20]

6.4 > 100 mg	2	83	Risk Ratio (M-H, Random, 95% CI)	2.42 [1.45, 4.05]
7 Loose stools/diarrhoea (total)	6	604	Risk Ratio (M-H, Random, 95% CI)	2.13 [1.10, 4.11]
8 Hard stools/constipation (total)	8	1036	Risk Ratio (M-H, Random, 95% CI)	2.07 [1.35, 3.17]
9 Hard stools/constipation (sensitivity analysis)	4	480	Risk Ratio (M-H, Random, 95% CI)	2.14 [1.04, 4.38]
10 Abdominal pain (total)	7	1190	Risk Ratio (M-H, Random, 95% CI)	1.55 [0.99, 2.41]
11 Nausea (total)	8	1214	Risk Ratio (M-H, Random, 95% CI)	1.19 [0.78, 1.82]
12 Change in stool colour (total)	4	359	Risk Ratio (M-H, Random, 95% CI)	6.92 [3.83, 12.52]
13 Headache (total)	4	526	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.58, 1.66]

Comparison 6. Iron status

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Ferritin in ng/ml (total)	42	3881	Mean Difference (IV, Random, 95% CI)	10.27 [8.90, 11.65]
2 Ferritin in ng/ml (cointervention)	42	3881	Mean Difference (IV, Random, 95% CI)	9.97 [8.70, 11.25]
2.1 Iron alone	37	3265	Mean Difference (IV, Random, 95% CI)	10.05 [8.55, 11.54]
2.2 Iron + vitamin C versus vitamin C	3	537	Mean Difference (IV, Random, 95% CI)	18.10 [-7.79, 44.00]
2.3 Iron + cointervention versus cointervention	3	79	Mean Difference (IV, Random, 95% CI)	6.81 [6.36, 7.26]
3 Ferritin in ng/ml (age)	42	3881	Mean Difference (IV, Random, 95% CI)	10.27 [8.90, 11.65]
3.1 12 to 18 years of age	7	1430	Mean Difference (IV, Random, 95% CI)	14.19 [9.70, 18.68]
3.2 50 to 55 years of age	0	0	Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
3.3 Mixed/unstated	35	2451	Mean Difference (IV, Random, 95% CI)	9.76 [7.89, 11.63]
4 Ferritin in ng/ml (baseline Hb)	42	3874	Mean Difference (IV, Random, 95% CI)	10.65 [9.31, 11.99]
4.1 Anaemic	4	202	Mean Difference (IV, Random, 95% CI)	13.74 [6.32, 21.16]
4.2 Non anaemic	24	1532	Mean Difference (IV, Random, 95% CI)	10.40 [7.90, 12.89]
4.3 Mixed/unstated	18	2140	Mean Difference (IV, Random, 95% CI)	11.36 [8.67, 14.05]
5 Ferritin in ng/ml (iron status)	42	3861	Mean Difference (IV, Random, 95% CI)	10.13 [8.81, 11.45]
5.1 Iron deficient	20	1065	Mean Difference (IV, Random, 95% CI)	8.40 [6.31, 10.49]
5.2 Not iron deficient	5	297	Mean Difference (IV, Random, 95% CI)	13.38 [6.74, 20.01]
5.3 Mixed/unstated	20	2499	Mean Difference (IV, Random, 95% CI)	12.88 [9.99, 15.78]
6 Ferritin in ng/ml (iron-deficiency anaemia)	42	3831	Mean Difference (IV, Random, 95% CI)	10.31 [8.99, 11.63]
6.1 Iron-deficiency anaemia	3	85	Mean Difference (IV, Random, 95% CI)	11.27 [3.26, 19.29]
6.2 Iron deficient, not anaemic	16	633	Mean Difference (IV, Random, 95% CI)	10.07 [6.77, 13.38]
6.3 Not iron deficient, not anaemic	2	117	Mean Difference (IV, Random, 95% CI)	12.27 [1.00, 23.54]
6.4 Mixed/unstated	25	2996	Mean Difference (IV, Random, 95% CI)	9.99 [8.38, 11.61]
7 Ferritin in ng/ml (dose)	42	3881	Mean Difference (IV, Random, 95% CI)	10.16 [8.79, 11.52]
7.1 < 30 mg	10	397	Mean Difference (IV, Random, 95% CI)	6.47 [3.18, 9.75]
7.2 31 mg to 60 mg	19	2262	Mean Difference (IV, Random, 95% CI)	12.36 [9.50, 15.22]
7.3 61 mg to 100 mg	6	381	Mean Difference (IV, Random, 95% CI)	10.14 [5.20, 15.08]
7.4 > 100 mg	8	841	Mean Difference (IV, Random, 95% CI)	13.50 [8.15, 18.86]
8 Ferritin in ng/ml (duration)	42	3881	Mean Difference (IV, Random, 95% CI)	10.27 [8.90, 11.65]
8.1 < 30 days (1 month)	7	794	Mean Difference (IV, Random, 95% CI)	7.60 [4.64, 10.57]

8.2 1 to 3 months	31	2829	Mean Difference (IV, Random, 95% CI)	12.17 [9.81, 14.53]
8.3 > 3 months	4	258	Mean Difference (IV, Random, 95% CI)	7.85 [1.31, 14.38]
9 Ferritin in ng/ml (type of iron)	42	3917	Mean Difference (IV, Random, 95% CI)	10.19 [8.84, 11.55]
9.1 Ferrous sulphate	27	2474	Mean Difference (IV, Random, 95% CI)	9.73 [8.32, 11.14]
9.2 Ferrous fumurate	1	47	Mean Difference (IV, Random, 95% CI)	9.60 [1.05, 18.15]
9.3 Other/not stated	16	1396	Mean Difference (IV, Random, 95% CI)	13.34 [8.61, 18.08]
10 Transferrin saturation (total)	23	1637	Mean Difference (IV, Random, 95% CI)	5.98 [3.93, 8.02]
11 Soluble transferrin receptor (mg/L) (total)	11	579	Std. Mean Difference (IV, Random, 95% CI)	-0.32 [-0.49, -0.16]
12 Total iron binding capacity (total)	19	960	Std. Mean Difference (IV, Random, 95% CI)	-0.64 [-1.38, 0.09]
13 Serum iron (total)	17	902	Std. Mean Difference (IV, Random, 95% CI)	0.47 [0.19, 0.74]
14 Erythrocyte protophyrin (ug/g Hb) (total)	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Comparison 7. Exercise performance - peak (maximal)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Absolute VO_2 max (L/min) (total)	8	276	Mean Difference (IV, Random, 95% CI)	0.11 [0.02, 0.20]
2 Relative VO_2 max ml/kg/min (total)	15	407	Mean Difference (IV, Random, 95% CI)	2.36 [0.55, 4.17]
3 Peak respiratory exchange ratio (RER) (total)	4	112	Mean Difference (IV, Random, 95% CI)	0.01 [-0.02, 0.03]
4 Maximum heart rate (total)	5	126	Mean Difference (IV, Random, 95% CI)	1.77 [-0.79, 4.33]
5 Lactate at longest point (total)	4	106	Mean Difference (IV, Random, 95% CI)	-0.00 [-0.72, 0.72]

Comparison 8. Exercise performance - submaximal

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage VO_2 peak (total)	5	126	Mean Difference (IV, Random, 95% CI)	-3.34 [-6.17, -0.51]
2 Heart rate (total)	6	212	Mean Difference (IV, Random, 95% CI)	-4.72 [-8.64, -0.80]
3 Energy consumption (kJ/min) (total)	2	61	Mean Difference (IV, Random, 95% CI)	-0.08 [-0.52, 0.36]
4 Respiratory exchange ratio (RER) (total)	5	136	Mean Difference (IV, Random, 95% CI)	-0.01 [-0.02, 0.01]
5 Achieved workload (total)	3	99	Mean Difference (IV, Random, 95% CI)	-4.70 [-16.37, 6.97]
6 Time to exhaustion (total)	2	38	Mean Difference (IV, Random, 95% CI)	3.46 [-6.42, 13.34]

Comparison 9. Anthropometric

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Height (cm) (total)	4	302	Mean Difference (IV, Random, 95% CI)	-0.32 [-2.25, 1.61]
2 Weight (kg) (total)	8	593	Mean Difference (IV, Random, 95% CI)	0.76 [-0.41, 1.92]
3 Weight (kg) (sensitivity analysis)	7	390	Mean Difference (IV, Random, 95% CI)	0.24 [-1.13, 1.60]
4 Body mass index (total)	6	520	Mean Difference (IV, Random, 95% CI)	0.53 [0.10, 0.96]
5 Body mass index (sensitivity analysis)	5	317	Mean Difference (IV, Random, 95% CI)	0.52 [-0.04, 1.07]

Comparison 10. Serum/plasma zinc

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Zinc levels (total)	4	151	Mean Difference (IV, Random, 95% CI)	-0.65 [-2.70, 1.40]

Comparison 11. Productivity

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Productivity	3	446	Std. Mean Difference (IV, Random, 95% CI)	0.07 [-0.12, 0.26]

Comparison 12. Malaria

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Malaria prevalence at end of therapy (Total)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 1.1. Comparison 1 Anaemia, Outcome 1 Anaemia at end of therapy (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 1 Anaemia

Outcome: 1 Anaemia at end of therapy (total)

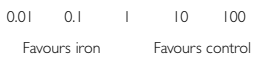
Study or subgroup	Iron n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Agarwal 2003	251/699	347/691		12.9 %	0.72 [0.63, 0.81]
Charoenlarp 1988	92/350	38/101		12.2 %	0.70 [0.51, 0.95]
Florencio 1981	2/39	11/20		5.4 %	0.09 [0.02, 0.38]
Gordeuk 1990	8/40	29/36		10.1 %	0.25 [0.13, 0.47]
Gunaratna 2015	85/184	97/184		12.7 %	0.88 [0.71, 1.08]
Jayatissa 1999	19/222	188/217		11.5 %	0.10 [0.06, 0.15]
Shah 2002	14/70	47/72		11.1 %	0.31 [0.19, 0.50]
Viteri 1999	0/37	5/44		1.9 %	0.11 [0.01, 1.88]
Wang 2012	19/34	30/35		12.1 %	0.65 [0.47, 0.90]
Zavaleta 2000	11/101	22/97		9.9 %	0.48 [0.25, 0.94]
Total (95% CI)	**1776**	**1497**		**100.0 %**	**0.39 [0.25, 0.60]**

Total events: 501 (Iron), 814 (Control)

Heterogeneity: $Tau^2 = 0.37$; $Chi^2 = 124.24$, df = 9 ($P<0.00001$); $I^2 = 93\%$

Test for overall effect: Z = 4.30 (P = 0.000017)

Test for subgroup differences: Not applicable



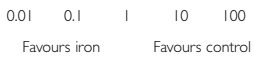
Analysis 1.2. Comparison 1 Anaemia, Outcome 2 Anaemia at end of therapy (sensitivity analysis).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 1 Anaemia

Outcome: 2 Anaemia at end of therapy (sensitivity analysis)

Study or subgroup	Iron n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Gunaratna 2015	85/184	97/184		0.88 [0.71, 1.08]



Analysis 1.3. Comparison 1 Anaemia, Outcome 3 Anaemia at end of therapy (cointervention).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 1 Anaemia

Outcome: 3 Anaemia at end of therapy (cointervention)

Study or subgroup	Iron n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Iron alone					
Agarwal 2003	251/699	347/691		12.9 %	0.72 [0.63, 0.81]
Charoenlarp 1988	92/350	38/101		12.2 %	0.70 [0.51, 0.95]
Gordeuk 1990	8/40	29/36		10.1 %	0.25 [0.13, 0.47]
Gunaratna 2015	85/184	97/184		12.7 %	0.88 [0.71, 1.08]
Shah 2002	14/70	47/72		11.1 %	0.31 [0.19, 0.50]
Viteri 1999	0/37	5/44		1.9 %	0.11 [0.01, 1.88]
Wang 2012	19/34	30/35		12.1 %	0.65 [0.47, 0.90]
Zavaleta 2000	11/101	22/97		9.9 %	0.48 [0.25, 0.94]
Subtotal (95% CI)	**1515**	**1260**		**83.0 %**	**0.57 [0.45, 0.74]**

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Study or subgroup	Iron n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Total events: 480 (Iron), 615 (Control)					
Heterogeneity: Tau² = 0.08; Chi² = 28.83, df = 7 (P = 0.00016); I² =76%					
Test for overall effect: Z = 4.35 (P = 0.000013)					
2 Iron + vitamin C versus vitamin C					
Florencio 1981	2/39	11/20		5.4 %	0.09 [0.02, 0.38]
Jayatissa 1999	19/222	188/217		11.5 %	0.10 [0.06, 0.15]
Subtotal (95% CI)	**261**	**237**		**17.0 %**	**0.10 [0.06, 0.15]**
Total events: 21 (Iron), 199 (Control)					
Heterogeneity: Tau² = 0.0; Chi² = 0.01, df = 1 (P = 0.94); I² =0.0%					
Test for overall effect: Z = 10.98 (P < 0.00001)					
3 Iron + cointervention versus cointervention					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Iron), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	**1776**	**1497**		**100.0 %**	**0.39 [0.25, 0.60]**
Total events: 501 (Iron), 814 (Control)					
Heterogeneity: Tau² = 0.37; Chi² = 124.24, df = 9 (P<0.00001); I² =93%					
Test for overall effect: Z = 4.30 (P = 0.000017)					
Test for subgroup differences: Chi² = 51.20, df = 1 (P = 0.00), I² =98%					

Analysis 1.4. Comparison 1 Anaemia, Outcome 4 Anaemia at end of therapy (age).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 1 Anaemia

Outcome: 4 Anaemia at end of therapy (age)

Study or subgroup	Iron n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 12 to 18 years of age					
Agarwal 2003	251/699	347/691		12.9 %	0.72 [0.63, 0.81]
Jayatissa 1999	19/222	188/217		11.5 %	0.10 [0.06, 0.15]
Shah 2002	14/70	47/72		11.1 %	0.31 [0.19, 0.50]
Zavaleta 2000	11/101	22/97		9.9 %	0.48 [0.25, 0.94]
Subtotal (95% CI)	**1092**	**1077**		**45.5 %**	**0.32 [0.11, 0.93]**
Total events: 295 (Iron), 604 (Control)					
Heterogeneity: Tau^2 = 1.13; Chi^2 = 93.51, df = 3 (P<0.00001); I^2 =97%					
Test for overall effect: Z = 2.09 (P = 0.037)					
2 50 to 55 years of age					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Iron), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
3 Mixed/unstated					
Charoenlarp 1988	92/350	38/101		12.2 %	0.70 [0.51, 0.95]
Florencio 1981	2/39	11/20		5.4 %	0.09 [0.02, 0.38]
Gordeuk 1990	8/40	29/36		10.1 %	0.25 [0.13, 0.47]
Gunaratna 2015	85/184	97/184		12.7 %	0.88 [0.71, 1.08]
Viteri 1999	0/37	5/44		1.9 %	0.11 [0.01, 1.88]
Wang 2012	19/34	30/35		12.1 %	0.65 [0.47, 0.90]
Subtotal (95% CI)	**684**	**420**		**54.5 %**	**0.51 [0.33, 0.78]**
Total events: 206 (Iron), 210 (Control)					
Heterogeneity: Tau^2 = 0.18; Chi^2 = 25.34, df = 5 (P = 0.00012); I^2 =80%					
Test for overall effect: Z = 3.06 (P = 0.0022)					
Total (95% CI)	**1776**	**1497**		**100.0 %**	**0.39 [0.25, 0.60]**
Total events: 501 (Iron), 814 (Control)					
Heterogeneity: Tau^2 = 0.37; Chi^2 = 124.24, df = 9 (P<0.00001); I^2 =93%					
Test for overall effect: Z = 4.30 (P = 0.000017)					
Test for subgroup differences: Chi^2 = 0.63, df = 1 (P = 0.43), I^2 =0.0%					

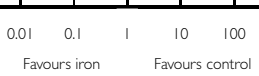
Analysis 1.5. Comparison 1 Anaemia, Outcome 5 Anaemia at end of therapy (baseline Hb).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 1 Anaemia

Outcome: 5 Anaemia at end of therapy (baseline Hb)

Study or subgroup	Iron n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Anaemic					
Wang 2012	19/34	30/35		12.1 %	0.65 [0.47, 0.90]
Subtotal (95% CI)	**34**	**35**		**12.1 %**	**0.65 [0.47, 0.90]**
Total events: 19 (Iron), 30 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.56 (P = 0.011)					
2 Non-anaemic					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Iron), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
3 Mixed/unstated					
Agarwal 2003	251/699	347/691		12.9 %	0.72 [0.63, 0.81]
Charoenlarp 1988	92/350	38/101		12.2 %	0.70 [0.51, 0.95]
Florencio 1981	2/39	11/20		5.4 %	0.09 [0.02, 0.38]
Gordeuk 1990	8/40	29/36		10.1 %	0.25 [0.13, 0.47]
Gunaratna 2015	85/184	97/184		12.7 %	0.88 [0.71, 1.08]
Jayatissa 1999	19/222	188/217		11.5 %	0.10 [0.06, 0.15]
Shah 2002	14/70	47/72		11.1 %	0.31 [0.19, 0.50]
Viteri 1999	0/37	5/44		1.9 %	0.11 [0.01, 1.88]
Zavaleta 2000	11/101	22/97		9.9 %	0.48 [0.25, 0.94]
Subtotal (95% CI)	**1742**	**1462**		**87.9 %**	**0.36 [0.22, 0.59]**
Total events: 482 (Iron), 784 (Control)					
Heterogeneity: Tau^2 = 0.43; Chi^2 = 124.02, df = 8 (P<0.00001); I^2 =94%					
Test for overall effect: Z = 4.10 (P = 0.000042)					
Total (95% CI)	**1776**	**1497**		**100.0 %**	**0.39 [0.25, 0.60]**
Total events: 501 (Iron), 814 (Control)					
Heterogeneity: Tau^2 = 0.37; Chi^2 = 124.24, df = 9 (P<0.00001); I^2 =93%					
Test for overall effect: Z = 4.30 (P = 0.000017)					
Test for subgroup differences: Chi^2 = 3.93, df = 1 (P = 0.05), I^2 =75%					

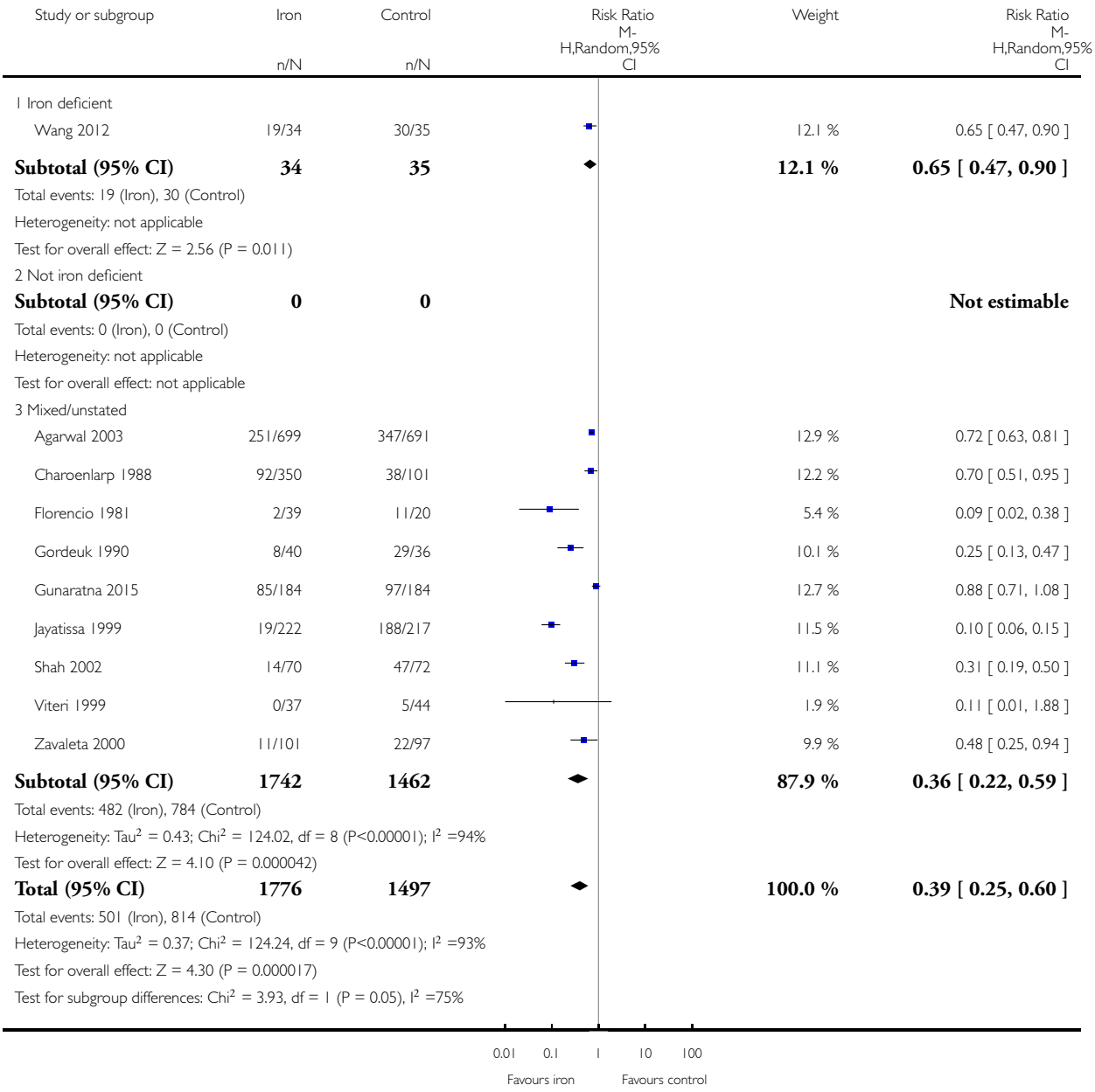


Analysis 1.6. Comparison 1 Anaemia, Outcome 6 Anaemia at end of therapy (iron status).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 1 Anaemia

Outcome: 6 Anaemia at end of therapy (iron status)



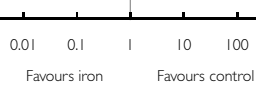
Analysis 1.7. Comparison 1 Anaemia, Outcome 7 Anaemia at end of therapy (iron-deficiency anaemia).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 1 Anaemia

Outcome: 7 Anaemia at end of therapy (iron-deficiency anaemia)

Study or subgroup	Iron n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Iron-deficiency anaemia					
Wang 2012	19/34	30/35		12.1 %	0.65 [0.47, 0.90]
Subtotal (95% CI)	**34**	**35**		**12.1 %**	**0.65 [0.47, 0.90]**
Total events: 19 (Iron), 30 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.56 (P = 0.011)					
2 Iron deficient, not anaemic					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Iron), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
3 Not iron deficient, not anaemic					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Iron), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
4 Mixed/unstated					
Agarwal 2003	251/699	347/691		12.9 %	0.72 [0.63, 0.81]
Charoenlarp 1988	92/350	38/101		12.2 %	0.70 [0.51, 0.95]
Florencio 1981	2/39	11/20		5.4 %	0.09 [0.02, 0.38]
Gordeuk 1990	8/40	29/36		10.1 %	0.25 [0.13, 0.47]
Gunaratna 2015	85/184	97/184		12.7 %	0.88 [0.71, 1.08]
Jayatissa 1999	19/222	188/217		11.5 %	0.10 [0.06, 0.15]
Shah 2002	14/70	47/72		11.1 %	0.31 [0.19, 0.50]
Viteri 1999	0/37	5/44		1.9 %	0.11 [0.01, 1.88]
Zavaleta 2000	11/101	22/97		9.9 %	0.48 [0.25, 0.94]
Subtotal (95% CI)	**1742**	**1462**		**87.9 %**	**0.36 [0.22, 0.59]**
Total events: 482 (Iron), 784 (Control)					
Heterogeneity: Tau^2 = 0.43; Chi^2 = 124.02, df = 8 (P<0.00001); I^2 =94%					
Test for overall effect: Z = 4.10 (P = 0.000042)					
Total (95% CI)	**1776**	**1497**		**100.0 %**	**0.39 [0.25, 0.60]**



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Study or subgroup	Iron n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Total events: 501 (Iron), 814 (Control)					
Heterogeneity: Tau² = 0.37; Chi² = 124.24, df = 9 (P<0.00001); I² =93%					
Test for overall effect: Z = 4.30 (P = 0.000017)					
Test for subgroup differences: Chi² = 3.93, df = 1 (P = 0.05), I² =75%					

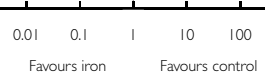
Analysis 1.8. Comparison 1 Anaemia, Outcome 8 Anaemia at end of therapy (dose).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 1 Anaemia

Outcome: 8 Anaemia at end of therapy (dose)

Study or subgroup	Iron n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 < 30 mg					
Viteri 1999	0/37	5/44		1.9 %	0.11 [0.01, 1.88]
Wang 2012	19/34	30/35		12.1 %	0.65 [0.47, 0.90]
Zavaleta 2000	11/101	22/97		9.9 %	0.48 [0.25, 0.94]
Subtotal (95% CI)	**172**	**176**		**24.0 %**	**0.57 [0.37, 0.88]**
Total events: 30 (Iron), 57 (Control)					
Heterogeneity: Tau² = 0.05; Chi² = 2.68, df = 2 (P = 0.26); I² =25%					
Test for overall effect: Z = 2.52 (P = 0.012)					
2 31 mg to 60 mg					
Gunaratna 2015	85/184	97/184		12.7 %	0.88 [0.71, 1.08]
Jayatissa 1999	19/222	188/217		11.5 %	0.10 [0.06, 0.15]
Subtotal (95% CI)	**406**	**401**		**24.2 %**	**0.30 [0.03, 3.45]**
Total events: 104 (Iron), 285 (Control)					
Heterogeneity: Tau² = 3.11; Chi² = 104.45, df = 1 (P<0.00001); I² =99%					
Test for overall effect: Z = 0.97 (P = 0.33)					



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Study or subgroup	Iron n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
3 61 mg to 100 mg					
Agarwal 2003	251/699	347/691		12.9 %	0.72 [0.63, 0.81]
Gordeuk 1990	8/40	29/36		10.1 %	0.25 [0.13, 0.47]
Subtotal (95% CI)	**739**	**727**		**23.0 %**	**0.44 [0.16, 1.25]**
Total events: 259 (Iron), 376 (Control)					
Heterogeneity: Tau^2 = 0.51; Chi^2 = 10.17, df = 1 (P = 0.001); I^2 =90%					
Test for overall effect: Z = 1.54 (P = 0.12)					
4 > 100 mg					
Charoenlarp 1988	92/350	38/101		12.2 %	0.70 [0.51, 0.95]
Florencio 1981	2/39	11/20		5.4 %	0.09 [0.02, 0.38]
Shah 2002	14/70	47/72		11.1 %	0.31 [0.19, 0.50]
Subtotal (95% CI)	**459**	**193**		**28.8 %**	**0.34 [0.14, 0.82]**
Total events: 108 (Iron), 96 (Control)					
Heterogeneity: Tau^2 = 0.48; Chi^2 = 14.25, df = 2 (P = 0.00080); I^2 =86%					
Test for overall effect: Z = 2.40 (P = 0.017)					
Total (95% CI)	**1776**	**1497**		**100.0 %**	**0.39 [0.25, 0.60]**
Total events: 501 (Iron), 814 (Control)					
Heterogeneity: Tau^2 = 0.37; Chi^2 = 124.24, df = 9 (P<0.00001); I^2 =93%					
Test for overall effect: Z = 4.30 (P = 0.000017)					
Test for subgroup differences: Chi^2 = 1.34, df = 3 (P = 0.72), I^2 =0.0%					

Analysis 1.9. Comparison 1 Anaemia, Outcome 9 Anaemia at end of therapy (duration).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 1 Anaemia

Outcome: 9 Anaemia at end of therapy (duration)

Study or subgroup	Iron n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 < 30 days (1 month)					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Iron), 0 (Control)					
Heterogeneity: not applicable					
Test for overall effect: not applicable					
2 1 to 3 months					
Charoenlarp 1988	92/350	38/101		12.2 %	0.70 [0.51, 0.95]
Florencio 1981	2/39	11/20		5.4 %	0.09 [0.02, 0.38]
Gordeuk 1990	8/40	29/36		10.1 %	0.25 [0.13, 0.47]
Jayatissa 1999	19/222	188/217		11.5 %	0.10 [0.06, 0.15]
Viteri 1999	0/37	5/44		1.9 %	0.11 [0.01, 1.88]
Subtotal (95% CI)	**688**	**418**		**41.2 %**	**0.20 [0.06, 0.64]**
Total events: 121 (Iron), 271 (Control)					
Heterogeneity: Tau^2 = 1.44; Chi^2 = 66.57, df = 4 (P<0.00001); I^2 =94%					
Test for overall effect: Z = 2.71 (P = 0.0067)					
3 > 3 months					
Agarwal 2003	251/699	347/691		12.9 %	0.72 [0.63, 0.81]
Gunaratna 2015	85/184	97/184		12.7 %	0.88 [0.71, 1.08]
Shah 2002	14/70	47/72		11.1 %	0.31 [0.19, 0.50]
Wang 2012	19/34	30/35		12.1 %	0.65 [0.47, 0.90]
Zavaleta 2000	11/101	22/97		9.9 %	0.48 [0.25, 0.94]
Subtotal (95% CI)	**1088**	**1079**		**58.8 %**	**0.63 [0.48, 0.82]**
Total events: 380 (Iron), 543 (Control)					
Heterogeneity: Tau^2 = 0.06; Chi^2 = 16.69, df = 4 (P = 0.002); I^2 =76%					
Test for overall effect: Z = 3.49 (P = 0.00048)					
Total (95% CI)	**1776**	**1497**		**100.0 %**	**0.39 [0.25, 0.60]**
Total events: 501 (Iron), 814 (Control)					
Heterogeneity: Tau^2 = 0.37; Chi^2 = 124.24, df = 9 (P<0.00001); I^2 =93%					
Test for overall effect: Z = 4.30 (P = 0.000017)					
Test for subgroup differences: Chi^2 = 3.56, df = 1 (P = 0.06), I^2 =72%					

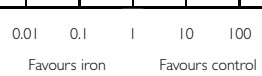
Analysis 1.10. Comparison 1 Anaemia, Outcome 10 Anaemia at end of therapy (type of iron).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 1 Anaemia

Outcome: 10 Anaemia at end of therapy (type of iron)

Study or subgroup	Iron n/N	control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Ferrous sulphate					
Florencio 1981	2/39	11/20		5.5 %	0.09 [0.02, 0.38]
Jayatissa 1999	19/222	188/217		11.8 %	0.10 [0.06, 0.15]
Shah 2002	14/70	47/72		11.3 %	0.31 [0.19, 0.50]
Zavaleta 2000	11/101	22/97		10.1 %	0.48 [0.25, 0.94]
Subtotal (95% CI)	**432**	**406**		**38.7 %**	**0.20 [0.09, 0.48]**
Total events: 46 (Iron), 268 (control)					
Heterogeneity: Tau^2 = 0.61; Chi^2 = 21.78, df = 3 (P = 0.00007); I^2 =86%					
Test for overall effect: Z = 3.65 (P = 0.00026)					
2 Ferrous fumurate					
Wang 2012	19/34	30/35		12.4 %	0.65 [0.47, 0.90]
Subtotal (95% CI)	**34**	**35**		**12.4 %**	**0.65 [0.47, 0.90]**
Total events: 19 (Iron), 30 (control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.56 (P = 0.011)					
3 Other					
Agarwal 2003	251/699	347/691		13.2 %	0.72 [0.63, 0.81]
Charoenlarp 1988	92/350	38/101		12.5 %	0.70 [0.51, 0.95]
Gordeuk 1990	8/40	29/36		10.3 %	0.25 [0.13, 0.47]
Gunaratna 2015	85/184	97/184		12.9 %	0.88 [0.71, 1.08]
Subtotal (95% CI)	**1273**	**1012**		**48.9 %**	**0.66 [0.50, 0.87]**
Total events: 436 (Iron), 511 (control)					
Heterogeneity: Tau^2 = 0.05; Chi^2 = 14.18, df = 3 (P = 0.003); I^2 =79%					
Test for overall effect: Z = 2.92 (P = 0.0035)					
Total (95% CI)	**1739**	**1453**		**100.0 %**	**0.40 [0.26, 0.62]**
Total events: 501 (Iron), 809 (control)					
Heterogeneity: Tau^2 = 0.36; Chi^2 = 122.26, df = 8 (P<0.00001); I^2 =93%					
Test for overall effect: Z = 4.15 (P = 0.000033)					
Test for subgroup differences: Chi^2 = 6.85, df = 2 (P = 0.03), I^2 =71%					



Analysis 2.1. Comparison 2 Haemoglobin, Outcome 1 Haemoglobin (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 2 Haemoglobin

Outcome: 1 Haemoglobin (total)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Agarwal 2003	699	123 (11)	691	116 (12)		2.9 %	7.00 [5.79, 8.21]
Berger 1997	65	191.7 (18.8)	65	184.9 (22.3)		1.4 %	6.80 [-0.29, 13.89]
Binkoski 2004	14	129 (16.84)	12	126 (16.97)		0.6 %	3.00 [-10.04, 16.04]
Booth 2014	25	135.8 (8.3)	24	136.8 (8.6)		2.0 %	-1.00 [-5.74, 3.74]
Bruner 1996	37	135 (8)	36	127 (7)		2.3 %	8.00 [4.55, 11.45]
Brutsaert 2003	10	139 (6.32)	10	134 (12.65)		1.1 %	5.00 [-3.76, 13.76]
Charoenlarp 1988	517	128.18 (11.81)	173	122.89 (14.06)		2.6 %	5.29 [2.96, 7.62]
Cooter 1978	5	130.75 (7.4)	5	130 (4.7)		1.3 %	0.75 [-6.93, 8.43]
DellaValle 2012	15	133 (6)	16	134 (8)		1.9 %	-1.00 [-5.96, 3.96]
Edgerton 1979	113	126.57 (12.7)	96	114.45 (20.17)		2.0 %	12.12 [7.45, 16.79]
Eftekhari 2006	47	142.5 (5.04)	47	129 (3.94)		2.8 %	13.50 [11.67, 15.33]
Elwood 1966	40	4 (1.5)	49	-1.6 (1.1)		2.9 %	5.60 [5.04, 6.16]
Florencio 1981	81	128.8 (5.8)	37	120 (5.6)		2.7 %	8.80 [6.60, 11.00]
Fogelholm 1992	14	139 (12.15)	17	128 (10.8)		1.2 %	11.00 [2.82, 19.18]
Fogelholm 1994	37	141.54 (14.32)	35	134 (14.47)		1.5 %	7.54 [0.89, 14.19]
Gordeuk 1987	34	125 (10.34)	19	126 (13.07)		1.5 %	-1.00 [-7.83, 5.83]
Gordeuk 1990	40	131 (8)	35	123 (9)		2.2 %	8.00 [4.12, 11.88]
Hinton 2000	22	135.2 (9.38)	19	130.8 (13.07)		1.4 %	4.40 [-2.66, 11.46]
Hinton 2007	10	136 (10)	10	131 (9)		1.2 %	5.00 [-3.34, 13.34]
Hoppe 2013	137.8333333 (14.25)		24	12	133 (13.5)		1.0 %	4.83 [-4.70, 14.36]
Jayatissa 1999	222	132 (9)	217	131 (11)		2.7 %	1.00 [-0.88, 2.88]
Jensen 1991	7	139 (3)	6	138 (6)		1.8 %	1.00 [-4.29, 6.29]
Kanani 2000	91	126.1 (7.63)	89	108.22 (10.38)		2.6 %	17.88 [15.21, 20.55]
Kang 2004	11	122 (9)	14	123 (12)		1.2 %	-1.00 [-9.23, 7.23]
Kianfar 2000	92	7.4 (6.76)	148	2 (8.22)		2.7 %	5.40 [3.49, 7.31]

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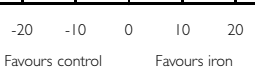
Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Klingshirn 1992	9	143.6 (12.8)	9	142.3 (11.1)		0.8 %	1.30 [-9.77, 12.37]
LaManca 1993	10	141 (6.32)	10	129 (12.64)		1.1 %	12.00 [3.24, 20.76]
Lanerolle 2000	281	135.42 (10.42)	284	131.95 (10.95)		2.8 %	3.47 [1.71, 5.23]
Larocque 2006	12	137.5 (7.41)	9	136.56 (7.53)		1.5 %	0.94 [-5.52, 7.40]
Leonard 2014	16	135 (3.53)	8	131.6 (3.9)		2.4 %	3.40 [0.19, 6.61]
Li 1994	40	127 (12)	40	113 (14)		1.7 %	14.00 [8.29, 19.71]
Maghsudlu 2008	185	132.9 (8)	182	131.9 (8)		2.8 %	1.00 [-0.64, 2.64]
Marks 2014	129	134.6 (8.7)	128	130 (9.9)		2.7 %	4.60 [2.32, 6.88]
McClung 2009	85	130 (9)	86	128 (11)		2.5 %	2.00 [-1.01, 5.01]
Mujica-Coopman 2015	28	152 (9)	27	149 (7)		2.1 %	3.00 [-1.25, 7.25]
Murray-Kolb 2007	56	129.92 (10.04)	57	132.29 (12.42)		2.1 %	-2.37 [-6.53, 1.79]
Newhouse 1989	19	135 (5)	18	131 (5)		2.4 %	4.00 [0.78, 7.22]
Radjen 2011	19	124.78 (7.94)	18	110.61 (5.49)		2.1 %	14.17 [9.79, 18.55]
Rowland 1988	7	134 (3)	7	127 (4)		2.3 %	7.00 [3.30, 10.70]
Rybo 1985	45	137 (9)	44	133 (10)		2.2 %	4.00 [0.04, 7.96]
R svik 2010	82	129 (6)	79	128 (7)		2.7 %	1.00 [-1.02, 3.02]
Taniguchi 1991	27	121 (11)	27	108 (12.5)		1.6 %	13.00 [6.72, 19.28]
Viteri 1999	37	137.5 (9.2)	44	135.8 (11.8)		2.0 %	1.70 [-2.88, 6.28]
Waldvogel 2012	74	135 (6.7)	71	130 (5.3)		2.7 %	5.00 [3.04, 6.96]
Walsh 1989	10	136 (6)	10	129 (6)		1.8 %	7.00 [1.74, 12.26]
Wang 2012	34	116.8 (16)	35	104.5 (12.9)		1.4 %	12.30 [5.43, 19.17]
Yadrick 1989	9	151 (6)	9	148 (15)		0.9 %	3.00 [-7.55, 13.55]
Yoshida 1990	6	133 (6)	6	137 (7)		1.3 %	-4.00 [-11.38, 3.38]
Zaman 2013	22	132.6 (7.4)	22	127.5 (8)		2.0 %	5.10 [0.55, 9.65]
Zavaleta 2000	101	129.47 (9.4)	97	125.19 (11)		2.5 %	4.28 [1.42, 7.14]
Zhu 1998	20	136.3 (8)	17	132.2 (7.6)		1.9 %	4.10 [-0.93, 9.13]
Total (95% CI)	**3635**		**3226**		◆	**100.0 %**	**5.30 [4.14, 6.45]**

Heterogeneity: $Tau^2 = 11.74$; $Chi^2 = 356.76$, df = 50 (P<0.00001); $I^2 = 86\%$

Test for overall effect: Z = 8.98 (P < 0.00001)

Test for subgroup differences: Not applicable



Analysis 2.2. Comparison 2 Haemoglobin, Outcome 2 Haemoglobin (sensitivity analysis).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 2 Haemoglobin

Outcome: 2 Haemoglobin (sensitivity analysis)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Bruner 1996	37	135 (8)	36	127 (7)		18.0 %	8.00 [4.55, 11.45]
DellaValle 2012	15	133 (6)	16	134 (8)		11.8 %	-1.00 [-5.96, 3.96]
Fogelholm 1992	14	139 (12.15)	17	128 (10.8)		5.5 %	11.00 [2.82, 19.18]
Marks 2014	129	134.6 (8.7)	128	130 (9.9)		24.8 %	4.60 [2.32, 6.88]
Waldvogel 2012	74	135 (6.7)	71	130 (5.3)		26.8 %	5.00 [3.04, 6.96]
Zaman 2013	22	132.6 (7.4)	22	127.5 (8)		13.2 %	5.10 [0.55, 9.65]
Total (95% CI)	**291**		**290**			**100.0 %**	**5.08 [2.99, 7.17]**

Heterogeneity: $Tau^2 = 3.24$; $Chi^2 = 10.72$, df = 5 (P = 0.06); $I^2 = 53\%$

Test for overall effect: Z = 4.76 (P < 0.00001)

Test for subgroup differences: Not applicable

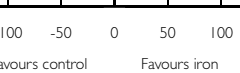
Analysis 2.3. Comparison 2 Haemoglobin, Outcome 3 Haemoglobin (cointervention).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 2 Haemoglobin

Outcome: 3 Haemoglobin (cointervention)

Study or subgroup	Iron		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
1 Iron alone							
Agarwal 2003	699	123 (11)	691	116 (12)		2.8 %	7.00 [5.79, 8.21]
Berger 1997	65	191.7 (18.8)	65	184.9 (22.3)		1.4 %	6.80 [-0.29, 13.89]
Binkoski 2004	14	129 (16.84)	12	126 (16.97)		0.6 %	3.00 [-10.04, 16.04]
Booth 2014	25	135.8 (8.3)	24	136.8 (8.6)		1.9 %	-1.00 [-5.74, 3.74]
Bruner 1996	37	135 (8)	36	127 (7)		2.3 %	8.00 [4.55, 11.45]
Brutsaert 2003	10	139 (6.32)	10	134 (12.65)		1.1 %	5.00 [-3.76, 13.76]
Charoenlarp 1988	517	128.18 (11.81)	173	122.89 (14.06)		2.6 %	5.29 [2.96, 7.62]
DellaValle 2012	15	133 (6)	16	134 (8)		1.9 %	-1.00 [-5.96, 3.96]
Edgerton 1979	113	126.57 (12.7)	96	114.45 (20.17)		2.0 %	12.12 [7.45, 16.79]
Eftekhari 2006	23	142 (6)	22	129 (3)		2.5 %	13.00 [10.25, 15.75]
Elwood 1966	40	4 (1.5)	49	-1.6 (1.1)		2.9 %	5.60 [5.04, 6.16]
Fogelholm 1992	14	139 (12.15)	17	128 (10.8)		1.2 %	11.00 [2.82, 19.18]
Fogelholm 1994	37	141.54 (14.32)	35	134 (14.47)		1.5 %	7.54 [0.89, 14.19]
Gordeuk 1987	34	125 (10.34)	19	126 (13.07)		1.4 %	-1.00 [-7.83, 5.83]
Gordeuk 1990	40	131 (8)	35	123 (9)		2.2 %	8.00 [4.12, 11.88]
Hinton 2000	22	135.2 (9.38)	19	130.8 (13.07)		1.4 %	4.40 [-2.66, 11.46]
Hinton 2007	10	136 (10)	10	131 (9)		1.1 %	5.00 [-3.34, 13.34]
Hoppe 2013	137.8333333 (14.25)		24	12	133 (13.5)	1.0 %	4.83 [-4.70, 14.36]
Jensen 1991	7	139 (3)	6	138 (6)		1.8 %	1.00 [-4.29, 6.29]
Kanani 2000	91	126.1 (7.63)	89	108.22 (10.38)		2.5 %	17.88 [15.21, 20.55]
Kang 2004	11	122 (9)	14	123 (12)		1.2 %	-1.00 [-9.23, 7.23]
Kianfar 2000	92	7.4 (6.76)	148	2 (8.22)		2.7 %	5.40 [3.49, 7.31]
Klingshirn 1992	9	143.6 (12.8)	9	142.3 (11.1)		0.8 %	1.30 [-9.77, 12.37]
LaManca 1993	10	141 (6.32)	10	129 (12.64)		1.1 %	12.00 [3.24, 20.76]



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Study or subgroup	Iron N	Iron Mean(SD)	Control N	Control Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Lanerolle 2000	281	135.42 (10.42)	284	131.95 (10.95)		2.7 %	3.47 [1.71, 5.23]
Larocque 2006	12	137.5 (7.41)	9	136.56 (7.53)		1.5 %	0.94 [-5.52, 7.40]
Leonard 2014	16	135 (3.53)	8	131.6 (3.9)		2.4 %	3.40 [0.19, 6.61]
Li 1994	40	127 (12)	40	113 (14)		1.7 %	14.00 [8.29, 19.71]
Maghsudlu 2008	185	132.9 (8)	182	131.9 (8)		2.7 %	1.00 [-0.64, 2.64]
Marks 2014	129	134.6 (8.7)	128	130 (9.9)		2.6 %	4.60 [2.32, 6.88]
McClung 2009	85	130 (9)	86	128 (11)		2.4 %	2.00 [-1.01, 5.01]
Mujica-Coopman 2015	28	152 (9)	27	149 (7)		2.1 %	3.00 [-1.25, 7.25]
Murray-Kolb 2007	56	129.92 (10.04)	57	132.29 (12.42)		2.1 %	-2.37 [-6.53, 1.79]
Newhouse 1989	19	135 (5)	18	131 (5)		2.4 %	4.00 [0.78, 7.22]
Radjen 2011	19	124.78 (7.94)	18	110.61 (5.49)		2.0 %	14.17 [9.79, 18.55]
Rowland 1988	7	134 (3)	7	127 (4)		2.2 %	7.00 [3.30, 10.70]
Rybo 1985	45	137 (9)	44	133 (10)		2.1 %	4.00 [0.04, 7.96]
R svik 2010	82	129 (6)	79	128 (7)		2.7 %	1.00 [-1.02, 3.02]
Viteri 1999	37	137.5 (9.2)	44	135.8 (11.8)		2.0 %	1.70 [-2.88, 6.28]
Waldvogel 2012	74	135 (6.7)	71	130 (5.3)		2.7 %	5.00 [3.04, 6.96]
Walsh 1989	10	136 (6)	10	129 (6)		1.8 %	7.00 [1.74, 12.26]
Wang 2012	34	116.8 (16)	35	104.5 (12.9)		1.4 %	12.30 [5.43, 19.17]
Zavaleta 2000	101	129.47 (9.4)	97	125.19 (11)		2.5 %	4.28 [1.42, 7.14]
Zhu 1998	20	136.3 (8)	17	132.2 (7.6)		1.9 %	4.10 [-0.93, 9.13]
Subtotal (95% CI)	**3239**		**2878**			**85.2 %**	**5.39 [4.22, 6.55]**
Heterogeneity: Tau^2 = 9.89; Chi^2 = 267.32, df = 43 (P<0.00001); I^2 =84%							
Test for overall effect: Z = 9.08 (P < 0.00001)							
2 Iron + vitamin C versus vitamin C							
Florencio 1981	81	128.8 (5.8)	37	120 (5.6)		2.6 %	8.80 [6.60, 11.00]
Jayatissa 1999	222	132 (9)	217	131 (11)		2.7 %	1.00 [-0.88, 2.88]
Taniguchi 1991	27	121 (11)	27	108 (12.5)		1.5 %	13.00 [6.72, 19.28]
Zaman 2013	22	132.6 (7.4)	22	127.5 (8)		2.0 %	5.10 [0.55, 9.65]
Subtotal (95% CI)	**352**		**303**			**8.8 %**	**6.59 [1.36, 11.82]**
Heterogeneity: Tau^2 = 24.46; Chi^2 = 34.88, df = 3 (P<0.00001); I^2 =91%							
Test for overall effect: Z = 2.47 (P = 0.013)							
3 Iron + cointervention versus cointervention							
Cooter 1978	5	130.75 (7.4)	5	130 (4.7)		1.3 %	0.75 [-6.93, 8.43]

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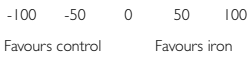
Study or subgroup	Iron N	Iron Mean(SD)	Control N	Control Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Eftekhari 2006	24	143 (4)	25	129 (5)		2.5 %	14.00 [11.47, 16.53]
Yadrick 1989	9	151 (6)	9	148 (15)		0.8 %	3.00 [-7.55, 13.55]
Yoshida 1990	6	133 (6)	6	137 (7)		1.3 %	-4.00 [-11.38, 3.38]
Subtotal (95% CI)	**44**		**45**			**5.9 %**	**3.80 [-6.41, 14.01]**
Heterogeneity: Tau^2 = 94.31; Chi^2 = 30.27, df = 3 (P<0.00001); I^2 =90%							
Test for overall effect: Z = 0.73 (P = 0.47)							
Total (95% CI)	**3635**		**3226**			**100.0 %**	**5.49 [4.35, 6.63]**
Heterogeneity: Tau^2 = 11.65; Chi^2 = 355.09, df = 51 (P<0.00001); I^2 =86%							
Test for overall effect: Z = 9.44 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 0.29, df = 2 (P = 0.86), I^2 =0.0%							



Analysis 2.4. Comparison 2 Haemoglobin, Outcome 4 Haemoglobin (age).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 2 Haemoglobin

Outcome: 4 Haemoglobin (age)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 12 to 18 years of age							
Agarwal 2003	699	123 (11)	691	116 (12)		2.9 %	7.00 [5.79, 8.21]
Bruner 1996	37	135 (8)	36	127 (7)		2.3 %	8.00 [4.55, 11.45]
Eftekhari 2006	47	142.5 (5.04)	47	129 (3.94)		2.8 %	13.50 [11.67, 15.33]
Jayatissa 1999	222	132 (9)	217	131 (11)		2.7 %	1.00 [-0.88, 2.88]
Kanani 2000	91	126.1 (7.63)	89	108.22 (10.38)		2.6 %	17.88 [15.21, 20.55]
Kianfar 2000	92	7.4 (6.76)	148	2 (8.22)		2.7 %	5.40 [3.49, 7.31]
Lanerolle 2000	281	135.42 (10.42)	284	131.95 (10.95)		2.8 %	3.47 [1.71, 5.23]
Larocque 2006	12	137.5 (7.41)	9	136.56 (7.53)		1.5 %	0.94 [-5.52, 7.40]
Walsh 1989	10	136 (6)	10	129 (6)		1.8 %	7.00 [1.74, 12.26]
Zavaleta 2000	101	129.47 (9.4)	97	125.19 (11)		2.5 %	4.28 [1.42, 7.14]
Subtotal (95% CI)	**1592**		**1628**			**24.7 %**	**6.99 [3.85, 10.13]**
Heterogeneity: Tau^2 = 23.13; Chi^2 = 176.74, df = 9 (P<0.00001); I^2 =95%							
Test for overall effect: Z = 4.36 (P = 0.000013)							
2 50 to 55 years of age							
Subtotal (95% CI)	**0**		**0**				**Not estimable**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
3 Mixed/unstated							
Berger 1997	65	191.7 (18.8)	65	184.9 (22.3)		1.4 %	6.80 [-0.29, 13.89]
Binkoski 2004	14	129 (16.84)	12	126 (16.97)		0.6 %	3.00 [-10.04, 16.04]
Booth 2014	25	135.8 (8.3)	24	136.8 (8.6)		2.0 %	-1.00 [-5.74, 3.74]
Brutsaert 2003	10	139 (6.32)	10	134 (12.65)		1.1 %	5.00 [-3.76, 13.76]
Charoenlarp 1988	517	128.18 (11.81)	173	122.89 (14.06)		2.6 %	5.29 [2.96, 7.62]
Cooter 1978	5	130.75 (7.4)	5	130 (4.7)		1.3 %	0.75 [-6.93, 8.43]
DellaValle 2012	15	133 (6)	16	134 (8)		1.9 %	-1.00 [-5.96, 3.96]
Edgerton 1979	113	126.57 (12.7)	96	114.45 (20.17)		2.0 %	12.12 [7.45, 16.79]
Elwood 1966	40	4 (1.5)	49	-1.6 (1.1)		2.9 %	5.60 [5.04, 6.16]

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Favours control Favours iron

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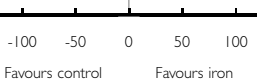
Study or subgroup	Iron		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
Florencio 1981	81	128.8 (5.8)	37	120 (5.6)		2.7 %	8.80 [6.60, 11.00]
Fogelholm 1992	14	139 (12.15)	17	128 (10.8)		1.2 %	11.00 [2.82, 19.18]
Fogelholm 1994	37	141.54 (14.32)	35	134 (14.47)		1.5 %	7.54 [0.89, 14.19]
Gordeuk 1987	34	125 (10.34)	19	126 (13.07)		1.5 %	-1.00 [-7.83, 5.83]
Gordeuk 1990	40	131 (8)	35	123 (9)		2.2 %	8.00 [4.12, 11.88]
Hinton 2000	22	135.2 (9.38)	19	130.8 (13.07)		1.4 %	4.40 [-2.66, 11.46]
Hinton 2007	10	136 (10)	10	131 (9)		1.2 %	5.00 [-3.34, 13.34]
Hoppe 2013	137.8333333 (14.25)	24	12	133 (13.5)		1.0 %	4.83 [-4.70, 14.36]
Jensen 1991	7	139 (3)	6	138 (6)		1.8 %	1.00 [-4.29, 6.29]
Kang 2004	11	122 (9)	14	123 (12)		1.2 %	-1.00 [-9.23, 7.23]
Klingshirn 1992	9	143.6 (12.8)	9	142.3 (11.1)		0.8 %	1.30 [-9.77, 12.37]
LaManca 1993	10	141 (6.32)	10	129 (12.64)		1.1 %	12.00 [3.24, 20.76]
Leonard 2014	16	135 (3.53)	8	131.6 (3.9)		2.4 %	3.40 [0.19, 6.61]
Li 1994	40	127 (12)	40	113 (14)		1.7 %	14.00 [8.29, 19.71]
Maghsudlu 2008	185	132.9 (8)	182	131.9 (8)		2.8 %	1.00 [-0.64, 2.64]
Marks 2014	129	134.6 (8.7)	128	130 (9.9)		2.7 %	4.60 [2.32, 6.88]
McClung 2009	85	130 (9)	86	128 (11)		2.5 %	2.00 [-1.01, 5.01]
Mujica-Coopman 2015	28	152 (9)	27	149 (7)		2.1 %	3.00 [-1.25, 7.25]
Murray-Kolb 2007	56	129.92 (10.04)	57	132.29 (12.42)		2.1 %	-2.37 [-6.53, 1.79]
Newhouse 1989	19	135 (5)	18	131 (5)		2.4 %	4.00 [0.78, 7.22]
Radjen 2011	19	124.78 (7.94)	18	110.61 (5.49)		2.1 %	14.17 [9.79, 18.55]
Rowland 1988	7	134 (3)	7	127 (4)		2.3 %	7.00 [3.30, 10.70]
Rybo 1985	45	137 (9)	44	133 (10)		2.2 %	4.00 [0.04, 7.96]
R svik 2010	82	129 (6)	79	128 (7)		2.7 %	1.00 [-1.02, 3.02]
Taniguchi 1991	27	121 (11)	27	108 (12.5)		1.6 %	13.00 [6.72, 19.28]
Viteri 1999	37	137.5 (9.2)	44	135.8 (11.8)		2.0 %	1.70 [-2.88, 6.28]
Waldvogel 2012	74	135 (6.7)	71	130 (5.3)		2.7 %	5.00 [3.04, 6.96]
Wang 2012	34	116.8 (16)	35	104.5 (12.9)		1.4 %	12.30 [5.43, 19.17]
Yadrick 1989	9	151 (6)	9	148 (15)		0.9 %	3.00 [-7.55, 13.55]
Yoshida 1990	6	133 (6)	6	137 (7)		1.3 %	-4.00 [-11.38, 3.38]
Zaman 2013	22	132.6 (7.4)	22	127.5 (8)		2.0 %	5.10 [0.55, 9.65]



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Study or subgroup	Iron N	Iron Mean(SD)	Control N	Control Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Zhu 1998	20	136.3 (8)	17	132.2 (7.6)		1.9 %	4.10 [-0.93, 9.13]
Subtotal (95% CI)	**2043**		**1598**			**75.3 %**	**4.69 [3.55, 5.83]**
Heterogeneity: Tau^2 = 7.27; Chi^2 = 155.67, df = 40 (P<0.00001); I^2 =74%							
Test for overall effect: Z = 8.07 (P < 0.00001)							
Total (95% CI)	**3635**		**3226**			**100.0 %**	**5.30 [4.14, 6.45]**
Heterogeneity: Tau^2 = 11.74; Chi^2 = 356.76, df = 50 (P<0.00001); I^2 =86%							
Test for overall effect: Z = 8.98 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 1.81, df = 1 (P = 0.18), I^2 =45%							

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Favours control Favours iron

Analysis 2.5. Comparison 2 Haemoglobin, Outcome 5 Haemoglobin (baseline Hb).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 2 Haemoglobin

Outcome: 5 Haemoglobin (baseline Hb)

Study or subgroup	Iron N	Iron Mean(SD)	Control N	Control Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Anaemic							
Florencio 1981	39	126.7 (6.8)	20	114.9 (5.8)		2.1 %	11.80 [8.48, 15.12]
Kianfar 2000	45	12 (1)	74	4 (8)		2.3 %	8.00 [6.15, 9.85]
Lanerolle 2000	51	129.3 (13.26)	57	119.86 (11.86)		1.8 %	9.44 [4.67, 14.21]
McClung 2009	18	122 (12)	17	116 (13)		1.1 %	6.00 [-2.30, 14.30]
Murray-Kolb 2007	56	129.92 (10.04)	57	132.29 (12.42)		1.9 %	-2.37 [-6.53, 1.79]
Radjen 2011	10	120.8 (7.77)	10	108.4 (3.92)		1.6 %	12.40 [7.01, 17.79]
Wang 2012	34	116.8 (16)	35	104.5 (12.9)		1.4 %	12.30 [5.43, 19.17]
Zavaleta 2000	20	123.7 (9.4)	15	110.4 (11)		1.3 %	13.30 [6.37, 20.23]

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Favours control Favours iron

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Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Subtotal (95% CI)	**273**		**285**			**13.5 %**	**8.67 [5.16, 12.18]**
Heterogeneity: Tau^2 = 18.64; Chi^2 = 35.67, df = 7 (P<0.00001); I^2 =80%							
Test for overall effect: Z = 4.84 (P < 0.00001)							
2 Non-anaemic							
Binkoski 2004	14	129 (16.84)	12	126 (16.97)		0.6 %	3.00 [-10.04, 16.04]
Booth 2014	25	135.8 (8.3)	24	136.8 (8.6)		1.8 %	-1.00 [-5.74, 3.74]
Bruner 1996	37	135 (8)	36	127 (7)		2.1 %	8.00 [4.55, 11.45]
Brutsaert 2003	10	139 (6.32)	10	134 (12.65)		1.1 %	5.00 [-3.76, 13.76]
DellaValle 2012	15	133 (6)	16	134 (8)		1.7 %	-1.00 [-5.96, 3.96]
Florencio 1981	42	120.8 (4.8)	17	126 (5.4)		2.2 %	-5.20 [-8.15, -2.25]
Fogelholm 1992	14	139 (12.15)	17	128 (10.8)		1.1 %	11.00 [2.82, 19.18]
Hinton 2000	22	135.2 (9.38)	19	130.8 (13.07)		1.3 %	4.40 [-2.66, 11.46]
Hinton 2007	10	136 (10)	10	131 (9)		1.1 %	5.00 [-3.34, 13.34]
Hoppe 2013	137.8333333 (14.25)		24	12	133 (13.5)	1.0 %	4.83 [-4.70, 14.36]
Jensen 1991	7	139 (3)	6	138 (6)		1.7 %	1.00 [-4.29, 6.29]
Kianfar 2000	47	3 (7)	74	0 (8)		2.2 %	3.00 [0.29, 5.71]
Klingshirn 1992	9	143.6 (12.8)	9	142.3 (11.1)		0.8 %	1.30 [-9.77, 12.37]
Lanerolle 2000	230	136.8 (9.15)	227	134.93 (8.37)		2.4 %	1.87 [0.26, 3.48]
Leonard 2014	16	135 (3.53)	8	131.6 (3.9)		2.1 %	3.40 [0.19, 6.61]
Maghsudlu 2008	185	132.9 (8)	182	131.9 (8)		2.4 %	1.00 [-0.64, 2.64]
McClung 2009	65	131 (6.5)	65	131.14 (7.28)		2.3 %	-0.14 [-2.51, 2.23]
Murray-Kolb 2007	17	125 (9)	13	121 (9)		1.4 %	4.00 [-2.50, 10.50]
Newhouse 1989	19	135 (5)	18	131 (5)		2.1 %	4.00 [0.78, 7.22]
Radjen 2011	9	129.22 (5.67)	8	113.38 (6.14)		1.6 %	15.84 [10.20, 21.48]
Rowland 1988	7	134 (3)	7	127 (4)		2.0 %	7.00 [3.30, 10.70]
R svik 2010	82	129 (6)	79	128 (7)		2.3 %	1.00 [-1.02, 3.02]
Waldvogel 2012	74	135 (6.7)	71	130 (5.3)		2.3 %	5.00 [3.04, 6.96]
Zavaleta 2000	81	130.9 (9.4)	82	127.9 (11)		2.1 %	3.00 [-0.14, 6.14]
Zhu 1998	20	136.3 (8)	17	132.2 (7.6)		1.7 %	4.10 [-0.93, 9.13]
Subtotal (95% CI)	**1081**		**1039**			**43.2 %**	**3.11 [1.67, 4.54]**
Heterogeneity: Tau^2 = 7.87; Chi^2 = 91.55, df = 24 (P<0.00001); I^2 =74%							
Test for overall effect: Z = 4.24 (P = 0.000023)							
3 Mixed/unstated							

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Favours control Favours iron

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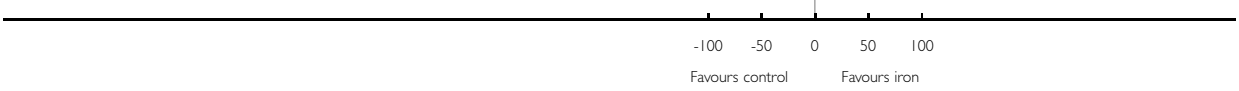
Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Agarwal 2003	699	123 (11)	691	116 (12)		2.4 %	7.00 [5.79, 8.21]
Berger 1997	65	191.7 (18.8)	65	184.9 (22.3)		1.3 %	6.80 [-0.29, 13.89]
Charoenlarp 1988	517	128.18 (11.81)	173	122.89 (14.06)		2.3 %	5.29 [2.96, 7.62]
Cooter 1978	5	130.75 (7.4)	5	130 (4.7)		1.2 %	0.75 [-6.93, 8.43]
Edgerton 1979	113	126.57 (12.7)	96	114.45 (20.17)		1.8 %	12.12 [7.45, 16.79]
Eftekhari 2006	47	142.5 (5.04)	47	129 (3.94)		2.3 %	13.50 [11.67, 15.33]
Elwood 1966	40	4 (1.5)	49	-1.6 (1.1)		2.5 %	5.60 [5.04, 6.16]
Fogelholm 1994	37	141.54 (14.32)	35	134 (14.47)		1.4 %	7.54 [0.89, 14.19]
Gordeuk 1987	34	125 (10.34)	19	126 (13.07)		1.4 %	-1.00 [-7.83, 5.83]
Gordeuk 1990	40	131 (8)	35	123 (9)		2.0 %	8.00 [4.12, 11.88]
Jayatissa 1999	222	132 (9)	217	131 (11)		2.3 %	1.00 [-0.88, 2.88]
Kanani 2000	91	126.1 (7.63)	89	108.22 (10.38)		2.2 %	17.88 [15.21, 20.55]
Kang 2004	11	122 (9)	14	123 (12)		1.1 %	-1.00 [-9.23, 7.23]
LaManca 1993	10	141 (6.32)	10	129 (12.64)		1.1 %	12.00 [3.24, 20.76]
Larocque 2006	12	137.5 (7.41)	9	136.56 (7.53)		1.4 %	0.94 [-5.52, 7.40]
Li 1994	40	127 (12)	40	113 (14)		1.6 %	14.00 [8.29, 19.71]
Marks 2014	129	134.6 (8.7)	128	130 (9.9)		2.3 %	4.60 [2.32, 6.88]
Mujica-Coopman 2015	28	152 (9)	27	149 (7)		1.9 %	3.00 [-1.25, 7.25]
Rybo 1985	45	137 (9)	44	133 (10)		1.9 %	4.00 [0.04, 7.96]
Taniguchi 1991	27	121 (11)	27	108 (12.5)		1.5 %	13.00 [6.72, 19.28]
Viteri 1999	37	137.5 (9.2)	44	135.8 (11.8)		1.8 %	1.70 [-2.88, 6.28]
Walsh 1989	10	136 (6)	10	129 (6)		1.7 %	7.00 [1.74, 12.26]
Yadrick 1989	9	151 (6)	9	148 (15)		0.8 %	3.00 [-7.55, 13.55]
Yoshida 1990	6	133 (6)	6	137 (7)		1.3 %	-4.00 [-11.38, 3.38]
Zaman 2013	22	132.6 (7.4)	22	127.5 (8)		1.8 %	5.10 [0.55, 9.65]
Subtotal (95% CI)	**2296**		**1911**			**43.2 %**	**6.30 [4.52, 8.08]**
Heterogeneity: Tau^2 = 14.23; Chi^2 = 220.14, df = 24 (P<0.00001); I^2 =89%							
Test for overall effect: Z = 6.93 (P < 0.00001)							
Total (95% CI)	**3650**		**3235**			**100.0 %**	**5.30 [4.11, 6.48]**
Heterogeneity: Tau^2 = 14.69; Chi^2 = 465.64, df = 57 (P<0.00001); I^2 =88%							
Test for overall effect: Z = 8.77 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 12.73, df = 2 (P = 0.00), I^2 =84%							



Analysis 2.6. Comparison 2 Haemoglobin, Outcome 6 Haemoglobin (iron status).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 2 Haemoglobin

Outcome: 6 Haemoglobin (iron status)

Study or subgroup	Iron		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
1 Iron deficient							
Binkoski 2004	14	129 (16.84)	12	126 (16.97)		0.6 %	3.00 [-10.04, 16.04]
Bruner 1996	37	135 (8)	36	127 (7)		2.2 %	8.00 [4.55, 11.45]
Brutsaert 2003	10	139 (6.32)	10	134 (12.65)		1.1 %	5.00 [-3.76, 13.76]
DellaValle 2012	8	134 (8)	8	132 (7)		1.3 %	2.00 [-5.37, 9.37]
Eftekhari 2006	47	142.5 (5.04)	47	129 (3.94)		2.6 %	13.50 [11.67, 15.33]
Fogelholm 1992	14	139 (12.15)	17	128 (10.8)		1.2 %	11.00 [2.82, 19.18]
Fogelholm 1994	37	141.54 (14.32)	35	134 (14.47)		1.4 %	7.54 [0.89, 14.19]
Hinton 2000	22	135.2 (9.38)	19	130.8 (13.07)		1.4 %	4.40 [-2.66, 11.46]
Hinton 2007	10	136 (10)	10	131 (9)		1.1 %	5.00 [-3.34, 13.34]
Klingshirn 1992	9	143.6 (12.8)	9	142.3 (11.1)		0.8 %	1.30 [-9.77, 12.37]
LaManca 1993	10	141 (6.32)	10	129 (12.64)		1.1 %	12.00 [3.24, 20.76]
Leonard 2014	16	135 (3.53)	8	131.6 (3.9)		2.3 %	3.40 [0.19, 6.61]
Marks 2014	73	134.4 (8.4)	71	127.1 (10.1)		2.3 %	7.30 [4.26, 10.34]
McClung 2009	32	126.81 (11.17)	31	121.41 (12.17)		1.6 %	5.40 [-0.37, 11.17]
Murray-Kolb 2007	42	128.6 (8.8)	41	128.5 (10.89)		2.0 %	0.10 [-4.17, 4.37]
Newhouse 1989	19	135 (5)	18	131 (5)		2.3 %	4.00 [0.78, 7.22]
Radjen 2011	19	124.78 (7.94)	18	110.61 (5.49)		2.0 %	14.17 [9.79, 18.55]
Taniguchi 1991	27	121 (11)	27	108 (12.5)		1.5 %	13.00 [6.72, 19.28]
Waldvogel 2012	74	135 (6.7)	71	130 (5.3)		2.6 %	5.00 [3.04, 6.96]
Wang 2012	34	116.8 (16)	35	104.5 (12.9)		1.4 %	12.30 [5.43, 19.17]
Zhu 1998	20	136.3 (8)	17	132.2 (7.6)		1.8 %	4.10 [-0.93, 9.13]

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Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Subtotal (95% CI)	**574**		**550**			**34.7 %**	**6.92 [4.76, 9.09]**
Heterogeneity: Tau^2 = 16.63; Chi^2 = 92.81, df = 20 (P<0.00001); I^2 =78%							
Test for overall effect: Z = 6.27 (P < 0.00001)							
2 Not iron deficient							
Marks 2014	56	134.5 (10.3)	57	133.5 (8.6)		2.2 %	1.00 [-2.50, 4.50]
McClung 2009	52	131 (7)	51	132 (7)		2.4 %	-1.00 [-3.70, 1.70]
Murray-Kolb 2007	14	134 (11)	16	142 (11)		1.2 %	-8.00 [-15.89, -0.11]
Rowland 1988	7	134 (3)	7	127 (4)		2.2 %	7.00 [3.30, 10.70]
R svik 2010	82	129 (6)	79	128 (7)		2.6 %	1.00 [-1.02, 3.02]
Subtotal (95% CI)	**211**		**210**			**10.6 %**	**0.84 [-2.26, 3.95]**
Heterogeneity: Tau^2 = 8.84; Chi^2 = 17.18, df = 4 (P = 0.002); I^2 =77%							
Test for overall effect: Z = 0.53 (P = 0.59)							
3 Mixed/unstated							
Agarwal 2003	699	123 (11)	691	116 (12)		2.7 %	7.00 [5.79, 8.21]
Berger 1997	65	191.7 (18.8)	65	184.9 (22.3)		1.4 %	6.80 [-0.29, 13.89]
Booth 2014	25	135.8 (8.3)	24	136.8 (8.6)		1.9 %	-1.00 [-5.74, 3.74]
Charoenlarp 1988	517	128.18 (11.81)	173	122.89 (14.06)		2.5 %	5.29 [2.96, 7.62]
Cooter 1978	5	130.75 (7.4)	5	130 (4.7)		1.2 %	0.75 [-6.93, 8.43]
Edgerton 1979	113	126.57 (12.7)	96	114.45 (20.17)		1.9 %	12.12 [7.45, 16.79]
Elwood 1966	40	4 (1.5)	49	-1.6 (1.1)		2.8 %	5.60 [5.04, 6.16]
Florencio 1981	81	128.8 (5.8)	37	120 (5.6)		2.5 %	8.80 [6.60, 11.00]
Gordeuk 1987	34	125 (10.34)	19	126 (13.07)		1.4 %	-1.00 [-7.83, 5.83]
Gordeuk 1990	40	131 (8)	35	123 (9)		2.1 %	8.00 [4.12, 11.88]
Hoppe 2013	137.8333333 (14.25)		24	12	133 (13.5)	1.0 %	4.83 [-4.70, 14.36]
Jayatissa 1999	222	132 (9)	217	131 (11)		2.6 %	1.00 [-0.88, 2.88]
Jensen 1991	7	139 (3)	6	138 (6)		1.8 %	1.00 [-4.29, 6.29]
Kanani 2000	91	126.1 (7.63)	89	108.22 (10.38)		2.4 %	17.88 [15.21, 20.55]
Kang 2004	11	122 (9)	14	123 (12)		1.2 %	-1.00 [-9.23, 7.23]
Kianfar 2000	92	7.4 (6.76)	148	2 (8.22)		2.6 %	5.40 [3.49, 7.31]
Lanerolle 2000	281	135.42 (10.42)	284	131.95 (10.95)		2.6 %	3.47 [1.71, 5.23]
Larocque 2006	12	137.5 (7.41)	9	136.56 (7.53)		1.5 %	0.94 [-5.52, 7.40]
Li 1994	40	127 (12)	40	113 (14)		1.7 %	14.00 [8.29, 19.71]
Maghsudlu 2008	185	132.9 (8)	182	131.9 (8)		2.6 %	1.00 [-0.64, 2.64]

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Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Mujica-Coopman 2015	28	152 (9)	27	149 (7)		2.0 %	3.00 [-1.25, 7.25]
Rybo 1985	45	137 (9)	44	133 (10)		2.1 %	4.00 [0.04, 7.96]
Viteri 1999	37	137.5 (9.2)	44	135.8 (11.8)		1.9 %	1.70 [-2.88, 6.28]
Walsh 1989	10	136 (6)	10	129 (6)		1.8 %	7.00 [1.74, 12.26]
Yadrick 1989	9	151 (6)	9	148 (15)		0.8 %	3.00 [-7.55, 13.55]
Yoshida 1990	6	133 (6)	6	137 (7)		1.3 %	-4.00 [-11.38, 3.38]
Zaman 2013	22	132.6 (7.4)	22	127.5 (8)		1.9 %	5.10 [0.55, 9.65]
Zavaleta 2000	101	129.47 (9.4)	97	125.19 (11)		2.4 %	4.28 [1.42, 7.14]
Subtotal (95% CI)	**2842**		**2454**			**54.7 %**	**4.92 [3.49, 6.35]**
Heterogeneity: Tau^2 = 9.85; Chi^2 = 202.66, df = 27 (P<0.00001); I^2 =87%							
Test for overall effect: Z = 6.74 (P < 0.00001)							
Total (95% CI)	**3627**		**3214**			**100.0 %**	**5.15 [4.00, 6.30]**
Heterogeneity: Tau^2 = 12.37; Chi^2 = 378.71, df = 53 (P<0.00001); I^2 =86%							
Test for overall effect: Z = 8.76 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 9.90, df = 2 (P = 0.01), I^2 =80%							

Analysis 2.7. Comparison 2 Haemoglobin, Outcome 7 Haemoglobin (iron-deficiency anaemia).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 2 Haemoglobin

Outcome: 7 Haemoglobin (iron-deficiency anaemia)

Study or subgroup	Iron		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
1 Iron-deficiency anaemia							
McClung 2009	18	122 (12)	17	116 (13)		1.1 %	6.00 [-2.30, 14.30]
Murray-Kolb 2007	17	125 (9)	13	121 (9)		1.5 %	4.00 [-2.50, 10.50]
Radjen 2011	10	120.8 (7.77)	10	108.4 (3.92)		1.7 %	12.40 [7.01, 17.79]
Wang 2012	34	116.8 (16)	35	104.5 (12.9)		1.4 %	12.30 [5.43, 19.17]
Subtotal (95% CI)	**79**		**75**			**5.6 %**	**9.01 [4.64, 13.37]**
Heterogeneity: $Tau^2 = 8.26$; $Chi^2 = 5.16$, df = 3 (P = 0.16); $I^2 = 42\%$							
Test for overall effect: Z = 4.05 (P = 0.000052)							
2 Iron deficient, not anaemic							
Binkoski 2004	14	129 (16.84)	12	126 (16.97)		0.6 %	3.00 [-10.04, 16.04]
Bruner 1996	37	135 (8)	36	127 (7)		2.2 %	8.00 [4.55, 11.45]
Brutsaert 2003	10	139 (6.32)	10	134 (12.65)		1.0 %	5.00 [-3.76, 13.76]
DellaValle 2012	8	134 (8)	8	132 (7)		1.3 %	2.00 [-5.37, 9.37]
Fogelholm 1992	14	139 (12.15)	17	128 (10.8)		1.1 %	11.00 [2.82, 19.18]
Hinton 2000	22	135.2 (9.38)	19	130.8 (13.07)		1.3 %	4.40 [-2.66, 11.46]
Hinton 2007	10	136 (10)	10	131 (9)		1.1 %	5.00 [-3.34, 13.34]
Klingshirn 1992	9	143.6 (12.8)	9	142.3 (11.1)		0.8 %	1.30 [-9.77, 12.37]
Leonard 2014	16	135 (3.53)	8	131.6 (3.9)		2.3 %	3.40 [0.19, 6.61]
McClung 2009	14	133 (6)	14	128 (7)		1.9 %	5.00 [0.17, 9.83]
Murray-Kolb 2007	25	131 (8)	28	132 (10)		1.8 %	-1.00 [-5.85, 3.85]
Newhouse 1989	19	135 (5)	18	131 (5)		2.3 %	4.00 [0.78, 7.22]
Radjen 2011	9	129.22 (5.67)	8	113.38 (6.14)		1.6 %	15.84 [10.20, 21.48]
Waldvogel 2012	74	135 (6.7)	71	130 (5.3)		2.6 %	5.00 [3.04, 6.96]
Zhu 1998	20	136.3 (8)	17	132.2 (7.6)		1.8 %	4.10 [-0.93, 9.13]
Subtotal (95% CI)	**301**		**285**			**23.8 %**	**5.15 [3.30, 6.99]**
Heterogeneity: $Tau^2 = 5.39$; $Chi^2 = 27.66$, df = 14 (P = 0.02); $I^2 = 49\%$							
Test for overall effect: Z = 5.47 (P < 0.00001)							

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Study or subgroup	Iron N	Iron Mean(SD)	Control N	Control Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
3 Not iron deficient, not anaemic							
McClung 2009	52	131 (7)	51	132 (7)		2.4 %	-1.00 [-3.70, 1.70]
Rowland 1988	7	134 (3)	7	127 (4)		2.2 %	7.00 [3.30, 10.70]
R svik 2010	82	129 (6)	79	128 (7)		2.6 %	1.00 [-1.02, 3.02]
Subtotal (95% CI)	**141**		**137**			**7.2 %**	**2.10 [-1.77, 5.97]**
Heterogeneity: Tau² = 9.60; Chi² = 11.96, df = 2 (P = 0.003); I² =83%							
Test for overall effect: Z = 1.06 (P = 0.29)							
4 Mixed/unstated							
Agarwal 2003	699	123 (11)	691	116 (12)		2.7 %	7.00 [5.79, 8.21]
Berger 1997	65	191.7 (18.8)	65	184.9 (22.3)		1.3 %	6.80 [-0.29, 13.89]
Booth 2014	25	135.8 (8.3)	24	136.8 (8.6)		1.9 %	-1.00 [-5.74, 3.74]
Charoenlarp 1988	517	128.18 (11.81)	173	122.89 (14.06)		2.5 %	5.29 [2.96, 7.62]
Cooter 1978	5	130.75 (7.4)	5	130 (4.7)		1.2 %	0.75 [-6.93, 8.43]
Edgerton 1979	113	126.57 (12.7)	96	114.45 (20.17)		1.9 %	12.12 [7.45, 16.79]
Eftekhari 2006	47	142.5 (5.04)	47	129 (3.94)		2.6 %	13.50 [11.67, 15.33]
Elwood 1966	40	4 (1.5)	49	-1.6 (1.1)		2.8 %	5.60 [5.04, 6.16]
Florencio 1981	81	128.8 (5.8)	37	120 (5.6)		2.5 %	8.80 [6.60, 11.00]
Fogelholm 1994	37	141.54 (14.32)	35	134 (14.47)		1.4 %	7.54 [0.89, 14.19]
Gordeuk 1987	34	125 (10.34)	19	126 (13.07)		1.4 %	-1.00 [-7.83, 5.83]
Gordeuk 1990	40	131 (8)	35	123 (9)		2.1 %	8.00 [4.12, 11.88]
Hoppe 2013	137.8333333 (14.25)		24	12	133 (13.5)	0.9 %	4.83 [-4.70, 14.36]
Jayatissa 1999	222	132 (9)	217	131 (11)		2.6 %	1.00 [-0.88, 2.88]
Jensen 1991	7	139 (3)	6	138 (6)		1.7 %	1.00 [-4.29, 6.29]
Kanani 2000	91	126.1 (7.63)	89	108.22 (10.38)		2.4 %	17.88 [15.21, 20.55]
Kang 2004	11	122 (9)	14	123 (12)		1.1 %	-1.00 [-9.23, 7.23]
Kianfar 2000	92	7.4 (6.76)	148	2 (8.22)		2.6 %	5.40 [3.49, 7.31]
LaManca 1993	10	141 (6.32)	10	129 (12.64)		1.0 %	12.00 [3.24, 20.76]
Lanerolle 2000	281	135.42 (10.42)	284	131.95 (10.95)		2.6 %	3.47 [1.71, 5.23]
Larocque 2006	12	137.5 (7.41)	9	136.56 (7.53)		1.5 %	0.94 [-5.52, 7.40]
Li 1994	40	127 (12)	40	113 (14)		1.6 %	14.00 [8.29, 19.71]
Maghsudlu 2008	185	132.9 (8)	182	131.9 (8)		2.7 %	1.00 [-0.64, 2.64]
Marks 2014	129	134.6 (8.7)	128	130 (9.9)		2.5 %	4.60 [2.32, 6.88]

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Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Mujica-Coopman 2015	28	152 (9)	27	149 (7)		2.0 %	3.00 [-1.25, 7.25]
Rybo 1985	45	137 (9)	44	133 (10)		2.1 %	4.00 [0.04, 7.96]
Taniguchi 1991	27	121 (11)	27	108 (12.5)		1.5 %	13.00 [6.72, 19.28]
Viteri 1999	37	137.5 (9.2)	44	135.8 (11.8)		1.9 %	1.70 [-2.88, 6.28]
Walsh 1989	10	136 (6)	10	129 (6)		1.7 %	7.00 [1.74, 12.26]
Yadrick 1989	9	151 (6)	9	148 (15)		0.8 %	3.00 [-7.55, 13.55]
Yoshida 1990	6	133 (6)	6	137 (7)		1.3 %	-4.00 [-11.38, 3.38]
Zaman 2013	22	132.6 (7.4)	22	127.5 (8)		1.9 %	5.10 [0.55, 9.65]
Zavaleta 2000	101	129.47 (9.4)	97	125.19 (11)		2.4 %	4.28 [1.42, 7.14]
Subtotal (95% CI)	**3092**		**2701**			**63.4 %**	**5.59 [4.15, 7.03]**
Heterogeneity: Tau^2 = 12.30; Chi^2 = 283.30, df = 32 (P<0.00001); I^2 =89%							
Test for overall effect: Z = 7.61 (P < 0.00001)							
Total (95% CI)	**3613**		**3198**			**100.0 %**	**5.44 [4.31, 6.56]**
Heterogeneity: Tau^2 = 11.76; Chi^2 = 365.57, df = 54 (P<0.00001); I^2 =85%							
Test for overall effect: Z = 9.46 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 5.56, df = 3 (P = 0.13), I^2 =46%							

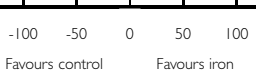
Analysis 2.8. Comparison 2 Haemoglobin, Outcome 8 Haemoglobin (dose).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 2 Haemoglobin

Outcome: 8 Haemoglobin (dose)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 < 30 mg							
Berger 1997	65	191.7 (18.8)	65	184.9 (22.3)		1.4 %	6.80 [-0.29, 13.89]
Booth 2014	25	135.8 (8.3)	24	136.8 (8.6)		1.9 %	-1.00 [-5.74, 3.74]
Brutsaert 2003	10	139 (6.32)	10	134 (12.65)		1.1 %	5.00 [-3.76, 13.76]
Cooter 1978	5	130.75 (7.4)	5	130 (4.7)		1.3 %	0.75 [-6.93, 8.43]
Fogelholm 1994	37	141.54 (14.32)	35	134 (14.47)		1.5 %	7.54 [0.89, 14.19]
Hinton 2000	22	135.2 (9.38)	19	130.8 (13.07)		1.4 %	4.40 [-2.66, 11.46]
Hinton 2007	10	136 (10)	10	131 (9)		1.1 %	5.00 [-3.34, 13.34]
Larocque 2006	12	137.5 (7.41)	9	136.56 (7.53)		1.5 %	0.94 [-5.52, 7.40]
Rybo 1985	45	137 (9)	44	133 (10)		2.2 %	4.00 [0.04, 7.96]
Taniguchi 1991	27	121 (11)	27	108 (12.5)		1.6 %	13.00 [6.72, 19.28]
Viteri 1999	37	137.5 (9.2)	44	135.8 (11.8)		2.0 %	1.70 [-2.88, 6.28]
Wang 2012	34	116.8 (16)	35	104.5 (12.9)		1.4 %	12.30 [5.43, 19.17]
Yadrick 1989	9	151 (6)	9	148 (15)		0.8 %	3.00 [-7.55, 13.55]
Zavaleta 2000	101	129.47 (9.4)	97	125.19 (11)		2.5 %	4.28 [1.42, 7.14]
Subtotal (95% CI)	**439**		**433**			**21.6 %**	**4.56 [2.50, 6.63]**
Heterogeneity: $Tau^2 = 5.77$; $Chi^2 = 22.01$, df = 13 (P = 0.06); $I^2 = 41\%$							
Test for overall effect: Z = 4.34 (P = 0.000014)							
2 31 to 60 mg							
Edgerton 1979	113	126.57 (12.7)	96	114.45 (20.17)		2.0 %	12.12 [7.45, 16.79]
Eftekhari 2006	47	142.5 (5.04)	47	129 (3.94)		2.7 %	13.50 [11.67, 15.33]
Hoppe 2013	137.8333333 (14.25)		24	12	133 (13.5)	1.0 %	4.83 [-4.70, 14.36]
Jayatissa 1999	222	132 (9)	217	131 (11)		2.7 %	1.00 [-0.88, 2.88]
Jensen 1991	7	139 (3)	6	138 (6)		1.8 %	1.00 [-4.29, 6.29]
Kanani 2000	91	126.1 (7.63)	89	108.22 (10.38)		2.5 %	17.88 [15.21, 20.55]
Kang 2004	11	122 (9)	14	123 (12)		1.2 %	-1.00 [-9.23, 7.23]



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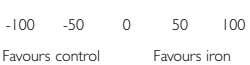
Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Kianfar 2000	92	7.4 (6.76)	148	2 (8.22)		2.7 %	5.40 [3.49, 7.31]
Klingshirn 1992	9	143.6 (12.8)	9	142.3 (11.1)		0.8 %	1.30 [-9.77, 12.37]
Lanerolle 2000	281	135.42 (10.42)	284	131.95 (10.95)		2.7 %	3.47 [1.71, 5.23]
Leonard 2014	8	133.7 (2.3)	4	131.6 (3.9)		2.1 %	2.10 [-2.04, 6.24]
Li 1994	40	127 (12)	40	113 (14)		1.7 %	14.00 [8.29, 19.71]
Marks 2014	129	134.6 (8.7)	128	130 (9.9)		2.6 %	4.60 [2.32, 6.88]
McClung 2009	85	130 (9)	86	128 (11)		2.4 %	2.00 [-1.01, 5.01]
Mujica-Coopman 2015	28	152 (9)	27	149 (7)		2.1 %	3.00 [-1.25, 7.25]
Murray-Kolb 2007	56	129.92 (10.04)	57	132.29 (12.42)		2.1 %	-2.37 [-6.53, 1.79]
Yoshida 1990	6	133 (6)	6	137 (7)		1.3 %	-4.00 [-11.38, 3.38]
Zaman 2013	22	132.6 (7.4)	22	127.5 (8)		2.0 %	5.10 [0.55, 9.65]
Zhu 1998	20	136.3 (8)	17	132.2 (7.6)		1.9 %	4.10 [-0.93, 9.13]
Subtotal (95% CI)	**1291**		**1309**			**38.3 %**	**4.93 [2.20, 7.66]**
Heterogeneity: Tau^2 = 30.74; Chi^2 = 234.16, df = 18 (P<0.00001); I^2 =92%							
Test for overall effect: Z = 3.53 (P = 0.00041)							
3 61 mg to 100 mg							
Agarwal 2003	699	123 (11)	691	116 (12)		2.8 %	7.00 [5.79, 8.21]
Binkoski 2004	14	129 (16.84)	12	126 (16.97)		0.6 %	3.00 [-10.04, 16.04]
Fogelholm 1992	14	139 (12.15)	17	128 (10.8)		1.2 %	11.00 [2.82, 19.18]
Gordeuk 1990	40	131 (8)	35	123 (9)		2.2 %	8.00 [4.12, 11.88]
LaManca 1993	10	141 (6.32)	10	129 (12.64)		1.1 %	12.00 [3.24, 20.76]
Leonard 2014	8	136.3 (4.2)	4	131.6 (3.9)		1.9 %	4.70 [-0.10, 9.50]
Radjen 2011	19	124.78 (7.94)	18	110.61 (5.49)		2.0 %	14.17 [9.79, 18.55]
R svik 2010	82	129 (6)	79	128 (7)		2.7 %	1.00 [-1.02, 3.02]
Waldvogel 2012	74	135 (6.7)	71	130 (5.3)		2.7 %	5.00 [3.04, 6.96]
Subtotal (95% CI)	**960**		**937**			**17.2 %**	**6.87 [4.24, 9.49]**
Heterogeneity: Tau^2 = 10.23; Chi^2 = 45.26, df = 8 (P<0.00001); I^2 =82%							
Test for overall effect: Z = 5.13 (P < 0.00001)							
4 > 100 mg							
Bruner 1996	37	135 (8)	36	127 (7)		2.3 %	8.00 [4.55, 11.45]
Charoenlarp 1988	517	128.18 (11.81)	173	122.89 (14.06)		2.6 %	5.29 [2.96, 7.62]
DellaValle 2012	15	133 (6)	16	134 (8)		1.9 %	-1.00 [-5.96, 3.96]
Elwood 1966	40	4 (1.5)	49	-1.6 (1.1)		2.9 %	5.60 [5.04, 6.16]



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Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Florencio 1981	81	128.8 (5.8)	37	120 (5.6)		2.6 %	8.80 [6.60, 11.00]
Gordeuk 1987	34	125 (10.34)	19	126 (13.07)		1.4 %	-1.00 [-7.83, 5.83]
Maghsudlu 2008	185	132.9 (8)	182	131.9 (8)		2.8 %	1.00 [-0.64, 2.64]
Newhouse 1989	19	135 (5)	18	131 (5)		2.4 %	4.00 [0.78, 7.22]
Rowland 1988	7	134 (3)	7	127 (4)		2.2 %	7.00 [3.30, 10.70]
Walsh 1989	10	136 (6)	10	129 (6)		1.8 %	7.00 [1.74, 12.26]
Subtotal (95% CI)	**945**		**547**			**22.9 %**	**4.85 [3.03, 6.67]**
Heterogeneity: Tau^2 = 5.79; Chi^2 = 50.98, df = 9 (P<0.00001); I^2 =82%							
Test for overall effect: Z = 5.22 (P < 0.00001)							
Total (95% CI)	**3635**		**3226**			**100.0 %**	**5.26 [4.12, 6.41]**
Heterogeneity: Tau^2 = 11.73; Chi^2 = 357.81, df = 51 (P<0.00001); I^2 =86%							
Test for overall effect: Z = 9.00 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 2.09, df = 3 (P = 0.55), I^2 =0.0%							

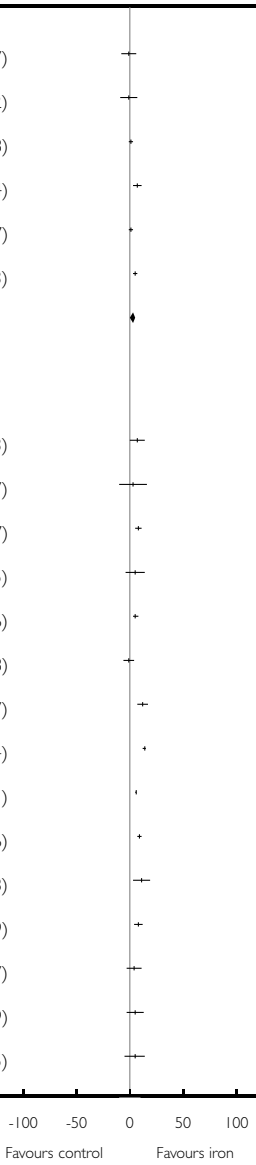
Analysis 2.9. Comparison 2 Haemoglobin, Outcome 9 Haemoglobin (duration).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 2 Haemoglobin

Outcome: 9 Haemoglobin (duration)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 < 30 days (1 month)							
Gordeuk 1987	34	125 (10.34)	19	126 (13.07)		1.5 %	-1.00 [-7.83, 5.83]
Kang 2004	11	122 (9)	14	123 (12)		1.2 %	-1.00 [-9.23, 7.23]
Maghsudlu 2008	185	132.9 (8)	182	131.9 (8)		2.8 %	1.00 [-0.64, 2.64]
Rowland 1988	7	134 (3)	7	127 (4)		2.3 %	7.00 [3.30, 10.70]
R svik 2010	82	129 (6)	79	128 (7)		2.7 %	1.00 [-1.02, 3.02]
Waldvogel 2012	74	135 (6.7)	71	130 (5.3)		2.7 %	5.00 [3.04, 6.96]
Subtotal (95% CI)	**393**		**372**			**13.2 %**	**2.60 [0.28, 4.91]**
Heterogeneity: $Tau^2 = 5.10$; $Chi^2 = 18.94$, df = 5 (P = 0.002); $I^2 = 74\%$							
Test for overall effect: Z = 2.20 (P = 0.028)							
2 1 to 3 months							
Berger 1997	65	191.7 (18.8)	65	184.9 (22.3)		1.4 %	6.80 [-0.29, 13.89]
Binkoski 2004	14	129 (16.84)	12	126 (16.97)		0.6 %	3.00 [-10.04, 16.04]
Bruner 1996	37	135 (8)	36	127 (7)		2.3 %	8.00 [4.55, 11.45]
Brutsaert 2003	10	139 (6.32)	10	134 (12.65)		1.1 %	5.00 [-3.76, 13.76]
Charoenlarp 1988	517	128.18 (11.81)	173	122.89 (14.06)		2.6 %	5.29 [2.96, 7.62]
DellaValle 2012	15	133 (6)	16	134 (8)		1.9 %	-1.00 [-5.96, 3.96]
Edgerton 1979	113	126.57 (12.7)	96	114.45 (20.17)		2.0 %	12.12 [7.45, 16.79]
Eftekhari 2006	47	142.5 (5.04)	47	129 (3.94)		2.8 %	13.50 [11.67, 15.33]
Elwood 1966	40	4 (1.5)	49	-1.6 (1.1)		2.9 %	5.60 [5.04, 6.16]
Florencio 1981	81	128.8 (5.8)	37	120 (5.6)		2.7 %	8.80 [6.60, 11.00]
Fogelholm 1992	14	139 (12.15)	17	128 (10.8)		1.2 %	11.00 [2.82, 19.18]
Gordeuk 1990	40	131 (8)	35	123 (9)		2.2 %	8.00 [4.12, 11.88]
Hinton 2000	22	135.2 (9.38)	19	130.8 (13.07)		1.4 %	4.40 [-2.66, 11.46]
Hinton 2007	10	136 (10)	10	131 (9)		1.2 %	5.00 [-3.34, 13.34]
Hoppe 2013	137.8333333 (14.25)		24	12	133 (13.5)		1.0 %	4.83 [-4.70, 14.36]



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Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Jayatissa 1999	222	132 (9)	217	131 (11)		2.7 %	1.00 [-0.88, 2.88]
Jensen 1991	7	139 (3)	6	138 (6)		1.8 %	1.00 [-4.29, 6.29]
Kanani 2000	91	126.1 (7.63)	89	108.22 (10.38)		2.6 %	17.88 [15.21, 20.55]
Kianfar 2000	92	7.4 (6.76)	148	2 (8.22)		2.7 %	5.40 [3.49, 7.31]
Klingshirn 1992	9	143.6 (12.8)	9	142.3 (11.1)		0.8 %	1.30 [-9.77, 12.37]
LaManca 1993	10	141 (6.32)	10	129 (12.64)		1.1 %	12.00 [3.24, 20.76]
Lanerolle 2000	281	135.42 (10.42)	284	131.95 (10.95)		2.8 %	3.47 [1.71, 5.23]
Larocque 2006	12	137.5 (7.41)	9	136.56 (7.53)		1.5 %	0.94 [-5.52, 7.40]
Li 1994	40	127 (12)	40	113 (14)		1.7 %	14.00 [8.29, 19.71]
Marks 2014	129	134.6 (8.7)	128	130 (9.9)		2.7 %	4.60 [2.32, 6.88]
McClung 2009	85	130 (9)	86	128 (11)		2.5 %	2.00 [-1.01, 5.01]
Mujica-Coopman 2015	28	152 (9)	27	149 (7)		2.1 %	3.00 [-1.25, 7.25]
Newhouse 1989	19	135 (5)	18	131 (5)		2.4 %	4.00 [0.78, 7.22]
Radjen 2011	19	124.78 (7.94)	18	110.61 (5.49)		2.1 %	14.17 [9.79, 18.55]
Rybo 1985	45	137 (9)	44	133 (10)		2.2 %	4.00 [0.04, 7.96]
Taniguchi 1991	27	121 (11)	27	108 (12.5)		1.6 %	13.00 [6.72, 19.28]
Viteri 1999	37	137.5 (9.2)	44	135.8 (11.8)		2.0 %	1.70 [-2.88, 6.28]
Walsh 1989	10	136 (6)	10	129 (6)		1.8 %	7.00 [1.74, 12.26]
Yadrick 1989	9	151 (6)	9	148 (15)		0.9 %	3.00 [-7.55, 13.55]
Yoshida 1990	6	133 (6)	6	137 (7)		1.3 %	-4.00 [-11.38, 3.38]
Zaman 2013	22	132.6 (7.4)	22	127.5 (8)		2.0 %	5.10 [0.55, 9.65]
Zhu 1998	20	136.3 (8)	17	132.2 (7.6)		1.9 %	4.10 [-0.93, 9.13]
Subtotal (95% CI)	**2269**		**1902**			**70.7 %**	**6.14 [4.70, 7.58]**
Heterogeneity: Tau^2 = 13.34; Chi^2 = 261.58, df = 36 (P<0.00001); I^2 =86%							
Test for overall effect: Z = 8.36 (P < 0.00001)							
3 > 3 months							
Agarwal 2003	699	123 (11)	691	116 (12)		2.9 %	7.00 [5.79, 8.21]
Booth 2014	25	135.8 (8.3)	24	136.8 (8.6)		2.0 %	-1.00 [-5.74, 3.74]
Cooter 1978	5	130.75 (7.4)	5	130 (4.7)		1.3 %	0.75 [-6.93, 8.43]
Fogelholm 1994	37	141.54 (14.32)	35	134 (14.47)		1.5 %	7.54 [0.89, 14.19]
Leonard 2014	16	135 (3.53)	8	131.6 (3.9)		2.4 %	3.40 [0.19, 6.61]
Murray-Kolb 2007	56	129.92 (10.04)	57	132.29 (12.42)		2.1 %	-2.37 [-6.53, 1.79]

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Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Wang 2012	34	116.8 (16)	35	104.5 (12.9)		1.4 %	12.30 [5.43, 19.17]
Zavaleta 2000	101	129.47 (9.4)	97	125.19 (11)		2.5 %	4.28 [1.42, 7.14]
Subtotal (95% CI)	**973**		**952**			**16.1 %**	**3.84 [0.94, 6.75]**
Heterogeneity: Tau^2 = 12.09; Chi^2 = 34.82, df = 7 (P = 0.00001); I^2 =80%							
Test for overall effect: Z = 2.59 (P = 0.0096)							
Total (95% CI)	**3635**		**3226**			**100.0 %**	**5.30 [4.14, 6.45]**
Heterogeneity: Tau^2 = 11.74; Chi^2 = 356.76, df = 50 (P<0.00001); I^2 =86%							
Test for overall effect: Z = 8.98 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 7.15, df = 2 (P = 0.03), I^2 =72%							

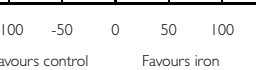
Analysis 2.10. Comparison 2 Haemoglobin, Outcome 10 Haemoglobin (type of iron).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 2 Haemoglobin

Outcome: 10 Haemoglobin (type of iron)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Ferrous sulphate							
Binkoski 2004	14	129 (16.84)	12	126 (16.97)		0.7 %	3.00 [-10.04, 16.04]
Bruner 1996	37	135 (8)	36	127 (7)		2.6 %	8.00 [4.55, 11.45]
DellaValle 2012	15	133 (6)	16	134 (8)		2.1 %	-1.00 [-5.96, 3.96]
Edgerton 1979	113	126.57 (12.7)	96	114.45 (20.17)		2.2 %	12.12 [7.45, 16.79]
Eftekhari 2006	47	142.5 (5.04)	47	129 (3.94)		3.0 %	13.50 [11.67, 15.33]
Florencio 1981	81	128.8 (5.8)	37	120 (5.6)		2.9 %	8.80 [6.60, 11.00]
Fogelholm 1992	14	139 (12.15)	17	128 (10.8)		1.3 %	11.00 [2.82, 19.18]



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Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Gordeuk 1987	17	125 (8.25)	9	126 (13.07)		1.1 %	-1.00 [-10.40, 8.40]
Hinton 2000	22	135.2 (9.38)	19	130.8 (13.07)		1.5 %	4.40 [-2.66, 11.46]
Hinton 2007	10	136 (10)	10	131 (9)		1.2 %	5.00 [-3.34, 13.34]
Jayatissa 1999	222	132 (9)	217	131 (11)		3.0 %	1.00 [-0.88, 2.88]
Jensen 1991	7	139 (3)	6	138 (6)		2.0 %	1.00 [-4.29, 6.29]
Kianfar 2000	92	7.4 (6.76)	148	2 (8.22)		3.0 %	5.40 [3.49, 7.31]
Klingshirn 1992	9	143.6 (12.8)	9	142.3 (11.1)		0.9 %	1.30 [-9.77, 12.37]
LaManca 1993	10	141 (6.32)	10	129 (12.64)		1.2 %	12.00 [3.24, 20.76]
Lanerolle 2000	281	135.42 (10.42)	284	131.95 (10.95)		3.0 %	3.47 [1.71, 5.23]
Li 1994	40	127 (12)	40	113 (14)		1.9 %	14.00 [8.29, 19.71]
Maghsudlu 2008	185	132.9 (8)	182	131.9 (8)		3.1 %	1.00 [-0.64, 2.64]
McClung 2009	85	130 (9)	86	128 (11)		2.7 %	2.00 [-1.01, 5.01]
Mujica-Coopman 2015	28	152 (9)	27	149 (7)		2.3 %	3.00 [-1.25, 7.25]
Newhouse 1989	19	135 (5)	18	131 (5)		2.6 %	4.00 [0.78, 7.22]
Radjen 2011	19	124.78 (7.94)	18	110.61 (5.49)		2.3 %	14.17 [9.79, 18.55]
Rowland 1988	7	134 (3)	7	127 (4)		2.5 %	7.00 [3.30, 10.70]
Viteri 1999	37	137.5 (9.2)	44	135.8 (11.8)		2.2 %	1.70 [-2.88, 6.28]
Waldvogel 2012	74	135 (6.7)	71	130 (5.3)		3.0 %	5.00 [3.04, 6.96]
Yadrick 1989	9	151 (6)	9	148 (15)		0.9 %	3.00 [-7.55, 13.55]
Zavaleta 2000	101	129.47 (9.4)	97	125.19 (11)		2.7 %	4.28 [1.42, 7.14]
Subtotal (95% CI)	**1595**		**1572**			**57.7 %**	**5.56 [3.74, 7.38]**
Heterogeneity: Tau^2 = 16.75; Chi^2 = 198.38, df = 26 (P<0.00001); I^2 =87%							
Test for overall effect: Z = 5.99 (P < 0.00001)							
2 Ferrous fumurate							
Cooter 1978	5	130.75 (7.4)	5	130 (4.7)		1.4 %	0.75 [-6.93, 8.43]
Wang 2012	34	116.8 (16)	35	104.5 (12.9)		1.6 %	12.30 [5.43, 19.17]
Subtotal (95% CI)	**39**		**40**			**2.9 %**	**6.66 [-4.66, 17.97]**
Heterogeneity: Tau^2 = 52.87; Chi^2 = 4.82, df = 1 (P = 0.03); I^2 =79%							
Test for overall effect: Z = 1.15 (P = 0.25)							
3 Other/not stated							
Agarwal 2003	699	123 (11)	691	116 (12)		3.2 %	7.00 [5.79, 8.21]
Berger 1997	65	191.7 (18.8)	65	184.9 (22.3)		1.5 %	6.80 [-0.29, 13.89]
Booth 2014	25	135.8 (8.3)	24	136.8 (8.6)		2.1 %	-1.00 [-5.74, 3.74]

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Study or subgroup	Iron N	Iron Mean(SD)	Control N	Control Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Charoenlarp 1988	517	128.18 (11.81)	173	122.89 (14.06)		2.9 %	5.29 [2.96, 7.62]
Elwood 1966	40	4 (1.5)	49	-1.6 (1.1)		3.2 %	5.60 [5.04, 6.16]
Fogelholm 1994	37	141.54 (14.32)	35	134 (14.47)		1.6 %	7.54 [0.89, 14.19]
Gordeuk 1987	17	125 (12.37)	9	126 (13.07)		0.9 %	-1.00 [-11.37, 9.37]
Gordeuk 1990	40	131 (8)	35	123 (9)		2.4 %	8.00 [4.12, 11.88]
Hoppe 2013	137.8333333 (14.25)		24	12	133 (13.5)	1.1 %	4.83 [-4.70, 14.36]
Kanani 2000	91	126.1 (7.63)	89	108.22 (10.38)		2.8 %	17.88 [15.21, 20.55]
Kang 2004	11	122 (9)	14	123 (12)		1.3 %	-1.00 [-9.23, 7.23]
Larocque 2006	12	137.5 (7.41)	9	136.56 (7.53)		1.7 %	0.94 [-5.52, 7.40]
Marks 2014	129	134.6 (8.7)	128	130 (9.9)		2.9 %	4.60 [2.32, 6.88]
Rybo 1985	45	137 (9)	44	133 (10)		2.4 %	4.00 [0.04, 7.96]
Taniguchi 1991	27	121 (11)	27	108 (12.5)		1.7 %	13.00 [6.72, 19.28]
Walsh 1989	10	136 (6)	10	129 (6)		2.0 %	7.00 [1.74, 12.26]
Yoshida 1990	6	133 (6)	6	137 (7)		1.4 %	-4.00 [-11.38, 3.38]
Zaman 2013	22	132.6 (7.4)	22	127.5 (8)		2.2 %	5.10 [0.55, 9.65]
Zhu 1998	20	136.3 (8)	17	132.2 (7.6)		2.1 %	4.10 [-0.93, 9.13]
Subtotal (95% CI)	**1837**		**1459**			**39.4 %**	**5.71 [3.93, 7.49]**
Heterogeneity: Tau^2 = 9.46; Chi^2 = 112.94, df = 18 (P<0.00001); I^2 =84%							
Test for overall effect: Z = 6.29 (P < 0.00001)							
Total (95% CI)	**3471**		**3071**			**100.0 %**	**5.63 [4.44, 6.82]**
Heterogeneity: Tau^2 = 11.27; Chi^2 = 320.63, df = 47 (P<0.00001); I^2 =85%							
Test for overall effect: Z = 9.29 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 0.05, df = 2 (P = 0.98), I^2 =0.0%							

Analysis 3.1. Comparison 3 Iron deficiency, Outcome 1 Iron deficiency at end of therapy (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 3 Iron deficiency

Outcome: 1 Iron deficiency at end of therapy (total)

Study or subgroup	Iron n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Ballin 1992	2/29	5/30		1.8 %	0.41 [0.09, 1.97]
Lanerolle 2000	28/275	56/274		17.7 %	0.50 [0.33, 0.76]
Leonard 2014	3/13	4/5		3.6 %	0.29 [0.10, 0.85]
Marks 2014	67/129	103/128		40.4 %	0.65 [0.54, 0.78]
Mujica-Coopman 2015	5/28	8/27		4.3 %	0.60 [0.23, 1.61]
Viteri 1999	1/37	7/44		1.1 %	0.17 [0.02, 1.32]
Wang 2012	23/34	31/35		31.1 %	0.76 [0.59, 0.99]
Total (95% CI)	**545**	**543**		**100.0 %**	**0.62 [0.50, 0.76]**

Total events: 129 (Iron), 214 (Control)

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 8.37$, df = 6 (P = 0.21); $I^2 = 28\%$

Test for overall effect: Z = 4.47 (P < 0.00001)

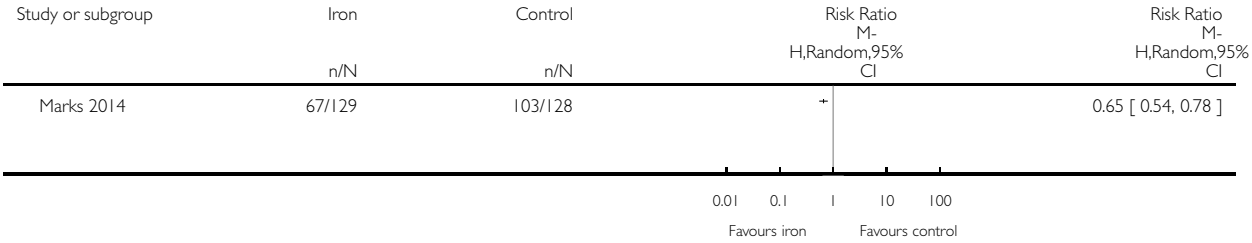
Test for subgroup differences: Not applicable

Analysis 3.2. Comparison 3 Iron deficiency, Outcome 2 Iron deficiency at end of therapy (sensitivity analysis).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 3 Iron deficiency

Outcome: 2 Iron deficiency at end of therapy (sensitivity analysis)

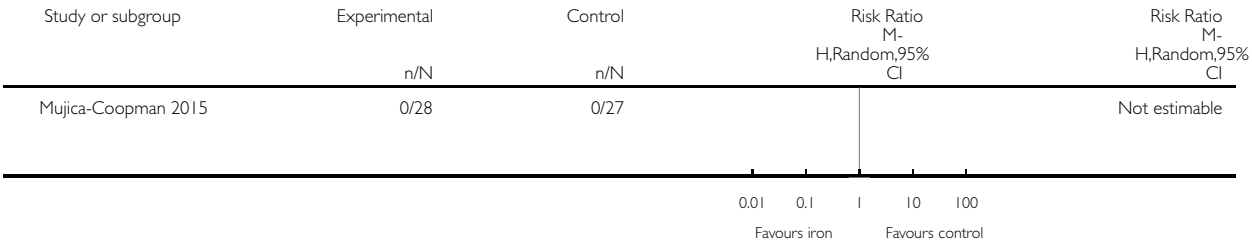


Analysis 4.1. Comparison 4 Iron-deficiency anaemia, Outcome 1 Iron-deficiency anaemia (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 4 Iron-deficiency anaemia

Outcome: 1 Iron-deficiency anaemia (total)

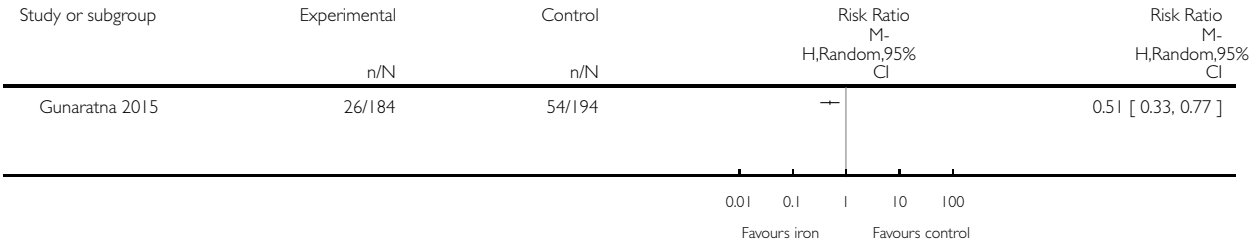


Analysis 4.2. Comparison 4 Iron-deficiency anaemia, Outcome 2 Microcytic anaemia (Total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 4 Iron-deficiency anaemia

Outcome: 2 Microcytic anaemia (Total)

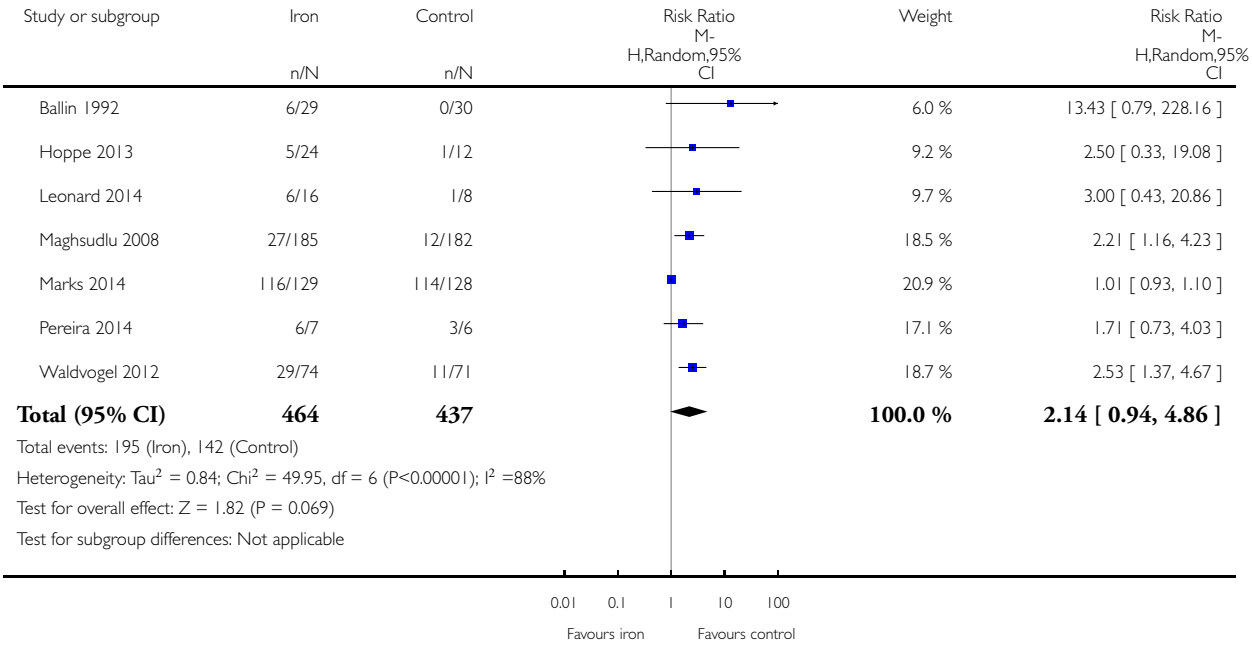


Analysis 5.1. Comparison 5 Side effects, Outcome 1 Any side effect (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 5 Side effects

Outcome: 1 Any side effect (total)

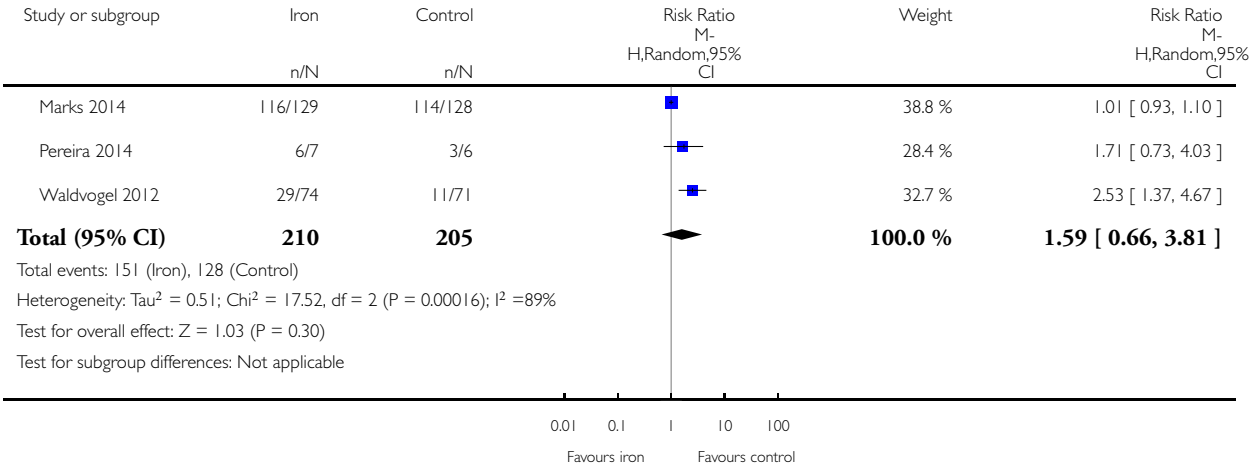


Analysis 5.2. Comparison 5 Side effects, Outcome 2 Any side effect (sensitivity analysis).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 5 Side effects

Outcome: 2 Any side effect (sensitivity analysis)

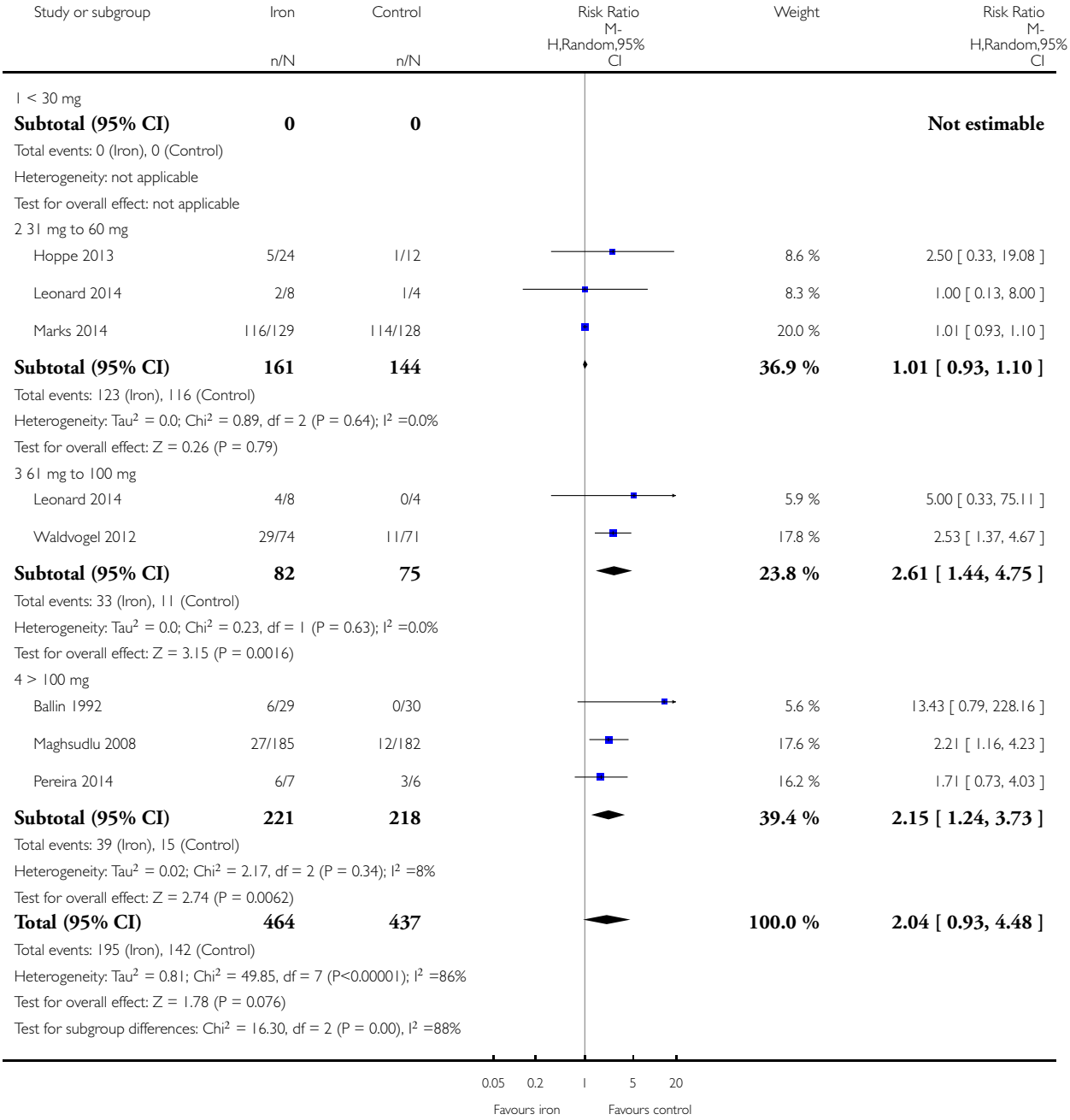


Analysis 5.3. Comparison 5 Side effects, Outcome 3 Any side effect (dose).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 5 Side effects

Outcome: 3 Any side effect (dose)

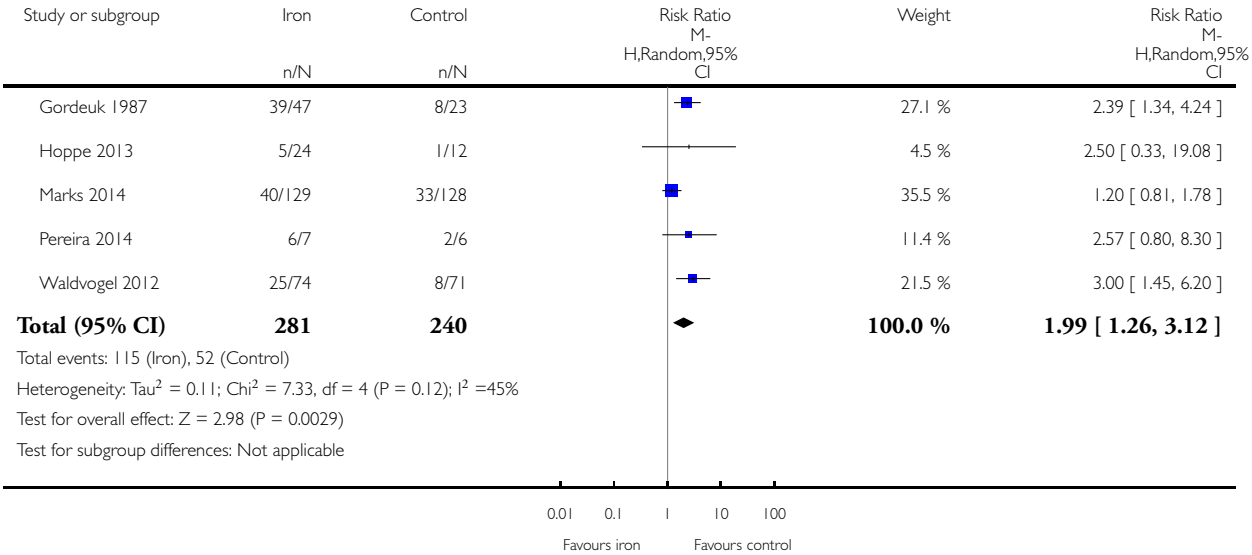


Analysis 5.4. Comparison 5 Side effects, Outcome 4 Gastrointestinal side effects (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 5 Side effects

Outcome: 4 Gastrointestinal side effects (total)

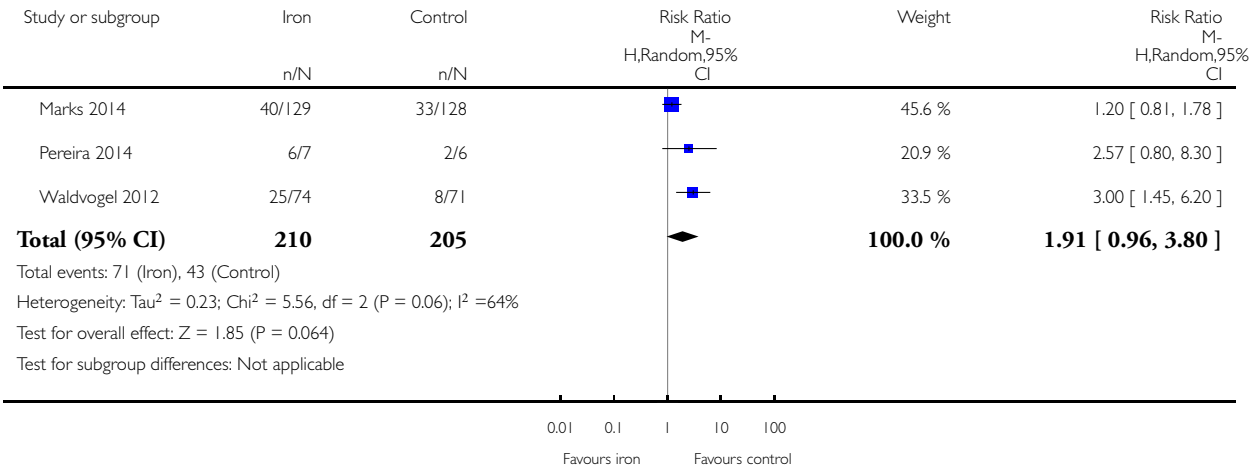


Analysis 5.5. Comparison 5 Side effects, Outcome 5 Gastrointestinal side effects (sensitivity analysis).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 5 Side effects

Outcome: 5 Gastrointestinal side effects (sensitivity analysis)

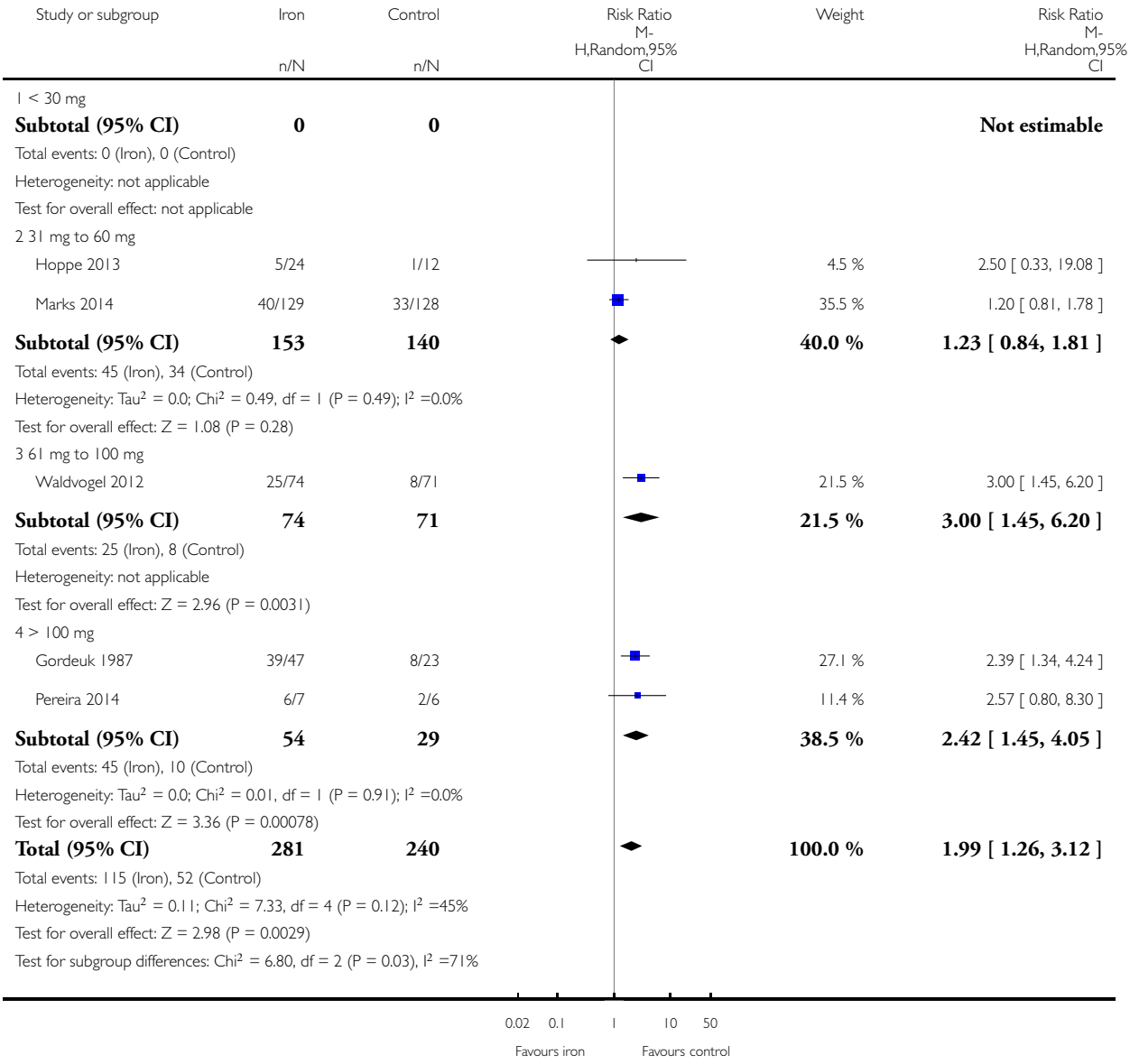


Analysis 5.6. Comparison 5 Side effects, Outcome 6 Gastrointestinal side effects (dose).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 5 Side effects

Outcome: 6 Gastrointestinal side effects (dose)

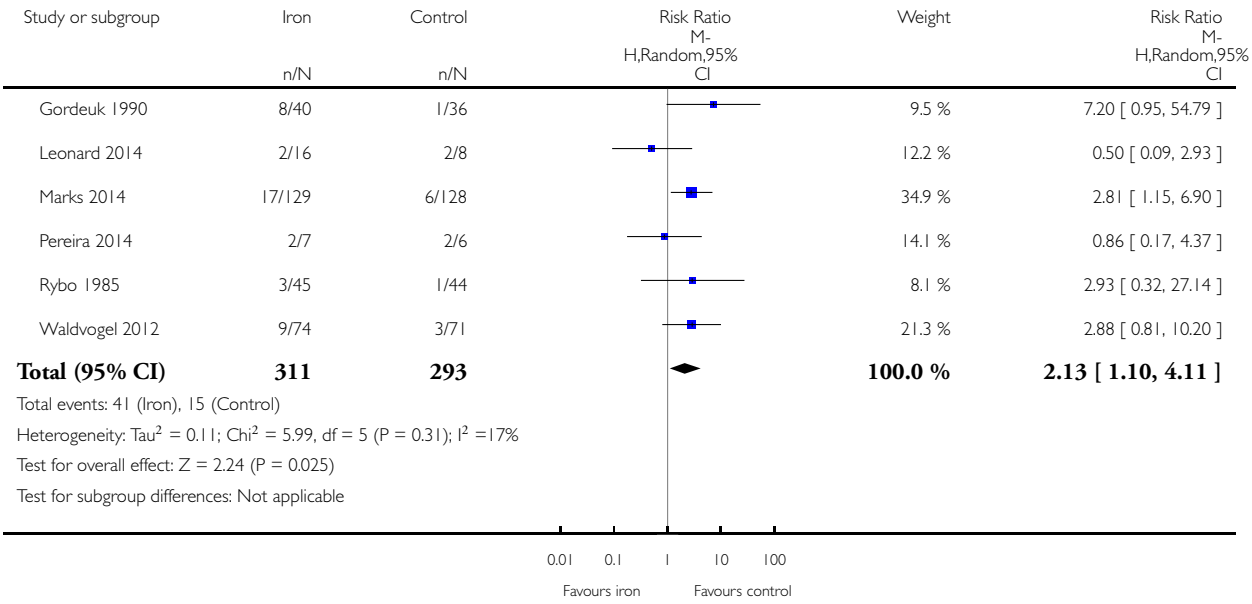


Analysis 5.7. Comparison 5 Side effects, Outcome 7 Loose stools/diarrhoea (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 5 Side effects

Outcome: 7 Loose stools/diarrhoea (total)

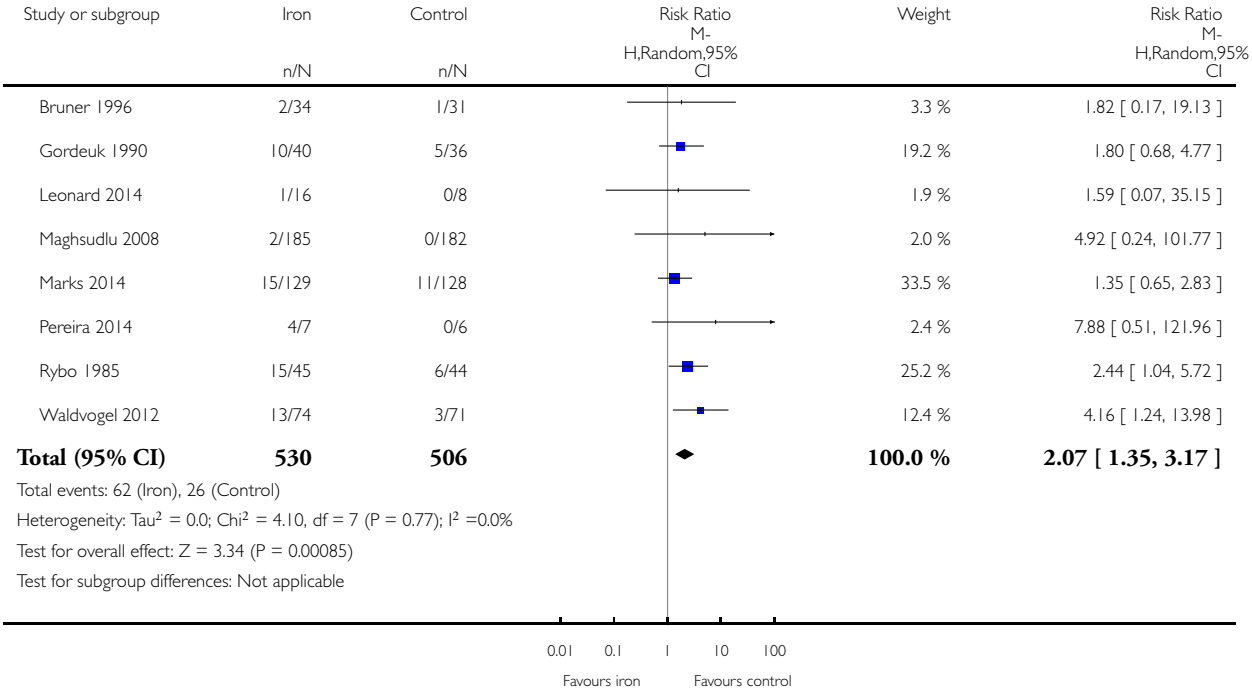


Analysis 5.8. Comparison 5 Side effects, Outcome 8 Hard stools/constipation (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 5 Side effects

Outcome: 8 Hard stools/constipation (total)

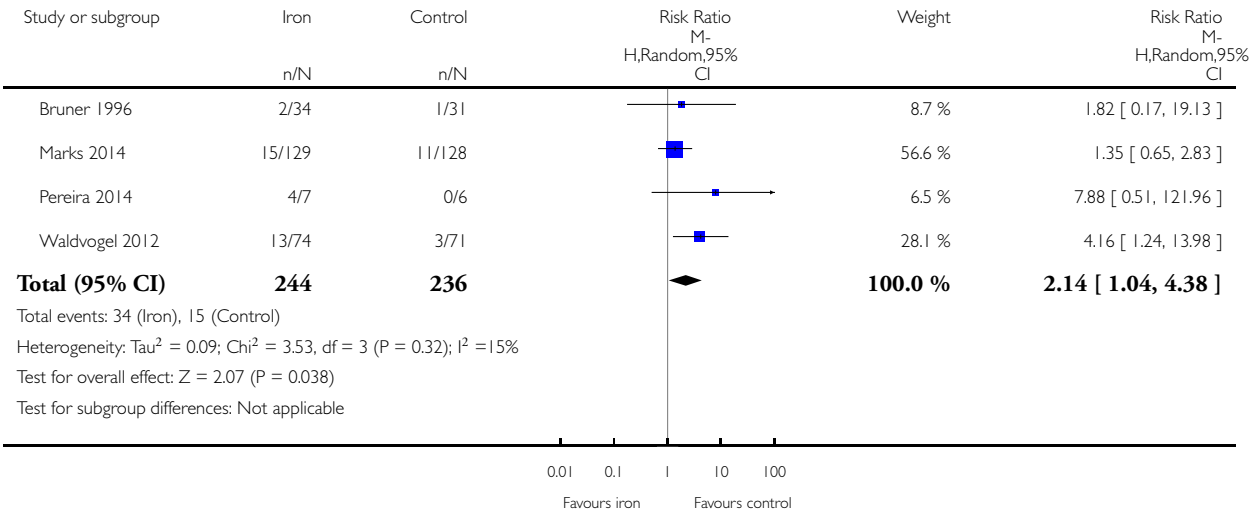


Analysis 5.9. Comparison 5 Side effects, Outcome 9 Hard stools/constipation (sensitivity analysis).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 5 Side effects

Outcome: 9 Hard stools/constipation (sensitivity analysis)

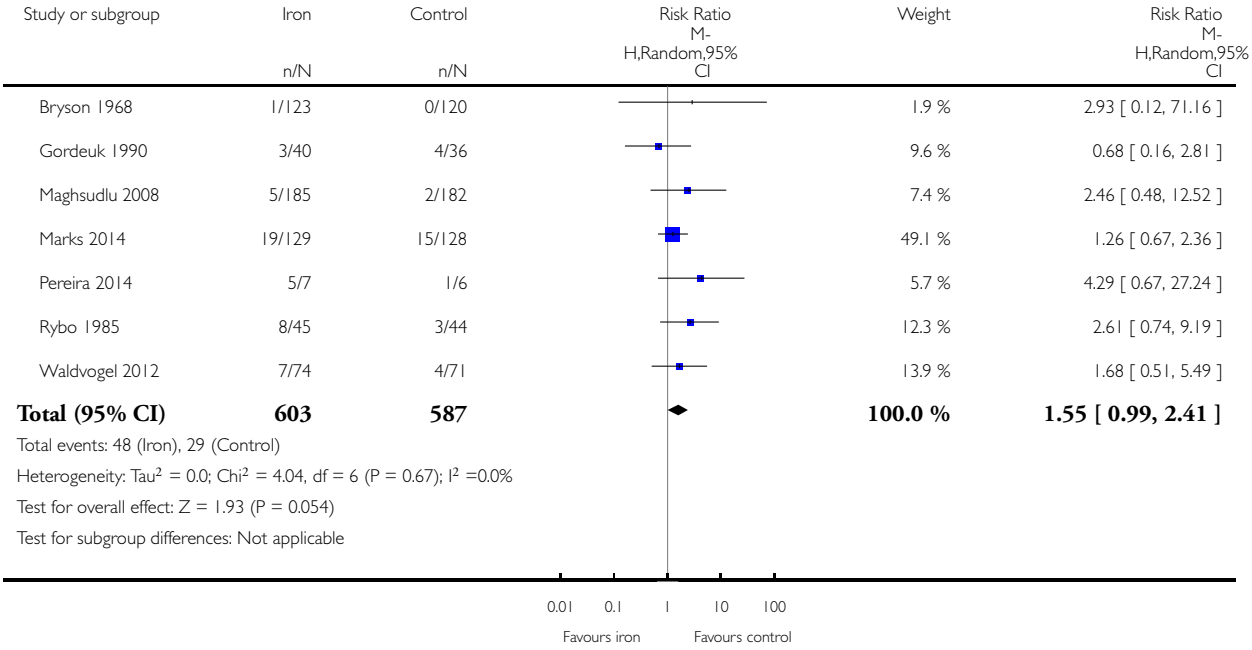


Analysis 5.10. Comparison 5 Side effects, Outcome 10 Abdominal pain (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 5 Side effects

Outcome: 10 Abdominal pain (total)

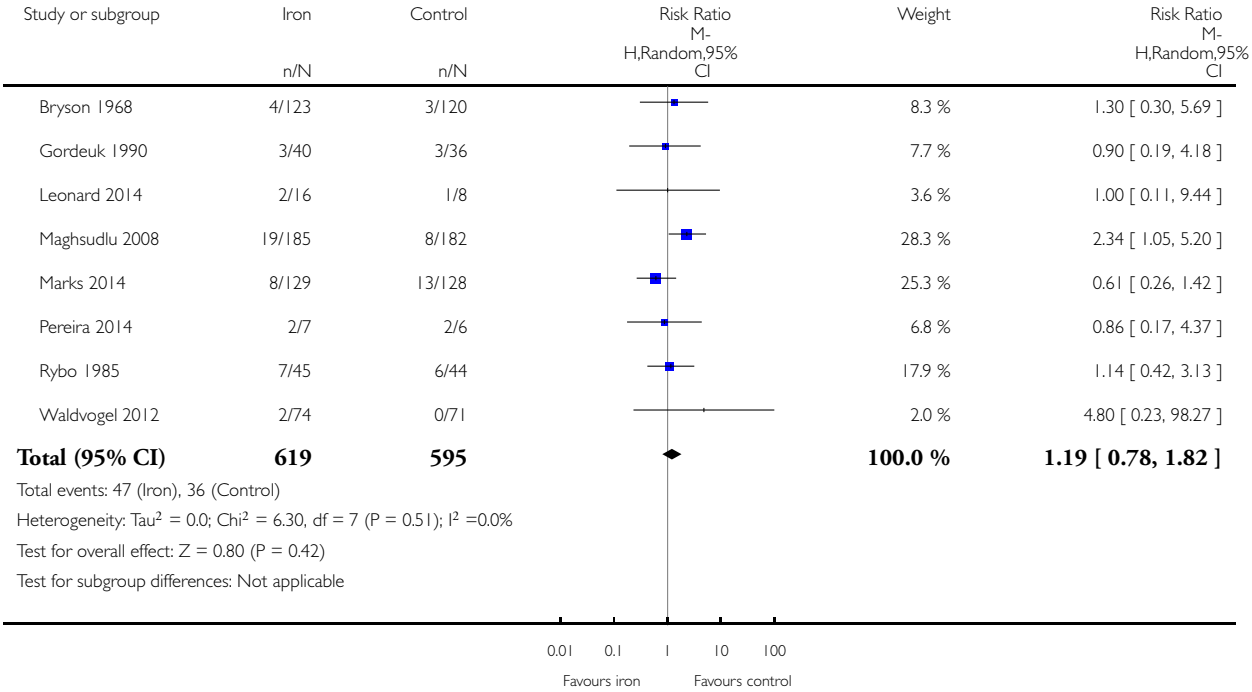


Analysis 5.11. Comparison 5 Side effects, Outcome 11 Nausea (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 5 Side effects

Outcome: 11 Nausea (total)

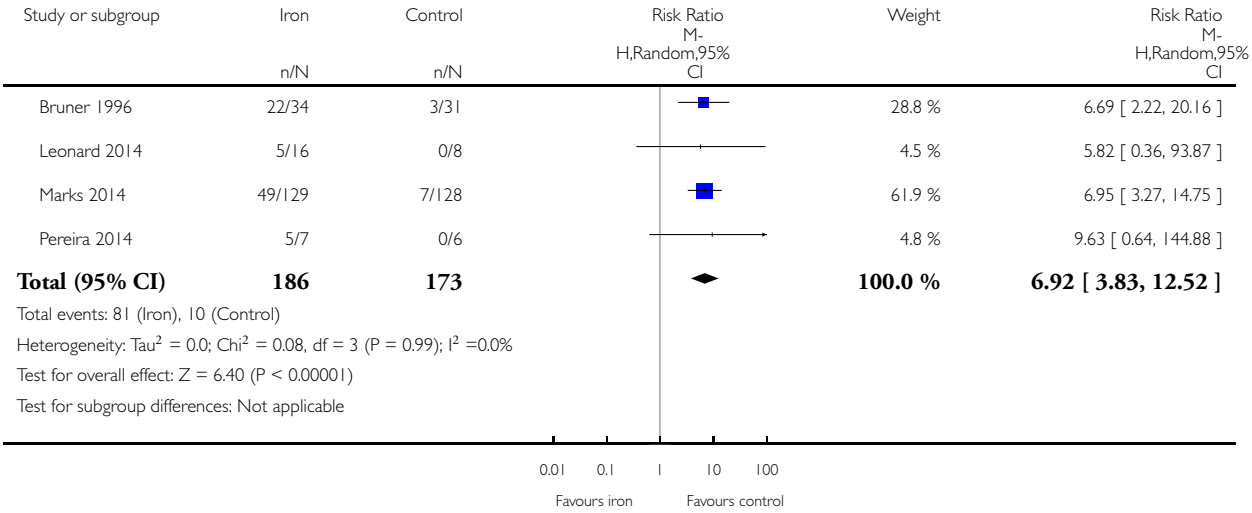


Analysis 5.12. Comparison 5 Side effects, Outcome 12 Change in stool colour (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 5 Side effects

Outcome: 12 Change in stool colour (total)



Analysis 5.13. Comparison 5 Side effects, Outcome 13 Headache (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 5 Side effects

Outcome: 13 Headache (total)

Study or subgroup	Iron n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Gordeuk 1987	13/47	7/23		47.1 %	0.91 [0.42, 1.97]
Gordeuk 1990	7/40	7/36		31.4 %	0.90 [0.35, 2.32]
Maghsudlu 2008	1/185	2/182		4.9 %	0.49 [0.04, 5.38]
Pereira 2014	4/7	2/6		16.6 %	1.71 [0.47, 6.30]
Total (95% CI)	**279**	**247**		**100.0 %**	**0.98 [0.58, 1.66]**

Total events: 25 (Iron), 18 (Control)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.11$, df = 3 (P = 0.78); $I^2 = 0.0\%$

Test for overall effect: Z = 0.09 (P = 0.93)

Test for subgroup differences: Not applicable

Analysis 6.1. Comparison 6 Iron status, Outcome 1 Ferritin in ng/ml (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 6 Iron status

Outcome: 1 Ferritin in ng/ml (total)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Binkoski 2004	14	32.3 (13.1)	12	17.2 (12.47)		1.4 %	15.10 [5.26, 24.94]
Booth 2014	25	25.4 (15.8)	24	18.4 (17.5)		1.5 %	7.00 [-2.35, 16.35]
Bruner 1996	37	27.3 (13.2)	36	12.1 (7.6)		3.0 %	15.20 [10.28, 20.12]
Brutsaert 2003	10	15.02 (7.02)	10	16.18 (7.24)		2.5 %	-1.16 [-7.41, 5.09]
Charoenlarp 1988	160	99.775 (54.13)	86	48 (33)		1.2 %	51.78 [40.87, 62.68]
DellaValle 2012	15	28 (8.6)	16	27.5 (13.1)		1.9 %	0.50 [-7.26, 8.26]
Eftekhari 2006	47	17.2 (1.28)	47	10.89 (0.55)		4.9 %	6.31 [5.91, 6.71]
Flink 2006	24	33 (14)	23	23.4 (15.8)		1.7 %	9.60 [1.05, 18.15]
Fogelholm 1992	14	26 (24.3)	17	11 (10.8)		0.8 %	15.00 [1.27, 28.73]
Fogelholm 1994	37	28.67 (16.22)	35	17 (9.31)		2.5 %	11.67 [5.60, 17.74]
Gordeuk 1987	34	13 (4.09)	19	10 (4.35)		4.3 %	3.00 [0.61, 5.39]
Hinton 2000	22	14.52 (7.04)	19	8.11 (3.92)		3.8 %	6.41 [2.98, 9.84]
Hinton 2007	10	20.82 (11.6)	10	15.18 (12.23)		1.3 %	5.64 [-4.81, 16.09]
Hoppe 2013	42.9166667 (29.79)		24	12	24 (13.5)	0.8 %	18.92 [4.76, 33.07]
Jayatissa 1999	222	93.4 (39.9)	217	56.3 (30.4)		2.3 %	37.10 [30.47, 43.73]
Jensen 1991	7	42 (23.81)	6	17 (14.7)		0.4 %	25.00 [3.80, 46.20]
Kang 2004	11	33.3 (33.4)	14	24.1 (15.8)		0.4 %	9.20 [-12.20, 30.60]
Kianfar 2000	92	21.83 (18.49)	142	2.37 (10.66)		3.4 %	19.46 [15.29, 23.63]
Klingshirn 1992	9	23.44 (6.65)	9	15.77 (10.45)		1.8 %	7.67 [-0.42, 15.76]
LaManca 1993	10	22.5 (10.75)	10	14.3 (6.95)		1.9 %	8.20 [0.27, 16.13]
Lanerolle 2000	275	27.48 (2.25)	274	15.98 (9.3)		4.8 %	11.50 [10.37, 12.63]
Larocque 2006	12	22.3 (9.11)	9	16.96 (6.21)		2.3 %	5.34 [-1.22, 11.90]
Leonard 2014	16	32.6 (8.66)	8	31.9 (5)		2.8 %	0.70 [-4.78, 6.18]
Li 1994	40	30 (20.8)	40	18.8 (17.9)		1.7 %	11.20 [2.70, 19.70]
Maghsudlu 2008	185	26.06 (1.77)	182	19.47 (1.57)		4.9 %	6.59 [6.25, 6.93]

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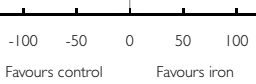
Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Marks 2014	129	17 (10.9)	128	10.6 (8.4)		4.3 %	6.40 [4.02, 8.78]
McClung 2009	85	32 (22.1)	86	26 (18.3)		2.5 %	6.00 [-0.09, 12.09]
Mujica-Coopman 2015	28	30.2 (21.2)	27	20.3 (13.5)		1.5 %	9.90 [0.54, 19.26]
Murray-Kolb 2007	56	35.4 (34.46)	57	21.16 (20.11)		1.3 %	14.24 [3.81, 24.67]
Newhouse 1989	19	37.7 (19.7)	18	17.2 (8.9)		1.4 %	20.50 [10.73, 30.27]
Radjen 2011	19	24.94 (5.83)	18	8.99 (2.05)		4.1 %	15.95 [13.16, 18.74]
Rowland 1988	7	26.6 (10.1)	7	8.6 (3.9)		1.8 %	18.00 [9.98, 26.02]
Swain 2007	9	4.6 (6.9)	12	0.5 (4.5)		2.9 %	4.10 [-1.08, 9.28]
Taniguchi 1991	27	5.4 (2.95)	27	3.25 (0.55)		4.8 %	2.15 [1.02, 3.28]
Verdon 2003	71	21 (9.2)	65	13.7 (6.9)		4.2 %	7.30 [4.58, 10.02]
Viteri 1999	37	14.81 (17.52)	44	-2.96 (13.53)		2.2 %	17.77 [10.85, 24.69]
Waldvogel 2012	74	28 (9.8)	71	12.9 (8.3)		4.0 %	15.10 [12.15, 18.05]
Walsh 1989	10	20.8 (12)	10	15.7 (9.9)		1.4 %	5.10 [-4.54, 14.74]
Yadrick 1989	9	41.5 (14.1)	9	28.2 (16.8)		0.8 %	13.30 [-1.03, 27.63]
Yoshida 1990	6	22 (5)	6	15 (6)		2.5 %	7.00 [0.75, 13.25]
Zaman 2013	22	45.2 (26.6)	22	30 (20.4)		0.8 %	15.20 [1.19, 29.21]
Zhu 1998	20	36.9 (24)	17	16.2 (13.5)		1.0 %	20.70 [8.38, 33.02]
Total (95% CI)	**1980**		**1901**			**100.0 %**	**10.27 [8.90, 11.65]**

Heterogeneity: $Tau^2 = 9.96$; $Chi^2 = 475.21$, df = 41 (P<0.00001); $I^2 = 91\%$

Test for overall effect: Z = 14.63 (P < 0.00001)

Test for subgroup differences: Not applicable



Analysis 6.2. Comparison 6 Iron status, Outcome 2 Ferritin in ng/ml (cointervention).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 6 Iron status

Outcome: 2 Ferritin in ng/ml (cointervention)

Study or subgroup	Iron		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
1 Iron alone							
Binkoski 2004	14	32.3 (13.1)	12	17.2 (12.47)		1.3 %	15.10 [5.26, 24.94]
Booth 2014	25	25.4 (15.8)	24	18.4 (17.5)		1.4 %	7.00 [-2.35, 16.35]
Bruner 1996	37	27.3 (13.2)	36	12.1 (7.6)		2.9 %	15.20 [10.28, 20.12]
Brutsaert 2003	10	15.02 (7.02)	10	16.18 (7.24)		2.3 %	-1.16 [-7.41, 5.09]
Charoenlarp 1988	160	99.775 (54.13)	86	48 (33)		1.1 %	51.78 [40.87, 62.68]
DellaValle 2012	15	28 (8.6)	16	27.5 (13.1)		1.8 %	0.50 [-7.26, 8.26]
Eftekhari 2006	23	16.8 (1.5)	22	11 (0.3)		4.9 %	5.80 [5.17, 6.43]
Flink 2006	24	33 (14)	23	23.4 (15.8)		1.5 %	9.60 [1.05, 18.15]
Fogelholm 1992	14	26 (24.3)	17	11 (10.8)		0.7 %	15.00 [1.27, 28.73]
Fogelholm 1994	37	28.67 (16.22)	35	17 (9.31)		2.3 %	11.67 [5.60, 17.74]
Gordeuk 1987	34	13 (4.09)	19	10 (4.35)		4.3 %	3.00 [0.61, 5.39]
Hinton 2000	22	14.52 (7.04)	19	8.11 (3.92)		3.7 %	6.41 [2.98, 9.84]
Hinton 2007	10	20.82 (11.6)	10	15.18 (12.23)		1.2 %	5.64 [-4.81, 16.09]
Hoppe 2013	42.9166667 (29.79)		24	12	24 (13.5)	0.7 %	18.92 [4.76, 33.07]
Jensen 1991	7	42 (23.81)	6	17 (14.7)		0.3 %	25.00 [3.80, 46.20]
Kang 2004	11	33.3 (33.4)	14	24.1 (15.8)		0.3 %	9.20 [-12.20, 30.60]
Kianfar 2000	92	21.83 (18.49)	142	2.37 (10.66)		3.3 %	19.46 [15.29, 23.63]
Klingshirn 1992	9	23.44 (6.65)	9	15.77 (10.45)		1.7 %	7.67 [-0.42, 15.76]
LaManca 1993	10	22.5 (10.75)	10	14.3 (6.95)		1.7 %	8.20 [0.27, 16.13]
Lanerolle 2000	275	27.48 (2.25)	274	15.98 (9.3)		4.8 %	11.50 [10.37, 12.63]
Larocque 2006	12	22.3 (9.11)	9	16.96 (6.21)		2.2 %	5.34 [-1.22, 11.90]
Leonard 2014	16	32.6 (8.66)	8	31.9 (5)		2.6 %	0.70 [-4.78, 6.18]
Li 1994	40	30 (20.8)	40	18.8 (17.9)		1.6 %	11.20 [2.70, 19.70]
Maghsudlu 2008	185	26.06 (1.77)	182	19.47 (1.57)		5.0 %	6.59 [6.25, 6.93]

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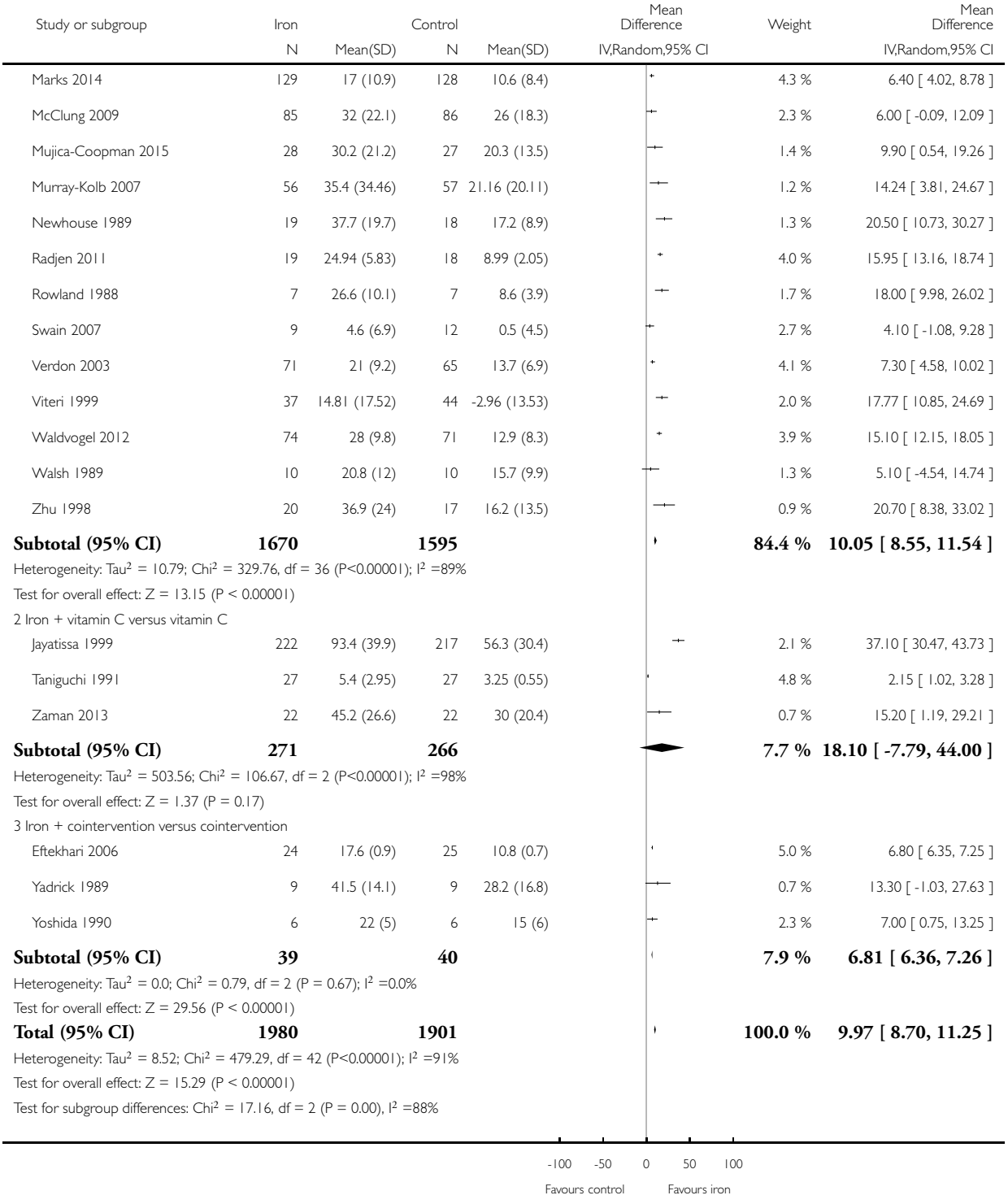


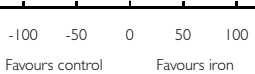
Analysis 6.3. Comparison 6 Iron status, Outcome 3 Ferritin in ng/ml (age).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 6 Iron status

Outcome: 3 Ferritin in ng/ml (age)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 12 to 18 years of age							
Bruner 1996	37	27.3 (13.2)	36	12.1 (7.6)		3.0 %	15.20 [10.28, 20.12]
Eftekhari 2006	47	17.2 (1.28)	47	10.89 (0.55)		4.9 %	6.31 [5.91, 6.71]
Jayatissa 1999	222	93.4 (39.9)	217	56.3 (30.4)		2.3 %	37.10 [30.47, 43.73]
Kianfar 2000	92	21.83 (18.49)	142	2.37 (10.66)		3.4 %	19.46 [15.29, 23.63]
Lanerolle 2000	275	27.48 (2.25)	274	15.98 (9.3)		4.8 %	11.50 [10.37, 12.63]
Larocque 2006	12	22.3 (9.11)	9	16.96 (6.21)		2.3 %	5.34 [-1.22, 11.90]
Walsh 1989	10	20.8 (12)	10	15.7 (9.9)		1.4 %	5.10 [-4.54, 14.74]
Subtotal (95% CI)	**695**		**735**		◆	**22.2 %**	**14.19 [9.70, 18.68]**
Heterogeneity: Tau^2 = 29.79; Chi^2 = 196.46, df = 6 (P<0.00001); I^2 =97%							
Test for overall effect: Z = 6.20 (P < 0.00001)							
2 50 to 55 years of age							
Subtotal (95% CI)	**0**		**0**				**Not estimable**
Heterogeneity: not applicable							
Test for overall effect: not applicable							
3 Mixed/unstated							
Binkoski 2004	14	32.3 (13.1)	12	17.2 (12.47)		1.4 %	15.10 [5.26, 24.94]
Booth 2014	25	25.4 (15.8)	24	18.4 (17.5)		1.5 %	7.00 [-2.35, 16.35]
Brutsaert 2003	10	15.02 (7.02)	10	16.18 (7.24)		2.5 %	-1.16 [-7.41, 5.09]
Charoenlarp 1988	160	99.775 (54.13)	86	48 (33)		1.2 %	51.78 [40.87, 62.68]
DellaValle 2012	15	28 (8.6)	16	27.5 (13.1)		1.9 %	0.50 [-7.26, 8.26]
Flink 2006	24	33 (14)	23	23.4 (15.8)		1.7 %	9.60 [1.05, 18.15]
Fogelholm 1992	14	26 (24.3)	17	11 (10.8)		0.8 %	15.00 [1.27, 28.73]
Fogelholm 1994	37	28.67 (16.22)	35	17 (9.31)		2.5 %	11.67 [5.60, 17.74]
Gordeuk 1987	34	13 (4.09)	19	10 (4.35)		4.3 %	3.00 [0.61, 5.39]
Hinton 2000	22	14.52 (7.04)	19	8.11 (3.92)		3.8 %	6.41 [2.98, 9.84]



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Study or subgroup	Iron N	Iron Mean(SD)	Control N	Control Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Hinton 2007	10	20.82 (11.6)	10	15.18 (12.23)		1.3 %	5.64 [-4.81, 16.09]
Hoppe 2013	42.9166667 (29.79)	24	12	24 (13.5)		0.8 %	18.92 [4.76, 33.07]
Jensen 1991	7	42 (23.81)	6	17 (14.7)		0.4 %	25.00 [3.80, 46.20]
Kang 2004	11	33.3 (33.4)	14	24.1 (15.8)		0.4 %	9.20 [-12.20, 30.60]
Klingshirn 1992	9	23.44 (6.65)	9	15.77 (10.45)		1.8 %	7.67 [-0.42, 15.76]
LaManca 1993	10	22.5 (10.75)	10	14.3 (6.95)		1.9 %	8.20 [0.27, 16.13]
Leonard 2014	16	32.6 (8.66)	8	31.9 (5)		2.8 %	0.70 [-4.78, 6.18]
Li 1994	40	30 (20.8)	40	18.8 (17.9)		1.7 %	11.20 [2.70, 19.70]
Maghsudlu 2008	185	26.06 (1.77)	182	19.47 (1.57)		4.9 %	6.59 [6.25, 6.93]
Marks 2014	129	17 (10.9)	128	10.6 (8.4)		4.3 %	6.40 [4.02, 8.78]
McClung 2009	85	32 (22.1)	86	26 (18.3)		2.5 %	6.00 [-0.09, 12.09]
Mujica-Coopman 2015	28	30.2 (21.2)	27	20.3 (13.5)		1.5 %	9.90 [0.54, 19.26]
Murray-Kolb 2007	56	35.4 (34.46)	57	21.16 (20.11)		1.3 %	14.24 [3.81, 24.67]
Newhouse 1989	19	37.7 (19.7)	18	17.2 (8.9)		1.4 %	20.50 [10.73, 30.27]
Radjen 2011	19	24.94 (5.83)	18	8.99 (2.05)		4.1 %	15.95 [13.16, 18.74]
Rowland 1988	7	26.6 (10.1)	7	8.6 (3.9)		1.8 %	18.00 [9.98, 26.02]
Swain 2007	9	4.6 (6.9)	12	0.5 (4.5)		2.9 %	4.10 [-1.08, 9.28]
Taniguchi 1991	27	5.4 (2.95)	27	3.25 (0.55)		4.8 %	2.15 [1.02, 3.28]
Verdon 2003	71	21 (9.2)	65	13.7 (6.9)		4.2 %	7.30 [4.58, 10.02]
Viteri 1999	37	14.81 (17.52)	44	-2.96 (13.53)		2.2 %	17.77 [10.85, 24.69]
Waldvogel 2012	74	28 (9.8)	71	12.9 (8.3)		4.0 %	15.10 [12.15, 18.05]
Yadrick 1989	9	41.5 (14.1)	9	28.2 (16.8)		0.8 %	13.30 [-1.03, 27.63]
Yoshida 1990	6	22 (5)	6	15 (6)		2.5 %	7.00 [0.75, 13.25]
Zaman 2013	22	45.2 (26.6)	22	30 (20.4)		0.8 %	15.20 [1.19, 29.21]
Zhu 1998	20	36.9 (24)	17	16.2 (13.5)		1.0 %	20.70 [8.38, 33.02]
Subtotal (95% CI)	**1285**		**1166**			**77.8 %**	**9.76 [7.89, 11.63]**
Heterogeneity: Tau^2 = 17.64; Chi^2 = 272.92, df = 34 (P<0.00001); I^2 =88%							
Test for overall effect: Z = 10.23 (P < 0.00001)							
Total (95% CI)	**1980**		**1901**			**100.0 %**	**10.27 [8.90, 11.65]**
Heterogeneity: Tau^2 = 9.96; Chi^2 = 475.21, df = 41 (P<0.00001); I^2 =91%							
Test for overall effect: Z = 14.63 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 3.19, df = 1 (P = 0.07), I^2 =69%							

Analysis 6.4. Comparison 6 Iron status, Outcome 4 Ferritin in ng/ml (baseline Hb).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 6 Iron status

Outcome: 4 Ferritin in ng/ml (baseline Hb)

Study or subgroup	Iron		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
1 Anaemic							
Kianfar 2000	47	21.7 (19.2)	70	0.8 (9.3)		2.4 %	20.90 [14.99, 26.81]
McClung 2009	18	14.5 (8.7)	17	9.7 (5.5)		2.8 %	4.80 [0.01, 9.59]
Murray-Kolb 2007	17	22.8 (17.7)	13	9.2 (7.7)		1.4 %	13.60 [4.20, 23.00]
Radjen 2011	10	24.32 (6.92)	10	8.33 (2.52)		2.9 %	15.99 [11.43, 20.55]
Subtotal (95% CI)	**92**		**110**			**9.5 %**	**13.74 [6.32, 21.16]**
Heterogeneity: Tau^2 = 47.25; Chi^2 = 19.76, df = 3 (P = 0.00019); I^2 =85%							
Test for overall effect: Z = 3.63 (P = 0.00028)							
2 Non anaemic							
Binkoski 2004	14	32.3 (13.1)	12	17.2 (12.47)		1.3 %	15.10 [5.26, 24.94]
Booth 2014	25	25.4 (15.8)	24	18.4 (17.5)		1.4 %	7.00 [-2.35, 16.35]
Bruner 1996	37	27.3 (13.2)	36	12.1 (7.6)		2.8 %	15.20 [10.28, 20.12]
Brutsaert 2003	10	15.02 (7.02)	10	16.18 (7.24)		2.3 %	-1.16 [-7.41, 5.09]
DellaValle 2012	15	28 (8.6)	16	27.5 (13.1)		1.8 %	0.50 [-7.26, 8.26]
Flink 2006	24	33 (14)	23	23.4 (15.8)		1.6 %	9.60 [1.05, 18.15]
Fogelholm 1992	14	26 (24.3)	17	11 (10.8)		0.8 %	15.00 [1.27, 28.73]
Hinton 2000	22	14.52 (7.04)	19	8.11 (3.92)		3.4 %	6.41 [2.98, 9.84]
Hinton 2007	10	20.82 (11.6)	10	15.18 (12.23)		1.2 %	5.64 [-4.81, 16.09]
Hoppe 2013	42.9166667 (29.79)		24	12	24 (13.5)	0.7 %	18.92 [4.76, 33.07]
Jensen 1991	7	42 (23.81)	6	17 (14.7)		0.4 %	25.00 [3.80, 46.20]
Kianfar 2000	43	23 (7.9)	72	3.9 (11.7)		3.3 %	19.10 [15.51, 22.69]
Klingshirn 1992	9	23.44 (6.65)	9	15.77 (10.45)		1.7 %	7.67 [-0.42, 15.76]
Leonard 2014	16	32.6 (8.66)	8	31.9 (5)		2.5 %	0.70 [-4.78, 6.18]
Maghsudlu 2008	185	26.06 (1.77)	182	19.47 (1.57)		4.4 %	6.59 [6.25, 6.93]

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Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
McClung 2009	66	36.76 (22.23)	65	30.2 (18.12)		2.0 %	6.56 [-0.38, 13.50]
Murray-Kolb 2007	39	41 (38.52)	44	24.7 (21.33)		0.8 %	16.30 [2.67, 29.93]
Newhouse 1989	19	37.7 (19.7)	18	17.2 (8.9)		1.3 %	20.50 [10.73, 30.27]
Radjen 2011	9	25.63 (4.64)	8	9.83 (0.84)		3.6 %	15.80 [12.71, 18.89]
Rowland 1988	7	26.6 (10.1)	7	8.6 (3.9)		1.7 %	18.00 [9.98, 26.02]
Swain 2007	9	4.6 (6.9)	12	0.5 (4.5)		2.7 %	4.10 [-1.08, 9.28]
Verdon 2003	71	21 (9.2)	65	13.7 (6.9)		3.7 %	7.30 [4.58, 10.02]
Waldvogel 2012	74	28 (9.8)	71	12.9 (8.3)		3.6 %	15.10 [12.15, 18.05]
Zhu 1998	20	36.9 (24)	17	16.2 (13.5)		0.9 %	20.70 [8.38, 33.02]
Subtotal (95% CI)	**769**		**763**			**49.9 %**	**10.40 [7.90, 12.89]**
Heterogeneity: Tau^2 = 24.43; Chi^2 = 166.60, df = 23 (P<0.00001); I^2 =86%							
Test for overall effect: Z = 8.17 (P < 0.00001)							
3 Mixed/unstated							
Charoenlarp 1988	160	99.775 (54.13)	86	48 (33)		1.1 %	51.78 [40.87, 62.68]
Eftekhari 2006	47	17.2 (1.28)	47	10.89 (0.55)		4.4 %	6.31 [5.91, 6.71]
Fogelholm 1994	37	28.67 (16.22)	35	17 (9.31)		2.3 %	11.67 [5.60, 17.74]
Gordeuk 1987	34	13 (4.09)	19	10 (4.35)		3.9 %	3.00 [0.61, 5.39]
Jayatissa 1999	222	93.4 (39.9)	217	56.3 (30.4)		2.1 %	37.10 [30.47, 43.73]
Kang 2004	11	33.3 (33.4)	14	24.1 (15.8)		0.4 %	9.20 [-12.20, 30.60]
LaManca 1993	10	22.5 (10.75)	10	14.3 (6.95)		1.7 %	8.20 [0.27, 16.13]
Lanerolle 2000	275	27.48 (2.25)	274	15.98 (9.3)		4.3 %	11.50 [10.37, 12.63]
Larocque 2006	12	22.3 (9.11)	9	16.96 (6.21)		2.1 %	5.34 [-1.22, 11.90]
Li 1994	40	30 (20.8)	40	18.8 (17.9)		1.6 %	11.20 [2.70, 19.70]
Marks 2014	129	17 (10.9)	128	10.6 (8.4)		3.9 %	6.40 [4.02, 8.78]
Mujica-Coopman 2015	28	30.2 (21.2)	27	20.3 (13.5)		1.4 %	9.90 [0.54, 19.26]
Taniguchi 1991	27	5.4 (2.95)	27	3.25 (0.55)		4.3 %	2.15 [1.02, 3.28]
Viteri 1999	37	14.81 (17.52)	44	-2.96 (13.53)		2.0 %	17.77 [10.85, 24.69]
Walsh 1989	10	20.8 (12)	10	15.7 (9.9)		1.3 %	5.10 [-4.54, 14.74]
Yadrick 1989	9	41.5 (14.1)	9	28.2 (16.8)		0.7 %	13.30 [-1.03, 27.63]
Yoshida 1990	6	22 (5)	6	15 (6)		2.3 %	7.00 [0.75, 13.25]
Zaman 2013	22	45.2 (26.6)	22	30 (20.4)		0.8 %	15.20 [1.19, 29.21]
Subtotal (95% CI)	**1116**		**1024**			**40.6 %**	**11.36 [8.67, 14.05]**

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Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Heterogeneity: Tau² = 21.34; Chi² = 306.21, df = 17 (P<0.00001); I² =94%							
Test for overall effect: Z = 8.28 (P < 0.00001)							
Total (95% CI)	**1977**		**1897**			**100.0 %**	**10.65 [9.31, 11.99]**
Heterogeneity: Tau² = 10.66; Chi² = 516.18, df = 45 (P<0.00001); I² =91%							
Test for overall effect: Z = 15.55 (P < 0.00001)							
Test for subgroup differences: Chi² = 0.82, df = 2 (P = 0.66), I² =0.0%							

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Favours control Favours iron

Analysis 6.5. Comparison 6 Iron status, Outcome 5 Ferritin in ng/ml (iron status).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 6 Iron status

Outcome: 5 Ferritin in ng/ml (iron status)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Iron deficient							
Binkoski 2004	14	32.3 (13.1)	12	17.2 (12.47)		1.3 %	15.10 [5.26, 24.94]
Bruner 1996	37	27.3 (13.2)	36	12.1 (7.6)		2.8 %	15.20 [10.28, 20.12]
Brutsaert 2003	10	15.02 (7.02)	10	16.18 (7.24)		2.3 %	-1.16 [-7.41, 5.09]
DellaValle 2012	8	25.1 (9.5)	8	20.7 (9.3)		1.4 %	4.40 [-4.81, 13.61]
Eftekhari 2006	47	17.2 (1.28)	47	10.89 (0.55)		4.7 %	6.31 [5.91, 6.71]
Flink 2006	24	33 (14)	23	23.4 (15.8)		1.6 %	9.60 [1.05, 18.15]
Fogelholm 1992	14	26 (24.3)	17	11 (10.8)		0.8 %	15.00 [1.27, 28.73]
Fogelholm 1994	37	28.67 (16.22)	35	17 (9.31)		2.4 %	11.67 [5.60, 17.74]
Hinton 2000	22	14.52 (7.04)	19	8.11 (3.92)		3.6 %	6.41 [2.98, 9.84]
Hinton 2007	10	20.82 (11.6)	10	15.18 (12.23)		1.2 %	5.64 [-4.81, 16.09]

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Favours control Favours iron

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Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Klingshirn 1992	9	23.44 (6.65)	9	15.77 (10.45)		1.7 %	7.67 [-0.42, 15.76]
LaManca 1993	10	22.5 (10.75)	10	14.3 (6.95)		1.7 %	8.20 [0.27, 16.13]
Leonard 2014	16	32.6 (8.66)	8	31.9 (5)		2.6 %	0.70 [-4.78, 6.18]
Marks 2014	73	12.7 (7.4)	71	6.9 (4.3)		4.2 %	5.80 [3.83, 7.77]
McClung 2009	32	18.48 (9.56)	31	13.04 (8.77)		3.0 %	5.44 [0.91, 9.97]
Murray-Kolb 2007	42	23.87 (20.41)	41	12.96 (12.67)		1.9 %	10.91 [3.62, 18.20]
Radjen 2011	19	24.94 (5.83)	18	8.99 (2.05)		3.9 %	15.95 [13.16, 18.74]
Taniguchi 1991	27	5.4 (2.95)	27	3.25 (0.55)		4.5 %	2.15 [1.02, 3.28]
Waldvogel 2012	74	28 (9.8)	71	12.9 (8.3)		3.8 %	15.10 [12.15, 18.05]
Zhu 1998	20	36.9 (24)	17	16.2 (13.5)		0.9 %	20.70 [8.38, 33.02]
Subtotal (95% CI)	**545**		**520**			**50.3 %**	**8.40 [6.31, 10.49]**
Heterogeneity: Tau^2 = 13.68; Chi^2 = 169.59, df = 19 (P<0.00001); I^2 =89%							
Test for overall effect: Z = 7.87 (P < 0.00001)							
2 Not iron deficient							
Marks 2014	56	22.7 (12.1)	57	15.1 (9.9)		3.2 %	7.60 [3.52, 11.68]
McClung 2009	52	40.3 (23.5)	51	33.8 (18.2)		1.7 %	6.50 [-1.61, 14.61]
Murray-Kolb 2007	14	70.3 (44.4)	16	42.2 (20.7)		0.3 %	28.10 [2.73, 53.47]
Newhouse 1989	19	37.7 (19.7)	18	17.2 (8.9)		1.3 %	20.50 [10.73, 30.27]
Rowland 1988	7	26.6 (10.1)	7	8.6 (3.9)		1.7 %	18.00 [9.98, 26.02]
Subtotal (95% CI)	**148**		**149**			**8.2 %**	**13.38 [6.74, 20.01]**
Heterogeneity: Tau^2 = 33.97; Chi^2 = 12.10, df = 4 (P = 0.02); I^2 =67%							
Test for overall effect: Z = 3.95 (P = 0.000077)							
3 Mixed/unstated							
Booth 2014	25	25.4 (15.8)	24	18.4 (17.5)		1.4 %	7.00 [-2.35, 16.35]
Charoenlarp 1988	160	99.775 (54.13)	86	48 (33)		1.1 %	51.78 [40.87, 62.68]
Gordeuk 1987	34	13 (4.09)	19	10 (4.35)		4.1 %	3.00 [0.61, 5.39]
Hoppe 2013	42.9166667 (29.79)	24	12	24 (13.5)		0.7 %	18.92 [4.76, 33.07]
Jayatissa 1999	222	93.4 (39.9)	217	56.3 (30.4)		2.1 %	37.10 [30.47, 43.73]
Jensen 1991	7	42 (23.81)	6	17 (14.7)		0.4 %	25.00 [3.80, 46.20]
Kang 2004	11	33.3 (33.4)	14	24.1 (15.8)		0.4 %	9.20 [-12.20, 30.60]
Kianfar 2000	92	21.83 (18.49)	142	2.37 (10.66)		3.2 %	19.46 [15.29, 23.63]
Lanerolle 2000	275	27.48 (2.25)	274	15.98 (9.3)		4.5 %	11.50 [10.37, 12.63]
Larocque 2006	12	22.3 (9.11)	9	16.96 (6.21)		2.2 %	5.34 [-1.22, 11.90]

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Favours control Favours iron

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Study or subgroup	Iron N	Iron Mean(SD)	Control N	Control Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Li 1994	40	30 (20.8)	40	18.8 (17.9)		1.6 %	11.20 [2.70, 19.70]
Maghsudlu 2008	185	26.06 (1.77)	182	19.47 (1.57)		4.7 %	6.59 [6.25, 6.93]
Mujica-Coopman 2015	28	30.2 (21.2)	27	20.3 (13.5)		1.4 %	9.90 [0.54, 19.26]
Swain 2007	9	4.6 (6.9)	12	0.5 (4.5)		2.7 %	4.10 [-1.08, 9.28]
Verdon 2003	71	21 (9.2)	65	13.7 (6.9)		3.9 %	7.30 [4.58, 10.02]
Viteri 1999	37	14.81 (17.52)	44	-2.96 (13.53)		2.0 %	17.77 [10.85, 24.69]
Walsh 1989	10	20.8 (12)	10	15.7 (9.9)		1.3 %	5.10 [-4.54, 14.74]
Yadrick 1989	9	41.5 (14.1)	9	28.2 (16.8)		0.7 %	13.30 [-1.03, 27.63]
Yoshida 1990	6	22 (5)	6	15 (6)		2.3 %	7.00 [0.75, 13.25]
Zaman 2013	22	45.2 (26.6)	22	30 (20.4)		0.7 %	15.20 [1.19, 29.21]
Subtotal (95% CI)	**1279**		**1220**			**41.5 %**	**12.88 [9.99, 15.78]**
Heterogeneity: Tau^2 = 27.10; Chi^2 = 274.29, df = 19 (P<0.00001); I^2 =93%							
Test for overall effect: Z = 8.72 (P < 0.00001)							
Total (95% CI)	**1972**		**1889**			**100.0 %**	**10.13 [8.81, 11.45]**
Heterogeneity: Tau^2 = 9.70; Chi^2 = 476.20, df = 44 (P<0.00001); I^2 =91%							
Test for overall effect: Z = 15.03 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 7.02, df = 2 (P = 0.03), I^2 =71%							

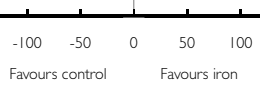
Analysis 6.6. Comparison 6 Iron status, Outcome 6 Ferritin in ng/ml (iron-deficiency anaemia).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 6 Iron status

Outcome: 6 Ferritin in ng/ml (iron-deficiency anaemia)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Iron-deficiency anaemia							
McClung 2009	18	14.5 (8.7)	17	9.7 (5.5)		2.8 %	4.80 [0.01, 9.59]
Murray-Kolb 2007	17	22.8 (17.7)	13	9.2 (7.7)		1.4 %	13.60 [4.20, 23.00]
Radjen 2011	10	24.32 (6.92)	10	8.33 (2.52)		2.9 %	15.99 [11.43, 20.55]
Subtotal (95% CI)	**45**		**40**			**7.2 %**	**11.27 [3.26, 19.29]**
Heterogeneity: Tau^2 = 39.88; Chi^2 = 11.31, df = 2 (P = 0.004); I^2 =82%							
Test for overall effect: Z = 2.76 (P = 0.0058)							
2 Iron deficient, not anaemic							
Binkoski 2004	14	32.3 (13.1)	12	17.2 (12.47)		1.3 %	15.10 [5.26, 24.94]
Bruner 1996	37	27.3 (13.2)	36	12.1 (7.6)		2.8 %	15.20 [10.28, 20.12]
Brutsaert 2003	10	15.02 (7.02)	10	16.18 (7.24)		2.3 %	-1.16 [-7.41, 5.09]
DellaValle 2012	8	25.1 (9.5)	8	20.7 (9.3)		1.4 %	4.40 [-4.81, 13.61]
Flink 2006	24	33 (14)	23	23.4 (15.8)		1.6 %	9.60 [1.05, 18.15]
Fogelholm 1992	14	26 (24.3)	17	11 (10.8)		0.8 %	15.00 [1.27, 28.73]
Hinton 2000	22	14.52 (7.04)	19	8.11 (3.92)		3.5 %	6.41 [2.98, 9.84]
Hinton 2007	10	20.82 (11.6)	10	15.18 (12.23)		1.2 %	5.64 [-4.81, 16.09]
Klingshirn 1992	9	23.44 (6.65)	9	15.77 (10.45)		1.7 %	7.67 [-0.42, 15.76]
Leonard 2014	16	32.6 (8.66)	8	31.9 (5)		2.6 %	0.70 [-4.78, 6.18]
McClung 2009	14	23.6 (8.3)	14	17.1 (10.4)		2.0 %	6.50 [-0.47, 13.47]
Murray-Kolb 2007	25	24.6 (22.4)	28	14.7 (14.2)		1.2 %	9.90 [-0.34, 20.14]
Newhouse 1989	19	37.7 (19.7)	18	17.2 (8.9)		1.3 %	20.50 [10.73, 30.27]
Radjen 2011	9	25.63 (4.64)	8	9.83 (0.84)		3.6 %	15.80 [12.71, 18.89]
Waldvogel 2012	74	28 (9.8)	71	12.9 (8.3)		3.7 %	15.10 [12.15, 18.05]
Zhu 1998	20	36.9 (24)	17	16.2 (13.5)		0.9 %	20.70 [8.38, 33.02]
Subtotal (95% CI)	**325**		**308**			**31.8 %**	**10.07 [6.77, 13.38]**
Heterogeneity: Tau^2 = 30.18; Chi^2 = 66.88, df = 15 (P<0.00001); I^2 =78%							
Test for overall effect: Z = 5.97 (P < 0.00001)							



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Study or subgroup	Iron N	Iron Mean(SD)	Control N	Control Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
3 Not iron deficient, not anaemic							
McClung 2009	52	40.3 (23.5)	51	33.8 (18.2)		1.7 %	6.50 [-1.61, 14.61]
Rowland 1988	7	26.6 (10.1)	7	8.6 (3.9)		1.7 %	18.00 [9.98, 26.02]
Subtotal (95% CI)	**59**		**58**			**3.4 %**	**12.27 [1.00, 23.54]**
Heterogeneity: Tau^2 = 49.19; Chi^2 = 3.91, df = 1 (P = 0.05); I^2 =74%							
Test for overall effect: Z = 2.13 (P = 0.033)							
4 Mixed/unstated							
Booth 2014	25	25.4 (15.8)	24	18.4 (17.5)		1.4 %	7.00 [-2.35, 16.35]
Charoenlarp 1988	160	99.775 (54.13)	86	48 (33)		1.1 %	51.78 [40.87, 62.68]
Eftekhari 2006	47	17.2 (1.28)	47	10.89 (0.55)		4.5 %	6.31 [5.91, 6.71]
Fogelholm 1994	37	28.67 (16.22)	35	17 (9.31)		2.3 %	11.67 [5.60, 17.74]
Gordeuk 1987	34	13 (4.09)	19	10 (4.35)		4.0 %	3.00 [0.61, 5.39]
Hoppe 2013	42.9166667 (29.79)		24	12	24 (13.5)	0.7 %	18.92 [4.76, 33.07]
Jayatissa 1999	222	93.4 (39.9)	217	56.3 (30.4)		2.1 %	37.10 [30.47, 43.73]
Jensen 1991	7	42 (23.81)	6	17 (14.7)		0.4 %	25.00 [3.80, 46.20]
Kang 2004	11	33.3 (33.4)	14	24.1 (15.8)		0.3 %	9.20 [-12.20, 30.60]
Kianfar 2000	92	21.83 (18.49)	142	2.37 (10.66)		3.1 %	19.46 [15.29, 23.63]
LaManca 1993	10	22.5 (10.75)	10	14.3 (6.95)		1.7 %	8.20 [0.27, 16.13]
Lanerolle 2000	275	27.48 (2.25)	274	15.98 (9.3)		4.4 %	11.50 [10.37, 12.63]
Larocque 2006	12	22.3 (9.11)	9	16.96 (6.21)		2.1 %	5.34 [-1.22, 11.90]
Li 1994	40	30 (20.8)	40	18.8 (17.9)		1.6 %	11.20 [2.70, 19.70]
Maghsudlu 2008	185	26.06 (1.77)	182	19.47 (1.57)		4.5 %	6.59 [6.25, 6.93]
Marks 2014	129	17 (10.9)	128	10.6 (8.4)		4.0 %	6.40 [4.02, 8.78]
Mujica-Coopman 2015	28	30.2 (21.2)	27	20.3 (13.5)		1.4 %	9.90 [0.54, 19.26]
Swain 2007	9	4.6 (6.9)	12	0.5 (4.5)		2.7 %	4.10 [-1.08, 9.28]
Taniguchi 1991	27	5.4 (2.95)	27	3.25 (0.55)		4.4 %	2.15 [1.02, 3.28]
Verdon 2003	71	21 (9.2)	65	13.7 (6.9)		3.8 %	7.30 [4.58, 10.02]
Viteri 1999	37	14.81 (17.52)	44	-2.96 (13.53)		2.0 %	17.77 [10.85, 24.69]
Walsh 1989	10	20.8 (12)	10	15.7 (9.9)		1.3 %	5.10 [-4.54, 14.74]
Yadrick 1989	9	41.5 (14.1)	9	28.2 (16.8)		0.7 %	13.30 [-1.03, 27.63]
Yoshida 1990	6	22 (5)	6	15 (6)		2.3 %	7.00 [0.75, 13.25]
Zaman 2013	22	45.2 (26.6)	22	30 (20.4)		0.7 %	15.20 [1.19, 29.21]

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Favours control Favours iron

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Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Subtotal (95% CI)	**1529**		**1467**			**57.7 %**	**9.99 [8.38, 11.61]**
Heterogeneity: Tau^2 = 8.03; Chi^2 = 349.91, df = 24 (P<0.00001); I^2 =93%							
Test for overall effect: Z = 12.13 (P < 0.00001)							
Total (95% CI)	**1958**		**1873**			**100.0 %**	**10.31 [8.99, 11.63]**
Heterogeneity: Tau^2 = 9.90; Chi^2 = 480.84, df = 45 (P<0.00001); I^2 =91%							
Test for overall effect: Z = 15.34 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 0.24, df = 3 (P = 0.97), I^2 =0.0%							

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Favours control Favours iron

Analysis 6.7. Comparison 6 Iron status, Outcome 7 Ferritin in ng/ml (dose).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 6 Iron status

Outcome: 7 Ferritin in ng/ml (dose)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
I < 30 mg							
Booth 2014	25	25.4 (15.8)	24	18.4 (17.5)		1.5 %	7.00 [-2.35, 16.35]
Brutsaert 2003	10	15.02 (7.02)	10	16.18 (7.24)		2.4 %	-1.16 [-7.41, 5.09]
Fogelholm 1994	37	28.67 (16.22)	35	17 (9.31)		2.5 %	11.67 [5.60, 17.74]
Hinton 2000	22	14.52 (7.04)	19	8.11 (3.92)		3.7 %	6.41 [2.98, 9.84]
Hinton 2007	10	20.82 (11.6)	10	15.18 (12.23)		1.3 %	5.64 [-4.81, 16.09]
Larocque 2006	12	22.3 (9.11)	9	16.96 (6.21)		2.3 %	5.34 [-1.22, 11.90]
Swain 2007	9	4.6 (6.9)	12	0.5 (4.5)		2.9 %	4.10 [-1.08, 9.28]
Taniguchi 1991	27	5.4 (2.95)	27	3.25 (0.55)		4.7 %	2.15 [1.02, 3.28]
Viteri 1999	37	14.81 (17.52)	44	-2.96 (13.53)		2.2 %	17.77 [10.85, 24.69]

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Favours control Favours iron

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Study or subgroup	Iron N	Iron Mean(SD)	Control N	Control Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Yadrick 1989	9	41.5 (14.1)	9	28.2 (16.8)		0.8 %	13.30 [-1.03, 27.63]
Subtotal (95% CI)	**198**		**199**			**24.3 %**	**6.47 [3.18, 9.75]**
Heterogeneity: Tau² = 16.93; Chi² = 36.32, df = 9 (P = 0.00003); I² =75%							
Test for overall effect: Z = 3.85 (P = 0.00012)							
2 31 mg to 60 mg							
Binkoski 2004	14	32.3 (13.1)	12	17.2 (12.47)		1.4 %	15.10 [5.26, 24.94]
Eftekhari 2006	47	17.2 (1.28)	47	10.89 (0.55)		4.9 %	6.31 [5.91, 6.71]
Flink 2006	24	33 (14)	23	23.4 (15.8)		1.7 %	9.60 [1.05, 18.15]
Hoppe 2013	42.9166667 (29.79)		24	12	24 (13.5)	0.8 %	18.92 [4.76, 33.07]
Jayatissa 1999	222	93.4 (39.9)	217	56.3 (30.4)		2.3 %	37.10 [30.47, 43.73]
Jensen 1991	7	42 (23.81)	6	17 (14.7)		0.4 %	25.00 [3.80, 46.20]
Kang 2004	11	33.3 (33.4)	14	24.1 (15.8)		0.4 %	9.20 [-12.20, 30.60]
Kianfar 2000	92	21.83 (18.49)	142	2.37 (10.66)		3.4 %	19.46 [15.29, 23.63]
Klingshirn 1992	9	23.44 (6.65)	9	15.77 (10.45)		1.8 %	7.67 [-0.42, 15.76]
Lanerolle 2000	275	27.48 (2.25)	274	15.98 (9.3)		4.7 %	11.50 [10.37, 12.63]
Leonard 2014	8	34.4 (10.2)	4	31.9 (5)		1.7 %	2.50 [-6.10, 11.10]
Li 1994	40	30 (20.8)	40	18.8 (17.9)		1.7 %	11.20 [2.70, 19.70]
Marks 2014	129	17 (10.9)	128	10.6 (8.4)		4.3 %	6.40 [4.02, 8.78]
McClung 2009	85	32 (22.1)	86	26 (18.3)		2.5 %	6.00 [-0.09, 12.09]
Mujica-Coopman 2015	28	30.2 (21.2)	27	20.3 (13.5)		1.5 %	9.90 [0.54, 19.26]
Murray-Kolb 2007	56	35.4 (34.46)	57	21.16 (20.11)		1.3 %	14.24 [3.81, 24.67]
Yoshida 1990	6	22 (5)	6	15 (6)		2.4 %	7.00 [0.75, 13.25]
Zaman 2013	22	45.2 (26.6)	22	30 (20.4)		0.8 %	15.20 [1.19, 29.21]
Zhu 1998	20	36.9 (24)	17	16.2 (13.5)		1.0 %	20.70 [8.38, 33.02]
Subtotal (95% CI)	**1119**		**1143**			**38.8 %**	**12.36 [9.50, 15.22]**
Heterogeneity: Tau² = 22.93; Chi² = 204.52, df = 18 (P<0.00001); I² =91%							
Test for overall effect: Z = 8.47 (P < 0.00001)							
3 61 mg to 100 mg							
Fogelholm 1992	14	26 (24.3)	17	11 (10.8)		0.8 %	15.00 [1.27, 28.73]
LaManca 1993	10	22.5 (10.75)	10	14.3 (6.95)		1.9 %	8.20 [0.27, 16.13]
Leonard 2014	8	30.7 (7)	4	31.9 (5)		2.2 %	-1.20 [-8.09, 5.69]
Radjen 2011	19	24.94 (5.83)	18	8.99 (2.05)		4.1 %	15.95 [13.16, 18.74]
Verdon 2003	71	21 (9.2)	65	13.7 (6.9)		4.1 %	7.30 [4.58, 10.02]

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Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Waldvogel 2012	74	28 (9.8)	71	12.9 (8.3)		4.0 %	15.10 [12.15, 18.05]
Subtotal (95% CI)	**196**		**185**			**17.0 %**	**10.14 [5.20, 15.08]**
Heterogeneity: Tau^2 = 28.57; Chi^2 = 38.49, df = 5 (P<0.00001); I^2 =87%							
Test for overall effect: Z = 4.02 (P = 0.000057)							
4 > 100 mg							
Bruner 1996	37	27.3 (13.2)	36	12.1 (7.6)		3.0 %	15.20 [10.28, 20.12]
Charoenlarp 1988	160	99.775 (54.13)	86	48 (33)		1.2 %	51.78 [40.87, 62.68]
DellaValle 2012	15	28 (8.6)	16	27.5 (13.1)		1.9 %	0.50 [-7.26, 8.26]
Gordeuk 1987	34	13 (4.09)	19	10 (4.35)		4.3 %	3.00 [0.61, 5.39]
Maghsudlu 2008	185	26.06 (1.77)	182	19.47 (1.57)		4.9 %	6.59 [6.25, 6.93]
Newhouse 1989	19	37.7 (19.7)	18	17.2 (8.9)		1.4 %	20.50 [10.73, 30.27]
Rowland 1988	7	26.6 (10.1)	7	8.6 (3.9)		1.8 %	18.00 [9.98, 26.02]
Walsh 1989	10	20.8 (12)	10	15.7 (9.9)		1.4 %	5.10 [-4.54, 14.74]
Subtotal (95% CI)	**467**		**374**			**19.9 %**	**13.50 [8.15, 18.86]**
Heterogeneity: Tau^2 = 46.61; Chi^2 = 104.30, df = 7 (P<0.00001); I^2 =93%							
Test for overall effect: Z = 4.94 (P < 0.00001)							
Total (95% CI)	**1980**		**1901**			**100.0 %**	**10.16 [8.79, 11.52]**
Heterogeneity: Tau^2 = 9.97; Chi^2 = 476.57, df = 42 (P<0.00001); I^2 =91%							
Test for overall effect: Z = 14.54 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 8.59, df = 3 (P = 0.04), I^2 =65%							

Analysis 6.8. Comparison 6 Iron status, Outcome 8 Ferritin in ng/ml (duration).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 6 Iron status

Outcome: 8 Ferritin in ng/ml (duration)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 < 30 days (1 month)							
Gordeuk 1987	34	13 (4.09)	19	10 (4.35)		4.3 %	3.00 [0.61, 5.39]
Kang 2004	11	33.3 (33.4)	14	24.1 (15.8)		0.4 %	9.20 [-12.20, 30.60]
Maghsudlu 2008	185	26.06 (1.77)	182	19.47 (1.57)		4.9 %	6.59 [6.25, 6.93]
Rowland 1988	7	26.6 (10.1)	7	8.6 (3.9)		1.8 %	18.00 [9.98, 26.02]
Taniguchi 1991	27	5.4 (2.95)	27	3.25 (0.55)		4.8 %	2.15 [1.02, 3.28]
Verdon 2003	71	21 (9.2)	65	13.7 (6.9)		4.2 %	7.30 [4.58, 10.02]
Waldvogel 2012	74	28 (9.8)	71	12.9 (8.3)		4.0 %	15.10 [12.15, 18.05]
Subtotal (95% CI)	**409**		**385**			**24.5 %**	**7.60 [4.64, 10.57]**
Heterogeneity: Tau² = 11.54; Chi² = 104.62, df = 6 (P<0.00001); I² =94%							
Test for overall effect: Z = 5.03 (P < 0.00001)							
2 1 to 3 months							
Binkoski 2004	14	32.3 (13.1)	12	17.2 (12.47)		1.4 %	15.10 [5.26, 24.94]
Bruner 1996	37	27.3 (13.2)	36	12.1 (7.6)		3.0 %	15.20 [10.28, 20.12]
Brutsaert 2003	10	15.02 (7.02)	10	16.18 (7.24)		2.5 %	-1.16 [-7.41, 5.09]
Charoenlarp 1988	160	99.775 (54.13)	86	48 (33)		1.2 %	51.78 [40.87, 62.68]
DellaValle 2012	15	28 (8.6)	16	27.5 (13.1)		1.9 %	0.50 [-7.26, 8.26]
Eftekhari 2006	47	17.2 (1.28)	47	10.89 (0.55)		4.9 %	6.31 [5.91, 6.71]
Flink 2006	24	33 (14)	23	23.4 (15.8)		1.7 %	9.60 [1.05, 18.15]
Fogelholm 1992	14	26 (24.3)	17	11 (10.8)		0.8 %	15.00 [1.27, 28.73]
Hinton 2000	22	14.52 (7.04)	19	8.11 (3.92)		3.8 %	6.41 [2.98, 9.84]
Hinton 2007	10	20.82 (11.6)	10	15.18 (12.23)		1.3 %	5.64 [-4.81, 16.09]
Hoppe 2013	42.9166667 (29.79)		24	12	24 (13.5)	0.8 %	18.92 [4.76, 33.07]
Jayatissa 1999	222	93.4 (39.9)	217	56.3 (30.4)		2.3 %	37.10 [30.47, 43.73]
Jensen 1991	7	42 (23.81)	6	17 (14.7)		0.4 %	25.00 [3.80, 46.20]
Kianfar 2000	92	21.83 (18.49)	142	2.37 (10.66)		3.4 %	19.46 [15.29, 23.63]

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Favours control Favours iron

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Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Klingshirn 1992	9	23.44 (6.65)	9	15.77 (10.45)		1.8 %	7.67 [-0.42, 15.76]
LaManca 1993	10	22.5 (10.75)	10	14.3 (6.95)		1.9 %	8.20 [0.27, 16.13]
Lanerolle 2000	275	27.48 (2.25)	274	15.98 (9.3)		4.8 %	11.50 [10.37, 12.63]
Larocque 2006	12	22.3 (9.11)	9	16.96 (6.21)		2.3 %	5.34 [-1.22, 11.90]
Li 1994	40	30 (20.8)	40	18.8 (17.9)		1.7 %	11.20 [2.70, 19.70]
Marks 2014	129	17 (10.9)	128	10.6 (8.4)		4.3 %	6.40 [4.02, 8.78]
McClung 2009	85	32 (22.1)	86	26 (18.3)		2.5 %	6.00 [-0.09, 12.09]
Mujica-Coopman 2015	28	30.2 (21.2)	27	20.3 (13.5)		1.5 %	9.90 [0.54, 19.26]
Newhouse 1989	19	37.7 (19.7)	18	17.2 (8.9)		1.4 %	20.50 [10.73, 30.27]
Radjen 2011	19	24.94 (5.83)	18	8.99 (2.05)		4.1 %	15.95 [13.16, 18.74]
Swain 2007	9	4.6 (6.9)	12	0.5 (4.5)		2.9 %	4.10 [-1.08, 9.28]
Viteri 1999	37	14.81 (17.52)	44	-2.96 (13.53)		2.2 %	17.77 [10.85, 24.69]
Walsh 1989	10	20.8 (12)	10	15.7 (9.9)		1.4 %	5.10 [-4.54, 14.74]
Yadrick 1989	9	41.5 (14.1)	9	28.2 (16.8)		0.8 %	13.30 [-1.03, 27.63]
Yoshida 1990	6	22 (5)	6	15 (6)		2.5 %	7.00 [0.75, 13.25]
Zaman 2013	22	45.2 (26.6)	22	30 (20.4)		0.8 %	15.20 [1.19, 29.21]
Zhu 1998	20	36.9 (24)	17	16.2 (13.5)		1.0 %	20.70 [8.38, 33.02]
Subtotal (95% CI)	**1437**		**1392**			**67.5 %**	**12.17 [9.81, 14.53]**
Heterogeneity: Tau^2 = 28.95; Chi^2 = 343.35, df = 30 (P<0.00001); I^2 =91%							
Test for overall effect: Z = 10.11 (P < 0.00001)							
3 > 3 months							
Booth 2014	25	25.4 (15.8)	24	18.4 (17.5)		1.5 %	7.00 [-2.35, 16.35]
Fogelholm 1994	37	28.67 (16.22)	35	17 (9.31)		2.5 %	11.67 [5.60, 17.74]
Leonard 2014	16	32.6 (8.66)	8	31.9 (5)		2.8 %	0.70 [-4.78, 6.18]
Murray-Kolb 2007	56	35.4 (34.46)	57	21.16 (20.11)		1.3 %	14.24 [3.81, 24.67]
Subtotal (95% CI)	**134**		**124**			**8.1 %**	**7.85 [1.31, 14.38]**
Heterogeneity: Tau^2 = 28.96; Chi^2 = 9.19, df = 3 (P = 0.03); I^2 =67%							
Test for overall effect: Z = 2.35 (P = 0.019)							
Total (95% CI)	**1980**		**1901**			**100.0 %**	**10.27 [8.90, 11.65]**
Heterogeneity: Tau^2 = 9.96; Chi^2 = 475.21, df = 41 (P<0.00001); I^2 =91%							
Test for overall effect: Z = 14.63 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 6.12, df = 2 (P = 0.05), I^2 =67%							

Analysis 6.9. Comparison 6 Iron status, Outcome 9 Ferritin in ng/ml (type of iron).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 6 Iron status

Outcome: 9 Ferritin in ng/ml (type of iron)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Ferrous sulphate							
Binkoski 2004	14	32.3 (13.1)	12	17.2 (12.47)		1.3 %	15.10 [5.26, 24.94]
Bruner 1996	37	27.3 (13.2)	36	12.1 (7.6)		2.9 %	15.20 [10.28, 20.12]
Brutsaert 2003	10	15.02 (7.02)	10	16.18 (7.24)		2.3 %	-1.16 [-7.41, 5.09]
DellaValle 2012	15	28 (8.6)	16	27.5 (13.1)		1.8 %	0.50 [-7.26, 8.26]
Eftekhari 2006	47	17.2 (1.28)	47	10.89 (0.55)		4.7 %	6.31 [5.91, 6.71]
Fogelholm 1992	14	26 (24.3)	17	11 (10.8)		0.8 %	15.00 [1.27, 28.73]
Gordeuk 1987	17	12 (4.123)	9	10 (4.35)		3.6 %	2.00 [-1.45, 5.45]
Hinton 2000	22	14.52 (7.04)	19	8.11 (3.92)		3.6 %	6.41 [2.98, 9.84]
Hinton 2007	10	20.82 (11.6)	10	15.18 (12.23)		1.2 %	5.64 [-4.81, 16.09]
Jensen 1991	7	42 (23.81)	6	17 (14.7)		0.4 %	25.00 [3.80, 46.20]
Kianfar 2000	92	21.83 (18.49)	142	2.37 (10.66)		3.3 %	19.46 [15.29, 23.63]
Klingshirn 1992	9	23.44 (6.65)	9	15.77 (10.45)		1.8 %	7.67 [-0.42, 15.76]
LaManca 1993	10	22.5 (10.75)	10	14.3 (6.95)		1.8 %	8.20 [0.27, 16.13]
Lanerolle 2000	275	27.48 (2.25)	274	15.98 (9.3)		4.6 %	11.50 [10.37, 12.63]
Leonard 2014	16	32.6 (8.66)	8	31.9 (5)		2.7 %	0.70 [-4.78, 6.18]
Li 1994	40	30 (20.8)	40	18.8 (17.9)		1.6 %	11.20 [2.70, 19.70]
Maghsudlu 2008	185	26.06 (1.77)	182	19.47 (1.57)		4.7 %	6.59 [6.25, 6.93]
McClung 2009	85	32 (22.1)	86	26 (18.3)		2.4 %	6.00 [-0.09, 12.09]
Mujica-Coopman 2015	28	30.2 (21.2)	27	20.3 (13.5)		1.4 %	9.90 [0.54, 19.26]
Murray-Kolb 2007	56	35.4 (34.46)	57	21.16 (20.11)		1.2 %	14.24 [3.81, 24.67]
Newhouse 1989	19	37.7 (19.7)	18	17.2 (8.9)		1.4 %	20.50 [10.73, 30.27]
Radjen 2011	19	24.94 (5.83)	18	8.99 (2.05)		3.9 %	15.95 [13.16, 18.74]
Rowland 1988	7	26.6 (10.1)	7	8.6 (3.9)		1.8 %	18.00 [9.98, 26.02]

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Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Verdon 2003	71	21 (9.2)	65	13.7 (6.9)		4.0 %	7.30 [4.58, 10.02]
Viteri 1999	37	14.81 (17.52)	44	-2.96 (13.53)		2.1 %	17.77 [10.85, 24.69]
Waldvogel 2012	74	28 (9.8)	71	12.9 (8.3)		3.8 %	15.10 [12.15, 18.05]
Yadrick 1989	9	41.5 (14.1)	9	28.2 (16.8)		0.7 %	13.30 [-1.03, 27.63]
Subtotal (95% CI)	**1225**		**1249**			**65.9 %**	**9.73 [8.32, 11.14]**
Heterogeneity: Tau^2 = 5.99; Chi^2 = 248.12, df = 26 (P<0.00001); I^2 =90%							
Test for overall effect: Z = 13.52 (P < 0.00001)							
2 Ferrous fumurate							
Flink 2006	24	33 (14)	23	23.4 (15.8)		1.6 %	9.60 [1.05, 18.15]
Subtotal (95% CI)	**24**		**23**			**1.6 %**	**9.60 [1.05, 18.15]**
Heterogeneity: not applicable							
Test for overall effect: Z = 2.20 (P = 0.028)							
3 Other/not stated							
Booth 2014	25	25.4 (15.8)	24	18.4 (17.5)		1.4 %	7.00 [-2.35, 16.35]
Charoenlarp 1988	160	99.775 (54.13)	86	48 (33)		1.2 %	51.78 [40.87, 62.68]
Fogelholm 1994	37	28.67 (16.22)	35	17 (9.31)		2.4 %	11.67 [5.60, 17.74]
Gordeuk 1987	17	14 (4.123)	9	10 (4.35)		3.6 %	4.00 [0.55, 7.45]
Hoppe 2013	42.9166667 (29.79)		24	12	24 (13.5)	0.8 %	18.92 [4.76, 33.07]
Jayatissa 1999	222	93.4 (39.9)	217	56.3 (30.4)		2.2 %	37.10 [30.47, 43.73]
Kang 2004	11	33.3 (33.4)	14	24.1 (15.8)		0.4 %	9.20 [-12.20, 30.60]
Larocque 2006	12	22.3 (9.11)	9	16.96 (6.21)		2.2 %	5.34 [-1.22, 11.90]
Marks 2014	129	17 (10.9)	128	10.6 (8.4)		4.1 %	6.40 [4.02, 8.78]
Newhouse 1989	19	37.7 (19.7)	18	17.2 (8.9)		1.4 %	20.50 [10.73, 30.27]
Swain 2007	9	4.6 (6.9)	12	0.5 (4.5)		2.8 %	4.10 [-1.08, 9.28]
Taniguchi 1991	27	5.4 (2.95)	27	3.25 (0.55)		4.6 %	2.15 [1.02, 3.28]
Walsh 1989	10	20.8 (12)	10	15.7 (9.9)		1.4 %	5.10 [-4.54, 14.74]
Yoshida 1990	6	22 (5)	6	15 (6)		2.3 %	7.00 [0.75, 13.25]
Zaman 2013	22	45.2 (26.6)	22	30 (20.4)		0.8 %	15.20 [1.19, 29.21]
Zhu 1998	20	36.9 (24)	17	16.2 (13.5)		1.0 %	20.70 [8.38, 33.02]
Subtotal (95% CI)	**750**		**646**			**32.5 %**	**13.34 [8.61, 18.08]**
Heterogeneity: Tau^2 = 72.79; Chi^2 = 213.64, df = 15 (P<0.00001); I^2 =93%							
Test for overall effect: Z = 5.53 (P < 0.00001)							
Total (95% CI)	**1999**		**1918**			**100.0 %**	**10.19 [8.84, 11.55]**
Heterogeneity: Tau^2 = 10.09; Chi^2 = 483.06, df = 43 (P<0.00001); I^2 =91%							
Test for overall effect: Z = 14.79 (P < 0.00001)							

-100 -50 0 50 100

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Study or subgroup	Iron		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
Test for subgroup differences: Chi^2 = 2.07, df = 2 (P = 0.35), I^2 =4%							

Analysis 6.10. Comparison 6 Iron status, Outcome 10 Transferrin saturation (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 6 Iron status

Outcome: 10 Transferrin saturation (total)

Study or subgroup	Iron		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
Binkoski 2004	14	32.3 (8.98)	12	32.6 (9.01)		4.2 %	-0.30 [-7.24, 6.64]
Booth 2014	23	47.4 (30.9)	24	34.6 (17.1)		1.6 %	12.80 [-1.56, 27.16]
Brutsaert 2003	10	39.6 (18.34)	10	27.4 (22.14)		1.1 %	12.20 [-5.62, 30.02]
Cooter 1978	5	30.9 (11.5)	5	41 (14.8)		1.3 %	-10.10 [-26.53, 6.33]
Eftekhari 2006	47	19.68 (7.16)	47	9.54 (0.9)		7.5 %	10.14 [8.08, 12.20]
Gordeuk 1990	40	24 (9)	36	20 (7)		6.5 %	4.00 [0.39, 7.61]
Hinton 2000	22	31.9 (19.69)	19	22 (16.13)		2.4 %	9.90 [-1.07, 20.87]
Hinton 2007	10	24.4 (15.7)	10	15.8 (8.4)		2.4 %	8.60 [-2.44, 19.64]
Jensen 1991	7	36 (13.23)	6	34 (14.7)		1.5 %	2.00 [-13.31, 17.31]
Klingshirn 1992	9	26.43 (13.39)	9	19.69 (5.39)		3.0 %	6.74 [-2.69, 16.17]
LaManca 1993	10	38 (15.49)	10	27.5 (11.7)		2.1 %	10.50 [-1.53, 22.53]
Lanerolle 2000	137	34.73 (12.79)	124	30.59 (10.33)		7.0 %	4.14 [1.33, 6.95]
Maghsudlu 2008	185	24.34 (0.96)	182	20.8 (1.06)		8.1 %	3.54 [3.33, 3.75]
McClung 2009	85	20.6 (10.3)	86	17.8 (9.4)		6.9 %	2.80 [-0.16, 5.76]

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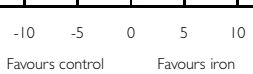
Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Mujica-Coopman 2015	28	28.6 (12)	27	24.9 (10.8)		4.8 %	3.70 [-2.33, 9.73]
Murray-Kolb 2007	56	28.9 (12.5)	57	21.9 (11.71)		5.9 %	7.00 [2.53, 11.47]
Newhouse 1989	19	34.1 (14.4)	18	21.4 (13)		3.2 %	12.70 [3.87, 21.53]
Radjen 2011	19	27.59 (8.92)	18	10.95 (4.2)		5.9 %	16.64 [12.18, 21.10]
Rybo 1985	45	39.9 (16.7)	44	23.4 (12.3)		4.7 %	16.50 [10.42, 22.58]
Swain 2007	9	-1.6 (1.5)	12	-0.02 (2.42)		7.7 %	-1.58 [-3.26, 0.10]
Walsh 1989	10	22.9 (7.1)	10	18.6 (6.1)		4.9 %	4.30 [-1.50, 10.10]
Zaman 2013	22	28 (12)	22	25.1 (12.1)		4.1 %	2.90 [-4.22, 10.02]
Zhu 1998	20	26.3 (16.9)	17	22.4 (11.7)		3.0 %	3.90 [-5.36, 13.16]
Total (95% CI)	**832**		**805**			**100.0 %**	**5.98 [3.93, 8.02]**

Heterogeneity: Tau^2 = 13.38; Chi^2 = 142.46, df = 22 (P<0.00001); I^2 =85%

Test for overall effect: Z = 5.73 (P < 0.00001)

Test for subgroup differences: Not applicable



Analysis 6.11. Comparison 6 Iron status, Outcome 11 Soluble transferrin receptor (mg/L) (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 6 Iron status

Outcome: 11 Soluble transferrin receptor (mg/L) (total)

Study or subgroup	Iron		Control		Std. Mean Difference	Weight	Std. Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
Booth 2014	25	1.03 (0.36)	24	1.19 (0.38)		8.5 %	-0.43 [-0.99, 0.14]
Brutsaert 2003	10	5.57 (2.65)	10	6.3 (2.12)		3.5 %	-0.29 [-1.17, 0.59]
DellaValle 2012	15	5.4 (1.7)	16	6.2 (1.7)		5.4 %	-0.46 [-1.17, 0.26]
Hinton 2000	22	6.78 (1.97)	19	7.98 (3.36)		7.1 %	-0.44 [-1.06, 0.19]
Hinton 2007	10	5.96 (1.17)	10	6.85 (1.78)		3.4 %	-0.57 [-1.46, 0.33]
Hoppe 2013	24	2.8458333 (1.454)	12	3.1 (1.755)		5.7 %	-0.16 [-0.85, 0.53]
Leonard 2014	8	1.3 (0.3)	8	0.7 (0.6)		2.3 %	1.20 [0.11, 2.29]
Mujica-Coopman 2015	28	5.8 (1.8)	27	6.5 (1.9)		9.6 %	-0.37 [-0.91, 0.16]
Murray-Kolb 2007	56	5.5 (2.3)	57	6.43 (2.3)		19.7 %	-0.40 [-0.77, -0.03]
R svik 2010	82	2.94 (0.8)	79	3.14 (0.85)		28.5 %	-0.24 [-0.55, 0.07]
Zhu 1998	20	4.51 (1.5)	17	5.83 (2.95)		6.3 %	-0.57 [-1.23, 0.09]
Total (95% CI)	**300**		**279**			**100.0 %**	**-0.32 [-0.49, -0.16]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 9.34$, df = 10 (P = 0.50); $I^2 = 0.0\%$

Test for overall effect: Z = 3.81 (P = 0.00014)

Test for subgroup differences: Not applicable

Analysis 6.12. Comparison 6 Iron status, Outcome 12 Total iron binding capacity (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 6 Iron status

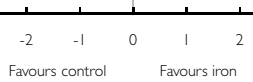
Outcome: 12 Total iron binding capacity (total)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Binkoski 2004	14	67.4 (11.22)	12	73.6 (11.43)		5.3 %	-0.53 [-1.32, 0.26]
Brutsaert 2003	10	58.6 (16.44)	10	64.7 (17.71)		5.2 %	-0.34 [-1.23, 0.54]
Cooter 1978	5	337.7 (36.8)	5	300.6 (47.7)		4.8 %	0.79 [-0.53, 2.10]
Gordeuk 1987	34	396.5 (61.23)	19	407 (78.46)		5.5 %	-0.15 [-0.71, 0.41]
Gordeuk 1990	40	328 (43)	36	371 (55)		5.5 %	-0.87 [-1.34, -0.40]
Hinton 2000	22	62.1 (17.82)	19	60.7 (13.07)		5.4 %	0.09 [-0.53, 0.70]
Hinton 2007	10	356.9 (66.1)	10	382 (73.3)		5.2 %	-0.34 [-1.23, 0.54]
Jensen 1991	7	412 (148.16)	6	355 (117.58)		5.0 %	0.39 [-0.71, 1.50]
Kang 2004	11	388 (75)	14	392 (50)		5.3 %	-0.06 [-0.85, 0.73]
Klingshirn 1992	9	274.86 (41.79)	9	328.04 (49.04)		5.1 %	-1.11 [-2.12, -0.10]
LaManca 1993	10	293.8 (44.27)	10	342.2 (52.49)		5.2 %	-0.95 [-1.89, -0.02]
Maghsudlu 2008	185	369.73 (6.79)	182	406.42 (8.88)		5.5 %	-4.64 [-5.03, -4.24]
Mujica-Coopman 2015	28	326.7 (33.5)	27	362.6 (47.1)		5.5 %	-0.87 [-1.42, -0.31]
Radjen 2011	19	56.71 (6.92)	18	68.49 (8.12)		5.3 %	-1.53 [-2.27, -0.79]
Rybo 1985	45	61.6 (10.1)	44	67.7 (12.5)		5.5 %	-0.53 [-0.96, -0.11]
Swain 2007	9	0.5 (6.6)	12	2.9 (2.77)		5.2 %	-0.48 [-1.36, 0.40]
Walsh 1989	10	345 (39)	10	368 (41)		5.2 %	-0.55 [-1.45, 0.35]
Yoshida 1990	6	400 (60)	6	410 (60)		5.0 %	-0.15 [-1.29, 0.98]
Zhu 1998	20	63.1 (17.6)	17	63.2 (15.4)		5.4 %	-0.01 [-0.65, 0.64]
Total (95% CI)	**494**		**466**			**100.0 %**	**-0.64 [-1.38, 0.09]**

Heterogeneity: $Tau^2 = 2.49$; $Chi^2 = 390.10$, df = 18 (P<0.00001); I^2 =95%

Test for overall effect: Z = 1.72 (P = 0.085)

Test for subgroup differences: Not applicable



Analysis 6.13. Comparison 6 Iron status, Outcome 13 Serum iron (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 6 Iron status

Outcome: 13 Serum iron (total)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Brutsaert 2003	10	22.7 (10.44)	10	15.8 (10.75)		4.9 %	0.62 [-0.28, 1.53]
Cooter 1978	5	102.3 (33.2)	5	118.8 (34.2)		3.3 %	-0.44 [-1.71, 0.82]
Gordeuk 1987	34	90.5 (44.3)	19	80 (34.87)		7.2 %	0.25 [-0.31, 0.81]
Gordeuk 1990	40	76 (24)	36	73 (25)		8.1 %	0.12 [-0.33, 0.57]
Hinton 2000	22	19.4 (12.66)	19	12.2 (7.84)		6.7 %	0.66 [0.03, 1.29]
Hinton 2007	10	86.3 (62.4)	10	57.1 (29.7)		4.9 %	0.57 [-0.33, 1.47]
Jensen 1991	7	126 (50.27)	6	112 (36.74)		3.9 %	0.29 [-0.81, 1.39]
Kang 2004	11	78 (31)	14	85 (476)		5.6 %	-0.02 [-0.81, 0.77]
Klingshirn 1992	9	71.43 (33.29)	9	63.57 (15.54)		4.8 %	0.29 [-0.64, 1.22]
LaManca 1993	10	110 (44.58)	10	93.5 (34.15)		5.0 %	0.40 [-0.49, 1.29]
Maghsudlu 2008	185	87.71 (3.8)	182	83.26 (4.71)		9.7 %	1.04 [0.82, 1.26]
Radjen 2011	19	15.49 (4.8)	18	7.41 (2.64)		5.5 %	2.03 [1.22, 2.83]
Rybo 1985	45	24.8 (11.7)	44	15.5 (7.5)		8.2 %	0.94 [0.50, 1.37]
Walsh 1989	10	79.3 (56.8)	10	68.3 (38.9)		5.0 %	0.22 [-0.66, 1.10]
Yoshida 1990	6	84 (36)	6	96 (36)		3.7 %	-0.31 [-1.45, 0.83]
Zaman 2013	22	18.2 (8.8)	22	17.8 (8)		7.0 %	0.05 [-0.54, 0.64]
Zhu 1998	20	15.5 (9.1)	17	13.5 (6.8)		6.6 %	0.24 [-0.41, 0.89]
Total (95% CI)	**465**		**437**			**100.0 %**	**0.47 [0.19, 0.74]**

Heterogeneity: $Tau^2 = 0.19$; $Chi^2 = 48.20$, df = 16 (P = 0.00004); $I^2 = 67\%$

Test for overall effect: Z = 3.31 (P = 0.00092)

Test for subgroup differences: Not applicable

Analysis 6.14. Comparison 6 Iron status, Outcome 14 Erythrocyte protophyrin (ug/g Hb) (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 6 Iron status

Outcome: 14 Erythrocyte protophyrin (ug/g Hb) (total)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Mean Difference IV,Random,95% CI
Berger 1997	65	2.06 (0.89)	65	2.19 (0.77)		-0.13 [-0.42, 0.16]

Analysis 7.1. Comparison 7 Exercise performance - peak (maximal), Outcome 1 Absolute VO2 max (L/min) (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 7 Exercise performance - peak (maximal)

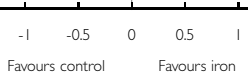
Outcome: 1 Absolute VO_2 max (L/min) (total)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
DellaValle 2012	15	3.4 (0.4)	16	3.3 (0.4)		10.1 %	0.10 [-0.18, 0.38]
Hinton 2000	22	2.48 (0.375)	19	2.56 (0.48)		11.3 %	-0.08 [-0.35, 0.19]
Hinton 2007	10	2.63 (0.8)	10	2.56 (0.76)		1.7 %	0.07 [-0.61, 0.75]
LaManca 1993	10	2.39 (0.38)	10	2.3 (0.38)		7.3 %	0.09 [-0.24, 0.42]
Li 1994	40	1.97 (0.34)	40	1.82 (0.35)		35.2 %	0.15 [0.00, 0.30]
Radjen 2011	19	3.05 (0.27)	18	2.84 (0.31)		22.8 %	0.21 [0.02, 0.40]
Rowland 1988	5	3.132 (0.377)	5	2.9 (0.52)		2.5 %	0.23 [-0.33, 0.79]
Zhu 1998	20	2.535 (0.482)	17	2.61 (0.443)		9.0 %	-0.07 [-0.37, 0.23]
Total (95% CI)	**141**		**135**			**100.0 %**	**0.11 [0.02, 0.20]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 4.96$, df = 7 (P = 0.66); $I^2 = 0.0\%$

Test for overall effect: Z = 2.38 (P = 0.017)

Test for subgroup differences: Not applicable



Analysis 7.2. Comparison 7 Exercise performance - peak (maximal), Outcome 2 Relative VO2 max ml/kg/min (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 7 Exercise performance - peak (maximal)

Outcome: 2 Relative VO_2 max ml/kg/min (total)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
DellaValle 2012	15	66.5 (5.4)	16	65.1 (6.2)		6.7 %	1.40 [-2.69, 5.49]
Fogelholm 1992	14	45.7 (12.69)	17	45.3 (10.935)		3.2 %	0.40 [-8.04, 8.84]
Hinton 2000	22	57.6 (8.44)	19	58.1 (10.46)		4.9 %	-0.50 [-6.38, 5.38]
Hinton 2007	10	42.41 (8.54)	10	37.92 (8.23)		3.8 %	4.49 [-2.86, 11.84]
Jensen 1991	7	38 (2)	6	29.3 (1.7)		9.0 %	8.70 [6.69, 10.71]
Klingshirn 1992	9	50.47 (4.6)	9	51.72 (4.15)		6.7 %	-1.25 [-5.30, 2.80]
LaManca 1993	10	41.72 (3.16)	10	39.48 (6.32)		6.4 %	2.24 [-2.14, 6.62]
Lyle 1992	20	42.7 (5.155)	14	43.2 (3.55)		8.0 %	-0.50 [-3.43, 2.43]
Newhouse 1989	19	52.7 (3.8)	18	50.6 (5.5)		7.9 %	2.10 [-0.96, 5.16]
Radjen 2011	19	47.04 (2.38)	18	44.48 (2.84)		9.3 %	2.56 [0.87, 4.25]
Rajaram 1995	16	38.1 (6)	13	35.2 (6.4)		6.2 %	2.90 [-1.65, 7.45]
Rowland 1988	5	54.3 (6.6)	5	52.6 (5.2)		3.8 %	1.70 [-5.66, 9.06]
Taniguchi 1991	27	37.6 (3.4)	27	37.8 (4)		9.1 %	-0.20 [-2.18, 1.78]
Walsh 1989	10	56.61 (3.7)	10	50.67 (2.4)		8.3 %	5.94 [3.21, 8.67]
Yoshida 1990	6	54.66 (4.66)	6	52 (2)		6.7 %	2.66 [-1.40, 6.72]
Total (95% CI)	**209**		**198**			**100.0 %**	**2.36 [0.55, 4.17]**

Heterogeneity: $Tau^2 = 8.39$; $Chi^2 = 58.26$, df = 14 (P<0.00001); $I^2 = 76\%$

Test for overall effect: Z = 2.55 (P = 0.011)

Test for subgroup differences: Not applicable

Analysis 7.3. Comparison 7 Exercise performance - peak (maximal), Outcome 3 Peak respiratory exchange ratio (RER) (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 7 Exercise performance - peak (maximal)

Outcome: 3 Peak respiratory exchange ratio (RER) (total)

Study or subgroup	Iron		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
DellaValle 2012	15	1.05 (0.07)	16	1.04 (0.07)		26.9 %	0.01 [-0.04, 0.06]
Hinton 2000	22	1.06 (0.09)	19	1.08 (0.09)		21.5 %	-0.02 [-0.08, 0.04]
Hinton 2007	10	1.23 (0.06)	10	1.2 (0.05)		27.9 %	0.03 [-0.02, 0.08]
LaManca 1993	10	1.21 (0.06)	10	1.21 (0.06)		23.7 %	0.0 [-0.05, 0.05]
Total (95% CI)	**57**		**55**			**100.0 %**	**0.01 [-0.02, 0.03]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.87$, df = 3 (P = 0.60); $I^2 = 0.0\%$

Test for overall effect: Z = 0.52 (P = 0.60)

Test for subgroup differences: Not applicable

Analysis 7.4. Comparison 7 Exercise performance - peak (maximal), Outcome 4 Maximum heart rate (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 7 Exercise performance - peak (maximal)

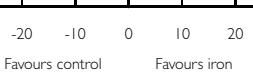
Outcome: 4 Maximum heart rate (total)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
DellaValle 2012	15	195.8 (7.8)	16	190.8 (9.8)		16.9 %	5.00 [-1.22, 11.22]
Hinton 2000	22	191.9 (6.52)	19	190.4 (7.8)		33.2 %	1.50 [-2.94, 5.94]
Hinton 2007	10	189 (9)	10	184 (11)		8.4 %	5.00 [-3.81, 13.81]
LaManca 1993	10	184 (3.16)	10	184 (6.32)		34.1 %	0.0 [-4.38, 4.38]
Rowland 1988	7	197 (10)	7	197 (8)		7.3 %	0.0 [-9.49, 9.49]
Total (95% CI)	**64**		**62**			**100.0 %**	**1.77 [-0.79, 4.33]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.33$, df = 4 (P = 0.68); $I^2 = 0.0\%$

Test for overall effect: Z = 1.35 (P = 0.18)

Test for subgroup differences: Not applicable



Analysis 7.5. Comparison 7 Exercise performance - peak (maximal), Outcome 5 Lactate at longest point (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 7 Exercise performance - peak (maximal)

Outcome: 5 Lactate at longest point (total)

Study or subgroup	Iron		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
DellaValle 2012	15	12.2 (1.7)	16	11.4 (2.1)		29.1 %	0.80 [-0.54, 2.14]
Klingshirn 1992	9	3.91 (1.42)	9	4.49 (0.65)		50.3 %	-0.58 [-1.60, 0.44]
LaManca 1993	10	9 (2.52)	10	8.5 (2.84)		9.4 %	0.50 [-1.85, 2.85]
Zhu 1998	20	9.9 (3.6)	17	9.8 (3.1)		11.2 %	0.10 [-2.06, 2.26]
Total (95% CI)	**54**		**52**			**100.0 %**	**0.00 [-0.72, 0.72]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.79$, df = 3 (P = 0.43); $I^2 = 0.0\%$

Test for overall effect: Z = 0.00 (P = 1.0)

Test for subgroup differences: Not applicable

Analysis 8.1. Comparison 8 Exercise performance - submaximal, Outcome 1 Percentage VO2 peak (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 8 Exercise performance - submaximal

Outcome: 1 Percentage VO_2 peak (total)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Hinton 2000	22	61.8 (7.04)	19	60.7 (6.71)		23.0 %	1.10 [-3.11, 5.31]
Klingshirn 1992	9	74.22 (3)	9	77.16 (3.73)		29.8 %	-2.94 [-6.07, 0.19]
LaManca 1993	10	76.2 (6.32)	10	80.8 (6.64)		16.2 %	-4.60 [-10.28, 1.08]
Rowland 1988	5	71.1 (10.4)	5	82.1 (9.1)		4.9 %	-11.00 [-23.11, 1.11]
Zhu 1998	20	83 (6.3)	17	88.5 (5.2)		26.0 %	-5.50 [-9.21, -1.79]
Total (95% CI)	**66**		**60**			**100.0 %**	**-3.34 [-6.17, -0.51]**

Heterogeneity: Tau^2 = 4.45; Chi^2 = 7.33, df = 4 (P = 0.12); I^2 =45%

Test for overall effect: Z = 2.31 (P = 0.021)

Test for subgroup differences: Not applicable

Analysis 8.2. Comparison 8 Exercise performance - submaximal, Outcome 2 Heart rate (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 8 Exercise performance - submaximal

Outcome: 2 Heart rate (total)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Hinton 2000	22	170 (14.07)	19	170 (13.07)		22.2 %	0.0 [-8.31, 8.31]
Hinton 2007	10	149 (13)	10	153 (15)		10.1 %	-4.00 [-16.30, 8.30]
LaManca 1993	10	164 (9.48)	10	172 (12.65)		16.0 %	-8.00 [-17.80, 1.80]
Li 1994	40	91.1 (8)	40	98 (65)		3.7 %	-6.90 [-27.20, 13.40]
Rowland 1988	7	165 (14)	7	175 (13)		7.7 %	-10.00 [-24.15, 4.15]
Zhu 1998	20	171 (9)	17	176 (10)		40.2 %	-5.00 [-11.18, 1.18]
Total (95% CI)	**109**		**103**			**100.0 %**	**-4.72 [-8.64, -0.80]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.27$, df = 5 (P = 0.81); $I^2 = 0.0\%$

Test for overall effect: Z = 2.36 (P = 0.018)

Test for subgroup differences: Not applicable

Analysis 8.3. Comparison 8 Exercise performance - submaximal, Outcome 3 Energy consumption (kJ/min) (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 8 Exercise performance - submaximal

Outcome: 3 Energy consumption (kJ/min) (total)

Study or subgroup	Iron		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
Hinton 2000	22	9.4 (1.41)	19	9.8 (1.74)		20.3 %	-0.40 [-1.38, 0.58]
Hinton 2007	10	1.9 (0.76)	10	1.9 (0.24)		79.7 %	0.0 [-0.49, 0.49]
Total (95% CI)	**32**		**29**			**100.0 %**	**-0.08 [-0.52, 0.36]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.51$, df = 1 (P = 0.47); $I^2 = 0.0\%$

Test for overall effect: Z = 0.36 (P = 0.72)

Test for subgroup differences: Not applicable

Analysis 8.4. Comparison 8 Exercise performance - submaximal, Outcome 4 Respiratory exchange ratio (RER) (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 8 Exercise performance - submaximal

Outcome: 4 Respiratory exchange ratio (RER) (total)

Study or subgroup	Iron		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
Hinton 2000	22	0.87 (0.09)	19	0.89 (0.09)		7.6 %	-0.02 [-0.08, 0.04]
Hinton 2007	10	0.919 (0.04)	10	0.9 (0.05)		14.7 %	0.02 [-0.02, 0.06]
Klingshirn 1992	9	0.94 (0.02)	9	0.96 (0.03)		41.8 %	-0.02 [-0.04, 0.00]
LaManca 1993	10	0.96 (0.06)	10	0.97 (0.06)		8.4 %	-0.01 [-0.06, 0.04]
Zhu 1998	20	0.89 (0.05)	17	0.89 (0.04)		27.5 %	0.0 [-0.03, 0.03]
Total (95% CI)	**71**		**65**			**100.0 %**	**-0.01 [-0.02, 0.01]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.88$, df = 4 (P = 0.58); $I^2 = 0.0\%$

Test for overall effect: Z = 1.08 (P = 0.28)

Test for subgroup differences: Not applicable

Analysis 8.5. Comparison 8 Exercise performance - submaximal, Outcome 5 Achieved workload (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 8 Exercise performance - submaximal

Outcome: 5 Achieved workload (total)

Study or subgroup	Iron		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
Hinton 2000	22	115 (28.1)	20	127 (31.3)		41.8 %	-12.00 [-30.06, 6.06]
Hinton 2007	10	97.7 (38.3)	10	92.2 (33.2)		13.8 %	5.50 [-25.92, 36.92]
Zhu 1998	20	137 (26)	17	138 (28)		44.4 %	-1.00 [-18.52, 16.52]
Total (95% CI)	**52**		**47**			**100.0 %**	**-4.70 [-16.37, 6.97]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.20$, df = 2 (P = 0.55); $I^2 = 0.0\%$

Test for overall effect: Z = 0.79 (P = 0.43)

Test for subgroup differences: Not applicable

Analysis 8.6. Comparison 8 Exercise performance - submaximal, Outcome 6 Time to exhaustion (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 8 Exercise performance - submaximal

Outcome: 6 Time to exhaustion (total)

Study or subgroup	Iron		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Random,95% CI		IV,Random,95% CI
Klingshirn 1992	9	83.23 (13.62)	9	80.44 (10.82)		75.6 %	2.79 [-8.57, 14.15]
LaManca 1993	10	51.4 (23.56)	10	45.85 (22.04)		24.4 %	5.55 [-14.45, 25.55]
Total (95% CI)	**19**		**19**			**100.0 %**	**3.46 [-6.42, 13.34]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.06$, df = 1 (P = 0.81); $I^2 = 0.0\%$

Test for overall effect: Z = 0.69 (P = 0.49)

Test for subgroup differences: Not applicable

Analysis 9.1. Comparison 9 Anthropometric, Outcome 1 Height (cm) (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 9 Anthropometric

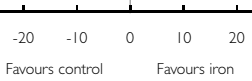
Outcome: 1 Height (cm) (total)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Berger 1997	65	149.5 (6.9)	65	148.7 (6.5)		30.1 %	0.80 [-1.50, 3.10]
Eftekhari 2006	47	154.5 (5.49)	47	156.9 (3.95)		34.4 %	-2.40 [-4.33, -0.47]
Hinton 2000	22	166.5 (7.03)	19	166.1 (6.97)		14.6 %	0.40 [-3.90, 4.70]
Radjen 2011	19	177 (6)	18	176 (4)		20.9 %	1.00 [-2.27, 4.27]
Total (95% CI)	**153**		**149**			**100.0 %**	**-0.32 [-2.25, 1.61]**

Heterogeneity: $Tau^2 = 1.84$; $Chi^2 = 5.87$, df = 3 (P = 0.12); $I^2 = 49\%$

Test for overall effect: Z = 0.32 (P = 0.75)

Test for subgroup differences: Not applicable



Analysis 9.2. Comparison 9 Anthropometric, Outcome 2 Weight (kg) (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 9 Anthropometric

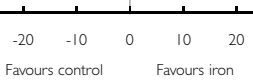
Outcome: 2 Weight (kg) (total)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Berger 1997	65	53.7 (9.8)	65	52.6 (9)		13.0 %	1.10 [-2.13, 4.33]
DellaValle 2012	15	67.3 (7.1)	16	67.8 (9.4)		4.0 %	-0.50 [-6.34, 5.34]
Eftekhari 2006	47	50.75 (5.47)	47	50.46 (3.98)		36.3 %	0.29 [-1.64, 2.22]
Hinton 2000	22	59 (5.63)	19	59.6 (7.85)		7.5 %	-0.60 [-4.84, 3.64]
Hinton 2007	10	61.4 (64)	10	67.4 (11.1)		0.1 %	-6.00 [-46.26, 34.26]
Kanani 2000	101	29.39 (7.74)	102	27.22 (8.58)		26.9 %	2.17 [-0.08, 4.42]
Radjen 2011	19	65.13 (7.64)	18	64.11 (6.11)		6.9 %	1.02 [-3.43, 5.47]
Zhu 1998	20	60.3 (6.3)	17	61.7 (8.8)		5.4 %	-1.40 [-6.41, 3.61]
Total (95% CI)	**299**		**294**			**100.0 %**	**0.76 [-0.41, 1.92]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 3.19$, df = 7 (P = 0.87); $I^2 = 0.0\%$

Test for overall effect: Z = 1.27 (P = 0.20)

Test for subgroup differences: Not applicable



Analysis 9.3. Comparison 9 Anthropometric, Outcome 3 Weight (kg) (sensitivity analysis).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 9 Anthropometric

Outcome: 3 Weight (kg) (sensitivity analysis)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Berger 1997	65	53.7 (9.8)	65	52.6 (9)		17.7 %	1.10 [-2.13, 4.33]
DellaValle 2012	15	67.3 (7.1)	16	67.8 (9.4)		5.4 %	-0.50 [-6.34, 5.34]
Eftekhari 2006	47	50.75 (5.47)	47	50.46 (3.98)		49.6 %	0.29 [-1.64, 2.22]
Hinton 2000	22	59 (5.63)	19	59.6 (7.85)		10.3 %	-0.60 [-4.84, 3.64]
Hinton 2007	10	61.4 (64)	10	67.4 (11.1)		0.1 %	-6.00 [-46.26, 34.26]
Radjen 2011	19	65.13 (7.64)	18	64.11 (6.11)		9.4 %	1.02 [-3.43, 5.47]
Zhu 1998	20	60.3 (6.3)	17	61.7 (8.8)		7.4 %	-1.40 [-6.41, 3.61]
Total (95% CI)	**198**		**192**			**100.0 %**	**0.24 [-1.13, 1.60]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.11$, df = 6 (P = 0.98); $I^2 = 0.0\%$

Test for overall effect: Z = 0.34 (P = 0.73)

Test for subgroup differences: Not applicable

Analysis 9.4. Comparison 9 Anthropometric, Outcome 4 Body mass index (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 9 Anthropometric

Outcome: 4 Body mass index (total)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Berger 1997	65	24.1 (5.4)	65	23.8 (3.8)		7.2 %	0.30 [-1.31, 1.91]
Eftekhari 2006	47	21.1 (1.79)	47	20.45 (1.43)		43.1 %	0.65 [0.00, 1.30]
Hinton 2007	10	23.2 (3.2)	10	23.9 (2.5)		2.9 %	-0.70 [-3.22, 1.82]
Hoppe 2013	24	22.3416667 (6.85)	12	21.4 (1.485)		2.3 %	0.94 [-1.92, 3.81]
Kanani 2000	101	14.7 (2.31)	102	14.16 (2.63)		39.9 %	0.54 [-0.14, 1.22]
Radjen 2011	19	20.76 (1.31)	18	20.59 (4.12)		4.7 %	0.17 [-1.82, 2.16]
Total (95% CI)	**266**		**254**			**100.0 %**	**0.53 [0.10, 0.96]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.33$, df = 5 (P = 0.93); $I^2 = 0.0\%$

Test for overall effect: Z = 2.40 (P = 0.017)

Test for subgroup differences: Not applicable

Analysis 9.5. Comparison 9 Anthropometric, Outcome 5 Body mass index (sensitivity analysis).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 9 Anthropometric

Outcome: 5 Body mass index (sensitivity analysis)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Berger 1997	65	24.1 (5.4)	65	23.8 (3.8)		11.9 %	0.30 [-1.31, 1.91]
Eftekhari 2006	47	21.1 (1.79)	47	20.45 (1.43)		71.7 %	0.65 [0.00, 1.30]
Hinton 2007	10	23.2 (3.2)	10	23.9 (2.5)		4.9 %	-0.70 [-3.22, 1.82]
Hoppe 2013	24	22.3416667 (6.85)	12	21.4 (1.485)		3.7 %	0.94 [-1.92, 3.81]
Radjen 2011	19	20.76 (1.31)	18	20.59 (4.12)		7.8 %	0.17 [-1.82, 2.16]
Total (95% CI)	**165**		**152**			**100.0 %**	**0.52 [-0.04, 1.07]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.33$, df = 4 (P = 0.86); $I^2 = 0.0\%$

Test for overall effect: Z = 1.82 (P = 0.068)

Test for subgroup differences: Not applicable

Analysis 10.1. Comparison 10 Serum/plasma zinc, Outcome 1 Zinc levels (total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 10 Serum/plasma zinc

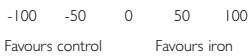
Outcome: 1 Zinc levels (total)

Study or subgroup	Iron N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Mujica-Coopman 2015	28	92.6 (21.8)	27	86.7 (11.9)		4.4 %	5.90 [-3.34, 15.14]
Prosser 2010	17	13.1 (0.412)	17	12.5 (0.412)		39.1 %	0.60 [0.32, 0.88]
Yadrick 1989	9	13.7 (1.2)	9	16.2 (3.3)		26.4 %	-2.50 [-4.79, -0.21]
Zaman 2013	22	12.8 (3.3)	22	14.4 (2.8)		30.1 %	-1.60 [-3.41, 0.21]
Total (95% CI)	**76**		**75**			**100.0 %**	**-0.65 [-2.70, 1.40]**

Heterogeneity: $Tau^2 = 2.79$; $Chi^2 = 13.56$, df = 3 (P = 0.004); $I^2 = 78\%$

Test for overall effect: Z = 0.62 (P = 0.54)

Test for subgroup differences: Not applicable

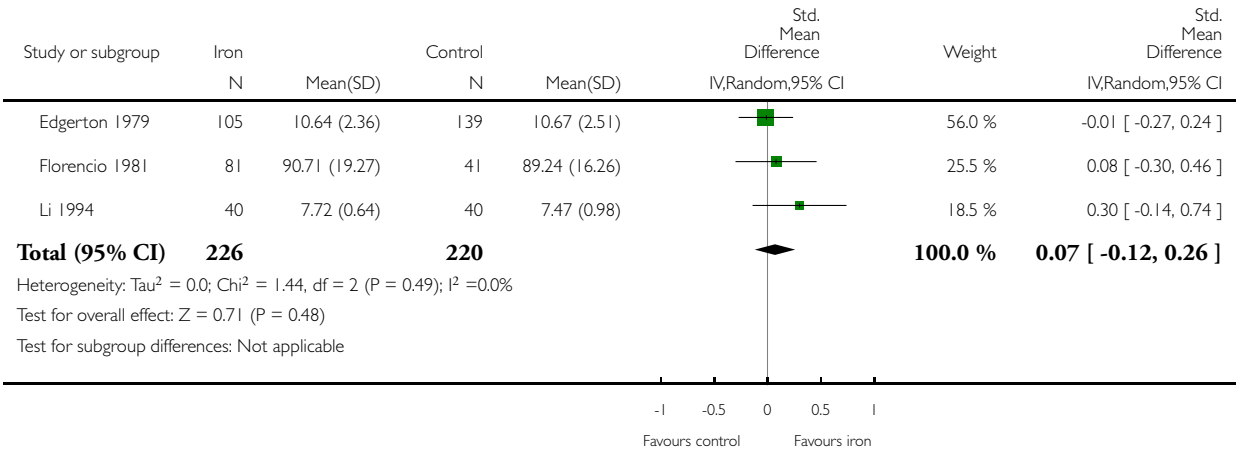


Analysis 11.1. Comparison 11 Productivity, Outcome 1 Productivity.

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 11 Productivity

Outcome: 1 Productivity

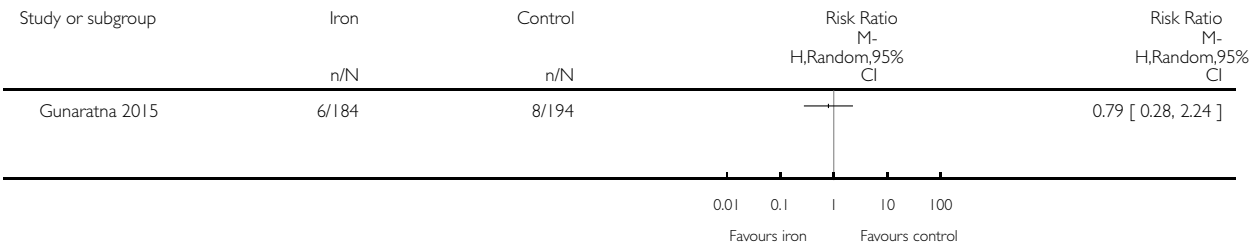


Analysis 12.1. Comparison 12 Malaria, Outcome 1 Malaria prevalence at end of therapy (Total).

Review: Daily iron supplementation for improving anaemia, iron status and health in menstruating women

Comparison: 12 Malaria

Outcome: 1 Malaria prevalence at end of therapy (Total)



APPENDICES

Appendix 1. Search strategies

Cochrane Central Register of Controlled Studies (CENTRAL)

CENTRAL 2012, Issue 2, searched 6 March 2012 [4417 records]
CENTRAL 2014, Issue 8, searched 17 September 2014 [1202 records]
CENTRAL 2015, Issue 10, searched 12 November 2015 [487 records]
#1MeSH descriptor: [Iron] this term only
#2MeSH descriptor: [Anemia, Iron-Deficiency] this term only
#3MeSH descriptor: [Iron, Dietary] this term only
#4MeSH descriptor: [Folic Acid] this term only
#5MeSH descriptor: [Micronutrients] this term only
#6MeSH descriptor: [Dietary Supplements] this term only
#7iron*
#8(folic* or folate* or folvite* or folacin* or pteroylglutamic*)
#9MeSH descriptor: [Trace Elements] this term only
#10(diet* near/3 supplement*)
#11micronutrient* or micro next nutrient* or multinutrient* or multi next nutrient*
#12MeSH descriptor: [Ferric Compounds] this term only
#13MeSH descriptor: [Ferrous Compounds] this term only
#14ferrous* or ferric* or fe
#15#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14
#16MeSH descriptor: [Drug Administration Schedule] this term only
#17MeSH descriptor: [Dose-Response Relationship, Drug] this term only
#18MeSH descriptor: [Time Factors] explode all trees
#19day or daily or week* or biweek* or bi next week* or intermittent* or alternat*
#20#16 or #17 or #18 or #19
#21#15 and #20
#22MeSH descriptor: [Menstruation] this term only
#23(menstruat* or menstrual*)
#24#22 or #23
#25(teen* or adolescen* or puberty or pubescen* or ADULT or MIDDLE next AGE*)
#26(girl* or woman* or women* or female*)
#27#25 and #26
#28#24 or #27
#29#21 and #28, in Trials

Ovid MEDLINE(R)

1948 to February Week 4 2012, searched 6 March 2012 [6714 records]
1946 to September Week 1 2014, searched 17 September 2014 [1737 records]
1946 to November Week 1 2015, searched 12 November 2015 [839 records]
1 iron/
2 anemia, iron deficiency/
3 iron, Dietary/
4 Folic acid/
5 Micronutrients/
6 Dietary Supplements/
7 iron$.tw.
8 (folic$ or folate$ or folvite$ or folacin$ or pteroylglutamic$).tw.

9 trace elements/
10 (diet$ adj3 supplement$).tw.
11 (micronutrient$ or micro-nutrient$ or multinutrient$ or multi-nutrient$).tw.
12 Ferric compounds/
13 Ferrous compounds/
14 (ferrous$ or ferric$ or fe).tw.
15 or/1-14
16 Drug Administration Schedule/
17 Dose-Response Relationship, Drug/
18 Time Factors/
19 (day or daily or week$ or bi-week$ or biweek$ or intermittent$ or alternate$).tw.
20 or/16-19
21 15 and 20
22 (iron adj3 (dose$ or dosage or administer$ or administration or frequency or regimen$)).tw.
23 21 or 22
24 adult/
25 middle aged/
26 adolescent/
27 (teen$ or adolescen$ or puberty or pubescen$).tw.
28 or/24-27
29 (girl$ or wom#n$ or female$).tw.
30 female/
31 29 or 30
32 28 and 31
33 Menstruation/
34 (menstruat$ or menstrual$).tw.
35 or/33-34
36 32 or 35
37 randomized controlled trial.pt.
38 controlled clinical trial.pt.
39 randomi#ed.ab.
40 placebo$.ab.
41 drug therapy.fs.
42 randomly.ab.
43 trial.ab.
44 groups.ab.
45 or/37-44
46 exp animals/ not humans.sh.
47 45 not 46
48 23 and 36 and 47

EMBASE (Ovid)

1980 to 2012 Week 9, searched 4 March 2012 [7146 records]
1980 to 2014 Week 37, searched 17 September 2014 [1826 records]
1980 to 2015 Week 45, searched 12 November 2015 [918 records]
1 iron/
2 iron intake/
3 iron deficiency anemia/
4 folic acid/
5 exp trace element/
6 diet supplementation/
7 iron$.tw.

8 (folic$ or folate$ or folvite$ or folacin$ or pteroylglutamic$).tw.
9 (diet$ adj3 supplement$).tw.
10 (micro-nutrient$ or micronutrient$ or multi-nutrient$ or multinutrient$).tw.
11 ferric ion/
12 ferrous ion/
13 (ferric$ or ferrous$ or fe).tw.
14 or/1-13
15 drug administration/
16 dose response/
17 (day or daily or week$ or biweek$ or bi-week$ or intermittent$ or alternat$).tw.
18 15 or 16 or 17
19 14 and 18
20 (iron adj3 (dose$ or dosage or administer$ or administration or frequency)).tw.
21 19 or 20
22 adult/
23 middle aged/
24 adolescent/
25 (teen$ or adolescen$ or puberty or pubescen$).tw.
26 or/22-25
27 female/
28 (girl$ or wom#n or female$).tw.
29 27 or 28
30 26 and 29
31 menstruation/
32 (menstruat$ or menstrual$).tw.
33 31 or 32
34 30 or 33
35 exp Clinical trial/
36 Randomized controlled trial/
37 Randomization/
38 Single blind procedure/
39 Double blind procedure/
40 Crossover procedure/
41 Placebo/
42 Randomi#ed.tw.
43 RCT.tw.
44 (random$ adj3 (allocat$ or assign$)).tw.
45 randomly.ab.
46 groups.ab.
47 trial.ab.
48 ((singl$ or doubl$ or trebl$ or tripl$) adj3 (blind$ or mask$)).tw.
49 Placebo$.tw.
50 Prospective study/
51 (crossover or cross-over).tw.
52 prospective.tw.
53 or/35-52
54 21 and 34 and 53
55 remove duplicates from 54

CINAHL (EBSCOhost)

1937 to current, searched 5 March 2012 [1210 records]
1937 to current, searched 17 September 2014 [456 records]

1937 to current, searched 12 November 2015 [180 records]
S47 S31 and S46
S46 S32 or S33 or S34 or S35 or S36 or S37 or S38 or S39 or S40 or S41 or S42 or S43 or S44 or S45
S45 TI (evaluat* study or evaluat* research) or AB (evaluate* study or evaluat* research) or TI (effectiv* study or effectiv* research) or AB (effectiv* study or effectiv* research) OR TI(prospectiv* study or prospectiv* research) or AB(prospectiv* study or prospectiv* research) or TI (follow-up study or follow-up research) or AB (follow-up study or follow-up research)
S44 placebo*
S43 crossover* or "cross over*"
S42 (MH "Crossover Design")
S41 (tripl* N3 mask*) or (tripl* N3 blind*)
S40 (trebl* N3 mask*) or (trebl* N3 blind*)
S39 (doubl* N3 mask*) or (doubl* N3 blind*)
S38 (singl* N3 mask*) or (singl* N3 blind*)
S37 (clinic* N3 trial*) or (control* N3 trial*)
S36 (random* N3 allocat*) or (random* N3 assign*)
S35 randomis* or randomiz*
S34 (MH "Meta Analysis")
S33 (MH "Clinical Trials+")
S32 MH random assignment
S31 S19 and S30
S30 S26 or S29
S29 S27 or S28
S28 menstruat* or menstrual*
S27 (MH "Menstruation")
S26 S22 and S25
S25 S23 or S24
S24 female* or wom#n or girl*
S23 (MH "Female")
S22 S20 or S21
S21 (teen* or adolescen* or puberty or pubescen* or adult* or middle age*)
S20 (AG adolescent) OR (AG middle aged) OR (AG adult) Limiters - Age Groups: Adult: 19-44 years, Middle Aged: 45-64 years
S19 S17 or S18
S18 (iron N3 dose*) or (iron N3 dosage) or (iron N3 administer*) or (iron N3 administration) or (iron N3 frequency)
S17 S11 and S16
S16 S12 or S13 or S14 or S15
S15 (day or daily or week* or biweek* or bi-week*or bi week* or intermittent* or alternat*)
S14 (MH "Time Factors")
S13 (MH "Dose-Response Relationship, Drug")
S12 (MH "Drug Administration Schedule")
S11 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10
S10 micro-nutrient* or micronutrient* or micro nutrient* multi-nutrient* or multinutrient* or multi nutrient*
S9 ferrous* or ferric* or "fe"
S8 diet* N3 supplement*
S7 folic* or folate* or folvite* or folacin* or pteroylglutamic*
S6 iron*
S5 (MH "Micronutrients")
S4 (MH "Trace Elements")
S3 (MH "Dietary Supplements")
S2 (MH "Folic Acid")
S1 (MH "Iron") OR (MH "Anemia, Iron Deficiency") OR (MH "Iron Compounds") OR (MH "Ferric Compounds") OR (MH "Ferrous Compounds")

Conference Proceedings Citation Index - Science (CPCI-S; Web of Science)

1990 to 2 March 2012, searched 6 March 2012 [154 records]
1990 to 12 September 2014, searched 17 September 2014 [5 records]
1990 to current, searched 12 November 2015 [2 records]
8 #7 AND #6 AND #3
7 TS=(random* or RCT or trial* or allocat* or assign* or placebo* or cross-over or crossover or "cross over" or factorial* or "double blind*" or "single blind")
6 #5 OR #4
5 TS=(menstruat* or menstrual*)
4 TS=(women or woman or female* or girl*)
3 #1 or #2
2 TS= (iron near/3 (dose* or dosage or administer* or administration or frequency or regimen*))
1 TS=((iron or ferrous or ferric or micronutrient* or multinutrient* or micro-nutrient* or multi-nutrient* or folic* or folate* or folvite* or folacin* or pteroylglutamic*) NEAR/5 (alternate* or week* or intermittent or biweek* or bi-week* or supplement*

Science Citation Index (SCI; Web of Science)

1970 to 2 March 2012, searched 6 March 2012 [1802 records]
1970 to 12 September 2014, searched 17 September 2014 [301 records]
1970 to 10 November 2015, searched 12 November 2015 [185 records]
8 #7 AND #6 AND #3
7 TS=(random* or RCT or trial* or allocat* or assign* or placebo* or cross-over or crossover or "cross over" or factorial* or "double blind*" or "single blind")
6 #5 OR #4
5 TS=(menstruat* or menstrual*)
4 TS=(women or woman or female* or girl*)
3 #1 or #2
2 TS= (iron near/3 (dose* or dosage or administer* or administration or frequency or regimen*))
1 TS=((iron or ferrous or ferric or micronutrient* or multinutrient* or micro-nutrient* or multi-nutrient* or folic* or folate* or folvite* or folacin* or pteroylglutamic*) NEAR/5 (alternate* or week* or intermittent or biweek* or bi-week* or supplement*))

Popline

(popline.org)
All available years, searched 6 March 2012 [33 records]
All available years, searched 18 September 2014 [21 records]
All available years, searched 12 November 2015 [14 records]
Advanced search: All fields : iron* OR folic* OR folate OR ferrous OR fe AND women OR woman OR menstru* OR girl* OR female* AND day OR daily OR week* OR biweek* OR bi weekly OR intermittent* OR alternat* AND random* OR trial* OR control* OR placebo*

World Health Organization (WHO) Regional Indexes

(globalhealthlibrary.net/php/index.php)
The following WHO regional indexes were searched for all available years on 25 May 2015, and again on 8 December 2015.
Literature in the Health Sciences in Latin America and the Caribbean (LILACS).
African Index Medicus (AIM; all available).
Western Pacific Region Index Medicus (WPRIM).
Index Medicus for the Eastern Mediterranean Region (IMEMR).
Index Medicus for South-East Asia Region (IMSEAR).
Searched on: Title : Iron AND Women

Worldcat

Searched 25 May 2015, and again on 8 December 2015.
Search on: Iron AND Women

DART-Europe E-theses Portal

Searched 25 May 2015, and again on 8 December 2015.
Searched on: Iron AND Women

Australasian Digital Theses Program

Searched 25 May 2015, and again on 8 December 2015.
Searched on: Iron AND Women

ProQuest Dissertations & Theses Global

Searched 25 May 2015, and again on 8 December 2015.
Searched on: Iron AND Women

WHO International Clinical Trials Registry Platform (ICTRP)

(apps.who.int/trialsearch)
Searched 25 May 2015, and again on 8 December 2015.
Searched on: Iron AND Women

Appendix 2. Unused methods archived for future updates of this review

In future updates of this review, we will conduct a sensitivity analysis to examine the following.

1. The effects of different ICC values for cluster studies.
2. The risk of publication bias by excluding unpublished studies.

WHAT'S NEW

Date	Event	Description
27 April 2016	Amended	In the abstract, we added information on the number of women included in the single analysis on iron-deficiency anaemia. We also reversed the order in which we present the results from the analyses on hard stools/constipation and loose stools/diarrhoea so these are consistent with the order in which they appear in the 'Summary of findings' table. Finally, we corrected the 'Summary of findings' table to ensure consistency of contents with the heading of column three (i.e. Number of participants (studies))

CONTRIBUTIONS OF AUTHORS

LMD-R and SRP conceived and designed the review.

CES, JS, MSYL SRP contributed to screening of studies and extraction of data.

MSYL and SRP entered data into RevMan and undertook the analysis.

LMD-R, MSYL and SRP wrote the manuscript.

All authors read and approved the final manuscript.

SRP has overall responsibility for this review.

DECLARATIONS OF INTEREST

The funders had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript.

Michael Sze Yuan Low is employed by Monash Health, an Australian government funded public hospital. MSYL has a PhD scholarship from the Royal Australasian College of Physicians/National Health and Medical Research Council Australia, which was used to fund research outside of this review.

Joanna Speedy is currently employed by the Australian Red Cross Blood Service, who sponsored and conducted one of the studies included in the review (Marks 2014), and was involved in conducting the study. Due to this potential conflict of interest Joanna Speedy was not involved in the decision to include this trial, extract data from this trial, or assess the risk of bias of this trial.

Claire E Styles is currently employed by the Australian Red Cross Blood Service, who sponsored and conducted one of the studies included in the review (Marks 2014), but was not involved in any aspect of this study.

Luz Maria De-Regil is a staff member of the Micronutrient Initiative (MI), an international not-for-profit organisation that delivers, with support of Global Affairs Canada, iron and folic acid through different programmes to children, women of reproductive age and pregnant women. None of these programmes met the inclusion criteria of this review and were not captured by the search process.

Sant-Rayn Pasricha's former institution received an unrestricted research grant in 2012, from Vifor Pharma Ltd for his work as a co-investigator on a phase II trial of IV iron carboxymaltose in patients with iron-deficiency anaemia. The work is unrelated to this review and is not included in the review.

Disclaimer: Luz Maria De-Regil is a full-time staff member of the Micronutrient Initiative. Jo Speedy, Claire Styles and Sant-Rayn Pasricha are staff of the Australian Red Cross Blood Service. The authors alone are responsible for the views expressed in this publication, and they do not necessarily represent the official position, decisions, policy or views of these organisations.

SOURCES OF SUPPORT

Internal sources

- Evidence and Programme Guidance, Department of Nutrition for Health and Development, World Health Organization, Switzerland.

Provided training and mentorship for the project

External sources

- Victoria Fellowship, Government of Victoria, Australia.

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Financial support for Dr Michael Low

- Monash Health, Australia.

Salary for Dr Michael Low

- CRB Blackburn Travelling Scholarship, The Royal Australasian College of Physicians, Australia.

Financial support for Dr Sant-Rayn Pasricha

- University of Melbourne Overseas Research Experience Scholarship, Australia.

Financial support for Dr Sant-Rayn Pasricha

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Financial support for Dr Sant-Rayn Prasricha

- NHMRC CJ Martin Early Career Fellowship, Australia.

Financial support for Dr Sant-Rayn Pasricha

- Bill and Melinda Gates Foundation, UK.

Financial support for Dr Sant-Rayn Pasricha

- CRB Blackburn Scholarship (National Health and Medical Research Council Gustav Nossal Award), Australia.

Financial support for Dr Michael Low

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

There were several differences between the pre-planned protocol (Pasricha 2012) and the review. These are as follows.

1. In the protocol, we planned three different comparisons: iron alone versus control/placebo alone; iron with a cointervention versus a cointervention alone; and overall iron versus control (combining these two comparisons). In the review, we opted to perform analysis on a single overall comparison (iron with or without a cointervention overall versus control/placebo with or without the same cointervention), and to treat the comparisons above as subgroups. This enabled a subgroup analysis to explore heterogeneity in effect sizes and outcomes, and simplifies the analysis for the reader. In addition, it increased the number of studies considered overall, especially for less commonly reported outcomes, and enabled us to provide an overall effect size of this intervention.

2. We formally assessed publication bias evident on funnel plots using statistical tests suggested by Egger, Peters and Harbord.

3. We added a subgroup of 'type of iron' (ferrous sulphate, ferrous fumarate, and others), as we have become aware through conversations with colleagues in the field that many potential users of our review were interested to discover whether different iron formulations could explain differences in efficacy and safety.

4. Given the rich data set of studies reporting on ferritin and the paucity of trials reporting on iron deficiency, we opted to undertake subgroup analysis reporting on this outcome in order to explore whether heterogeneity in this outcome could be explained by any of the pre-specified subgroups.

5. Finally, because of the availability of data and interest in the outcomes, we attempted to analyse the effects of iron on fatigue and on productivity.

INDEX TERMS

Medical Subject Headings (MeSH)

*Dietary Supplements [adverse effects]; Anemia, Iron-Deficiency [blood; *therapy]; Hemoglobin A; Iron [*administration & dosage; adverse effects; *deficiency]; Menstruation [*blood]; Randomized Controlled Trials as Topic

MeSH check words

Adolescent; Adult; Female; Humans; Middle Aged