

A Systematic Review of the Effects of Iron Therapy on Fatigue in Adults with Iron Deficiency and Normal Haemoglobin

Systematisk översikt om effekt av järnbehandling på trötthet hos vuxna med järnbrist och normalt hemoglobin

- Katarina Sztaniszláv, Dorothea Lagrange, Rebecka Klang, Rolf Ahlzén, Louise Olsson
HTA-enheten Camtö

The following have contributed to this report:

Literature search: Liz Holmgren and Karin Emilsson, The Medical Library, Örebro university

Clinical effect: Katarina Sztanisláv, MD, PhD, Dorothea Lagrange, MD, Louise Olsson, MD, PhD

Statistical review: Rebecka Klang, MSc

Ethics: Rolf Ahlzén, MD, PhD

Layout: Printing Office (Repro) Örebro University

Internal review:

Lars Breimer, MD, PhD

External review:

Manar Bitar, MD, senior consultant, Clinical Chemistry, Laboratory Medicine, Örebro University Hospital

Bengt Rasmussen, MD, PhD, senior consultant, Division of Hematology, Department of Medicine, Örebro University Hospital

Medical fact box:

Lars Englund MD, general practitioner, Jakobsgårdarna Primary Care Centre, Borlänge

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Contact: camto@regionorebrolan.se

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<https://www.regionorebrolan.se/camto>



Centre for Assessment of Medical Technology in Örebro

University Hospital Örebro

S-701 85 Örebro

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Abbreviations and glossary

BMS	Brunell Mood Scale
FSS	Fatigue Severity Scale. 10-item questionnaire scored on a Likert scale.
FVNS	Fatigue Visual Numeric Scale
Hb	Haemoglobin
IDNA	Iron deficiency no anaemia
MFI-20	Multidimensional Fatigue Inventory
MFSI	Multidimensional Fatigue Symptom Inventory. Measures general, physical, emotional, and mental fatigue, and vigour in the previous seven days. Each subscale comprises six items rated from 0 (not at all) to 4 (extremely), yielding a total score between 0 and 24 for each subscale. Total fatigue score is calculated by subtracting the vigour subscale score from the sum score of the other four subscales.
PFS	Piper Fatigue Score
RCT	Randomised Controlled Trial

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Abstract

Background

The benefits of iron supplementation in iron-deficient individuals without anaemia remain unclear. This systematic review aimed to evaluate the effects of oral and intravenous iron on fatigue in this population, while also assessing laboratory parameters.

Methods

Librarians at Örebro University conducted a literature search in MEDLINE, Embase and Cochrane Library for randomised controlled trials (RCTs) published between February 2016 and February 2026. The review adhered to PRISMA guidelines. Two independent researchers assessed study eligibility and risk of bias using the RoB2 tool. A narrative synthesis was conducted.

Results

Out of 647 articles, four RCTs were found relevant. One was excluded due to unacceptably high risk of bias, and the remaining three had moderate to high risk. A total of 516 participants, mainly women of reproductive age and healthy blood donors were included in studies evaluating intravenous iron versus placebo. A multitude of fatigue assessment scores were applied.

No study demonstrated a statistically significant effect of intravenous iron on fatigue, irrespective of fatigue assessment instrument or follow-up duration. A statistically significant increase in ferritin levels was observed after ≥ 6 weeks in participants receiving intravenous iron compared with placebo. No clinically relevant increase in hemoglobin was observed.

Conclusions

Three randomised controlled trials demonstrate that intravenous iron increases ferritin levels compared with placebo but has no effect on fatigue in patients with iron deficiency without anaemia. No randomised trials assessing oral iron supplementation for fatigue in this population have been published in the last ten years.

Plain Language Summary in Swedish/ Populärvetenskaplig sammanfattning

Bakgrund

Järnbrist är en vanlig orsak till anemi (brist på röda blodkroppar, lågt hemoglobinvärde). Behandling med järn förbättrar då både symtom, som t ex trötthet, och blodvärden. Däremot är det oklart om personer som enbart har lågt järnvärde men normalt hemoglobin har någon nytta av järnbehandling. Trötthet är en mycket vanlig sökorsak i sjukvården och påträffas ett lågt järnvärde förekommer att man behandlar det med järn, även om patienten har ett normalt hemoglobinvärde.

Syftet med denna systematiska översikt var därför att sammanställa studier som undersökt effekten av järnbehandling – både i tablettform och intravenöst – på trötthet hos personer med järnbrist men utan anemi.

Metod

Bibliotekarier vid Örebro universitet sökte efter studier publicerade mellan februari 2016 och februari 2026 i tre vetenskapliga databaser. Urvalet av relevanta studier genomfördes enligt riktlinjer för systematiska översikter. Två oberoende granskare bedömde både vilka studier som skulle inkluderas och risken för snedvridna resultat i studierna.

Resultat

Totalt 647 studier påträffades varav fyra var relevanta. En av studierna fick dock tas bort på grund av oacceptabelt hög risk för snedvridna resultat. Tre randomiserade studier med samtligt 516 deltagare ingick i den slutliga analysen. Deltagarna bestod främst av kvinnor i fertil ålder eller friska blodgivare. Samtliga studier undersökte intravenös järnbehandling jämfört med placebo, och inga motsvarande studier med järntabletter påträffades. Ett flertal olika skalor användes för att kartlägga tröttheten.

Ingen av studierna rapporterade att deltagare som fått intravenös järnbehandling upplevde minskad trötthet, oavsett vilket bedömningsinstrument som användes eller hur länge deltagarna följdes upp. Behandling med intravenöst järn gav förbättrade järnvärden efter minst sex veckors uppföljning. Hemoglobinvärdena ökade något, men utan klinisk betydelse.

Slutsats

Tre randomiserade studier visar att intravenös järnbehandling hos personer med järnbrist utan anemi förbättrar järnvärden i jämförelse med placebo, men att det inte minskar upplevd trötthet i denna patientgrupp.

Medical Fact Box in Swedish/Medicinsk faktaruta

Lars Englund MD, general practitioner, Jakobsårdarna Primary Care Centre, Borlänge

En vanlig klinisk situation för en allmänläkare är en patient som söker för onormal trötthet. Den kliniska bedömningen och undersökningen vid det första läkarbesöket ger inga ledtrådar till en eventuell diagnos och funktionsnedsättningen är ofta inte tydlig heller. Inte sällan är det en ung patient med allmänna funderingar utan att det i konsultationen kommer fram någon särskild oro om t ex cancersjukdom eller annan allvarlig åkomma. Begreppet "brist" är dock en vanlig frågeställning. En ung kvinna jag träffade förstod hur allvarlig hennes trötthet var när "inte ens energidryck hjälper".

Bland de "trötthetsprover" som ordineras finns ofta Hb, CRP, TSH, T4, Kreatinin, Vitamin B12, Folat, Glukos eller HbA1c, eventuellt leukocyter och trombocyter, delvis beroende på fynd i anamnes eller status. Ett prov som alltid finns med är Ferritin eller andra mått på järnstatus.

En inte ovanlig situation, och särskilt hos kvinnor som menstruerar, är då ett något lågt värde på Ferritin men ett normalt Hb. Vid en rundfråga bland kollegor på vårdcentralen är våra rutiner när det gäller behandling i den situationen olika. Någon föreslår direkt Ferinject, dvs järntillförsel intravenöst, andra rekommenderar järntabletter. En del patienter har redan från början bestämt sig för att de inte vill ha järntabletter utan vill direkt gå på Ferinject. En kollega påpekar att det är först vid anemi som behandling är indicerad och en annan kollega föreslår att unga kvinnor med denna anamnes kan rekommenderas att ta en järntablett dagligen under menstruationsdagarna, men utan recept. Andra ger kostrekommendationer.

Frågan om huruvida behandling av järnbrist utan anemi verkligen ger minskad trötthet var alltså osäkra på, det bedömdes nog mest vara en placeboeffekt. Att få ett vetenskapligt välgrundat råd för hur vi ska agera bedömdes vara en viktig fråga.

Background

Iron deficiency is one of the most common causes of anaemia. Iron replacement therapy improves laboratory values and anaemia-related symptoms, such as fatigue and reduced physical capacity. However, the effects of iron therapy in individuals with iron deficiency without anaemia (IDNA) have not been clearly established.

A 2019 Cochrane review [1] including randomised controlled trials was unable to draw firm conclusions regarding the effect of intravenous iron therapy in individuals with IDNA. Other systematic reviews [2, 3] have reported some effects of iron supplementation on fatigue in this patient group. The findings, however, are not entirely clear-cut and vary depending on study design, population, and oral or intravenous administration.

Objective

The objective of this systematic review is to summarise studies investigating the effect of oral or intravenous iron therapy primarily on fatigue in individuals with iron deficiency without concomitant anaemia.

Method

This systematic review was preregistered in Researchweb 2026-01-19

(www.researchweb.org/is/fourol/project/286970).

Research question:

What is the effect of intravenous or oral iron supplementation on fatigue in individuals with iron deficiency and normal haemoglobin?

The following PICOS was defined:

- **Population** Non-anemic adults aged ≥ 18 years with iron deficiency (low ferritin levels) and no clinical suspicion of serious disease
- **Intervention** Intravenous or oral iron supplementation
- **Control** Placebo
- **Outcome** Self-reported fatigue using validated scales
Haemoglobin
Ferritin
- **Study design** RCTs

Exclusion criteria

- Studies involving patients with serious illnesses, e.g. chronic kidney disease, hypothyroidism, heart failure, or malignancy.
- Studies on patients with a notable decrease in haemoglobin within the reference range, indicating serious disease.
- Studies on patients with conditions that could explain symptoms of fatigue.
- Pregnant women.
- Observational studies, systematic reviews, letters, comments, abstracts.
- Studies in languages other than English.

Literature search

A literature search was conducted by librarians at the Medical Library, Örebro University, in MEDLINE, Embase, and the Cochrane Library for the period 1 February, 2016, to 23 February, 2026. Search strategies are provided in Appendix 1.

Selection

Two independent reviewers (LO, DL) screened all identified studies. Titles and abstracts were assessed for relevance, and publications deemed relevant by either reviewer were retrieved in full text. Two reviewers (KSz, DL) then independently assessed full-text articles for eligibility based on the research question, PICOS, and the inclusion and exclusion criteria. Any disagreements were resolved by consensus. Reference lists of relevant systematic reviews and primary studies were screened to identify additional studies. The selection process is presented in a PRISMA diagram.

Risk of bias assessment

All studies deemed eligible underwent risk-of-bias assessment. It was assessed independently by two reviewers (KSz, DL) using the Swedish version (SBU) of the RoB2 tool for randomised controlled trials [4]. Any disagreements were resolved by consensus.

Statistical review

A statistician (RK) reviewed the statistical aspects of relevant studies, including sample size calculations, statistical methods, reporting, and interpretation. Continuous baseline variables were assessed using Carlisle's method [5], in which extreme values of the calculated combined p-value may indicate potential issues with randomisation. Cut-off values were defined as a combined p-value of ≤ 0.05 or ≥ 0.95 .

Conflicts of interest

Information on conflicts of interest and study funding were extracted by one reviewer (KSz).

Publishing journals

The journals in which the identified studies were published were reviewed, particularly regard to potential predatory journals. Directory of Open Access Journals, Cabells' Predatory Reports [6], and the Norwegian list of approved journals [Norska listan - Försvarshögskolan](#) were used.

Data extraction

Basic characteristics and relevant outcome data were extracted by one reviewer (KSz) and independently checked by a second reviewer (DL).

Analysis

A narrative analysis was conducted, as the included studies were too heterogeneous to allow for quantitative synthesis.

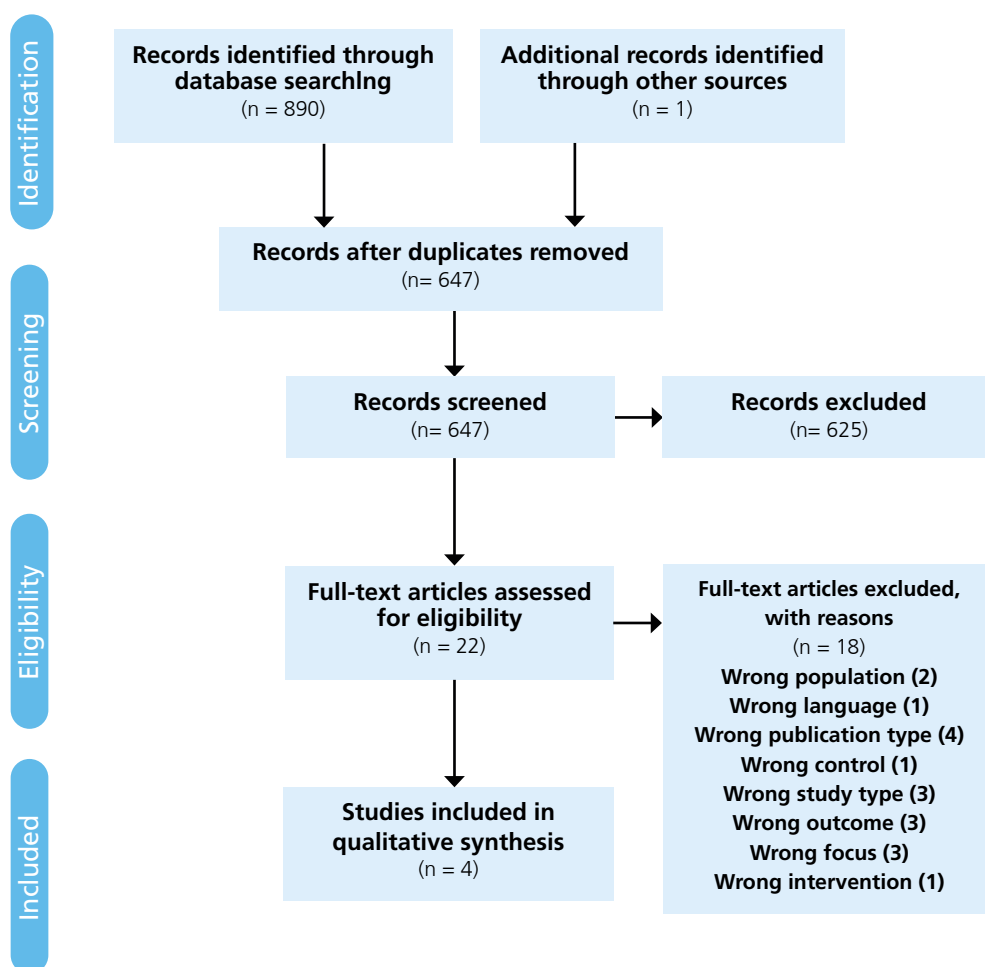
Ongoing studies

Ongoing randomised trials were identified in ClinicalTrials.gov, and ongoing systematic reviews in PROSPERO on April 28, 2026.

Results

Assessment of relevant studies

The literature search yielded 890 unique records, one additional record was identified through reference screening, and 647 records remained after removal of duplicates. One additional record was identified through reference list screening. A total of 22 records were assessed in full text, of which four were found to be relevant (Figure 1). Excluded articles, with reasons for exclusion, are presented in Appendix 2. None of the first or corresponding authors of the four included studies were listed in the Retraction Watch Database (18 March, 2026).



Figur 1 Study flow chart

Two studies were conducted in Europe [7, 8], one in Australia [9], and one in Pakistan [10] (Table 1). Two of the studies [9, 10] included women of reproductive age, while the other two focused on healthy blood donors [7, 8]. In one of these studies [8], men were also included, accounting for 218 (53%) of the study population.

The two blood donor studies included participants recruited between 2011-2013 [8], and 2013-2016 [7]. The studies involving women of reproductive age were conducted more recently. Three of the studies evaluated the effect of intravenous iron [7-9] whereas Sultana et al from 2026 [10] did not specify the route of administration.

The studies were heterogeneous regarding outcome measures, including fatigue, which was assessed using different scales and at somewhat varying follow-up times. The Gybel-Brask study from 2018 [7] reported fatigue as a secondary outcome measure.

Cut-off values for haemoglobin and ferritin used for inclusion varied between the studies, particularly for ferritin. It was $\leq 60 \mu\text{g/L}$ in the study by Gybel-Brask study from 2018 [7], whereas in the recent study by Dugan 2025 [9], it was $\leq 20 \mu\text{g/L}$.

Table 1 Basic characteristics of relevant studies (n=4).

Author, year, country	Study period	Participants % F, age, characteristics	Cut-off values for inclusion	Intervention n	Placebo n	Follow-up	Outcome
Sultana, 2026, Pakistan [10]	March 2023-Feb 2024	N=220 F: 100% Age 18-45 yrs IDNA, FSS ≥ 36	NR	N=110 iron therapy (not defined)	N=110	2 mths	*Fatigue Severity Scale (FSS) Hb S-ferritin
Dugan, 2025, Australia [9]	Jan 2021-Nov 2022	N=26 F: 100% Age 18-45 yrs Regular weekly exercise >3 hrs	Hb ≥ 115 g/L S-ferritin ≤ 20 μ g/L	N=14 1000 mg iron isomaltoside iv	N=12	4 days 4 weeks 3 mths **	*Fatigue (MFI-20, PFS, BMS fatigue) Hb S-Ferritin
Keller, 2020, Switzerland [8]	Dec 2011-Jan 2013	N=405 F: 47% Mean age: 42 yrs Healthy blood donors with IDNA	Women: Hb ≥ 121 g/L Men: ≥ 135 g/L S-ferritin ≤ 50 μ g/L	N=203 800 mg ferric carboxymaltose iv	N=202	6-8 weeks	Primary outcome: Self-rated average fatigue level *** Secondary outcomes: Self-perceived change in fatigue by MFSI-SF Hb S-Ferritin
Gybel-Brask, 2018, Denmark [7]	June 2013-Dec 2016	N=85 F: 100% Mean age: 23 - 25 yrs First-time blood donors with IDNA	P-ferritin ≤ 60 μ g/L	N=43 1000 mg iron isomaltoside iv	N=42	3, 12, 24 weeks	Primary outcome: Hb change baseline to 24 weeks Secondary outcome: Hb change baseline to 12 weeks Ferritin Fatigue (change base-line to 12 and 24 weeks) (FVNS, FSS)

Legend: BMS: Brunell Mood Scale, fatigue, FSS: Fatigue Severity Scale, FVNS: fatigue visual numeric scale, IDNA: iron deficiency no anaemia, LSmean: least square mean, MFI-20: Multidimensional Fatigue Inventory, MFSI: 30-item Multidimensional Fatigue Symptom Inventory-Short-Form, PFS: Piper Fatigue Score

* No primary or secondary endpoints specified.

** Follow-up blood assessment only to assess the variability of S-ferritin decay.

*** Average fatigue during the past 7 days using a numeric rating scale (NRC) from 1 (no fatigue at all) to 10 (extreme fatigue).

Risk of bias assessment

Risk of bias (RoB) is presented in Figure 2.

In the study by Sultana from 2026 [10], the description of the randomisation process is inadequate and baseline data are missing. The study flow diagram contains incorrect figures. The dropout rate was relatively high (32/110 in the placebo group and 24/110 in the intervention group). The study protocol ([Study Details | NCT06596161 | Iron Therapy and Fatigue in Women of Reproductive Age | ClinicalTrials.gov](#)) was published after the study had been completed and the results were known. The results are reported solely as comparisons between pre- and post-intervention values, without any analysis between the groups. The study is therefore excluded due to an unacceptably high risk of bias, low methodological quality, and the absence of group comparisons.

Randomisation in the study by Dugan 2025 [9] was conducted using an independent internet-based service by the study's unblinded researchers (who are also co-authors of the study) to randomly assign participants to study groups. The article does not specify whether allocation was concealed, and the risk of bias in the randomisation domain is assessed as moderate. Participants were blinded to the intervention during the study. However, the researcher (and co-author) who administered the study drug were not blinded. It is considered unlikely, however, that this affected the outcomes.

The study had a pre-registered protocol (ACTRN 12620001357943, [ANZCTR - Registration](#)). According to this study protocol, follow-ups and outcome measurements were to be conducted after four days, four weeks, and three months. However, the published article reports three-month data only for ferritin. The article presents data on fatigue measured using the MFI-20 (Multidimensional Fatigue Inventory), even though this outcome measure is not specified in the study protocol. The overall risk of bias in the study was assessed as high.

In the study by Keller 2020 [8], fatigue was assessed using self-reported scales. The study participants were blinded and therefore the risk of bias was found low for this domain. A protocol ([Study Details | NCT01519830 | Iron Substitution in Blood Donors | ClinicalTrials.gov](#)) was submitted approximately six weeks after participant recruitment began. Haemoglobin and serum ferritin were not listed as outcome measures in the protocol. Risk of bias in this study is therefore considered moderate.

The study by Gybel-Brask 2018 [7] assessed fatigue as a secondary outcome measure among blinded participants. The study was not statistically powered for these secondary outcomes. The study had a moderate dropout rate. A protocol ([Study Details | NCT01895231 | A Study of Intravenous Iron Isomaltoside 1000 \(Monofer®\) Administered by Infusions to Iron-deficient Blood Donors | ClinicalTrials.gov](#)) was submitted for registration approximately three weeks after the study began. The protocol stated that participants with ferritin levels below 30 µg/L would be included, but this was changed to 60 µg/L because fewer participants than expected had ferritin levels below 30 µg/L. This is reported in the publication. However, data were analyzed using several statistical methods, and this means it cannot be ruled out that the reported results were selected from among several possible analyses. Overall, the risk of bias in this study is assessed as high.

Figure 2 Risk of bias assessment

Author, Year	Randomisation	Deviation from plan	Missing data	Outcome measurement	Outcome report	Overall risk of bias
Sultana, 2026 [10]	●	●	●	●	●	
Dugan, 2025 [9]	●	●	●	●	●	●
Keller, 2020 [8]	●	●	●	●	●	●
Gybel-Brask, 2018 [7]	●	●	●	●	●	●

● low

● moderate

● high

unacceptably high

Statistical review of relevant studies

The statistical review is summarised in Table 2.

The study by Sultana 2026 [10] did not adequately report the sample size calculation, it only stated that such a calculation was performed without presenting the required the number of participants derived from it. The results were analyzed only within groups relative to baseline, rather than between-group comparisons. Within-group analyses alone do not allow for comparisons between groups [11]. The continuous variables showed unusually large differences between groups at baseline (combined p-value 0.999998 using Carlisle’s test), but the reason for this cannot be determined.

The study by Dugan 2025 [9] used linear mixed models, which are likely to be overly complex given the small sample size. In regression analyses, it is generally recommended to have at least around 10 participants per parameter to reduce the risk of overfitting and unstable estimates [12]. This limits the reliability of the study’s results.

No correction for multiple testing was reported in the study by Keller from 2020 [8]. Such corrections are important to reduce the risk of false positive findings when multiple statistical tests are performed. No other statistical issues were noticed.

In the study by Gybel-Brask 2018 [7], no reference or justification was provided for the chosen effect size used in the sample size calculation, nor was any correction for multiple testing reported.

Table 2 Review of statistical domains of the included studies

Author, Year	Distribution of continuous baseline variables *	Planned and achieved sample size	Choice of statistical analysis methods	Reporting and author's interpretation of statistical aspects
Sultana, 2026 [10]	Dissimilar groups (0.999998)	Needed sample size not reported Reference for choice of effect size missing (220 randomised)	No between group comparisons	Method-related limitations on interpretation No mention of multiplicity correction
Dugan, 2025 [9]	OK (0.30)	No issues noted 24 needed (26 randomised)	Overly complex given the sample size	Method-related limitations on interpretation
Keller, 2020 [8]	OK (0.55)	No issues noted 326 needed or 400 for subgroups to also be powered (405 randomised)	No issues identified	No mention of multiplicity correction
Gybel-Brask 2018 [7]	OK (0.83)	Reference for choice of effect size missing 74 needed (85 randomised)	No issues identified	No mention of multiplicity correction

* Calculation based on Carlisle's method. Interpretation: Low values (<0.05) indicate that the groups (intervention and control) are similar at baseline while higher values (>0.95) indicate that the groups are dissimilar.

Conflict of Interest

Conflicts of interest in the identified studies are presented in Table 3. The studies had between 4 and 10 authors, and between 10% and 29% of them reported financial conflicts of interest in relation to the companies Vifor Pharma or Pharmacosmos. These two companies are competitors in the market for intravenous iron preparations. One employee from Pharmacosmos was listed as an author in one of the studies.

Table 3 Financial conflict of interest as declared in relevant studies

Author, Year	Authors n	Financial COI* n (%)	Employees ** n (%)	Funding
Sultana, 2026 [10]	5	0 (0%)	0 (0%)	No
Dugan, 2025 [9]	7	2 (29%) Vifor Pharma	0 (%)	No
Keller, 2020 [8]	10	1 (10%) Vifor Pharma	0 (%)	Humanitarian Foundation of the Swiss Red Cross, Switzerland. Vifor Pharma provided the drugs.
Gybel-Brask, 2018 [7]	4	0	1 (25%) *** Pharmacosmos	Medical writing assistance from Pharmacosmos

* Financial COI as declared by authors in relation to study sponsor, and percentage of all authors

** Authors employed by study sponsors, and percentage of all authors

*** Another author was employed by the company after the trial was finalized.

Journals

The studies were published in four journals, two of which were hybrid journals and two of which were open-access journals listed in DOAJ (Table 4). None of the journals were listed in Cabell's Predatory Reports. The Norwegian list ([Norska listan - Försvarshögskolan](#)) classified one of the journals at Level 2, two at Level 1 and one as under evaluation.

Table 4 Characteristics of journals publishing the identified studies

Author, Year	Journal	Type of journal	DOAJ*	Cabell's Predatory Reports	Norwegian list**
Sultana, 2026 [10]	Journal of the Pakistan Medical Association	Open Access	Yes	No	1
Dugan, 2025 [9]	British Journal of Sports Medicine	Hybrid	Irrelevant	No	2
Keller, 2020 [8]	Scientific Reports	Open Access	Yes	No	1‡
Gybel-Brask, 2018 [7]	Transfusion	Hybrid	Irrelevant	No	1

* Relevant for Open Access journals only

** Norwegian list: 0 not approved, 1 the majority of legitimate, peer-reviewed scientific journals, 2 leading scientific publication channels

‡ "Under discussion" in the Norwegian list database

Summary of the assessment of relevant studies

In summary, four relevant studies were identified, but one (Sultana, 2026) was excluded from further analysis due to an unacceptably high risk of bias. The results of the remaining three studies are presented in the next section.

Results reported in the included studies

Effect of intravenous iron therapy on fatigue

The findings are summarised in Table 5.

The study by Dugan 2025 [9] reported no significant differences in the Multidimensional Fatigue Inventory-20 (MFI-20), Piper Fatigue Score (PFS), or Brunell Mood Scale/ Fatigue (BMS/ Fatigue) between intravenous iron therapy compared to placebo after four weeks in recreationally active women of reproductive age with IDNA.

In the study by Keller 2020 [8], self-rated mean fatigue scores were 3.9 ± 1.8 in the iron group and 4.0 ± 2.2 in the placebo group, showing no differences between the groups 6 to 8 weeks after treatment in healthy blood donors. As a secondary outcome measure, fatigue was also assessed using the Multidimensional Fatigue Symptom Inventory-Short-Form (MFSI), but no significant difference was found between the groups either.

The study by Gybel-Brask 2018 [7], which had a longer follow-up period, showed no significant effect of intravenous iron therapy on the Fatigue Visual Numeric Scale or in various domains of the Fatigue Severity Scale after 12 or 24 weeks.

In the study by Dugan, the Multidimensional Fatigue Inventory-20/General score showed a decrease in the intervention group from 13.2 to 11.5 ($\Delta 1.7$), and for the placebo group from 12.6 to 11.8 ($\Delta 0.8$) after 4 weeks. For the Piper Fatigue Score/total fatigue, a decrease was reported for the iron group from 5.23 to 4.06 ($\Delta 1.17$) after 4 weeks and for the placebo group from 3.94 to 3.79 ($\Delta 0.15$).

In the study by Keller, the self-rated fatigue decreased in both groups, from 4.4 to 3.9 in the iron group ($\Delta 0.5$) and from 4.6 to 4.0 ($\Delta 0.6$) in the placebo group, which was not clinically relevant.

The mean fatigue symptoms scores in the study by Gybel-Brask appeared to decrease from baseline during the trial for both treatment groups.

Table 5 Effect of intravenous iron versus placebo on fatigue

Author, Year	Time point	Outcome measures	Intervention	Placebo	p-value
Dugan, 2025 [9]	4 wks	MFI-20* (mean $\pm$ SE):			
		general	11.5 $\pm$ 0.8	11.8 $\pm$ 0.9	0.8
		physical fatigue	9.2 $\pm$ 1	9.6 $\pm$ 1.1	0.8
		reduced activity	9.1 $\pm$ 1	9.3 $\pm$ 1.1	0.9
		reduced motivation	9.6 $\pm$ 0.9	8.9 $\pm$ 0.9	0.6
		mental fatigue	11.5 $\pm$ 0.6	11.2 $\pm$ 0.6	0.8
		PFS* (mean $\pm$ SE):			
		total fatigue	4.1 $\pm$ 0.4	3.8 $\pm$ 0.5	0.7
		behavioural severity	3.3 $\pm$ 0.5	3.5 $\pm$ 0.5	0.8
		affective meaning	4.6 $\pm$ 0.5	3.9 $\pm$ 0.6	0.4
		sensory	4.3 $\pm$ 0.5	4.4 $\pm$ 0.5	0.9
		cognitive mood	4.2 $\pm$ 0.5	3.6 $\pm$ 0.5	0.4
		BMS fatigue (mean $\pm$ SE)	8.6 $\pm$ 0.9	8.3 $\pm$ 0.9	0.8
Keller, 2020 [8]	6–8 wks	Fatigue level** (mean $\pm$ SD)	3.9 $\pm$ 1.8	4.0 $\pm$ 2.2	0.8
		MFSI (mean $\pm$ SD):			
		total	11.0 $\pm$ 12.0	11.3 $\pm$ 12.3	NS
		general	9.2 $\pm$ 3.3	9.3 $\pm$ 4.0	NS
		physical	7.3 $\pm$ 2.2	7.3 $\pm$ 1.8	NS
		emotional	8.3 $\pm$ 2.9	8.1 $\pm$ 2.9	NS
		mental	8.6 $\pm$ 2.5	8.5 $\pm$ 2.5	NS
		vigorous	22.4 $\pm$ 4.0	22.1 $\pm$ 4.7	NS
Gybel-Brask, 2018 [7]	12 wks	FVNS*** (LS mean)	-1	-0.14	0.07
		FSS (LS mean):			
		Exercise brings on my fatigue	-0.3	-0.2	0.8
		I am easily fatigued	-0.3	-0.6	0.3
		Fatigue interferes with my physical functioning	-0.1	-0.2	0.8
		Fatigue causes frequent problems for me	-0.1	0.1	0.3
		Fatigue interferes with my work, family, social life	-0.3	0.46	0.02
	24 wks	FVNS*** (LS mean)	-0.8	-0.5	0.6
		FSS (LS mean)			
		Exercise brings on my fatigue	-0.5	-0.4	0.7
		I am easily fatigued	-0.6	-0.5	0.9
		Fatigue interferes with my physical functioning	-0.6	-0.5	0.5
		Fatigue causes frequent problems for me	-0.2	-0.1	0.7
		Fatigue interferes with my work, family, social life	-0.2	0.2	0.2

Legend: BMS: Brunell Mood Scale, fatigue, FSS: Fatigue Severity Scale, FVNS: fatigue visual numeric scale, LSmean: least square mean, MFI-20: Multidimensional Fatigue Inventory, MFSI: 30-item Multidimensional Fatigue Symptom Inventory-Short-Form; PFS: Piper Fatigue Score

* Data presented as estimated means (SE) from linear mixed models

** Self-rated fatigue during the past 7 days on a numeric rating scale between 1 (no fatigue) to 10 (extreme fatigue)

*** Data presented as change from baseline to right before the second (12 weeks) and third (24 weeks) blood donation, data are shown as least square mean (LS Mean)

Effect of intravenous iron therapy on haemoglobin and ferritin levels

The findings are summarised in Table 6.

In the study by Dugan [9], no significant difference in haemoglobin levels was found between the intervention and placebo groups after 4 weeks. Only ferritin was measured after 3 months. Participants in the placebo group had been unblinded after 4 weeks, received intravenous iron and therefore, no difference in serum ferritin levels was observed between the groups at 3 months.

In the study by Keller 2020 [8], both haemoglobin (142 ± 11 vs. 137.2 ± 12 , $p < 0.001$) and ferritin (142 ± 55 vs. 28 ± 61.3 , $p < 0.001$) were statistically significantly higher 6–8 weeks after iron intravenously compared with placebo.

In the 2018 study by Gybel-Brask 2018 [7], the change in Hb levels from baseline to 12 and 24 weeks was significantly higher among those who received intravenous iron compared to placebo (12 weeks $p = 0.03$, 24 weeks $p < 0.0001$). Plasma ferritin concentrations also differed significantly after 12 (146.9 vs. 11.9 , $p < 0.0001$) and 24 weeks (62 vs. 2.3 , $p < 0.0001$).

Table 6 Effect of intravenous iron vs placebo on Hb and (plasma/serum) ferritin levels

Author, Year	Time point	Haemoglobin (g/L)			Ferritin (µg/L)		
		Intervention	Control	p	Intervention	Control	p
Dugan, 2025 [9]	4 wks*	130±2	126±2	0.35	218.2±32.5	18.4±1.5	NR
	3 mths	NR	NR	NR	114.3±17.4	188.8±7.7	NR
Keller, 2020 [8]	6–8 wks	142.7±10.9	137.2±12	<0.001	142.6±55	28.6±61.3	<0.001
Gybel-Brask, 2018 [7]	12 wks**	1.7	1.4	0.03	146.9	11.9	<0.0001
	24 wks**	1.8	0.5	<0.0001	62	2.3	<0.0001

* Data presented as estimated means (SE) from linear mixed models

** Data presented as change from baseline to right before the second (12 weeks) and third (24 weeks) blood donation, data are shown as least square mean (LS Mean)

Ongoing studies

An ongoing clinical trial registered on ClinicalTrials.gov (Study Details | NCT07263529 | Risk of Anaemia and Effects of Oral Iron Therapy in Non-Anemic Iron-Deficient Women (18-55 Years) | ClinicalTrials.gov) is investigating the risk of developing anaemia in women aged 18–55 with iron deficiency, as well as the effects of iron therapy with oral iron (ferrous sulfate), including on fatigue. The study is being conducted in two phases at a center in Istanbul, Turkey. First, there is a two-month period of dietary counseling to increase iron intake. Participants are then divided into four groups based on blood test results, ranging from isolated iron deficiency to overt anaemia. The estimated study completion was expected in February 2026.

Three systematic reviews are currently underway that examine the effect of iron supplementation in adults with iron deficiency without anaemia. A systematic review from Portugal titled “Impact of iron supplementation on fatigue, physical performance, and cognitive function in adults with iron deficiency without anemia: a Systematic Review and Meta-Analysis (<https://www.crd.york.ac.uk/PROSPERO/view/CRD420251268022>) began in December 2025 and is scheduled to conclude in December 2026.

Another review from Taiwan, “Oral iron supplementation for the reduction of fatigue: a systematic review and meta-analysis” (<https://www.crd.york.ac.uk/PROSPERO/view/CRD420261361251>) examines the effect of oral iron supplementation on fatigue in adults with iron deficiency, with or without anaemia, and began in April 2026.

The third systematic review from the Czech Republic, “Iron Supplementation for Fatigue in Non-Anemic Iron-Deficient Women: A Systematic Review and Meta-analysis of Randomized Controlled Trials” (<https://www.crd.york.ac.uk/PROSPERO/view/CRD420261360155>) focuses on the effect of iron treatment on fatigue in women with iron deficiency but without anaemia, starting in April 2026 and scheduled to conclude preliminary in June 2026.

Summary of Findings

Outcome	Number of studies Participants (n)	RoB	Directness	Consistency	Precision	Summary
Fatigue	3 RCT (n=516)	Moderate risk: 1 RCT High risk: 2 RCTs	Yes*	Yes	-	No effect on fatigue
Haemoglobin levels	3 RCT (n=516)	Moderate risk: 1 RCT High risk: 2 RCTs	Yes*	Yes	-	Haemoglobin increased after iv iron
Ferritin levels	3 RCT (n=516)	Moderate risk: 1 RCT High risk: 2 RCTs	Yes*	Yes	-	Ferritin increased after iv iron

* studies performed in OECD member countries

Discussion

Four relevant randomised controlled trials that met our PICOS criteria were identified, one of which was excluded due to an unacceptably high risk of bias.

The included three studies showed substantial heterogeneity regarding inclusion criteria, choice of outcome measures, and follow-up duration, which is worth noting. Definition of iron deficiency (different cut-off values for ferritin) also varied across studies. The World Health Organization defines iron deficiency as a ferritin level $<15 \mu\text{g/L}$ in adults [13], however, in UptoDate, a ferritin concentration below $30 \mu\text{g/L}$ are used as a cut-off [14]. Only one RCT in our systematic review used a ferritin cutoff of $<20 \mu\text{g/L}$ [9]; in the other two [7, 8], the cutoff values were considerably higher ($50 \mu\text{g/L}$, or $60 \mu\text{g/L}$, respectively).

Despite heterogeneity among the studies, the findings suggest that intravenous iron therapy does not have a significant effect on self-reported fatigue in individuals with iron deficiency without anaemia, despite concurrent improvements in haemoglobin and ferritin levels. This finding appears to be consistent across assessment scales and persists at follow-up for up to 24 weeks. However, the study by Gysel-Brask 2018 was not powered for patient-reported outcomes and the study by Dugan 2025 included a relatively small number of participants. In the study by Keller 2020, iron deficiency was defined as $\text{S-ferritin} \leq 50 \mu\text{g/L}$, however nearly 45 % of participants had ferritin concentrations $<15 \mu\text{g/L}$ and no difference in fatigue between the groups was observed.

Self-reported fatigue, measured using different scales, decreased in both in the intravenous iron and the placebo groups across the included studies. In the study by Keller 2020 [8], this difference was not clinically relevant, while the two other two studies neither defined nor discussed the clinical relevance of the differences.

Previously published systematic reviews, including the Cochrane review from 2019 [1], show conflicting results. While some systematic reviews [2, 3, 15, 16] based on older RCTs involving primarily premenopausal women given oral iron therapy report a positive effect on fatigue, the Cochrane review [1], which included a broader patient population, including even those with chronic heart failure and post-cardiac surgery, found limited support for the use of intravenous iron supplementation in non-anemic individuals with iron deficiency. The differences between the reviews may possibly be explained by differences in population and intervention (oral versus intravenous iron).

It should be noted that we did not find any RCT from the past decade examining the effect of oral iron therapy among patients with iron deficiency but no anaemia. The lack of recent studies makes it difficult to determine whether the positive effects of oral iron therapy reported in older studies are still relevant.

In summary, this systematic review focused on adults with iron deficiency without anaemia and without evidence of serious comorbidities contributing to low ferritin levels. The findings suggest that intravenous iron therapy in this population does not reduce fatigue, despite improved laboratory parameters. Overall, the results from the three included RCTs do not support the use of intravenous iron to reduce fatigue in otherwise healthy individuals.

Knowledge gaps

Two areas were identified as knowledge gaps:

- No recent randomised studies investigating the effect of oral iron therapy on fatigue in individuals with iron deficiency without anaemia were identified.
- Ferritin thresholds varied across studies, and there appears to be no clear or consistent definition of what constitutes iron deficiency in generally healthy populations.

Ethical reflections

Fatigue is a non-specific symptom, and the possible reasons behind it are almost innumerable. When patients present with fatigue, a standard set of routine laboratory tests is often performed, and ferritin is typically included among these.

If low iron stores in themselves, irrespective of haemoglobin levels, truly cause fatigue, iron supplementation should have a prompt positive effect. In this study, no such effect was observed. Furthermore, no effect was observed in either the treatment group or the placebo arm. This is somewhat surprising, given that injection therapy typically has a placebo effect on general symptoms, such as fatigue.

What if the studies had demonstrated a clear placebo effect? The present consensus concerning the unethical nature of placebo treatments is based on the conviction that clinical medicine must "play with open cards", and not in any way deceive patients. The consequences of such deception on a broader scale would be disastrous for clinical practice, for which mutual trust is a fundamental ethical principle.

When low ferritin values are detected, the clinician must evaluate how much further investigation is warranted. It must be determined whether the low ferritin level reflects pathological losses, such as gastrointestinal bleeding, or an imbalance between normal losses (e.g. in women of reproductive age) and iron intake. The risk of overlooking and masking serious conditions through iron treatment must be considered, and established clinical principles must be upheld.

On the other hand, it must be noted that low ferritin values without anaemia do not constitute a specific diagnosis according to ICD-10. "Treating" laboratory values may lead to unnecessary medicalisation. This systematic review suggests that such treatment does not reduce fatigue; as long as haemoglobin levels remain within the normal range in otherwise healthy individuals, the biological plausibility that low ferritin per se causes fatigue seems unlikely.

11. Bland J, Altman D. Comparisons against baseline within randomised groups are often used and can be highly misleading. *Trials*. 2011;12:264 <https://doi.org/https://10.1186/1745-6215-12-264>.
12. Babyak MA. What you see may not be what you get: a brief, nontechnical introduction to overfitting in regression-type models *Psychosom Med* 2004;66:411-21 <https://doi.org/https://10.1097/01.psy.0000127692.23278.a9>. .
13. World Health Organisation. WHO guideline on use of ferritin concentrations to assess iron status in individuals and population. 2020. <https://doi.org/https://iris.who.int/server/api/core/bitstreams/ccf25949-dfa7-4409-8b86-ade1a48dbd8f/content>.
14. Auerbach M, DeLoughery TG. Diagnosis of iron deficiency and iron deficiency anemia in adults. UpToDate. https://doi.org/https://www.uptodate.com/contents/diagnosis-of-iron-deficiency-and-iron-deficiency-anemia-in-adults?search=iron%20deficiency%20anemia&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2&searchCorrelationId=5f5df57d-8c4d-4c31-b167-fed5be3b1b57&searchCorrelationTerm=iron%20deficiency%20anemia&utm_source=substack&utm_medium=email#H4008843982.
15. Pratt JJ, Khan KS. Non-anaemic iron deficiency - a disease looking for recognition of diagnosis: a systematic review. *Eur J Haematol*. 2016;96:618-28 <https://doi.org/https://10.1111/ejh.12645>.
16. Yokoi K, Konomi A. Iron deficiency without anaemia is a potential cause of fatigue: meta-analyses of randomised controlled trials and cross-sectional studies. *Br J Nutr*. 2017 2017;117:1422-31 <https://doi.org/https://10.1017/S0007114517001349>.

Appendices

Appendix 1 Literature search

Database: Database(s): Ovid MEDLINE(R) ALL 1946 to December 18, 2024

Host: Ovid

Date searched: 2026-02-23

Limits applied: publications in English language, Publication Year from 2016 to 2026

Field Codes: /:Mesh-term; exp: Exploded Mesh-term; ab: Abstract; kf: Keyword heading word; ti: Title;

Concept	#	Search	Results
Iron deficiency	1	Iron Deficiencies/	6867
	2	(hypoferrinemia or sideropaenia or sideropenia). ab,kf,ti.	127
	3	1 or 2	6967
	4	Iron/ or exp Ferritins/	130760
	5	(decreased or deficient* or deplet* or inadequa* or insufficien* or low or marginal).ab,kf,ti.	6326226
	6	4 and 5	42056
	7	((Iron or Fe or ⁵⁶ Fe or ferro or ferrum or ferritin* or iso ferritin* or apoferritin* or immunoferritin or myoferritin or proteoferrin or sanifer or unifer) adj4 (decreased or deficient* or deplet* or inadequa* or insufficien* or low or marginal)).ab,kf,ti.	48652
	8	3 or 6 or 7	70061
Non-anaemic	9	(non-anaemic or non-anemic or "without anaemia" or "without anemia" or "no anaemia" or "no ane- mia").ti,ab,kf.	3579
	10	8 and 9	1421
	11	(latent adj3 "iron deficient*").ab,kf,ti.	182
	12	10 or 11	1594
Limits	13	limit 12 to (english language and yr="2016 -Cur- rent")	748
RCT- filter	14	(randomized controlled trial or controlled clinical trial).pt.	745975
	15	(randomized or placebo or randomly or trial or groups).ab.	4124822
	16	drug therapy.fs.	2905107
	17	14 or 15 or 16	6559320
	18	exp animals/ not humans.sh.	5426824
	19	17 not 18	5759017
Combined Sets	20	13 and 19	338

*Glanville J, Kotas E, Featherstone R, Dooley G. Which are the most sensitive search filters to identify randomized controlled trials in MEDLINE? J Med Libr Assoc. 2020 Oct 1;108(4):556-563. doi: 10.5195/jmla.2020.912. PMID: 33013212. Se appendix A: Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity-and precision-maximizing version (2008 revision); Ovid format

Database: Embase

Host: Embase.com

Date searched: 2026-02-23

Limits applied: publications in English language, Publication Year from 2016 to 2026

Field Codes: /de: Emtree term; /exp: Exploded Emtree term; ab: Abstract; kw: Author Keyword; ti: Title;

Concept	#	Search	Results
	1	'iron deficiency'/de OR 'hypoferremia'/de	25426
	2	hypoferremia:ti,ab,kw OR sideropaenia:ti,ab,kw OR sideropenia:ti,ab,kw	658
	3	#1 OR #2	25832
	4	'iron'/de OR 'ferritin'/de OR 'apoferritin'/de	304899
	5	decreased:ti,ab,kw OR deficient*:ti,ab,kw OR deplet*:ti,ab,kw OR inadequa*:ti,ab,kw OR insufficien*:ti,ab,kw OR low:ti,ab,kw OR marginal:ti,ab,kw	8370798
	6	#4 AND #5	107052
	7	((iron OR fe OR 56fe OR ferro OR ferrum OR ferritin* OR isoferritin* OR apoferritin* OR immunoferritin OR mycoferritin OR proteoferrin OR sanifer OR unifer) NEAR/4 (decreased OR deficient* OR deplet* OR inadequa* OR insufficien* OR low OR marginal)):ti,ab,kw	72803
	8	#3 OR #6 OR #7	140406
	9	'non anaemic':ti,ab,kw OR 'non anemic':ti,ab,kw OR 'without anaemia':ti,ab,kw OR 'without anemia':ti,ab,kw OR 'no anaemia':ti,ab,kw OR 'no anemia':ti,ab,kw	6573
	10	#8 AND #9	2785
	11	(latent NEAR/3 'iron deficient*'):ti,ab,kw	315
	12	#10 OR #11	3064
	13	#12 NOT 'conference abstract'/it AND [english]/lim AND [2016-2026]/py	1008
	14	'randomized controlled trial'/exp	1151879
	15	'controlled clinical trial'/de	461574
	16	random*:ti,ab,tt	2592328
	17	'randomization'/de	101963
	18	'intermethod comparison'/de	319270
	19	placebo:ti,ab,tt	478441
	20	compare:ti,tt OR compared:ti,tt OR comparison:ti,tt (evaluated:ab OR evaluate:ab OR evaluating:ab OR assessed:ab OR assess:ab) AND (compare:ab OR compared:ab OR comparing:ab OR comparison:ab)	729542
	21	(open NEXT/1 label):ti,ab,tt	3492688
	22	((double OR single OR doubly OR singly) NEXT/1 (blind OR blinded OR blindly)):ti,ab,tt	195714
	23	'double blind procedure'/de	379652
	24		319052

25	(parallel NEXT/1 group*):ti,ab,tt	54734
26	crossover:ti,ab,tt OR 'cross over':ti,ab,tt (assign* OR match OR matched OR allocation) NEAR/6 (alternate OR group OR groups OR inter- vention OR interventions OR patient OR patients OR subject OR subjects OR participant OR partici- pants)):ti,ab,tt	160848
27	assigned:ti,ab,tt OR allocated:ti,ab,tt	585099
28	(controlled NEAR/8 (study OR design OR trial)):ti,ab,tt	631774
29	volunteer:ti,ab,tt OR volunteers:ti,ab,tt	672232
30	'human experiment'/de	330149
31	trial:ti,tt	746245
32	#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32	592865
33	((random* NEXT/1 sampl* NEAR/8 ('cross sec- tion*' OR questionnaire* OR survey OR surveys OR database OR databases)):ti,ab,tt) NOT ('compar- ative study'/de OR 'controlled study'/de OR 'ran- domised controlled':ti,ab,tt OR 'randomized con- trolled':ti,ab,tt OR 'randomly assigned':ti,ab,tt)	7843521
34	'cross-sectional study'/de NOT ('randomized controlled trial'/exp OR 'controlled clinical trial'/ de OR 'controlled study'/de OR 'randomised controlled':ti,ab,tt OR 'randomized con- trolled':ti,ab,tt OR 'control group':ti,ab,tt OR 'control groups':ti,ab,tt)	3953
35	'case control*':ti,ab,tt AND random*:ti,ab,tt NOT (('randomised controlled':ti,ab,tt OR 'randomized controlled':ti,ab,tt)	495787
36	'systematic review':ti,tt NOT (trial:ti,tt OR study:ti,tt)	25238
37	nonrandom*:ti,ab,tt NOT random*:ti,ab,tt	365529
38	'random field*':ti,ab,tt	21762
39	('random cluster' NEAR/4 sampl*):ti,ab,tt	3319
40	review:ab AND review:it NOT trial:ti,tt	1840
41	'we searched':ab AND (review:ti,tt OR review:it)	1380146
42	'update review':ab	62537
43		156

44	(databases NEAR/5 searched):ab (rat:ti,tt OR rats:ti,tt OR mouse:ti,tt OR mice:ti,tt OR swine:ti,tt OR porcine:ti,tt OR murine:ti,tt OR sheep:ti,tt OR lambs:ti,tt OR pigs:ti,tt OR pig- lets:ti,tt OR rabbit:ti,tt OR rabbits:ti,tt OR cat:ti,tt OR cats:ti,tt OR dog:ti,tt OR dogs:ti,tt OR cattle:ti,tt OR bovine:ti,tt OR monkey:ti,tt OR monkeys:ti,tt OR trout:ti,tt OR marmoset*:ti,tt) AND 'animal experi- ment'/de	89016
45	'animal experiment'/de NOT ('human experiment'/de OR 'human'/de)	1341608
46	#34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR	2840369
47	#46	5100481
48	#33 NOT #47	6923921
49	#13 AND #48	350

*ISSG: Embase RCT filter for Embase.com, 30 April 2023 revision by Glanville, J. et al.

<https://sites.google.com/a/york.ac.uk/issg-search-filters-resource/home/rcts/embase-rct-filter#h.33an36c3ldl>

Database: Cochrane Library

Host: Wiley

Date searched: 2026-02-26

Limits applied: Publication Year from 2016 to 2026

Field Codes: /MeSH descriptor: [] explode all trees: Exploderad Mesh-term; MeSH descriptor: [] this term only: unexplode Mesh-term; ab: Abstract; kw: Keywords; ti: Title

Concept	#	Search	Results
Iron deficiency	1	MeSH descriptor: [Iron Deficiencies] explode all trees	2166
	2	(hypoferrinemia or sideropaenia or sideropenia):ti,ab,kw	5
	3	#1 or #2	2167
	4	MeSH descriptor: [Iron] in all MeSH products	3277
	5	MeSH descriptor: [Ferritins] explode all trees	1340
	6	#4 or #5	3850
	7	(decreased or deficient* or deplet* or inadequa* or insufficien* or low or marginal):ti,ab,kw	489310
	8	#6 and #7	2674
	9	((iron or Fe or ⁵⁶ Fe or ferro or ferrum or ferritin* or iso-ferritin* or apo-ferritin* or immuno-ferritin or myco-ferritin or proteo-ferrin or sanifer or unifer) NEAR/4 (decreased or deficient* or deplet* or inadequa* or insufficien* or low or marginal)):ti,ab,kw	6301
	10	#3 or #8 or #9	6921
Non-anaemic	11	(non-anaemic or non-anemic or "without anaemia" or "without anemia" or "no anaemia" or "no anemia"):ti,ab,kw	667
Combined Sets	12	#10 and #11	370
	13	(latent NEAR/3 iron NEXT deficient*):ti,ab,kw	18
	14	#12 or #13	384
Limits	15	#14 with Publication Year from 2016 to 2026, in Trials and English. Ongoing studies from WHO and Trials.gov are excluded	146

Appendix 2 Excluded studies after full-text reading, with reasons

Year	Publication	Reason for exclusion	
1	2026	Kedir, Shemsu, Tamiru, Dessalegn, Ademe, Beyene Wondafrash, Abate, Kalkidan Hassen. School-Based Weekly Iron–Folic Acid Supplementation and Its Effect on Mental Health Outcomes Among Adolescent Girls in Central Ethiopia: A Cluster-Randomized Controlled Trial. Journal of Nutrition and Metabolism 2026; 9500345. https://doi.org/10.1155/jnme/9500345	Wrong population, wrong focus, wrong intervention
2	2025	Kapoor MP, Sugita M, Kawaguchi M, Timm D, Kawamura A, Abe A, Okubo T. Influence of iron supplementation on fatigue, mood states and sweating profiles of healthy non-anemic athletes during a training exercise: A double-blind, randomized, placebo-controlled, parallel-group study. Contemp Clin Trials Commun 2023; 32:101084. doi: https://10.1016/j.conctc.2023.101084	Wrong population
3	2025	Reznichenko, G, Tursunov, R, Reznichenko, Y, Smiyan, S, Gordiychuk, O, Odinaeva, N, Borodin, A. Experience of correction of latent (non-anaemic) iron deficiency in adolescent girls and young women. REPRODUCTIVE ENDOCRINOLOGY 2025; (81): 27–34. https://doi.org/10.18370/2309-4117.2025.81.27-34	Wrong language, wrong population
4	2024	Akram, S, Akhtar, AM, & Zakar, R. Randomized controlled trial on the treatment of Hypoferritinemia without Anemia: Comparing oral and intravenous iron supplementation among reproductive age women in Pakistan. Pakistan Journal of Medical Sciences 2024; 41(1), 286–294. https://10.12669/pjms.41.1.11083	Wrong publication type
5	2024	Jyothi, GS, Shelatkar, R, Kalavathy, HR et al. A clinical study evaluating low dose ferrous fumarate vs. standard iron supplements in iron-deficient non-anemic to mild anemic adults. Sci Rep 2024; 14: 15674. https://doi.org/10.1038/s41598-024-65878-5	Wrong control, wrong population
6	2024	Karregat J, Meulenbeld A, Abubakar J, Quee FA, van den Hurk K. Iron deficiency-related symptoms in non-anemic whole blood donors. Transfusion 2024; 64(10):1920-1930. https://10.1111/trf.17983	Wrong study type, wrong focus
7	2023	Csulak E, Takács T, Babis B, Horváth L, et al Iron deficiency in young basketball players: Is a 100 µg/L ferritin cut-off appropriate for iron supplementation?: Results of a randomized placebo-controlled study. Clin Cardiol 2023;46(9):1116-1123. https://10.1002/clc.24117	Wrong outcome, wrong population
8	2023	Howaldt, S, Cody, M, Mitchell, JA. Iron Uptake from Ferric Maltol in Patients with Iron Deficiency with or without Anemia: post Hoc analysis of a Multicenter, Open-Label, Randomized, Phase 1 Clinical Study. Blood 2023; 142 (Supplement 1): 5234. https://doi.org/10.1182/blood-2023-185768	Wrong focus, wrong population, wrong publication type

9	2023	Stefan, MW, Gundermann, DM, Sharp, MH, Jennings, BA, Gheith, RH et al. Assessment of the Efficacy of a Low-Dose Iron Supplement in Restoring Iron Levels to Normal Range among Healthy Premenopausal Women with Iron Deficiency without Anemia. <i>Nutrients</i> 2023; 15, 2620. https://doi.org/10.3390/nu15112620	Wrong intervention, wrong outcome
10	2022	Lanz P, Wiecezorek M, Sadlon A, de Godoi Rezende Costa Molino C, et al. Iron Deficiency and Incident Infections among Community-Dwelling Adults Age 70 Years and Older: Results from the DO-HEALTH Study. <i>J Nutr Health Aging</i> 2022;26(9):864-871. https://10.1007/s12603-022-1836-2	Wrong focus
11	2020	Arcani R, Suchon P, Venton G, Soubrier C, Gaigne L et al. Efficacy of intravenous iron therapy in non-anaemic iron-deficient patients with fatigue. <i>Neth J Med</i> 2020 Feb;78(1):34-36.	Wrong study type
12	2020	D'Amato T, Kon E, Martorelli F, Monteleone G, Simili V, Tasso F, Di Matteo B, Scardino M. Effect of intravenous ferric carboxymaltose supplementation in non-anaemic iron deficient patients undergoing hip and knee arthroplasty. <i>J Biol Regul Homeost Agents</i> 2020 Jul-Aug;34(4 Suppl. 3):69-77. Congress of the Italian Orthopaedic Research Society.	Wrong focus, wrong outcome, wrong study type
13	2017	Macher S, Drexler C, Lindenau I, Sipurzynski S, Stojakovic T, Holter M, Moritz M, Schlenke P, Amrein K. High-dose intravenous iron versus oral iron in blood donors with iron deficiency: the ironwoman randomised, controlled trial. <i>Vox sanguinis</i> 2017; 112, 113-114. https://doi.org/10.1111/vox.12530	Wrong publication type, wrong control
14	2017	Pompano, L, Haas, JD. The impact of iron supplementation and daily aerobic exercise on physical fitness in non-anemic Chinese women. <i>Annals of nutrition & metabolism</i> 2017; 71:1083. https://10.1159/000480486	Wrong publication type
15	2016	Cho YW, Allen RP, Earley CJ. Clinical efficacy of ferric carboxymaltose treatment in patients with restless legs syndrome. <i>Sleep Med</i> 2016 Sep;25:16-23. https://10.1016/j.sleep.2016.06.021	Wrong outcome, wrong population
16	2016	Sharma, R., Stanek, J.R., Koch, T.L., Grooms, L. and O'Brien, S.H. Intravenous iron therapy in non-anemic iron-deficient menstruating adolescent females with fatigue. <i>Am. J. Hematol.</i> 2016, 91: 973-977. https://doi.org/10.1002/ajh.24461	Wrong study type, wrong population
17	2016	Trenkwalder, C. Winkelmann, J. Oertel, W. Virgin, G., Roubert, B., Mezzacasa, A. Single-dose ferric carboxymaltose for the treatment of restless legs syndrome in iron deficient non-anaemic patients-a randomized, placebo-controlled trial. <i>Journal of Sleep Research</i> 2016;. 25: 67-68. https://10.1111/jsr.12446	Wrong publication type, wrong outcome
18	2016	Waldvogel, S., Rochat, B., Peduzzi, D., Vaucher, P., Tissot, J.-D. and Favrat, B. Effects of oral supplementation of iron on hepcidin blood concentrations among non-anaemic female blood donors: a randomized controlled trial. <i>Vox Sang</i> 2016; 110: 166-171. https://doi.org/10.1111/vox.12348	Wrong outcome

