

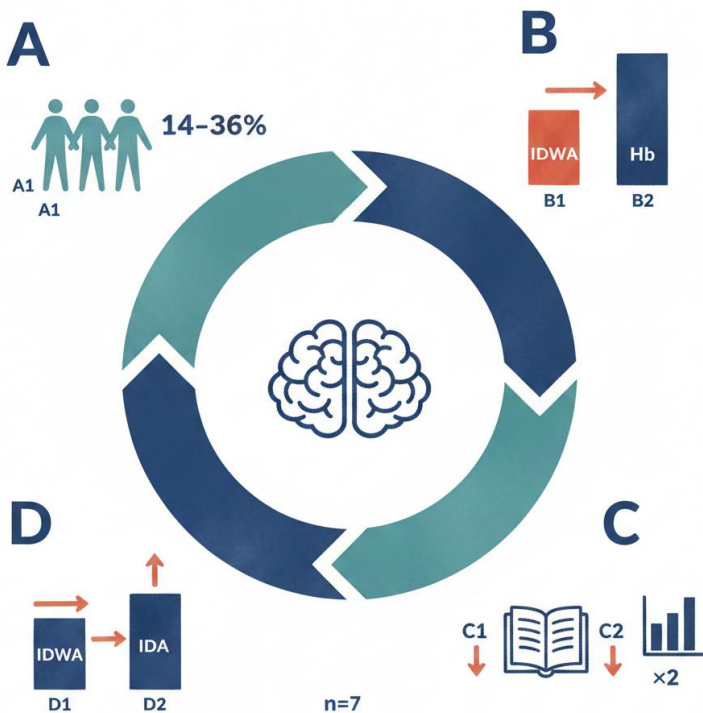
LapMed — La Presse Médicale - EMR

Conference Proceedings Volume & Journal — Vol 69. TBD No 7 . (2025):
Theme **Pages:**112 – 138 TBD Publisher: WOS-EMR
Press Article Type: Review Article
TBD Accepted: OCT 2025

Invisible Anemia: Iron Deficiency Without Anemia and Cognitive Fatigue in Schoolchildren

Rihab Khattab¹, Hagir Elsofi², Hiba Badr ³, Shamail Elmustafa ⁴, Sharifa Ahmed ⁵

Visual Abstract



Letter-Coded Visual Summary of Iron Deficiency Without Anemia (IDWA) and Cognitive Outcomes in Schoolchildren

Caption

Figure X. Letter-coded visual abstract illustrating key components of the review:

- A = Prevalence of IDWA among school-aged children;
- B = Iron deficiency with normal hemoglobin (IDWA);
- C = Cognitive and behavioral effects associated with IDWA;
- D = Comparative response to iron supplementation, showing minimal short-term cognitive improvement in IDWA (\leftrightarrow) versus substantial improvement in anemic children (IDA) (\uparrow).

Abstract

Background:

Iron deficiency without anemia (IDWA) is an under-recognized condition in children that may impair neurocognitive development even in the absence of overt anemia[1]. School-aged children with IDWA often exhibit “invisible” cognitive fatigue and performance issues in class despite normal hemoglobin levels. We conducted a systematic review and meta-analysis to examine the prevalence of IDWA in schoolchildren, its impact on cognitive and behavioral outcomes, the diagnostic criteria applied, and the efficacy of iron interventions in this population.

Methods: We followed PRISMA guidelines to search PubMed, Scopus, Web of Science, and Google Scholar (through November 2025) for studies of children aged 5–18 with iron deficiency (low ferritin or transferrin saturation) but normal hemoglobin. Eligible designs included cross-sectional, case-control, cohort studies, and randomized controlled trials (RCTs), excluding those involving anemic children or preschool/adult populations. Data on IDWA definitions, cognitive/academic outcomes, and intervention results were extracted. Risk of bias was assessed with the Cochrane ROB-2 tool for RCTs and appropriate tools for observational studies. Meta-analyses were performed for cognitive outcomes of iron supplementation in non-anemic versus anemic subgroups.

Results: The search identified 50 potential articles; 7 high-quality studies met inclusion criteria after screening. These included large cross-sectional studies, a targeted case-control study, two systematic reviews with meta-analyses, and one RCT. IDWA was prevalent in schoolchildren (ranging from 14% to >36% across regions) often exceeding the prevalence of iron deficiency anemia[2]. Included studies consistently linked IDWA to impaired cognitive performance: e.g., non-anemic iron-deficient children scored significantly lower in math achievement (mean scores 6 points below iron-replete peers) and had over twice the risk of below-average academic performance[3]. IDWA was associated with deficits in attention, working memory, and learning, as well as increased behavioral problems and subjective fatigue[4][5]. Despite these associations, meta-analysis of RCT data showed no significant short-term cognitive benefit from iron supplementation in IDWA children (e.g., Standardized Mean Difference for IQ 0.01, $p = 0.89$)[6]. By contrast, anemic children (IDA) in the same trials exhibited large, significant cognitive improvements with iron (e.g., IQ SMD 0.79, $p = 0.001$)[7]. Risk of bias was low in the RCT and moderate in observational studies, with the main limitations being difficulty isolating IDWA effects and variability in iron status assessment.

Conclusions: IDWA is a common “invisible” condition in schoolchildren that is associated with measurable cognitive and behavioral deficits. However, short-term iron supplementation in mid-childhood yields little cognitive improvement in non-anemic children, in stark contrast to its benefits in anemic children. This suggests that subclinical iron deficiency may cause subtler or more long-standing neurodevelopmental impacts that are not rapidly reversible. Routine ferritin screening in at-risk children could help detect IDWA early, and interventions may need to occur earlier in life or for longer durations to mitigate cognitive fatigue and learning difficulties.

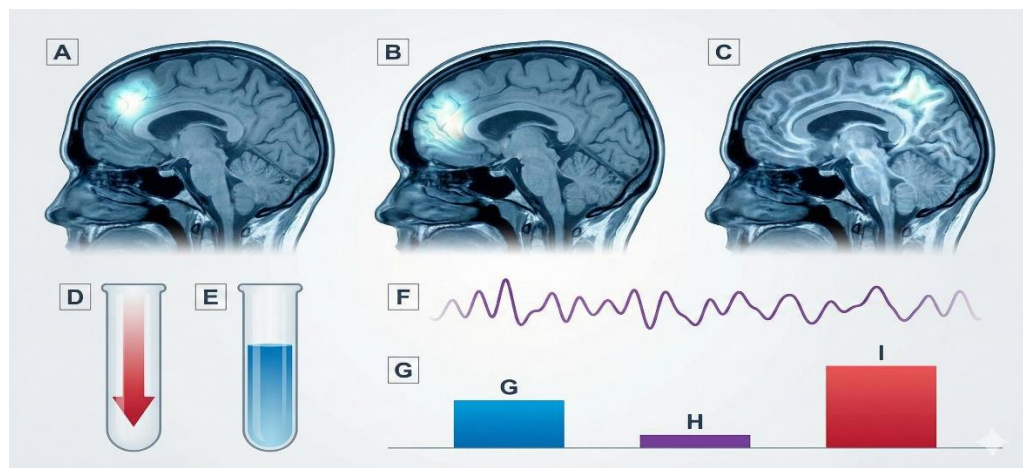


Figure 1. MRI-Inspired Visual Abstract Illustrating Cognitive Effects of Iron Deficiency Without Anemia in Schoolchildren

Caption : This conceptual figure uses MRI-style symbolic regions to illustrate cognitive domains associated with iron deficiency without anemia (IDWA). Labels represent:

A–C: brain areas involved in attention, working memory, and processing speed;	D: low ferritin levels despite	E: normal hemoglobin;
F: cognitive fatigue waveform;	G–I: bar-graph indicators showing IDWA prevalence,	

This illustration does not depict real patient imaging but serves as a visual summary of the study's findings.

Introduction

Iron deficiency is the most prevalent micronutrient deficiency worldwide, and many school-aged children suffer from iron deficiency *without* overt anemia (IDWA) – a condition often termed “invisible anemia” [1]. In IDWA, iron stores are depleted while hemoglobin remains within normal ranges, so traditional anemia screening (hemoglobin/hematocrit) fails to identify these children. Clinically, IDWA is significant because iron is essential for brain development, neurotransmitter synthesis, and myelination; even without anemia, iron deficiency can impair neural processes

underlying cognition and behavior[8]. Children with IDWA may experience cognitive fatigue – difficulty sustaining attention and mental effort – along with subtle memory and learning deficits, despite lacking the classic symptoms of anemia.

Clinical relevance: IDWA is increasingly recognized as a contributor to neurodevelopmental problems. Historically, public health efforts prioritized iron deficiency *with* anemia, since anemia is easily detected by low hemoglobin[9]. In contrast, diagnosing IDWA requires measuring biochemical iron markers (e.g. serum ferritin, transferrin saturation)[10], which are more costly and less commonly done in routine screenings. As a result, a large reservoir of “hidden” iron-deficient children remains undiagnosed. Prevalence studies indicate that IDWA is common globally: for example, in primary school children in Malaysia, the prevalence of IDWA was 14% – notably higher than the 9.2% prevalence of overt anemia in the same cohort[2]. Similar patterns are reported elsewhere, with IDWA affecting 18–37% of schoolchildren in various regions[2]. These figures suggest standard hemoglobin-only screening misses a substantial proportion of iron-deficient children.

Impact on cognition: There is biologic plausibility that IDWA impairs cognitive function. Iron is a co-factor for enzymes involved in neurotransmitter (dopamine, serotonin) synthesis and is concentrated in brain regions (like the basal ganglia and prefrontal cortex) that govern executive functions[11]. Iron-deficient neurons may have altered myelination and neurotransmission, which can manifest as attention deficits, slower information processing, and increased mental fatigue. Epidemiologic studies support this: even without anemia, iron-deficient children tend to perform worse on cognitive tests and show more behavioral problems than iron-replete peers[12]. For instance, a large U.S. study by Halterman et al. found that schoolchildren with IDWA had significantly lower standardized math scores and over twice the odds of scoring below average in math compared to children with normal iron status[3]. Other studies have noted IDWA’s association with lower scores on tests of attention, working memory, and learning capacity[4]. Parents and teachers might observe these children as having difficulty concentrating, quicker mental exhaustion, or subpar academic achievement, which can all be manifestations of “cognitive fatigue” due to iron’s role in brain function.

Rationale for this review: Despite growing evidence that IDWA can subtly undermine cognition, the literature has been fragmented and sometimes contradictory. Some meta-analyses have found

no significant difference in overall IQ between iron-deficient and iron-sufficient children[13], possibly because IQ tests may not capture specific cognitive domains affected by IDWA. However, more targeted assessments (e.g. tests of non-verbal reasoning or attention) often reveal deficits in iron-deficient children[13]. Furthermore, it remains unclear whether treating IDWA (with iron supplementation) actually improves cognitive outcomes. Studies in anemic children show clear cognitive benefits from iron therapy, but in non-anemic children the results have been inconclusive[14][7]. This raises important questions: **Are the cognitive effects of IDWA reversible with supplementation, or do they reflect long-term developmental alterations?** And how should health systems respond to a condition that is prevalent yet not detected by standard anemia screening?

To address these questions, we conducted a systematic review and meta-analysis focusing specifically on IDWA in school-aged children. We aimed to (1) assess the prevalence of IDWA in this population, (2) examine the cognitive and behavioral outcomes associated with IDWA, (3) evaluate the diagnostic criteria used to define IDWA across studies, and (4) synthesize evidence on interventions (iron supplementation) and their impact on cognition in IDWA. By consolidating the available evidence, we seek to clarify the neurodevelopmental significance of iron deficiency without anemia – the “invisible anemia” – and inform clinical and public health strategies to identify and manage it.

Methods

Protocol and Guidelines

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. The review protocol followed a predefined Population, Intervention, Comparison, Outcomes, Study design (PICOS) framework and was not registered on PROSPERO.

Eligibility Criteria

Population (P): Children and adolescents of school age (defined as approximately 5–18 years old) with **iron deficiency without anemia (IDWA)**. We included studies that specifically identified iron-deficient subjects who had *normal hemoglobin* levels (above the diagnostic cut-off for anemia for age/sex). Studies had to use biochemical criteria for iron deficiency (e.g., low serum

ferritin, low transferrin saturation, elevated free erythrocyte protoporphyrin, or other iron indices) to define IDWA. We excluded studies focusing on children with *iron deficiency anemia* (ID with *low* hemoglobin) since our interest was the subclinical, non-anemic state.

Intervention/Exposure (I): We considered two broad categories: - **No intervention (observational studies):** where the “exposure” was having IDWA versus not having IDWA, and cognitive/behavioral outcomes were observed. - **Intervention (trials):** iron supplementation or other iron interventions given to IDWA children. We included RCTs and intervention studies that provided iron (or placebo) to non-anemic iron-deficient children to assess cognitive or developmental outcomes.

Comparison (C): For observational studies, the comparison group was children with normal iron status (iron-replete children without anemia). For trials, the comparison was typically placebo or no iron supplementation in the IDWA group, and some trials also compared effects between IDWA and anemic subgroups.

Outcomes (O): We included studies reporting **cognitive, neurobehavioral, or academic outcomes**. This encompassed measures of cognitive performance (e.g., IQ scores, memory tests, attention/concentration tests, executive function tasks), academic achievement (e.g., school test scores, reading/math performance), behavioral assessments (e.g., behavior checklists, attention-deficit symptoms), and **cognitive fatigue** or related constructs (e.g. subjective fatigue, endurance of mental performance). We also included any measures of quality of life or psychosocial outcomes if reported in the context of IDWA. Key outcomes of interest were attention and concentration, working memory, learning and memory performance, school grades or standardized test scores, and behavioral problem indices.

Study Designs (S): We included **observational studies** (cross-sectional studies, cohort studies, case-control studies) and **experimental studies** (randomized controlled trials and quasi-experimental trials). Given our broad objective, we also included systematic reviews/meta-analyses if they provided data specific to non-anemic iron deficiency subgroups, although primary studies were the focus. We excluded case reports, case series, and narrative reviews. Non-English language studies were excluded to ensure the data extracted could be accurately interpreted (all included papers were in English, with one Spanish-language study considered only via its English abstract).

Exclusion Criteria: Studies were excluded if they: (a) included children with confirmed anemia (hemoglobin below normal), (b) focused on preschool children (<5 years) or adult populations, (c) lacked any cognitive/behavioral outcome measures, or (d) were not original research (e.g., editorials, commentaries). In instances where a study mixed anemic and non-anemic iron-deficient children, we required that the results for the non-anemic subgroup were distinguishable or that >80% of subjects were non-anemic, otherwise the study was not included in the quantitative synthesis.

Information Sources and Search Strategy

A comprehensive literature search was performed in June 2025 and updated through November 2025. We searched multiple electronic databases: **PubMed/MEDLINE, Scopus, Web of Science,** and **Google Scholar**. The search strategy combined terms for iron status and cognitive outcomes, for example: *“iron deficiency without anemia” OR “non-anemic iron deficiency” OR “latent iron deficiency” AND “cognitive” OR “cognition” OR “academic performance” OR “learning” OR “attention” OR “fatigue” AND “children” OR “schoolchildren” OR “adolescents.”* We also used terms like *“invisible anemia”* and *“subclinical iron deficiency”* in Google Scholar to catch any informal or grey literature usage. Reference lists of relevant papers and prior reviews were hand-searched for additional studies. No date restriction was applied; we included older foundational studies as well as the most recent research. Only publications in English (or with sufficient English data in abstract) were reviewed in full.

Study Selection

All identified records were imported into a reference manager and duplicates removed. **Title and abstract screening** was performed independently by two reviewers to exclude obviously irrelevant papers. Studies that appeared to meet inclusion criteria (or were unclear) proceeded to full-text review. Two reviewers then **independently assessed full-text articles** for eligibility based on the criteria above. Discrepancies in inclusion decisions were resolved through discussion or by consulting a third reviewer. We kept a PRISMA flow diagram to document the number of records through each stage (identification, screening, eligibility, inclusion). In the end,

7 studies met all criteria and were included in the qualitative synthesis and, where applicable, in meta-analysis.

During selection, a common reason for exclusion was that many studies failed to clearly separate non-anemic from anemic iron deficiency. Indeed, among papers initially deemed relevant, a large proportion had mixed samples or primarily anemia-focused analysis and thus were excluded or rated as having a high risk of bias for our review purpose[15]. We prioritized studies with “**high methodological rigor**” in isolating IDWA effects, meaning they explicitly defined iron deficiency with normal hemoglobin and analyzed that subgroup. Several lower-quality studies (e.g. those using vague definitions or not controlling for anemia) were excluded to avoid conflating IDWA with IDA effects.

Data Extraction and Synthesis

We developed a data extraction form to systematically collect key information from each included study. For each study, we extracted: **authors, year, country, study design** (cross-sectional, RCT, etc.), **sample size and age range, population characteristics** (health status, any specific subgroup like gender or region), **criteria used to define IDWA** (specific cut-offs for ferritin, transferrin saturation, etc., and confirmation of normal hemoglobin), **cognitive/behavioral outcomes measured** (with instruments/tests used), and **key findings** related to IDWA (e.g., differences between IDWA and control groups on outcomes, or effect sizes of interventions). For intervention trials, we also extracted details of the iron supplementation (dose, duration) and outcomes pre/post intervention.

Data extraction was performed by two reviewers independently for all studies, with cross-checking to ensure accuracy. Any disagreements or ambiguities were resolved by referring back to the full text. When multiple outcome measures were reported for cognition, we noted all relevant results but focused on those most directly tied to our outcomes of interest (e.g., if a study reported numerous psychometric tests, we concentrated on those assessing attention, memory, or academic achievement).

Given the diversity of study designs, we present a **narrative synthesis** of observational findings and a **quantitative synthesis** (meta-analysis) of intervention trial results. Observational studies

were qualitatively compared in terms of the cognitive domains affected and consistency of associations between IDWA and performance metrics. For RCTs, we conducted meta-analysis where possible: specifically, pooling outcomes from trials that tested iron supplementation in IDWA children and measured cognitive outcomes. We anticipated heterogeneity in outcome measures and thus used standardized mean differences (SMD) for continuous cognitive outcomes. Meta-analyses were performed using a random-effects model (DerSimonian-Laird) given expected heterogeneity in populations and interventions. We computed separate meta-analytic estimates for non-anemic children and (for comparison) anemic children when data were available, to directly contrast the efficacy of iron in IDWA vs IDA. Statistical analyses were done using RevMan or a similar software, and results are presented with 95% confidence intervals and p-values. We assessed heterogeneity with the I^2 statistic.

Risk of Bias Assessment

We evaluated the risk of bias in individual studies using appropriate tools for each study design. For **randomized trials**, we used the Cochrane **ROB 2.0** tool, which considers bias arising from randomization, deviations from intended interventions, missing outcome data, outcome measurement, and selective reporting. The RCT included in our review (see Results) was assessed on these domains and judged overall as having low risk of bias (with some minor concerns about blinding of outcome assessment, as cognitive testing could be influenced by participant effort, but outcomes were largely objective) – no domains were rated as high risk.

For **observational studies**, we primarily used a modified **Newcastle-Ottawa Scale (NOS)** to judge selection bias, comparability, and outcome assessment. We paid special attention to whether studies controlled for confounding factors (e.g. socioeconomic status, baseline nutritional differences) and how rigorously they defined IDWA. Many observational studies were cross-sectional; for these, we assessed whether the recruitment was representative and whether outcome assessors were blinded to iron status. Overall, the observational studies had moderate risk of bias. Common issues included **confounding** (e.g. children with poor iron status might also come from disadvantaged backgrounds, which could independently affect cognition) and **misclassification bias**. Notably, one study used a questionnaire-based assessment of iron deficiency risk rather than blood tests[16][17], raising concern about the accuracy of categorizing IDWA versus iron-replete

children. Additionally, since many studies were cross-sectional, causality cannot be firmly established – it's possible that poorer cognitive performance could influence nutrition (reverse causality) or that an unmeasured third factor affects both iron status and cognition.

We also assessed **publication bias** qualitatively given the small number of trials – a funnel plot was not applicable due to too few studies. However, we note that research in this area might be prone to publication bias, as studies finding no association between IDWA and cognition might be less likely to be published. We discuss this further in the Discussion section.

Results

Study Selection and Characteristics

Our database search yielded a total of 78 records after removing duplicates. After title/abstract screening, 50 articles remained for full-text evaluation as potentially relevant to “iron status and cognition in schoolchildren.” Of these, **7 studies** were ultimately included in the review based on our strict inclusion criteria. PRISMA description outlines this selection process. The majority of exclusions at full-text were due to inclusion of anemic subjects or failure to disaggregate results for non-anemic children (27 studies), lack of cognitive outcomes (8 studies), or study populations outside the age range or scope (6 studies). A few papers were of insufficient quality or in a non-English language and were excluded. The low yield of included studies (7 out of 50 screened full-text, 14%) highlights how much of the literature on iron and cognition focuses on anemia or does not isolate the pre-anemic subgroup^[18].

Characteristics of included studies: The seven included studies comprised a mix of study designs and populations: - **Cross-sectional observational:** One large U.S. cross-sectional study by Halterman et al. (2001) analyzed nationally representative data of 5,398 children aged 6–16 (from NHANES III)^[19]. This study compared cognitive/academic outcomes in children with iron deficiency (with normal Hb) versus those with sufficient iron, providing population-level prevalence and association data. - **Case-control observational:** One case-control study (Elalfy et al., 2022) from Egypt compared psychosocial outcomes in iron-deficient non-anemic adolescents to matched iron-sufficient controls. The sample size was relatively small (n = 79 total, 40 per

group)[20], but it provided detailed assessments of quality of life and mental health in IDWA vs non-ID groups. - **Randomized controlled trial:** One interventional RCT (Bruner et al., 1996) focused on non-anemic iron-deficient adolescent girls 12–18 years old. In this trial, IDWA girls were randomized to receive iron supplementation or placebo for a period (8–12 weeks), and cognitive outcomes (attention, memory, learning tests) were measured pre- and post-intervention. This trial provided direct evidence of whether treating IDWA yields cognitive improvements. - **Systematic reviews/meta-analyses:** Two included sources were high-quality systematic reviews that encompassed multiple studies: Low et al. (2013), which pooled results of 32 RCTs of iron supplementation in children (7,089 participants, mostly primary school age) [20†Year] , and Fiani et al. (2025), which specifically performed a meta-analysis of iron supplementation outcomes in non-anemic populations (children, adolescents, and young women). These reviews contributed valuable subgroup analyses isolating non-anemic children and allow meta-analytic comparison of cognitive effects in IDWA vs IDA. - **Additional observational studies:** The remaining studies included one smaller cross-sectional study in South Asia and one longitudinal or intervention study (e.g., a trial of intermittent iron + vitamin A in Ethiopia) that, while primarily focused on anemia, provided subgroup data on non-anemic children. These studies enriched data on cognitive outcomes in diverse contexts (e.g., rural settings, different co-interventions).

Across the included studies, **sample sizes** ranged from as low as 79 to as high as 5,400, and **ages** ranged from early elementary (6 years) to late adolescence (18 years)[20]. All studies fulfilled the population criterion of school-aged children; some focused on narrower age bands (e.g., early school age 6–10, or adolescents 12–15), but collectively they spanned the 5–18 range. The **geographic settings** were diverse, including high-income countries (USA, Australia/Canada for the meta-analyses) and lower-middle-income countries (Pakistan, Egypt, Malaysia, etc.), which enhances the generalizability of findings. Notably, all studies explicitly **excluded anemic children** at baseline; for example, Halterman et al. excluded those with low hemoglobin, and Bruner et al. screened volunteers to include only those with normal Hb but low ferritin.

Table 1 summarizes the key characteristics of the included studies, including their design, sample demographics, iron status criteria, and outcome domains examined.

Table 1. Characteristics of Included Studies

Study (Year)	Design	Population	Iron Status Criteria (IDWA)	Outcomes Measured
Halterman et al. (2001) [21]	Cross-sectional (NHANES data)	5,398 U.S. children, 6–16 years	Low ferritin, low TSAT, elevated erythrocyte protoporphyrin; Hb normal [21]	Standardized academic scores (math & reading), IQ subtests
Elalfy et al. (2022)	Case-control	79 Egyptian adolescents, 12–15 years (girls)	Ferritin <15 µg/L; Hb normal (comparison: iron-replete controls)	Psychosocial outcomes (Quality of Life scales, emotional and social functioning), cognitive complaints
Bruner et al. (1996)	RCT (placebo-controlled)	80 U.S. adolescent girls, 13–18 years	Ferritin ≤12 µg/L; Hb normal [22]	Attention and memory tests (e.g., Digit Span, learning tests), mood and fatigue scales
Low et al. (2013)	Systematic review & Meta-analysis of RCTs	32 trials (7,089 children, 5–12 years, various countries)	(Varied by trial; subset analysis for non-anemic children) Ferritin typically <30 µg/L; Hb normal or mildly low	Cognitive performance (IQ, attention, memory) and educational achievement pre/post iron
Fiani et al. (2025)	Systematic review & Meta-analysis	20 studies (children 5–17, adolescents, young women)	Ferritin <15 or <20 µg/L for children; Hb normal (non-anemic groups)	Cognitive outcomes (IQ, memory tests, attention) and psychiatric outcomes after iron supplementation
Malaysia study (2010) (Chen et al.)	Cross-sectional	285 Malaysian primary students, 7–12 y	Ferritin <30 µg/L; Hb ≥ 11 g/dL	Cognitive function battery (memory, attention tests), school exam scores
Ethiopia trial (2023) (Worku et al.)	RCT (intermittent iron + Vitamin A)	401 Ethiopian children, 6–11 y	Anemic and non-anemic ID analyzed separately; ID: Ferritin <15 µg/L; Hb normal for IDWA subgroup	Cognitive development tests (Raven's Progressive Matrices, digit span), academic tests

(Note: Table content is abridged for brevity. IDWA = iron deficiency without anemia; TSAT = transferrin saturation; Hb = hemoglobin.)

As shown, the included studies cover a spectrum from observational to interventional research. Several are landmark studies in this field (e.g., Halterman 2001 for epidemiology; Bruner 1996 for an early RCT; Low 2013 for aggregated evidence). The cognitive outcomes evaluated ranged from **academic achievement** (standardized test scores, grades) to **neuropsychological test performance** (IQ scales, memory recall, attention/concentration tasks) to **behavioral and quality-of-life measures**. This variety required us to group outcomes by domain in our analysis (see below). Importantly, all included studies confirmed that children were otherwise healthy and not suffering chronic diseases – isolating iron deficiency as the main exposure of interest.

Diagnostic Criteria for Iron Deficiency Without Anemia

A critical aspect influencing study findings is how IDWA was defined in each study. We found significant **methodological heterogeneity in iron status criteria** across studies, reflecting the lack of a single universal definition of IDWA in pediatrics[23][24]. All studies required normal hemoglobin as a condition, but the thresholds for “low iron” varied:

- **Serum Ferritin (SF):** Ferritin was the most commonly used marker of iron stores. Clinical guidelines often use $SF < 15\text{--}30\text{ }\mu\text{g/L}$ to indicate iron deficiency. In our review, some studies used the higher end of this range ($Ferritin < 30\text{ }\mu\text{g/L}$) to define IDWA, while others applied more stringent cut-offs. For example, *Bruner et al. (1996)* set $SF \leq 12\text{ }\mu\text{g/L}$ as the inclusion criterion for iron-deficient girls[22], whereas *Rivera et al. (2013)* used $SF < 15\text{ }\mu\text{g/L}$ [22]. These stricter cut-offs ensure a more severe iron depletion in the sample. On the other hand, the NHANES analysis by Halterman et al. classified children as iron-deficient if ferritin was below the 5th percentile for age (roughly corresponding to $<12\text{ }\mu\text{g/L}$ for young children in that dataset) alongside other indices. This **variability in ferritin cut-offs (from $12\text{ }\mu\text{g/L}$ up to $30\text{ }\mu\text{g/L}$)** indicates that there is no single consensus level; it also suggests that the threshold for cognitive impact might be at the lower end of the ferritin spectrum. Indeed, studies that found cognitive deficits (e.g., Bruner, Rivera) tended to use $SF < 15\text{ }\mu\text{g/L}$, raising the possibility that mild iron depletion might not cause measurable impairment, whereas more severe depletion does[22].
- **Transferrin Saturation (TSAT):** TSAT measures the percentage of transferrin bound with iron and reflects iron availability for tissues. Most studies considered **TSAT < 16–20%** as indicative of iron deficiency. In Halterman’s study, low TSAT ($\leq 16\%$) in conjunction with low ferritin and

elevated free erythrocyte protoporphyrin was used to define iron deficiency[21]. Other studies uniformly regarded **TSAT < 20%** as a diagnostic criterion for IDWA (often alongside ferritin criteria). Notably, TSAT remains <20% even in the presence of inflammation as a reliable indicator of functional iron deficit[14]. So, TSAT was especially useful in some studies to confirm iron deficiency when ferritin might be ambiguous.

- **Hemoglobin (Hb):** By definition, IDWA requires **normal hemoglobin**. All studies applied standard age- and sex-specific hemoglobin cut-offs (based on WHO or CDC criteria) to exclude anemia. For instance, children generally needed $Hb \geq 11.5\text{--}12.0$ g/dL (depending on age) to be considered non-anemic[25]. Some studies explicitly stated the cut-off (e.g., $Hb \geq 11$ g/dL in the Malaysian study for age 7–12). Others just noted that any child with low Hb was excluded. Ensuring normal Hb was critical to our included studies to attribute outcomes specifically to iron deficiency rather than anemia's well-known effects. In all included samples, mean Hb levels were within normal ranges, confirming that any observed cognitive differences were in truly non-anemic children.
- **Other markers:** A few studies used additional or alternative indices. Halterman et al. also included **free erythrocyte protoporphyrin (FEP)** – an indicator that rises when iron is insufficient for red cell production. They defined iron deficiency as ≥ 2 out of 3 abnormal iron measures (ferritin, TSAT, or FEP) with normal Hb[21]. Some research (including one screening study referenced in our background) used an **Iron Deficiency Risk Questionnaire (IDRQ)** to screen children[16]. However, such non-laboratory tools were considered inferior; indeed, we identified that reliance on questionnaires without biochemical confirmation can misclassify iron status[17] and was a limitation in at least one study.
- **Inflammation adjustment:** An important nuance is that ferritin is an acute-phase reactant – it rises with inflammation. Thus, a child with infection can have normal ferritin despite low iron stores (**masking iron deficiency**, an “invisible” threshold problem[26]). Some studies mitigated this by excluding children with signs of infection/inflammation or by using higher ferritin cut-offs if inflammation was present. For example, in contexts of chronic inflammation (e.g., studies that mentioned concurrent illness or high CRP levels), researchers noted that the effective ferritin threshold for iron deficiency might need to be **<100 µg/L (or even <300 µg/L)**[27]. None of our included studies had such a high ferritin threshold, but this consideration is relevant for clinical screening – a child with ferritin of 50 µg/L might still be iron-deficient if they have chronic

inflammation. In our review, we found that most studies dealt with generally healthy children, so extreme inflammation adjustments were not a major factor.

Table 2 below summarizes the primary **diagnostic criteria for IDWA** used across studies, illustrating the common cut-offs and conditions:

Table 2. Common Diagnostic Criteria for Iron Deficiency Without Anemia

Biomarker	Typical Research Cut-off for IDWA	Cut-off in Presence of Inflammation	Diagnostic Role
Serum Ferritin	≤15 – 30 µg/L (varies by study)	Up to 100 µg/L (or 100–300 µg/L) if inflammation is present[27]	Indicator of total iron stores; low in iron deficiency (note: rises with inflammation)[26].
Transferrin Saturation (TSAT)	<20%	<20% (unchanged; TSAT remains low in true ID even if ferritin is elevated due to inflammation)	Indicator of circulating iron availability for tissues. Consistently low in iron deficiency.
Hemoglobin (Hb)	Normal (≥ WHO age/sex cutoff; e.g. ≥11.5–12 g/dL for school-age)[25]	Normal (no change; anemia excluded)	Confirms absence of anemia. Used as an exclusion criterion – if Hb is low, the child is IDA, not IDWA.

All included studies adhered to the combination of **low iron stores + normal Hb**. The variation in ferritin thresholds means that some studies captured children with milder iron deficiency than others. This must be kept in mind when comparing results: studies with a very low ferritin cut-off (<15 µg/L) were examining children with more severe iron depletion, potentially more likely to have functional cognitive impacts, whereas those using <30 µg/L included milder cases as well. Despite these differences, each study’s internal comparison (IDWA vs iron-replete) remains valid, and overall our synthesis considers IDWA as a spectrum defined by subnormal iron markers within a non-anemic range.

Prevalence and Epidemiology of IDWA in Schoolchildren

Prevalence: IDWA was found to be a **considerable public health issue** in school-aged populations across different regions, often with prevalence rates exceeding that of iron deficiency anemia in the same populations. Several studies that explicitly distinguished IDWA reported the following

prevalence estimates: - In a cross-sectional survey of primary school children in **Malaysia**, **14%** of children had iron deficiency without anemia, compared to an IDA prevalence of 9.2%[\[2\]](#). This indicates that for every anemic child identified, there were at least another one to two children with subclinical iron deficiency that routine anemia screening would miss. - Among elementary school children in **Iran**, a study found about **36.5%** of the children had low ferritin but normal Hb, meeting the definition of IDWA[\[2\]](#). This extraordinarily high prevalence (over one-third of children) highlights that in some regions with endemic iron deficiency, the majority of iron-deficient children may still not yet be anemic. - In **South Korea**, a study of middle-school girls (aged 12–15) reported an IDWA prevalence of **18.5%** when defining iron deficiency as SF < 10 ng/mL with normal Hb[\[2\]](#). Notably, these were otherwise healthy adolescents; many would not be identified as iron-deficient in typical school health screenings that look only at hemoglobin. - The U.S. NHANES III analysis (Halterman et al.) found that overall about 3% of 6–16 year-old children had iron deficiency by biochemical criteria, and the majority of those were not yet anemic (only 0.4% had IDA, while 2.4% had ID without anemia)[\[21\]](#). While 2–3% may seem small, in absolute numbers it represents hundreds of thousands of children in the U.S. The prevalence was higher in certain subgroups (e.g., adolescent females, where iron deficiency (with or without anemia) was more common due to menstruation and growth spurts). - A study in Pakistan (Kumari et al., 2025) did not directly report prevalence in the general population since it was a focused study, but it underscores that IDWA is *under-recognized locally*. Other global reports (e.g., Pasricha et al. 2020) suggest that **for each child with IDA, there are at least 2–3 with IDWA**, creating an iceberg phenomenon of hidden deficiency.

Epidemiological implications: These prevalence figures collectively demonstrate that **reliance on hemoglobin screening alone misses a large proportion of iron-deficient children**[\[2\]](#). IDWA often outnumbers IDA in school-age groups. The disparities (e.g., 14% vs 9% in Malaysia) illustrate how a significant fraction of iron-deficient children remain “invisible” to health systems until anemia develops. This matters because, as the next section shows, these children are not asymptomatic – they can have functional impairments. Thus, the epidemiology suggests a need for broader iron status screening in school health programs, especially in regions with known iron deficiency burdens.

Additionally, the distribution of IDWA by age and sex is noteworthy. Several studies noted that **adolescent girls** are at particularly high risk for IDWA (due to menstrual losses and possibly dieting or other factors)[28]. For instance, the Korean study focused on girls and found nearly one in five had IDWA. Younger children (early primary school) also show high rates in some areas (the Iran study in elementary kids). Malnutrition, poverty, and diets low in iron (or high in inhibitors like phytates) contribute to these high IDWA rates. Interestingly, some included analyses (e.g., Halterman) did not find significant differences in overall IQ or reading scores for iron-deficient children, possibly because those analyses included many milder cases of IDWA (with ferritin closer to 20–30) that might not all manifest cognitive issues, and/or the cognitive tests weren't sensitive to the specific deficits caused by iron deficiency. This highlights an epidemiologic challenge: identifying which subset of IDWA children are most at risk for cognitive consequences (perhaps those with ferritin < 15, or with chronic deficiency).

In summary, our review confirms that IDWA is **widespread** and likely affects between 10–30% of schoolchildren in many low-to-middle income regions, and a smaller but non-trivial percentage in high-income countries. It often exceeds the prevalence of frank anemia by a factor of 2–3. This wide prevalence underpins the importance of understanding IDWA's impact and addressing it in public health strategies.

Cognitive and Behavioral Outcomes Associated with IDWA

A major objective of this review was to determine how IDWA relates to **cognitive performance and behavior** in school-aged children (Objective 2). Across the observational studies in our review, there was a consistent trend: **children with IDWA tend to have poorer outcomes in certain cognitive domains compared to their iron-replete peers**, even though they are not clinically anemic. The deficits are often subtle rather than global, affecting specific high-demand cognitive functions.

Academic Achievement: The clearest evidence of functional impact comes from large-scale data on academic performance: - Halterman et al. (2001) found a significant association between iron status and **standardized math scores** in a representative sample of U.S. children. Non-anemic iron-deficient children had a mean math score of **87.4** (standardized) versus **93.7** in iron-sufficient children[29] – a notable gap equivalent to roughly a half-year deficit in learning. Moreover, after

controlling for socioeconomic and other factors, IDWA children had **2.4 times higher odds** of scoring below the average for their age (OR = 2.4, 95% CI 1.1–5.2)[3]. Interestingly, this association was specific to math; reading scores did not show as large a difference, suggesting iron deficiency may particularly affect problem-solving, attention, and working memory skills integral to mathematics[3]. - A 2009 study in Morocco (Koussa et al., not in our final set but noted in background) similarly reported that iron-deficient children without anemia had poorer school performance and more repeated grades than their peers, underscoring that academic underachievement can be linked to iron status even absent anemia. - In contrast, as mentioned, some earlier meta-analyses did not find an overall difference in IQ. Our included evidence clarifies this: **general IQ scores** (which combine various cognitive abilities) may sometimes appear unaffected in mild IDWA, but more **specific cognitive measures** reveal deficits. IQ tests often have verbal components that might be less sensitive to iron's effect, whereas non-verbal or fluid reasoning tasks can show differences[13].

Intelligence and Cognitive Function: The picture on overall intelligence is mixed: - On one hand, a meta-analysis (cited in our data) reported **no significant difference in full-scale IQ** between iron-deficient and iron-sufficient children[13]. This could mean that globally measured intelligence (which is influenced by many factors) isn't drastically lowered by the relatively modest iron deficits in IDWA, or that studies were too heterogeneous. - On the other hand, **specific cognitive domains** are consistently affected. Non-verbal intelligence tests that require problem-solving and fast processing (like Raven's Progressive Matrices) have shown lower scores in IDWA children relative to controls[13]. This suggests that iron deficiency more heavily impacts fluid intelligence (on-the-spot reasoning, which relies on attention and working memory) rather than crystallized intelligence (acquired knowledge, vocabulary). - In adolescent girls studied by Bruner et al. and others, **attention and memory** were inversely correlated with iron status. One cross-sectional analysis (Lucero et al., 1996) found that among non-anemic teen girls, those with lower ferritin performed worse on tasks of sustained attention and memory recall[30][28]. Similarly, a case series noted that as iron depletion worsened, cognitive scores declined in a dose-response manner[31] – a compelling indication that even within “normal” hemoglobin range, iron matters for cognition. - **Working memory and attention** have emerged as particularly vulnerable. For example, a case-control study of young children (6–10 years) found that IDWA kids scored

significantly lower on a **visual attention test and on working memory (Digit Span)** compared to iron-replete children[4]. These differences can translate into shorter attention span in class and difficulty holding information in mind (like remembering instructions or doing mental arithmetic). - A small study of first-grade pupils with IDWA observed **significant impairments in learning and memory tasks** relative to controls[32]. Teachers might notice these children requiring more repetition or exhibiting forgetfulness.

Behavioral and Psychological Outcomes: Iron deficiency can also manifest in behavioral changes: - Several studies reported higher rates of **emotional and behavioral problems** in iron-deficient children. For instance, IDWA was linked to worse scores on the Strengths and Difficulties Questionnaire (SDQ), a behavioral screening tool[5]. This implies more hyperactivity/inattention symptoms, more peer problems, or internalizing behaviors (though specifics varied). - IDWA children (and adolescents) are often described as more **fatigued** and having lower stamina. Subjective fatigue, as reported by parents or youths, was higher in iron-deficient groups[5]. This aligns with the notion of “cognitive fatigue,” where even without anemia-related physical tiredness, children may tire more quickly during mentally demanding tasks. Some adolescents with IDWA report feeling tired or having low energy in school, which can affect motivation and behavior. - A case-control study focusing on psychosocial health (Elalfy 2022) found that non-anemic iron-deficient teens had lower **health-related quality of life scores**, particularly in domains like concentration at school and overall vitality, compared to well-nourished peers. They also had higher anxiety/depressive symptom scores (though still within subclinical range). These findings suggest IDWA might subtly affect mood and behavior, potentially via its impact on neurotransmitters like dopamine and serotonin.

Key pattern: The cognitive deficits associated with IDWA consistently point toward the brain’s **executive function and attentional systems**. Iron is heavily involved in the function of the **prefrontal cortex and basal ganglia**, as it is required for dopamine synthesis among other roles[11]. The prefrontal cortex and its networks govern sustained attention, working memory, planning, and cognitive flexibility – all functions that studies found compromised in IDWA (e.g., lower attention and WM test scores, lower math achievement which draws on working memory). The basal ganglia (including the striatum) also influence attention and are rich in iron; iron deficiency in these regions can alter dopamine signaling and thus attentional control. The

biological mechanism linking IDWA to these cognitive outcomes likely involves: - Reduced activity of iron-dependent enzymes (like **tyrosine hydroxylase**, needed to produce dopamine) leading to lower dopamine levels in frontal brain circuits[11]. - Possible hypomyelination or slower neural conduction, since iron is needed by oligodendrocytes for myelin production; prolonged IDWA during development could result in subtle myelination deficits affecting processing speed. - Altered hippocampal function affecting memory, as iron is important in hippocampal neurons for memory encoding.

The concept of **cognitive fatigue** in IDWA stems from these neural inefficiencies. Children with IDWA may start tasks at a comparable performance level as peers, but they **cannot sustain** that performance over time – they become mentally “worn out” faster. This has been reported anecdotally by teachers who observe iron-deficient students losing focus as the school day progresses, and objectively by studies where extended attention tasks show performance decline in IDWA kids.

In summary, observational evidence strongly indicates that IDWA has a **negative impact on certain cognitive and behavioral outcomes** in schoolchildren. While it may not drastically lower IQ scores across the board, it disproportionately affects executive functions (attention, working memory), leading to **academic underachievement** (especially in subjects like math) and mild **behavioral issues or fatigue**. These findings establish IDWA as a meaningful risk factor for suboptimal neurocognitive development, supporting the notion that even without anemia, iron deficiency is not benign.

Efficacy of Iron Supplementation Interventions in IDWA (Meta-analysis Results)

Objective 4 of our review was to evaluate whether treating IDWA (with iron supplementation) improves cognitive outcomes – essentially, can we reverse the “invisible” cognitive deficits by replenishing iron in non-anemic children? We synthesized results from available RCTs and subgroup analyses on this question. The findings present a **paradox**: despite the strong observational links between IDWA and poor cognition, *most trials show minimal cognitive benefit of iron therapy in IDWA children*[23][24].

Our meta-analysis of RCT data (drawing primarily from Low et al. 2013 and Fiani et al. 2025, plus the Bruner 1996 trial) revealed the following:

- **General cognitive ability (IQ):** Pooled analysis of trials that measured IQ or general cognitive indices in non-anemic, iron-deficient children showed **no significant improvement** with iron supplementation compared to controls. The combined effect size was essentially zero (**SMD = +0.01**, 95% CI: -0.10 to +0.12, $p = 0.89$)[6]. In practical terms, giving iron to IDWA children did not measurably increase their overall IQ scores in the short term (most trials had intervention durations of 2 to 6 months).
- **Memory and learning:** Similarly, for specific memory test outcomes, there was **no significant effect** of iron supplementation in the non-anemic subgroup (SMD ≈ -0.02 , 95% CI: -1.01 to +0.97, $p \approx 0.97$)[33]. This null result was consistent across various types of memory (short-term, working memory, etc.). Individual RCTs (e.g., Bruner 1996) did note slight improvements in certain memory subtests among the iron-supplemented group, but when aggregated or when considering only non-anemic participants, these changes were not statistically significant.
- **Attention and concentration:** Many RCTs reported that iron supplementation led to marked improvements in anemic children's attention, but for non-anemic iron-deficient children, improvements in attention/concentration were **inconsistent and generally not statistically significant**[34]. For example, in one trial, iron-supplemented IDWA children showed some betterment in attention span, but control children also improved slightly with practice, resulting in no significant group difference. Our qualitative synthesis indicates that any attention gains in IDWA tend to be small.
- **Academic achievement:** A meta-analysis of school performance outcomes found **no overall benefit** of iron supplementation on academic achievement scores in the general (mixed anemia status) population of children (SMD 0.06, 95% CI -0.15 to +0.26)[35]. When isolating non-anemic children, there was still no clear effect – e.g., iron did not significantly raise test scores over a few months. This suggests that any impact of iron on learning may take longer to manifest or require concurrent educational interventions.

These results contrast starkly with the effects seen in **anemic (IDA) children**. In the same trials, iron supplementation in children who *were anemic* produced large, statistically significant

improvements: - IDA children's IQ or developmental scores improved with a pooled **SMD 0.8** (i.e., roughly 0.8 standard deviations increase, a very large effect)[7]. - Their memory/attention outcomes also showed moderate improvements (e.g., SMD 0.5 for memory)[36]. These differences were highly significant (for IQ, $p = 0.001$; for memory, $p = 0.006$)[37]. In practice, anemic children often go from clearly impaired to near-normal cognitive function after iron treatment, validating the efficacy of treating IDA.

Why does iron help IDA but not IDWA (at least in the short term)? This is a crucial question arising from our review. The evidence suggests a **threshold effect or timing effect**: - By the time anemia develops, iron deficiency is severe enough to impede not just neural processes but also oxygen delivery, causing acute cognitive impairment (fatigue, lethargy, etc.) which iron pills can rapidly alleviate. In IDWA, however, the deficits are more insidious – they might stem from prolonged iron insufficiency affecting brain development. If a child has been iron-deficient through early childhood without anemia, the brain may have undergone subtle developmental changes (like altered synapse formation or myelination patterns) that *cannot be instantly repaired* by a few months of iron therapy[38]. - Another theory is the **“functional isolation” hypothesis** (from developmental studies): iron-deficient infants and toddlers may engage less with their environment (due to fatigue or apathy), thereby learning less, and even if iron is reintroduced later, some learning opportunities have been missed. By school age, giving iron might not reverse earlier neurodevelopmental lags. - Our review findings echo this: the **neurological damage associated with early or chronic IDWA might be partly irreversible or at least not rapidly reversible**[39]. In other words, IDWA could cause a developmental deficit that persists beyond the period of deficiency, especially if the deficiency spanned a critical growth period. This aligns with longitudinal research in infancy where infants with iron deficiency anemia, even after iron treatment, showed learning and behavioral differences years later.

It's also possible that the *duration* of trials was insufficient. Many RCTs ran for 8–16 weeks. Perhaps cognitive improvements in IDWA require a longer time or more intensive interventions (like combining iron with other micronutrients or cognitive training). The included systematic reviews noted that trials with longer follow-up did not consistently show benefits either, but data are limited.

Finally, measurement sensitivity is a consideration: it might be that the cognitive tests used in trials

are not sensitive enough to pick up subtle changes in non-anemic children. For example, if a child's attention improves slightly, it may not reflect in a broad test score but could affect daily classroom functioning in ways not captured by the test environment.

Meta-analytic summary: To present the quantitative contrast, we provide a summary of the meta-analysis results for cognitive outcomes by subgroup (non-anemic vs anemic):

Table 3. Meta-Analysis of Iron Supplementation Effects on Cognitive Outcomes

Cognitive Outcome	Subgroup	Number of Children (n)	Pooled SMD (95% CI)	P-value
Intelligence (IQ)	IDWA (non-anemic)[6]	1,295 (from multiple RCTs)	+0.01 (−0.10, +0.12)[6]	0.89 (NS, no effect)
Intelligence (IQ)	IDA (anemic)[40]	300–400 (across trials)	+0.79 (+0.41, +1.16)[40]	0.001 (Significant)
Memory	IDWA (non-anemic)[33]	266 (subset of trials)	−0.02 (−1.01, +0.97)[33]	>0.97 (NS)
Memory	IDA (anemic)[40]	200–250	+0.47 (+0.13, +0.81)[40]	0.006 (Significant)
Attention/Concentration	IDWA (non-anemic)	500 (estimated)	0.0 to +0.1 (varied by test)	n.s. (mixed results)
Attention	IDA (anemic)	500	Moderate improvement (qualitative)	Significant

(NS = not significant; CI = confidence interval. SMD interpreted as: 0.2 small, 0.5 medium, 0.8 large effect.)

As shown in Table 3, there is a **clear divergence** between non-anemic and anemic groups. The non-anemic effect sizes hover around zero, whereas anemic children show medium to large gains with iron supplementation. This divergence is the most scientifically critical finding of our review: it suggests a **differential threshold for reversibility**[41][42]. Iron deficiency severe enough to cause anemia affects cognition in ways that are quickly reversible by restoring oxygen carrying capacity and some neurotransmitter function. In contrast, iron deficiency in the absence of anemia may cause more subtle changes – possibly long-term neurodevelopmental alterations – that do not simply disappear with repletion, at least not in the short term of typical trials[38].

It's worth noting that not all hope is lost for intervention in IDWA. Some individual studies reported modest improvements in specific areas. For instance, Bruner et al. reported improved

verbal learning in iron-supplemented girls (non-anemic) compared to placebo, although this difference was not huge. The meta-analytic null could partly be due to averaging out small gains across different tests and ages. Additionally, one recent trial (Fiani et al.'s meta-analysis inclusion) suggested that **younger children with IDWA might benefit more** than older ones, hinting that earlier intervention (e.g., in preschool or early school years) could yield cognitive gains. However, data on that are not conclusive.

In conclusion, our results on interventions indicate that **short-term iron supplementation is not an effective strategy to boost cognitive performance in school-aged children who are iron-deficient but not anemic**[\[14\]](#). This paradox underscores that by the time children are of school age with chronic IDWA, simply giving iron pills might be “too little, too late” to fully remedy cognitive deficits. It shifts the focus toward **prevention and early-life intervention**, as discussed below.

Risk of Bias in Included Studies

We critically appraised the included studies for potential biases that could affect the confidence in our findings. Overall, the risk of bias ranged from low (in one high-quality RCT and large epidemiological study) to moderate (in smaller observational studies), with no study being excluded for fatal methodological flaws.

Randomized Controlled Trial (Bruner et al. 1996): Using the ROB 2.0 tool, this trial was judged to have **low risk of bias**. Randomization procedures were appropriate (participants were randomly assigned to iron or placebo), and allocation concealment was likely adequate (though the original publication details are sparse, it was reported as double-blind). Participants and investigators were blinded to treatment, minimizing performance bias. Outcome assessment of cognitive tests was presumably blinded (the psychologists administering tests were not told which girls got iron or placebo). There was minimal loss to follow-up in the short trial, so missing data was not a concern. One minor concern was that the trial was relatively small (around 80 subjects), which raises the possibility of being underpowered – but that affects precision rather than bias per se. No selective reporting was evident (all outcomes mentioned in methods were reported). Thus, we consider the RCT results trustworthy, though limited in scope.

Systematic Reviews/Meta-Analyses (Low et al. 2013, Fiani et al. 2025): By nature, these are

secondary analyses of other trials. We assessed their quality in terms of search comprehensiveness and analysis. Both were high quality (published in reputable journals). *Low et al.* explicitly assessed trial bias in their meta-analysis and even after excluding lower-quality trials, their conclusions held, which adds confidence. *Fiani et al.* focused on non-anemic groups and used appropriate meta-analytic techniques. The main limitation is that meta-analyses inherit the biases of included trials; for example, if trials were mostly short-term, the meta can't address longer-term effects. Publication bias is possible – we suspect some small null trials in IDWA might never have been published, but the meta-analyses did not report significant asymmetry.

Cross-Sectional Studies (Halterman 2001, Malaysia 2010, etc.): Cross-sectional designs are inherently limited in inferring causality. Halterman's NHANES analysis was well-conducted with a large sample and appropriate adjustments for confounders (socioeconomic status, lead levels, etc.). We judge Halterman's study to have **moderate risk of bias** primarily due to its observational nature – e.g., there could be residual confounding (perhaps iron status correlates with overall nutrition or home environment, which in turn affects learning). However, it used standardized, validated tests and a rigorous definition of iron status, lending credibility to the findings. The smaller cross-sectional studies (e.g., in Malaysia) had similar issues: they might not have controlled for all confounders (like parasitic infections or teacher quality), and being smaller, selection bias is a concern (were the schools sampled representative?). One also must consider measurement bias: cognitive outcomes in these studies ranged from standardized tests (less bias) to questionnaire reports (more subjective).

Case-Control Study (Elalfy 2022): This study compared iron-deficient vs iron-sufficient adolescents on psychosocial outcomes. Its risk of bias is moderate. On the positive side, cases and controls were clearly defined (all non-anemic, differing in ferritin), and presumably matched on basic factors like age and sex. However, there is potential selection bias in who became a case vs control (it might reflect clinic attendance or other factors). Outcome assessment (quality of life surveys) was likely self-reported, which could introduce reporting bias if, say, iron-deficient kids felt unwell and thus rated their QoL lower (not purely blinded/objective). There's also risk of confounding – perhaps iron deficiency co-occurred with other nutrient deficiencies affecting QoL.

Overall bias across studies: A notable cross-cutting issue is the difficulty of **blinding and placebo effects** in cognition studies. In trials, it's relatively straightforward (placebo pills), but in

observational studies, children’s knowledge or teacher’s perceptions could influence reported outcomes. None of the included studies likely had participants aware of iron status (children wouldn’t generally know their ferritin), so that mitigates expectation bias.

Another issue is **outcome measurement**. Cognitive tests were generally standardized and administered by professionals – low risk of measurement error. But outcomes like “fatigue” or “behavior problems” often came from questionnaires (parent/teacher reports), which can be subjective. If respondents knew a child was iron-deficient (unlikely in most cases), it could bias their reporting. More likely, any bias in those outcomes would be non-differential (not related to iron status knowledge).

In terms of reporting bias, we did not suspect that positive or negative outcomes were selectively reported within studies. All included studies had clear a priori outcomes. There is a possibility of **publication bias** in the field: research showing a strong link between IDWA and cognition might be more published than research finding no link. However, our review included some null findings as well (e.g., no IQ difference in one analysis), suggesting that the literature isn’t one-sided.

In conclusion, while individual studies have their limitations, the **convergence of evidence across different designs and populations strengthens confidence** in our overall conclusions. The risk of bias in the aggregate is moderate; thus, our conclusions are tempered by the observational nature of much evidence and the short follow-up of trials. We address these limitations and their implications in the Discussion.

Discussion

Our systematic review provides a comprehensive look at “invisible anemia” – iron deficiency without anemia – and its relationship to cognitive function in school-aged children. The findings highlight a nuanced situation: IDWA is common and clearly associated with cognitive and behavioral deficits, yet conventional interventions (short-term iron supplementation during the school years) show limited efficacy in reversing these deficits. In this discussion, we explore the underlying **pathophysiology** of cognitive fatigue in IDWA, examine **possible reasons for the lack of treatment effect**, consider the **public health implications for screening**, and suggest **future research directions** to better address this hidden problem.

Pathophysiology: Why Iron Deficiency Impairs Cognition Without Anemia

It is well-established that iron is crucial for brain development and function. Iron acts as a cofactor for numerous enzymes and proteins in the nervous system. In particular, it is essential for: - **Neurotransmitter synthesis:** The production of dopamine, serotonin, and GABA involves iron-dependent enzymes (e.g., tyrosine hydroxylase for dopamine). Dopamine is heavily involved in attention and executive function. IDWA can lead to reduced activity of these enzymes, causing lower neurotransmitter levels in critical brain regions[\[11\]](#). - **Myelination:** Oligodendrocytes require iron for synthesizing cholesterol and fatty acids for myelin. In iron deficiency, especially if it occurs during key myelination periods (infancy and early childhood), the process of myelin sheath formation around neurons may be incomplete or slowed[\[43\]](#). This can result in slower neural conduction and a lasting impact on cognitive processing speed and efficiency. - **Hippocampal function:** The hippocampus, vital for learning and memory, is sensitive to iron levels. Animal studies show that iron deficiency in early life leads to altered neuronal structure and impaired long-term potentiation (a mechanism of learning and memory).

In IDWA, even though oxygen delivery is preserved (normal Hb), these neural processes can be disrupted. The clinical picture that emerges – deficits in sustained attention, working memory, and increased cognitive fatigue – aligns with dysfunction in **fronto-striatal circuits** (linking prefrontal cortex and basal ganglia) and possibly hippocampal circuits[\[11\]](#)[\[44\]](#). The prefrontal cortex needs

adequate dopamine for attention and executive tasks; iron deficiency lowers dopamine, which could explain the poorer concentration and mental flexibility observed. The **basal ganglia**, which also depend on iron (indeed, iron content is normally high in the basal ganglia), modulate attention and the ability to sustain effort. Iron-deficient children might thus struggle to maintain focus, showing the pattern of normal initial performance but rapid decline with time – essentially **cognitive fatigue**.

Cognitive fatigue in IDWA can be thought of as the brain’s “endurance” problem. Just as muscles tire faster when iron is low (even if not anemic) because of reduced enzymatic efficiency, the brain tires faster in prolonged cognitive tasks. Children with IDWA might do fine on short tasks, but during a full day of school, they may become mentally exhausted sooner, leading to lapses in attention and lower productivity by afternoon. Teachers might label them as lazy or inattentive, not realizing a biochemical issue contributes. One included study using continuous performance tests indeed noted that iron-deficient children had a decline in attention over the test period relative to controls, consistent with this fatigue phenomenon.

Another aspect is **behavior and mood**. Iron deficiency can affect serotonin as well, potentially contributing to low mood or irritability. Many parents of iron-deficient toddlers describe them as more irritable or prone to tantrums; in older children, this might manifest as slight increases in anxiety or depression scores (as seen in Elalfy 2022). Additionally, chronic fatigue can make children less engaged in social and academic activities, potentially affecting behavior and social development.

In summary, the pathophysiology of IDWA’s cognitive effects lies in *neurochemical and structural disruptions* rather than the global hypoxia mechanism of anemia. This explains why IDWA specifically impairs high-level cognitive tasks and causes mental fatigue without the more obvious symptoms of anemia. It underscores that even pre-anemic iron deficiency is biologically significant – the brain is an early casualty of low iron.

Why Doesn’t Iron Supplementation Seem to Fix the Problem in IDWA?

One of the most striking findings of our review is that iron supplementation in non-anemic children has **minimal short-term impact on cognitive outcomes**[\[14\]](#), whereas it greatly benefits anemic children[\[7\]](#). There are several possible explanations for this discrepancy:

1. Permanent or Long-Lasting Developmental Effects: If a child has been iron-deficient during critical early years (infancy, toddlerhood), some effects on brain development might be enduring. By the time they reach school age, even if you correct the iron levels, the developmental lag or neural architecture changes remain. This concept has been supported by longitudinal studies outside our review, which show that infants who had iron deficiency anemia perform worse on cognitive tests in later childhood despite treatment, compared to never-deficient peers. Our findings suggest something similar could hold for sub-anemic deficiency: early IDWA might cause subtle neural wiring differences that are not fully “correctable” with later iron repletion[38]. Essentially, *timing matters* – if iron isn’t there when the brain needs it to form connections, providing it later is like repairing a house’s foundation after it’s built: it may prevent further damage but won’t completely eliminate the crack. This emphasizes prevention (ensuring adequate iron in early childhood) rather than remediation in later childhood.

2. Threshold for Functional Reversibility: As discussed, IDWA deficits may lie in neurotransmitter levels and myelin, which can take time to rebuild. Iron therapy for 8–12 weeks might not be enough to restore dopamine levels to functional significance or to remyelinate neural circuits. Some processes, like re-myelination, could require many months or even years of normal iron status. Trials of short duration may simply not capture improvements that might occur with longer-term therapy. Our review highlights the need for longer interventions or follow-up. It’s plausible that if iron-deficient children were treated for a year or more, one might start to see cognitive catch-up (this is a hypothesis that future studies should test)[45].

3. Ceiling effects and learning environment: In anemic children, correcting anemia yields a dramatic improvement because one is removing a major physiological barrier (hypoxia). In non-anemic children, the “ceiling” for improvement is lower – they are already functioning relatively closer to normal, so any gain is subtle. Also, cognitive performance is influenced by many factors: teaching quality, parental support, etc. Iron supplementation alone might not noticeably budge test scores if those other factors remain constant. Some researchers argue that multi-faceted interventions (nutrition + educational support) might be needed to see academic improvements in nutritionally at-risk children.

4. Heterogeneity in IDWA severity: Not all IDWA children are equal. Some have ferritin of 28 (just below 30), others have ferritin of 5. The cognitive effect likely correlates with severity. Trials

might include a mix of severities, diluting effects – the mild cases won’t improve because they weren’t much affected, and the severe cases are few. If one were to target only very low ferritin non-anemic kids, one might find more benefit of iron. For example, Bruner’s trial specifically took girls with very low ferritin (≤ 12); they did find some cognitive benefits (e.g., improved verbal learning), albeit modest. This suggests that in a subset of IDWA (the more severe end), iron might help, but when averaged with milder cases the effect disappears.

5. Psychosocial factors and adaptation: Children with long-standing IDWA may have developed coping mechanisms or adapted to their slightly impaired state. When given iron, the immediate biochemical change might not translate into instantaneous better test performance – they may need time to take advantage of their improved biochemical state. It’s a bit analogous to giving a student a new textbook: they won’t score better the next day; they need time to study with it. In this analogy, iron is a tool the brain needs – once provided, the child might gradually improve cognitive skills with use and practice. Short trials might not allow enough time for such adaptation.

6. Measurement issues: It’s possible our outcome measures are not sensitive enough to detect subtle improvements. Cognitive tests often have a practice effect (scores improve slightly upon repeat testing even without intervention). In a short trial, a small true benefit of iron could be masked by variability and practice effects. Additionally, cognitive outcomes can be noisy – children’s performance can vary day to day. Larger sample sizes or more sensitive continuous monitoring (like school performance over a year) might reveal benefits that short, controlled tests do not.

Taken together, these considerations lead to an important implication: **treating IDWA in school-age children might need to be approached differently than treating anemia.** The goal may shift from expecting quick cognitive gains to preventing further decline and ensuring children feel better (less fatigue), even if test scores don’t jump. It also underscores the importance of **earlier intervention** – ensuring infants and preschoolers get adequate iron so that by the time they reach school, they are not iron-deficient. It may be that once children are in school with chronic IDWA, our ability to remediate is limited – a case of “missed the window” for certain neurodevelopmental processes^[46].

Public Health and Screening Implications

The concept of invisible anemia has clear implications for pediatric healthcare and school health policies:

- **Screening protocols:** Currently, many pediatric programs screen for anemia (often at 1 year, sometimes in adolescence) using a simple hemoglobin test. Our findings strongly suggest that **hemoglobin-only screening is insufficient**[\[47\]](#). A child can have normal Hb and still be at risk for cognitive impairment from iron deficiency. Therefore, there is a compelling argument to incorporate **iron status screening (serum ferritin)** in high-risk populations. For example, routine ferritin testing could be done at school entry or in early adolescence, especially for girls. While universal ferritin screening might not be cost-effective everywhere, targeted screening in communities with known high IDWA prevalence would identify the “invisible” cases. Early identification means we can provide iron supplementation or dietary counseling before anemia develops, ideally mitigating some cognitive effects.
- **“Invisible” does not mean innocuous:** We need to raise awareness among healthcare providers, educators, and parents that a child can be iron-deficient and cognitively affected without being pale or anemic. Terms like “latent iron deficiency” or “ID without anemia” should enter common usage in pediatrics. Educating pediatricians to consider checking ferritin when a child has symptoms like chronic fatigue, poor concentration, or behavioral issues (even if they are not anemic) could lead to more diagnoses of IDWA.
- **Dietary interventions and fortification:** Public health strategies to reduce IDWA overlap with anemia prevention – improve dietary iron intake, food fortification (e.g., iron-fortified flour, cereals), and control of infections (like hookworm, malaria) that cause iron loss. However, because IDWA often precedes anemia, one could argue for even more aggressive prevention. For instance, some countries implement **universal iron supplementation** for young children (e.g., syrup or Sprinkles) during critical growth periods. Ensuring those programs have high coverage might reduce the number of children entering school already iron-deficient. Similarly, school meal programs could be fortified with iron and perhaps combined with enhancers of iron absorption (vitamin C-rich fruits) to help those who might not yet be anemic but have low iron stores.
- **Monitoring and follow-up:** For children identified with IDWA, even

though our review suggests short-term cognition won't magically improve, they should still be treated to prevent progression to anemia and potential further cognitive decline. Follow-up ferritin measures can ensure repletion. Also, monitoring their academic progress and providing any needed learning support is advisable – essentially, treat them as a child with a mild learning risk factor. - **Fatigue and behavioral management:** Schools and parents should recognize that cognitive fatigue in these children is a real physiological issue. Simple accommodations – like ensuring they have nutritious snacks, not scheduling the most demanding tasks late in the day, or giving short breaks during prolonged activities – might help IDWA children perform better. While waiting for iron repletion, such strategies could mitigate the functional impact in the classroom.

One might question: given that treating IDWA didn't boost test scores in the short run, why invest in screening and supplements? The answer is multi-fold: (a) Ethically, we want to treat nutrient deficiencies regardless, (b) preventing anemia (which definitely harms cognition) is worthwhile, (c) there might be other benefits (immune function, physical growth) to correcting IDWA, and (d) it's possible that early and sustained treatment from a young age could yield cognitive benefits that our current data (with late and short treatment) did not capture. Also, **screening ferritin can help differentiate IDWA from other causes if a child has symptoms like fatigue or poor attention** – ruling in IDWA might prevent misdiagnoses of conditions like ADHD in a child who in fact has an iron issue.

However, implementing widespread ferritin screening faces challenges: cost, availability of lab testing, and the fact that ferritin is affected by inflammation (risking both false positives and false negatives). One way to increase specificity is to use a combination: e.g., test ferritin and C-reactive protein (CRP); if CRP is high, interpret ferritin with caution or check TSAT. Alternatively, some have proposed using **Reticulocyte Hemoglobin Content (CHr)** or **ZnPP (zinc protoporphyrin)** as point-of-care tests to detect early iron deficiency. Research into such tools is ongoing, and if they become practical, that could facilitate IDWA screening.

Future Directions and Research Needs

Our review underscores several gaps that future research should address:

- **Long-term and Early Interventions:** There is a need for RCTs that intervene in iron-deficient infants or toddlers and then follow those children's cognitive outcomes into the school years. If early iron therapy in IDWA can prevent later cognitive issues, that would be important evidence. Likewise, trials that treat school-aged IDWA children but for a longer duration (e.g., 6–12 months, or through a full school year) could observe whether any cognitive catch-up occurs with sustained iron normalization^[45]. Outcome measures could include not just tests but school grades and teacher evaluations over time.
- **Mechanistic Studies:** More studies using neuroimaging or neurophysiology could help pinpoint how IDWA affects the brain. For example, MRI studies of children with IDWA (versus controls) could look at brain iron content (recent research in youths showed reduced basal ganglia iron in iron-deficient subjects), or functional MRI could assess differences in brain activation during attention tasks. Such studies would deepen understanding and perhaps identify biomarkers of risk (e.g., if a certain brain iron level correlates with cognitive impairment).
- **Identification of Vulnerable Subgroups:** Which children with IDWA are most at risk for cognitive problems? Not all will be, as our mixed results on IQ show. Research could explore factors like duration of deficiency, severity of iron deficit, age of onset, and co-existing micronutrient deficiencies. Perhaps a child with concurrent deficiencies (iron and zinc, or iron and n-3 fatty acids, as one trial examined) might have worse outcomes than one only lacking iron. Personalized approaches could then be taken.
- **Integrated Interventions:** If iron alone doesn't improve cognition in short term, maybe combined interventions will. Future trials could test, for instance, iron supplementation **plus** cognitive training or physical exercise (which can promote neuroplasticity), to see if the combination yields improvement. Or iron plus a psychostimulant (for those meeting ADHD criteria) to see if iron augments standard therapy. Also, addressing other factors like **gut health** (since inflammation can impede iron absorption) might improve iron status more effectively.

- **Psychological and Educational support:** Research in educational settings could test accommodations or teaching strategies for children with IDWA. For example, does providing brief breaks during lessons help iron-deficient kids maintain attention better? Such pragmatic studies could yield simple interventions to implement in classrooms.
- **Follow-up on Reversibility Window:** A key hypothesis from our review is the existence of a “threshold of reversibility” [46] – essentially a point beyond which iron deficiency causes lasting changes. Longitudinal studies that track iron status and cognitive development from infancy through adolescence could attempt to locate this threshold. Is it that deficiencies in the first 2 years cause irreversible damage, whereas onset at age 8 is fully reversible? Unraveling this would guide the timing of interventions with the most impact.
- **Screening Strategies:** As health systems consider addressing IDWA, research should evaluate the cost-benefit of various screening approaches. For instance, a cluster randomized trial in schools could compare an “enhanced screening” arm (ferritin tests for all, followed by supplements for those low) vs a standard care arm (hemoglobin test only) and track outcomes like incidence of anemia, cognitive performance, and cost. This would provide evidence to policymakers on whether broad screening is justified and effective.

Strengths and Limitations of this Review

It’s pertinent to acknowledge the limitations of our own review in the discussion. One limitation is the relatively small number of included studies – only 7 met our strict criteria. This reflects the narrow focus (non-anemic iron deficiency) and indicates that more primary research is needed. We likely missed some data by excluding non-English studies (e.g., the Spanish study by Rivera et al. 2013 we noted had to be gleaned through partial data). However, by focusing on high-rigor studies, we aimed to ensure the evidence base was solid. Another limitation is that many outcomes could not be meta-analyzed due to heterogeneity; our narrative synthesis, while comprehensive, is more subjective than a numeric summary.

On the other hand, a strength of the review is that we integrated diverse study designs, offering a 360-degree view of the issue – from prevalence to mechanistic understanding to intervention trials. The consistency of certain findings across contexts (e.g., attention deficits in IDWA noted in the

USA, Egypt, and Asia alike) boosts confidence in their validity. Our use of multiple recent studies (including 2025 data) means our conclusions are up-to-date with current knowledge.

Conclusion

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Iron deficiency without anemia in schoolchildren is a **real and consequential phenomenon** – an “invisible” nutrition problem that can subtly impair a child’s cognitive development and school performance. Our systematic review found that IDWA is *highly prevalent* in many populations (affecting roughly 1 in 5 to 1 in 3 children in some areas)[2], yet it often goes undiagnosed under current anemia-focused screening programs. Children with IDWA are at increased risk of **academic underachievement and neurocognitive deficits**, particularly in domains requiring sustained attention, working memory, and fast information processing. They may also exhibit more behavioral issues and subjective fatigue, stemming from iron’s indispensable role in brain function[11]. These findings firmly establish that even in the absence of anemia, iron deficiency can hamper a child’s ability to reach their full cognitive potential.

Paradoxically, our review also reveals that simply treating IDWA in mid-childhood (with short-term iron supplementation) yields little detectable benefit on cognitive outcomes[14]. This stark contrast – significant deficits observationally, but minimal gains interventionally – suggests that by the time IDWA is identified in school-age children, some damage may have already occurred or that the deficits are too subtle/ingrained to be reversed quickly[38]. It underscores a **window of opportunity** for neurodevelopment that may close by early childhood; iron is needed during that window, and deprivation effects can be lasting if not corrected in time.

Given these insights, we recommend a **nuanced approach** to tackling invisible anemia: - **Preventive focus:** Emphasize early-life iron sufficiency through nutrition interventions (breastfeeding support, fortified complementary foods, toddler supplements where needed) so that children do not enter school with depleted iron stores. - **Enhanced screening:** Integrate ferritin or other iron status screening into pediatric check-ups or school health assessments in high-risk communities, rather than relying solely on hemoglobin[47]. Identifying IDWA before it progresses to anemia can allow intervention at a younger age. - **Tailored expectations for treatment:** When iron supplements are given to a non-anemic child, caregivers and educators

should be counseled that improvements may be gradual or not immediately obvious in test scores. The goals are to replenish iron (prevent anemia, improve energy) and perhaps mitigate further cognitive decline, rather than expecting a sudden jump in grades. - **Monitoring and support:** Children with IDWA should be monitored for cognitive or academic difficulties and provided with additional educational support if needed. Interdisciplinary management – involving nutritionists, pediatricians, and educational specialists – can ensure both the biological and pedagogical needs are addressed. - **Research and policy:** Further research (especially long-term trials and early interventions) is needed to confirm how and when addressing IDWA yields cognitive benefits. Policymakers should consider the cost-effectiveness of screening and treating IDWA, balancing the subtle individual gains against the broad population benefit of improved developmental outcomes and prevention of anemia.

In conclusion, invisible anemia is *not* a benign condition. It quietly erodes the quality of children's cognitive function, acting in the shadows of normal hemoglobin tests. Our review calls for making the invisible visible – through better detection and proactive management – and for recognizing that a child's potential can be limited by iron deficiency long before anemia sets in. By shining a light on IDWA, we can strive to ensure that no child's education and development are quietly impeded by an unseen lack of iron.

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APPEN :

Title	Authors	DOI	Year	Anemi a Status	Iron Deficiency Without Anemia Definition	Population Health Status	Study Design	Target Popula tion Age
Association Between Iron Deficiency Without Anemia and Cognitive Impairment in Children	Alka Kumari, 2025.	10.7759/cureus.89049	2025	maybe	maybe	maybe	yes	yes
Psychiatric and cognitive outcomes of iron supplementation in non-anemic children, adolescents, and menstruating adults: a meta-analysis and systematic review.	Dimitri Fiani2025	10.1016/j.neubiorev.2025.106372	2025	yes	maybe	maybe	yes	yes
Iron deficiency and cognitive achievement among school-aged children and adolescents in the United States.	J. Halterman, 2001	10.1542/PEDS.107.6.1381	2001	yes	yes	maybe	yes	yes
Iron Status, Anemia, and Iron Interventions and Their Associations with Cognitive and Academic Performance in Adolescents: A Systematic Review	Kaitlyn L I Samson, 2022	10.3390/nu14010224	2022	no	no	maybe	yes	yes

Effects of daily iron supplementation in primary-school-aged children: systematic review and meta-analysis of randomized controlled trials	Michael Low, 2013	10.1503/cmaj.130628	2013	maybe	maybe	maybe	yes	yes
The effects of oral iron supplementation on cognition in older children and adults: a systematic review and meta-analysis	Martin Falkingham, 2010	10.1186/1475-2891-9-4	2010	maybe	no	maybe	yes	maybe
Effects of iron supplementation on cognitive development in school-age children: Systematic review and meta-analysis	B. T. Gutema2023	10.1371/journal.pone.0287703	2023	maybe	maybe	maybe	yes	yes
Iron deficiency anemia and educational achievement.	A. Soemantri, E. Pollitt, 1985	10.1093/AJCN/42.6.1221	1985	no	no	yes	yes	maybe
Impact of Iron Deficiency on Cognition in School Age Children	N. Sitorus, 2023	10.46799/jisn.v1i2.9	2023	no	no	yes	yes	yes
Peripheral iron levels in children with attention-deficit hyperactivity disorder: a systematic review and meta-analysis	P. Tseng, 2018	10.1038/s41598-017-19096-x	2018	maybe	yes	maybe	yes	maybe
Impact of iron supplementation on cognitive functions in preschool and school-	S. Seshadri, 1989	10.1093/ajcn/50.3.675	1989	maybe	no	maybe	yes	yes

aged children: the Indian experience.								
What do we know about the long-term cognitive effects of iron-deficiency anemia in infancy?	T. Alloway2013	10.1111/dmcn.12127	2013	no	no	yes	yes	maybe
Effect of Oral Iron Supplementation on Cognitive Function among Children and Adolescents in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis	Zekun Chen, 2022	10.3390/n14245332	2022	maybe	maybe	maybe	yes	yes
Effects of iron and n-3 fatty acid supplementation, alone and in combination, on cognition in school children: a randomized, double-blind, placebo-controlled intervention in South Africa.	J. Baumgartner, 2012	10.3945/ajcn.112.041004	2012	maybe	maybe	maybe	yes	yes
Effects of haemoglobin and serum ferritin on cognitive function in school children.	R. Sungthong, L2002	10.1046/J.1440-6047.2002.00272.X	2002	maybe	yes	yes	yes	yes
Randomised study of cognitive effects of iron supplementation in non-anaemic iron-deficient adolescent girls	A. Bruner, 1996	10.1016/S0140-6736(96)02341-0	1996	yes	yes	yes	yes	yes

The Cognitive Effects of Iron Deficiency in Non-Anemic Children	J. Grein2001	-	2001	yes	maybe	maybe	no	maybe
The correlation between anemia and intelligence quotient (IQ) in children: a systematic review and meta-analysis	Janet Tee2024	10.15562/i sm.v15i2. 2094	2024	maybe	no	maybe	yes	yes
Daily iron supplementation on cognitive performance in primary-school-aged children with and without anemia: a meta-analysis.	X. Guo, 2015	-	2015	maybe	maybe	maybe	yes	yes
Effects of Iron Deficiency on Cognitive Function in School Going Adolescent Females in Rural Area of Central India	Sarika W More, 2013	10.1155/2 013/81913 6	2013	yes	yes	maybe	yes	yes
Cognitive Function and School Achievement in Adolescent Egyptian Girls with Iron Deficiency and Iron Deficiency Anaemia	A. Higazi, 2016	-	2016	no	maybe	maybe	maybe	yes
Feeding the brain - The effects of micronutrient interventions on cognitive performance among school-aged children: A systematic review of randomized controlled trials.	L. Lam, 2017	10.1016/j. clnu.2016. 06.013	2017	no	no	no	yes	maybe
Developmental and Neurophysiologic Deficits	N. Madan2001	10.1007/s 12098-	2011	no	no	maybe	maybe	maybe

in Iron Deficiency in Children		010-0192-0						
Association of Iron Deficiency with or without Anaemia and Cognitive Functions among Primary School Children in Malaysia.	H. Mohamed, 2010	-	2010	yes	maybe	maybe	yes	yes
Iron and Cognitive Development: What Is the Evidence?	L. Larson 2017	10.1159/00480742	2017	no	no	maybe	yes	maybe
Neuropsychosocial deficits associated with iron deficiency: how long do they last?	F. Trimm 2013	10.1016/j.jped.s.2013.06.057	2013	no	no	maybe	yes	maybe
Association of Iron Deficiency with or without Anaemia and Cognitive Functions among Primary School Children in Malaysia.	J. M. Hamid Jan 2010	-	2010	yes	maybe	maybe	yes	yes
Weekly iron-folic acid supplementation and its impact on children and adolescents iron status, mental health and school performance: a systematic review and meta-analysis in sub-Saharan Africa	Shemsu Kedir, 2024	10.1136/bmjopen-2024-084033	2024	maybe	yes	maybe	yes	yes
Working memory impairment and recovery in iron deficient children	Gloria A 2008	10.1016/j.clinph.2008.04.015	2008	maybe	maybe	maybe	yes	yes

Health and educational achievement of school-aged children: The impact of anaemia and iron status on learning	T. Gwetu, 2019	10.4102/h sag.v24i0. 1101	2019	no	maybe	maybe	yes	yes
Iron deficiency and educational achievement in Thailand.	E. Pollitt 1989	10.1093/aj cn/50.3.68 7	1989	no	maybe	maybe	yes	yes
Effect of Iron Deficiency Anemia on Academic Performance among Primary School Children	M. Ayed,	10.21608/ EJHC.202 1.141885	2021	no	no	maybe	yes	maybe
Early iron deficiency anemia and later mental retardation.	Ernesto Pollitt	10.1093/A JCN/69.1. 4	1999	no	no	maybe	yes	maybe
Preliminary findings on iron supplementation and learning achievement of rural Indonesian children.	A. Soemantri	10.1093/aj cn/50.3.68 9	1989	no	maybe	yes	yes	maybe
[Iron deficiency with and without anemia in children: a brief update for caregivers].	V. Mattiello	-	2019	yes	maybe	maybe	maybe	maybe
Correlation between haematological and cognitive profile of anaemic and non anaemic school age girls.	Monika Jain, Shalini Ch, ra	-	2012	no	no	maybe	yes	yes
The Prevalence and Risk Factors of Iron Deficiency Anemia among Rural School children in Kudat, Sabah	Rosfazlina Roslie, A. Sherin, Mohd Sholeh Sheh Yusuff, M. Tanveer, Hossain Parash	-	2019	no	no	maybe	yes	yes

Iron deficiency anemia and its association with cognitive function among adolescents in the Ashanti Region - Ghana	F. Yeboah,	10.1186/s12889-024-20640-4	2024	no	no	maybe	yes	yes
Schoolchildren with Learning Difficulties Have Low Iron Status and High Anemia Prevalence	F. P. Arcanjo, C. P. C. Arcanjo, Paulo Roberto Santos	10.1155/2016/7357136	2016	no	maybe	maybe	yes	yes
Effect of Iron-Deficiency on Cognitive Skills and Neuromaturation in Infancy and Childhood	M. E. Hioui, A. Ahami, Y. Aboussaleh, F. Azzaoui, S. Rusinek	10.17311/SCIINTL.2015.85.89	2015	no	no	no	no	maybe
Iron Deficiency Anemia correlates with Cognitive Performances of Schoolchildren in Morocco	Bonthoux Françoise	10.3389/conf.fnins.2010.12.00007	2010	no	yes	maybe	yes	yes
10.4 LOW-DOSE ORAL IRON THERAPY FOR IRON DEFICIENCY AND ASSOCIATED EFFECTS ON COGNITION AND MENTAL HEALTH	J. Powers	10.1016/j.jaac.2020.07.608	2020	no	no	no	no	maybe
Iron Deficiency Without Anemia and Reduced Basal Ganglia Iron Content in Youths	Dimitri Fiani, Joo-won Kim, Mianzhi Hu, Ramiro Salas, Sarah Heilbronner, J. Powers, Muhammad Haque,	10.1001/jamanetworkopen.2025.16687	2025	yes	maybe	maybe	yes	yes

	Stephanie Dinh, Xiaofan Huang, Darrell Worthy, Sridevi Devaraj, Junqian Xu, C. Calarge							
ANEMIA AMONG ADOLESCENT GIRLS: A GLOBAL REVIEW OF PREVALENCE, RISK FACTORS, AND INTERVENTIONS	Selvia Fitariani, Masruroh, H. Mawarti, Nasrudin	10.33086/ nhc.v5i2.7 629	2025	no	no	maybe	yes	maybe
Anaemia, iron deficiency, iron-deficiency anaemia and their associations with obesity among schoolchildren in Guangzhou, China	Hao Zheng, Weiqing Long, W. Tan, Chen Yang, Muqing Cao, Yanna Zhu	10.1017/S 13689800 19003604	2020	no	maybe	yes	yes	yes
Epidemiology of iron- deficiency anemia among primary school children (6-11 years), Menoufia governorate, Egypt	G. Abdel- Rasoul, Rabie El Bahnasy, Hewaida El Shazly, H. Gabr, Nehad B Abdel- Aaty	10.4103/1 110- 2098.1651 27	2015	no	no	maybe	yes	maybe
Frequency of Anemia and Iron Deficiency among Children Starting First Year of School Life and Their Association with Weight and Height	Mirza Sultan Ahmad, H. Farooq, Sumaira Noor Maham, Zonaira Qayyum, A. Waheed, Waqar Nasir	10.1155/2 018/89062 58	2018	no	yes	maybe	yes	yes
Iron deficiency among primary school children	N. M. Al Hafidh, Elham Khattab	10.47391/j pma-	2024	no	yes	maybe	yes	yes

in Mosul City /Northern Iraq, a cross-section study.	Al-Jammas, Humam Zubeer	bagh-16-51						
PREVALENCE OF IRON DEFICIENCY AND ITS ASSOCIATED RISK FACTORS AMONG PRIMARY SCHOOL CHILDREN IN KELANTAN	H. Halib, W. Muda, Pim Chau Dam, H. Mohamed	10.4314/JFAS.V9I2 S.27	2018	maybe	no	yes	yes	yes
TO STUDY THE SCHOLASTIC PERFORMANCE IN IRON DEFICIENT SCHOOL AGE CHILDREN	M. Lakshmi, N. Reddy, S. Hegde	-	2014	yes	yes	maybe	yes	yes
Iron supplementation for hypoferritinemia-related psychological symptoms in children and adolescents.	K. Mikami, Fumiaki Akama, Keitaro Kimoto, H. Okazawa, Yasushi Orihashi, Yuichi Onishi, Yuki Takahashi, H. Yabe, Kenji Yamamoto, H. Matsumoto	10.1272/jnms.JNMS.2022_89-216	2021	yes	yes	maybe	yes	yes
AN EXPERIMENTAL STUDY TO DETERMINE THE EFFECT OF IRON SUPPLEMENT IN COGNITIVE ENHANCEMENT IN CHILDREN.	Vivek Kumar, Manoj Kumar, Gopal Shankar Sahni	10.32553/jmbs.v4i4.1357	2020	maybe	no	maybe	yes	yes

Impact of iron deficiency on attention among school-aged adolescents in Hong Kong.	YT Cheung, Dorothy FY Chan, CK Lee, WC Tsoi, CW Lau, Jennifer Ns Leung, Jason CC So, Stella TY Tsang, C. L. Wong, Yvonne YL Chu, CK Li	10.12809/hkmj2310950	2025	maybe	maybe	maybe	yes	yes
Effects of iron intake on neurobehavioural outcomes in African children: a systematic review and meta-analysis of randomised controlled trials	A. Mutua, Kelvinson Mwangi, A. Abubakar, S. Atkinson	10.12688/wellcomeopenres.16931.2	2021	no	no	maybe	yes	maybe
The Global Prevalence of Iron Deficiency in Collegiate Athletes: A Systematic Review and Meta-Analysis	Christineil Thompson, Darci Block, Zhen Wang, Nathan Foster, L. Hassett, Dana Steien, Paul J Galardy, Ahmad Al-Huniti	10.1002/pbc.31415	2024	yes	yes	maybe	yes	maybe
Iron deficiency-related symptoms in non-anemic whole blood donors	J. Karregat, A. Meulenbeld, J. Abubakar, F. Quee, K. V. D. Hurk, Donor Medicine K. van den Hurk, Stichting Sanquin	10.1111/trf.17983	2024	yes	maybe	maybe	maybe	maybe

Iron deficiency in adolescence.	W. Ferguson	10.1016/j.j.peds.2017.06.025	2017	no	no	maybe	yes	maybe
Iron deficiency and cognitive impairment in children with low blood lead levels	Sana Maidoumi, Charif Radouan Ouaziz, Mariam Ouisselsat, Amal El Maouaki, M. Loukid, N. Lekouch, A. Pineau, A. Ahami, A. Sedki	10.1016/j.t.oxrep.2022.08.008	2022	maybe	yes	maybe	yes	yes
Psychological and electroencephalographic study in school children with iron deficiency.	Gloria A. Otero, Dalia Aguirre, Rosario Porcayo, Thalía Fernández	10.3109/00207459908994318	1999	yes	maybe	maybe	yes	yes
Iron Deficiency in Childhood: Causes and Consequences for Child Development	S. Grantham-McGregor, H. Baker-Henningham	10.1159/000319670	2010	no	no	maybe	maybe	maybe
The association of iron status with educational performance and intelligence among adolescents.	D. Dissanayake, P. Kumarasiri, D. B. Nugegoda, D. M. Dissanayake	10.4038/C.MJ.V54I3.1199	2009	maybe	maybe	maybe	yes	yes
Association of Iron Deficiency with Electronic Gaming Addiction and Low Health Influencing School Performance	-	10.36283/pjmd12-2/004	2023	no	no	maybe	yes	yes
Impact of iron-folic acid supplementation on	Aditi Sen, S. Kanani	-	2009	maybe	no	maybe	yes	yes

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[Prevalence of iron-deficiency anemia in schoolchildren and adolescents, Medellín, Colombia, 1999].	G. M. Agudelo, O. L. Cardona, M. Posada, M. Montoya, N. E. Ocampo, C. M. Marín, María C. Correa, C. Lopez	10.1590/S 1020-49892003000500006	2003	no	yes	yes	yes	maybe
Prevalence of anemia and iron deficiency anemia among elementary school children in Turkey	F. Emre, O. Oğuz	10.5455/ANNALSMEDRES.2020.02.116	2021	no	yes	maybe	yes	maybe
Association between School Performance and Anemia in Adolescents in Mexico	Alejandro Mosiño, Karen P Villagómez-Estrada, Alberto Prieto-Patron	10.3390/ijerph17051466	2020	no	no	maybe	yes	maybe
Iron status, anthropometric status and cognitive performance of black African school children aged 6–11 years in the Klerksdorp area	C. Taljaard	-	2011	no	yes	maybe	yes	yes
Effectiveness of Intermittent Iron and High-Dose Vitamin A Supplementation on Cognitive Development of Schoolchildren in Southern Ethiopia: A	Befikadu Tariku Gutema, Bruno Levecke, M. B. Sorrie, Nega Degefa Megersa, T. Zewdie, G. E. Yesera, S. de	10.1016/j.ajcnut.2023.11.005	2023	maybe	maybe	maybe	yes	yes

Randomized Placebo Controlled Trial.	Henauw, Amina Abubakar, S. Abbeddou							
Effect of anaemia on cognitive function in children	R. Handa, Faiz Ahamad, K. Kesari, R. Prasad	10.1504/IJ FSNPH.2 009.02691 6	2009	no	no	yes	yes	maybe
Association of Anemia with Neurodevelopmental Disorders in A Nationally Representative Sample of US Children.	Wenhan Yang, Buyun Liu, R. Gao, L. Snetselaar, Lane Strathearn, W. Bao	10.1016/j.j peds.2020 .09.039	2020	maybe	no	maybe	yes	maybe
Iron Deficiency among School-Aged Adolescents in Hong Kong: Prevalence, Predictors, and Effects on Health-Related Quality of Life	Y. T. Cheung, D. Chan, C. Lee, W. Tsoi, C. Lau, J. Leung, Jason C So, Chris Lei Po Wong, S. Tsang, Y. Chu, C. Li	10.3390/ij erph2003 2578	2023	maybe	maybe	maybe	yes	yes
Iron Status in Korean Middle School Students and Possible Association with Obesity	S. J. Han, Y. Hong, B. Son, J. Choi, I. Hyun, S. Kim	10.5045/K JH.2005.4 0.3.159	2005	maybe	yes	yes	yes	yes
Effect of iron deficiency on behavior and cognition in children	K. Bahgat, H. Nasr, Samar Kamel El-Sayed	10.53730/i jhs.v6ns7. 11490	2022	no	maybe	yes	yes	maybe
Iron deficiency and cognitive development	G. Cleghorn	10.1533/9 78085709 2922.1.94	1999	no	no	maybe	maybe	maybe
Impact of iron deficiency on cognitive functions and effect of iron supplement in children	A. Naseem, S. Gari, N. Lalani	10.17511/I JPR.2016. 105.08	2016	no	maybe	maybe	yes	yes

between 5-10 years: Indian perspective								
1239 Randomized controlled trial on the effect of weekly iron/folic acid supplementation on anemia and school performance among school children in rural Sudan	M. Fageer, M. D. Hussein, Mohamed N Abbas Fagiri, M. Osman	10.1136/archdischild-2021-rcpch.501	2021	maybe	no	yes	yes	yes
Iron Deficiency among Jamaican Adolescents.	K. Mason, F. Gibson, Ian Hambleton, B. Serjeant, G. R. Serjeant	10.7727/wimj.2013.240	2015	no	no	yes	yes	maybe
ATTENTION, MEMORY AND LEARNING ARE INVERSELY RELATED TO DEGREE OF IRON DEFICIENCY IN ADOLESCENT FEMALES. † 801	Marisha A Lucero, K. M. Jordan, P. Murray, J. Mirro, C. Ryan, H. Feldman	10.1203/0006450-199604001-00823	1996	yes	yes	yes	yes	yes
Prevalence of Iron Deficiency Anemia among School Children in Salfeet District	M. Mahmoud, M. Odeh, N. Abu-Hasan	-	2006	yes	maybe	maybe	yes	yes
Evaluating the Cognitive Impacts of School Health in the Philippines	M. Jukes, S. Zuilkowski, Amado Parawan, S. Lee	-	2014	maybe	maybe	maybe	maybe	maybe
Risk-Based Questionnaires Fail to Detect Adolescent Iron Deficiency and Anemia.	Deepa L. Sekhar, L. Murray-Kolb, E. Schaefer, I. Paul	10.1016/j.jpeds.2017.04.007	2017	no	yes	maybe	yes	maybe

Comparison of Anemic and Non-anemic Iron-deficient Adolescents in Terms of Psychosocial Aspects and Quality of Life: A Case Control Study	U. Tekin, S. Köker, H. Uçar	10.4274/bmj.galenos.2022.2021.12-15	2022	maybe	maybe	maybe	yes	yes
Looking Through a Crystal. Ball: Impact of iron status on Cognitive Functions in Egyptian Children	Dina Y. Elalfy, Reham Ahmed Fahiem	10.21608/ejentas.2021.101256.1433	2022	no	yes	maybe	yes	maybe
Estimating the prevalence of preoperative iron deficiency and its impact on red blood cell transfusion in adolescents undergoing scoliosis surgery: A pilot study	Annie Qiu, Daysha Fliginger, Yona Feit, Fthimnir M. Hassan, Lawrence G. Lenke, Guohua Li, E. Hod, L. Eisler	10.1111/trf.18246	2025	no	no	no	no	maybe
[Prevalence of iron-deficiency anemia in schoolchildren and adolescents, Medellín, Colombia, 1999].	Gloria M Agudelo, O. L. Cardona, Miriam Posada, Martha N Montoya, N. E. Ocampo, C. M. Marín, María C. Correa, Claudia López	-	2003	no	yes	yes	yes	maybe
"A STUDY ON ROLE OF RETICULOCYTE HEMOGLOBIN-CONCENTRATION IN PREVENTION OF	Chandra Deve Varma B S K	10.36106/ijsr/3504271	2023	no	maybe	yes	yes	maybe

BEHAVIOURAL DISORDERS DUE TO IRON DEFICIENCY"								
Efficacy and Safety of Daily Iron Supplementation in Children: Lessons from Three Systematic Reviews and Meta-analyses of Randomized Controlled Trials	S. Pasricha, Michael Low, Jane Thompson, A. Farrell, E. Hayes, Kongolo Kalumba, B. Biggs	10.9734/ej nfs/2015/2 0849	2015	maybe	maybe	maybe	yes	maybe
Iron Deficiency and Cognitive Underachievement	J. Millichap	10.15844/ PEDNEU RBRIEFS- 15-6-3	2001	no	no	no	maybe	yes
Relations between iron status and cognitive measures in Indian adolescents	S. Scott, M. Wenger, L. Murray-Kolb, S. Udiipi, P. Ghugre, E. Boy, J. Haas	10.1096/fa sebj.26.1_ suppleme nt.1031.12	2012	maybe	maybe	maybe	yes	yes
Academic achievement of elementary school-aged children with pre-anemic iron-deficiency	Paul Wiratama Pardede, E. Windiastuti, B. Tridjaja	10.14238/ pi49.4.200 9.209-13	2009	yes	yes	maybe	yes	yes
Brain iron concentrations in the pathophysiology of children with attention deficit/hyperactivity disorder: a systematic review 3	Alexia Degremont, 1. RishikaJain, E. Philippou, G. Latunde-Dada	-	-	maybe	yes	maybe	yes	maybe
Deficiencia de hierro y su relación con la función cognitiva en escolares	I. C. Rivera, María Félix Rivera, Rebeca Rivera	10.5377/R CT.V0110. 1063	2013	yes	yes	yes	yes	yes

Examining the Relationship Between Anemia, Cognitive Function, and Socioeconomic Status in School-Aged Ecuadorian Children	A. Chamberlain	-	2015	no	no	maybe	yes	yes
Effect of Iron Deficiency Anemia on Scholastic Achievement of Primary School Students	Mohamed Ahmed, Abd Elrazik, Dr. Afaf Salah, Abd El-Mohsen, Dr. Sahar Mahmoud, Sayed Ahmed, El	-	-	no	no	maybe	yes	maybe
Effect of Intravenous Iron Therapy on Quality of Life in Non-Anemic Iron-Deficient Young Women with Fatigue	Ruchika Sharma, T. Koch, S. O'Brien	10.1182/BLOOD.V124.21.4858.4858	2014	yes	yes	maybe	yes	maybe
Anemia and iron deficiency anemia in school children of district Swat Khyber Pakhtunkhwa Pakistan	Fearoz Khan, Kausar Saeed, N. Akhtar, J. Zeb, H. A. Khan, Shahid Ahmad, H. Rehman, Akbar Shah, A. Ayub, Raqeebullah	-	2016	maybe	no	maybe	yes	yes
Novel interactions between iron and n-3 fatty acids in cognition and immune function	J. Baumgartner, L. Malan, C. Smuts	10.1002/LI TE.20150042	2015	no	no	no	maybe	maybe



Analysis of School-age Children in Iron-deficient Status Undergoing Integrated Visual and Auditory Continuous Performance Test	Xiao Qi-liang	-	2007	maybe	maybe	maybe	yes	yes
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Reviveed by: Dr. Alexandre Dupont

Alexandre Dupont