

WHO GUIDELINE¹: DAILY IRON SUPPLEMENTATION IN INFANTS AND CHILDREN

EXECUTIVE SUMMARY

Approximately 300 million children globally had anaemia in 2011. Deficiency in iron, a mineral necessary to carry oxygen in haemoglobin, is thought to be the most common cause of anaemia. Iron deficiency can result from inadequate intake or absorption of dietary iron, increased need in periods of growth, increased losses from menstruation in adolescent girls, or infection by intestinal helminths, such as schistosomiasis or hookworm infestation, in areas endemic to these parasites.

Iron is an essential nutrient for development and cell growth in the immune and neural systems, as well as in regulation of energy metabolism and exercise. The economic costs of iron deficiency anaemia from annual physical productivity losses have been calculated to be around US\$ 2.32 per capita, or 0.57% of gross domestic product in low- and middle-income countries. The WHO has consistently recommended oral iron supplementation as one of the interventions that can reduce the prevalence of anaemia.

Iron is required for the survival and virulence of many pathogens. Concerns have been expressed on a possible increased risk of malaria with iron interventions in malaria-endemic areas, particularly among iron-replete children. On the other hand, screening to identify iron deficiency in children prior to iron supplementation is not feasible in many malaria-endemic settings. Given the importance and magnitude of anaemia globally, particularly in areas where malaria transmission is intense, an assessment of all available evidence has been carried out, to examine the safety and effectiveness of iron supplementation in children, including in malaria-endemic areas.

Purpose of the guideline

This guideline aims to help Member States and their partners in their efforts to make informed decisions on the appropriate nutrition actions to achieve the [Sustainable Development Goals](#) (SDGs) (1), the global targets set in the [Comprehensive implementation plan on maternal, infant and young child nutrition](#) (2) and the [Global strategy for women's, children's, and adolescents' health \(2016–2030\)](#) (3). The recommendations in this guideline are intended for a wide audience, including policy-makers, their expert advisers, and technical and programme staff at organizations involved in the design, implementation and scaling-up of programmes for anaemia prevention and control, and in nutrition actions for public health.

The recommendations supersede those of previous WHO guidelines on iron supplementation in children where they pertain specifically to daily oral iron supplementation among infants and children.

Guideline development methodology

WHO developed the present evidence-informed recommendations using the procedures outlined in the [WHO handbook for guideline development](#) (4). The steps in this process included: (i) identification of priority questions and outcomes; (ii) retrieval of the evidence; (iii) assessment and synthesis of the evidence; (iv) formulation of recommendations, including research priorities; and planning for (v) dissemination; (vi) implementation, equity and ethical considerations; and (vii) impact evaluation and updating of the guideline. The Grading of Recommendations Assessment, Development and Evaluation ([GRADE](#)) methodology was followed (5), to prepare evidence profiles related to preselected topics, based on up-to-date systematic reviews.

¹ This publication is a World Health Organization (WHO) guideline. A WHO guideline is any document, whatever its title, containing WHO recommendations about health interventions, whether they be clinical, public health or policy interventions. A standard guideline is produced in response to a request for guidance in relation to a change in practice, or controversy in a single clinical or policy area, and is not expected to cover the full scope of the condition or public health problem. A recommendation provides information about what policy-makers, health-care providers or patients should do. It implies a choice between different interventions that have an impact on health and that have ramifications for the use of resources. All publications containing WHO recommendations are approved by the WHO Guidelines Review Committee.

The guideline development group consisted of content experts, methodologists and representatives of potential stakeholders and beneficiaries. One guideline group participated in a meeting concerning this guideline, held in Geneva, Switzerland, on 20–25 February 2010, where the guideline was scoped. A second guideline group participated in a meeting held in Geneva, Switzerland, on 14–18 March 2011, to discuss the safety of iron supplementation in children living in areas of high malaria transmission, and a third meeting was convened in Geneva, Switzerland, on 23–26 June 2014, where the guideline was finalized. Two experts served as technical peer-reviewers of the draft guideline.

Available evidence

The available evidence comprised four systematic reviews that followed the procedures of the [Cochrane handbook for systematic reviews of interventions](#) (6) and assessed the effects of daily iron supplementation in infants, preschool-age and school-age children, as well as the effect of iron on the incidence and severity of malaria, including deaths in children living in malaria-endemic settings. The reviews included individually randomized and cluster-randomized controlled trials. All studies compared a group of children who received iron supplementation to a group that did not receive iron. For systematic reviews done prior to 2013, the WHO Secretariat conducted an additional search on PubMed (June 2014) prior to the meeting of the guideline development group. In addition, in August 2015, a full literature search was performed as part of the review of evidence for malaria and iron supplementation. These searches did not identify any relevant additional studies.

The overall quality of the available evidence for daily iron supplementation in children and in malaria-endemic settings varied from high to very low for the critical outcomes of anaemia, iron deficiency and iron deficiency anaemia. The quality of evidence was moderate to very low for morbidity, mortality and growth measurements. The evidence for clinical malaria as an outcome in studies conducted in malaria-endemic settings was considered of high to moderate quality.

Recommendations¹

- Daily iron supplementation is recommended as a public health intervention in infants and young children aged 6–23 months, living in settings where anaemia is highly prevalent,² for preventing iron deficiency and anaemia (*strong recommendation, moderate quality of evidence*).

Suggested supplementation scheme: 10–12.5 mg elemental iron given daily for 3 consecutive months in a year

- Daily iron supplementation is recommended as a public health intervention in preschool-age children aged 24–59 months, living in settings where anaemia is highly prevalent,² for increasing haemoglobin concentrations and improving iron status (*strong recommendation, very low quality of evidence*).

Suggested supplementation scheme: 30 mg elemental iron given daily for 3 consecutive months in a year

- Daily iron supplementation is recommended as a public health intervention in school-age children aged 60 months and older, living in settings where anaemia is highly prevalent,² for preventing iron deficiency and anaemia (*strong recommendation, high quality of evidence*).

Suggested supplementation scheme: 30–60 mg elemental iron given daily for 3 consecutive months in a year

- In malaria-endemic areas, the provision of iron supplementation in infants and children should be done in conjunction with public health measures to prevent, diagnose and treat malaria (*strong recommendation, high quality of evidence*).

¹ These recommendations supersede those of previous WHO guidelines on iron supplementation in children.

² Where the prevalence of anaemia is 40% or higher in this age group. For the latest estimates, please refer to the [Vitamin and Mineral Nutrition Information System](#) (VMNIS) hosted at WHO (7).

Remarks

The remarks in this section are intended to give some considerations for implementation of the recommendations, based on the discussion of the guideline development group.

- Daily oral iron supplementation is a preventive strategy for implementation at the population level. If a child is diagnosed with anaemia, national guidelines for the treatment of anaemia should be followed.
- If the prevalence of anaemia is 20–40%, intermittent regimens of iron supplementation can be considered.
- The selection of the most appropriate delivery platform should be context specific, with the aim of reaching the most vulnerable populations and ensuring a timely and continuous supply of supplements.
- In malaria-endemic areas, iron supplementation does not increase the risk of clinical malaria or death when regular malaria-surveillance and treatment services are provided. Oral iron interventions should not be given to children who do not have access to malaria-prevention strategies (e.g. provision of insecticide-treated bednets and vector-control programmes), prompt diagnosis of malaria illness, and treatment with effective antimalarial drug therapy.
- The risk of clinical malaria is not more likely among iron-replete children given iron supplementation in malaria-endemic areas. There is no need to screen for anaemia prior to iron supplementation in settings where anaemia is highly prevalent.
- Since malaria infection occurs in early infancy and is especially dangerous at this age, in malaria-endemic areas, iron supplements should only be given to infants who sleep under insecticide-treated bednets, and where all episodes of malaria illness can be promptly treated with effective antimalarial drug therapy according to national guidelines.
- In the presence of comprehensive surveillance and prompt diagnosis and treatment of malaria, there was no compelling evidence of increased risk of adverse events from iron supplementation. Insufficient and inequitable health-care services are associated with an increase in risks in general.

Research priorities

Discussions between the members of the WHO guideline development group and the external review group highlighted the limited evidence available in some knowledge areas, meriting further research on iron supplementation in infants and children, particularly in the following areas:

- the optimal dose, schedule and duration of iron supplementation; the effect of different doses and durations of iron supplementation on different severity, prevalence or causes of anaemia in all WHO regions;
- additional data on the safety of iron supplementation (liver damage; iron overload after continuing the supplementation programme for a number of years; iron supplementation given in conjunction with other interventions; insulin resistance; effects in non-anaemic or non-iron-deficient children);
- the effect of adding other micronutrients to the iron supplement on haemoglobin concentrations and the prevalence of anaemia;
- implementation research on effective behaviour-change strategies for sustained adherence and innovative delivery mechanisms for iron supplements;
- additional long-term studies on functional outcomes (e.g. cognitive and motor development).