

# Efficacy and effectiveness of interventions to control iron deficiency and iron deficiency anemia

**I**ron deficiency, including its most severe form—iron deficiency anemia (IDA)—is the most common and widespread micronutrient deficiency worldwide.<sup>1</sup> Iron deficiency is more prevalent in population groups that have high iron requirements because of rapid growth or blood loss. The population groups most vulnerable to developing iron deficiency are infants, children, and women of reproductive age.

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Low dietary intake of bioavailable iron is a major factor in the etiology of iron deficiency. Correcting such deficits requires large-scale interventions, and many countries have implemented supplementation and food fortification programs for this purpose. The high iron requirement of pregnant women is of special concern, and women are generally advised to take iron supplements during pregnancy and, in some circumstances, during early lactation as well.<sup>1</sup> Similarly, food fortification programs can target specific population groups, such as programs that encourage the use of fortified complementary food for infants and young children. Food fortification can also be used to increase iron intake in the general population through the fortification of staple food, such as cereal flour, or of widely used condiments.

Although many countries have long-term experience with iron supplementation and, to a lesser extent, food fortification programs, little information about the usefulness of such interventions is available. This document highlights some of the important principles in developing a program to control iron deficiency. In particular, evidence-based information about the *efficacy* of an intervention is needed to develop an effective program, and information about its *effectiveness* is required for carrying out economic analyses as well as for determining overall program performance.

### **Definition: Efficacy**

Efficacy has been defined as *the extent to which a specific intervention, procedure, regimen, or service produces a beneficial effect under ideal conditions.*<sup>2</sup> In this context “ideal conditions” refers to situations in which all individuals targeted by the intervention comply with the treatment regimen to which they are assigned. Thus, efficacy refers only to biological factors, not to behavioral factors.

For example, the efficacy of using an iron supplementation regimen or of regularly consuming an iron-fortified food can be evaluated by monitoring iron status under strictly controlled conditions—that is, by monitoring the extent to which iron deficiency and/or IDA is reduced or prevented in the treatment group compared with the control group. The efficacy of iron interventions can also be determined through measures of other biological outcomes, such as cognitive development and growth.

A well-designed efficacy study is one that is randomized, double-blind, and placebo-controlled and in which intake is carefully supervised and monitored. Participants in the treatment group receive iron supplements or an iron-fortified food, and subjects in the control groups receive placebo supplements or unfortified food during the study.

## Definition: Effectiveness

Effectiveness has been defined as *the extent to which a specific intervention, procedure, regimen, or service, when deployed in the field, does what it is intended to do for a defined population.*<sup>2</sup> Unlike efficacy, effectiveness is affected by compliance, which is influenced by behavioral factors that are in turn affected by access to the intervention, supply, cost, and other factors. Compliance can differ between population groups and settings. Even if an intervention has been demonstrated to be efficacious, its effectiveness can be limited if compliance is low. For example, the use of iron supplements during pregnancy has been shown to be efficacious in reducing anemia, but pooled data from the past 30 years do not conclusively demonstrate program effectiveness.<sup>3</sup> The shortfall in effectiveness has been attributed largely to inadequate supply of iron supplements.<sup>4</sup>

The effectiveness of iron supplementation or food fortification programs is considerably more difficult to evaluate than their efficacy, because changes in iron status (or other biological indicators) are measured in uncontrolled settings—that is, in real-life situations. *Trial effectiveness*, which is efficacy adjusted for compliance during a research trial,<sup>5</sup> must be differentiated from *program effectiveness*, because compliance in the study population can be influenced during the evaluation.

Given the numerous logistical difficulties and the great expense involved in organizing large-scale effectiveness studies, this type of evaluation is rarely made. Instead, effectiveness may be monitored and cost-benefit analyses conducted during implementation of an efficacious intervention to control iron deficiency.

## Efficacy and effectiveness of iron supplementation

Although both daily and weekly iron supplementation regimens have been demonstrated to be efficacious in vulnerable population groups, existing data do not demonstrate that large-scale programs with iron supplementation are generally effective.<sup>6</sup> Researchers attempting to explain this finding have suggested a variety of contributing factors, including the following:

- A lack of the supplements themselves, as a result of poor or ineffective procurement and distribution systems.<sup>4</sup>
- Failure to use specific indicators of iron deficiency in monitoring or evaluating programs. Anemia is often used as a proxy for IDA. However, because the etiology of anemia is often multifactorial, supplementation with iron alone will be inadequate to prevent and control anemia where iron deficiency is not the only cause of anemia.<sup>7</sup>

Unlike efficacy, effectiveness is affected by compliance, which is influenced by behavioral factors that are in turn affected by access to the intervention, supply, cost, and other factors.

- Failure to concentrate efforts on the individuals who are iron deficient. Although the overall effectiveness of iron supplementation programs targeting all pregnant women may be limited, the benefit to iron-deficient individuals can be significant.<sup>8</sup>
- Poor compliance with the supplementation regimen.<sup>6</sup>
- Absence of counseling on possible negative side effects, such as nausea, constipation, and diarrhea.<sup>9</sup>
- Poor access to and use of prenatal health care services.

### **Efficacy and effectiveness of iron fortification of food**

Food fortification is often suggested as the best long-term approach to increasing iron intake. However, few data are available to show the efficacy of increased iron intake from iron-fortified food—either targeted food or staple food—in improving iron status. A carefully controlled six-month study confirmed that NaFeEDTA-fortified fish sauce was efficacious in improving iron status among anemic Vietnamese women.<sup>10</sup> These findings support earlier reports on the usefulness of NaFeEDTA as an iron fortificant for condiments.<sup>11</sup> The efficacy of salt that has been dual fortified with iodine and microencapsulated ferrous sulfate has also been demonstrated recently, in Moroccan schoolchildren.<sup>12</sup>

It is important to bear in mind that efficacy has been demonstrated only for water-soluble iron compounds added to condiments. The efficacy of less soluble iron compounds (that are not freely water soluble or are insoluble in water) added to cereal flours is unknown.<sup>13</sup> The evaluation of iron-fortified targeted food is also limited. Only one study has demonstrated that a water-insoluble iron fortificant, electrolytic iron, added to an infant cereal contributed substantially to preventing IDA in infants.<sup>14</sup>

No large-scale iron fortification programs have been evaluated for effectiveness. Compliance with food fortification programs can be assumed to be considerably better than with iron supplementation, because less active involvement by the consumer is required. However, important factors that influence compliance include the cost as well as the sensory properties (taste, appearance, and odor) of the iron-fortified food vehicle itself as well as effects on food prepared from or consumed together with the iron-fortified food vehicle.

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## Summary

- Effective interventions are needed to control iron deficiency.
- Information about the *efficacy* of an intervention is needed to develop an effective program. Although iron supplementation has been demonstrated to be efficacious in many studies, more information is needed about the efficacy of food fortification.
- Even if an efficacious intervention is implemented, its *effectiveness* and cost-benefit will be limited if the program is not properly implemented. Factors that act as barriers and facilitators to the success of iron supplementation and food fortification programs need to be evaluated in different settings, and innovative ways to minimize the former and maximize the latter must be explored.

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Factors that act as barriers and facilitators to the success of iron supplementation and food fortification programs need to be evaluated in different settings.

## About INACG

The International Nutritional Anemia Consultative Group (INACG) is dedicated to reducing the prevalence of iron deficiency anemia and other nutritionally preventable anemias worldwide. It sponsors international meetings and scientific reviews and convenes task forces to analyze issues related to etiology, treatment, and prevention of nutritional anemias. Examination of these issues is important to the establishment of public policy and action programs.

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