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Iron Deficiency Anaemia

Assessment, Prevention, and Control

A guide for programme managers

United Nations Children's Fund

United Nations University

World Health Organization

IDA

This document deals primarily with indicators for monitoring interventions to combat iron deficiency, including iron deficiency anaemia, but it also reviews the current methods of assessing and preventing iron deficiency in the light of recent significant scientific advances. Criteria for defining IDA, and the public severity of anaemia based on prevalence estimates, are provided. Approaches to obtaining dietary information, and guidance in designing national iron deficiency prevention programmes, are presented.

Strategies for preventing iron deficiency through food-based approaches, i.e. dietary improvement or modification and fortification, and a schedule for using iron supplements to control iron deficiency and to treat mild-to-moderate iron deficiency anaemia, are discussed. For each strategy, desirable actions are outlined and criteria are suggested for assessment of the intervention. Attention is given to micronutrient complementarities in programme implementation, e.g., the particularly close link between the improvement of iron status and that of vitamin A.

Finally, this document recommends action-oriented research on the control of iron deficiency, providing guidance in undertaking feasibility studies on iron fortification in most countries.

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Assessment, Prevention and Control

A guide for programme managers

i Executive summary

This document deals primarily with indicators for monitoring interventions to combat iron deficiency, including iron deficiency anaemia. However, it also reviews the current methods of preventing iron deficiency in the light of recent significant scientific advances. It summarizes regional prevalences of anaemia, and briefly discusses the principal factors affecting its prevalence.

Indicators for assessing iron deficiency are presented, together with their thresholds of abnormality in various age, gender, and physiological status; the relationships between them; and their applicability in different settings according to resource availability.

It also presents approaches for obtaining dietary information and guidance on designing national iron deficiency prevention programmes. Iron requirements and recommended iron intakes from diets of different bioavailability are summarized.

Criteria for defining iron deficiency anaemia are provided, and a slight modification from those previously recommended by WHO is proposed. Also proposed are criteria for defining the public health severity of anaemia, on the basis of prevalence estimates. Acceptable methods for assessing anaemia and iron status, both on the basis of clinical examinations and blood tests, are discussed. Threshold values for the interpretation of these indices are given.

Strategies for preventing iron deficiency through food-based approaches, i.e. dietary improvement or modification and fortification, are discussed. For example, modifiers that affect the bioavailability of food-iron sources are reviewed, and suggestions for altering meal patterns to improve absorbability are offered.

A schedule for using iron supplements to control iron deficiency, and to treat mild-to-moderate IDA according to age, gender, and physiological status, is provided. For each strategy, desirable actions are outlined and criteria suggested for assessment of the intervention. In this connection, indicators for use in monitoring programme implementation are described.

In most countries, some aspects of each of the main types of intervention will be needed to control the problem of iron deficiency. Particular attention is devoted to micronutrient complementarities in programme implementation. For example, the particularly close link between improving iron status and improving vitamin A status is explored.

Finally, recommendations are made for action-oriented research on the control of iron deficiency, and for undertaking feasibility studies on iron fortification in countries. Increased advocacy, exchange of information, development of human resources, and action-oriented research are recommended for accelerating the achievement of the goals for reducing iron deficiency.

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V Abbreviations

CDC	Centers for Disease Control and Prevention (USA)
CSM	Corn-soy-milk
DALY	Disability adjusted life years
ID	Iron deficiency
IDA	Iron deficiency anaemia
EP	Erythrocyte protoporphyrin
FAO	Food and Agriculture Organization of the United Nations
G6PD	Glucose-6 phosphate dehydrogenase
Hb	Haemoglobin
Hct	Haematocrit
IDD	Iodine deficiency disorders
INACG	International Nutritional Anaemia Consultative Group
IQ	Intelligence quotient
Na-Fe EDTA	Sodium ferric ethylenediaminetetraacetic acid
JECFA	Joint FAO/WHO Expert Committee on Food Additives
MCH	Maternal and child health
MCHC	Mean corpuscular haemoglobin concentration
MCV	Mean corpuscular volume
MDIS	Micronutrient Deficiency Information System
NGO	Nongovernmental organization
PHC	Primary health care
RBC	Red blood cells
SF	Serum ferritin
SI	Serum iron
TIBC	Total iron binding capacity
TR	Transferrin receptor
TS	Transferrin saturation
T_3	Triiodothyronine
UNICEF	United Nations Children's Fund
UNU	United Nations University
VAD	Vitamin A deficiency
WHO	World Health Organization
WSB	Wheat-soy blend

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vii Preface

This document is based in large part on a consultation convened in Geneva from 6-10 December 1993, jointly organized by the World Health Organization (WHO), the United Nations Children's Fund (UNICEF), and the United Nations University (UNU).

Since the meeting there have been significant new data emerging in key areas, which have been published in scientific literature and presented in international meetings. It was recognized that this information was relevant and should also be included. Therefore, the final text has been updated and contains new material, together with the conclusions reached and recommendations made by the Consultation.

Iron deficiency, and specifically iron deficiency anaemia, remains one of the most severe and important nutritional deficiencies in the world today. Every age group is vulnerable. Iron deficiency impairs the cognitive development of children from infancy through to adolescence. It damages immune mechanisms, and is associated with increased morbidity rates.

During pregnancy, iron deficiency is associated with multiple adverse outcomes for both mother and infant, including an increased risk of haemorrhage, sepsis, maternal mortality, perinatal mortality, and low birth weight. It is estimated that nearly all women are to some degree iron deficient, and that more than half of the pregnant women in developing countries suffer from anaemia. Even in industrialized countries, the iron stores of most pregnant women are considered to be deficient. Finally, as much as a 30% impairment of physical work capacity and performance is reported in iron-deficient men and women.

The economic implications of iron deficiency and of the various intervention strategies to combat it, suggest that food-based approaches and targeted supplementation are particularly cost-effective. The highest benefit-to-cost ratio is attained with food fortification.

In the last two decades, the importance of iron deficiency and anaemia as a public health problem has been increasingly recognized by health authorities and policy makers. This is reflected in the goals on the reduction of iron deficiency anaemia endorsed by Heads of State, ministers in the World Declaration and Plan of Action from the World Summit for Children (1990) and in the World Declaration and Plan of Action for Nutrition from the International Conference on Nutrition (1992).

The document aims at providing scientists and national authorities worldwide with an up-to-date and authoritative review of iron deficiency anaemia, together with guidelines and recommendations. It is also intended for managers of national programmes dealing with the prevention and control of micronutrient malnutrition, as well as for policy makers. It is meant to help them to implement effective measures for fighting iron deficiency anaemia. We hope that the information included in this manual will contribute to our common effort to eliminate iron deficiency anaemia.

1 Introduction

In 1992, World Health Resolution WHA45.33 urged Member States to:

> *establish, as part of the health and nutrition monitoring system, a micronutrient monitoring and evaluation system capable of assessing the magnitude and distribution of iodine, vitamin A and iron deficiency disorders, and monitor the implementation and impact of control programmes . . .*

For their part, WHO and UNICEF, together with key partners, convened a series of consultations on appropriate indicators for assessing and monitoring micronutrient deficiencies and their control programmes. Consultations on iodine deficiency disorders and vitamin A deficiency were held first, in 1992 *(1,2)*.

A third consultation on iron deficiency was held a year later, in December 1993, providing the basis for the present document. Also included is important new information emerging since the consultation

Iron deficiency affects a significant part, and often a majority, of the population in nearly every country in the world. Programmes for the prevention of iron deficiency, particularly iron supplementation for pregnant women, are under way in 90 of 112 countries that reported to WHO in 1992 *(3)*. Most of these programmes, however, are neither systematically implemented nor well monitored or evaluated.

Scientific consensus on the prevention of iron deficiency anaemia was described in a 1989 WHO monograph *(4)*. Since then, however, knowledge of the consequences of iron deficiency - even in the absence of anaemia - has evolved, while fortification technology has improved considerably.

Furthermore, national, regional, and global efforts to overcome micronutrient malnutrition have gathered accelerated momentum. As a result, an overall review of the strategies for preventing iron deficiency - together with a closer examination of prevalence indicators and methods of monitoring programmes of prevention - have become appropriate and timely.

The general objective of the 1993 consultation was to review and accelerate global processes for preventing iron deficiency, with the goal of substantially reducing the problem during the forthcoming decade.

The specific objectives of the consultation were as follows:

- To review appropriate target groups for iron deficiency and anaemia assessment and surveillance, and appropriate prevalence indicators, criteria, and thresholds.
- To review and make general recommendations on suitable laboratory methods for assessment of key indicators.
- To identify the steps by which the main strategies - improved food consumption and dietary practices, food fortification, supplementation, and public health measures - could be more effectively implemented at each level.
- To identify appropriate indicators for monitoring programme implementation.
- To identify high-priority, action-oriented, and operational research needed to enable and accelerate effective programme implementation.
- To determine critical needs in human resources development for prevention of iron deficiency.

2 Concepts used in defining iron nutritional status

Iron status can be considered as a continuum from iron deficiency with anaemia, to iron deficiency with no anaemia, to normal iron status with varying amounts of stored iron, and finally to iron overload - which can cause organ damage when severe. Iron deficiency is the result of long-term negative iron balance. Iron stores in the form of haemosiderin and ferritin are progressively diminished and no longer meet the needs of normal iron turnover.

From this critical point onward, the supply of iron to the transport protein apotransferrin is compromised. This condition results in a decrease in transferrin saturation and an increase in transferrin receptors in the circulation and on the surface of cells, including the erythron.

All tissues express their need for iron in exactly the same way, i.e. by the same type of transferrin receptors on cell surfaces in proportion to actual iron need. Accordingly, a compromised supply of iron to the erythron is associated with a similarly insufficient supply of iron to all other tissues.

Functionally, the lack of mobilizable iron stores will eventually cause a detectable change in classical laboratory tests, including measurement of haemoglobin, mean corpuscular haemoglobin concentration, mean corpuscular volume, total iron-binding capacity, transferrin saturation, and zinc-erythrocyte protoporphyrin.

Iron deficiency is defined as a condition in which there are no mobilizable iron stores and in which signs of a compromised supply of iron to tissues, including the erythron, are noted. The more severe stages of iron deficiency are associated with anaemia.

When iron-deficient erythropoiesis occurs, haemoglobin concentrations are reduced to below-optimal levels. When individual haemoglobin levels are below two standard deviations (-2SD) of the distribution mean for haemoglobin in an otherwise normal population of the same gender and age who are living at the same altitude, iron deficiency anaemia is considered to be present.

In a normal population, 2.5% of the population would be expected to be below this threshold. Hence, iron deficiency anaemia would be considered a public health problem only when the prevalence of haemoglobin concentration exceeds 5.0% of the population (see Table 3).

The prevalence of iron deficiency anaemia in a population is therefore a statistical rather than a physiological concept, although it reflects that proportion of the population that has iron-deficient erythropoiesis. Iron deficiency anaemia should be regarded as a subset of iron deficiency. That is, it represents the extreme lower end of the distribution of iron deficiency.

Because anaemia is the most common indicator used to screen for iron deficiency, the terms anaemia, iron deficiency, and iron deficiency anaemia are sometimes used interchangeably. There are, however, mild-to-moderate forms of iron deficiency in which, although anaemia is absent, tissues are still functionally impaired.

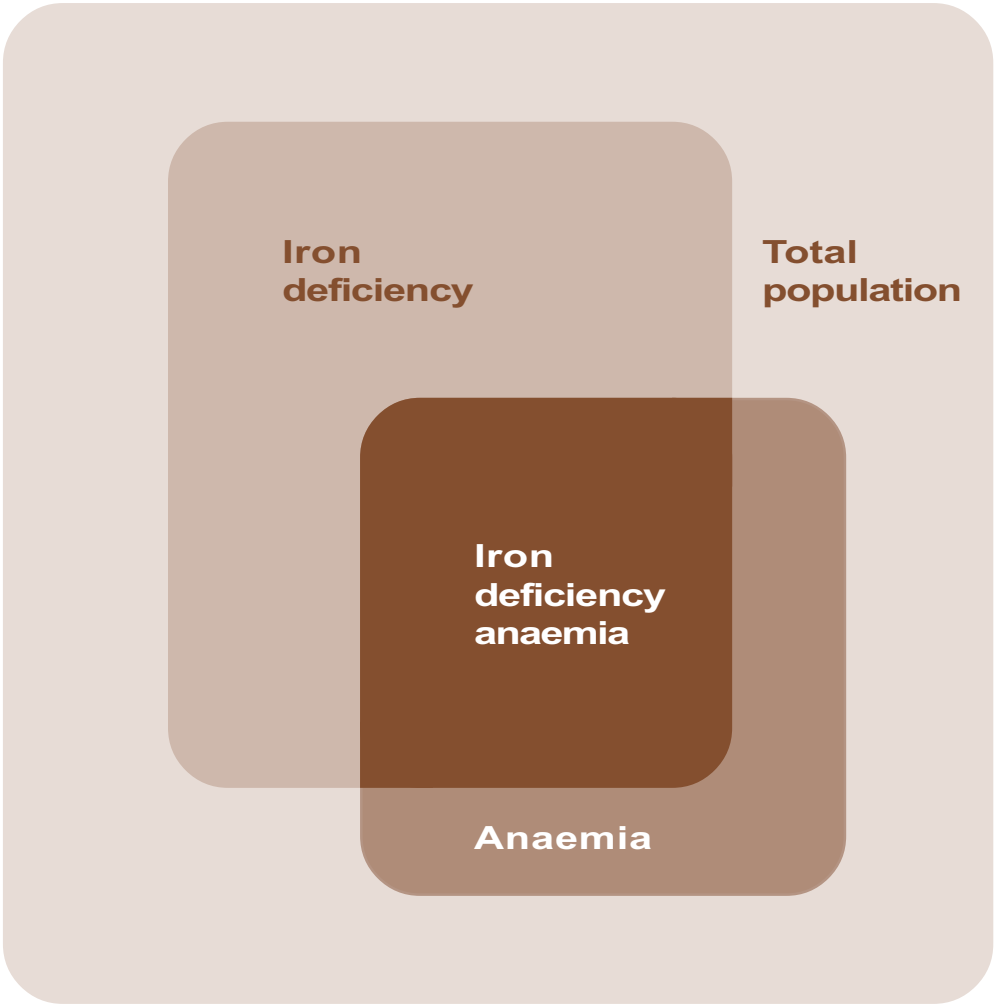
In addition, although iron deficiency anaemia accounts for most of the anaemia that occurs in underprivileged environments, several other possible causes should be noted. These include haemolysis occurring with malaria; glucose-6-phosphate dehydrogenase deficiency; congenital hereditary defects in haemoglobin synthesis; and deficits in other nutrients, e.g. vitamins A, $B_{12,}$ and C, and folic acid.

Blood loss such as that associated with schistosomiasis, hookworm infestation, haemorrhage in childbirth, and trauma, can also result in both iron deficiency and anaemia. Lastly, as with vitamin A deficiency, inhibition of the normal metabolism of iron can result in anaemia. These causes of anaemia are not addressed in detail in this guidebook.

The relationship between anaemia and iron deficiency in a population is illustrated in Figure 1 on the opposite page *(5)*. In particular, it is noted that the extent of the overlap between iron deficiency and iron deficiency anaemia varies considerably from one population to another and according to gender and age groups.

The degree of overlap between rates of total anaemia and of iron deficiency anaemia also varies with the population observed. The greatest overlap occurs in populations in which dietary iron absorbability is low or blood loss is common due to hookworm infestation.

Figure 1. Conceptual diagram of the relationship between iron deficiency and anaemia in a hypothetical population



Source: Adapted from Yip R. Iron nutritional status defined. In: Filer IJ, ed. *Dietary Iron: birth to two years.* New York, Raven Press, 1989:19-36.

3 Functional consequences of iron deficiency

The pallor of anaemia was associated with weakness and tiredness long before its cause was known. Now it is recognized that even without anaemia, mild to moderate iron deficiency has adverse functional consequences *(6).*

Iron deficiency adversely affects

- the cognitive performance, behaviour, and physical growth of infants, preschool and school-aged children;
- the immune status and morbidity from infections of all age groups; and
- the use of energy sources by muscles and thus the physical capacity and work performance of adolescents and adults of all age groups.

Specifically, iron deficiency anaemia during pregnancy

- increases perinatal risks for mothers and neonates; and
- increases overall infant mortality.

Moreover, iron-deficient animals and humans have impaired gastrointestinal functions and altered patterns of hormone production and metabolism. The latter include those for neurotransmitters and thyroidal hormones which are associated with neurological, muscular, and temperature-regulatory alterations that limit the capacity of individuals exposed to the cold to maintain their body temperature. In addition, DNA replication and repair involve iron-dependent enzymes.

3.1 Cognitive development

In experimental animals, iron has been shown to play a key role in brain function. Several areas of the brain contain iron, sometimes in large quantities. Iron-deficient animals show alterations both in neurotransmitters and behaviour that do not usually respond to iron replenishment.

There is strong evidence that findings from animal studies also apply to humans. For example, iron deficiency anaemia has been conclusively seen to delay psychomotor development and impair cognitive performance of infants in Chile *(7),* Costa Rica *(8),* Guatemala *(9)*, and Indonesia *(10)*; of preschool and school-aged children in Egypt *(11)*, India *(12)*, Indonesia (*13*,*14*), Thailand *(15)*, and the USA *(16*,*17)*.

Adolescent girls whose diet was supplemented with iron felt less fatigued; their ability to concentrate in school increased and their mood improved *(18)*. Neurological malfunction in young children, adolescents, and adults - as determined by electrophysiological measurements - has also been documented as being associated with iron deficiency *(19)*.

In Costa Rica, children who had moderate anaemia as infants achieved lower scores on intelligence (IQ) tests and other cognitive performance upon entry in school than did children who were non-anaemic during infancy. This finding emerged even when the tests were controlled for a comprehensive set of socioeconomic factors *(11)*. This result was recently confirmed in Chile *(20)*. On the other hand, in Thailand the poor performance in Thai language and mathematics tests of children with low haemoglobin levels was not reversed by iron supplementation *(15)*.

Thus, iron deficiency can impair cognitive performance at all stages of life. Moreover, the effects of iron deficiency anaemia in infancy and early childhood are not likely to be corrected by subsequent iron therapy. An estimated 10-20% of preschool children in developed countries, and an estimated 30-80% in developing countries, are anaemic at 1 year of age *(21)*. These children will have delayed psychomotor development, and when they reach school age they will have impaired performance in tests of language skills, motor skills, and coordination, equivalent to a 5 to 10 point deficit in IQ.

3.2 Resistance to infection

Morbidity from infectious disease is increased in iron-deficient populations *(22-26)*, because of the adverse effect of iron deficiency on the immune system *(27-30)*. In these situations, leukocytes have a reduced capacity to kill ingested microorganisms *(31-34)* and lymphocytes a decreased ability to replicate when stimulated by a mitogen. Also in such cases, there occurs a lowered concentration of cells responsible for cell-mediated immunity *(31, 35-37)* and a depressed skin-test response to common antigens *(31,35)*. Iron supplementation and milk or cereal fortification among deficient children has been reported to reduce morbidity from infectious disease *(38)*.

3.3 Work capacity and productivity

A linear relationship has been reported between iron deficiency and work capacity for agricultural workers in Colombia *(39)*, Guatemala *(40)*, Indonesia *(41)*, Kenya *(42,43)*, and Sri Lanka *(44-46)*. Work capacity returned rapidly to normal with iron supplementation. Similarly, iron supplementation increased work output among road workers and rubber tappers in Indonesia *(24)*; tea pickers in Indonesia *(26,41)* and Sri Lanka *(44-46)*; agricultural workers in India *(47)*, Guatemala *(40)*, and Colombia *(39)*; and industrial workers in Kenya *(48)*, China *(49)*, and other countries. Gains in productivity and take-home pay ranged from 10% to 30% of previous levels.

Compared with non-anaemic women, anaemic female workers in China were 15% less efficient in performing their work. They spent 6% less energy on their out-of-work activities, had 4% lower maximal work capacity, and had 12% lower overall productivity, as compared to levels achieved after anaemia was corrected by iron treatment for 4 months *(49)*. Similarly, non-anaemic iron-deficient adolescent female runners significantly improved their levels of endurance and physical performance after supplementation with iron, as compared with those of a placebo control group *(50)*.

3.4 Pregnancy

Iron deficiency in childbearing women increases maternal mortality *(51)*, prenatal and perinatal infant loss, and prematurity *(52,53)*. Forty percent of all maternal perinatal deaths are linked to anaemia. Favourable pregnancy outcomes occur 30-45% less often in anaemic mothers, and their infants have less than one-half of normal iron reserves *(54)*.

Such infants require more iron than is supplied by breast milk, at an earlier age, than do infants of normal birth weight *(55)*. Moreover, if pregnancy-induced iron deficiency is not corrected, women and their infants suffer all the consequences described above.

3.5 Growth

Growth improved in iron-deficient children who were given supplementary iron in Indonesia *(56)*, Kenya *(57)*, and Bangladesh *(58)*, as well as in the United Kingdom *(59)* and the United States *(60)*. Whether or not an effect of iron supplementation is observed apparently depends on local factors. These include frequency of diarrhoea and other infections, age at iron depletion, and other dietary factors.

3.6 Endocrine and neurotransmitters

Iron deficiency alters the production of triiodothyronine (T_3) and thyroid function in general, and the production and metabolism of catecholamines and other neurotransmitters. This results in impaired temperature response to a cold environment.

In both experimental animals and human subjects, those with iron deficiency anaemia more readily become hypothermic and have a depressed thyroid function *(61-65)*. This condition may be the cause of some of the discomfort from cold felt by poorly nourished individuals at temperatures in which well-nourished persons are quite comfortable.

3.7 Heavy-metal absorption

An important consequence of iron deficiency is an apparent increased risk of heavy-metal poisoning in children. Iron-deficient individuals have an increased absorption capacity that is not specific to iron. Absorption of other divalent heavy metals, including toxic metals such as lead and cadmium, is also increased *(66)*.

Prevention of iron deficiency, therefore, reduces the number of children susceptible to lead poisoning. Such prevention may also help to reduce their lead burden after exposure to high levels of lead from chipped lead paints, pollution from automobile fumes (such as occurs in many cities), or other excessive exposure to lead in the environment *(67)*.

4 Economic implications of iron deficiency

National socioeconomic development, as well as personal health and self-fulfilment, are impaired by iron deficiency. The negative impact on national development can be estimated from:

- the number of individuals affected in various age and gender categories;
- the severity of the deficiency; and
- the duration and consequences of the condition.

The economic implications of such conditions include:

- the costs incurred by the public and private sectors in therapeutic measures for the prevalent level of anaemia;
- the societal consequences of increased maternal mortality and resultant restraints on productivity; and
- the long-term projected negative consequences of impaired mental development on human capital formation.

The estimation of disability adjusted life years (DALYs) is an expression of years of life lost (YLL) and years lived with disability (YLD). DALYs provide an overall view of the magnitude of economic losses to a population *(68)*.

Other indirect social and health consequences of impaired health and vitality are difficult to estimate and are often not considered. For example, among resource-poor societies the premature death of a mother and the lower income-generating capacity of iron-deficient and anaemic workers translates into greater rates of disease and overall undernutrition.

This vicious circle impairs individual, family, and community, as well as overall socioeconomic development. Consequently, estimates of only the economic cost of iron deficiency are conservative understatements of the true handicap imposed on society.

Costs of interventions specifically directed at nutrition and health education, dietary diversification, and other public health interventions that also result in improvements in iron nutrition, are not considered here. Data are lacking to allow even a rough approximation of the effectiveness of these measures for controlling iron deficiency. However, the general consensus is that if these interventions are competently carried out, they are highly cost-effective and sustainable.

There is a general scarcity of information both on the actual cost of programmes for the control of iron deficiency, and on the benefits obtained by its correction. Various programme budgetary considerations include the costs of:

- iron compounds required to treat anaemia and control iron deficiency;
- provision of iron fortification programmes;
- facilities, personnel time, logistics support; and
- programme monitoring and evaluation.

Iron compounds are no more than 7% of the total cost of supplementation programmes. In the case of iron fortification, the proportion of the cost of the most expensive iron compound may reach 27% of the total cost of the product because of the much lower cost of the other components. Generally, ongoing expenditures incurred in the treatment of anaemic subjects, and those involved in purchasing pharmaceutical preparations containing iron, are ignored, even though these may be significant.

The percentage efficiency of each intervention to control iron deficiency should also be considered when developing cost-benefit estimates. For example, successfully implemented iron supplementation programmes are considered to be at least 70% effective in the short term. As another example, general iron fortification programmes are considered to be 93% effective in the long term.

Estimates of benefits are made on the basis of projections from the correction of deficits caused by iron deficiency. These projections include lives saved; incomes increased; and deficits prevented in mental performance at all ages, including learning capacity at school. Resultant savings in treatment costs when iron deficiency is prevented should also be considered when calculating benefits to society.

Once both costs and benefits of various programmes have been estimated, the cost-benefit ratio of interventions can be derived. Several attempts have been made to develop models for comparative purposes among interventions *(69,70)*, as applied to an 'average' developing world population. These models involve prevalence of iron deficiency by age group, using neither the lower nor the higher costs of the various intervention components.

Estimates of fixed costs, e.g. depreciation and maintenance of health-post buildings and vehicles, monitoring, and costs of health-post personnel, are estimated on the assumption that programmes to control iron deficiency share these costs with three other programmes: family planning, antenatal care, and maternal-infant care. Accordingly, each programme incurs only one-quarter of the total estimated fixed costs.

When programmes are primarily community-based, costs are estimated to be further reduced by three-quarters. The 'average' fortification programme will include the cost of the most expensive compound, iron-EDTA (sodium iron ethylenediaminetetraacetic acid).

Table 1 on the following page presents estimates of the relative effectiveness and cost of various strategies, in terms of DALYs gained by each, and the cost per DALY.

Table 1. Relative effectiveness and cost per Disability Adjusted Life Year (DALY) of various prevention strategies

Intervention	Number of DALYs gained	Cost per DALY	
		Per day	*Per week*
Short-term			
Benefits or costs			
Prenatal supplementation	511	100	51
Widespread supplementation	4665	88	24
Universal fortification plus prenatal supplementation	5038	16	11
Universal fortification plus residual supplementation	5394	39	16
Long-term			
Human capital formation			
Supplementation	2679	37	17
Fortification	3332	9	-

Source: Murray & Lopez *(68)*.

5 Prevalence and epidemiology of iron deficiency

5.1 Prevalence

Iron deficiency is the most common and widespread nutritional disorder in the world *(71)*. As well as affecting a large number of children and women in non-industrialized countries, it is the only nutrient deficiency which is also significantly prevalent in virtually all industrialized nations. There are no current global figures for iron deficiency, but using anaemia as an indirect indicator it can be estimated that most preschool children and pregnant women in non-industrialized countries, and at least 30-40% in industrialized countries, are iron deficient *(21, 51)*.

Nearly half of the pregnant women in the world are estimated to be anaemic: 52% in non-industrialized - as compared with 23% in industrialized - countries (see Table 2a, below, and 2b, following page). In industrialized countries, however, most pregnant women are thought to suffer from some degree of iron deficiency. For example, 75% of pregnant women attending universities in Paris showed evidence of depleted iron stores *(72)*.

Table 2a. Estimated percentages of anaemia prevalence (1990-95) based on blood haemoglobin concentration (21, 51)

	Percentage of total affected population in:	
	Industrialized countries	Non-industrialized countries
Children *(0-4 years)*	20.1	39.0
Children *(5-14 years)*	5.9	48.1
Pregnant women	22.7	52.0
All women *(15-59 years)*	` 10.3	42.3
Men *(15-59 years)*	4.3	30.0
Elderly *(+60 years)*	12.0	45.2

Table 2b. Estimated prevalence of anaemia (1990-1995) by WHO Region based on blood haemoglobin concentration (21,51)

WHO Regions	Total affected population, *in thousands*					
	Children *(0-4 years)*	Children *(5-14 years)*	Pregnant Women	All women *(15-59 years)*	Men *(15-59 years)*	Elderly *(+60 years)*
Africa	45 228	85 212	10 800	57 780	41 925	13 435
Americas	14 200	40 633	4 500	53 787	19 443	12 617
South-East Asia	111 426	207 802	24 800	214 991	184 752	60 208
Europe	12 475	12 867	2 400	27 119	13 318	18 095
Eastern Mediterranean	33 264	37 931	7 700	60 196	41 462	11 463
Western Pacific	29 793	156 839	9 700	158 667	174 400	78 211
Overall	**245 386**	**541 284**	**59 900**	**572 540**	**475 300**	**194 029**

Anaemia is particularly prominent in south Asia. In India, for example, up to 88% of pregnant and 74% of non-pregnant women are affected. Throughout Africa, about 50% of pregnant and 40% of non-pregnant women are anaemic. West Africa is the most affected, and southern Africa the least. In Latin America and the Caribbean, prevalences of anaemia in pregnant and non-pregnant women are about 40% and 30% respectively. The highest levels are in the Caribbean, reaching 60% in pregnant women on some islands *(51, 21)*.

Prevalence data for various age groups are not available for all countries. However, the prevalence rate among preschool children is usually similar to, or higher than, the rate among pregnant women. Epidemiological mapping of prevalence requires cut-off levels, or criteria for grading the public health severity of anaemia. Table 3 provides a provisional schema for this purpose.

In most industrialized countries, the prevalence of anaemia among pregnant women is around 20%. It is therefore considered reasonable to classify these populations as having a medium prevalence, since a prevalence of up to 5% may not necessarily be regarded as abnormal in any population.

Table 3. Proposed classification of public health significance of anaemia in populations on the basis of prevalence estimated from blood levels of haemoglobin or haematocrit [a]

Category of public health significance	Prevalence of anaemia (%)
Severe	> or = 40
Moderate	20.0 – 39.9
Mild	5.0 – 19.9
Normal	< or = 4.9

[a] *Based on cut-off levels of haemoglobin and haematocrit given in Table 6.*

5.2 Epidemiology

The prevalence of iron deficiency varies greatly according to host factors: age, gender, physiological, pathological, environmental, and socioeconomic conditions. Iron requirements and recommended iron intakes are summarized in Table 4, and the factors that influence them are discussed beginning on page 20.

Table 4. Iron requirements and recommended iron intakes by age and gender group

Groups	Age (*years*)	Mean body weight (*kg*)	Required iron intake for growth (*mg/day*)	Median iron losses (*mg/day*)	
				Basal	Menstrual
Children	0.5-1	9.0	0.55	0.17	
	1-3	13.3	0.27	0.19	
	4-6	19.2	0.23	0.27	
	7-10	28.1	0.32	0.39	
Males	11-14	45.0	0.55	0.62	
	15-17	64.4	0.60	0.90	
	18+	75.0		1.05	
Females	11-14[b]	46.1	0.55	0.65	
	11-14	46.1	0.55	0.65	0.48
	15-17	56.4	0.35	0.79	0.48
	18+	62.0		0.87	0.48
Post menopause		62.0		0.87	
Lactating		62.0		1.15	

[a] Total absolute requirements include requirement for growth, basal losses and, in female, menstrual losses.
[b] Non-menstruating.
[c] Bioavailability of dietary iron during this period varies greatly.

Table 4 (continued). Iron requirements and recommended iron intakes by age and gender group

Total absolute requirements[a] (*median*) (*mg/day*)	Recommended iron intakes to cover requirements of 97.5% of populations for diets of different bioavailability *(mean +2 SD) (mg/day)* Level of dietary iron bioavailabilty %			
	High 15%	Intermediate 12%	Low 10%	Very low 5%
0.72	6.2[c]	7.7[c]	9.3[c]	18.6[c]
0.46	3.9	4.8	5.8	11.6
0.50	4.2	5.3	6.3	12.6
0.71	5.9	7.4	8.9	17.8
1.17	9.7	12.2	14.6	29.2
1.50	12.5	15.7	18.8	37.6
1.05	9.1	11.4	13.7	27.4
1.20	9.3	11.7	14.0	28.0
1.68	21.8	27.7	32.7	65.4
1.62	20.7	25.8	31.0	62.0
1.46	19.6	24.5	29.4	58.8
0.87	7.5	9.4	11.3	22.6
1.15	10.0	12.5	15.0	30.0

Adapted from: Vitamin and mineral requirements in human nutrition, FAO/WHO (to be published)

Source: References *(4,73)*.

5.2.1 Age

Full-term infants are normally born with adequate iron stores in the liver and haematopoietic tissue, because of destruction of fetal red blood cells soon after birth. This leads to deposition of iron in these tissues, especially if the cord is ligated after it stops pulsating.

Breast milk is relatively low in iron, although the iron in breast milk is much better absorbed than that in cows' milk. Iron deficiency commonly develops after six months of age if complementary foods do not provide sufficient absorbable iron, even for exclusively breastfed infants.

Iron requirements on a body weight basis are proportional to growth velocity. Accordingly, in addition to women in their reproductive years as a result of physiological losses, iron deficiency is most common in the preschool years and during puberty. Another peak may occur in old age, when diets frequently deteriorate in quality and quantity.

5.2.2 Gender

Following menarche, adolescent females often do not consume sufficient iron to offset menstrual losses. As a result, a peak in the prevalence of iron deficiency frequently occurs among females during adolescence.

5.2.3 Physiological state

Substantial amounts of iron are deposited in the placenta and fetus during pregnancy. This results in an increased need of about 700-850 mg in body iron over the whole pregnancy.

Overall, iron absorption is increased during pregnancy, when menstruations stop. Pregnant women still do not absorb sufficient additional iron, however, and the risk of iron deficiency increases.

Lactation results in loss of iron via breast milk. Consequently, for some women a deficiency developed during pregnancy may be perpetuated during lactation. In terms of iron balance, however, lactational amenorrhea more than compensates for iron lost through breast milk.

5.2.4 Pathological state

Common infections, especially those which are chronic and recurrent, may impair haematopoiesis and consequently cause anaemia. Malaria by haemolysis and some parasitic infections, e.g. hookworm, trichuriasis, amoebiasis, and schistosomiasis (both vesical and intestinal forms), cause blood loss directly. This blood loss contributes to iron deficiency.

Other important causes of anaemia include genetic factors, e.g thalassemia, sickle cell trait, and glucose-6-phosphate dehydrogenase deficiency (G6PD). Because these genetic factors are not due to iron deficiency, they are not discussed in this guidebook.

These other causes of anaemia are mentioned, however, as a reminder that they should be considered when choosing and focusing on population groups for assessment and surveillance purposes. In this way, more appropriate interventions can be developed.

It should also be noted that these genetic conditions, except for thalassemia major - which is rare - do not prevent the development of iron deficiency, and may coincide with it.

5.2.5 Environmental factors

A given diet may be low in iron or may contain adequate amounts of iron which are of low bioavailability (see Chapter 8). Other nutrients necessary for haematopoiesis may also be deficient. These include folic acid, vitamins A, B_{12}, and C, protein, and copper and other minerals *(73).*

Trauma or childbirth can result in acute or chronic blood loss, with consequent iron deficiency and anaemia

5.2.6 Socioeconomic status

Iron deficiency is most common among groups of low socioeconomic status.

6 Assessment, surveillance, and indicators

6.1 Individual and population-based assessment

Surveillance of iron deficiency involves an ongoing process of recording and assessing iron status in an individual or a community. Worldwide, the most common method of screening individuals or populations for iron deficiency involves determining the prevalence of anaemia by measuring blood haemoglobin or haematocrit levels.

A major limitation of each of these two tests, however, lies in the fact that anaemia is not a specific indication of iron deficiency. As noted in Chapter 5, other nutrient deficiencies and most infectious diseases can also result in significant anaemia.

One common practice in assessing whether or not anaemia is due to iron deficiency involves monitoring the response in haemoglobin or haematocrit levels after 1 or 2 months of oral supplementation with iron. An increase of 10 g/l in haemoglobin or 3% in haematocrit is indicative of iron deficiency. Individual management in resource-poor countries is likely to be based mainly upon either haemoglobin or haematocrit assessment - or both - and upon their response to initial iron therapy.

Another limitation of haemoglobin or haematocrit measurements is that levels change only when they are very low at the outset, and when iron deficiency is already severe. In resource-adequate situations, the usual practice involves the use of further, specific, and more sensitive tests for individual assessment. These include serum ferritin, transferrin saturation, and others.

This guidebook, however, deals primarily with population-based assessments. It does not elaborate on the selection, specificity, and sensitivity of various tests for individual assessment.

6.2 Purposes of biological assessments

Biological assessments are made to:

- Determine the magnitude, severity, and distribution of iron deficiency and anaemia, and preferably its main causes. This information can serve as a basis for planning policies and interventions, and as a baseline against which to assess their impact.
- Identify populations more affected or at greater risk. This information enables national authorities to select priority areas for action, especially if resources are limited.
- Monitor trends in prevalence and evaluate the impact of interventions. Other programme indicators are also needed for monitoring programme implementation.
- Measure progress towards achieving the goals adopted by the International Community.
- Provide the basis for advocacy programmes for iron deficiency and anaemia prevention in affected and vulnerable populations.

The approaches used in surveillance range from the routine collection and analysis of indicators in health centres (especially antenatal clinics) and analysis of laboratory records, to periodic special community-based assessments and the integration of iron status or anaemia assessment in other population-based surveys.

Clinic-based data are generally not representative of an entire population. However, periodic assessments using the same methods in the same service context may enable trends to be effectively followed. Any assessment should include an analysis of factors causing or contributing to anaemia, in addition to iron deficiency.

6.3 Selection of subjects for assessment

6.3.1 Vulnerability

Vulnerability to iron deficiency varies greatly with each stage of the life cycle. This variation is due to changes in iron stores, level of intake, and needs relating to growth or iron losses. In general, children aged 6 months through 5 years of age *(74)* and women of childbearing age *(75)* - especially during pregnancy - are the most vulnerable groups.

Unless born preterm or with low birth weight, most infants are at low risk before 6 months of age because their iron stores are usually still adequate from the perinatal period. Accordingly, the earliest age to begin assessment of iron status is normally between 6 and 9 months; assessment may begin earlier (e.g. from 4 months) in communities with low iron status.

Among children under 5 years of age, the greatest prevalence of iron deficiency occurs during the second year of life, due to low iron content in the diet and rapid growth during the first year. In areas with a high prevalence of hookworm infestation, school-aged children as well as adults can also develop significant iron deficiency *(76).*

6.3.2 Accessibility

For monitoring purposes, infants and pregnant women are the most accessible groups because they frequently attend primary health care and maternal and child health clinics where assessments can be conducted. Non-pregnant women can sometimes be monitored through family planning services. School-aged children can be reached through school health services. Preschool children and adult men are the least accessible groups because they have no regular contact with the health care system.

6.3.3 Representativeness

For survey or surveillance purposes, the sampled population should be representative of those populations targeted for a universal or specific intervention programme. Although there are significant variations in iron status and prevalence of anaemia across age groups and strata, iron status across communities with similar dietary patterns tends to be comparable among those of the same socioeconomic status. Traditionally-designed nutritional surveys based on 30 to 60 clusters are adequate for assessing iron status.

Prevalence rates for one subgroup (by age or gender) cannot be used as a proxy for the rest of the population because risks of iron deficiency vary widely. In most developing countries, the prevalence of iron deficiency is high for both infants and women of childbearing age because of low iron intake relative to increased iron requirements.

In industrialized countries, however, infants are relatively more affected. Occasionally there are populations in which infants and preschool children have high rates of iron deficiency anaemia even though the rate is low among adult women *(77).* Dietary patterns of infants, preschool children, and adults in such situations are very different. Hence, high iron intake among adults offers no assurance of adequate iron in the diets of infants or preschool children.

In most settings where malaria, hookworm, or schistosomiasis are not significant contributors to anaemia in adults, high prevalence rates of iron deficiency anaemia are usually only found in women of childbearing age. Adult men who are free of diseases associated with blood loss are not appreciably affected by relatively low iron intake; they have lower normal iron requirements to compensate for iron losses *(78).*

6.4 General issues in defining iron status indicators

Even though there may be many causes of anaemia, dietary iron deficiency is usually either the main or a major contributing factor. Other significant nutritional deficiencies (e.g. low intakes of folic acid and vitamins A, B_{12}, and C) and infectious diseases (e.g. malaria and hookworm) may also contribute to anaemia.

Iron deficiency anaemia reflects the severe end of the spectrum of depletion. Where rates greater than 30-40% occur in a defined age-gender group, most non-anaemic individuals in that group will be sufficiently iron-deficient to be at risk of adverse functional consequences *(78).* In these situations, even without specific assessment or in the presence of other factors contributing to anaemia, the institution of a broad spectrum of interventions to improve the iron nutrition of vulnerable sub-populations is justified.

Several well-established laboratory indices for assessing and monitoring iron status are available. Of these, however, only haemoglobin or haematocrit tests can be routinely performed in field settings. More precise, multiple biochemical tests of iron status can only be conducted in resource-adequate countries or under special research or survey conditions *(79).*

The usefulness and limitations of using anaemia as a surrogate for iron status has been established by studies which have concurrently assessed iron status and performed other available iron-related tests. These other tests include mean corpuscular volume, mean corpuscular haemoglobin, serum ferritin, transferrin saturation, erythrocyte protoporphyrin, and (more recently) transferrin receptors.

6.5 The spectrum of iron nutritional status

In normal individuals, the iron used for haemoglobin formation accounts for about two-thirds of total body iron. In men, about one-third of body iron may be deposited as haemosiderin or ferritin in stores that can be mobilized when there occurs a need to supply iron in a functionally active form.

About 14% of iron is used for other vital physiological functions *(80).* In addition, a small pool of iron in plasma is in transit, and bound to the iron carrier transferrin *(81).*

Measurements of haemoglobin, serum ferritin, serum iron, and transferrin (total iron-binding capacity) enable iron status to be characterized in detail *(82).* However, each of these determinations has well-recognized limitations under field conditions, i.e. single or combined measurements of iron status show that response to therapeutic trials is greater than expected.

As previously noted, iron deficiency anaemia represents the extreme low end of the spectrum of iron status. The severity of anaemia is differentiated by the severity of the reduction in haemoglobin level.

The term “anaemia” is sometimes used synonymously with “iron deficiency anaemia”. Clearly, however, these terms do not cover the same reality. There are about 2-5 times more iron-deficient than iron-deficient-anaemic individuals. There are also many causes of anaemia besides iron deficiency, particularly in tropical regions.

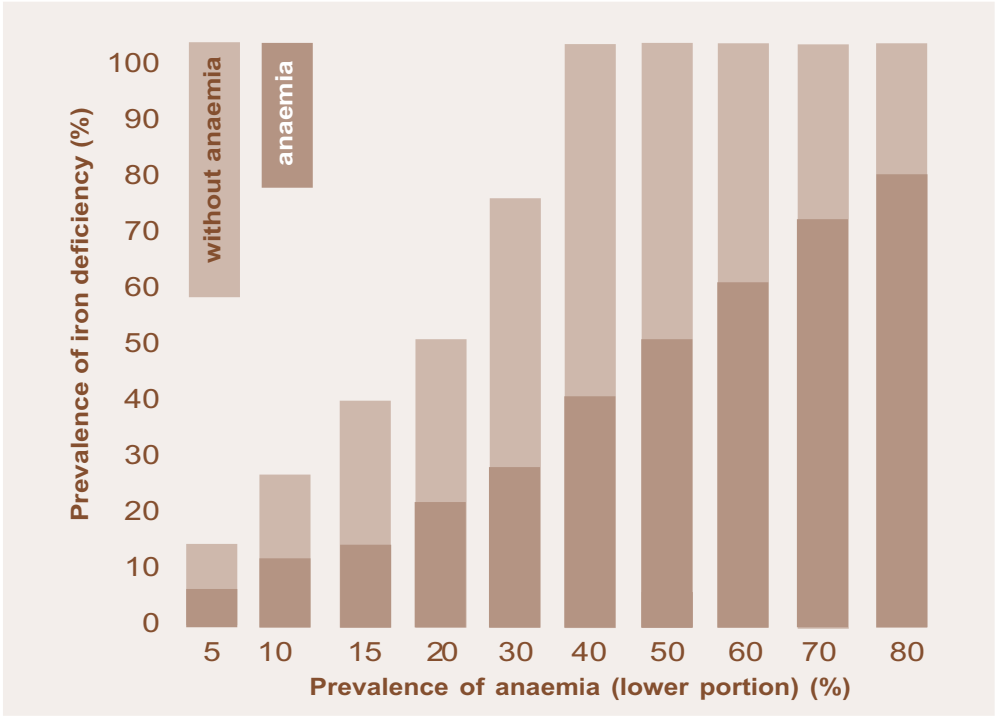
In any case, however, iron deficiency is the predominant nutritional deficiency causing anaemia and is present even when other causes of anaemia are recognized. There are, however, mild-to-moderate forms of iron deficiency in which anaemia is absent.

Data collected in US national surveys revealed that 30-40% of children under 5 years of age, and women of childbearing age who had evidence of iron deficiency, were also anaemic *(83).* This relationship provides a basis for estimating the prevalence of iron deficiency - with or without anaemia - by using the prevalence of iron deficiency anaemia.

Assuming that this relationship is valid for other populations with a higher prevalence of iron deficiency, some degree of iron deficiency would be present in about 50% of the population of these age and gender groups if anaemia prevalence exceeds 20%, and in virtually the entire population of the same age and gender groups if anaemia prevalence exceeds 40% (Figure 2).

In addition, the relative proportion of anaemia due to iron deficiency increases as the prevalence of anaemia increases. Up to a prevalence of iron deficiency anaemia of 40%, the prevalence of iron deficiency will be about 2.5 times that of anaemia.

Figure 2. Projected prevalence of iron deficiency based on prevalence of iron deficiency anaemia



Source: Yip R, based on the second US National Health and Nutrition Survey (NHANES II), and Pizarro et al. *(84).*

The hypothetical relationship noted above does not apply to prevalence rates for overall anaemia. Anaemia from other causes must be excluded before the proportion of the population that is iron-deficient can be derived from Figure 2.

The programmatic implications of this projection are as follows. When the prevalence of iron deficiency anaemia reaches the 20-30% level in the age-gender group under evaluation, it may be more effective - and possibly more efficient - to provide universal supplementation to that entire group than to screen for individual case-management purposes.

A decision analysis using the US national survey data reached a similar conclusion *(85)*. The same analysis also concluded that screening becomes ineffective by the time the prevalence of anaemia is lower than 5%, because most of the cases are not related to iron deficiency.

Screening for programmatic purposes should therefore be considered for anaemia prevalences between 5% and 20%. A prevalence within this range suggests appropriate interventions based on dietary modifications, provision of iron-fortified foods, targeted iron supplementation, and control of infections.

6.6 Application of iron-related indicators to specific settings

Variations in the prevalence of iron deficiency worldwide, the availability of laboratories for testing, and the occurrence of factors other than iron deficiency that cause anaemia, require that iron-related indicators be divided into three categories. These categories of indicators are applied in settings considered to be resource-poor, resource-intermediate, or resource-adequate. Resource-adequate settings correspond to the commonly-used term “developed country”, while the other two settings are usually classified as situations which are typical of “less developed” countries.

The reason for this differentiation lies in the wide variation of resources among and within “less developed” countries. For example, the towns and cities may be resource-intermediate while the rural areas more resource-poor.

Table 5 summarizes which iron status indicators to apply, according to resource availability. It is also assumed that the three levels of resources, i.e. poor, intermediate, and adequate, roughly correspond to the three degrees of severity of anaemia: severe, moderate, and mild.

Table 5. Assessing iron status on the basis of resource availability in a country

	Resource conditions[a]		
Level of resources	Poor	Intermediate	Adequate
Prevalence of anaemia	Severe	Moderate	Mild
	Clinical decisions		
Screening	Clinical examination[b]	Haemoglobin or haematocrit for screening	Haemoglobin or haematocrit for screening Additional tests[c]: *Serum ferritin* *Transferrin saturation*
Confirmation or diagnostic	Haemoglobin or haematocrit Clinical response to iron administration	Haemoglobin or haematocrit response to iron administration	Haemoglobin or haematocrit response to iron administration Serum ferritin Erythrocyte protoporphyrine Transferrin saturation Transferrin receptor
	Public health and population-based decisions		
Special assessment or survey	Haemoglobin or haematocrit	Haemoglobin or haematocrit Optional: *Mean cell volume* *Serum ferritin* *Transferrin saturation* *Erythrocyte protoporphyrine*[d]	Haemoglobin or haematocrit Mean cell volume Serum ferritin Transferrin saturation Erythrocyte protoporphyrine Transferrin receptor
Diagnosis of causes of anaemia		Response to iron supplement [e,f]	
Long-term surveillance	Haemoglobin or haematocrit from PHC or MCH centres	Haemoglobin or haematocrit from PHC or MCH centres at selected sites	Haemoglobin or haematocrit from clinics[g]

Footnotes to Table 5 *(opposite)*

a Relative terms that correspond approximately to the level of development according to UN Classification (United Nations Development Programme. *Human Development Report.* New York, Oxford University Press, 1999).

b Severe prevalence of anaemia (> 40%) justifies universal iron supplementation without screening individuals. The clinical assessment of anaemia lacks sensitivity and, therefore, a prevalence of 2%-3% of cases clinically detected represents a severe problem.

c Serum ferritin or transferrin saturation in addition to haemoglobin or haematocrit is of interest in individuals for detecting mild forms of iron deficiency or iron overload.

d Specific iron biochemistry tests may lose some sensitivity in populations that also have high rates of infections.

e Anaemia response to treatment for malaria or hookworm should be considered in areas with a known incidence of these conditions.

f Where nutritional deficiencies, such as of folic acid, vitamin C, or vitamin A, are believed to contribute to anaemia, multiple supplementation should be considered.

g Consistent use of the same procedures, (e.g. compilation of data from clinics, even if inadequate for statistical assessment) may nevertheless reveal trends useful for population surveillance.

7 Methods of assessing iron status

7.1 Assessment of anaemia

7.1.1 Criteria of anaemia

It is well known that normal haemoglobin distributions vary with age and gender, at different stages of pregnancy, and with altitude and smoking *(86,87)*. There is also evidence of a genetic influence. In the United States, for example, individuals of African extraction have haemoglobin values 5 to 10 g/l lower than do those of European origin. This contrast is not related to iron deficiency *(88)*.

The correct interpretation of haemoglobin or haematocrit values, therefore, requires the consideration of modulating factors in selecting appropriate cut-off values. Those values at sea level for haemoglobin and haematocrit corresponding to anaemia, are presented in Table 6. Table A3 in Annex 3 reflects haemoglobin and haematocrit levels at various altitudes.

Table 6. Haemoglobin and haematocrit levels below which anaemia is present in a population[a]

Age or gender group	Haemoglobin g/l	Haematocrit mmol/l	Haematocrit l/l
Children 6 months to 59 months	110	6.83	0.33
Children 5–11 years	115	7.13	0.34
Children 12–14 years	120	7.45	0.36
Non-pregnant women (above 15 years of age)	120	7.45	0.36
Pregnant women	110	6.83	0.33
Men (above 15 years of age)	130	8.07	0.39

[a] Conventional conversion factors: 100 g haemoglobin = 6.2 mmol haemoglobin = 0.30 l/l haematocrit. Adapted from reference *(89)*, by splitting the age group for children 5-14 years and applying a haemoglobin cut-off level for those 5-11 years which has been lowered by 5 g/l to reflect the findings in non-iron-deficient children in the USA (cf. Table A1 in Annex 3).

Severe anaemia in pregnancy is defined as haemoglobin <70 g/l and requires medical treatment. Very severe anaemia is defined as haemoglobin <40 g/l. Very severe anaemia in pregnant women is a medical emergency due to the risk of congestive heart failure; maternal death rates are greatly increased.

Annex 3 provides age-related criteria for normal haemoglobin and haematocrit levels developed by the Centers for Disease Control and Prevention in Atlanta, USA *(79)*. Criteria for stages of pregnancy, and adjustment factors for altitude and smoking are also provided. For populations of African extraction, recent analysis indicates that achieving a similar screening performance (sensitivity and specificity) requires a haemoglobin criterion that is 10 g/l (0.62 mmol/l) lower than those shown in Table 6 *(90,91).*

7.1.2 Clinical examination to detect severe anaemia

Severe anaemia is a major risk factor associated with greatly increased morbidity and mortality for young children and pregnant women. Prompt recognition of the condition, and treatment and clinical follow-up of individuals, are crucial in avoiding complications such as high-output heart failure. Subjects with severe anaemia can usually be detected by clinical examination for significant pallor of the eyelids, tongue, nail beds, and palms.

For clinically detecting haemoglobin levels of 50-80 g/l during childhood, a sensitivity and specificity of 60%-70% is reported. For those <50 g/l, a sensitivity of 93% and a specificity of 57% is reported *(92)*. Among Ethiopian refugee women in Somalia, a sensitivity of 53% and specificity of 91% are reported *(78).* In young children, palm pallor is preferred to eyelid pallor as a clinical diagnostic sign, due to the frequency of conjunctivitis which causes redness even in anaemic subjects.

In resource-poor settings where routine laboratory testing of haemoglobin or haematocrit is not feasible, clinical signs should be regularly used to screen individual women and children. The purpose of this screening should be to identify high-risk subjects before the onset of life-threatening complications.

Considering the increased risk of human immunodeficiency virus (HIV) transmission via blood transfusion, and the risk of short-term mortality from transfusion itself *(93),* clinical examination to identify and manage cases of severe anaemia may provide one strategy to reduce the need for transfusion. The use of clinical indicators is recommended for screening for treatment of subjects with severe anaemia, but it is not recommended for population-based surveys of anaemia.

7.1.3 Haemoglobin measurement

The prevalence of anaemia in a population is best determined by using a reliable method of measuring haemoglobin concentration *(94).* Compared with the cost and difficulty of biochemically assessing the prevalence of iodine deficiency and vitamin A deficiency, the determination of the prevalence of anaemia in a population is relatively simple and inexpensive.

The only methods generally recommended for use in surveys to determine the population prevalence of anaemia by haemoglobinometry are the cyanmethemoglobin method in the laboratory and the HemoCue system.

The cyanmethemoglobin method for determining haemoglobin concentration is the best laboratory method for the quantitative determination of haemoglobin. It serves as a reference for comparison and standardization of other methods *(94).*

A fixed quantity of blood is diluted with a reagent (Drabkins solution) and haemoglobin concentration is determined after a fixed time interval in an accurate, well-calibrated photometer.

The HemoCue system is a reliable quantitative method for determining haemoglobin concentrations in field surveys *(95),* based on the cyanmethemoglobin method. The HemoCue system consists of a portable, battery-operated photometer and a supply of treated disposable cuvettes in which blood is collected.

The system is uniquely suited to rapid field surveys because the one-step blood collection and haemoglobin determination do not require the addition of liquid reagents. Survey field staff without specialized laboratory training have been successfully trained to use this device.* This equipment can be obtained through UNICEF.

The HemoCue system gives satisfactory accuracy and precision when evaluated against standard laboratory methods *(96)*. Long-term field experience has also shown the instrument to be stable and durable. These features make it possible to include haemoglobin determinations in multipurpose health and nutrition surveys.

* In 1998, the cost of the photometer was approximately US$320 and a supply of disposable cuvettes US$0.30 per test.

There exists a range of other quantitative and semi-quantitative methods for determining haemoglobin concentration. A report of the strengths and weaknesses of the various methods that may have an application in clinical practice is available.[1] Again, however, only the two methods described above are generally recommended.

7.1.4 Haematocrit or packed cell volume

Haematocrit or packed cell volume is a commonly performed clinical assessment frequently used in surveys of anaemia because of its simplicity and the widespread availability of the necessary equipment. Haematocrit measurement is an acceptable and recommended method for anaemia determination, but has no advantage compared to haemoglobin measurement. Moreover, reliable haematocrit determination requires a stable power supply.

For haematocrit determination, blood is collected in anticoagulant-treated capillary tubes and spun in a small, specially designed centrifuge. The volume of packed cells as a portion of the total volume of blood is measured and expressed as l/l whole blood.

Many referral hospitals have electronic cell counters. Provided that they are well calibrated and maintained, these devices can yield rapid and reliable indications of mean cell volume (MCV) and the number of red blood cells (RBC) from which a "calculated haematocrit" (MCV x RBC concentration) can be obtained. In general, centrifuge haematocrit and calculated haematocrit based on electronic counters are closely matched.

Although in most populations the prevalence of anaemia determined by using haematocrit or haemoglobin concentration (using the cut-off values given in Table 6), will be similar, results may not be identical. This difference in anaemia prevalence, obtained by using these two methods, may add to the complexity of a survey report and make the results more difficult for decision-makers to interpret. Accordingly, there is little advantage in determining haematocrit as well as haemoglobin during surveys.

A potential source of error in haemoglobin and haematocrit determination lies in inadequate technique in obtaining capillary blood. Care must be taken to ensure adequate puncture of the tissue and spontaneous blood flow from the wound. The key to accuracy is blood sampling from finger- or heel-prick *(97).*

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[1] *Anemia detection in health services. Guidelines for Program Managers, 2nd edition.* Program for Appropriate Technology in Health (PATH), OMNI, USAID, December 1996.

7.2 Specific tests or procedures for assessing iron status

Iron status can be determined by several well-established tests in addition to measurement of haemoglobin or haematocrit. Unfortunately, however, there is no single standard test to assess iron deficiency without anaemia. The use of multiple tests only partially overcomes the limitation of a single test *(79)* and is not an option in resource-poor settings.

Moreover, iron-related tests do not all correlate closely with one another because each reflects a different aspect of iron metabolism *(98).* In anaemic individuals, such tests are used to confirm or help clarify the type or cause of anaemia.

Although these tests are utilized for special surveys in populations, they are not routinely conducted on a large scale because of their relatively high cost. This cost usually limits their use to settings with adequate resources. Even where feasible, most iron biochemical tests are of limited use in resource-poor settings. In such situations, other nutrient deficiencies and high rates of infections can interfere with the interpretation of such tests relative to iron status.

The following sections describe specific tests or procedures for assessing iron status.

7.2.1 Serum ferritin

The serum ferritin level is the most specific biochemical test that correlates with relative total body iron stores. A low serum ferritin level reflects depleted iron stores and hence is a precondition for iron deficiency in the absence of infection. Serum apoferritin is an acute-phase reactant protein and is therefore elevated in response to any infectious or inflammatory process. Consequently, serum ferritin in the normal range reflects only iron sufficiency in the absence of these conditions. Interpretation of serum ferritin levels is thus problematic in populations in which, with the exception of parasitic infections and malaria, the incidence of infection or inflammation is high.

Interpretation of serum ferritin as an indicator of the relative extent of depletion of iron stores is presented in Table 7 (following page). The generally accepted cut-off level for serum ferritin, below which iron stores are considered to be depleted, is <15 μg/l. Kits used for serum ferritin determination should be carefully calibrated against the WHO standard shown in Table 7.

Table 7. Relative extent of iron stores on the basis of serum ferritin concentration

Iron stores	Serum ferritin (μg/l)			
	Less than 5 years of age		*More than 5 years of age*	
	Male	*Female*	*Male*	*Female*
Depleted iron stores	< 12	< 12	<15	<15
Depleted iron stores in the presence of infection	< 30	< 30	-	-
Severe risk of iron overload	-	-	> 200 (adult male)	>150 (adult female)

Significant variations in serum ferritin levels relating to vulnerability to iron deficiency occur across age and gender groups. Infants, young children, and pregnant women usually have serum ferritin values near or in the range reflective of depletion; however, a low level *per se* does not imply functional iron deficiency. Only when the mobilizable iron supply for physiological function is inadequate is iron deficiency considered present.

Serum ferritin measurement is the preferred method for detecting depleted iron stores. However, it is of limited usefulness during pregnancy because it diminishes late in pregnancy, even when bone marrow iron is present.

7.2.2 Erythrocyte protoporphyrin

Levels of erythrocyte protoporphyrin, the precursor of haem, become elevated when the iron supply is inadequate for haem production. With adequate iron, erythrocyte protoporphyrin levels, like those of haemoglobin, are maintained within a well-defined normal range in healthy individuals. Table 8, on the following page, reflects the several equivalent units in which erythrocyte protoporphyrin cut-off levels can be expressed. In general, an elevated erythrocyte protoporphyrin level correlates well with low serum ferritin, and can serve to screen for moderate iron deficiency without anaemia *(99).*

Three commonly encountered conditions, in addition to iron deficiency, can cause a significant elevation of erythrocyte protoporphyrin: infection or inflammation, lead poisoning, and haemolytic anaemia. For this reason, the measurement of erythrocyte protoporphyrin is most useful in settings where iron deficiency levels are common and where infections, lead poisoning and other forms of anaemia are rare.

Until recently, erythrocyte protoporphyrin was measured by a complex and costly procedure that limited its use to that of a reference method. A simplified haematofluorometer that directly measures erythrocyte protoporphyrin fluorescence is now available. This device has enabled the widespread use of erythrocyte protoporphyrin testing in outpatient settings in the USA *(100).*

The severity of iron deficiency on the basis of erythrocyte protoporphyrin measurement is reflected in Table 8, below. Erythrocyte protoporphyrin levels are considered normal if only mild iron depletion is present (i.e. with serum ferritin levels of 12-24 mg/l). In the absence of infection, measurement of erythrocyte protoporphyrin is the preferred method for detecting iron deficiency once serum ferritin drops below the cut-off value, indicating inadequate iron supply to tissues.

Table 8. Changes in iron status by age group on the basis of erythrocyte protoporphyrin

Iron status	Erythrocyte protoporphyrin	
	< 5 years of age	*⊕ 5 years of age*
Iron overload or excess	Normal	Normal
Normal	Normal	Normal
Mild iron deficiency without anaemia	Normal	Normal
Moderate iron deficiency without anaemia	>70 µg/dl red blood cell >2.6 µg/g haemoglobin >61 mmol/mol haem	>80 µg/dl red blood cell >3.0 µg/g haemoglobin >70 mmol/mol haem
Severe iron deficiency with anaemia	>70 µg/dl red blood cell >2.6 µg/g haemoglobin >61 mmol/mol haem	>80 µg/dl red blood cell >3.0 µg/g haemoglobin >70 mmol/mol haem

7.2.3 Serum iron, transferrin, and transferrin saturation

Iron deficiency results in a reduction in serum iron (SI) levels, an elevation in transferrin (total iron-binding capacity [TIBC]) levels, and hence a net reduction in transferrin saturation (i.e. SI/TIBC). However, the diurnal variation both in serum iron and transferrin saturation is considerable. In addition, there is a marked overlap in these indices between normal and iron-deficient subjects. This overlap diminishes the usefulness of these indices in establishing or rejecting a diagnosis of iron deficiency.

Transferrin saturation is of great value, however, as the first screening step for hereditary haemochromatosis. Cut-off values of between 60% and 70% have been widely used for this purpose. In screening for iron deficiency, individuals with more marked anaemia (responding to iron therapy with a haemoglobin increase >20 g/l) usually have a transferrin saturation <16%.

7.2.4 Serum transferrin receptors

The measurement of serum transferrin receptors is a recent addition to the available selection of tests for iron deficiency. However, epidemiological studies have yielded limited information concerning the usefulness of this test in discriminating between iron-deficient and iron-replete subjects.

An increase in serum transferrin receptors is a sensitive response during the early development of iron deficiency. Serum transferrin receptor levels increase progressively as the supply of iron to the tissues becomes progressively more deficient *(101).*

Major advantages of measuring serum transferrin receptors involve the facts that the assay is not significantly affected by infection or inflammatory processes, and it does not vary with age, gender, or pregnancy *(102, 103).* However, serum transferrin receptor levels may be elevated when there is increased red cell production, turnover, or both, such as in the case of haemolytic anaemia *(104).*

There are several methods for measuring serum transferrin. The most commonly used method is based on the ELISA assay (enzyme-linked immunosorbant assay). The values obtained will vary according to the method used, however, since there is no uniform standard available for their measurement. Similarly, there is currently no universally agreed reference value for serum transferrin.

7.2.5 Red cell indices

Among all the red cell indices measured by electronic blood counters, mean corpuscular volume and mean corpuscular haemoglobin are the two most sensitive indices of iron deficiency. Reduction in mean corpuscular volume occurring in parallel with anaemia is a late phenomenon in the development of iron deficiency. Reference values for mean corpuscular volume and mean corpuscular haemoglobin are presented in Table A5 in Annex 3.

7.2.6 Bone marrow iron stain

A bone marrow stain for iron has been regarded as the reference against which to evaluate other iron tests. Absence of stainable iron reflects absent iron stores. For this reason, the bone marrow stain correlates best with serum ferritin, which is another measure of iron stores *(105)*. For obvious reasons, bone marrow iron-staining is not useful in simple population-based surveys.

7.3 Defining iron deficiency when multiple indices are available

As shown in Tables 6-8 in this Chapter, and Tables A1-A5 in Annex 3, there are for different population groups generally accepted cut-off values to define "iron deficiency" for each specific test described in the preceding sections. As indicated above, however, each test has limitations in terms of its sensitivity and specificity.

The best indicator for detecting iron deficiency is serum ferritin when measured in the absence of infection. Under the same conditions, elevated erythrocyte protoporphyrin indicates iron-deficient erythropoiesis or elevated levels of lead. However, erythrocyte protoporphyrin is less specific than serum ferritin. Transferrin saturation is even less reliable as an indicator of iron deficiency because of intra- and inter-day variability in serum iron. Mean corpuscular haemoglobin begins to decrease when iron reserves are depleted and iron deficiency has developed. However, mean corpuscular haemoglobin may not reach abnormally low levels until some time after iron deficiency sets in.

As a consequence of the limitations of each test, when they are considered jointly to define iron deficiency, sensitivity is low although specificity increases. Examples of such joint consideration include the model based on low transferrin saturation and high erythrocyte protoporphyrin, and the ferritin model based on low serum ferritin and transferrin saturation and high erythrocyte protoporphyrin.

These models underestimate iron deficiency as observed by haemoglobin response to iron administration. They therefore present no advantage over measurement of serum ferritin for diagnosing iron deficiency in populations.

A definition of iron deficiency based on multiple indicators is useful for population-based assessment when it is feasible to measure several indices. The best combination would be haemoglobin, serum transferrin receptors, and serum ferritin or bone-marrow iron. Such a combination would reflect functional impairment, tissue avidity for iron, and iron storage, respectively. Usually, this approach is not feasible in settings with resource constraints (see Table 5).

7.4 Haemoglobin response to iron and other supplements or interventions

One established approach to the diagnosis of iron deficiency in individuals or populations involves monitoring changes in haemoglobin or haematocrit after oral iron supplementation *(106).* An increase of at least 10 g/l in haemoglobin or 0.03 l/l in haematocrit after 1 or 2 months of supplementation is indicative of iron deficiency.

In settings where there are multiple causes of anaemia, iron supplementation may only partially correct the haematological deficit. For example, a combined iron and vitamin A supplement for pregnant women in Indonesia was needed where both deficiencies were common *(107).* Table 9 shows the response according to the combination of supplements given.

Table 9. Proportion of anaemic pregnant women who responded to oral iron and vitamin A supplements and became non-anaemic

Treatment	*Number of subjects*	*Anaemic cases that responded (haemoglobin >110 g/l*
Placebo	62	16%
Vitamin A only	63	35%
Iron only	63	68%
Iron and vitamin A	63	97%

Source: Suharno et al. *(107)*

This Indonesian example illustrates the importance of assessing the potential multiple etiology of anaemia. This is necessary in populations with a high prevalence of possible etiologic factors, in order to decide whether multiple interventions are needed concurrently. These concurrent interventions may involve the use of other micronutrients in addition to iron; or the control of malaria, hookworm, or other infections; or both.

7.5 Assessing population iron status by using haemoglobin distributions

Estimates of haemoglobin are commonly included in nutrition surveys of children, whereas surveys specific for anaemia usually examine both children and women. The prevalence of anaemia serves as an index of the severity of iron deficiency in the whole population.

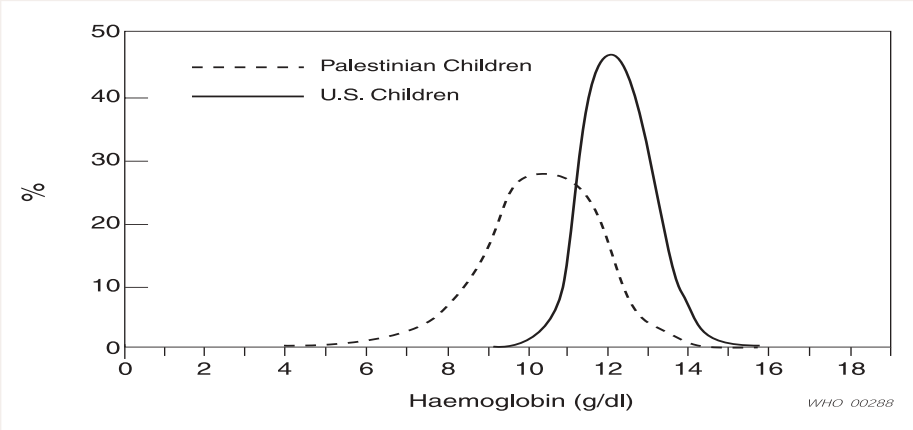
Where multiple factors may contribute significantly to anaemia, it is possible to differentiate anaemia attributable to iron deficiency from anaemia due to other factors. The latter include deficiencies of folic acid, vitamins A, $B_{12,}$ and C; or infections including malaria, hookworm, and schistosomiasis. This differentiation can be achieved by observing blood smears, by means of a small supplementation trial, or by conducting specific tests.

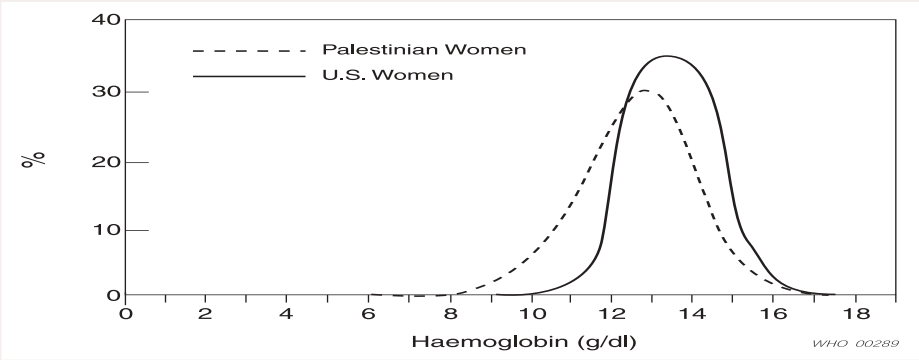
Where poor availability of dietary iron is the main etiologic factor, children and women are disproportionately affected, while the haemoglobin levels of adult men are virtually unaffected. Where other factors contribute significantly, adult men are less likely to be spared.

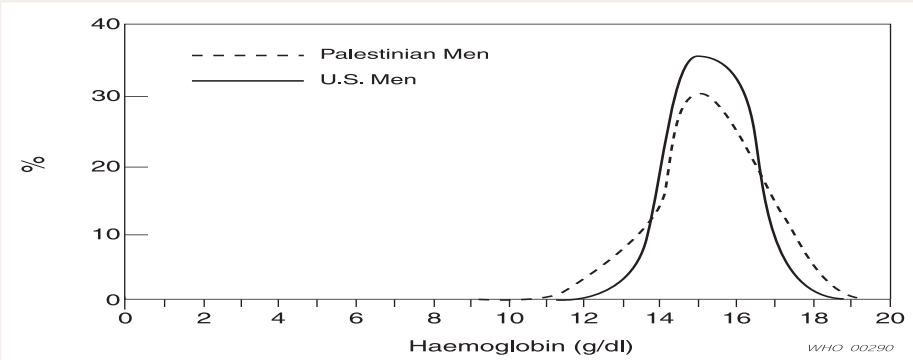
A useful approach inolves comparison of the haemoglobin distribution among children, women, and men from the population under study with a non-anaemic reference population. This approach allows inferences to be made as to which factors are likely to be responsible for a high anaemia prevalence.

One example involves the comparison of haemoglobin distributions among children, women, and men in a Palestinian refugee population in which iron deficiency was the sole cause of anaemia. Another involves an Ethiopian refugee population in which a combination of both iron and vitamin C deficiencies coexisted, with the vitamin C deficiency affecting men as well as women and children. Figures 3a and 3b *(78)* on the following two pages compare the haemoglobin distributions for each of these two refugee populations with US reference distributions.

Figure 3a. Haemoglobin distribution in Palestinian vs US children, women, and men

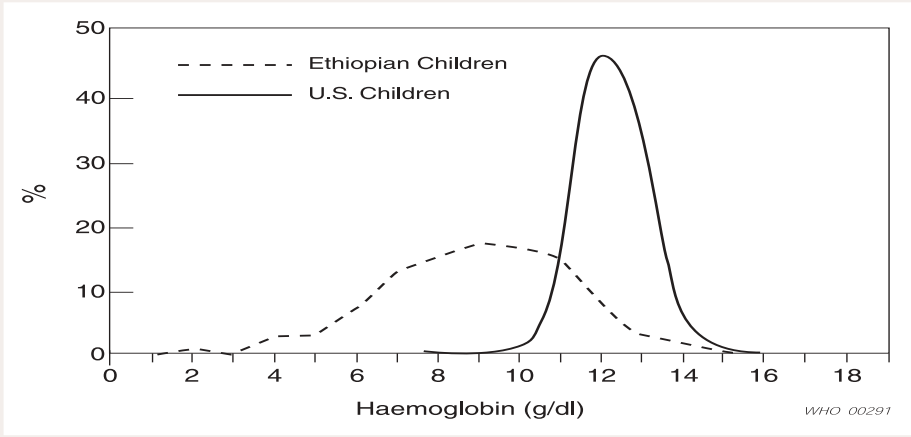


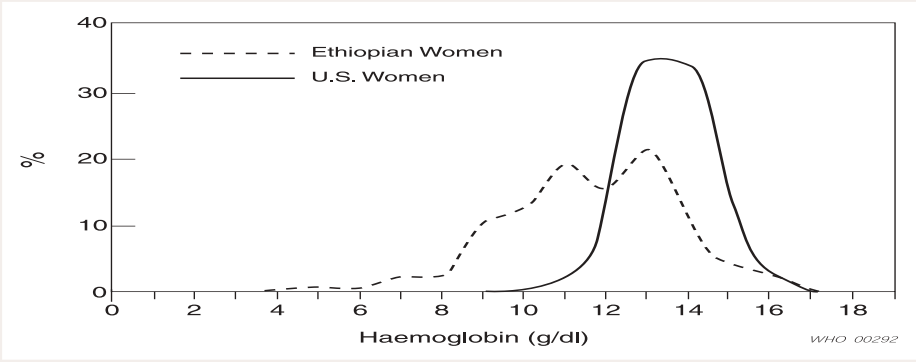


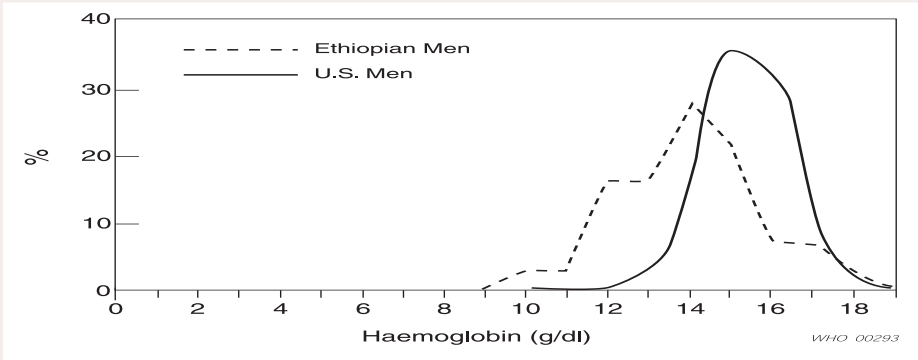


Source: Yip (78)

Figure 3b. Haemoglobin distribution in Ethiopian vs US children, women, and men







Source: Yip (78)

8 Prevention strategies

Iron deficiency, like most nutritional deficiencies of public health concern, is mainly a consequence of poverty. Even in developed countries, it affects a significant proportion of people in groups which are particularly vulnerable.

Prevention strategies must, if they are to be sustainable, involve the input and resources of a wide range of sectors and organizations. This is especially true for iron deficiency. For example, the agriculture, health, commerce, industry, education, and communication sectors should be included in any strategy. These, in turn, should work in concert with communities and with local nongovernmental organizations.

Efforts should be targeted to:

- reduce poverty;
- improve access to diversified diets;
- improve health services and sanitation; and
- promote better care and feeding practices.

These are fundamental elements of any programme to improve nutritional well-being in general, but are especially important in the improvement of iron status in particular.

8.1 Food-based approaches

8.1.1 Dietary improvement

Food-based approaches represent the most desirable and sustainable method of preventing micronutrient malnutrition. Such approaches are designed to increase micronutrient intake through the diet.

Food-based approaches should therefore include strategies to:

- improve the year-round availability of micronutrient-rich foods;
- ensure the access of households, especially those at risk, to these foods; and
- change feeding practices with respect to these foods.

One of the greatest strengths of these food-based strategies lies in their potential to result in multiple nutritional benefits. These benefits can, in turn, achieve both short-term impact and long-term sustainability.

In practice, food-based approaches should first address the production, preservation, processing, marketing, and preparation of food. Secondly, they should address feeding practices, such as intra-family food distribution and care for vulnerable groups.

Applied to iron deficiency, efforts should be directed towards promoting the availability of, and access to, iron-rich foods. Examples include meat and organs from cattle, fowl, fish, and poultry; and non-animal foods such as legumes and green leafy vegetables.

Similarly, focus should be upon foods which enhance the absorption or utilization of iron. Examples include those of animal origin, and non-animal foods - such as some fruits, vegetables, and tubers - that are good sources of vitamins A and C, and folic acid. Finally, effective nutrition education - and information on health and nutrition for both supply and demand aspects of programmes - may be needed to increase the demand for and consumption of such foods.

The first step in this process involves obtaining and analysing information on the various foods consumed and on the way they are processed, mixed, and prepared for a meal. Annex 4 suggests proposed strategies for obtaining such information, adapted from the approach currently used with success in some programmes to promote consumption of foods rich in vitamin A.

The interpretation of values concerning iron status which have been obtained using this methodology will vary according to the bioavailability of iron from local food mixtures and meal patterns. Accordingly, this approach should be adapted to, and its value assessed under, local conditions.

Once all the information has been analysed, appropriate recommendations can be made for changing dietary components and the timing of their consumption, altering food processing or preparation, or changing meal patterns. The focus should be on changes that will improve the bioavailability, as well as the amount, of iron in the diet.

Interpretation of bioavailability is limited by the scarcity of accurate information concerning the content of phytates and iron-binding polyphenols in various foods. Such information is urgently needed to facilitate the promotion of correct food choices.

Recommendations should be adapted to regional and local variations in diet, the age group concerned, seasonal availability, and other factors that cause food intake and meal patterns to vary. It should be noted that food-frequency questionnaires are not a sufficient base from which to draw inferences on likely iron status unless they are combined with information on meal composition and food consumption patterns.

Methods of food preparation and processing influence the bioavailability of iron. Cooking, fermentation, or germination can, by thermal or enzymatic action, reduce the phytic acid and the hexa- and penta-inositol phosphate content. All inositol phosphates inhibit iron absorption in proportion to the total number of phosphate groups. Processing procedures that lower the number of phosphate groups improve bioavailability of non-haem iron *(108).*

Building food-based approaches around the needs and activities of women can be especially effective. This is particularly important in recognition of the multiple roles women play as food providers and primary caregivers.

For example, promoting home gardens and small animal husbandry, and improving food preservation and home or community processing technologies, can be especially useful in improving iron status. These interventions are enhanced by efforts to generate additional income for women and by effective nutrition education.

The primary goal of dietary modification to improve and maintain the iron status of a population involves changes in behaviour, leading to an increase in the selection of iron-containing foods and a meal pattern favourable to increased bioavailability. Although sometimes difficult to achieve, such changes in dietary habits can bring about important sustainable improvements, not only in iron status but also for nutrition in general. Such changes must be rooted in issues that take into account food security, actual availability, and education.

Bioavailability of food iron is strongly influenced by enhancers and inhibitors in the diet. Presently, there is no satisfactory *in vitro* method for predicting the bioavailability of iron in a meal.

Iron absorption can vary from 1% to 40%, depending on the mix of enhancers and inhibitors in the meal. Therefore, the adequacy - i. e. bioavailability - of iron in usual diets can be improved by altering meal patterns to favour enhancers, lower inhibitors, or both.

Enhancers of iron absorption include:

- haem iron, present in meat, poultry, fish, and seafood;
- ascorbic acid or vitamin C, present in fruits, juices, potatoes and some other tubers, and other vegetables such as green leaves, cauliflower, and cabbage; and
- some fermented or germinated food and condiments, such as sauerkraut and soy sauce (note that cooking, fermentation, or germination of food reduces the amount of phytates).

Inhibitors of iron absorption include:

- phytates, present in cereal bran, cereal grains, high-extraction flour, legumes, nuts, and seeds;
- food with high inositol content;
- iron-binding phenolic compounds (tannins); foods that contain the most potent inhibitors resistant to the influence of enhancers include tea, coffee, cocoa, herbal infusions in general, certain spices (e.g. oregano), and some vegetables; and
- calcium, particularly from milk and milk products.

Examples of simple but effective alterations in meal patterns that enhance iron absorption might include:

- separate tea drinking from mealtime - one or two hours later, the tea will not inhibit iron absorption because most of the food will have left the stomach;
- include in the meal fruit juices such as orange juice, or another source of ascorbic acid such as tubers, cabbage, carrots, or cauliflower;
- consume milk, cheese, and other dairy products as a between-meal snack, rather than at mealtime; and
- consume foods containing inhibitors at meals lowest in iron content, e.g. a breakfast of a low-iron cereal (bread or corn tortilla) consumed with tea or milk products; this meal pattern can provide adequate calcium without hampering iron nutrition.

Other actions that indirectly affect iron status might include:

- parasitic disease control programmes, in particular those directed to hookworm, schistosomiasis and malaria control; these programmes can enhance iron deficiency anaemia control programme effectiveness in a population with moderate to severe levels of infection; and
- incentive policies and improved farming systems that favour the development, availability, distribution, and use of foods that enhance iron absorption.

A step-by-step practical approach, that might be followed in any setting, would be to:

- assess food availability and eating practices, and describe a typical daily meal pattern with emphasis on populations at highest risk;
- analyse the content of the foods and meals, in terms of iron and potential enhancers and inhibitors;
- estimate bioavailability *(109);*
- determine ways in which nutritional status can be modified, through composition of meals (given local food availability, costs, and cultural factors); timing of the consumption of certain foods; and food preparation practices;
- implement appropriate dietary modifications; and
- assess iron status (haemoglobin or haematocrit levels) before and after implementing modified practices.

Indicators of the progress of programme implementation through dietary improvement should be developed and interpreted locally and nationally. These indicators should be periodically reviewed and adapted to reflect changing programme needs. The indicators should be simple and inexpensive, in order to be feasible. One or two indicators to monitor each primary type of intervention are likely to be sufficient. Rapid appraisal techniques are often appropriate for this purpose.

8.1.2 Food fortification

There is a consensus that enrichment (or fortification) of food is an effective long-term approach to improving the iron status of populations. Once a fortification programme is established, it is a cost-effective and sustainable means of achieving this purpose. The technical, operational, and financial feasibility should, however, be carefully assessed before embarking on such a fortification programme.

An effective iron fortification programme requires the cooperative efforts of governments, the food industry (producers, processors, and marketers) and consumers. Appropriate food vehicles and fortificants must be selected.

Legislation that permits, regulates, or requires the addition of iron fortificants to foods is essential, as are effective enforcement mechanisms. Legislative action to ensure the quality and safety of iron-fortified foods, and honest and fair practices in marketing them, may also be needed.

Essential requirements for implementing fortification strategies include the identification of an appropriate food vehicle that reaches the target population, that is centrally processed, and that is widely available and consumed in relatively predictable amounts by vulnerable population groups. It is essential that the final product not be significantly changed in terms of its organoleptic quality, shelf life, or price; and that the food as prepared be acceptable to the population.

The dietary habits of the population are an important consideration in selecting a food for fortification. For example, possible appropriate food vehicles range from wheat flour or pasta and condiments like sugar, salt, curry powder, haldi, monosodium glutamate (MSG), to bouillon cubes and soy sauce.

In subsistence farming areas in most developing countries, a fortified-food approach has limited potential because few households ever consume commercially processed foods. Instead, fortified food supplements can be effectively and widely distributed through general food distribution programmes, e.g. school lunch or other supplemental or emergency feeding programmes.

Several iron fortificants have been used successfully in a variety of national programmes. Examples are as follows.

- Rice in the Philippines is fortified with a standard ferrous sulphate mix.
- Where bread and pasta are abundantly consumed, and flour is milled in only a few places, several iron fortificants have been added successfully during the milling process. Ferrous sulphate is adequate if the turnaround time between milling and bread consumption is relatively short (3 to 4 months), as in Chile.

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- If flour (wheat or maize) is stored for a long time, metallic iron (Sweden, UK, and USA) or ferrous fumarate (Venezuela) have been used. When flour is used as a vehicle, the general population is the target group, but this approach does not reach infants and young children, who usually consume little bread.

Iron-EDTA

Sodium iron ethylenediaminetetraacetic acid (NaFeEDTA), known as iron-EDTA, is a potentially valuable fortificant that has hitherto had limited use. Compared to other fortificants, it is better absorbed and not sensitive to many food iron inhibitors. Accordingly, it is particularly interesting in populations whose staple foods are based on cereals and legumes.

Because iron-EDTA is well absorbed and not reactive, it does not cause fat (e.g. in bread) to become rancid. Therefore, it is suitable for use in other (not previously fortified) foods. It is also chemically stable, which allows for long storage of foods. Condiments such as curry powder in South Africa have been successfully fortified with iron-EDTA, as has sugar in Guatemala *(110)*. However, additional information is needed on its efficacy and safety before it can be recommended.

Studies on multiple fortification have been boosted by the advent of several new technologies including the development of iron-EDTA. Double fortification with iron-EDTA and vitamin A in Guatemala *(110)* and with iodide and metallic iron in India *(111)* has already been examined.

The concern that iron-EDTA might inhibit bioavailability (i.e. that it might promote the loss) of other minerals such as zinc or calcium, is allayed by studies in humans with stable isotope tracers *(112)*. In a long-term study in Guatemala, zinc blood levels actually rose after 30 months following the consumption of iron-EDTA fortified sugar *(110*).

In fact, other animal and human data confirm improved absorption of zinc-iron-EDTA. However, further research is necessary to understand how iron-EDTA interacts with other micronutrients.

In some industrialized countries, EDTA has been extensively used as a stabilizer. The Joint FAO/WHO Expert Committee on Food Additives (JECFA) examined the existing data on iron-EDTA and found no objection to its use at a level of 2.5 mg/kg of body weight per day *(113)*.

Fortified foods for young children

Normal-birth-weight infants who are exclusively breastfed do not need iron supplements for the first 4 to 6 months of life. When complementary feeding begins, and certainly after 6 months of age, infants need an additional source of iron to maintain adequate iron nutrition and prevent iron deficiency anaemia.

Since cereals are widely used as early complementary foods, they should be fortified during their commercial preparation, by extrusion, cooking, or mixing processes. Centrally processed milk-based foods designed for infants and preschool children should also be fortified. Other forms of iron have been used for infant cereals: small-particle-size metallic iron is the form most widely used.

An iron complex with ammonium-orthophosphate - which is less reactive and has better absorbability - is used successfully in Sweden, and its use should be explored elsewhere. Iron pyrophosphate and orthophosphate should not be used, because of their poor bioavailability.

Finally, the practice of including iron-rich complementary foods for young children should be encouraged, both at home and in the community. Ferrous sulphate is the most widely used fortificant for cows' milk or modified infant formula.

Emergency foods

In emergency situations, the provision of food supplements that are adequate in energy and protein but not in essential micronutrients, may provoke or aggravate micronutrient deficiencies. For example, while the growth of young children may be enhanced, without provision of the additional micronutrients needed to support that growth, clinical deficiencies may be precipitated.

As recommended by the WHO/FAO International Conference on Nutrition (Rome, 1992), the nutrient content of emergency food aid for refugees and displaced persons should

> *meet the nutritional requirements, if necessary through fortification or ultimately through supplementation. Governments, in collaboration with the international community, should provide sustainable assistance to refugees and displaced persons, giving high priority to the prevention of malnutrition and the outbreak of micronutrient deficiency diseases.*

Such fortification might include not only iron, but also vitamins A, C, or both, the B vitamins, iodine, and other nutrients, depending on the anticipated risk of these deficiencies and based upon local circumstances. However, the cost of providing fortified foods is high - if funds are limited, their use for this purpose might entail a reduction of overall food supplies available for distribution, as well as delays in delivery.

Food aid

When supplemental foods are used under normal conditions, as for example in food-for-work or supplementary feeding programmes, they should be fortified with iron to prevent the risk of deficiency. The World Food Programme provides vitamin A-fortified skimmed milk and iodized salt in countries with populations at risk of these deficiencies. Cereal-legume blends, including corn-soy-milk and wheat-soy, are also commonly fortified with minerals and vitamins.

Few governments have a clear policy or programme for dietary improvement or food fortification to alleviate iron deficiency. In view of the new knowledge and technologies available, it is timely for all countries whose population is affected by iron deficiency - and who have not yet defined a food-based strategy - to undertake a feasibility study of the possibilities for dietary improvement and food fortification *(114).*

8.2 Iron supplementation

Iron supplementation is the most common strategy currently used to control iron deficiency in developing countries. This is likely to remain the case until either significant improvements are made in the diets of entire populations or food fortification is achieved.

Supplementation is most often used to treat existing iron deficiency anaemia. It should also be considered as a preventive public health measure to control iron deficiency in populations at high risk of iron deficiency and anaemia. Supplementation programmes, especially for pregnant women, operate in developed as well as in developing countries. For example, Sweden has been implementing iron supplementation and fortification of many foods for many years. This practice may explain a relatively low prevalence of iron deficiency anaemia in that country.

Various delivery systems and modalities, under conditions of varied efficiency, reach a wide range of target groups. Small controlled studies of supplementation have been shown to be particularly successful, and a few large-scale supplementation programmes clearly demonstrating positive biological impact are reported from some developing countries. Countries should identify specific problems and constraints limiting the effectiveness of supplementation programmes and those key elements responsible for successes and failures. Only then will information be sufficient to introduce effective and efficient solutions, if traditional approaches and practices are to continue.

Traditionally, target groups for supplementation programmes have been pregnant women and infants. This practice is due to the short- and long-term health benefits of these programmes for both groups. To a large extent, they are reached with relative ease through the health system in urban areas.

However, it has become increasingly evident that the main target group for supplementation to prevent iron deficiency should be all women of childbearing age (in addition to infants older than 6 months, preschool children, and adolescent girls). This target group should not be limited to pregnant women, who are often accessible only through the health system and late in pregnancy.

One problem is that all of these groups are often difficult to contact through the health services. An exception involves adolescent girls, who may be reached through the school system.

Therefore, efforts should concentrate on supplementation programmes for women of childbearing age. If women enter pregnancy with adequate iron reserves, iron supplements provided during pregnancy will be more efficient at improving the iron status of the mother and of the fetus. As a result, the risk of maternal anaemia at delivery and of anaemia in early infancy will be reduced.

8.2.1 Iron supplementation to prevent iron deficiency anaemia

It is important to differentiate between supplementation that aims at *preventing* anaemia by correcting iron deficiency before iron deficiency anaemia is manifest, and *therapeutic supplementation*, which aims at correcting established iron deficiency anaemia (115).

Therapeutic supplementation should be part of the health care delivery system. Supplementation to prevent iron deficiency without anaemia may be a community-based initiative which needs innovative approaches in order to deliver timely preventive supplements to groups at risk.

Women's organizations, schools, and religious and community leaders are all potentially important players in delivering supplements to correct iron deficiency. Approaches based on self-purchase of supplements through community stores should also be evaluated.

Several trials utilizing supplements on a weekly - rather than daily - basis are now in progress *(116, 117).* However, the demonstrated effectiveness of weekly programmes, based on self-administered iron supplements under programme conditions, is awaited before being recommended as a public health measure.

Table 10. Dosage schedules for iron supplementation to prevent iron deficiency anaemia

Age groups	Indications for supplementation	Dosage schedule	Duration
Low-birth-weight infants	Universal supplementation	Iron: 2 mg/kg body weight/day	From 2 months of age up to 23 months of age
Children from 6 to 23 months of age	Where the diet does not include foods fortified with iron or where anaemia prevalence is above 40%	Iron: 2 mg/kg body weight/day	From 6 months of age up to 23 months of age
Children from 24 to 59 months of age	Where anaemia prevalence is above 40 %	Iron: 2 mg/kg body weight/day up to 30 mg	3 months
School-aged children (above 60 months)	Where anaemia prevalence is above 40 %	Iron: 30 mg/day Folic acid: 250 µg/day	3 months
Women of childbearing age	Where anaemia prevalence is above 40 %	Iron: 60 mg/day Folic acid: 400 µg/day	3 months
Pregnant women	Universal supplementation	Iron: 60 mg/day Folic acid: 400 µg/day	As soon as possible after gestation starts - no later than the 3rd month - and continuing for the rest of pregnancy
Lactating women	Where anaemia prevalence is above 40 %	Iron: 60 mg/day Folic acid: 400 µg/day	3 months post-partum

Dosage schedules for iron supplementation (Table 10, opposite)

Low-birth-weight infants

A daily dosage of 2 mg iron/kg of body weight in the form of a liquid preparation should be given to all low-birth-weight infants, starting at 2 months and continuing to 23 months of age (universal supplementation).

Infants and children below 2 years of age

Where the diet does not include fortified foods, or prevalence of anaemia in children approximately 1 year of age is severe (above 40%), supplements of iron at a dosage of 2 mg/kg of body weight/day should be given to all children between 6 and 23 months of age. There have been some reports of stained teeth after iron supplementation with some solutions. Good oral hygiene and the use of ferrous carbonate can prevent this condition. Ferrous carbonate is not soluble, but present as a suspension or a solution of iron-EDTA *(118)*.

Children above 2 years of age

The recommended WHO regimen *(4)* - based on daily supplementation as summarized in Table 10 - should be followed. However, supervised weekly, or biweekly supplementation of preschool and school-aged children and adolescent girls has been reported to be effective in several countries *(115,119,120)*.

Women of childbearing age: pregnant women

A total amount of about 700-850 mg of iron is needed to meet the iron requirements of a mother and fetus during pregnancy, at delivery, and during the perinatal period. Iron needs during the first trimester are lower than pre-pregnancy needs; they increase the most during the second half of the pregnancy and especially during the last trimester. For unknown reasons, dietary iron absorption in iron-sufficient women is reduced during the first trimester and increased in the second half of pregnancy.

The average woman of reproductive-age needs about 350-500 mg additional iron to maintain iron balance during pregnancy. Potentially, this iron could be provided either from the mother's iron stores or from iron supplements. However, it is not reasonable to expect that this additional iron can come from iron stores, since they very seldom reach this level in women in either developed or developing countries (the mean iron content of the body reserves - ferritin and haemosiderin - is often only around 200-250 mg).

Furthermore, in developing countries 25-30% of women have no iron reserves at all. Because the situation is especially serious among pregnant teenagers, it is important to promote all measures - with emphasis on pubertal girls - that will improve iron reserves before pregnancy.

All pregnant women (universal supplementation) should be given 60 mg iron and 400 μg folic acid daily during the second half of pregnancy to control iron deficiency anaemia. There is some evidence, however, that smaller doses of 30 mg daily could achieve similar results *(86,121)*.

Combined with other micronutrients, folic acid should always be given with iron during pregnancy. This combination is important because of the increased folic acid requirement of pregnant women and the fact that both deficiencies are common in pregnancy. In addition, folic acid supplementation prior to pregnancy will also have an impact on maternal folic acid status, which is expected to reduce the risk of neural tube defects *(120).*

Women of childbearing age: lactating women

In populations with a severe prevalence of anaemia (>40%), it is recommended that iron supplementation begin during pregnancy. Supplementation should continue during lactation for at least three months post-partum, at the same dosage - 60 mg iron and 400 μg folic acid daily - as during pregnancy.

Women of childbearing age: non-pregnant women

In areas where the prevalence of anaemia among women of childbearing age is severe (> 40%), preventive iron supplementation of 60 mg/day iron with 400 μg folic acid for 3 months should be considered.

Adolescents

Where prevalence of anaemia in pubertal girls is severe (>40%), preventive iron supplementation of 60 mg/day iron with 400 μg folic acid for 3 months should be considered. Adolescent boys should also receive preventive iron supplementation where prevalence of anaemia among them is severe (>40%). As with adolescent girls, supplementation should continue throughout adolescence, following the same schedule of 60 mg/day iron with 400 μg folic acid for 3 months.

8.2.2 Problems associated with iron supplementation

Delivery system

Much of the success of an iron supplementation programme depends on the effectiveness of the delivery system. The framework of the programme will be provided by the health system of the country in question. It may also include primary health care facilities and community health workers, such as traditional birth attendants and volunteers *(121)*. Ideally, iron supplementation should be community-based: the community should embrace the need for the programme and provide support on its behalf.

To this end, involving other human resources in the community should be seriously considered. These include the school system, women's clubs, religious organizations, and nongovernmental organizations, together with formal and informal community leaders. Involvement and participation of the private health system will also help to achieve maximum coverage.

Adherence

Irregular consumption of prescribed iron supplements, due in part to side-effects (Table 11), has plagued most supplementation programmes. For this reason, definitive results of tests of iron preparations with fewer side-effects are eagerly awaited. Even if new iron preparations are more expensive than ferrous sulphate, they may ultimately be more cost-effective if they improve adherence *(122).*

Table 11. Possible side-effects associated with iron medication

- Epigastric discomfort, nausea, diarrhoea, or constipation may appear with a daily dose of 60 mg or more. If these symptoms occur, supplement should be taken with meals.
- Faeces may turn black, which is not harmful. Treatment should continue.
- All iron preparations inhibit the absorption of tetracyclines, sulphonamides, and trimethoprim. Thus, iron should not be given together with these agents.
- High-dose vitamin C supplements should not be taken with iron tablets, because this would likely cause epigastric pain.

The side-effects of iron tablets generally increase with higher dosages. These side-effects can be reduced if supplements are taken with meals, but absorption is reduced by about 40% *(125).* If the supplement is administered in the form of a single tablet, it is best ingested at bedtime.

Adherence frequently diminishes due to intolerence when more than one iron tablet of 60 mg is required. Under such circumstances, prescribing one daily tablet instead of two is justified as a general policy or for the particular subjects who experience intolerance. One tablet taken consistently is preferable to the risk of total rejection or non-acceptance of supplements.

Awareness and motivation

Motivating the target group to take iron tablets according to the prescribed schedule, thereby improving adherence, is of utmost importance. Accordingly, communities, families, mothers, and health workers need to be well informed about the health benefits - as well as the side-effects - of iron supplementation for both the mother and fetus.

One approach is a comprehensive education and information programme, organized through the health and other community infrastructures. Such a programme should emphasize the benefits of iron supplementation and provide advice concerning possible side-effects. Community leaders, volunteer health workers or local cadres, schoolteachers, and students can reinforce these messages as a demonstration of their involvement in and commitment to the community.

The training of community workers involved in programme implementation is essential. Social marketing techniques can be used to great advantage. Of course, the design of messages should take into account local terms, perceptions, and cultural factors related to anaemia.

Quality and packaging of iron supplements

Improvements are needed in the quality of iron tablets, especially in their stability (e.g. avoidance of cracking, and disintegration, and absorption of moisture) and other physical characteristics (e.g. their colour and odour). Development of improved packaging to minimize deterioration before distribution, and innovative and safe ways of dispensing the tablets, is also needed.

The design and testing of all of these aspects of iron supplementation are significant in improving adherence. They are especially important in preventing accidental iron poisoning, particularly in children.

Risk of iron overload with iron supplementation

The above-mentioned supplementation strategies are not considered to be associated with any increased risk of iron overload (see Annex 2).

Monitoring and evaluation

Iron supplementation programmes should be carefully assessed, and their efficiency and effectiveness monitored, to improve critical aspects of the system.

8.2.3 Other complementary public health interventions

Iron supplementation programmes should be integrated into broader public health programmes which are directed to the same population target groups. Iron supplementation during pregnancy and lactation is a major component in reducing maternal morbidity and mortality. Emphasis should therefore be placed upon increasing the capacity of antenatal, postnatal, and child health clinics to provide iron supplementation for mothers and children.

For maximum effectiveness, links should be established with programmes such as those targeting:

- malaria prophylaxis;
- hookworm control;
- immunization;
- environmental health;
- control of micronutrient malnutrition; and
- community-based primary health care.

Community participation within the framework of the concept of primary health care (and beyond) should be actively encouraged.

8.2.4 Integration with other micronutrient control programmes

Preventive supplementation is particularly well-suited to strategies that combine multiple micronutrient interventions. Accordingly, efforts should be intensively directed to this area. Programmes that involve preparations containing iron, folic acid, and vitamins A and C, directed to infants, children, and pregnant and lactating women, are highly desirable.

Similarly, much more attention should be focused on the use of multiple micronutrient-fortified food preparations in supervised feeding programmes (e.g. in schools and emergency situations). The involvement in this effort of the pharmaceutical and food industries and of food-aid donors should be fostered. Also encouraged should be the active participation of educational institutions, such as home-science colleges and departments.

In emergency situations (e.g. among refugees, displaced, or war-affected populations) infants and young children are particularly vulnerable to iron and other micronutrient deficiencies. Food aid provided in these situations should be nutritionally adequate to prevent iron deficiency anaemia and other micronutrient deficiency disorders.

To determine appropriate complementary action in micronutrient programmes, it is necessary to conduct a careful analysis based on a conceptual framework that compares:

- the etiology of each micronutrient deficiency;
- vulnerable groups;
- groups most appropriate for assessment and monitoring purposes (surveillance groups); and
- suitable intervention strategies.

Table 12 compares complementary actions involving the three micronutrient deficiencies currently of major public health significance, i.e. iodine, iron, and vitamin A. Combined approaches to overcoming micronutrient malnutrition - especially deficiencies in vitamin A and C, folic acid, iron, and zinc - should be emphasized *(105,124,125),* especially since the foods to be promoted and other necessary actions are often similar for these nutrients.

Table 12. Iodine, iron and vitamin A deficiencies: etiology, vulnerable groups, and appropriate groups for surveillance purposes

Iodine deficiency	Iron deficiency	Vitamin A deficiency
	Etiology	
Geographic	Dietary Increased losses	Dietary Increased losses
	Vulnerable groups	
Entire population	Pregnant and lactating women	Pregnant and lactating women
	Infants	Infants less than 6 months old
	Preschool children	Preschool children
	Women of childbearing age, including adolescent girls	
	Surveillance groups	
School-aged children	Pregnant women Preschool children	Preschool children

8.2.5 Iron supplementation to correct iron deficiency anaemia

As mentioned earlier in this chapter, it is important to differentiate between supplementation for the *prevention* of iron deficiency anaemia and supplementation for its *correction*. The amounts of iron supplementation recommended to treat iron deficiency anaemia for adults is 120 mg/day iron for 3 months. For infants and younger children, it is 3 mg/kg/day, not to exceed 60 mg daily.

9 Action-oriented research needs

This chapter identifies needs for action-oriented research in the fields of iron deficiency and anaemia. These research needs are presented in relation to the various intervention strategies described in the preceding chapters.

9.1 Dietary improvement

- Develop simple methods of dietary assessment, including screening foods or meals for their value as important sources of bioavailable iron and other nutrients.
- Develop laboratory methods for assessing iron bioavailability from individual meals.
- Update analytical databases on food, condiments, and spices, with respect to iron content and availability, as well as content of folic acid, vitamin C, tannins, phytates, vitamin A, and carotenoids.
- Evaluate traditional forms of food preparation that may favourably affect bioavailability of iron, which are decreasing in use (e.g. fermentation); and explore ways in which these methods can be made more practical and/or less time-consuming.
- Investigate methods of improving dietary patterns (e.g. food selection and preparation, addition of enhancers or removal of inhibitors of iron absorption).
- Research practical methods of food preparation that will reduce the content of tannins and phytates, such as the use of commercial phytase, malting of cereals, prolonged cooking at high and low temperatures, germination and fermentation.

- Expand knowledge about interactions among and between nutrients and/or non-nutrient factors (e.g. condiments and vitamins A and C, which influence micronutrient bioavailability, especially that of iron).
- Conduct operational research to improve community nutrition and related education, and implement a social marketing approach with the ultimate goal of improving the quality and quantity of the food supply and its use.
- Explore methods of introducing adventitious iron sources, such as the use of iron cooking pots.
- Evaluate approaches to improving the delivery and adoption of agricultural inputs and technologies by nutritionally vulnerable or iron-deficit households.
- Develop means to extend outreach to women farmers through agriculture extension services.
- Explore methodologies for improving the marketing of foods rich in iron and vitamins A and C.
- Improve methods for documenting the cost-effectiveness of horticultural interventions.

9.2 Iron fortification

- Expand research on iron-EDTA to include not only its current areas of application, but also its use in non-traditional vehicles (e.g. an adequate fortificant, its effect on absorption of other minerals, and the effectiveness of its absorption to influence meal iron bioavailability compared with that from ferrous sulphate).
- Continue research to determine how EDTA promotes the absorption of the non-haem iron pool.

- Continue to explore the potential for multiple fortification of foods with micronutrients.
- Improve fortification technology to make fortification feasible in remote areas and in the community (e.g. premixes for home fortification use and microencapsulation).
- Conduct pilot fortification studies to assess biological effectiveness, acceptability, and costs.
- Develop methods for quality assurance control of fortification.

9.3 Iron supplementation

- Assess relative effectiveness of weekly supplements in various vulnerable population groups and under various conditions of programme implementation.
- Conduct operational research on ways to improve the effectiveness and efficiency of preventive and therapeutic iron supplementation programmes.
- Explore new approaches to iron supplementation, which may have better absorption and fewer side-effects.
- Determine the cost-effectiveness of universal supplementation of infants in areas where a high prevalence of iron deficiency is found among them.
- Conduct operational research on practical surveillance systems, use of sentinel sites, etc.
- Undertake operational research on community-based infrastructures for the distribution of iron and folic acid to pregnant women, and monitoring its effects among them.

- Study effects of zinc supplementation in areas where iron deficiency is highly prevalent.
- Conduct bioavailability tests on preparations containing multiple micronutrients.
- Study combined pharmaceutical micronutrient preparations and super-fortified foods, including their feasibility, stability, and effectiveness.
- Study the role, effectiveness, and cost-effectiveness of treating hookworm infections as a means of alleviating or preventing anaemia and iron deficiency.

10 General recommendations

In order to reduce substantially the prevalence of iron deficiency anaemia, and in support of national programmes for the prevention of iron deficiency, the following actions are recommended:

10.1 For governments

- Undertake appropriate studies to collect or update information on the prevalence and severity of anaemia in various age groups and by gender in the principal ecological zones and socioeconomic groups of the country; results should be made rapidly available and used as the basis for advocacy and programme planning and monitoring.

- Formulate and implement, as part of the national plan of action for nutrition, a programme for the prevention of iron deficiency, based on a combination of dietary improvement, food fortification (where feasible) and iron supplementation; public health measures integrated into maternal and child health, and primary health care programmes as described in Annex 5, should also be part of the plan.

- Establish a surveillance system to ensure appropriate monitoring of iron status and of programme implementation, using indicators outlined in this report; locally applicable programme indicators should be further developed.

- Undertake a feasibility study of iron fortification programmes with emphasis upon reaching at least the major vulnerable populations.

- Review, and strengthen as necessary, national legislation or regulations dealing with fortification and the marketing of appropriate fortified foods; strengthen appropriate food control and quality assurance systems; and foster effective working relationships with the food industry and consumer groups.

- Develop appropriate support activities, e.g. human resources development (training of programme managers, sector specialists, extension agents, and laboratory and field staff, each for his or her respective role); advocacy; information, education, and communication; and applied research; and provide at least the minimum facilities necessary to those activities, including those for anaemia assessment.

- Develop suitable managerial mechanisms, including integration into appropriate community programmes, e.g. those promoting sustainable agriculture and rural development, primary health care, maternal and child health, and prevention of other micronutrient deficiencies.

- Mobilize the effective participation of community groups, the private sector, and nongovernmental organizations, in these programmes.

10.2 For supporting organizations and institutions

- Stimulate and provide technical, material, and financial support for the formulation, implementation, and monitoring and evaluation of national and local programmes.

- Assist in mobilizing and training necessary human resources.

- Provide support for appropriate applied and operational research.
- Ensure the organization of necessary global, regional, and subregional advocacy, and of appropriate meetings, communications, and information systems.
- Develop rosters of available human resources in various categories, and in all countries, and ensure the widespread circulation of those rosters.
- Initiate, if possible, systems for continuous collection and periodic dissemination of information on the prevention of iron deficiency, and systems to ensure adequate communication on iron deficiency prevention initiatives, especially through widely circulated periodicals, bulletins, and newsletters.
- Ensure that adequate and appropriate global and national information systems are established in connection with iron deficiency, including information on the implementation of prevention programmes.
- Foster action-oriented research, and networking to increase collaborative efforts and cross-cultural trials.

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annexes

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annex 2 The practical significance of iron overload for iron fortification and supplementation programmes

As is the case for several other essential nutrients, it is important to take note of the possibility of too much as well as too little iron. Data on the relationships between iron excess and infections, the occurrence of genetic and metabolic disorders leading to iron overload, and some controversial reports of a relationship between iron stores and chronic diseases have been misinterpreted to suggest that interventions aimed at reducing iron deficiencies are undesirable. This has adversely affected efforts to improve iron nutrition, even in areas with serious iron deficiency. Failure to clarify these issues can interfere with needed programmes of iron supplementation and fortification for populations at risk of iron deficiency. None of the relationships cited above is a contraindication to efforts to improve iron nutrition through diets supplying more available iron, by iron fortification of appropriate vehicles, or by supplementation at recommended levels.

Iron and infection

It is not only the host that needs iron for biochemical functions, but also the infectious agent. Without it, replication is inhibited. In fact, withholding iron from the infectious agent is an important mechanism of normal resistance to infections *(1,2)*. Conalbumin and lactoferrin have stronger iron-binding properties than do most bacterial siderophores and are normally highly unsaturated and function as iron-withholding rather than iron-transporting agents. Lactoferrin, known to be released upon degranulation of leucocytes in septic areas, is an important component of human milk and resists proteolytic destruction in the gastrointestinal tract *(3)*. The extremely high iron-binding capacity of serum transferrin is also important because it removes free iron ions from plasma.

In iron-deficient or severely malnourished individuals, humeral and cell-mediated immunity is reduced and leucocyte function is impaired. Under these conditions the withholding of iron required for replication of an infectious agent becomes even more important *(4)*. The exacerbation of malaria with a high case-fatality rate in Somali refugees given therapeutic doses of iron has been described *(5,6)*. Parenteral iron given to children with kwashiorkor, who are characterized by low transferrin levels and impaired immunity, has also been associated with mortality from overwhelming infection *(6,7)*. However, in field studies in which 100 mg of iron was given daily to adults or proportionately less to school and preschool children, a prompt and sustained decrease in morbidity from diarrhoea and respiratory disease was consistently observed *(8,9)*.

Iron supplementation at this level evidently promotes recovery of immune function without providing enough iron to increase the severity of existing or subsequent infections. The fact that therapeutic doses of either oral or parenteral iron should not be given to individuals of any age with severe anaemia or severe protein-energy malnutrition is in no way a contraindication to the doses normally used in supplementation. The danger of an adverse effect on resistance to infection is irrelevant to levels of iron intake associated with fortification, even with multiple fortified food sources.

Iron and chronic disease

There has been increasing concern in recent years that a subset of the population in developed countries or upper-income populations in developing countries with overall adequate iron status may be adversely affected by high levels of iron in the food supply. There are two aspects to this concern: one related to individuals with undiagnosed iron overload metabolic disorders; and the other to an observed association between laboratory indicators of high iron stores and a variety of chronic diseases.

Normal individuals have a mechanism for reducing iron absorption when iron stores are adequate that prevents iron overload. In fact, food iron absorption in normal populations is estimated to be nearly nil when serum ferritin levels are greater than 60 g/l. However, the gene for idiopathic haemochromatosis has a homozygote frequency estimated to be between 100 and 500 per 100 000 in some northern European populations. Persons with idiopathic haemochromatosis have reduced protective inhibition of iron absorption and may develop iron overload, especially if taking frequent iron tablets for long periods. For this reason some have suggested that, because of the increased risk to such individuals, iron fortification should be withheld, even from iron-deficient populations.

The objection is the same as that used earlier to resist iodization of salt because of the occasional individual susceptible to iodine-induced hyperthyroidism. Relatively rare diseases should be dealt with medically and not serve to prevent a needed public health measure that benefits or is benign for the population as a whole. The same is true for diet in relation to several other metabolic diseases and for foods to which some individuals are commonly allergic.

In developed countries, where the iron content of the diet is higher and the iron status is better than in developing countries, screening of individuals at risk for iron overload can be done by measuring transferrin saturation or serum ferritin. In most developing countries, where dietary iron content and availability are low, the additional iron to improve iron nutriture is unlikely to pose a risk even for those genetically susceptible to iron overload.

It has also been suggested that there is the possibility of a relationship between high iron intakes and the risk of coronary heart disease *(10)* and some kinds of cancer *(11-14)* on the basis of the notion that increased body iron stores, as judged from serum ferritin levels, are associated with increased risk. Although these studies are inconclusive and contradictory *(15)*, they have raised concern because these chronic diseases are now the leading causes of mortality in many countries. It is possible that rather than high iron levels acting causally, chronic disease processes themselves alter iron metabolism giving rise to an apparent association. It is noteworthy that neither morbidity nor mortality from coronary heart disease is increased among subjects with hereditary haemochromatosis (Hallberg, personal communication).

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annex 3

Variations in haemoglobin and haematocrit levels

This annex presents tabled data which describe in quantitative terms variations in haemoglobin and haematocrit levels according to age, gender, stage of gestation, smoking, and altitude. Described in Tables A1 through A5, respectively, are:

A1 Normal age- and gender-related changes of haemoglobin and haematocrit values for children and adults

A2 Normal gestation-related changes of haemoglobin and haematocrit values

A3 Normal increases of haemoglobin and haematocrit values related to long-term altitude exposure

A4 Adjustments for haemoglobin and haematocrit values for smokers

A5 Normal age- and gender-related red cell indices for children and adults

Table A1. Normal age- and gender-related changes of haemoglobin and haematocrit values for children and adults[a]

Females

	0.50–0.99 years	*1.00–1.99 years*	*2.00–4.99 years*	*5.00–7.99 years*	*8.00–11.99 years*	*12.00–14.99 years*	*15.00–17.99 years*	*18.00-44.99 years*
				Haemoglobin (g/l)				
Mean	122	123	124	125	128	134	135	135
-2SD	105	107	107	109	110	115	117	117
				Haematocrit (l/l)				
Mean	0.357	0.359	0.363	0.372	0.384	0.390	0.395	0.400
-2SD	0.310	0.320	0.320	0.330	0.340	0.340	0.340	0.340

Males

	0.50–0.99 years	*1.00–1.99 years*	*2.00–4.99 years*	*5.00–7.99 years*	*8.00–11.99 years*	*12.00–14.99 years*	*15.00–17.99 years*	*18.00-44.99 years*
				Haemoglobin (g/l)				
Mean	122	123	124	125	128	140	148	153
-2SD	105	107	107	109	110	120	123	132
				Haematocrit (l/l)				
Mean	0.357	0.359	0.363	0.372	0.384	0.405	0.430	0.445
-2SD	0.310	0.320	0.320	0.330	0.340	0.350	0.370	0.390

[a] Based on the US second National Health and Nutrition Examination Survey (NHANES II), after excluding those with abnormal tests related to iron. (Centers for Disease Control. CDC Criteria for anemia in children and childbearing age women. MMWR, 1989, 38: 400-404; Yip R, Johnson C, Dallman PR. Age-related changes in laboratory values used in the diagnosis of anemia and iron deficiency. American Journal of Clinical Nutrition, 1984, 39:427-436).

Table A2. Normal gestation-related changes of haemoglobin and haematocrit values[a]

	Gestation (weeks)							
	12	*16*	*20*	*24*	*28*	*32*	*36*	*40*
Haemoglobin (g/l)								
Mean	122	118	116	116	118	121	125	129
-2SD	108	104	103	103	105	108	112	116
Haematocrit (l/l)								
Mean	0.367	0.354	0.348	0.348	0.355	0.364	0.375	0.387
-2SD	0.325	0.315	0.310	0.310	0.315	0.325	0.335	0.350

[a]Adapted from Centers for Disease Control. CDC Criteria for anemia in children and childbearing age women. *MMWR*, 1989, 38:400-404.

Table A3. Normal increases of haemoglobin and haematocrit values related to long-term altitude exposure[a]

Altitude (metres)	Increase in haemoglobin (g/l)	Increase in haematocrit (l/l)
<1000	0	0
1000	+ 2	+0.005
1500	+ 5	+0.015
2000	+ 8	+0.025
2500	+13	+0.040
3000	+19	+0.060
3500	+27	+0.085
4000	+35	+0.110
4500	+45	+0.140

[a]Adapted from Hurtado A , Merino C, Delgado E. Influence of anoxemia on haematopoietic activities. *Archives of Internal Medicine*, 1945, 75:284-323. Centers for Disease Control. CDC Criteria for anemia in children and childbearing age women. *MMWR*, 1989, 38:400-404.

Table A4. Adjustments for haemoglobin and haematocrit values for smokers

	Haemoglobin *(g/l)*	Haematocrit *(l/l)*
Non-smoker	0	0
Smoker (all)	+0.3	+0.010
1/2 - 1 packet/day	+0.3	+0.010
1-2 packets/day	+0.5	+0.015
⊕ 2 packets/day	+0.7	+0.020

Table A5. Normal age- and gender-related red cell indices for children and adults[a]

	Female and male			
	1–1.9 years	*2–4.9 years*	*5–7.9 years*	*8–11.9 years*
RBC count				
Mean	4.34	4.34	4.41	4.52
-2SD	3.8	3.7	3.1	3.8
MCV (fl)				
Mean	79	81	82	84
-2SD	67	73	74	76
MCH (pg)				
Mean	27.4	28.1	28.6	28.7
-2SD	22	25	25	26
MCHC (g/l)				
Mean	34.4	34.5	34.5	34.5
-2SD	32	32	32	32

	Female			Male		
	12-14.9 *years*	**15-17.9 *years***	**>18 *years***	**12-14.9 *years***	**15-17.9 *years***	**>18 *years***
RBC count						
Mean	4.47	4.48	4.42	4.71	4.92	4.99
-2SD	3.9	3.9	3.8	4.1	4.2	4.3
MCV (fl)						
Mean	86	88	90	85	87	89
-2SD	77	78	81	77	79	80
MCH (pg)						
Mean	29.4	30.0	30.6	29.1	29.9	30.5
-2SD	26	26	26	26	27	27
MCHC (g/l)						
Mean	34.1	33.9	33.9	34.4	34.4	34.5
-2SD	32	32	32	32	32	32

[a] Based on the US second National Health and Nutrition Examination Survey (NHANES II) after excluding those with abnormal tests related to iron; Yip R, Johnson C, Dallman PR. Age-related changes in laboratory values used in the diagnosis of anemia and iron deficiency. *American Journal of Clinical Nutrition*, 1984, 39:427-436.

annex 4

Approaches for obtaining information

Information on local dietary patterns and on the availability and consumption of iron-containing foods is essential in establishing a food-based intervention programme to improve iron status. Information is needed on availability in an area or a population at the market and household levels; on general meal patterns of vulnerable groups; and on semi-quantitative and qualitative intakes of iron-containing foods and foods that inhibit or enhance iron absorption.

A.4.1 Market and household food availability

Surveys, conducted in markets, households, or both, are useful in establishing the availability of iron-containing foods and those that contain the major enhancers and inhibitors of iron absorption. At the market level, information can be collected by interviewing vendors to obtain a list of the important foods acquired by communities of concern, and a rough estimate of quantities available by season and their unit costs for the size of the population served by the market.

Vendors may also provide information on quantities usually purchased by families. The focus should be on animal products (meat, poultry, and fish and other seafood), cereals, legumes, nuts and seeds, green leafy and yellow vegetables, and fruits (especially citrus). Foods should be identified in the local language and, when possible, by their scientific name.

Surveys at the household level should first use focus groups of women and elders to generate a list of important foods available in households from the market, home production, hunting and gathering, and imported foods. Information collected should include seasonal availability of foods, the usual quantity acquired and prepared for the family, and how frequently the foods are consumed. A random selection of households should be visited at various seasons to ascertain which iron sources are available. Questions should be asked to ascertain whether the household consumes those sources present, and especially the frequency of their consumption by young children and women.

Generally, there are no major feasibility obstacles in conducting market and household food availability surveys. Such surveys require participation of a local assistant, guided by a nutritionist and with back-up by an in-country botanist who can provide botanical sampling for identification if required.

Adequate training is critical to prepare staff to be good facilitators and recorders at focus group discussions. The facilitator must speak the local language. In urban areas, consideration should be given to the specific shopping districts frequented by the sampled communities.

A4.2 Dietary patterns of vulnerable groups

Information on dietary patterns of vulnerable groups can be obtained through general focus group discussions. Emphasis should be on regular food use practices during pregnancy and lactation, complementary feeding of infants, and post-weaning diets of young children. Information is needed on food preparation, frequency of consumption of iron-rich foods in season, and usual portion sizes, and should include an estimate of the proportion of community members that ascribe to each practice. Special attention should be given to the use of tea, coffee, herbal teas, spices, and fermented foods.

This information is most useful when obtained from the community or region and stratified by ethnic group, ecological zone, socioeconomic status, and by specifically vulnerable groups, in particular pregnant women, infants, and preschool children. Obtaining the information requires the cooperation and goodwill of local leaders, and skilled focus group leaders who have nutrition experience and are familiar with the local language and customs.

A4.3 Food beliefs and attitudes

Information on food beliefs and attitudes is best collected in focus group discussions with women and elders in the communities surveyed, and also health personnel and teachers. The accumulated facts should be stratified by ethnic group, socioeconomic status, and ecological zone, and should be based on separate sessions for each vulnerable group (pregnant or lactating women, infants, and preschool children), depending on the quantity of information and discussion time needed. Focus group discussions should include beliefs and attitudes towards iron-rich foods and the relationships between iron-rich foods and health in general. It should seek ideas from the community about how best to improve use of iron-containing foods and foods having the auxiliary nutrients and factors that modulate iron bioavailability.

This approach is particularly dependent on interest and support from the local leadership and the skill of focus group leaders. The information gathered, which should include the percentage of community members who hold specific food-related beliefs, will greatly assist in developing dietary intervention programmes.

A4.4. Semi-quantitative and qualitative food consumption levels

There are a number of qualitative and semi-quantitative methods for making rapid assessments of the consumption of iron-containing foods for use both on a household basis and for specific at-risk groups. Rapid survey procedures are also designed to assess the usual frequency with which specific foods are consumed within households or by individuals over a defined period, e.g. days, weeks, or months. Even though this is not a quantitative survey of food consumption, with trained interviewers the estimates can be made semi-quantitative.

The primary purpose, however, is to determine whether the consumption of iron-rich foods, and those containing enhancers or inhibitors of absorption, is frequent enough in households as a whole, or in at-risk individuals within households, to meet their probable needs. This determination can serve to rank the risk of a diet inadequate in iron sources and absorption promoters or excessive in inhibitors of absorption. This information is useful, together with other indicators of anaemia and iron deficiency, for understanding the underlying causes of the problem and designing appropriate food-based interventions to prevent and control iron deficiency.

One example of this approach is the “recall method” summarized here. The “population” to be surveyed may be an entire community (i.e. all households in a community) or a selected sample of households representing a whole area (e.g. a district). In the latter case the cluster sample approach is appropriate. At least 30 children in each of the age groups of interest is suggested, in order to achieve a minimum sample of 150-200 children under 3 years of age (less than or equal to 35 months). These children, who constitute about 10% of the population, should be from separate households.

The initial universe, therefore, should be a population of at least 3 000 (i.e. 3 000 households). Thirty clusters of seven households each should provide the number of children needed, and the clusters could be selected to represent a district. A multistage random cluster sampling of villages, and of households within villages, is then undertaken. After a preliminary visit to each of the communities concerned, an interview is conducted with the mother (or the caregiver) of each child under 3 years of age in the randomly selected households.

The interviews should be conducted at home or in a neutral public place, not in a health facility. They should not be conducted by a regular health worker.

The latter circumstances are likely to produce biased answers in an attempt to please the interviewer. The interviewer should be fluent in the language of the person being interviewed and questions should be asked in the local language. Care must be taken to avoid asking leading questions or prompting replies.

The recall method gives quick and useful information, because it can be conducted overnight in a village. However, the following limitations should be carefully borne in mind:

- The method represents consumption patterns over only a limited period, usually 1 week or less. If there are important seasonal variations, the procedure should be repeated at 3- to 4-month intervals.
- Unless surveyors are trained to collect the data in a semi-quantitative manner, the data concern frequency of consumption only.
- Bias should be avoided in selecting villages and households interviewed (e.g. village notables tend to want to be included in the sample); random sampling is essential.
- Short-term intake can be atypical of the usual diet, especially in times of illness or during festive occasions.
- If there is a special market in the village on a particular day, the timing of the visit in relation to that of the market may influence results.
- Analysis should be according to broad food groups and ranges of iron content within food groups from food composition tables.
- Such an approach does not directly provide information on why certain foods are or are not given before a certain age.

annex 5 Strategies and guidelines for national IDA control programmes

Although the treatment of iron deficiency anaemia is technically simple, its prevention through interventions is more demanding and depends on concerted strategies and multisectoral involvement. A focused, effective, and affordable national strategy is needed. The experience of several countries has been used in formulating the following general guidelines.

A5.1 Situation analysis

The first step in developing a national strategy is to prepare a situation analysis to establish justification for a programme and to support decision-making. Components of needed information include as much of the following as possible:

Epidemiology of IDA

Magnitude and severity; age and gender distribution; regional differences; causes (e.g. iron deficiency, combined micronutrient deficiency, infection, parasitic infestation); dietary patterns; information on bioavailability of iron; related micronutrients (e.g. vitamin C, vitamin A, zinc); enhancers and inhibitors of iron absorption (e.g. phytates, inositol phosphate, iron-binding phenolic compounds).

Health infrastructure and delivery system

Distribution of health facilities, transport and storage capacity, management, and access of the population to health services.

Technical feasibility

Logistics (equipment, protocols); training and supervision; people (current technical ability of the personnel involved), considering current and past experience in IDA control.

Economic feasibility

Government health budget and financing; private sector and community contributions.

Community and individual concerns about iron fortification, supplementation or therapy

Perception, attitude, cultural issues, and what people recognize as undesirable symptoms or patterns of distress related to anaemia; possibility for community action or involvement, or both.

Political concern and commitment

Inter- and intra-ministerial collaboration in efforts to control IDA.

A5.2 Goals and objectives

Based on the situation analysis, achievable and realistic goals and specific and quantifiable objectives can be formulated. The overall objective is unlikely to be the complete elimination of IDA, because this is certainly not achievable in most countries in the near future. However, the objectives should set attainable achievement targets for the most vulnerable groups in definite time periods in terms of both prevalence and processes (actions).

A5.3 Components of a strategy for IDA control

Programmes to control iron deficiency are usually based on several major strategies. Each country, according to its stage of development and the results of its own situation analysis, should formulate an appropriate short- and long-term strategy, incorporating some or all of the following elements.

A5.3.1 Dietary modification

Dietary modification activities require not only information on real food availability by groups at risk but also on dietary patterns, the bioavailability of iron in local diets, and cultural aspects and local preferences. Information, education, and communication at all levels play key roles in promoting a healthy diet. Evidence to date indicates that well-conducted education and communication campaigns can indeed change knowledge, attitudes, and behaviour, and can thereby improve nutritional status.

Local dietary factors

Local dietary factors influencing the bioavailability of dietary iron, including both enhancers and inhibitors, should be identified. Common practices in food selection and preparation (including meal composition and preparation with respect to these factors), iron-rich foods available throughout the year and staples - and their interaction - should be assessed.

Appropriate dietary modification activities should seek to:

- increase, where possible, intakes of locally available haem-iron food products, e.g. meat, liver, blood curd, etc;
- increase intake of vitamin C-rich foods and other foods that promote iron absorption (e.g. fermented food products); and
- reduce as much as possible consumption of iron absorption inhibitors (e.g. phytates and iron-binding phenolic compounds).

Behavioural aspects

Modifying dietary patterns that are usually culturally ingrained and may have existed for hundreds of years is not so easily achievable. Beliefs, preferences, restrictions, taboos, and cultural issues governing food consumption should be understood and appreciated. An approach is needed that is solidly based on formative research, messages that are targeted to specific groups, and a good understanding of the possibilities and limits of behavioural objectives.

Intersectoral action

This component should include, in particular, agricultural extension to promote the production and consumption of iron- and other micronutrient-rich foods; school garden and lunch programmes; community development programmes; and community involvement. Meal preparation demonstrations are needed. These should include homemade complementary foods and school menus rich in micronutrients, based on local foods. School lunch programmes should include community participation, so that their impact will be carried over into the household. Governments should invest not only in terms of money for the school to run the programme, but also in well-thought-out guidelines and suggestions. The latter should include many alternatives, among which managers can select in order to conform to their specific situations.

Promoting breastfeeding and use of iron-rich complementary foods

Breast milk usually supplies adequate iron during the first 6 months of life. Accordingly, emphasis on preventing iron deficiency in infants and preschool children should include promotion of both breastfeeding and the preparation in the home of iron-rich complementary foods.

Nutrition communication to promote consumption of animal products (e.g. meat, liver, blood curd) and vegetables rich in iron, vitamin C, and vitamin A in home-based weaning food should be encouraged. Fermentation or germination of some foods might also be helpful.

A5.3.2 Fortification

Iron fortification can be an effective way of preventing iron deficiency, and does not necessarily require cooperation of the individual. Recent technical developments to overcome undesirable changes in fortified food and success with salt iodization make it more realistic for countries to consider and adopt this strategy. This development is especially significant in reaching urban populations.

Prerequisites for successful fortification include a suitable food vehicle; a bioavailable iron source compatible with the vehicle; careful market research; preparation of appropriate standards and regulations; and long-term commitment.

A5.3.3 Iron supplementation

Targeting (in descending order of priority)

- Pregnant and lactating women, and low-birth-weight infants.
- Infants 6-12 months of age.
- Women of childbearing age, starting from adolescence.
- School-aged children.

Approach

- Universal supplements for pregnant and lactating women and low-birth-weight infants.
- Supplementation for women of childbearing age including adolescent girls and school-aged children, if anaemia prevalence exceeds 40%.
- Screening - only if anaemia prevalence is mild or moderate (<20%) and protocols and guidelines for action are available.

Delivery system

- Integration with the activities of primary health care and maternal and child health clinics.
- Using channels outside the health system, building on existing programmes in the communities.
- Sharing facilities, training and supervision.
- Providing adequate supplies and logistics.
- Ensuring shelf-life under prevailing climatic conditions.
- Identifying and addressing factors leading to low adherence.
- Forewarning on side-effects (black faeces and dyspepsia) by providers.
- Creating awareness, linking iron deficiency anaemia to conditions which people recognize as undesirable symptoms or patterns of distress.
- Stressing undesirable consequences of IDA during pregnancy and delivery for infants.
- Encouraging positive expectations as a result of supplements.
- Motivating and training personnel for IDA prevention.

A5.3.4 Other public health measures

- Reduction of the prevalence of infectious diseases in general (e.g. diarrhoeal and respiratory diseases, measles).
- Reduction in the prevalence of hookworms, trichuriasis, and schistosomiasis infestations. Ideally, parasite control should be complemented with primary preventive measures to break the transmission cycle and environmental health measures to reduce parasitism (especially hookworms). This is particularly important for pregnant women, who should receive an appropriate anti-helminthic after the third month of pregnancy

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- Reduction in the prevalence of malaria, which is a major cause of anaemia, particularly in Africa.

A5.3.5 Support measures

Advocacy and social communications

At all levels, from that of the community to that of national policy-makers, it is necessary to identify the target and communication objective for each, the main messages, the methods and media to be used, and the materials required. A strong political will at the highest level is mandatory; without it, the programme cannot hope for national coverage, adequate budgeting, or intersectoral collaboration.

A strong advocacy effort is therefore essential, starting from the highest levels down to local political leaders and communities. Advocacy statements should be devised; examples include:

> "Iron deficiency anaemia is compromising physical and cognitive development and performance, especially in the coming generation ."

and

> "Iron deficiency anaemia in adults contributes to low work productivity and has a negative impact on the economy."

Training of personnel

It is important to train personnel from various sectors (e.g. health, agriculture, commerce, and industry), as well as community leaders, to motivate the participation of households, communities, the private sector, and nongovernmental organizations.

Infrastructure

The minimum necessary infrastructure (e.g. haemoglobinometry down to district or sub-district levels) should be provided.

Management mechanisms

A task force for preventing iron deficiency anaemia - or, better still, for preventing micronutrient malnutrition in general - could be created. This task force would lead the advocacy effort, as well as plan and oversee implementation of action programmes.

The task force should be multisectoral, with members from government departments, academic and research institutes, the private sector (including professional groups and industry), nongovernmental organizations, and others. Expert groups may be formed to provide technical guidance to the task force.

A5.3.6 Monitoring and evaluation

Monitoring and evaluation is best incorporated into, or conducted partly by, the existing built-in supervisory and reporting system. However, a complementary independent sentinel surveillance system, linked with monitoring of other micronutrient deficiencies, should be encouraged. Monitoring and evaluation should encompass both programme implementation and epidemiological information.

Haemoglobin or haematocrit determinations on a public health basis are, in any case, important for monitoring trends in anaemia prevalence and assessing the effectiveness of interventions. Serum ferritin measurements, which provide a more sensitive and specific measure of tissue iron deprivation, should be taken systematically - on the basis of a limited subsample - for evaluation purposes. If feasible, serum transferrin receptor levels should also be determined as another indicator.

Data to be collected by the routine reporting system include:

- supply and logistics;
- coverage;
- process indicators, especially provider and client compliance; and
- impact indicators.

If possible, coverage indicators should also take into consideration the size of floating populations and underprivileged groups. Determining compliance can assist in deciding whether sustaining a programme or approach will be cost-effective, or whether programme modifications have improved or detracted from performance.

For supply and logistics in supplementation programmes, special emphasis should be placed upon:

- monthly monitoring of stocks at each level of distribution;
- scheduling of orders to ensure regular supply; and
- quality control measures by periodic sample checking, including a check on the condition and authenticity of supplies of supplements.

Data on food beliefs and preferences, and semi-quantitative and qualitative food-consumption data, should be obtained from time to time using rapid assessment methods.