NUTRITIONAL ANAEMIAS:
TOOLS FOR EFFECTIVE PREVENTION AND CONTROL

World Health Organization

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CONTENTS

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SCOPE AND PURPOSE

This reference document aims to help Member States and their partners in their efforts to make informed decisions on the appropriate nutrition actions to prevent and control nutritional anaemias. The suggestions, steps and course of actions proposed here are intended for health workers covering a wide audience, including policy-makers, economists and technical and programme staff in ministries and organizations involved in the design, implementation and scaling-up of nutrition actions for public health, to help in the design and implementation of a comprehensive nutrition-based strategy for combating nutritional anaemias.

The document presents the key aspects to be taken into account when considering implementation of a programme for detection and control of anaemia at national or regional level. This manual is intended to contribute to discussions among stakeholders when selecting or prioritizing interventions to be undertaken in their specific context.

ANAEMIA AS A PUBLIC HEALTH PROBLEM

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A naemia – a condition in which the haemoglobin (Hb) concentration in the blood is lower than normal – affects roughly one third of the world's population *(1, 2)* and over 800 million women and children *(3)*. Anaemia is associated with poor cognitive and motor development outcomes in children, can cause fatigue and low productivity, and, when it occurs in pregnancy, is associated with poor birth outcomes (including low birth weight and prematurity) as well as maternal and perinatal mortality *(4)*. In 2010, anaemia was estimated to account for more than 68 million years lived with disability, more than the estimate for major depression, chronic respiratory diseases and injuries combined *(1)*. As such, anaemia has significant consequences for human health as well as social and economic development in low-, middle- and high-income countries.

1.1 CLASSIFICATION AND ETIOLOGY OF ANAEMIA

Anaemia is diagnosed when the concentration of haemoglobin falls below established cut-off values (see section 1.5). When the haemoglobin concentration decreases, the capacity of the blood to carry oxygen to tissues is compromised, resulting in symptoms such as fatigue, reduced physical work capacity, and shortness of breath, among others.

Anaemia develops through three main mechanisms: ineffective erythropoiesis (when the body makes too few red blood cells), haemolysis (when red blood cells are destroyed) and blood loss. Nutritional deficiencies, diseases and genetic haemoglobin disorders are the most common contributors to anaemia *(2)*. Iron deficiency, haemoglobinopathies and malaria are considered as the three top causes of anaemia globally *(1)* and are discussed broadly below. Anaemias are frequently classified by their cause (e.g. nutritional anaemias or haemolytic anaemias), but can also be distinguished by the size, shape and colour of the red blood cells. For example, in *microcytic* anaemias like iron-deficiency anaemia, the amount of haemoglobin in each red blood cell is reduced and the cells are smaller than normal. Iron-deficiency anaemia is also classified as *hypochromic*, since the red blood cells are less red in colour (Figure 1) *(5)*. *Megaloblastic* anaemia (red cells are larger than normal) is characteristic of folate or vitamin B_{12} deficiencies.

1.1.1. NUTRIENT DEFICIENCIES

"Nutritional anaemias" result when the intake of certain nutrients is insufficient to meet the demands for synthesis of haemoglobin and erythrocytes *(4)*. Iron deficiency is the most common cause (nutritional or otherwise) of anaemia and is estimated to contribute to approximately 50% of all cases of anaemia among non-pregnant and pregnant women, and 42% of cases in children under 5 years of age worldwide *(3, 6)*. However, the proportion of anaemia due to iron deficiency will vary, depending on the age and sex of the group being studied, the region of the world in which they live and the prevalence of other causes of anaemia in that particular area *(7)*. Deficiencies of vitamins A, B_2 (riboflavin), B_6 (pyridoxine), B_{12} (cobalamin), C, D and E, folate and copper can also result in anaemia, owing to their specific roles in production of haemoglobin or erythrocytes. The mechanisms by which specific nutrients cause anaemia are further explained in section 2.1.

1.1.2. DISEASE

Infectious diseases can cause anaemia through multiple mechanisms, including impaired nutrient absorption and metabolism, ineffective erythropoiesis, or increased nutrient losses. Acute and chronic infections can also contribute to what is commonly called "anaemia of chronic disease" or "anaemia of chronic inflammation", whereby pro-inflammatory cytokines alter iron metabolism so that iron is sequestered in stores as ferritin, and the production and lifespan of red blood cells are reduced *(8)*. Anaemia of chronic disease/inflammation is characterized by a normochromic, normocytic anaemia

Figure 1. Types, diagnostic features and differential diagnoses of anaemia

Adapted from De Regil LM, Peña-Rosas JP, Garcia-Casal MN. Anemias de origen nutricio. In: Kaufer-Horwitz M, Pérez-Lizaur AB, Arroyo P, editors. Nutriología médica, 4th ed. Mexico City: Editorial Panamericana; 2014:401–33 *(5)*.
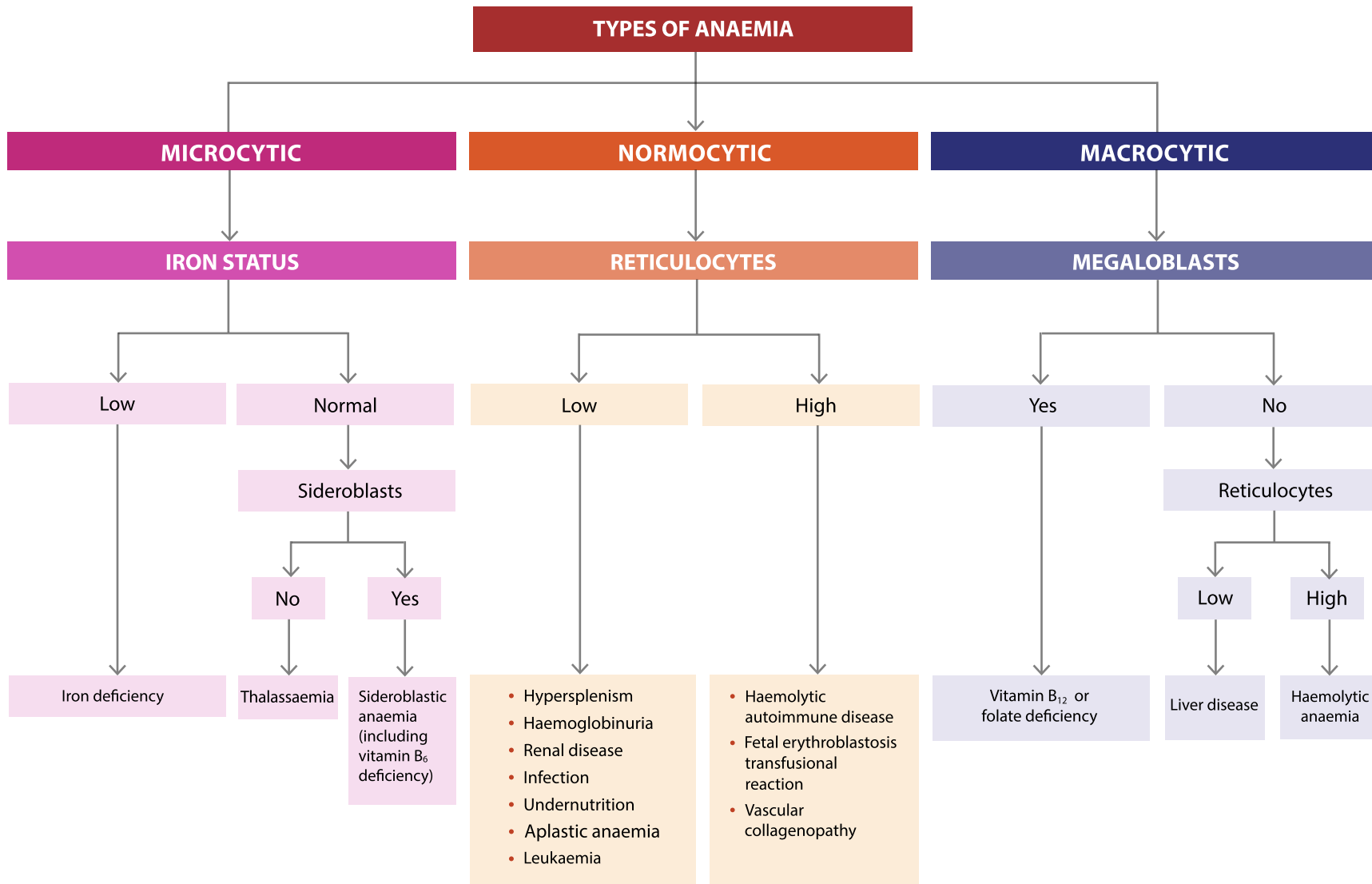
with low red blood cell counts and is the second most prevalent anaemia after iron-deficiency anaemia *(8)*. The mechanisms through which common infections in low- and middle-income countries (including malaria, tuberculosis (TB), HIV and parasite infections) contribute to anaemia are further discussed in section 2.2.

1.1.3. GENETIC HAEMOGLOBIN DISORDERS

Structural variation or reduced production of the globin chains of haemoglobin can also result in anaemia. Globally, more than 300 000 children are estimated to be born each year with a serious inherited haemoglobin disorder, and approximately 80% of these births occur in low- or middle-income countries *(9)*. Sickle cell disorders, which are associated with chronic haemolytic anaemia, are the most common genetic haemoglobin disorder, found predominantly in sub-Saharan Africa, followed by β- and α-thalassaemia, which are primarily concentrated in south-east Asia *(9)*. Roughly 5% of the global population is estimated to carry a significant haemoglobin variant; the percentage is much higher in Africa (18%) and Asia (7%) *(4)*. The mechanisms by which genetic haemoglobin disorders cause anaemia are discussed in more detail in section 2.3.

1.2 VULNERABLE GROUPS

The population groups most vulnerable to anaemia include children under 5 years of age, particularly infants and children under 2 years of age, adolescents, women of reproductive age (15–49 years), and pregnant women. Other at-risk groups include the elderly, though the prevalence and etiology of anaemia among older adults are not as well characterized.

1.2.1 INFANTS AND YOUNG CHILDREN UNDER 2 YEARS OF AGE

This age group is particularly vulnerable to developing anaemia. Iron-deficiency anaemia is common in infants and young children, owing to the high iron requirements needed for their rapid growth and development, particularly during the first 2 years of life. In addition, typical complementary foods fed to children are frequently low in iron content (in quantity and bioavailability) and have high contents of inhibitors of iron absorption. Low birth weight and prematurity also negatively impact the iron stores present at birth, thus further compromising the iron status of very young children, particularly in countries where intrauterine growth restriction is common.

1.2.2 CHILDREN UNDER 5 YEARS OF AGE

Though children over 2 years of age generally have a lower prevalence of anaemia than the youngest children, as a group, children aged under 5 years bear the largest burden of anaemia globally *(1)*.

1.2.3 ADOLESCENTS AND WOMEN OF REPRODUCTIVE AGE (NON-PREGNANT AND PREGNANT)

This group is also at increased risk of developing iron deficiency and anaemia, for several reasons. Regular blood loss that occurs with menstruation increases iron losses and thus iron requirements. Periods of high growth and development during adolescence and pregnancy incur significant additional iron needs (e.g. for the fetus, placenta and expanded maternal blood volume in pregnancy). Women may also experience significant iron loss from bleeding in childbirth, and diets that are low in bioavailable iron are common among women and adolescents in many low- and middle-income countries *(10)*. In some settings, intra-household food allocation may be based on differential valuation of household members; women, girls and the elderly are more likely to be negatively affected by this

unequal distribution *(11–13)*. Pregnant adolescents are at particular risk of developing anaemia *(14)*, not only because of their dual iron requirements (for their own growth and for the growth of the fetus), but because they are also less likely to access antenatal care *(15)*.

1.2.4 OLDER ADULTS

Individuals over 65 years of age (or 60 years in some national and international classifications) are considered older adults *(16)*. Anaemia in this group may represent a substantial burden in the future, owing to the increasing size of the elderly population globally, as well as increasing lifespans. Global data on the prevalence and causes of anaemia among the elderly are limited, but it is known that the prevalence of anaemia increases with age, starting at the age of 50 years, and that anaemia affects men in this age group more commonly than women *(17)*. Roughly one third of anaemia cases in the elderly in the United States of America (USA) are due to nutritional deficiencies, primarily iron (but also folate and vitamin B_{12}); one third are due to chronic inflammation or chronic kidney disease; and one third are considered "unexplained anaemia of the elderly", a form of hypoproliferative normocytic anaemia not due to nutritional deficiency, chronic kidney disease or inflammatory disease, in which the erythropoietin response to anaemia is compromised *(18)*. In contrast, in one study of older adults in Uganda, "unexplained anaemia" accounted for more than half of anaemia cases *(19)*.

The determinants and etiology of anaemia in these vulnerable groups is discussed in more detail in section 2.1.

1.3 HEALTH CONSEQUENCES OF ANAEMIA

Anaemia was recently quantified to account for close to 9% of the total global disability burden from all conditions *(1)* and thus has significant consequences for human health as well as social and economic development. Anaemia has been associated with negative outcomes in several population groups – including maternal mortality, low birth weight and premature birth, as well as delayed child development; yet, a causal link has not been established for all outcomes, despite strong biological plausibility.

1.3.1 MATERNAL AND PERINATAL OUTCOMES

Anaemia during pregnancy has been associated with poor maternal and birth outcomes, including premature birth, low birth weight and maternal, perinatal and neonatal mortality *(20)*. Anaemia is a particularly important complication of malaria in pregnant women, especially those who are pregnant for the first time, who are susceptible to severe anaemia *(15)*. However, despite strong biological plausibility for a causal link between maternal haemoglobin concentration and adverse maternal and birth outcomes, a causal relationship has not been established for all outcomes, and results are inconsistent. Nevertheless, a 10 g/L increase in haemoglobin has been estimated to decrease the risk of maternal mortality by 29%, and perinatal mortality by 28% *(21, 22)*. Anaemia in the first or second trimester significantly increases the risk of low birth weight and preterm birth *(23)*. Prenatal iron supplementation increases birth weight and significantly reduces the risk of low birth weight, but not preterm birth *(23, 24)*.

Finally, postpartum anaemia is associated with decreased quality of life, including increased tiredness, breathlessness, palpitations and infections *(25)*. Women who have anaemia postpartum may also experience greater stress and depression *(26)*, and be at greater risk of postpartum depression *(27)*. Mothers with anaemia may also be less responsive, more controlling and more "negative" towards their infants, which can have negative implications for infant development *(28)*.

1.3.2 CHILD DEVELOPMENT

A large number of observational studies have shown associations between iron deficiency, iron-deficiency anaemia and poor cognitive and motor development outcomes in children. Iron deficiency causes alterations to brain structure and function, which may be irreversible even with iron treatment, particularly if the deficiency occurs during infancy when neurogenesis and differentiation of different brain regions are occurring *(29)*. Nevertheless, a clear causal relationship has not been established between iron-deficiency anaemia and delayed cognitive or behavioural development *(30)*. Studies that have examined the effects of iron supplementation on motor and mental development in young children have shown inconsistent effects on child development *(31)*. Of eight double-randomized trials of iron supplementation in children aged under 4 years *(21)*, five showed benefits in motor development, one showed benefits in language development, and one showed benefits in mental development. Among anaemic children aged 5–12 years, iron supplementation improved global cognitive scores and intelligence quotient as well as measures of attention and concentration *(32)*.

1.3.3 CHILD MORBIDITY, MORTALITY AND PHYSICAL GROWTH

Iron is essential for aspects of immune function, yet the relationship with disease is complex. Past reviews have failed to establish a clinically important relationship between states of iron deficiency and susceptibility to infections *(33)*. Iron supplementation has also been linked to increased morbidity among iron-replete children and in areas where infectious morbidity is high *(31, 34, 35)*. However, haemoglobin concentrations below 50 g/L were linked to increased child mortality *(36)*, and the risk of death as a function of haemoglobin for children aged 1 month to 12 years is estimated as a reduction of 24% for every 10 g/L increase in haemoglobin concentration *(37)*.

In children aged less than 5 years, iron supplementation has not been found to improve growth, even among children with anaemia, and some studies have shown an adverse effect on growth, especially in iron-replete children *(34)*. Among children of primary-school age, iron supplementation has been shown to increase height-for-age and weight-for age (the latter only among children with anaemia) *(32)*.

1.3.4 WORK PRODUCTIVITY AND PHYSICAL ACTIVITY

The causal relationship between iron-deficiency anaemia and physical work has been well documented *(38)*. Iron-deficiency anaemia affects physical performance, through affecting tissue oxidative capacity (a result of iron deficiency) as well as the capacity of red cells to carry oxygen to tissues (a result of anaemia) *(38)*. Impairment of oxygen-carrying capacity of the red cells impairs aerobic capacity in tissues, while impairment of tissue oxidative capacity alters endurance and energetic efficiency *(38)*. Such impairments have significant consequences for economies where physical labour is common (see section 1.4). Daily iron supplementation also improves exercise performance among women of reproductive age *(39)*.

1.3.5 OTHER MORBIDITY AND MORTALITY OUTCOMES

Among older persons, anaemia is associated with a higher risk of death, increased hospitalizations and disability *(17)*, a greater risk of falls and impaired muscle strength, impairment of executive function, and dementia *(40)*.

1.4 ECONOMIC AND DEVELOPMENTAL CONSEQUENCES OF ANAEMIA

Because of the effects of anaemia on work productivity in adults and cognitive development in children, attempts have been made to quantify the economic impact of anaemia in terms of income or wage losses from decreased productivity or impaired cognitive development. The median physical and cognitive losses associated with anaemia and iron deficiency have been estimated at US$ 3.64 per head, or 0.81% of gross domestic product (GDP) in selected developing countries *(41)*. In India, where anaemia is very prevalent, the lifetime costs of iron-deficiency anaemia between the ages of 6 and 59 months amounted to 8.3 million disability-adjusted life-years (DALYs) and annual production losses of US$ 24 billion in 2013 (corresponding to 1.3% of GDP) *(42)*.

1.5 ASSESSMENT OF ANAEMIA

Anaemia is most frequently assessed at a population level through measurement of blood haemoglobin concentration. Anaemia can also be diagnosed, though less frequently, using haematocrit (packed cell volume), mean cell volume, blood reticulocyte count, blood film analysis or haemoglobin electrophoresis.

Haemoglobin is known to naturally vary by age, sex, elevation and smoking status, as well as physiological status (e.g. pregnancy). Thus, a haemoglobin concentration below established sex-, age-, and pregnancy-specific cut-off values is indicative of anaemia (Table 1).

TABLE 1. Haemoglobin levels (g/L) to diagnose anaemia at sea level

Population, age	No anaemia	Anaemia		
		Mild	**Moderate**	**Severe**
Children, 6–59 months	≥110	100–109	70–99	<70
Children, 5–11 years	≥115	110–114	80–109	<80
Children, 12–14 years	≥120	110–119	80–109	<80
Non-pregnant women, 15 years and above	≥120	110–119	80–109	<80
Pregnant women	≥110	100–109	70–99	<70
Men, 15 years and above	≥130	110–129	80–109	<80

Source: Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Geneva: World Health Organization; 2011 *(43)*.

These thresholds, first established in 1968 by the World Health Organization (WHO) *(44)*, and modified slightly in 2001 *(45)*, are applied widely globally, though researchers have questioned whether additional or separate criteria are needed for certain population groups. For example, individuals of African heritage have haemoglobin concentrations that are significantly lower than for individuals of European descent *(46, 47)*. It has been suggested to include adjustments for ethnicity to the WHO thresholds for determining anaemia (Table 2) *(7)*. WHO is currently reviewing the evidence about cut-off points to diagnose anaemia in different settings. Such discussion may be critical, not only for correctly identifying individuals with anaemia but also for implementation of interventions. The most common nutritional intervention for anaemia – supplementation – although effective in reducing anaemia, may also have deleterious effects, particularly in iron-replete individuals and in settings where morbidity from infectious disease is high *(35)*.

TABLE 2. Suggested adjustments for several ethnic groups to the thresholds of haemoglobin concentration used by WHO to define anaemia

Ethnic group	Suggested adjustment (g/L)
African American	−10.0
East Asian American	0
Hispanic American	0
Japanese American	0
American Indian	0
Jamaican girls (13–14 years)	−10.7
Indonesian from West Indonesia	0
Thai	0
Vietnamese	−10.0
Greenland men	− 8.0
Greenland women	− 6.0

Source: Assessing the iron status of populations. Second edition including literature reviews. Report of a Joint World Health Organization/Centers for Disease Control and Prevention technical consultation on the assessment of iron status at the population level, Geneva, Switzerland, 6–8 April 2004. Geneva: World Health Organization; 2007 *(7)*.

Haemoglobin concentration is relatively easy to measure in the field, using relatively inexpensive equipment, and can be done on either capillary or venous blood. It also does not require highly skilled individuals to perform the measurement. However, while essential to diagnose anaemia, haemoglobin measurement cannot alone determine the *cause* of the anaemia. For example, haemoglobin concentration is frequently used as a proxy indicator of iron deficiency and iron-deficiency anaemia, and the terms "anaemia" and "iron-deficiency anaemia" are frequently and incorrectly used interchangeably. Haemoglobin concentration alone is not a suitable indicator for assessing iron status or diagnosing iron-deficiency anaemia because of the overlap of haemoglobin concentrations in normal and iron-deficient individuals, and the high prevalence of anaemia of chronic disease (or inflammation) in areas where poverty, malnutrition and disease are prevalent *(48)*.

In order to determine whether anaemia is caused by iron deficiency, additional measurements of iron status are needed, such as serum ferritin or serum transferrin receptor, which are the most commonly used indicators. Serum ferritin is a measure of the amount of iron in body stores; when infection is not present, ferritin increases when iron stores are present, and falls as they are depleted *(7)*. Serum ferritin concentrations below 15 µg/L for individuals over 5 years of age, and below 12 µg/L for children aged under 5 years, are generally considered to be indicative of depleted iron stores *(45)*. The level of transferrin receptor in serum reflects the intensity of erythropoiesis and demand for iron; levels of transferrin receptor rise after iron stores have been depleted *(7)*. Iron status can also be assessed through measurements of total iron-binding capacity, transferrin saturation, zinc protoporphyrin concentration, erythrocyte protoporphyrin concentration, or bone marrow biopsy *(4, 45)*. Figure 2 provides an illustration of how different indices of iron status change with progressing deficiency towards iron-deficiency anaemia.

Figure 2. Indices for assessing iron status at various stages of deficiency

	IRON STATUS			
	NORMAL	**STAGE I**	**STAGE II**	**STAGE III**
		Storage depletion (low Fe storage)	Mild functional Fe deficiency (Fe-deficient)	Functional Fe deficiency (Fe-deficient anaemia)
STORAGE IRON				
TRANSPORT IRON				
FUNCTIONAL IRON				
HAEMATOLOGICAL CHANGES	Normal	↓ Ferritin	↓ Ferritin; ↓ SI; ↓ Tsat; ↓ Hep; ↑ TIBC; ↑ sTfR; ↑ rbZP	↓ Ferritin; ↓ SI; ↓ Tsat; ↓ Hep; ↓ Hb; ↓ MCV; ↓ MCH; ↑ sTfR; ↑ rbZP

REPLETE   DEPLETED

Fe: iron; Hb: haemoglobin; Hep: hepcidin; MCH: mean corpuscular hemoglobin; MCV: mean corpuscular volume; rbZP: red blood cell zinc protoporphyrin; SI: serum iron; sTfR: serum transferrin receptor; TIBC: total iron-binding capacity; Tsat: transferrin saturation.

When assessing iron status, markers of infection and inflammation (such as C-reactive protein, CRP, or alpha-1 acid glycoprotein, AGP) should also be measured. Ferritin is an acute-phase protein, and its concentration rises in response to infection/inflammation. CRP provides an indication of acute disease, while AGP indicates chronic infection and may better reflect the changes in the concentration of ferritin during infections; however, reliable assessment of iron status during infection is problematic and requires further study *(7)*. There are different approaches to deal with ferritin cut-off values in cases of inflammation *(49, 50)*. Markers of infection/inflammation are also useful in determining whether the anaemia could be due to chronic or acute disease, rather than a nutritional deficiency, though separating these causes can be challenging.

For assessing the iron status of populations, the best approach is to measure the concentration of haemoglobin, serum ferritin and/or transferrin receptor (the latter particularly in settings where infection and inflammation are common) *(7)*. For monitoring the effect of interventions on iron status at the population level, WHO recommends using serum ferritin in combination with haemoglobin *(7)*. A proposed method for interpreting ferritin and transferrin receptor concentrations in population surveys is provided in Table 3 *(51)*.

TABLE 3. Proposed interpretation* of low serum ferritin and high transferrin receptor concentrations in population surveys

Percentage (%) of serum ferritin values below threshold[b]	Percentage (%) of transferrin receptor values above threshold[c]	Interpretation
<20[d]	<10	Iron deficiency is not prevalent
<20[d]	≥10	Iron deficiency is prevalent; inflammation is present
≥20[e]	≥10	Iron deficiency is prevalent
≥20[e]	<10	Iron depletion is prevalent

* This classification is based on experience measuring ferritin and transferrin receptor in research studies and requires validation in population surveys.

[a] Thresholds for serum ferritin: <12 µg/L for children aged under 5 years; <5 µg/L for all other individuals.

[b] Use thresholds recommended by manufacturers as there is not currently an international standard reference.

[c] <30% for pregnant women.

[d] ≥30% for pregnant women.

Source: Assessing the iron status of populations. Second edition including literature reviews. Report of a Joint World Health Organization/Centers for Disease Control and Prevention technical consultation on the assessment of iron status at the population level, Geneva, Switzerland, 6–8 April 2004. Geneva: World Health Organization; 2007 *(7).*

Unlike haemoglobin, many measurements of nutritional status (including biomarkers for iron status) have traditionally been performed on venous blood (which is more challenging to collect and transport in the field), and are expensive and require sophisticated laboratory equipment, as well as skilled technicians. However, there is increasing development of "field-friendly" methods for assessment of nutritional status *(7, 52).*

At the individual level in many settings, neither haematological nor biochemical assessments are possible, and diagnosis of anaemia is based on clinical signs and medical history. For children, palmar pallor is assessed for diagnosis of anaemia *(53)*, and for pregnant women, clinical assessment of anaemia during prenatal care includes fatigue, shortness of breath, conjunctival and palmar pallor and increased respiratory rate *(54)*. Clinical examination is limited, however, in its ability to detect anaemia; in populations where the prevalence of severe anaemia is less than 10%, the sensitivity of clinical pallor to detect anaemia ranged from 60% to 80% and the specificity was 92–94% *(4)*.

1.6 MAGNITUDE AND DISTRIBUTION OF ANAEMIA

1.6.1 WOMEN AND CHILDREN

The most recent estimates for 2016 indicate that anaemia affects 33% of women of reproductive age globally (about 613 million women between 15 and 49 years of age). In Africa and Asia, the prevalence is highest at over 35% *(1)*. Severe anaemia, which is associated with substantially worse mortality and cognitive and functional outcomes, affects 0.8–1.5% of these same population groups *(3)*.

In a recent WHO report presenting 2011 data on the prevalence of anaemia, the WHO African Region, South-East Asia Region and Eastern Mediterranean Region had the lowest mean haemoglobin concentrations, as well as the highest prevalences of anaemia among women and children *(6)*. The WHO African Region had the countries with the lowest haemoglobin levels and highest prevalences of anaemia. Children under 5 years of age in the WHO African Region represented the highest *proportion*

of individuals affected with anaemia (62.3%), while the greatest *number* of children and women with anaemia resided in the WHO South-East Asia Region, including 190 million non-pregnant women, 11.5 million pregnant women, and 96.7 million children aged under 5 years. At the country level, the majority of WHO Member States (141 to 182, depending on the population group) had a moderate-to-severe public health problem with anaemia among women and children aged under 5 years, according to WHO classifications *(3, 6)* (Table 4). All countries for which country-level estimates were generated had a prevalence of anaemia of at least 5%, indicating at least a mild public health problem.

TABLE 4. Classification of anaemia as a problem of public health significance

Prevalence of anaemia (%)	Category of public health significance
≤4.9	No public health problem
5.0–19.9	Mild public health problem
20.0–39.9	Moderate public health problem
≥40	Severe public health problem

Source: World Health Organization, Centers for Disease Control and Prevention. Worldwide prevalence of anaemia 1993–2005. WHO Global Database on Anaemia. Geneva: World Health Organization; 2008 *(51)*.

Progress on reducing the incidence of anaemia has been made in some regions, while further improvements are still needed in others. At a global level, in all age and gender groups, anaemia is estimated to have decreased roughly seven percentage points between 1990 and 2010, from 40% to 33% *(1)*. During roughly the same period (1995 to 2011), anaemia was estimated to have decreased by 4–5 percentage points in the three highest-risk groups (children aged under 5 years, pregnant women, non-pregnant women of reproductive age) *(3)*. At a regional level, Africa (central and west, and east) and south Asia had the lowest mean haemoglobin concentrations, as well as the highest prevalences of anaemia among high-risk groups in both 1995 and 2011, despite significant improvements for children in the African regions (larger than in any other region) *(3)*. No improvement was seen among some groups with low haemoglobin levels and high prevalence of anaemia in 1995, including non-pregnant women in west Africa, central Asia, the Middle East and north Africa; and pregnant women in southern Africa and south Asia. Haemoglobin concentrations among children appear to have declined in southern Africa, while the largest improvements in women's haemoglobin levels were seen in central America and the Caribbean, east Africa, east and south-east Asia and Oceania *(3)*. The global average of the prevalence of anaemia in women of reproductive age increased slightly between 2005 and 2016, although the increase was not statistically significant. It declined from 42% to 38% in Africa and from 25% to 22% in Latin America and the Caribbean, although this was offset by slight increases in all other regions *(1)*.

1.6.2 OLDER ADULTS

Anaemia among older adults is less well documented, but it is known that the prevalence of anaemia among adults aged over 50 years rises with advancing age, particularly among men *(17)*. Data from predominantly high-income countries estimate that 17% (ranging from 3% to 50%) of individuals aged over 65 years in the community have anaemia, with a significantly higher prevalence among older adults in nursing homes (47%) *(40)*. Data from low-income and middle-income countries are limited, though WHO estimated that roughly 24% of older adults (over 60 years of age) globally had anaemia in 2005 *(55)*. In Uganda, 20% of adults aged over 50 years had anaemia (24% of men and 17% of women) *(19)*. Though the proportion of elderly individuals affected is lower than that seen among children or pregnant women, both the proportion and the number of older adults affected are rising worldwide. Lifetimes are also lengthening, indicating a potentially substantial burden in this population group in the future *(17)*.

DETERMINANTS OF ANAEMIA

2
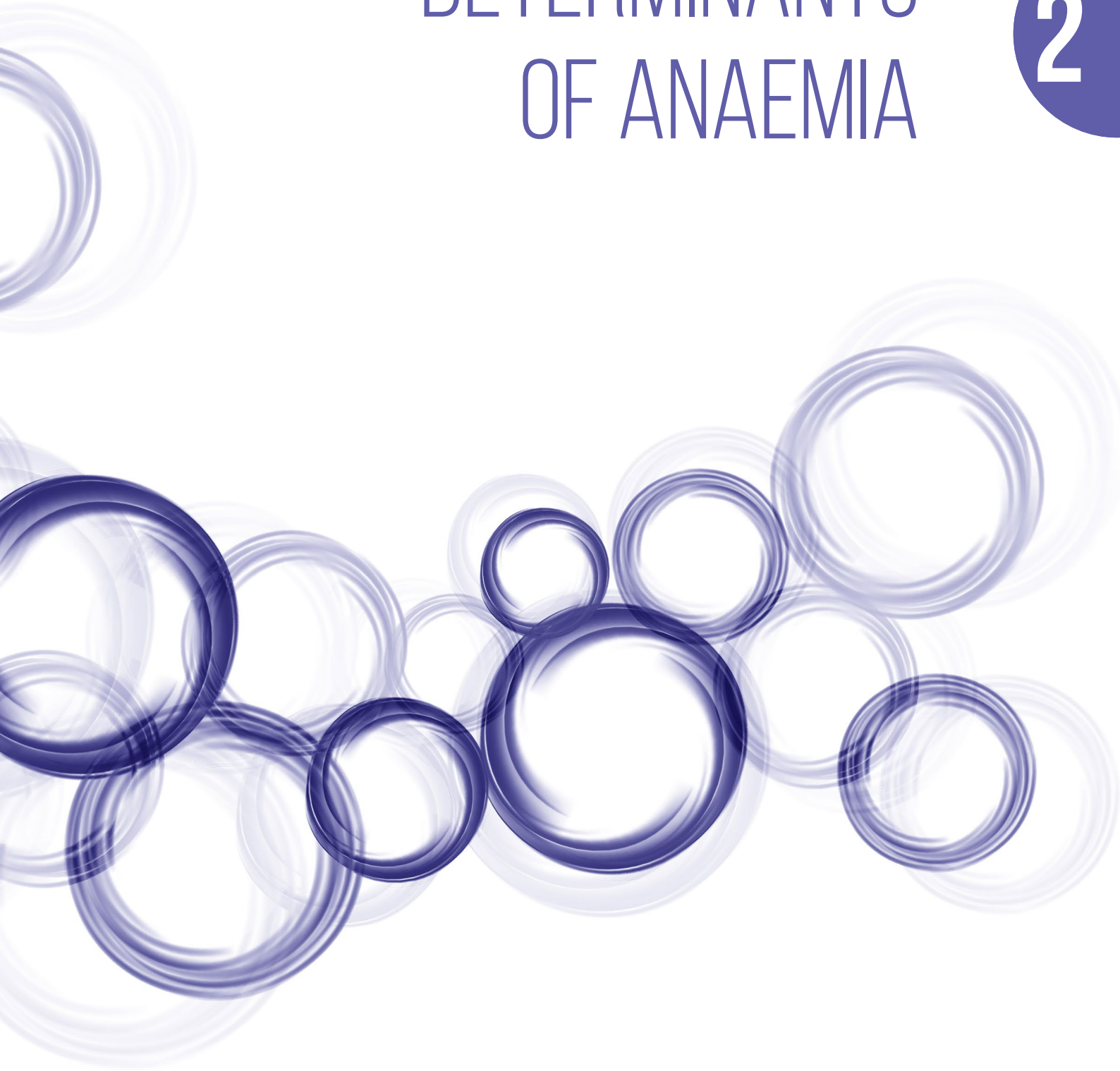
The etiology of anaemia is complex and the role of different determinants can vary from one setting to the next. The prevalence and distribution of anaemia is affected by a broad range of factors, including biological, socioeconomic and contextual/ecological determinants, with many acting simultaneously. Thus, interventions to tackle anaemia (discussed in section 3) must identify and address, in an integrated manner, the range of potential and unique risk factors at play in a particular setting and address their independent and overlapping effects.

2.1 BIOLOGICAL DETERMINANTS OF ANAEMIA

Anaemia is influenced by multiple biological factors, including nutrition, physical growth, physiological processes (e.g. pregnancy, menstruation, lactation), sex, age and race. Anaemia results when the production of erythrocytes is outpaced by their destruction or loss. Thus, factors that can affect the development of anaemia act by decreasing production of erythrocytes or increasing their destruction or loss, or in some cases both.

2.1.1 NUTRIENT DEFICIENCIES

"Nutritional anaemias" result when the intake of certain nutrients is insufficient to cover the demands for synthesis of haemoglobin and erythrocytes *(4)*. Iron deficiency is the most common nutritional deficiency leading to anaemia. Other nutritional deficiencies that can also lead to anaemia include deficiencies of vitamins A, B_6, B_{12}, C, D and E, folate, riboflavin and copper, though some of these nutrient deficiencies are uncommon and may not play a significant role in the burden of anaemia globally. In many cases, where diets are poor in micronutrients, multiple micronutrient deficiencies are likely to have a synergistic effect on the development of anaemia *(4)*.

While inadequate dietary intake of these nutrients is a primary pathway leading to anaemia, nutritional anaemias can also result from increased nutrient losses (e.g. blood loss from parasites, haemorrhage associated with childbirth, or heavy menstrual losses, all leading to iron deficiency), impaired absorption (e.g. lack of intrinsic factor to aid vitamin B_{12} absorption or high intake of anti-nutrients such as phytate, impairing iron absorption), as well as altered nutrient metabolism (e.g. vitamin A deficiency affecting mobilization of iron stores).

2.1.1.1 IRON

Iron is a key nutrient required for haemoglobin, and thus production of red blood cells; it is an essential part of the haemoglobin molecule. Conditions that require an increase in red blood cells – for example, growth of tissue mass of an infant, or growth of a fetus during pregnancy – increase iron requirements. Iron deficiency develops when dietary iron intake cannot meet iron needs (e.g. owing to poor diet, or impaired absorption from high intake of phytates or phenolic compounds), especially during periods of life when iron requirements are especially high (i.e. during infancy and pregnancy), or iron losses exceed iron intake (e.g. from blood loss from parasites, childbirth or menstruation) over a period of time. In the late stages of iron deficiency, when the body's store of iron has been depleted, the supply of iron to support production of red blood cells is compromised and, as a result, haemoglobin concentration decreases. Iron-deficiency anaemia is characterized as a hypochromic, microcytic anaemia.

Poor iron status can be transferred intergenerationally from mother to child. The extent to which maternal iron deficiency and/or iron-deficiency anaemia during pregnancy affects fetal iron status is debated; infants born to women with iron-deficiency anaemia have been shown, in several studies, to be at increased risk of iron deficiency and anaemia *(56, 57)* but not all studies show a relationship between maternal iron deficiency and later infant/child iron status *(58)*. Infants who are born

prematurely or with low birth-weight (<2500 g) have compromised iron stores at birth and are also at increased risk of becoming iron deficient and anaemic (also see section 2.1.3).

Iron deficiency is estimated to contribute to approximately 50% of all cases of anaemia among non-pregnant and pregnant women, and 42% of cases in children aged under 5 years *(3, 6)*. However, a systematic review based on representative surveys that reported the prevalence of iron deficiency, iron-deficiency anaemia, and anaemia among preschool children and non-pregnant women of reproductive age from countries ranked as low, medium and high by the Human Development Index, showed that the proportion of anaemia attributable to iron deficiency was lower in countries where the prevalence of anaemia was >40%, especially in rural populations *(59)*; this suggested that the proportion of anaemia associated with iron deficiency could be lower than the previously assumed 50% in countries with low, medium or high Human Development Index ranking *(59)*. Furthermore, in some countries, for example Cambodia, it has been suggested that the high prevalence of anaemia in women and children cannot be explained solely by micronutrient deficiencies and haemoglobin disorders *(60, 61)*.

The role of iron in cases of severe anaemia is greater (>50% for children and non-pregnant women, and >60% for pregnant women) *(3)*. Thus, while in many cases, iron-deficiency anaemia and anaemia are viewed synonymously, it is important to remember that roughly half of anaemia cases will *not* be caused by iron deficiency *nor* can they be corrected by providing additional iron.

2.1.1.2 VITAMIN A

Multiple mechanisms for the role of vitamin A deficiency in the development of anaemia have been documented *(62)*. Retinoids have been shown to modulate erythropoiesis, and lack of vitamin A, because of its important role in immune function, could contribute to the development of anaemia of infection (also see section 2.2) in individuals who are deficient in vitamin A *(62)*. Vitamin A also plays a role in iron metabolism, with decreased mobilization of iron from stores in the liver and spleen during vitamin A deficiency,[1] which could also contribute to the development of anaemia *(62)*. In contrast to iron-deficiency anaemia, which is marked by a depletion of iron stores (decreased serum ferritin), anaemia due to vitamin A deficiency is marked by an increase in iron stores in the liver and spleen, and increased serum ferritin concentrations *(63)*.

Vitamin A deficiency is prevalent in many low- and middle-income countries, particularly among preschool children, pregnant women and women of reproductive age. In 2013, the prevalence of deficiency was 29% among children aged 6–59 months in low-income and middle-income countries. In 2013, the prevalence of deficiency was highest in sub-Saharan Africa (48%) and south Asia (44%) *(64)*. Vitamin A supplementation has been shown to increase haemoglobin concentrations in many different settings and populations, including when it is administered in the absence of iron supplements *(65)*.

2.1.1.3 B VITAMINS (RIBOFLAVIN, B₁₂, FOLATE, B₆)

Deficiencies of several B vitamins may play a role in the development of anaemia.

Riboflavin (vitamin B_2) deficiency may contribute to development of anaemia, through its effects on iron metabolism, including decreasing iron mobilization from stores, decreasing iron absorption and increasing iron losses *(66)*, as well as impairing globin production *(65)*. Riboflavin supplements provided along with iron supplements have been shown to have a greater effect on haemoglobin concentration than iron supplements alone *(66)*. Riboflavin deficiency is particularly common in areas where intakes of meat and milk/dairy products are low, and has been documented in pregnant and lactating women, infants, school-aged children and the elderly *(67)*.

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[1] Countries at risk of vitamin A deficiency included those with a 2005 GDP below US$ 15 000.

Both vitamin B_{12} (cobalamin) deficiency and folate deficiency can lead to macrocytic (megaloblastic) anaemia, as deficiencies of these nutrients affect DNA synthesis, cell division and thus erythropoiesis. Vitamin B_{12} deficiency most commonly results from low dietary intake of the nutrient, particularly if the diet is low in animal-source food, but can also result from malabsorption, particularly in the elderly, among whom gastric atrophy is common *(68)*. Data on the prevalence of vitamin B_{12} deficiency at the national level are lacking; however, in five out of seven countries with national data, the reported prevalence of vitamin B_{12} deficiency is 5% or greater among different age and biological groups *(69)*.

Similarly, folate deficiency was estimated to be of public health significance in six out of eight countries with national data *(69)*. Folate deficiency tends to be more common in populations that rely on unfortified wheat or rice as a staple food and that also consume low amounts of legumes and green leafy vegetables *(68)*. Pregnant women, preterm infants and individuals living in malaria-endemic regions are also at high risk of folate deficiency *(65)*.

However, the contribution of deficiencies of vitamin B_{12} and folate to the global incidence of anaemia is thought to be minimal, except in the case of women and their infants and children consuming vegetarian diets that are deficient in vitamin B_{12} *(70)*. A review of the evidence for deficiency of vitamin B_{12} and folate and anaemia indicates that a high prevalence of vitamin B_{12} or folate deficiency does not necessarily correlate to a high prevalence of these types of anaemia *(70)*.

Vitamin B_6 is essential for synthesis of haem, and can cause the same microcytic, hypochromic anaemia as iron deficiency, as well as normocytic or sideroblastic anaemia *(65)*. Vitamin B_6 deficiency is rare, and the public health significance of this deficiency for anaemia is unknown *(65)*.

2.1.1.4 VITAMINS C, D AND E

Vitamin C is known to affect iron metabolism, particularly enhancing absorption of non-haem iron, but also increasing mobilization of iron from stores *(65)*. Vitamin C deficiency can also contribute to haemolysis, through oxidative damage to erythrocytes and also capillary haemorrhaging leading to blood loss *(65)*. Populations at risk of vitamin C deficiency include pregnant women, infants fed exclusively with cow's milk, the elderly and smokers. Vitamin C supplementation has been shown to increase haemoglobin concentration and serum ferritin in children and non-pregnant women *(65)*.

Low levels of vitamin D have been associated with anaemia in children and adults from the USA, and individuals with chronic kidney disease, end-stage heart failure, and type 2 diabetes from several countries *(71)*. The mechanism linking vitamin D deficiency to decreased haemoglobin concentration is not entirely understood, but there is evidence indicating that low levels of vitamin D may lead to decreased local calcitriol production in the bone marrow, which may limit erythropoiesis *(71)*.

Anaemia associated with vitamin E deficiency is characterized as a haemolytic anaemia, owing to the protective effect of vitamin E on polyunsaturated fatty acids in the membranes of red blood cells *(65)*. Deficiency of vitamin E is thought to be largely limited to premature and low-birth-weight infants, and individuals with pathological malabsorption syndromes, as vitamin E is common in foods, particularly vegetable and seed oils *(65)*. Vitamin E is routinely provided to premature/low-birth-weight infants in high-income countries, to avoid "anaemia of prematurity"*(65)*.

2.1.1.5 COPPER

Copper is needed for several enzymes that are required for iron metabolism, including caeruloplasmin, which is responsible for the oxidation of ferrous iron and the transfer of iron from storage to sites of haemoglobin synthesis (72), and is thus essential for normal iron metabolism and erythropoiesis. One clinical sign of copper deficiency is anaemia (most often normocytic and hypochromic, but sometimes normochromic and microcytic (72, 73)). However, copper deficiency is rare, with high-risk individuals including premature and low-birth-weight infants fed milk diets, infants and children recovering from malnutrition, individuals receiving prolonged total parenteral nutrition, infants with prolonged diarrhoea, and individuals with malabsorption syndromes (e.g. coeliac disease or non-tropical sprue) (72). High iron or zinc intakes can also interfere with copper absorption, just as high intakes of divalent metals (copper, calcium, zinc, manganese), which share the same transporter as iron, can interfere with iron absorption and produce iron deficiency.

2.1.2 OTHER FORMS OF MALNUTRITION

2.1.2.1 UNDERNUTRITION: STUNTING, WASTING AND UNDERWEIGHT

Stunting, wasting and underweight are manifestations of undernutrition that are assessed through body measurements and have been associated with anaemia in some studies (74, 75) but not all (76). These manifestations of poor nutritional status are associated with anaemia, owing to similar causal factors. Stunting results from a variety of factors and conditions occurring particularly during the first 2 years of life, including poor maternal nutrition, inadequate home and community environments, inadequate complementary feeding practices leading to poor intake of micronutrients and animal-source foods, contaminated water and poor sanitation, suboptimal breastfeeding practices, and clinical and subclinical infections (77). Wasting reflects "acute malnutrition" or undernutrition that has resulted from a shorter-term state of nutrient deficiency that causes weight (particularly muscle and fat stores) to be inadequate for a child's height. Wasting is thought to share some of the same causes as stunting (78), such as illness, food insecurity and poor dietary intake, although the severity, frequency and speed of onset of illness, and the severity and seasonality of the food security situation in which a child is living, may lead to wasting rather than stunting (78). Underweight (low-weight-for-age) can reflect a child whose weight is too low for their height (wasted), or a child who is short for their age (stunted), and thus has low body mass, or a combination of both.

2.1.2.2 OVERWEIGHT AND OBESITY

Though at seemingly opposite ends of the over- and undernutrition spectrum, overweight, obesity and iron deficiency are linked, with data from multiple countries showing an increased risk for iron deficiency in overweight and obese individuals (children, adolescents and adults) (79). The link between these conditions is probably through hepcidin, a peptide hormone that is responsible for iron homeostasis and produced primarily in the liver (80). Hepcidin regulates the activity of the only known iron exporter, ferroportin-1, downregulation of which decreases iron in plasma and increases iron in stores (79). Hepcidin expression is increased by higher body iron levels, and inflammation (decreasing ferroportin-1 expression and thus decreasing iron absorption and iron bioavailability in plasma) and is decreased by anaemia and hypoxia (increasing ferroportin-1 expression and thus increasing iron absorption and iron bioavailabilty in plasma) (79). In obese individuals, hepcidin levels are elevated as compared to lean individuals; in one study, overweight children had elevated hepcidin levels and poorer iron status than children of normal weight, despite having similar dietary iron intake to normal-weight children (81). Obesity is also associated with subclinical inflammation, which can increase hepcidin levels (81). Research suggests that iron deficiency in overweight/obese individuals is

due to hepcidin-mediated reduction in iron absorption and/or sequestration and increased hepcidin production by the liver (and to a lesser degree, adipose tissue), though the link between weight gain and iron status is still not completely understood *(79)*. In addition, while obesity is associated with iron deficiency, haemoglobin concentrations generally tend to be within the normal range *(79, 80)*.

2.1.3 GROWTH, PHYSIOLOGICAL STATE, SEX, AGE AND RACE

In groups at high risk of anaemia, multiple factors are frequently acting simultaneously to affect the risk of anaemia. For example, children aged under 5 years (particularly those under 2 years), adolescents and women of reproductive age (12–49 years of age) are high-risk groups for anaemia because of the combined effects of growth, physiological state and sex in these groups.

2.1.3.1 GROWTH

During growth, nutrient demands, particularly for iron, increase in order to meet the need for haemoglobin and erythropoiesis required for expansion of blood volume and muscle and tissue development. Children under 2 years of age have a very high rate of growth, and between 6 and 24 months of age, iron requirements per kilogram of body weight are higher than at other stages of life *(82)*. Meeting the nutrient requirements of young children in many low-income countries where dietary quality is poor is challenging, given the small quantities of food they eat. Low-birth-weight and premature infants are at greater risk because they have smaller iron stores to begin with at birth. After 2 years of age, the rate of growth slows, the haemoglobin concentration tends to increase, and the prevalence of anaemia decreases. Thus, in periods of rapid growth, such as those that occur during infancy and adolescence, anaemia commonly develops when nutrient needs for erythropoiesis – primarily iron – cannot be met.

2.1.3.2 PHYSIOLOGICAL PROCESSES

Physiological processes that occur during the life-cycle can also affect the development of anaemia. Menstruation increases iron losses, thus increasing the risk of anaemia in females when they reach menarche and throughout their reproductive years. Adolescent females are at particular risk of anaemia because of their iron needs for growth as well as increased iron losses from menstruation. The risk of anaemia is further exacerbated if adolescent females become pregnant, as pregnancy incurs significant nutrient needs, again for iron, to meet the requirements of expanding blood volume for the mother and also the growth and development of the fetus. In addition, many females (adolescents and adults) enter pregnancy with iron stores that are already inadequate. Over the course of pregnancy, women's iron needs increase from 0.8 mg per day during the first trimester to close to 10 times higher (7.5 mg/day) in the third trimester *(4)*. Iron is needed for production of breast milk during lactation; however, amenorrhoea during this period reduces the iron requirement for lactating women compared to pregnancy. Tables 5 and 6 show iron requirements by age, sex and physiological status. However, short durations between pregnancies (which do not allow recuperation of iron stores), as well as high numbers of pregnancies, are also associated with increased risk of anaemia.

TABLE 5. Requirements for total absorbed iron and recommended nutrient intakes by age, sex and physiological status

| Group and age (years) | Requirements for absorbed iron (mg/day) | | Recommended nutrient intake (mg/day) for a dietary iron by bioavailability | | | |
	Median requirement	95th percentile	15%	12%	10%	5%
Infants and children						
0.5–1	0.72	0.93	6.2	7.7	9.3	18.6
1–3	0.46	0.58	3.9	4.8	5.8	11.6
4–6	0.50	0.63	4.2	5.3	6.3	12.6
7–10	0.71	0.89	5.9	7.4	8.9	17.8
Males						
11–14	1.17	1.46	9.7	12.2	14.6	29.2
15–17	1.50	1.88	12.5	15.7	18.8	37.6
18+	1.05	1.37	9.1	11.4	13.7	27.4
Females						
11–14 (premenarche)	1.20	1.40	9.3	11.7	14.0	28.0
11–14 (after menarche)	1.68	3.27	21.8	27.7	32.7	65.4
15–17	1.62	3.10	20.7	25.8	31.0	62.0
18+	1.46	2.94	19.6	24.5	29.4	58.8
Postmenopausal	0.87	1.13	7.5	9.4	11.3	22.6
Lactating	1.15	1.50	10.0	12.5	15.0	30.0

Source: World Health Organization, Food and Agricultural Organization of the United Nations. Vitamin and mineral requirements in human nutrition, 2nd ed. Geneva: World Health Organization; 2004 *(83)*.

TABLE 6. Iron requirements (absorbed and recommended dietary allowances) during pregnancy

Pregnancy	Median absorbed iron requirement (mg/day)	Median dietary iron requirement (mg/day)[a]	Recommended dietary allowance (mg/day)[b]
First trimester	1.2	6.4 (18% bioavailablity)	
Second trimester	4.7	18.8 (25% availability)	27 (25% bioavailability)
Third trimester	5.6	22.4 (25% bioavailabilty)	

[a] In the first trimester, the requirement is estimated using the absorption efficiency for non-pregnant females, and increased to 25% for second and third trimesters due to increased iron demand.

[b] Recommended dietary allowance is set by estimating the requirement for absorbed iron at the 97.5 percentile, 25% absorption and rounding.

Source: Iron. In: Institute of Medicine (US) Panel on Micronutrients. Dietary reference intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. Washington (DC): National Academy Press; 2001:290–393 *(84)*.

2.1.3.3 SEX

The risk of anaemia is also patterned by sex, and through much of the life-course, women have a greater prevalence of anaemia than men. Physiological processes like menstruation and pregnancy increase the risk of anaemia for females compared to males in the rough age range of 15–49 years. While an individual's sex has not been traditionally thought to affect their risk of anaemia until puberty, when menstruation increases iron losses for females, male infants and young children may be at greater risk of lower haemoglobin concentrations and/or poor iron status as compared to their female peers *(75, 85–88)*. An assessment of iron stores in infants during the first year of life found that male infants had consistently lower iron stores and estimated body iron, and higher rates of iron deficiency than female infants. Male infants had significantly lower iron endowment even at 1 month of life, indicating a role of factors in utero for determining iron status at birth *(58)* – potentially hormonal influences on erythropoietic activity *(85)*. In the elderly, men have higher rates of anaemia (see section 2.1.3.4). Apart from physiological sex differences, gender norms or cultural practices that govern household food distribution or other dietary, feeding or care practices may also contribute to gender differences in anaemia.

2.1.3.4 AGEING

The ageing process can also affect the risk of anaemia, both through "natural" manifestations of ageing, and through pathological processes (comorbidities) that occur with increased frequency among the elderly (though it can difficult to separate the two). Haemoglobin concentration is seen to decline with advancing age, starting roughly in the fifth decade of life, with a more marked decline among men *(17, 88)*. Thus, in contrast to anaemia patterns among younger adults (i.e. <50 years of age), where the prevalence of anaemia is higher in women, older men have a greater prevalence of anaemia than older women. The decline in haemoglobin, including the more pronounced decline seen among men, is thought to be partially due to decreased numbers of bone marrow erythroid progenitors, which are seen more commonly in elderly men compared to elderly women *(89)*. Haematopoietic stem cells also appear to have increased erythropoietin resistance with age, and ageing limits the ability of the kidneys to produce sufficient erythropoietin to meet the increased need *(90)*. Finally, ageing is associated with increased pro-inflammatory cytokine expression (regardless of health status), which contributes to the development of anaemia of chronic disease/inflammation *(90)*.

Elderly individuals can also be at increased risk of anaemia because of comorbidities, including gastric atrophy causing malabsorption of nutrients, gastrointestinal blood loss, myelodysplastic syndromes, and chronic conditions (e.g. chronic inflammation or chronic kidney disease) *(18)*. Owing to these sex differences, as well as associations with mortality risk at both low and high haemoglobin concentrations *(90)*, some researchers have suggested that the haemoglobin cut-off values for the elderly may need to be revisited to define the optimal haemoglobin value that defines an abnormal concentration in elderly individuals *(91)*. Currently, WHO cut-off values use a different haemoglobin concentration for postmenopausal women (<120 g/L) than similarly-aged men (<130 g/L) *(17)*.

2.1.3.5 RACE

Race is an additional biological factor that determines haemoglobin distribution and, consequently, the prevalence of anaemia. Black individuals have lower haemoglobin concentrations than white individuals; these differences are not explained by health, nutrition or socioeconomic status, and are observed across the age spectrum *(17)*. Even after accounting for iron status and known gene mutations such as α-thalassaemia, glucose-6-phopsphate deficiency and sickle-cell trait, which occur more commonly in populations of African descent (and are discussed further in section 2.3), differences in haemoglobin by race still existed in one study of more than 32 000 individuals *(92)*. The most widely used criteria for defining anaemia set by WHO do not currently take race into account *(43)*.

2.2 DISEASE (INFECTION AND INFLAMMATION)

Disease can cause anaemia through multiple mechanisms. Disease or infection can impair nutrient absorption and metabolism or increase nutrient losses (such as with intestinal parasites). Infectious processes or chronic disease can also cause what is referred to as "anaemia of chronic disease/inflammation", whereby pro-inflammatory cytokines alter iron metabolism so that iron is sequestered in stores as ferritin, and the production and lifespan of red bloods are reduced *(8)*. Acute and chronic infections, such as malaria, cancer, TB, HIV, chronic kidney disease and chronic heart failure can all lead to anaemia. For many of these diseases – particularly malaria and parasitic infections– the physical setting determines the risk of disease and thus patterns of anaemia risk (also see section 2.4).

2.2.1 SOIL-TRANSMITTED HELMINTH INFECTIONS

Hookworm (*Necator americanus* and *Ancylostoma duodenale*) is the primary soil-transmitted helminth that is associated with blood (and iron) loss, and iron-deficiency anaemia. It has been estimated that a single hookworm can cause blood loss of 0.03–0.26 mL/day *(93)*. Based on this estimate of faecal loss of haemoglobin, light-intensity hookworm infections (1 to <2000 eggs per gram of faeces) are related to a loss of less than 2 mg of haemoglobin per gram of faeces, while heavy-intensity hookworm infections (>4000 eggs per gram of faeces) correspond to a loss of more than 5 mg of haemoglobin per gram of faeces *(94)*. (DALYs) expansion was provided earlier, a measure of overall disease burden expressed as the number of years lost due to ill health or early death, from *A. duodenale* or *N. americanus* infection have been most recently estimated at 1.8 million, which corresponds to an important proportion of the DALYs attributable to soil-transmitted helminth infections *(95)*. The intensity of infection and species of hookworm, as well as coinfection with multiple parasites *(75)*, determine the severity of blood loss. In west Africa, roughly 4% of cases of anaemia are attributable to hookworm *(75)*.

2.2.2 SCHISTOSOMIASIS

Another parasitic infection that can also lead to anaemia is schistosomiasis, which primarily occurs in sub-Saharan Africa, with an estimated 192 million cases per year among children and young adults *(4)*. Schistosomiasis similarly leads to blood loss, but may also contribute to anaemia through splenic sequestration of erythrocytes, increased haemolysis or anaemia of chronic disease *(4)*. The exact mechanisms of schistosomiasis-induced anaemia are not well understood.

2.2.3 MALARIA

Malaria is one of the primary causes of anaemia globally *(1)*. The number of malaria cases globally fell from an estimated 262 million in 2000 to 214 million in 2015, a decline of 18%. Most cases in 2015 are estimated to have occurred in the WHO African Region (88%), followed by the WHO South-East Asia Region (10%) and the WHO Eastern Mediterranean Region (2%) *(96)*. Malaria is a primary cause of anaemia in east and west Africa in particular *(6)*. Roughly 15% of cases of anaemia in preschool children in west Africa are estimated to be attributable to malaria *(75)*. *Plasmodium falciparum* is the most pathogenic species of the parasites causing malaria, and infection with *P. falciparum* can lead to severe anaemia, subsequent hypoxia and congestive heart failure *(4)*. Malaria disturbs iron metabolism in multiple ways *(97)* and the mechanism for malaria-related anaemia is probably related to both increased haemolysis (erythrocyte destruction) and decreased production of red blood cells *(4)*. Hepcidin is upregulated in malaria infection, which probably contributes to anaemia through redistribution of iron to macrophages, and decreasing or preventing iron uptake from the diet *(97)*.

Although earlier studies showed increased risk of malaria-related adverse events with iron supplementation, a recent systematic review showed no difference in the risk of clinical malaria

between groups receiving daily iron supplementation and those receiving placebo or supplementation without iron, in children living in malaria hyperendemic or holoendemic areas *(98)*. The current WHO recommendation for children in malaria-endemic areas is provision of iron supplementation in conjunction with public health measures to prevent, diagnose and treat malaria *(99)*. Malaria control in endemic areas can reduce anaemia and severe anaemia by over a quarter and by 60%, respectively *(100)*.

2.2.4 HIV

Anaemia is one of the most common haematological abnormalities among persons living with HIV, affecting anywhere between 1.3% and 95% of these individuals, and typically characterized as a normochromic and normocytic anaemia, with a low reticulocyte count, normal iron stores and an impaired erythropoietin response *(101)*. Anaemia in persons living with HIV is thought to result from several factors that are both indirectly and directly related to the virus. Indirect effects of HIV infection on anaemia include: opportunistic infections, which are common among persons living with HIV, leading to anaemia (e.g. malaria, hookworm); nutritional deficiencies contributing to anaemia development; and antiretroviral therapy having a negative effect on erythropoiesis *(101)*. The HIV virus also appears to have direct effects on anaemia, by affecting haematopoietic progenitor cells and decreasing responsiveness to erythropoietin *(101)*. Finally, HIV infection is linked to pro-inflammatory cytokines and altered iron metabolism, leading to "anaemia of chronic disease/inflammation" *(101)*. Anaemia among persons living with HIV is a predictor of progression to AIDS, as the degree of anaemia is correlated with disease progression *(101)*, as well as being independently associated with mortality *(102)*.

2.2.5 TUBERCULOSIS

Anaemia is common among patients with TB and may be more common among those who are coinfected with TB and HIV *(103)*; in one study from Malawi, more than three quarters (77%) of TB patients without HIV had anaemia, while 88% of TB/HIV-coinfected patients had anaemia *(104)*. In Indonesia, 60% of malnourished TB patients had anaemia *(105)*, while in Uganda, 71% of TB/HIV-coinfected patients had anaemia *(106)*. Anaemia among pulmonary TB patients is thought to result from increased blood loss from haemoptysis (blood in sputum); decreased production of red blood cells; poor appetite and food intake, leading to poor nutrient status (of iron, but also of other nutrients, including selenium in one study *(104)*); and anaemia of chronic disease/inflammation *(103)*.

2.2.6 LOW-GRADE INFLAMMATION

Iron metabolism is closely associated with immune response. Both deficiency and excess of iron affect the inflammatory response and susceptibility to infections. Also, iron's pro-oxidant effect increases the inflammatory response. Low iron status and anaemia in obesity have been associated with the inflammatory response *(107, 108)*. There are nutritional factors that can affect or modulate the immune system. These include total calorie intake (both excess and deficit), total fat, fat type, vitamins A, B_6, C, D and E, carotenoids, iron, zinc and selenium *(109)*.

2.3 GENETIC HAEMOGLOBIN DISORDERS

Inherited genetic haemoglobin disorders, such as sickle cell trait or thalassaemias, are one of the top three causes of anaemia globally *(2)*. Roughly 5% of the global population is estimated to carry a significant haemoglobin variant; the percentage is higher in Africa (18%) and Asia (7%) *(4)*. More than 300 000 children are estimated to be born each year with either sickle cell anaemia or one of its variants (which affects 180 000 births annually in sub-Saharan Africa), or a form of thalassaemia (affecting primarily south and south-east Asia) *(9, 95)*. However, some of these estimates, based on studies completed before 1980, may underestimate

the current incidence of these conditions, as child survival has improved in many of the countries in which these disorders are most common *(9)*. In many low-income countries, diagnosis and management of these conditions is inadequate or unavailable *(9)*.

2.4 SOCIAL, BEHAVIOURAL AND ENVIRONMENTAL DETERMINANTS OF ANAEMIA

A broad range of socioeconomic, behavioural and environmental determinants make some individuals and population groups more vulnerable to anaemia. Such determinants include, for instance, lack of sufficient income, low education level, discrimination based on gender norms or race, unhealthy behaviours such as smoking, poor living conditions and inadequate access to water, sanitation and hygiene. Environmental factors such as altitude, and emergency or disaster settings (either induced or natural), also contribute to the prevalence of anaemia.

2.4.1 SOCIAL AND BEHAVIOURAL DETERMINANTS

Socioeconomic status is tightly linked to anaemia, and affects the prevalence of anaemia through several pathways. Poverty is a major determinant of health. It is associated with poor living and working conditions, including poor water, sanitation and hygiene, and inadequate infrastructure, which can lead to increased disease. It is also connected to adverse health and nutrition behaviours (including smoking or poor dietary practices, both of which can affect haemoglobin concentration), food insecurity and poor dietary quality (including limited access to fortified foods and animal-source foods). Poverty is also linked to inadequate access to health-care services (including limited access to anaemia prevention and treatment services, including iron supplements, deworming, insecticide-treated bed nets, as well as reproductive care). In a pooled analysis of demographic and health survey (DHS) data sets, women and children in the lowest wealth quintiles had a risk of anaemia 25% and 21% higher, respectively, than women and children in the highest wealth quintiles *(4)*.

Education is also a determinant of health. Lack of formal education or a low education level is also associated with development of anaemia. From the same analysis of DHS data sets, women with no education were 8% more likely to have anaemia, and their children were 9% more likely to have anaemia than women with secondary or higher education *(4)*. Low maternal education level may affect mothers' ability to access and understand health and nutrition information, and ultimately negatively affect their children's quality of diet *(110)*. Mothers' education level may also influence decision-making and compliance with recommended health practices (such as iron supplementation or reproductive health practices), as well as caretaking practices (including feeding and hygiene behaviours).

Ethnicity and race are perceived and valued differently in most societies. Ethnicity is socially constructed around shared values and social practices, and may or may not be associated with a common racial background. Varying from setting to setting, population groups belonging (or thought to belong) to specific ethnic, cultural or religious groups are at greater risk of suffering discrimination and thus enjoying fewer opportunities for generating income (poor-valued jobs); for accessing or increasing their education; for accessing certain services such as health care, social services or community campaigns; and for promoting healthy behaviours *(111)*, to name a few. The association of these factors with anaemia occurs through multiple pathways. Discrimination may prevent access to services or reduce the quality and utilization of health care. Ethnicity may also signify differences in dietary practices (e.g. vegetarianism, fasting) or other care practices that could affect the risk of anaemia, or represent a true biological difference in anaemia risk due to genetic factors (e.g. inherited haemoglobin disorders). In Viet Nam, women of ethnic minorities were 1.5 times more likely to have anaemia than women of the majority ethnic group, even after controlling for other sociodemographic and dietary characteristics *(112)*. The authors speculated that biological factors –

differences. In India, social caste, independent of household wealth and parental education and other maternal and socioeconomic determinants, is a risk factor for anaemia (mild, moderate and severe) in children, indicating that caste-based discrimination may affect the development of anaemia *(113)*. Religion is one of the shared values and social practices that has also been associated with anaemia risk in some settings, probably related to meat consumption, fasting and avoidance of certain foods *(114)*.

Rural residence has been associated with a greater prevalence of anaemia *(75, 86)*. Urban residents may have greater access to services (including health care, as well as water, sanitation and hygiene), decreased exposure to some infectious agents (e.g. soil-transmitted parasites), and a more varied diet than rural residents, all of which are factors that can decrease the risk of anaemia.

Gender inequality and cultural practices related to marriage and pregnancy also play a role in the development of anaemia in some settings. Women and adolescent girls are already at increased physiological risk of anaemia in settings where their access to health care, education and household resources is limited. In households where food-distribution practices or other dietary or feeding practices favour men and boys, the risk of developing anaemia is exacerbated for women of any age group. In addition, the dietary practices of children frequently mirror those of their mother (owing to shared environments) and can also reflect the mother's knowledge of anaemia and practices to prevent it *(115)*. Thus, the opportunities that are provided to the mother in terms of access to information and education to improve health and nutrition outcomes extend beyond the mother to her child. As described previously, adolescent girls are at high risk of anaemia because of their rate of growth and increased iron losses from menstruation. In settings where early marriage and childbearing are common, the risk of anaemia will be increased. Prevailing gender norms usually affect women's rights and opportunities to access appropriate care for their health throughout the life-course, including sexual and reproductive health services. Women's access to health care is usually mediated by discriminating gender norms, which can exacerbate the effect of other factors such as the distance to and availability of health care.

Dietary patterns can affect iron intake or bioavailability for cultural, traditional or religious reasons. For example, inclusion of coffee or tea during meals, cooking in copper or iron pots and use of calcium to prepare staple foods as tortillas could affect the iron content and bioavailability of iron in foods. Regarding cultural beliefs, the use of certain food combinations or household food-distribution patterns could affect iron intake *(116–118)*.

Smoking increases blood levels of carboxyhaemoglobin, owing to the inhalation of carbon monoxide, so an increase in haemoglobin concentration occurs *(119)*. An adjustment in haemoglobin concentration has been proposed according to the frequency of cigarette use. For those who smoke between half and one pack of cigarettes per day (20 cigarettes/pack), 3 g/L of haemoglobin concentration is subtracted; for those who smoke between 1 and 2 packets per day 5 g/L is subtracted, and for those who smoke more than 2 packs per day, 7 g/L is subtracted. The diagnosis of anaemia is then made using the cut-off values applied to the rest of the population (Tables 1 and 2). Additional adjustments by altitude may be necessary (Table 7) *(43)*.

2.4.2 ENVIRONMENTAL FACTORS

Though the prevalence of anaemia is generally estimated at the national or subnational level, it is known that it varies spatially at much lower levels of aggregation, based on the spatial distribution of the many biological factors (e.g. areas where malaria or intestinal parasites are endemic) and socioeconomic factors associated with anaemia, as previously discussed. The risk of anaemia has been geographically mapped, based on the spatial distribution of two of its primary risk factors – disease and malnutrition *(75)* – and in the future, genetic haemoglobin disorders (which are also specific to particular regions) may also contribute to developing refined models.

2.4.2.1 EMERGENCY SETTINGS

Particular environmental settings where other social determinants play a major role are also associated with increased incidence of anaemia. Individuals affected by emergencies (both induced and natural) or humanitarian crises, as well as displaced persons living in refugee settings, have increased risk of nutritional deficiencies and anaemia. In the aftermath of an emergency, food shortages are a common occurrence, owing to loss of livelihoods, food crops and food supplies. Infrastructure and access to basic services (like water, sanitation and hygiene) can be damaged or no longer existent, leading to increased risk of disease (particularly diarrhoea), which contributes to malabsorption and malnutrition, as well as increased mortality. Micronutrient deficiencies that can cause anaemia can easily develop during these situations, or become worse if they are already present, particularly for those groups with greater nutrient needs and higher risk of anaemia (particularly children aged under 2 years, and pregnant and lactating women) *(120)*. Anaemia is also common in camps for refugees/displaced persons *(121–123)*, but also among refugee populations dispersed among neighbourhoods *(124)*. In refugee camps, access to nutritious foods, particularly iron-rich foods and fresh fruits and vegetables, is limited, and refugees commonly rely on food rations, with little access (owing to physical and financial constraints) to other food markets or food sources *(122)*. Increased disease risk (particularly diarrhoeal morbidity) is also common in these settings. Refugees outside of camps may also experience continued increased risk of anaemia and other nutritional problems, owing to food insecurity affecting dietary diversity; lack of employment and income leading to poverty; and inadequate health care and education *(124)*.

2.4.2.2 GEOGRAPHICAL SETTING: ALTITUDE

Because haemoglobin is responsible for transporting oxygen to tissues, its concentration varies according to residential elevation above sea level. The higher the altitude of the place of residence, the lower the environmental oxygen tension and, therefore, the body will respond with an increase in the body haemoglobin concentration *(125, 126)*. A desirable increase in haemoglobin concentration by altitude has been proposed, based on the correction factors recorded by various authors *(127)*. At altitudes between 1000 m and 1499 m above sea level, subtract 2 g/L from haemoglobin measurements. At altitudes between 1500 m and 1999 m above sea level, subtract 5 g/L from haemoglobin measurements; between 2000 m and 2499 m, subtract 8 g/L; between 2500 m and 2999 m, subtract 13 g/L, and so on (Table 7). This distribution is not a linear relationship; that is, the increase in haemoglobin concentration per metre above sea level is not the same at low altitudes as at high altitudes.

TABLE 7. Altitude adjustments to measure haemoglobin concentrations

Altitude (metres above sea level)	Measured haemoglobin adjustment (g/L)
<1000	0
1000	−2
1500	−5
2000	−8
2500	−13
3000	−19
3500	−27
4000	−35
4500	−45

Source: Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Geneva: World Health Organization; 2011 *(43)*.

SOLUTIONS
TO ANAEMIA

3
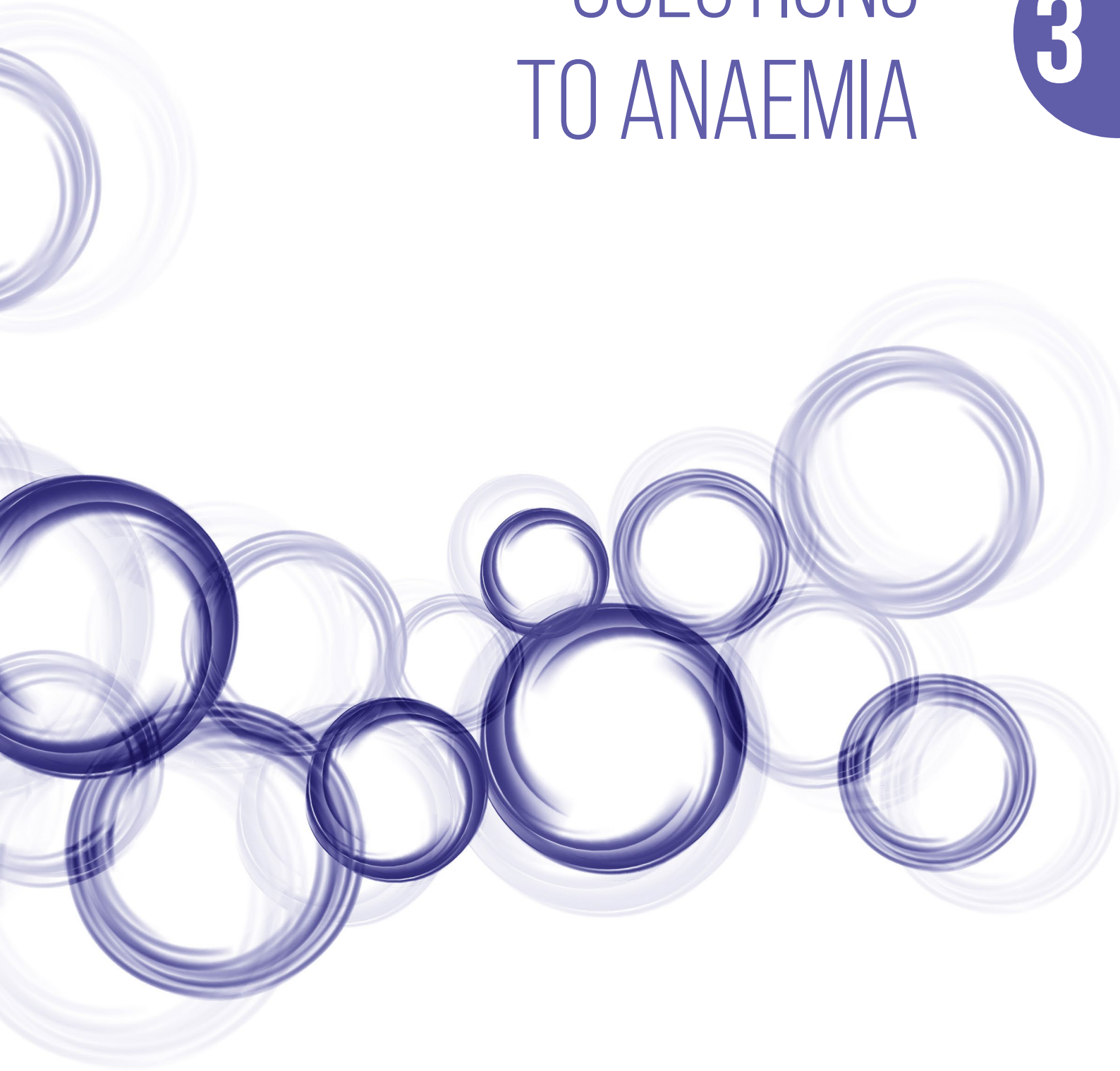
The previous two sections have outlined the magnitude and distribution of anaemia, its consequences and varied causes. Globally, nutrition, disease and genetic haemoglobin disorders are the three main contributors to anaemia, which is fundamentally linked to poverty. To effectively address anaemia at the country or regional level, a more detailed picture of the unique determinants of anaemia in a particular setting is needed. Each setting will need to assess the most relevant contributing factors and, in selecting the most appropriate interventions, engage a wide range of sectors for effective action (e.g. nutrition, health, water, sanitation and hygiene, poverty alleviation, agriculture, industry, education).

This section outlines:

- **nutrition-specific** solutions to anaemia, which tackle the immediate causes of anaemia, principally poor dietary intake of haematopoietic nutrients like iron or vitamin A, as well as infant feeding practices and access to fortified foods;

- **nutrition-sensitive** solutions to anaemia, which address underlying and basic causes of anaemia from a wide range of sectors, including disease control (e.g. malaria, intestinal helminths), water, sanitation and hygiene, as well as intersectoral strategies that address root causes such as poverty and gender norms.

The most effective programmes to prevent anaemia are those that are comprehensive and combine nutrition-specific and nutrition-sensitive interventions and involve a wide range of sectors and actors. Determination of the right mix of strategies should be done through a situation analysis, which considers the magnitude, prevalence and distribution of anaemia and related nutrient deficiencies; food consumption levels, including micronutrient intake; dietary habits, practices and behaviours of vulnerable groups; as well as socioeconomic data to identify constraints and opportunities *(128)*. Section 4 discusses steps and considerations for choosing solutions to implement in a particular setting.

3.1 NUTRITION-SPECIFIC SOLUTIONS TO ANAEMIA

Nutrition-specific interventions aim to address the most proximal causes of anaemia, principally poor dietary intake of haematopoietic nutrients like iron or vitamin A, as well as infant feeding practices and access to fortified foods. Interventions that increase dietary diversity, improve infant feeding practices, and improve the bioavailability and intake of micronutrients, through fortification or supplementation, are nutrition-specific interventions. Social and behaviour-change communication strategies that aim to change nutrition-related behaviours and practices also fall within nutrition-specific approaches.

3.1.1 FOOD-BASED STRATEGIES

Inadequate dietary intake of the micronutrients needed for production of red blood cells and haemoglobin is a primary pathway leading to anaemia. In many settings in low- and middle-income countries, diets are poor in micronutrients, low in dietary diversity (i.e. monotonous) and high in anti-nutrient components like phytate, which impairs the absorption of micronutrients such as iron. While iron deficiency is the leading nutrient deficiency leading to anaemia, diets that are deficient in one micronutrient are also likely to be deficient in other micronutrients that may also contribute to the development of anaemia. "Food-based strategies" to prevent anaemia aim to increase the availability and consumption of a nutritionally adequate micronutrient-rich diet made up of a variety of available foods *(128)*. Such strategies have as a goal increasing dietary diversity – i.e. increasing the variety and types of foods consumed and improving the year-round availability of micronutrient-rich foods – and enhancing the diet by improving the bioavailability of nutrients, through including components in the diet that improve absorption, or utilizing preparation, processing or storage techniques that reduce the impact of anti-nutrient factors. Food-based strategies may also increase the access of households

and individuals, particularly those at most risk of anaemia, to micronutrient-rich foods, including fortified foods, and also change feeding practices related to these foods *(45)*. The food-based strategies relevant to anaemia discussed here include:

- dietary diversification and enhancing the bioavailability of micronutrients;
- infant and young child feeding practices: breastfeeding and complementary feeding;
- food fortification.

3.1.1.1 DIETARY DIVERSIFICATION AND ENHANCING THE BIOAVAILABILITY OF MICRONUTRIENTS

The main nutrients of concern for nutritional anaemia are iron, vitamin A, vitamin B_{12} and folate. Increasing the intake of foods that are rich in these nutrients will help to meet nutrient requirements and thus prevent anaemia, though the extent to which nutrient needs can be met by food-based approaches varies by nutrient as well as by target group. For example, requirements for vitamin A can be feasibly met through plant-source foods; however, it is much more difficult to meet requirements for iron from plant sources alone, and for some groups, animal-source foods or fortified foods will be necessary *(129)*. This is the case for young children, who have particularly high needs for iron and consume very small amounts of food (see section 3.1.1.2). Pregnant women also have very high iron requirements, and daily prenatal supplementation with iron and folic acid is recommended in most settings, to prevent anaemia and improve birth outcomes. Nevertheless, dietary diversification through increasing consumption of vegetables, fruits and animal-source foods, and accompanying strategies to improve the bioavailability of nutrients in the diet, should be always be part of strategies to prevent anaemia, since inadequate dietary intake is the primary pathway for development of nutritional anaemia. There are also benefits of dietary diversification beyond prevention of anaemia, including improved growth among children and reducing the consumption of less nutritious foods that are related to overweight and chronic disease *(129)*.

IRON

Meat, fish and poultry are rich sources of bioavailable iron. Plant sources of iron are generally less well absorbed, though including "enhancers" such as the organic acids citric, malic or ascorbic acid (i.e. vitamin C) may improve the absorption of iron from these foods *(129)*. In addition, adding haem iron from animal-source foods (especially from beef, but also from lamb, pork, liver and chicken) to foods containing non-haem iron will also increase the overall bioavailability and absorption of iron from a meal *(130)*. Methods of food processing – such as soaking, fermentation, germination or thermal or mechanical processing – can also improve the bioavailability and absorption of iron *(131)*. Finally, avoiding combination of known inhibitors of non-haem iron – such as tea or coffee – with meals will improve iron absorption *(130)*. A combination of strategies – increasing iron-rich foods in the diet, adding "enhancers", avoiding "inhibitors" and exploiting beneficial processing techniques – will be the best approach for improving iron status. For infants and young children, meeting their iron requirements is particularly challenging, and strategies to meet their iron needs should also include food fortification (see section 3.1.1.2).

VITAMIN A

Requirements for vitamin A can be met from plant-source foods (e.g. green leafy vegetables, orange/yellow fruits and vegetables) in the form of pro-carotenoids, though dairy products, eggs, fish oil and liver are particularly rich sources of retinol *(129)*. Consumption of fat improves the absorption of carotenoids from the diet, and short cooking times and steaming rather than boiling may reduce oxidation and loss of carotenoids in foods *(131)*.

VITAMIN B$_{12}$ AND FOLATE

Vitamin B$_{12}$ is only found in animal-source foods; shellfish, beef liver, other meats, fish and poultry, as well as dairy products are rich sources of this vitamin. Folate is naturally found in legumes and green leafy vegetables, whole grains and fruits and fruit juices such as oranges.

KEY ACTIONS AND RECOMMENDATIONS: DIETARY DIVERSIFICATION AND ENHANCING THE BIOAVAILABILITY OF MICRONUTRIENTS

- Increase the production and consumption of iron-rich foods, primarily animal-source foods such as meat (especially red meat), poultry and fish, but also iron-rich plant sources such as legumes.

- Increase the production and consumption of foods that are rich in vitamin A/carotenoid, such as green leafy vegetables, orange-fleshed fruits and vegetables (e.g. orange-fleshed sweet potatoes), dairy products, eggs, liver and fish oils.

- Add fruits and vegetables that are rich in citric or ascorbic acid (e.g. citrus fruits) to the diet, to increase the absorption of non-haem iron. Vitamin C degrades with cooking, so consumption of uncooked (or lightly cooked) fruits and vegetables with high vitamin C content should be encouraged (assuming considerations of food hygiene and food safety are addressed).

- Identify and promote culturally appropriate and feasible methods of food processing and preparation, to improve bioavailability and absorption.

  o *Iron*: germination, fermentation and soaking may improve absorption.

  o *Vitamin A*: short cooking times and steaming rather than boiling will maintain pro-vitamin A activity.

- Avoid combining known inhibitors of iron absorption with meals that are high in iron content; for example:

  o separate tea and coffee drinking from meal times; consumption 1–2 hours later will not inhibit iron absorption;

  o consume dairy products (milk, cheese and other foods made from milk) as a between-meal snack, not at a meal time.

ADDITIONAL RESOURCES ON DIETARY DIVERSIFICATION AND LINKS TO WHO GUIDANCE

- Allen LH, de Benoist B, Dary O, Hurrell R. Guidelines on food fortification with micronutrients. Geneva: World Health Organization, Food and Agricultural Organization of the United Nations; 2006 (http://apps.who.int/iris/bitstream/10665/43412/1/9241594012_eng.pdf?ua=1.

- Promoting a healthy diet for the WHO Eastern Mediterranean Region: user-friendly guide. Cairo: World Health Organization Regional Office for the Eastern Mediterranean; 2012 (http://apps.who.int/iris/bitstream/10665/119951/1/emropub_2011_1274.pdf?ua=1).

- Final report of the Mixed Committee of the League of Nations on the relation of nutrition to health, agriculture and economic policy. Geneva: League of Nations; 1937 (https://archive.org/details/finalreportofmix00leaguoft).

- FAO/WHO International symposium on sustainable food systems for healthy diets and improved nutrition, 1–2 December 2016, Rome, Italy (http://www.who.int/nutrition/events/2016-sustainable-food-systems-symposium-dec2016-rome/en/).

3.1.1.2 INFANT AND YOUNG CHILD FEEDING: BREASTFEEDING AND COMPLEMENTARY FEEDING

Children under 2 years of age are one of groups that are most vulnerable to iron deficiency. Thus, appropriate feeding practices – including exclusive breastfeeding for the first 6 months of life, and optimal complementary feeding – during the first 2 years of life are crucial for avoiding the development of iron deficiency, anaemia, micronutrient deficiencies and other forms of undernutrition.

BREASTFEEDING

Normal-birth-weight (>2500 g), full-term (37 weeks' gestation or more) infants are generally born with iron stores that are adequate for approximately the first 4–6 months of life. During this time, iron stores are the primary source of iron for the infant's growth and development, and dietary iron needs are minimal. Breast milk is not high in iron, but the iron is thought to be relatively well absorbed: between 12% and 56% of breast-milk iron is estimated to be absorbed *(132)*. Exclusive breastfeeding during the first 6 months of life is protective of iron status, as iron from other complementary foods or liquids will not be as well absorbed and can interfere with the absorption of breast-milk iron *(133)*. In addition, early introduction of cow's milk in young infants can cause intestinal blood loss, further compromising iron status *(134)*.

In contrast, low-birth-weight infants and premature infants will have compromised iron stores at birth, owing to their reduced size and/or premature delivery. It is recommended that these infants receive an external source of iron (e.g. iron supplements) before 6 months of age (see section 3.1.2).

KEY ACTIONS AND RECOMMENDATIONS: BREASTFEEDING

- Infants should be exclusively breastfed for the first 6 months of life, to achieve optimal growth, development and health *(135)*.

- After 6 months of age, infants should receive nutritionally adequate and safe complementary foods, while continuing to breastfeed for up to 2 years or beyond.

- Low-birth-weight infants will need an external source of iron before 6 months of age (see section 3.1.2).

ADDITIONAL RESOURCES ON BREASTFEEDING AND LINKS TO WHO GUIDANCE

- World Health Organization e-Library of Evidence for Nutrition Actions (eLENA). Exclusive breastfeeding for optimal growth, development and health of infants. Guidance on exclusive breastfeeding (http://www.who.int/elena/titles/exclusive_breastfeeding/en/).

- World Health Organization e-Library of Evidence for Nutrition Actions (eLENA). Early initiation of breastfeeding to promote exclusive breastfeeding (http://www.who.int/elena/titles/early_breastfeeding/en/).

- World Health Organization e-Library of Evidence for Nutrition Actions (eLENA). Continued breastfeeding for healthy growth and development of children (http://www.who.int/elena/titles/continued_breastfeeding/en/).

COMPLEMENTARY FEEDING

The period of complementary feeding (beginning at 6 months of age) is a high-risk period for development of undernutrition and increased disease. In many settings, the nutritional quality of first foods provided to infants – typically cereal-based gruels – is poor: very low in energy, macronutrients like protein and fat, and micronutrients, particularly iron. Complementary foods need to provide an increasingly greater proportion of a child's daily nutrient needs as the child ages. For some nutrients, like iron, the proportion of nutrient requirement that needs to come from complementary foods is already very high in infancy – roughly 97% of the iron requirements of a 9–11-month-old infant need to come from complementary foods *(136)*. Hygiene practices and water safety may also not be adequate, leading to increased risk of infection from foods and liquids that are provided.

Comprehensive recommendations for meeting nutritional needs through complementary foods are laid out in the *Guiding principles for complementary feeding of the breastfed child (136)* and *Guiding principles for feeding non-breastfed children 6–24 months of age (137)*. While these guidelines are important for ensuring nutritionally adequate complementary feeding practices, there are recommendations that are particularly relevant to the prevention of anaemia, as outlined in the '"Key actions and recommendations" box.

KEY ACTIONS AND RECOMMENDATIONS: COMPLEMENTARY FEEDING

- Feed a variety of foods, including:

  - meat, poultry, fish or eggs daily (or as often as possible); if animal-source foods are not available/accessible, fortified foods or home fortificants (i.e. point-of-use fortificants, such as micronutrient powders or lipid-based nutrient supplements) may be needed;

  - vitamin-A-rich fruits and vegetables daily (or as often as possible); if animal-source foods are not available/accessible, fortified foods or home fortificants (i.e. point-of-use fortificants, such as micronutrient powders or lipid-based nutrient supplements) may be needed;

  - foods containing adequate fat content to ensure 30–45% of total energy intake from fat (including fat intake from breast milk); adequate fat intake aids absorption of fat-soluble vitamins that may play a role in the development of anaemia, such as vitamins A, D and E.

- Avoid giving drinks with low nutrient value that can interfere with nutrient absorption (e.g. tea and coffee can interfere with iron absorption) or decrease appetite for more nutritious foods/liquids.

ADDITIONAL RESOURCES ON COMPLEMENTARY FEEDING AND LINKS TO WHO GUIDANCE

- Guiding principles for feeding non-breastfed children 6–24 months of age. Geneva: World Health Organization; 2005 (http://apps.who.int/iris/bitstream/10665/43281/1/9241593431. pdf?ua=1&ua=1).

- Guiding principles for complementary feeding of the breastfed child. Pan-American Health Organization; 2003 (http://www.who.int/nutrition/publications/guiding_principles_compfeeding_ breastfed.pdf)

3.1.1.3 FOOD FORTIFICATION

Micronutrient fortification – the process of deliberately increasing the content of essential micronutrients in a food, in order to improve the nutritional quality of the food supply and to provide a public health benefit with minimal risk to health *(137)* – is one of the most cost-effective and sustainable approaches to improving the nutritional status of populations. Fortification of staple foods can provide a consistent supply of nutrients if fortified products are consumed regularly, avoiding disruptions in nutrient availability due to seasonality. Fortification also has the potential to improve the nutritional status of a large portion of the population, if foods that are widely distributed and consumed are selected as fortification vehicles. Thus, fortification of food staples (e.g. wheat or corn flour, rice, salt) with one or several nutrients is a common approach (referred to as "mass" or "universal fortification") for improving the nutritional intake of the general population, and is effective, simple and inexpensive once established.

For specific groups – for example, young children – where nutrient needs are higher and their intake of food staples may be more limited, "targeted" or "point-of-use" fortification (the latter also known as "home fortification") may be more appropriate. "Biofortification" is the process by which the nutritional quality of food crops is improved through agronomic practices, conventional plant breeding, or modern biotechnology. Biofortification differs from conventional fortification in that biofortification aims to increase nutrient levels in crops during plant growth rather than through manual means during processing of the crops. This can be achieved through one of three main non-mutually exclusive agronomic methods: (i) application of fertilizer to the soil or leaves; (ii) conventional or traditional plant breeding; or (iii) genetic engineering, which includes genetic modification and transgenesis.

"MASS" OR "UNIVERSAL" FORTIFICATION

Mass or universal fortification entails addition of one or more micronutrients to a food that is commonly consumed by the general public (e.g. cereals, condiments or milk) and is most effective when mandated and regulated by the government at the national level *(138, 139)*. Mass fortification is generally preferable when the majority of the population has an unacceptable public health risk of being or becoming deficient in specific micronutrients *(138)* and also consumes significant quantities of industrially processed foods *(140)*. Selection of food vehicles and nutrient levels requires an understanding of many different factors, including: the nutritional needs and deficiencies of the population; the usual consumption profile of the proposed food vehicle; sensory and physical effects of the fortificant nutrients on the food vehicle; fortification of other food vehicles; population consumption of vitamin and mineral supplements; and costs *(139)*.

For fortification with iron, the form of iron used as the fortificant and the amount of iron added to the food vehicle is critical to determining the level of impact of the fortification programme. The effectiveness of many iron-fortification programmes is hampered by using forms of iron with low bioavailability, insufficient consumption of the food vehicle, and inadequate levels of fortification for given consumption levels *(139)*. However, reductions in iron deficiency and anaemia in several countries with flour-fortification programmes – including Chile, Costa Rica, Denmark, Sweden and the USA *(140, 141)* – among women and children provide evidence of the effectiveness of the approach. A review of nationally representative data from countries with and without flour-fortification programmes showed that the prevalence of anaemia has decreased significantly in countries that fortify wheat and/or maize flour with micronutrients *(142)*.

Folic acid has been added to wheat and maize flour to increase the intake of folate by women and prevent neural tube defects and other congenital anomalies *(143)*. There are limited data on adding vitamin B_{12} to flour to improve the intake and status of this vitamin, but such fortification appears to be a feasible approach *(143)*. Vitamin A has been used to fortify oils, fats (e.g. margarine), condiments, milk and sugar, and wheat and maize flours can be considered as vehicles for delivery of vitamin A to

populations at risk of vitamin A deficiency *(143)*. Fortification of sugar with vitamin A has been shown to improve vitamin A status in women and preschool children in Guatemala *(144)*.

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KEY ACTIONS AND RECOMMENDATIONS: MASS FORTIFICATION

- Fortification of wheat and maize flour should be considered when industrially produced flour is regularly consumed by large population groups in a country *(139, 143)*.

- Iron fortification of wheat flour should be considered at the national or regional level only if there is laboratory evidence of a high prevalence of iron deficiency and iron-deficiency anaemia in women or children (iron-deficiency anaemia >5%) *(140)*.

- Iron-fortification programmes should aim to decrease the prevalence of iron deficiency in the target at-risk populations to levels reported in industrialized countries (<10% iron deficiency and <5% iron-deficiency anaemia). These levels should be reached in 2 to 3 years after the start of the fortification programme *(140)*.

- The first choices for iron fortificants for wheat flour are NaFeEDTA, ferrous sulfate and ferrous fumarate. NaFeEDTA is the only iron compound recommended for fortification of high-extraction wheat flour *(140)*.

- Retinyl acetate and retinyl palmitates, along with provitamin A (β-carotene) are the main forms of vitamin A available for use as food fortificants.

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ADDITIONAL RESOURCES ON FORTIFICATION AND LINKS TO WHO GUIDANCE:

- WHO guideline: fortification of maize flour and corn meal with vitamins and minerals. Geneva: World Health Organization; 2016 (http://apps.who.int/iris/bitstream/10665/251902/1/9789241549936-eng.pdf?ua=1).

- Neufeld LM, Aaron GJ, Garrett GS, Baker SK, Dary O, Van Ameringen M. Food fortification for impact: a data-driven approach. Bull World Health Organ. 2016;94:631–2. doi:10.2471/BLT.15.164756.

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TARGETED FORTIFICATION

Targeted fortification programmes fortify food vehicles targeted at specific subgroups of the population, to increase the intake of that particular group while not affecting the intake of the population as a whole *(45)*. Examples of targeted fortification include fortified complementary foods for infants and young children and fortified foods for school feeding, for emergency feeding or for displaced persons/refugees (i.e. fortified blended foods such as corn–soy blend or ready-to-eat foods used in emergencies, such as high-energy biscuits). Targeted fortification is particularly useful for groups that have particular nutrient needs (e.g. the high iron requirements of infants and children aged under 2 years) that are difficult to meet through universal fortification alone, owing to low consumption of the staple food, or when higher levels of fortification are needed for the vulnerable group. In the case of emergency feeding and feeding displaced persons/refugees, fortified foods that are targeted to the affected groups may

help to alleviate the nutritional impact of limited access to nutritious foods, particularly iron-rich foods and fresh fruits and vegetables. Fortified grain–soy blends (e.g. corn–soy blend, wheat–soy blend) are examples of foods used for feeding in emergency and refugee settings.

KEY ACTIONS AND RECOMMENDATIONS: TARGETED FORTIFICATION

For complementary feeding

- Use fortified complementary foods or vitamin–mineral supplements for infants aged 6–23 months as needed. Unfortified complementary foods that are predominantly plant based generally provide insufficient amounts of certain key nutrients (particularly iron, zinc and calcium) to meet the recommended nutrient intakes during the age range of 6–23 months *(136)*.

Emergency settings

- Pregnant women in emergency settings should be provided with fortified blended food commodities, *in addition* to the basic general ration, that are designed to provide 10–12% (up to 15%) of energy from protein and 20–25% energy from fat. The fortified blended food should be fortified to meet two thirds of daily requirements for all micronutrients.

- Blended foods provided as food aid, especially if they are fortified with essential nutrients, can be useful for feeding older infants and young children. However, their provision should not interfere with promoting the use of local ingredients and other donated commodities for preparing suitable complementary foods.

ADDITIONAL RESOURCES ON TARGETED FORTIFICATION AND LINKS TO WHO GUIDANCE

- World Health Organization, United Nations High Commissioner for Refugees, United Nations Children's Fund, World Food Programme. Food and nutrition needs in emergencies. Geneva: World Health Organization; 2004 (http://apps.who.int/iris/bitstream/10665/68660/1/a83743.pdf?ua=1).

- Guiding principles for feeding infants and young children during emergencies. Geneva: World Health Organization; 2004 (http://apps.who.int/iris/bitstream/10665/42710/1/9241546069. pdf?ua=1).

POINT-OF-USE (HOME) FORTIFICATION

"Point-of-use" or "home" fortification involves adding fortificants (e.g. in powdered or lipid-based form) to food immediately prior to consumption (i.e. at the "point-of use"), most commonly in home settings, but point-of-use fortification has also been used in school/institutional settings for meals prepared on site. Multiple micronutrient powders are single-dose packets of vitamins and minerals in powdered form that can be sprinkled onto any semi-solid food consumed at home, school or at any other point of use *(145, 146)*. Lipid-based nutrient supplements (LNS) are a family of products that contain a range of vitamins and minerals in addition to energy, protein and essential fatty acids *(147)*. The majority of energy in LNS comes from fat, though the total energy provide by LNS used for home-fortification purposes ("small quantity LNS") is approximately 120 kcal from a 20 g "dose".

Point-of-use fortification with multiple micronutrient powders has been shown to be effective at preventing anaemia and improving iron status in children aged under 2 years and children aged 2–12 years *(148, 149)*. Point-of-use fortification may have several advantages over other methods of fortification, especially for groups that are particularly vulnerable to anaemia, like infants and young children. Because these supplements are added immediately prior to consumption, issues of shelf stability and adverse effects of the fortificant on the food (e.g. oxidation of fats, colour changes or off-tastes) are minimized. The fortificant can also be tailored to the specific needs of the target group, in both the range of vitamins and minerals provided as well as the amount. For young children who consume small amounts of food, adding the fortificant directly to their portion of food ensures that they consume the level of nutrients they need.

KEY ACTIONS AND RECOMMENDATIONS: POINT-OF-USE FORTIFICATION

Children aged under 2 years

- In populations where anaemia is a public health problem, point-of-use fortification of complementary foods with iron-containing micronutrient powders in infants and young children aged 6–23 months is recommended, to improve iron status and reduce anaemia *(150)*. A suggested supplementation scheme and MNP composition is provided.

Suggested scheme for home fortification with multiple micronutrient powders of foods consumed by infants and children aged 6–23 months	
Supplement composition per sachet[a]	• Iron: 10 to 12.5 mg of elemental iron[a] • Vitamin A: 300 µg retinol • Zinc: 5 mg elemental zinc • With or without other micronutrients to achieve 100% of the RNI [b, c]
Duration and time interval between periods of intervention	Programme target of 90 sachets/doses over a 6-month period
Settings	Areas where the prevalence of anaemia in children aged under 2 years or under 5 years is 20% or higher

[a] 12.5 mg of elemental iron equals 37.5 mg of ferrous fumarate or 62.5 mg of ferrous sulfate heptahydrate or equivalent amounts in other iron compounds. In children aged 6–12 months, sodium iron EDTA (NaFeEDTA) is generally not recommended. If NaFeEDTA is selected as a source of iron, the EDTA intake (including other dietary sources) should not exceed 1.9 mg EDTA/kg/day.

[b] Recommended nutrient intake (RNI). Multiple micronutrient powders can be formulated with or without other vitamins and minerals in addition to iron, vitamin A and zinc, to achieve 100% of the RNI, and also taking into consideration the technical and sensory properties.

[c] Where feasible, likely consumption from other sources, including home diet and fortified foods, should be taken into consideration for establishing the composition of the sachet.

Children aged 2–12 years

- In populations where anaemia is a public health problem, point-of-use fortification of foods with iron-containing micronutrient powders in children aged 2–12 years is recommended, to improve iron status and reduce anaemia. A suggested scheme for point-of-use fortification of foods with iron-containing micronutrient powders in children aged 2–12 years is provided.

Suggested scheme for point-of-use fortification of foods with iron-containing micronutrient powders in children aged 2–12 years	
Supplement composition per sachet[a]	• Iron: 10 to 12.5 mg of elemental iron for children aged 2–4 years; and 12.5 to 30 mg elemental iron for children aged 5–12 years[a] • Vitamin A: 300 µg retinol • Zinc: 5 mg elemental zinc • With or without other micronutrients to achieve 100% of the RNI[b, c]
Regimen	Programme target of 90 sachets/doses over a 6-month period
Settings	Areas where the prevalence of anaemia in children under 5 years of age, is 20% or higher

[a]   12.5 mg of elemental iron equals 37.5 mg of ferrous fumarate or 62.5 mg of ferrous sulfate heptahydrate or equivalent amounts in other iron compounds. If s. If sodium iron EDTA (NaFeEDTA) is selected as a source of iron, the dose of elemental iron should be reduced by 3–6 mg due to its higher bioavailability. The appropriate range of NaFeEDTA is an area of research need.

[b]   Recommended nutrient intake (RNI). Multiple micronutrient powders can be formulated with or without other vitamin and minerals in addition to iron, vitamin A and zinc to achieve 100% of the RNI, and also taking into consideration the technical and sensory properties.

[c]   Where feasible, likely consumption from other sources, including home diet and fortified foods, should be taken into consideration for establishing the composition of the sachet.

Source: World Health Organization. E-Library of Evidence for Nutrition Actions (eLENA). Multiple micronutrient powders for point-of-use fortification of foods consumed by children 6–23 months of age. Geneva: World Health Organization; 2016 (http://www.who.int/elena/titles/micronutrientpowder_infants/en/ *(145)*.

- In malaria-endemic areas, the provision of iron in any form, including micronutrient powders for point-of-use fortification, should be implemented in conjunction with measures to prevent, diagnose and treat malaria. Provision of iron through these interventions should not be made to children who do not have access to malaria-prevention strategies (e.g. provision of insecticide-treated bednets and vector-control programmes), prompt diagnosis of malaria illness, and treatment with effective antimalarial drug therapy.

- Programmes involving the use of MNP for home fortification of foods should be preceded by an evaluation of the nutritional status among children aged under 5 years and of existing measures to control anaemia and vitamin A deficiency, such as hookworm-control programmes, the provision of supplements and the use of other products for home fortification of foods and fortified complementary foods, to ensure that the daily micronutrient needs are met and not exceeded (see section 3.1.2).

Pregnant women

- Routine use of MNP is not recommended as an alternative to standard iron and folic supplementation during pregnancy for improving maternal and infant health outcomes *(151)*.

BIOFORTIFICATION

Biofortification refers to the indirect addition of essential nutrients or other substances to foods, for the purpose of nutritional or health enhancement. When referring to agriculture, "biologic fortification" or "biofortification" indicates crops that have been nutritionally enhanced using agronomic practices, conventional plant-breeding practices or modern biotechnology. Crops that have been biofortified with nutrients include beans, cassava, maize, rice, sweet potato and wheat. In addition to iron, crops have been biofortified with zinc, pro-vitamin A carotenoids and amino acids and proteins. Advantages to biofortification include targeting low-income households that consume staple foods as a large proportion of their diet; low recurrent costs once seeds are developed; sustainability, as biofortified crops can be planted year after year, even if funding is limited or government or international agency attention wanes; and reaching populations that may be out of the reach of commercially fortified products *(152)*. Sweet potato enriched with pro-vitamin A has been shown to increase the vitamin A liver stores of primary school children *(153)* and high-iron rice can improve the iron status of women of reproductive age *(154)*.

3.1.2 MICRONUTRIENT SUPPLEMENTATION: IRON (AND FOLIC ACID)

Supplementation with iron (with or without folic acid) is a very common strategy employed to prevent iron-deficiency anaemia in settings where iron is known to be deficient in the diet, and anaemia is prevalent, particularly among vulnerable groups. Provision of iron supplements to children aged under 2 years has been shown to increase haemoglobin concentrations and iron stores, and reduce the risk of anaemia, iron deficiency and iron-deficiency anaemia *(31)*. In pregnant women, supplementation with iron and folic acid is associated with a reduced risk of iron deficiency and anaemia. In the past decade, debate has arisen as to the appropriate dose, frequency (e.g. daily versus intermittent) and coverage of iron supplementation (e.g. universal versus targeted) for groups at risk of iron deficiency, particularly young children, in different settings (e.g. malaria-endemic versus non-malaria-endemic areas). Such debate was spurred by evidence of adverse effects of iron supplementation in children on morbidity – particularly in settings where malaria or infectious disease is prevalent *(155)* – as well as growth *(31)*. More recent evidence has indicated that iron supplementation does not adversely

affect malarial morbidity and mortality in children when regular malaria surveillance and treatment are provided *(76)*. The adverse effects of iron supplements on growth in young children aged under 2 years still remain uncertain *(31)*.

The following set of recommendations is separated by target group: children aged 6–23 months, preschool and school-age children, nonpregnant women and adolescent girls, pregnant women, postpartum women and low-birth-weight and very-low-birth-weight infants. Supplementation programmes should ideally form part of an integrated programme of antenatal and neonatal care (for supplementation in pregnant and postpartum women) or part of school or community programmes (for preschool and school-age children). The selection of the most appropriate delivery platform should be context specific, however, with the aim of ensuring that the most vulnerable members of the populations are reached. For example, if the education system is selected as the delivery channel, efforts should be made to reach children who do not attend school. In addition to provision of iron supplements, antenatal and neonatal care programmes should also promote adequate gestational weight gain, screening of all women for anaemia at antenatal and postpartum visits, use of complementary measures to control and prevent anaemia (e.g. hookworm control), and a referral system to manage cases of severe anaemia *(156)*. School and community programmes should ensure that the daily nutritional needs of preschool or school-age children are met and not exceeded, through the evaluation of nutritional status and intake, as well as consideration of existing anaemia and measures to control micronutrient deficiency (such as provision of vitamin A supplements, fortified foods and anthelminthic therapy). In malaria-endemic areas, the provision of iron supplements should be implemented in conjunction with measures to prevent, diagnose and treat malaria (control of malaria and intestinal helminths is described in further detail in section 3.2.1).

The supplementation guidelines presented next represent *preventive* strategies for implementation at the population level. Treatment guidelines – in terms of dose, frequency and duration of the supplement to be provided – differ from the preventive guidelines presented here and are outlined in the relevant WHO documents provided under "Additional resources on iron supplementation and links to WHO guidance".

KEY ACTIONS AND RECOMMENDATIONS: IRON AND FOLIC ACID SUPPLEMENTATION

Children aged 6–23 months

- Daily iron supplementation is recommended as a public health intervention in infants and young children aged 6–23 months, living in settings where the prevalence of anaemia is 40% or higher in this age group,[a] for preventing iron deficiency and anaemia *(99)*. A suggested scheme for daily iron supplementation in children aged 6–23 months is provided next.

[a] In the absence of prevalence data in this group, consider proxies for high risk of anaemia. For the most recent estimates, visit the WHO-hosted Vitamin and Mineral Nutrition Information System (VMNIS) *(157)*.

Suggested scheme for daily iron supplementation in infants and young children aged 6–23 months	
Supplement composition	10–12.5 mg elemental iron,[a] drops or syrup
Frequency	Daily, one supplement per day
Duration and time interval between periods of supplementation	3 consecutive months per year
Settings	Populations where the prevalence of anaemia is 40% or higher in this age group

[a]   10–12.5 mg of elemental iron equals 50–62.5 mg of ferrous fumarate, 30–37.5 mg of ferrous sulfate heptahydrate or 83.3–104.2 mg of errous gluconate.

• In malaria-endemic areas, the provision of iron supplementation in infants and children should be done in conjunction with public health measures to prevent, diagnose and treat malaria.

Preschool and school-age children
• In daily iron supplementation is recommended as a public health intervention in preschool-age children aged 24–59 months, and school-aged children (aged 5–12 years) living in settings where the prevalence of anaemia in infants and young children is ≥40%, for preventing iron deficiency and anaemia *(99)*. Suggested schemes for daily supplementation in preschool and school-aged children are provided next.

Suggested schemes for daily iron supplementation in preschool and school-age children		
Supplement composition	30 mg of elemental iron[a]	30–60 mg of elemental iron[a]
Supplement form	Drops/syrups	Tablets/capsules
Frequency	Daily, one supplement per day	
Duration and time interval between periods of supplementation	3 consecutive months per year	
Target group	Preschool-age children (24–59 months)	School-age children (5–12 years)
Settings	Where the prevalence of anaemia in preschool or school age children is ≥40%	

[a]   30-60 mg of elemental iron equals 150–300 mg of ferrous fumarate, 90–180 mg of ferrous sulfate heptahydrate or 250–500 mg of ferrous gluconate.

• In malaria-endemic areas, the provision of iron supplements should be implemented in conjunction with measures to prevent, diagnose and treat malaria.

• Where infection with hookworm is endemic (prevalence ≥20%), it may be more effective to combine iron supplementation with anthelminthic treatment in children above the age of 5 years. Universal anthelminthic treatment, irrespective of infection status, is recommended at least annually in these areas *(158, 159)*.

- In settings where the prevalence of anaemia in preschool (age 24–59 months) or school-age (age 5–12 years) children is ≥20%, WHO recommends the intermittent use of iron supplements as a public health intervention to improve iron status and reduce the risk of anaemia among children *(160)*. Suggested schemes for intermittent supplementation in preschool and schoolaged children are provided next.

Suggested schemes for intermittent iron supplementation in preschool and school-age children		
Supplement composition	25 mg of elemental iron[a]	45 mg of elemental iron[b]
Supplement form	Drops/syrups	Tablets/capsules
Frequency	One supplement per week	
Duration and time interval between periods of supplementation	3 months of supplementation followed by 3 months of no supplementation, after which the provision of supplements should restart. If feasible, intermittent supplements could be given throughout the school or calendar year	
Target group	Preschool-age children (24–59 months)	School-age children (5–12 years)
Settings	Where the prevalence of anaemia in preschool or school-age children is ≥20%	

[a] 25 mg of elemental iron equals 75 mg of ferrous fumarate, 125 mg of ferrous sulfate heptahydrate or 210 mg of ferrous gluconate.
[b] 45 mg of elemental iron equals 135 mg of ferrous fumarate, 225 mg of ferrous sulfate heptahydrate or 375 mg of ferrous gluconate.

- In malaria-endemic areas, the provision of iron supplements should be implemented in conjunction with adequate measures to prevent, diagnose and treat malaria.

Menstruating women and adolescent girls (non-pregnant women of reproductive age)

- Daily iron supplementation is recommended as a public health intervention in menstruating adult women and adolescent girls living in settings where the prevalence of anaemia is ≥40% in this age group, for the prevention of anaemia and iron deficiency *(161)*. A suggested scheme for daily supplementation in menstruating women is provided next.

Menstruating women and adolescent girls (non-pregnant women of reproductive age)	
Supplement composition	30–60 mg elemental iron[a]
Frequency	Daily, one supplement per day
Duration and time interval between periods of supplementation	3 consecutive months in a year
Target group	Non-pregnant, menstruating women and adolescent girls (aged 12–49 years)
Settings	Populations where the prevalence of anaemia is 40% or higher in this age group

[a] 30–60 mg of elemental iron equals 90–180 mg of ferrous fumarate, 150–300 mg of ferrous sulfate heptahydrate or 250–500 mg of ferrous gluconate.

- In malaria-endemic areas, the provision of iron and folic acid supplements should be implemented in conjunction with adequate measures to prevent, diagnose and treat malaria.

- In populations where the prevalence of anaemia among non-pregnant women and adolescents of reproductive age (12–49 years) is ≥20%, intermittent supplementation with iron and folic acid is recommended as a public health intervention in menstruating women, to improve their haemoglobin concentrations and iron status and reduce the risk of anaemia *(162)*. A suggested scheme for intermittent supplementation in menstruating women is provided next.

Suggested scheme for intermittent iron and folic acid supplementation in menstruating women and adolescent girls	
Supplement composition	Iron: 60 mg of elemental iron[a] Folic acid: 2800 µg (2.8 mg)
Frequency	One supplement per week
Duration and time interval between periods of supplementation	3 months of supplementation followed by 3 months of no supplementation, after which the provision of supplements should restart
Settings	Populations where the prevalence of anaemia among non-pregnant women of reproductive age is 20–39%

[a] 60 mg of elemental iron equals 180 mg of ferrous fumarate, 300 mg of ferrous sulfate heptahydrate or 500 mg of ferrous gluconate.

Pregnant women

- Daily oral iron and folic acid supplementation with 30–60 mg of elemental iron and 400 µg (0.4 mg) folic acid is recommended for pregnant women and adolescent girls within the context of routine antenatal care, to prevent maternal anaemia, puerperal sepsis, low birth weight and preterm birth *(163)*.

- In settings where anaemia in pregnant women is a severe public health problem (i.e. where at least 40% of pregnant women have a blood haemoglobin concentration <110 g/L), a daily dose of 60 mg of elemental iron is preferred over a lower dose. The suggested scheme for daily supplementation in pregnant women is presented next.

Suggested scheme for daily iron and folic acid supplementation in pregnant women	
Supplement composition	Iron: 30–60 mg of elemental iron[a] Folic acid: 400 µg (0.4 mg)
Frequency	One supplement daily
Duration	Throughout pregnancy; supplementation with iron and folic acid should begin as early as possible

[a] 30 mg of elemental iron equals 90 mg of ferrous fumarate, 150 mg of ferrous sulfate heptahydrate or 250 mg of ferrous gluconate.

- Intermittent oral iron and folic acid supplementation with 120 mg of elemental iron and 2800 g (2.8 mg) of folic acid once weekly is recommended for pregnant women, to improve maternal and neonatal outcomes if daily iron is not acceptable due to side-effects, and in populations with an anaemia prevalence among pregnant women of less than 20% *(163)*. A suggested scheme for intermittent iron and folic acid supplementation in non-anaemic pregnant women is provided next.

Suggested scheme for *intermittent* iron and folic acid supplementation in non-anaemic pregnant women	
Supplement composition	Iron: 120 mg of elemental iron[a,b] Folic acid: 2800 µg (2.8 mg)
Frequency	One supplement once a week
Duration	Throughout pregnancy; supplementation with iron and folic acid should begin as early as possible
Settings	Countries where the prevalence of anaemia among pregnant women is lower than 20%

[a] 120 mg of elemental iron equals 360 mg of ferrous fumarate, 600 mg of ferrous sulfate heptahydrate, or 1000 mg of ferrous gluconate.
[b] Haemoglobin concentrations should be measured prior to the start of supplementation to confirm non-anaemic status.

- In malaria-endemic areas, the provision of iron and folic acid supplements should be implemented in conjunction with adequate measures to prevent, diagnose and treat malaria.

Postpartum women

- Oral iron supplementation, either alone or in combination with folic acid supplementation, may be provided to postpartum women for 6–12 weeks following delivery, to reduce the risk of anaemia in settings where gestational anaemia is of public health concern (≥20%) *(164)*.

Low-birth-weight and very-low-birth-weight infants

- Low-birth-weight infants (weighing between 1.5 and 2.5 kg) should be given iron supplements (2 mg/kg body weight per day) from 2 months to 23 months of age *(165)*.

- Very-low-birth-weight infants (weighing between 1.0 and 1.5 kg) who are fed their mother's own milk or donor human milk should be given 2–4 mg/kg per day iron supplementation starting at 2 weeks until 6 months of age *(166)*.

ADDITIONAL RESOURCES ON IRON SUPPLEMENTATION AND LINKS TO WHO GUIDANCE

- World Health Organization. E-Library of Evidence for Nutrition Actions (ELENA). Micronutrient supplementation in low-birth-weight and very-low-birth-weight infants (http://www.who.int/elena/titles/supplementation_lbw_infants/en/).

3.1.3 SOCIAL AND BEHAVIOUR-CHANGE COMMUNICATION STRATEGIES

While increasing awareness of appropriate nutrition practices and behaviours and providing key interventions to improve nutritional status is essential, evidence suggests that these alone will not be sufficient to create lasting changes in behaviours. A social and behaviour-change communication strategy should accompany nutrition-specific interventions aimed at preventing anaemia. These strategies can promote optimal infant and young child feeding practices (breastfeeding and complementary feeding); optimal dietary practices and behaviours, including during pregnancy and lactation; and awareness and correct use of iron supplements and/or home fortificants (e.g. MNP); along with other practices such as hand washing with soap, prompt attention to fever in malaria settings, and measures to manage diarrhoea, particularly among younger children (see section 3.2.2). Among pregnant women, social and behaviour-change communication strategies have been shown to be effective in increasing consumption of nutrient-rich foods, iron-fortified foods and iron supplements during pregnancy *(167)*. Among children, social and behaviour-change communication strategies – particularly those utilizing interpersonal communication approaches – have been used effectively to increase early initiation of breastfeeding, the duration of exclusive breastfeeding, and the duration of any breastfeeding *(167)*. Social and behaviour-change communication strategies have also been used to increase consumption of animal-source foods, fruits and vegetables, and improve utilization of nutrient supplements among young children *(167)*.

KEY ACTIONS AND RECOMMENDATIONS: SOCIAL AND BEHAVIOUR-CHANGE COMMUNICATION

- Social and behaviour-change communication strategies should be developed for a particular context, using formative research or ethnographic work prior to implementation *(167)*.

- Multiple social and behaviour-change communication approaches and channels (e.g. interpersonal communication, media, community/social mobilization) to change behaviours are more effective than using one approach alone *(167)*.

- Targeting multiple contacts in addition to the target group (e.g. targeting husbands and mothers-in-law in addition to pregnant women or mothers) has a greater effect *(167)*.

ADDITIONAL RESOURCES ON SOCIAL AND BEHAVIOUR-CHANGE COMMUNICATION AND LINKS TO WHO GUIDANCE

- World Health Organization. Sponsored symposium. Strategic behaviour change approaches to optimize the impact of micronutrient interventions. In collaboration with the Micronutrient Initiative, 2 June 2014, Addis Ababa, Ethiopia (http://www.who.int/nutrition/events/2014_WHOMI_symposium_behaviour_change_micronutrient_intervention/en/).

- Accelerating nutrition improvements: best practices for scaling up. Examples from Ethiopia, Uganda and the United Republic of Tanzania. Geneva: World Health Organization; 2016 (WHO/NMH/NHD/16.4; http://apps.who.int/iris/bitstream/10665/252535/1/WHO-NMH-NHD-16.4-eng.pdf?ua=1).

- United Nations Children's Fund. Communication for development (https://www.unicef.org/cbsc/index_65736.html).

3.2 NUTRITION-SENSITIVE SOLUTIONS TO ANAEMIA

Nutrition-sensitive solutions to anaemia address the underlying and basic causes of anaemia that require input from a wide range of sectors, including disease control (e.g. malaria, intestinal helminths), water, sanitation and hygiene, reproductive health, intersectoral strategies that address root causes such as poverty, lack of education and gender norms. Actions and recommendations listed here are not representative of the breadth of activities needed to address any one cause – for example, malaria or water, sanitation and hygiene – but are focused on activities that most directly relate to the prevention of anaemia and are within the purview of those working within the health-care system. Additional documents and guidelines are provided following the summaries of key actions and recommendations.

3.2.1 PARASITIC INFECTIONS: MALARIA, SOIL-TRANSMITTED HELMINTH INFECTIONS AND SCHISTOSOMIASIS

3.2.1.1 MALARIA

Malaria is one of the primary causes of anaemia globally *(1–3)*. Ninety per cent of all malaria deaths occur in sub-Saharan Africa *(95)* and malaria is a primary cause of anaemia in east and west Africa in particular. Pregnant women are particularly vulnerable to malaria, owing to reduced immunity during pregnancy, and malaria during pregnancy increases not only the risk of anaemia and death for the mother, but also the risk of spontaneous abortion, stillbirth, premature delivery and low birth weight of her baby. Infants and children are also at high risk of adverse effects from malaria, including anaemia.

The relationship between malaria and iron is complex (see section 2.2.3) and interventions to address iron-deficiency anaemia must also take into account the prevalence of malaria in each setting. Malaria control in endemic areas can reduce anaemia and severe anaemia by over 25% and by 60%, respectively *(100)*. In addition, when regular malaria surveillance and treatment are provided, iron supplementation does not adversely affect malarial morbidity and mortality in children *(76)*. Thus, in settings in which malaria is endemic and iron supplementation is warranted, provision of iron supplements should be accompanied by measures to prevent, diagnose and treat malaria. Such measures include vector control with insecticide-treated nets or indoor residual spraying (IRS), chemoprevention (e.g. intermittent preventive treatment in pregnancy/for infants) and case management.

Vector control is the key intervention for global malaria control and accounts for close to 60% of global investment in malaria control *(168)*. Long-lasting insecticidal nets reduce the transmission of malaria parasites, mainly by killing or blocking mosquitoes that attempt to feed upon humans under nets *(169)*. IRS[1] kills mosquitoes and reduces their longevity when they rest on insecticide-sprayed surfaces inside houses or other structures, usually after they have fed on the occupants *(168)*. Use of long-lasting insecticidal nets reduces maternal anaemia among pregnant women, as well as placental infection and low birth weight *(170)*.

Intermittent preventive treatment in pregnancy (IPTp, i.e. administration of sulfadoxine–pyrimethamine during the second and third trimester of pregnancy) is a form of chemoprevention that has been shown to reduce severe maternal anaemia, low birth weight and perinatal mortality *(170)*. Intermittent preventive treatment for infants (IPTi) with sulfadoxine–pyrimethamine provides protection against clinical malaria and anaemia in the first year of life, and also reduces hospital admissions *(170)*.

Effective strategies for malaria case-management need to ensure access to appropriate, effective treatment at each level of health care *(171)*. WHO recommends that all suspected cases of malaria be treated on the basis of a confirmed diagnosis by microscopy examination or rapid diagnostic testing

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[1] Indoor residual spraying (IRS) is the application of a long-lasting, residual insecticide to resting surfaces for potential malaria vectors, such as internal walls, eaves and ceilings of all houses or structures (including domestic animal shelters) where such vectors might come into contact with the insecticide *(168)*. It is not discussed in depth in this manual, as it is outside of the purview of the intended audience.

of a blood sample *(172)*. In children and non-immune populations, correct diagnosis is essential, as *P. falciparum* malaria can quickly become fatal *(172)*.

KEY ACTIONS AND RECOMMENDATIONS: MALARIA CONTROL

- **Vector control:** malaria-control programmes should prioritize delivering either long-lasting insecticidal net or indoor residual spraying (IRS) at high coverage and to a high standard *(173)*. Long-lasting insecticidal nets are discussed here; see the additional resources section for additional information on IRS and combining both interventions.

- **Long-lasting insecticide treated nets:** in areas targeted for long-lasting insecticidal nets, achieve universal coverage (i.e. access to and use of long-lasting insecticidal nets by all those at risk) of long-lasting insecticidal nets should be achieved in malaria-endemic areas *(174)*.

  o All infants at their first immunization, and all pregnant women as early as possible in pregnancy, should each receive one long-lasting insecticidal nets, through immunization and antenatal care visits.

  o Insecticide-treated nets should be used as early in pregnancy as possible, and continue to be used throughout pregnancy and in the postpartum period for both mother and child.

  o Malaria-control programmes should apply a combination of mass free distributions and continuous distributions of long-lasting insecticidal nets through multiple channels.

  o Other channels for distribution – through school, churches/mosques, occupations or communities – should also be explored.

- **Chemoprevention**: in areas of high transmission, chemoprevention should be used for pregnant women and young children, including intermittent preventive treatment in pregnancy and infancy, and seasonal malaria chemoprevention *(170)*.

  o All possible efforts should be made to increase access to intermittent preventive treatment in pregnancy (IPTp) as part of antenatal care in all areas of Africa with moderate to high malaria transmission *(175)*.

  o IPTp with sulfadoxine–pyrimethamine should be provided at each scheduled antenatal care visit during the second and third trimester of pregnancy.

  o *Seasonal malarial chemoprevention* (i.e. intermittent administration of a full treatment course of an antimalarial medicine e.g. amodiaquine plus sulfadoxine–pyrimethamine, during the malaria season to prevent malarial illness, with the objective of maintaining therapeutic concentrations of antimalarial drug in the blood throughout the period of greatest malarial risk) is recommended for children aged 3–59 months living in areas of highly seasonal malaria transmission in the Sahel subregion *(176)*.

  o *Intermittent preventive treatment for infants* (IPTi) with sulfadoxine–pyrimethamine is recommended in areas with moderate to high transmission, where resistance to sulfadoxine–pyrimethamine is low and where seasonal malarial chemoprevention is not currently implemented *(170)*. IPTi with sulfadoxine–pyrimethamine should be delivered at routine childhood immunization clinics, at the time of the second and third diphtheria–tetanus–pertussis (DTP) and measles vaccination.

- **Case-management:** all cases of suspected malaria in all epidemiological settings should be examined for evidence of infection with malaria parasites, by either microscopy or rapid diagnostic testing *(172)*.

3.2.1.2 SOIL-TRANSMITTED HELMINTH INFECTIONS AND SCHISTOSOMIASIS

Hookworm (*Necator americanus* and *Ancylostoma duodenale*) and schistosomiasis are associated with blood (and iron) loss, and iron-deficiency anaemia. Hookworms are common in tropical and subtropical areas, particularly sub-Saharan Africa and south-east Asia. Poverty and poor water, sanitation, hygiene and infrastructure are also important determinants for transmission of hookworm. Hookworm infection contributes to maternal anaemia; estimates from Asia and Africa suggest that the between one third and one half of moderate to severe cases of anaemia in pregnant women and in preschool and school-age children are due to hookworm infestation *(177)*. However, systematic reviews of large-scale distribution of anthelminthic drugs to at-risk populations have not shown a difference in haemoglobin levels between those given a dose of deworming drugs and those given a placebo or receiving no treatment. Periodic preventive chemotherapy, or repeated large-scale administration of anthelminthic drugs to at-risk populations, can dramatically reduce the burden of soil-transmitted helminth infections. This can potentially decrease morbidity among individuals who are heavily infected by soil-transmitted helminths, if linked with multisectoral programmes that maximize and sustain the benefits of a decreased burden of soil-transmitted helminth infections, such as a range of water, sanitation and hygiene services and practices *(178–181)*.

WHO's strategy for controlling soil-transmitted helminth infections is through periodic treatment of at-risk populations living in endemic areas *(182, 183)*. At-risk groups include: preschool and school-aged children and women of childbearing age (including pregnant women in their second and third trimesters and lactating women). Periodic deworming can be easily integrated with child health days or vitamin A supplementation programmes for preschool children, or integrated with school-based health programmes. Schools provide an important entry point for deworming activities, as they provide easy access to health and hygiene education components, such as the promotion of hand washing and improved sanitation.

Schistosomiasis occurs primarily in sub-Saharan Africa and ranks second only to malaria as the most common parasitic disease. In addition to blood loss caused by the parasite, schistosomiasis has additional mechanisms that lead to anaemia, not all of which are completely understood. Schistosomiasis is significantly associated with anaemia as well as other adverse effects, including diarrhoea, pain, fatigue, undernutrition and reduced exercise tolerance *(184)*.

For schistosomiasis, control includes large-scale drug treatment of at risk populations (i.e. preventive chemotherapy with praziquantel), snail control, improved sanitation, and health and hygiene education. Target populations include school-age children and adults considered to be at-risk, including pregnant and lactating women and groups with occupations involving contact with infested water, including fisherman, farmers, irrigation workers or women in their domestic tasks, or entire communities in endemic areas *(185)*.

Soil-transmitted helminth infections in at-risk population groups *(182)*

- *Preventive chemotherapy (deworming)*, using annual or biannual[a] single-dose albendazole (400 mg) or mebendazole (500 mg),[b] is recommended as a public health intervention for all young children (12–23 months of age), preschool (24–59 months of age) and school-age children living in areas where the baseline prevalence of any soil-transmitted infection is 20% or higher among children, in order to reduce the worm burden of soil-transmitted helminth infections.

[a] Biannual administration is recommended where the baseline prevalence is over 50%.
[b] A half-dose of albendazole (i.e. 200 mg) is recommended for children younger than 24 months of age.

- *Preventive chemotherapy (deworming)*, using annual or biannual[a] single-dose albendazole (400 mg) or mebendazole (500 mg), is recommended as a public health intervention for all non-pregnant adolescent girls (10–19 years of age) and non-pregnant women of reproductive age (15–49 years of age) living in areas where the baseline prevalence of any soil-transmitted helminth infection is 20% or higher among non-pregnant adolescent girls and non-pregnant women of reproductive age, in order to reduce the worm burden of soil-transmitted helminth infection.

[a] Biannual administration is recommended where the baseline prevalence is over 50%.

- *Preventive chemotherapy (deworming)*, using single-dose albendazole (400 mg) or mebendazole (500 mg), is recommended as a public health intervention for pregnant women, after the first trimester, living in areas where both: (i) the baseline prevalence of hookworm and/or T. trichiura infection is 20% or higher among pregnant women, and (ii) anaemia is a severe public health problem, with a prevalence of 40% or higher among pregnant women,[a] in order to reduce the worm burden of hookworm and *T. trichiura* infection.

[a] For the most recent estimates of prevalence of anaemia, visit the WHO-hosted Vitamin and Mineral Nutrition Information System (VMNIS) *(157)*.

- Delivering preventive chemotherapy to adolescent girls and women of reproductive age entails extra care and precaution in ensuring that women and girls receiving anthelminthic medicines are not pregnant. Policy-makers may decide to withhold preventive chemotherapy among adolescent and women of reproductive age when the pregnancy status or gestational age of women and girls is uncertain, or in areas where rates of unplanned pregnancies are high and coverage of antenatal care is low.

- Education on health and hygiene should be provided, to reduce transmission and reinfection by encouraging healthy behaviours.

- Adequate sanitation and access to safe water should also be provided (see section 3.2.2).

- Anthelminthic medicines can be given to those coinfected with HIV, who are otherwise eligible for inclusion in large-scale preventive chemotherapy interventions *(186)*.

Considerations for the control of soil-transmitted helminths and schistosomiasis

- Preventive chemotherapy, or the periodic large-scale administration of anthelminthic medicines to populations at risk, can dramatically reduce the burden of worms caused by soil-transmitted helminth infections. In areas of varying soil-transmitted helminth endemicity, no average benefit of preventive chemotherapy was detected for outcomes related to morbidity, nutritional outcomes or development in the entire population (composed of infected and uninfected individuals). However, a decreasing worm burden of soil-transmitted helminths decreases morbidity among individuals who are heavily infected by soil-transmitted helminths. Because preventive chemotherapy does not break the cycle of infection and reinfection, populations living in contaminated environments continue to be at risk of infection and need frequent administrations of anthelminthic medicines.

- Long-term solutions to schistosomiasis and soil-transmitted helminthiases require improvements in water, sanitation and hygiene. Moreover, multisectoral, integrated programmes will be needed to maximize and sustain the benefits of a decreased worm burden of soil-transmitted helminth infections.
- Preventive chemotherapy is an important but insufficient part of a comprehensive package to eliminate morbidity due to schistosomiasis and soil-transmitted helminths in at-risk populations.
- Adequate sanitation and access to safe water should be provided (see section 3.2.2).

ADDITIONAL RESOURCES ON SOIL-TRANSMITTED HELMINTH INFECTIONS AND SCHISTOSOMIASIS AND LINKS TO WHO GUIDANCE

- World Health Organization. Neglected tropical diseases (http://www.who.int/neglected_diseases/diseases/en/).
- World Health Organization. Intestinal worms. Strategy (http://www.who.int/intestinal_worms/strategy/en/).
- World Health Organization. Schistosomiasis. Strategy. Control and preventive chemotherapy (http://www.who.int/schistosomiasis/strategy/en/).
- World Health Organization. Recommended treatment strategy for schistosomiasis in preventive chemotherapy (http://www.who.int/schistosomiasis/strategy/p41_sch.pdf?ua=1).

3.2.2 WATER, SANITATION AND HYGIENE

Water, sanitation and hygiene are related to the development of anaemia in multiple ways. Hookworms and schistosomiasis contribute to anaemia and are associated with poor water, sanitation and hygiene access and practices, which are concentrated in poor and disadvantaged populations. Safe water reduces the odds of schistosomiasis infection and water, sanitation and hygiene access and practices are associated with lower odds of soil-transmitted helminth infections *(188)*.

In addition, anaemia may be linked to poor water, sanitation and hygiene through the development of environmental enteropathy (also referred to as tropical enteropathy), a subclinical condition characterized by increased gut permeability and impaired absorptive and barrier functions of the small intestine lining, thought to result from ingesting large amounts of faecal bacteria from poor sanitation and hygiene practices *(189)*. Environmental enteropathy causes chronic immune stimulation, which probably contributes to the anaemia of inflammation (i.e. anaemia of chronic disease) *(190)*.

While some water, sanitation and hygiene activities may be outside the purview of the health sector, there are key practices related to water, sanitation and hygiene that are relevant to improving nutritional status that can be promoted through health and nutrition activities. For example promoting improvements in key hygiene behaviours (e.g. hand washing), treatment and use of safe water, and using hygienic methods of disposal of faeces and urine, are practices and behaviours that are important to the prevention of anaemia and can be incorporated into health-sector activities. Water, sanitation and hygiene can be incorporated into nutrition counselling, promotion and assessments, as well as health visits. For example, hand washing can be promoted as an "essential nutrition action" and included in nutritional counselling and promotion materials, and safe water kits (containing a water-treatment product, soap and a water storage container) can be distributed at prenatal care visits for pregnant women *(191)*.

KEY ACTIONS AND RECOMMENDATIONS: WATER, SANITATION AND HYGIENE

- **Promote optimal hand washing:** optimal hand-washing practices include the following *(190)*:
    - o use soap or ash every time hands are washed
    - o wash hands under poured or flowing water
    - o wash hands before handling, preparing or eating food; and before feeding someone or giving medicines; and wash hands often during food preparation
    - o wash hands after going to the toilet, cleaning a person who has defecated, blowing your nose, coughing, sneezing or handling an animal or animal waste, and both before and after tending to someone who is sick.

- **Promote treatment of water and safe storage of drinking water in the household** *(191)***:**
    - o treat all drinking water using an effective treatment method, such as chlorination, boiling, solar disinfection using heat and ultraviolet radiation, filtration using different types of filters, or combined chemical coagulation, flocculation and disinfection
    - o store treated water in an appropriate vessel, preferably with a narrow neck and a tap
    - o if the container does not have a tap, pour the water into a clean pitcher to serve, or use a ladle to dispense water; hang the ladle on the wall
    - o do not touch the inside of the container with hands.

- **Promote safe, hygienic methods of sanitation/faeces management** *(188)***:**
    - o reduce open defecation and prevent urination/defecation near bodies of water (for schistosomiasis control) *(192)*
    - o hygienic latrines should be used by all household members, with modifications made for children and people with limited mobility; latrines should meet minimum standards, including a cleanable platform, cover over the pit, housing that provides privacy, and a hand-washing station nearby; maintain clean latrines with a clear pathway
    - o when latrines are not available, bury faeces away from the house
    - o hepatic schistosomiasis is transferred when faeces contaminate snail-infested waters, and urinary schistosomiasis can be transmitted through urine; thus, urine and faeces should be prevented from entering snail-infested waters *(192)*.

- **Promote wearing of shoes (for control of soil-transmitted helminths):**
    - o soil-transmitted helminths can be acquired from eggs in faeces that are in soil; wearing shoes and safely disposing of faeces will prevent transmission of soil-transmitted helminths *(192)*.

- **Discourage standing in rivers/lakes to play or wash clothes (for schistosomiasis control)** *(188)*

- **Promote optimal food-hygiene practices** *(193, 194)***:** food hygiene is particularly important for preparation of food for young children or for individuals with compromised immune systems, as many microorganisms can be transmitted through food.
    - o Keep hands and food preparation areas clean.
    - o Wash hands before and during food preparation.

- o Wash all surfaces and equipment used to prepare or serve food, with soap and water and, if possible, with bleach.

- o Protect food from insects, pests and other animals, by covering it with netting or a cloth, or keeping it in containers.

- o Separate raw and cooked food (during preparation and storage).

- o Cook food thoroughly (especially meat, poultry, eggs, fish and seafood) and reheat cooked food thoroughly.

- o Keep foods at safe temperatures:

  - do not leave cooked food at room temperature for more than 2 h

  - reheat cooked food that has been stored, before re-serving

  - do not thaw frozen food at room temperature.

- o Prepare fresh food for infants and young children and other people with compromised immune systems, and do not store it after cooking.

- o Use safe water and raw materials: wash raw vegetables/fruits with treated water or peel the skin before eating.

3.2.3 REPRODUCTIVE HEALTH PRACTICES

Females are at higher risk of anaemia compared to males, throughout almost the entire life-cycle. Physiological factors, such as menstruation and pregnancy, increase iron needs, thus increasing the risk of anaemia in women throughout their reproductive years. Early onset of childbearing – i.e. during adolescence – is a particular risk for developing anaemia because of the iron needs for growth of the adolescent mother herself, as well as iron needs for pregnancy, including growth and development of the fetus. In addition, many females (adolescents and adults) enter pregnancy with iron stores that are already inadequate. Finally, short durations between pregnancies, which do not allow recuperation of iron stores, as well as high numbers of pregnancies, are also associated with increased risk of anaemia.

Many reproductive health practices have a role to play in the prevention of anaemia in women throughout the adolescent and adult period, including: delaying the age of first pregnancy, ensuring optimal access to and coverage with quality prenatal care when a woman does become pregnant, ensuring that evidence-based delivery and postnatal care practices are employed, and promoting optimal birth spacing. Several of these practices affect not only the anaemia risk of the mother, but also that of her child. Reproductive health-care visits also provide opportunities to integrate nutrition or other public health interventions, for example, iron and folic acid supplementation or distribution of long-lasting insecticidal nets in malaria-endemic areas.

KEY ACTIONS AND RECOMMENDATIONS: REPRODUCTIVE HEALTH PRACTICES

Pre-pregnancy: components of pre-pregnancy care that are relevant to prevention/treatment of anaemia are listed next.

- **Delaying the age of first pregnancy:** childbirth at an early age is associated with greater health risks for the mother as well as her infant, including pregnancy complications that can lead to death, and low birth weight of the infant *(195)*. WHO-recommended strategies to prevent early pregnancy include the following (for a full list of recommendations see reference *(195)*):

    o formulating and enforcing laws and policies to prohibit marriage of girls aged under 18 years

    o influencing family and community norms and informing and empowering girls to delay marriage until 18 years of age

    o increasing educational opportunities for girls through formal and non-formal channels, and strengthening efforts to retain girls in school, to delay marriage and childbearing

    o providing interventions with curriculum-based sexuality and health education, with promotion of contraception to adolescents

    o offering and promoting postpartum and post-abortion contraception to adolescents

    o improving health-service delivery to adolescents, as a means of facilitating their access to, and use of, contraceptive information and services

    o providing information to all pregnant adolescents about the importance of using skilled antenatal and childbirth care.

- **Iron and folic acid supplementation:** intermittent or daily iron and folic acid supplementation is recommended as a public health intervention in menstruating women living in settings where anaemia is highly prevalent, to improve their haemoglobin concentrations and iron status and reduce the risk of anaemia (see section 3.1.2). There is some evidence of additional benefit of MMN supplements containing 13–15 different micronutrients (including iron and folic acid) over iron and folic acid supplements alone, but there is also some evidence of risk, and some important gaps in the evidence. In populations with a high prevalence of nutritional deficiencies, policy-makers might consider the benefits of multiple micronutrient supplements on maternal health outweigh the disadvantages, and may choose to give these supplements that include iron and folic acid *(163)*.

Prenatal care: components of prenatal care that are relevant to prevention/treatment of anaemia are listed next.

- **Iron and folic acid supplementation:** on confirmation of pregnancy, women should receive routine antenatal care, including daily or intermittent iron and folic acid supplementation, depending on the prevalence of anaemia in the region and their anaemia status (see section 3.1.2).

- **Screening for anaemia:** WHO recommends that all pregnant women be screened for anaemia at each prenatal visit *(54)*.

    o At the initial prenatal care visit, haemoglobin should be measured.

    o On all subsequent visits, clinical signs of anaemia, such as conjunctival or palmar pallor, should be assessed.

    o Women who are diagnosed with anaemia should be treated appropriately with iron and folic acid supplements (see section 3.1.2).

- **Nutritional counselling:** pregnant women should be advised to eat a greater amount and variety of foods, particularly those that are rich in iron, such as meat and fish *(53)*. Discussing food taboos during pregnancy that could be nutritionally harmful, as well as including family members in discussions related to the diet of the pregnant woman, is advised (also see section 3.1.1.1).

- **Deworming/antihelminthic treatment (in areas where soil-transmitted helminth infections are endemic):** preventive chemotherapy (deworming) is recommended as a public health intervention for all pregnant women, after the first trimester, living in areas where both: (i) the baseline prevalence of hookworm and/or *T. trichiura* infection is 20% or higher among pregnant women, and (ii) anaemia is a severe public health problem, with a prevalence of 40% or higher among pregnant women, in order to reduce the worm burden of hookworm and *T. trichiura* infection (see section 3.2.1).

- **Malaria prevention/treatment/case management (in malaria-endemic areas):** women in their second and third trimesters should receive IPTp as appropriate, as well as receiving and utilizing long-lasting insecticidal nets as early in pregnancy as possible (see section 3.2.1).

Perinatal and postnatal care: components of perinatal and postnatal care that are relevant to prevention/treatment of anaemia of the mother and infant are listed next.

- **Optimal timing of umbilical cord clamping:** delayed cord clamping should be provided as a part of essential neonatal care in all births (pre-term and term) and all types of deliveries (vaginal and caesarean) *(196)*. Delaying cord clamping allows blood flow between the placenta and neonate to continue, which can improve iron status in the infant for up to 6 months after birth. This may be particularly relevant for infants living in low-resource settings with reduced access to iron-rich foods. Preterm infants also have significant benefits from delayed cord clamping, included reduced intra-cranial bleeding and decreased need for blood transfusions.

  o Delayed umbilical cord clamping (not earlier than 1 min after birth) is recommended for improved maternal and infant health and nutrition outcomes *(195)*.

  o Delayed cord clamping applies equally to preterm and full-term births and caesarean and vaginal deliveries.

  o Delayed cord clamping is consistent with practices that are recommended to prevent postpartum haemorrhage (see below).

- **Prevention of postpartum haemorrhage:** women with anaemia during pregnancy are at increased risk of greater blood loss at delivery and in the immediate postpartum period *(197, 198)*. Postpartum haemorrhage (defined as a blood loss of 500 mL or more within 24 h after delivery) is strongly associated with severe maternal morbidity (including severe anaemia) and long-term disability, as well as maternal death *(198)*. Recommended practices to prevent postpartum haemorrhage include (for a full set of recommendations see reference *(198)*):
  - the use of uterotonic drugs for the prevention of postpartum haemorrhage in all births is recommended, and oxytocin is the recommended uterotonic drug; all women giving birth should be offered uterotonic drugs during the third stage of labour;
  - controlled cord traction is recommended for vaginal births in settings where skilled birth attendants are available and if the care provider and pregnant women regard a small reduction in blood loss and a small reduction in the third stage of labour as important; otherwise it is not recommended:
  - delayed cord clamping is recommended for all births;
  - surveillance of uterine tonus through abdominal palpation is recommended in all women, for early identification of postpartum uterine atony.
- **Birth spacing:** short birth-to-pregnancy intervals (<18 months) have been associated with preterm birth, small for gestational age and low birth weight (all of which are associated with development of anaemia in early infancy); very short birth-to-pregnancy intervals (<6 months) have been associated with increased maternal anaemia *(199)*.
  - WHO recommends that after a live birth, an interval of at least 24 months should pass before attempting the next pregnancy, in order to reduce the risk of adverse maternal, perinatal and infant outcomes *(199)*.

ADDITIONAL RESOURCES ON REPRODUCTIVE HEALTH-CARE PRACTICES RELEVANT TO ANAEMIA AND LINKS TO WHO GUIDANCE

- WHO recommendations on antenatal care for a positive pregnancy experience. Geneva: World Health Organization; 2016 (http://apps.who.int/iris/bitstream/10665/250796/1/9789241549912-eng.pdf?ua=1).

3.2.4 INTERSECTORAL ACTIONS

As described in section 2.4.1, there are many social, economic and cultural determinants of anaemia. Poverty; poor living and working conditions, including poor water, sanitation and hygiene and inadequate infrastructure; inadequate access to health-care services; lack of education; gender inequality that limits female empowerment and prevents access to education, health, nutrition, household income and other resources can all be all linked to poor nutritional status and risk of anaemia. Alleviating these socioeconomic and cultural problems requires the action of multiple different sectors, in addition to the health sector. However, the health sector can contribute in multiple ways: e.g. by promoting and advocating for policies and practices that support women's empowerment and gender equality; supporting equal education for males and females; preventing early marriage and childbearing and unwanted pregnancies (see section 3.2.3); and improving the health and nutrition literacy of women and girls, and also of men and communities.

KEY ACTIONS AND RECOMMENDATIONS: INTERSECTORAL ACTIONS

- **Improve gender equality and women's empowerment** *(200)*:
  - o increase the health and nutrition literacy of women, families and communities, particularly with respect to maternal and infant/child nutritional needs and the causes and consequences of anaemia and how it can be prevented
  - o increase the value placed on daughters to create more equitable access to food and health services, including intrahousehold food distribution, and use of prenatal and pregnancy care services
  - o eliminate child marriages and prevent early marriage and childbearing (also see section 3.2.3)
  - o increase gender equality within relationships, by engaging men and boys and improving active involvement of fathers, and increasing awareness of maternal and child nutrition and health issues, particularly anaemia
  - o reduce harmful gender norms and practices surrounding pregnancy and the postpartum period, particularly any food taboos that restrict certain foods or quantities of foods and could lead to anaemia
  - o advocate and support governments and communities in overcoming barriers in policy, social norms and taboos that discriminate against the health of women.

- **Support educational opportunities for girls and women:** women who are more educated are more likely to marry later, postpone childbearing and have fewer and spaced children, and better able to take timely decisions about accessing health-care services *(200)*.

- **Support income-generating activities for women:** giving women access to income can allow them to pay for healthy food, essential medicines, nutritional supplements and health-care services for themselves and their families *(200)*.

- **Raise awareness among policy-makers and communities** about the significant negative health, social and economic consequences of anaemia and how it can be prevented and treated.

DEVELOPMENT OF AN ANAEMIA-CONTROL STRATEGY

4
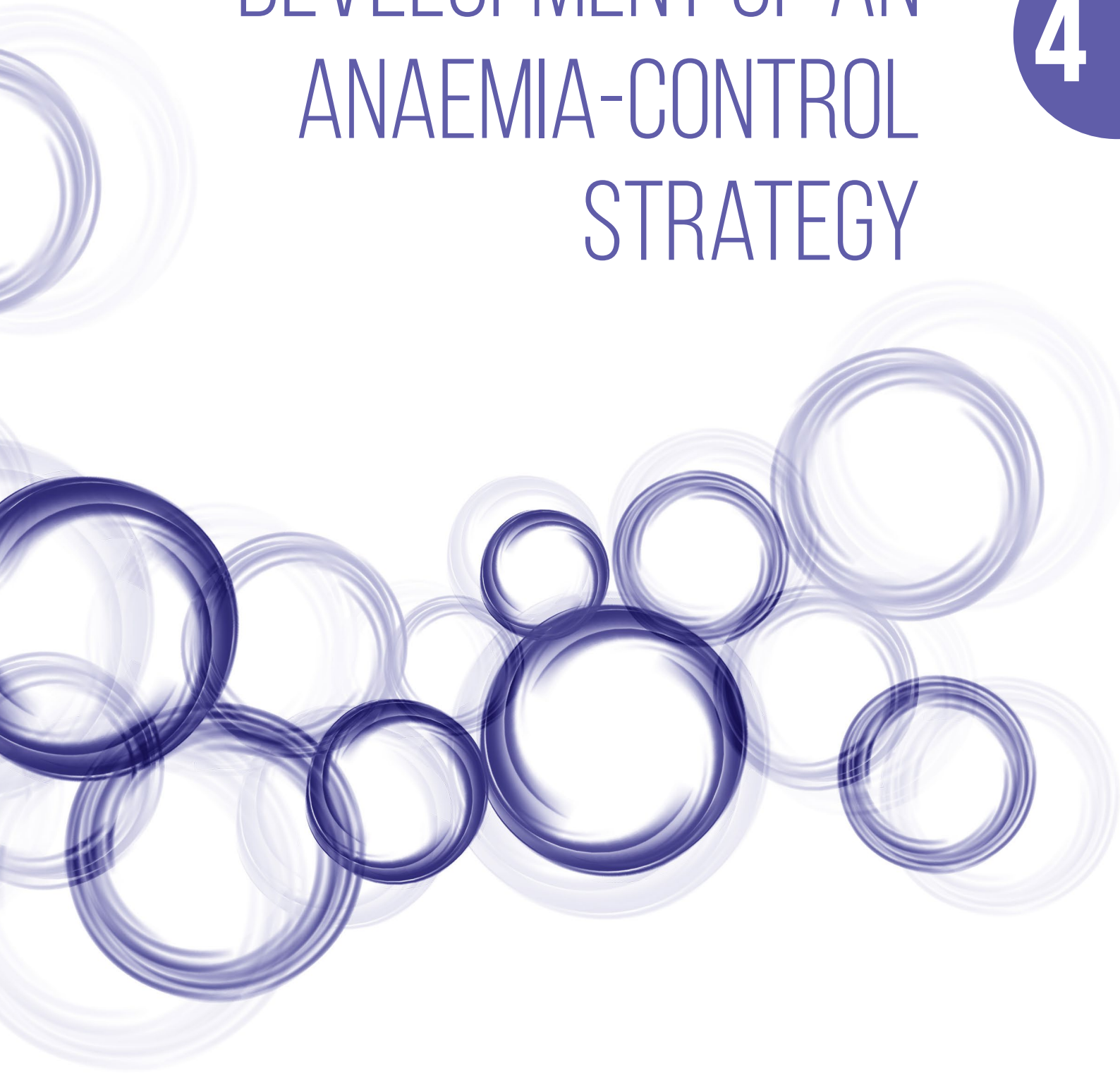
As discussed in the previous section, effectively addressing anaemia at the country or regional level requires a detailed picture of the specific determinants of anaemia in that particular setting. Knowing the primary causes will allow selection of interventions that will be the most effective, as well as development of a strategy to engage the multiple sectors needed for implementation (e.g. nutrition, health, water, sanitation and hygiene, as well as, poverty alleviation, agriculture, industry and education).

Another key part of selecting interventions is to understand how best to implement them in a given setting. The process of determining the right mix of strategies to prevent anaemia, and how to implement them in a chosen setting, is the focus of this section. A model for developing an anaemia-control strategy serves as the framework for this process. Monitoring and evaluation of anaemia-control programmes is the focus of section 5.

4.1 MODEL FOR DEVELOPING ANAEMIA-CONTROL STRATEGIES

For coordinated action to address prevention and control of anaemia, development of an anaemia-control strategy (at national or regional level) is recommended *(201, 202)*. Such a strategy should be built upon an understanding of the anaemia situation in the particular setting (prevalence, geographical distribution and target groups), primary causes of anaemia, and current programmes already addressing anaemia and how they can be improved or changed. A broad group of stakeholders from multiple sectors and institutions should develop the strategy, and determine priority actions, responsible parties, desired outcomes, monitoring and evaluation plans and timelines for implementation. Each party should have clear and very well defined responsibilities and tasks. Close interrelations and clear levels of reporting are desirable. The components of this model are discussed in further detail in the subsections that follow.

4.1.1 ASSESS AND UNDERSTAND THE PROBLEM: SITUATIONAL ANALYSIS

Anaemia-control strategies need to reflect the primary causes of anaemia in a particular population. Identification of the specific role of different determinants is challenging, however, and in most settings, iron deficiency should be assumed to contribute to anaemia (and more so in groups that are most vulnerable to iron deficiency – e.g. pregnant women, infants) unless otherwise documented. Conducting a situational analysis should aim to gather existing information not only about the prevalence and distribution of anaemia, but also about existing anaemia-control programmes and barriers and facilitators to their improvement. The steps listed next collect important information for developing an anaemia-control strategy.

4.1.1.1 DETERMINE THE PREVALENCE OF ANAEMIA AND IDENTIFY PRIORITY TARGET GROUPS AND REGIONS/AREAS

National anaemia surveys (or other smaller surveys if national surveys are not available) should be used to assess the extent and distribution of anaemia in a country. Target groups are those most affected by anaemia, which include (in decreasing order of priority) pregnant women and children aged under 2 years; lactating women and women recently engaged or married; women of reproductive age; adolescents; children aged 2–10 years; elderly individuals; and men *(201)*. If possible, national survey data should also be used to identify regions where anaemia is most concentrated (e.g. rural or isolated regions), so efforts can be appropriately targeted.

4.1.1.2 DETERMINE THE PRIMARY CAUSES OF ANAEMIA AND THEIR RELATIVE IMPORTANCE

While iron deficiency is a primary contributor to anaemia in low- and middle-income country settings, at least half of anaemia cases will not be solved by solely addressing iron status. Data on other nutritional deficiencies (e.g. vitamin A) should be reviewed, as should dietary patterns/habits related to development of anaemia

(e.g. dietary restrictions during pregnancy, complementary feeding practices, consumption of animal-source foods). Data on other primary causes of anaemia – malaria, helminth infections, haemoglobinopathies, and chronic infections such as HIV or TB – should complement nutritional information, to determine the relative importance of these conditions as well as their geographical distribution.

4.1.1.3 ASSESS CURRENT PROGRAMMES ADDRESSING ANAEMIA AND POTENTIAL IMPROVEMENTS

If anaemia-control programmes already exist, it is essential to understand what is/is not working and how these programmes can be improved. Formative research and institutional research techniques – qualitative and quantitative – can be used to assess how and what nutrition and health services are being provided, what health-care workers know about anaemia (its causes, how to prevent it and what the consequences are), and what advice/counselling they give to patients. Part of this step should also include determining what other sectors/programmes are not currently addressing anaemia but can potentially be involved in an anaemia-control strategy (e.g. infectious disease, reproductive health, the private sector) and what delivery platforms they offer. Finally, an assessment of resources and capacity available to institutions that could become involved in anaemia-control efforts is useful *(202)*.

4.1.1.4 ASSESS CURRENT KNOWLEDGE ABOUT ANAEMIA AND BARRIERS TO PREVENTION AND CONTROL

Qualitative research can be used to better understand how anaemia is perceived in the general population, as well as among policy-makers and health workers (e.g. do people understand the causes and consequences of anaemia?); how prevention is viewed (e.g. are iron supplements acceptable to the population? do people feel it is important to prevent anaemia?); and what barriers to accessing services may exist (e.g. high costs, gender inequality which prohibits access to needed services, political commitment). Such information can help to tailor interventions to the given context, identify other sectors/services that may need to be integrated into anaemia prevention, and identify particular aspects of anaemia where more awareness and commitment are needed.

4.1.2 RAISE AWARENESS AND CONDUCT HIGH-LEVEL ADVOCACY

In many situations, the causes and impact of anaemia may not be well understood – by the general public, but also by health workers/professionals and policy-makers. Many interventions, using many different channels, can be employed to increase awareness of the importance of addressing anaemia – for example, using known personalities as "anaemia champions"; using popular media to disseminate messages on anaemia; or using other public health events/campaigns to distribute information on anaemia *(200)*. Formative research conducted during the situation analysis about what different people know about anaemia and its causes and consequences can feed into this process. High-level advocacy targeting policy-makers, ministries, donors, academia, religious leaders and the private sector should aim to obtain national-level political commitment so that the anaemia-control strategy is supported and more stable *(202)*. Advocacy can also be directed at the public, to increase their use of, and demand for, anaemia services, as well as at health professionals, to increase or improve their implementation of anaemia-prevention actions.

4.1.3 CREATE AN ANAEMIA TASK FORCE AND DEVELOP PARTNERSHIPS

To address the multifactorial causes of anaemia effectively, close coordination and cooperation between the multiple relevant sectors – nutrition, agriculture, reproductive health, child health, malaria, education, parasite control, water, sanitation and hygiene – and groups – government agencies, nongovernmental organizations (NGOs), donors and the private sector – is needed. Past experiences of developing anaemia-control strategies have found that achieving genuine collaboration between a core group of stakeholders to develop the anaemia-control strategy and implement a national anaemia programme is one of the most challenging aspects, but also one of the most crucial *(202)*.

4.1.4 DETERMINE PROGRAMMATIC INTERVENTIONS AND DEVELOP IMPLEMENTATION PLANS

The intersectoral anaemia task force needs to decide which anaemia-prevention and control activities are a priority to implement, who is responsible for carrying them out and what the timeline is for their implementation. During this process, specific objectives should be identified that have a timeframe and can be measured as part of monitoring and evaluation (see section 5) – for example, increased awareness among pregnant women of the consequences of anaemia, or increased training for community health-care workers on detecting clinical signs of anaemia. Constructing a logic model – a pictorial depiction of how programme inputs and activities will lead to desired outcomes – based on the situational analysis results and the planned activities, helps to guide not only programme development but also programme monitoring and evaluation (logic models and programme monitoring and evaluation are discussed in more detail in section 5). The task force should also establish how the different partners – government agencies and NGOs – will collaborate and carry out interventions in an integrated manner *(202)*. Each planned activity should have a workplan and budget, and must described in terms of timing, responsible parties, cost and indicators of success *(201)*.

4.1.5 DEVELOP A MONITORING AND EVALUATION PLAN

Monitoring and evaluation is the focus of section 5. Briefly, a monitoring and evaluation plan needs to include performance indicators, and should ideally integrate with existing information systems. *Monitoring* is an ongoing exercise, and a plan for regular monitoring should be developed during the planning of the anaemia-control programme; *evaluation* is a more rigorous exercise conducted periodically to assess impact, which in this case is changes in the prevalence of anaemia or a shift in the population's haemoglobin curve among target groups.

4.2 EXAMPLES OF NATIONAL ANAEMIA-CONTROL PLANS

4.2.1 BANGLADESH

Bangladesh adopted a national strategy for anaemia prevention and control in 2006, with the aim of reducing the prevalence of anaemia by 25% by 2015 among high-risk groups, including pregnant and lactating women, infants and young children under 2 years of age, adolescent girls and newly-wed women *(203)*. At the time the strategy was implemented, anaemia was estimated to affect 46% of pregnant women, 64% of children aged 6–23 months, 42% of children aged 24–59 months, 30% of adolescent girls and 33% of non-pregnant women *(203)*. The strategy was developed by the Ministry of Family Health and Welfare in coordination with participants from multiple sectors including other government sectors (local government and rural development, education), international agencies (WHO, United Nations Children's Fund, World Bank), national and international NGOs, professional medical organizations and research institutes. It was built upon past efforts for prevention and control of anaemia and identified comprehensive strategies that addressed the multiple causes of anaemia in Bangladesh:

- micronutrient supplementation to high-risk groups

- counselling on the importance of taking iron and folic acid supplements

- anaemia screening for children, adolescent girls and women

- dietary improvement, including optimal breastfeeding and complementary feeding, and increased dietary diversity and access to micronutrient-rich foods, including through household food production/crop diversification

- mass fortification

- parasite control

- family planning and safe motherhood efforts, to delay the age of first pregnancy, space births and reduce bleeding at delivery.

4.2.2 PANAMA

As part of its *National Plan on Nutrition and Food Security, 2009–2015*, Panama implemented several strategies that included actions to address anaemia, with the objectives of reducing postpartum anaemia by 40% and reducing anaemia by 30% in children aged under 3 years *(204)*. The National Plan was created by a group of 30 organizations that included government sectors, NGOs, academic organizations, businesses/private sector and international organizations. The National Plan subsumed other plans related to anaemia control, most importantly the *National Plan for Prevention and Control of Micronutrient Deficiencies, 2009–2015 (205)*, which proposed several anaemia-control strategies in prioritized districts and targeted populations (indigenous populations, areas of high poverty or areas with high levels of undernutrition), to prevent and reduce iron-deficiency anaemia in neonates and increase iron stores in infants aged under 6 months, as well as to reduce anaemia in children aged under 5 years (particularly those under 3 years), school-age children and pregnant women *(205)*. Activities to reach the anaemia-related objectives of the *National Plan on Nutrition and Food Security, 2009–2015* included:

- universal implementation of delayed umbilical cord clamping

- iron supplementation for infants (starting at 4 months of age), children (daily or weekly), women of reproductive age (weekly) and pregnant and lactating women (daily)

- distribution of a fortified food (Nutricereal) targeted to children aged under 3 years and pregnant/lactating women in prioritized areas

- distribution of multiple micronutrient powders to preschool children

- mass fortification with micronutrients

- prevention and treatment of intestinal parasite infections in children aged under 3 years

- counselling of pregnant women on optimal dietary practices

- monitoring haemoglobin in pregnant women and women of reproductive age.

4.2.3 THAILAND

Thailand recognized anaemia as a serious nutritional concern in 1982 and established anaemia reduction as a national goal *(201)*. To meet its objective, Thailand used a variety of strategies to increase use of iron and folic acid supplements, focusing primarily on pregnant women. Village health volunteers were used to identify pregnant women and encourage them to attend antenatal care, reaching 98% coverage of pregnant women receiving antenatal care, and 84% coverage of those attending four antenatal care visits. Free iron and folic acid supplements were provided to all pregnant women, regardless of their haemoglobin levels, and the way in which health workers counselled women to take iron and folic acid was improved through qualitative research. Thailand also decentralized the supply and logistics of iron and folic acid supplements, to allow provincial offices to estimate their own needs, and had easily accessible back-up supplies. Between 1986 and 1996/97, Thailand reduced the prevalence of anaemia by 50% in pregnant women and anaemia also declined among children aged under 5 years *(201)*.

MONITORING AND EVALUATION OF ANAEMIA-CONTROL PROGRAMMES

5

Section 4 described the steps of creating and implementing an anaemia control programme. A crucial complement to that process is developing a monitoring and evaluation (M&E) plan to be implemented concurrently with the programme. *Monitoring* is an ongoing routine exercise of collecting information on a programme to assess processes and outputs. *Evaluation* is a more rigorous exercise conducted periodically to assess the impact of a programme on desired outcomes. Both are essential practices in public health.

Monitoring and evaluation of programmes allows practitioners to learn from past experience, to make decisions based on data, and to guide and tailor programme efforts based on desired outcomes. M&E can also increase the effectiveness of programmes by improving service delivery and planning and can address social inequity through improved allocation of resources. Effective programme evaluation that demonstrates results to stakeholders is a systematic way to improve and account for public health actions *(205)*.

This section first outlines key components of a M&E plan for anaemia-control programmes. A M&E plan describes how the entire M&E system should function alongside the anaemia-control programme. Secondly, it presents a framework for programme evaluation that can be part of an anaemia-control programme's M&E plan. This framework is based on the Centers for Disease Control and Prevention's (CDC's) *Framework for program evaluation in public health (206)*.

The WHO/CDC electronic catalogue of indicators for micronutrient programmes, referred to as the "eCatalogue of Indicators" contains a non-comprehensive register of standard process and impact indicators for tracking the performance of public health programmes implementing micronutrient interventions for anaemia-control programmes. This eCatalogue of Indicators is a dynamic digital resource and new indicators are being progressively added as they become available (see https://extranet.who.int/indcat/).

## 5.1 KEY COMPONENTS OF A MONITORING AND EVALUATION PLAN FOR ANAEMIA-CONTROL PROGRAMMES

Though the discussion of M&E in this manual comes after the discussion of programme development and implementation, it is essential to address M&E early on in the conceptualization and planning of a programme. Many parts of M&E discussed in this section – for example, constructing a logframe or developing a programme description – are processes that should be done early in programme development, but will become very useful when developing indicators for monitoring or a design for evaluation.

5.1.1 LOGIC MODEL

A logic model depicts graphically the relationships between a programme's "inputs" (i.e. the resources invested in the programme), a programme's activities, the direct results of the programme's activities, and the intended changes or benefits to be seen in the target population. In other words, a logic model is a visual representation of the interrelated pathways through which the programme is supposed to achieve its outcomes *(206, 207)*.

For the purposes of M&E, logic models are useful for developing indicators at each stage of the programme's process (discussed further in sections 5.1.2 and 5.2). But ideally, logic models are created earlier during programme development. A logic model can engage stakeholders to coordinate and reach consensus about programme objectives, activities, outcomes and limitations, and also helps stakeholders understand the links between programme components and activities that are required to effect change *(207)*. A logical framework also known as LogFrame, is a useful tool during programme implementation, to make adjustments or corrections to programme components, or to help identify challenges or risks that might prevent outcomes from being achieved, and assumptions about the conditions necessary to achieve impact *(208)*.

Figure 3. Logic model for components of an anaemia-control plan that includes iron and folic acid supplementation for children aged under 5 years, women of reproductive age and pregnant women and behaviour-change communication on increasing dietary intake of iron/micronutrients in these target groups
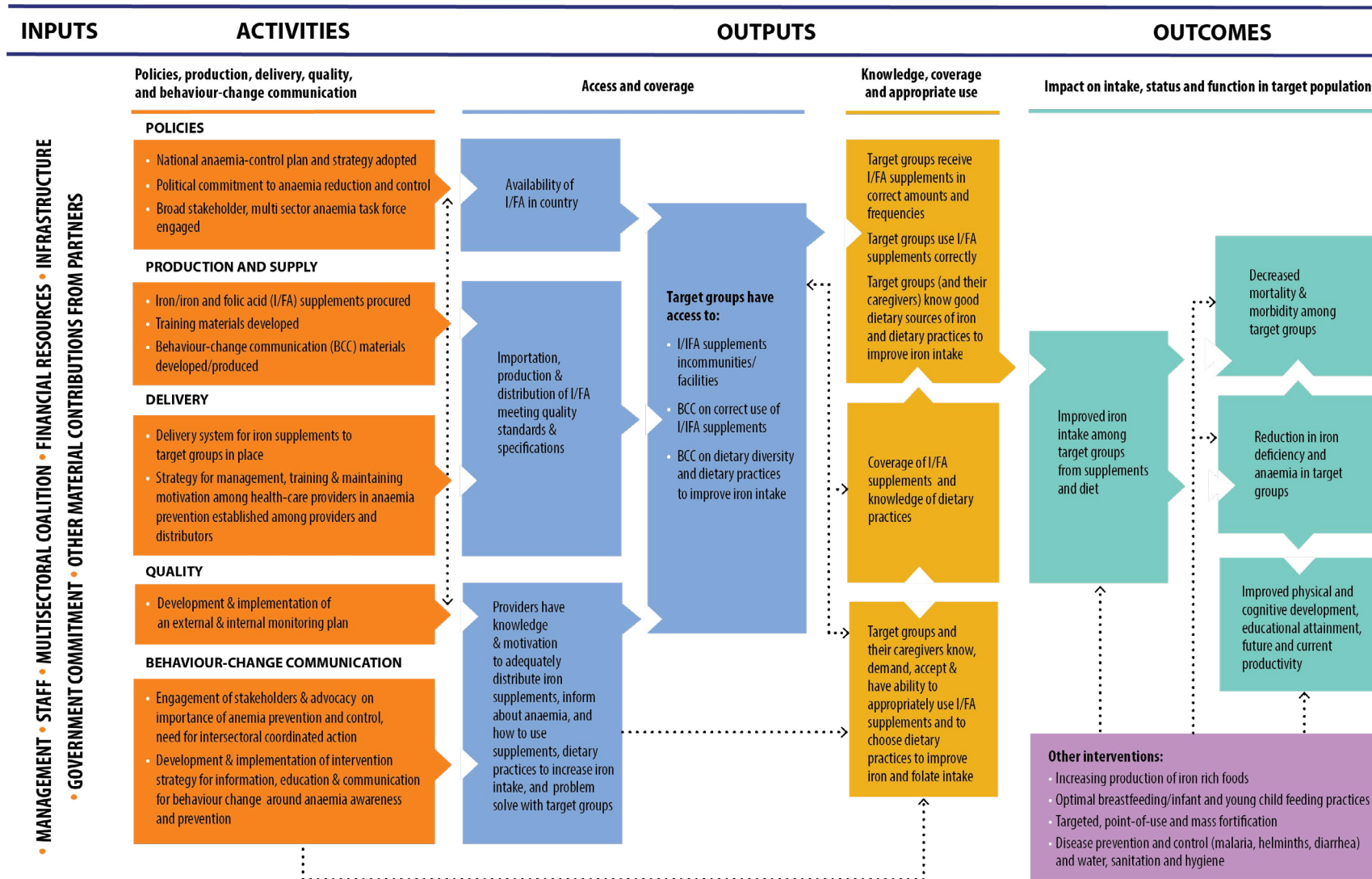
The components of a logic model can vary. One example developed by WHO and CDC includes inputs, activities, outputs and outcomes *(207, 209)*. Figure 3 shows an adaptation of the CDC/WHO model for an anaemia-control programme.

Briefly, the model includes the following items:

- *inputs*: the resources available to and invested in the programme, including personnel, equipment, funding, infrastructure and indirect and direct suppport from partners. In the case of anaemia-control, examples of input may be: staff trained in nutrition, equipment for assessing anaemia, and existing programme infrastructure allowing access to target populations;

- *activities*: what the programme actually does, including actions, events and programme implementation. These activities may relate to policies, products and supplies, delivery systems, quality control, and planning behaviour change. For anaemia control, activities could include anaemia-screening events, establishing legislation on food fortification, distributing mineral supplements, establishing anaemia-related policies and protocols for screening or treatment, and developing behaviour-change communication around anaemia control and prevention;

- *outputs*: either products or direct services resulting from the programme activities, which in turn can affect access to and coverage of an intervention, or knowledge and appropriate use of an intervention by health personnel. For example, in the case of anaemia control, outputs may include increased numbers of staff trained in causes and treatment of anaemia, an increased proportion of health clinics offering anaemia screening, an increased proportion of pregnant women receiving iron supplements, and increased awareness of the consequences of anaemia among the target group or health-care professionals working with the target group;

- *outcomes*:[1] the expected benefits or changes among programme participants, either during or after the programme. These changes can be in in behaviours, knowledge, skills, intake of micronutrients, nutritional status, health conditions or functions. Outcomes can be shorter- or longer-term effects, and can be intended or unintended, positive or negative. In the case of anaemia, outcomes include increased intake of iron-fortified foods, increased use of iron supplements by pregnant women, or decreased prevalence of anaemia among children and pregnant women.

Additional resources on creating a logic model are provided at the end of this section.

5.1.2 PERFORMANCE INDICATORS

Performance indicators are measures of inputs, processes/activities, outputs and outcomes of a given programme or strategy. Having *specific*, *well-defined* indicators that are *measurable* and can be *reliably assessed* (i.e. data sources exist and are accessible) is essential for assessing progress, setting targets and identifying problems. The logic model can be used as a template for developing indicators that reflect the process of programme activities leading to expected effects. Different indicators assess a programme at different points in the logic model and can allow detection of smaller changes than simply measuring one outcome variable. Table 8 provides definitions of different types of indicators and examples of generic indicators that could be appropriate for an anaemia-control programme. However, indicators are programme specific and should be developed taking into account the specific interventions, context and desired outcomes.

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[1] "Impacts" are sometimes listed as a separate category in some logic models, generally indicating long-term effects of the programme, for example on health/nutrition conditions. In the WHO/CDC logic model described here *(209)*, impacts are considered a subset of outcomes.

TABLE 8. Definitions and examples of performance indicators

Type of indicator	Definition	Examples of indicators in an anaemia-control programme
Input	Measures the quantity, quality and timeliness of resources available to and invested in the programme, including personnel, equipment, funding, infrastructure and indirect and direct support from partners	• Number of large-scale wheat/maize flour mills in the country • Government commitment to anaemia control • Health-system infrastructure reaching target populations • Multisector coalition on anaemia control established and active
Activity (process)	Measures the progress of activities in a programme and the way these are carried out, including actions, events policies, products and supplies, delivery systems, quality control and planning behaviour change	• Number of health workers trained and supervised in anaemia prevention and control • Number of iron-fortified foods available in the marketplace • Percentage or number of food companies fortifying staple foods or processed foods with iron • Percentage of target group screened for anaemia
Output	Measures the quantity, quality and timeliness of the products – goods or services – that are the result of a programme	• Percentage of target group receiving the recommended number of iron and folic acid tablets • Percentage of target group receiving treatment or presumptive treatment for hookworm infections/malaria • Percentage of samples of fortified wheat flour that meet fortification specifications

Type of indicator	Definition	Examples of indicators in an anaemia-control programme
Outcome	Measures the expected benefits or changes (in behaviours, knowledge, skills, micronutrient intake, nutritional/health status or functions) among programme participants, either during or after the programme	• Percentage of target group who have adequate knowledge of anaemia and anaemia-prevention and control measures • Percentage of target group that consume sufficient iron-rich foods daily • Percentage of pharmacies or small shops that market and sell iron and folic acid tablets • Percentage of food companies that produce iron-fortified products with adequate levels of fortificant • Percentage of target group that has anaemia, disaggregated by mild, moderate and severe anaemia • Shift in population's haemoglobin curve

Adapted from: De-Regil LM, Peña-Rosas JP, Flores-Ayala R, del Socorro Jefferds ME. Development and use of the generic WHO/CDC logic model for vitamin and mineral interventions in public health programmes. Public Health Nutr. 2014;17(3):634–9 *(207)* and Galloway R. Anemia prevention and control: what works. Part II. Tools and resources. Washington (DC): The World Bank; 2003 *(210)*.

5.1.3 DATA FLOW AND MANAGEMENT

Another critical piece of a comprehensive M&E plan is delineating how monitoring data will be collected and by whom. A plan also needs to be in place outlining how data will be passed up to programme management and eventually donors. Finally, a process for making decisions based on collected data – e.g. redistributing resources to underserved areas, increasing training of staff – should also be clarified, so that the flow of data is not unidirectional. Outlining the roles and responsibilities of critical staff members in this process is also essential. For example, data on the number of iron and folic acid tablets distributed to pregnant women may be collected by programme field staff and then reported to supervisors on a weekly basis, who then compile activity reports on a monthly basis. Responsibilities that relate to data flow and management include collecting data, checking them for errors/inconsistencies, reviewing reports and making decisions based on the data collected. Data management also includes details about how data will be stored (electronically, or hard copies), including any potential privacy issues, as well as how and by whom the data will be analysed.

Programme evaluation, as previously described, is a periodic assessment of the impact of a programme on the desired outcomes. While evaluation may appear to be a later-stage activity to be addressed and developed once the programme is up and running, for a variety of reasons, evaluation should be discussed and planned during the preliminary stages of development. The conclusions that can be made from an evaluation depend very strongly on the design chosen, which must be considered from the very start of the programme.

The framework considered in this section – a six-step framework developed by CDC – has components that may be carried out early in programme development. For example, engaging the stakeholders and describing the programme should occur early on but are essential for setting the stage for an effective and useful evaluation. The framework involves the six steps listed next (adapted from reference *(206)*).

1. ENGAGE THE STAKEHOLDERS

Prior to conducting an evaluation, it is essential to consider the input of all stakeholders involved in the programme. Different stakeholders may have different perspectives on the programme's objectives, operations and outcomes, and those views need to be understood and addressed, so that the results of evaluation are well accepted by all parties. Stakeholders may include those who are involved in programme operations, those served by or affected by the programme, and primary users of the evaluation. Activities to engage stakeholders may include directly involving them in the design and conduct of the evaluation, or keeping them informed of the progress of evaluation.

2. DESCRIBE THE PROGRAMME

Describing the programme – its mission and objectives – in sufficient detail to understand its goals and strategies, establishes a frame of reference for all subsequent decisions in the evaluation. A description of the programme may have been developed during the conceptualization of the programme, but should include several components: a statement of need – that is, the problem that the programme addresses; a description of the expected effects by time (short term, medium term, long term), including unintended consequences; a description of the programme activities; available resources for the programme to conduct its activities; the stage of development of the programme, which may affect the goal of the evaluation; the context in which the programme exists, including environmental influences such as politics or socioeconomic conditions; and a logic model (see section 5.1).

3. FOCUS THE EVALUATION DESIGN

The issues of greatest concern to stakeholders should be the primary focus of the evaluation, while taking into account the time and resources available. Knowing the intended use of the evaluation and creating a strategy that will be useful, feasible, ethical and accurate is key. When developing the design for the evaluation, stakeholders should consider: the purpose of the evaluation; the users of the evaluation; the way in which the evaluation results will be used and applied; the questions they would like the evaluation to address; and the methods that will be employed to collect data. The methods employed in an evaluation should meet the needs of the primary users, uses and questions of the evaluation. The choice of design – experimental, quasi-experimental or observational – has significant implications for what claims can be made from the evaluation's results, and should be decided upon early in the stages of programme development.

4. GATHER CREDIBLE EVIDENCE

Depending on the primary questions of the evaluation and the reasons for asking them, the best way to gather credible evidence may vary. For anaemia, multiple methods are relevant, from personal interviews to observation, document analysis and clinical/biochemical assessment. Using multiple methods for collecting data, and encouraging stakeholder participation can increase the perceived credibility and acceptance of the evaluation results. Aspects of data collection that should be considered include indicators, sources of data, the quality and quantity of data, and logistics. Indicators should meaningfully address the evaluation questions; sources of data should be justified clearly; standard operating procedures for data collection need to be established to ensure data quality; and the amount of data required to answer the evaluation questions needs to be established at the outset of data collection.

5. JUSTIFY THE CONCLUSIONS

The evidence gathered needs to be analysed, synthesized and interpreted; the methods for doing so should be agreed upon before data collection begins, so that the necessary data are collected. Evaluation results are more likely to be used and accepted by stakeholders when the conclusions of an evaluation are consistent with shared values of the stakeholders – for example, the needs of participants, the programme objectives, or programme targets or criteria of performance. Making recommendations – or identifying actions to consider based on the results of the evaluation – requires more information (e.g. other competing priorities or effective alternatives, as well as the situational context) than simply the results of evaluation.

6. ENSURE USE OF THE PROGRAMME AND SHARE LESSONS LEARNT

A deliberate effort should be made to make stakeholders aware of the evaluation's findings, as well as to ensure that the results are appropriately used. Some of this process should begin in the early stages of evaluation design. For example, anticipating what actions may result from the findings of evaluation in terms of programme design can prepare stakeholders, by thinking through how they will use the evaualation's eventual evidence. Such forethought can also identify any areas where the evaluation may be incomplete and allow for modifications prior to implementation. How and in what format (e.g. written report, audiovisual materials, online content) the evaluation results will be disseminated should be discussed by intended users and stakeholders early on in the evaluation process. Evaluation results should be communicated in ways that meet the information needs of important audiences.

Finally, anaemia-control programmes must be subject to constant evaluation and CHANGED as appropriate (based on evidence), in order to make decisions to adjust, maintain, expand or terminate the programme, as needed.

ADDITIONAL RESOURCE ON MONITORING AND EVALUATION AND LINK TO WHO GUIDANCE

- World Health Organization. Evidence-Informed Policy Network (http://www.who.int/evidence/en/).

- WHO evaluation practice handbook. Geneva: World Health Organization, 2013 (http://apps.who.int/iris/bitstream/10665/96311/1/9789241548687_eng.pdf?ua=1, accessed 23 October 2017).

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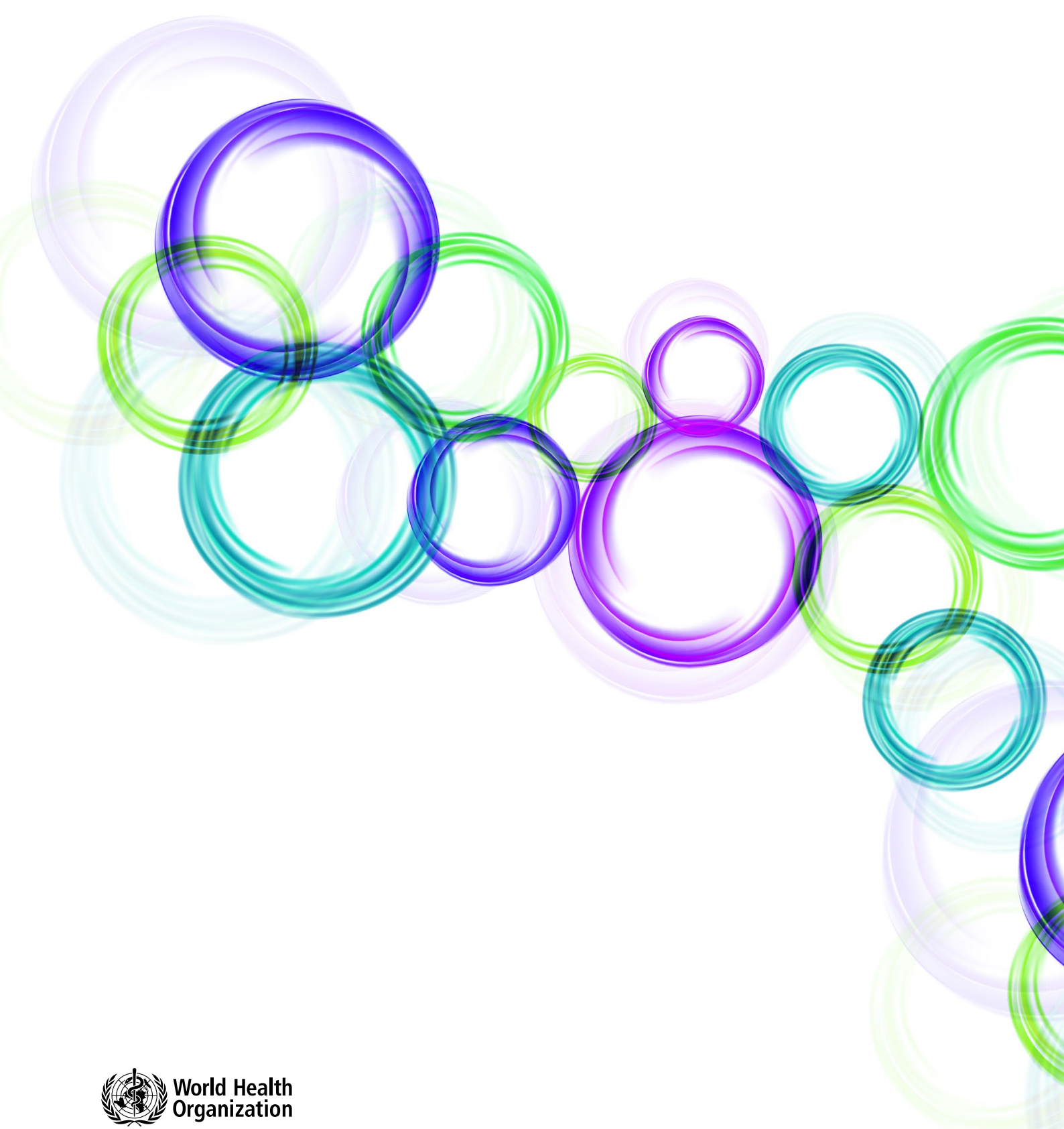
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