# Guidance on appropriate use and considerations for limiting anaemia testing, assessment and screening using haemoglobin in public health anaemia reduction efforts for adolescents

Technical briefing note

**[August 2023]**

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## WHAT IS ANAEMIA?

Anaemia is a condition where the number of red blood cells or the concentration of the iron-rich protein haemoglobin within them is lower than normal. Haemoglobin is necessary for transporting oxygen from the lungs to the cells and tissues, and when its concentration falls, the capacity of the blood to carry oxygen decreases, resulting in symptoms such as fatigue, weakness, dizziness and shortness of breath.[1]

Anaemia increases the risk of disease and disability and can result in poor productivity among individuals, negatively impacting how they can participate and contribute to families and communities. In the long term, this leads to significant losses to the well-being and economic productivity of individuals, communities and countries.

In adolescent pregnancy, anaemia can lead to poor reproductive outcomes, with complications for the mother and the baby, including preterm birth, low birth weight, and maternal and neonatal mortality.[2] In 2019, the global anaemia prevalence was 29.9% among women of reproductive age, 29.6% among non-pregnant women of reproductive age and 36.5% among pregnant women.[3]

## WHAT CAUSES ANAEMIA?

Anaemia can be caused by blood loss, blood cell destruction, inadequate blood cell production or a combination of the three. Nutritional deficiencies, particularly iron deficiency, are the most common cause of anaemia due to inadequate blood cell production, although deficiencies in folate and vitamins B12 and A are also important causes. Haemoglobinopathies (e.g., sickle cell anaemia and thalassemia) are an important cause of anaemia due to blood cell destruction, and infectious diseases — such as malaria, tuberculosis, HIV and parasitic infections — are the main causes of anaemia due to blood loss.[1]

## WHAT IS HAEMOGLOBIN?

Haemoglobin is a protein found in red blood cells that carries oxygen in our body and gives blood its red colour.[4] The optimal haemoglobin concentration needed to meet physiologic needs varies by age, sex, altitude of residence, smoking habits and pregnancy status.[1] Thus, a haemoglobin concentration that is below the established sex, age and pregnancy-specific cut-off values is indicative of anaemia.[i] Table 1 shows haemoglobin levels to diagnose anaemia for different age groups.[5]

Table 1: Anaemia classification based on haemoglobin level (g/dl)*

| Population, age | No anaemia | Mild | Moderate | Severe |
|---|---|---|---|---|
| Children, 5–11 years | ≥11.5 | 11.0–11.4 | 8.0–10.9 | <8.0 |
| Children, 12–14 years | ≥12.0 | 11.0–11.9 | 8.0–10.9 | <8.0 |
| Non-pregnant women and adolescent girls, 15 years and above | ≥12.0 | 11.0–11.9 | 8.0–10.9 | <8.0 |

[i] The World Health Organization (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 implementing interventions that target anaemia.

| | | | | |
|---|---|---|---|---|
| **Pregnant women and adolescent girls** | ≥11.0 | 10.0–10.9 | 7.0–9.9 | <7.0 |
| **Adolescent boys and men, 15 years as above** | ≥13.0 | 11.0–12.9 | 8.0–10.9 | <8.0 |

*Note: values are adjusted from g/L to g/dl.

Adapted from: World Health Organization. (2011). Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. https://apps.who.int/iris/handle/10665/85839

## WHAT IS IRON DEFICIENCY ANAEMIA?

Iron is an essential element of the human body which has important functions, such as oxygen transport, DNA synthesis and muscle metabolism.

Iron deficiency is the most common cause of anaemia worldwide. It primarily occurs when an individual's increased need for iron — such as during rapid periods of growth and development like early childhood, adolescence or pregnancy and certain illnesses — cannot be met, but it can also occur during other stages in life.[6] Iron deficiency has also been shown to affect cognitive and physical development in children and to reduce productivity in adults.[1]

The terms "iron-deficiency anaemia" and "anaemia" are sometimes incorrectly used synonymously. The prevalence of anaemia has also frequently been used as a proxy for iron-deficiency anaemia, but this is incorrect: the proportion of anaemia attributed to iron deficiency anaemia varies considerably between populations according to gender, age and burden of infectious diseases.[7, 8]

## WHAT CAUSES IRON DEFICIENCY?

Iron deficiency can be caused:

1. When dietary iron cannot meet the body's iron demands. This is especially the case during periods of life when iron requirements are high, such as early childhood adolescence and pregnancy.
2. High iron losses due to acute blood loss. This includes childbirth, injury or haemorrhage, heavy menstruation and some parasitic diseases.
3. High intake of inhibitors of iron absorption.
4. Malabsorption. Iron is absorbed in the body through the duodenum, which is the first section of the small intestine. Malabsorption of iron occurs when there is a problem in the duodenum or a decrease in the production of stomach acids, impacting how iron is absorbed in the small intestine. For instance, celiac disease, inflammatory bowel disease and stomach ulcers affect nutrient absorption.[9, 10]

## SCREENING VS. DIAGNOSTIC TESTS

Screening is intended for asymptomatic people (those showing no or disguised symptoms), while diagnostic tests are intended for people showing symptoms in need of a diagnosis.

The goal of screening is the early detection of a condition or disease in order to suggest lifestyle changes to reduce the risk or to treat it most effectively. Screening measures are not considered diagnostic, but they are used to identify a subset of the population who should have additional follow up measures to assess their eligibility for an intervention, treatment or test to determine the presence or absence of disease.[11]

A haemoglobin test measures the volume of haemoglobin in red blood cells to find out how much haemoglobin is in the blood and to identify when its levels are low. This is measured in

grams per deciliter (g/dl) or grams per liter (g/l) of blood. Refer to Table 1 for the World Health Organization (WHO) haemoglobin cut-off levels to diagnose anaemia in different age groups.

## WHAT IS FERRITIN?

Due to its high reactivity, iron is always bound to a protein depending on its role and location in the body. Iron circulates in the plasma bound to transferrin and is stored in cells as ferritin. Serum ferritin levels indicate iron stores — they are low in iron-deficient individuals and high in iron-loaded individuals — which makes them useful for identifying iron deficiency or overload. Accurate measurements of this protein, along with markers of inflammation, can guide the appropriate interventions for anaemia and iron deficiency anaemia in both individual patients and at a population level.[6]

It is important to note that when significant inflammation is present, serum ferritin levels may not reflect accurate iron stores.[12]

## IS HAEMOGLOBIN CONCENTRATION A SUITABLE INDICATOR FOR ASSESSING IRON STATUS OR IRON DEFICIENCY ANAEMIA?

Haemoglobin concentration is not a suitable indicator for assessing iron status or iron deficiency anaemia. It can and should only be used to detect anaemia but it does not provide information on causes and types of anaemia.

Haemoglobin concentration is relatively easy to measure in the field, and it can be done on either capillary or venous blood. Using capillary or finger prick techniques, such as HemoCue, requires less specialized training than venous blood draws and can provide instant readings without blood storage, transport and laboratory analyses. However, some studies have expressed concern around the accuracy of HemoCue, particularly for severe anaemia.[13, 14, 15] However, while haemoglobin measurement is essential for identifying an individual with anaemia, it alone cannot determine the cause of the anaemia: additional clinical and laboratory measures at the individual and population levels are required to diagnose and assess public health anaemia profiles and causes of anaemia.[10]

## WHAT ADDITIONAL MEASUREMENTS ARE NEEDED TO DETERMINE IRON DEFICIENCY ANAEMIA?

In order to determine whether anaemia is caused by iron deficiency, additional measurements of iron status are needed. Venous blood measures, such as serum ferritin or serum transferrin receptors, are the most commonly used indicators.[ii]

Serum ferritin is a measure of the amount of iron in body stores. When infection is not present, serum ferritin levels increase when iron stores are sufficient and fall as they are depleted.[iii] The level of transferrin receptor in serum reflects the intensity of erythropoiesis (the production of red blood cells) and the demand for iron for this process. The levels of transferrin receptor rise after iron stores have been depleted.[10, 16]

When assessing iron status, markers of infection and inflammation (such as C-reactive protein or alpha-1 acid glycoprotein) should also be measured, particularly in areas where poverty, malnutrition and diseases are prevalent.

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[ii] Transferrin is the main iron transport protein found in the blood.

[iii] 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, particularly in areas where poverty, malnutrition and disease are prevalent. The determination of iron status is challenging when concomitant infection and inflammation are present because of confounding effects of the acute-phase response on the interpretation of most iron indicators.

## WHAT IS WEEKLY IRON FOLIC ACID SUPPLEMENTATION?

Weekly iron and folic acid supplementation for adolescents, or WIFAS, is the provision of oral supplements to prevent and reduce anaemia. These supplements consist of 60 mg of elemental iron and 2.8 mg of folic acid, as recommended by WHO,[17] although some countries use 60 mg of elemental iron and 0.4 mg of folic acid as an interim dose where the WHO-recommended formulation of WIFAS is not available.[iv] It is also recommended by the WHO as a preventative public health intervention for adolescent girls and menstruating women living in areas where the prevalence of anaemia in adolescent girls and women of reproductive age (15 to 49 years) is 20% or greater.

The current guidelines for intermittent iron and folic acid supplementation indicate that the supplement should be taken at minimum once weekly, usually on a predetermined day and time. This should take place for a period of three months, followed by a three-month period with no supplementation, for a total of six months per year. Alternatively, supplements can be given throughout the school calendar year if feasible, with the break from the supplements aligned with school vacations. This is the preferred supplementation scheme for many programs.

Some countries also may provide WIFAS every week for up to 52 weeks. For adolescents, it is recommended for girls from 10 to 19 years of age. [18,19]

## SHOULD WE SCREEN ALL GIRLS FOR ANAEMIA BEFORE STARTING WEEKLY IRON FOLIC ACID SUPPLEMENTATION?

No, screening all girls before delivering WIFAS is not recommended. Because WIFAS is preventive and not a targeted program, screening is not performed because it is not cost-effective where anaemia in adolescent girls and women of reproductive age (15 to 49 years) is more than 20%. Therefore, individual girls are not tested for anaemia through this program prior to receiving weekly supplements. However, should a girl present with signs and symptoms of anaemia, she should be referred to a local health center for follow-up, so that she can be assessed, properly diagnosed and given treatment, as appropriate.

Anaemia disproportionately impacts girls and women, and there are inequities in accessing care. Understanding anaemia in countries and its multiple causes and etiologies — which can range from dietary causes and infections to maternal and women's health, the environment and unknown factors — are important. Anaemia screening using haemoglobin testing in a population does not give us this much needed information about the causes of anaemia. This would instead need to come from population-level surveys from a random representative sample that includes several blood measures in addition to haemoglobin.

## WHAT ARE THE POTENTIAL CONCERNS RELATED TO ANAEMIA SCREENING?

The concerns related to anaemia screening are:

1. There are ethical considerations when testing/screening for anaemia without having systems, structures and supplies in place for treating individuals. Screening of all individuals or adolescent girls should not be part of a program unless adequate measures are in place to treat those who are anaemic. Most countries do not have the appropriate protocols, supplementation supplies or referrals in place to treat anaemia in adolescents. It is also worth noting that if following evidence-based protocols, such as providing daily supplementation of iron folic acid for three months, the health facility will need to test again after three months. If the adolescents are still anaemic, then additional measures, assessments or interventions may be required.[17]

[iv] WIFAS containing 2.8 mg folic acid is seven times more effective in increasing red blood cell folate concentrations to levels above WHO recommendations for preventing neural tube defects than WIFAS with 0.4 mg of folic acid.

2. Investing in screening for all individuals comes with a high cost in human and financial resources, and there are also considerations for environmental biohazard waste. Investing in screening also means that funds and human time will be diverted away from other evidence-based actions that could be part of anaemia reduction strategies. There is no evidence-based recommendation to use anaemia screening of all individuals within a population or intervention target group where a public health intervention to reduce anaemia is being delivered, such as WIFAS. For adolescents, this is not seen as an appropriate addition that would result in increased coverage or adherence, specifically since WIFAS is being delivered primarily as a public health approach to reduce anaemia and we would therefore plan on giving all girls the weekly supplement, regardless of their HemoCue reading and anaemia status. With WIFAS as a preventive intervention at the public health level, individual screening is not cost-efficient.

3. Using haemoglobin testing among adolescent girls to screen for anaemia could risk them choosing to avoid school on screening days, or it could lead to negative perceptions of the project. It has been suggested that individuals can be motivated by seeing their blood levels or a change in blood levels, but this could have the opposite affect among those who are not anaemic at the start of intervention. They may question why they are taking iron products, and some may not see a change after consuming supplements (especially if we are preventing a further decline). This would require strong counseling services, but this type of counseling is mostly absent in schools, and it is not currently part of facility training or protocols. All these factors could potentially add to school absenteeism.

## WHEN SHOULD HAEMOGLOBIN BE MEASURED AMONG ADOLESCENTS?

Haemoglobin testing is recommended:

1. **At the individual level**:
    a. If an individual has signs and symptoms of anaemia and needs clinical diagnosis to confirm treatment and management method.
    b. To assess any change/increase in the haemoglobin level following the completion of therapeutic treatment or the management of anaemia in clinical settings. If the person is still anaemic, then additional measures, assessments or interventions may be required.

2. **At the population level**: having data on anaemia from random sampling from a cross-sectional survey can give us information on the population prevalence of anaemia burden. Subregional or national level sampling can also help indicate areas with a higher prevalence of anaemia. There is a lack of adolescent data on anaemia and iron deficiency anaemia. This makes it crucial for decision makers leading anaemia reduction efforts to assess anaemia prevalence data within adolescent health surveys and broader population health and nutrition surveys, or to invest in cross-sectional surveys with a random sampling approach to gather adolescent population data.

## SUMMARY AND RECOMMENDATIONS

There are multiple causes of anaemia, and an accurate characterization of anaemia is important to understand the burden and epidemiology of the problem, for planning appropriate public health interventions and for clinical care of people across the life course.

At the individual level, clinicians should understand the causes of anaemia in order to diagnose, manage and treat anaemia. At the public health level, actions toward anaemia diagnosis and control will require global, regional and country actions that should cover general and context-specific characteristics.[20]

WIFAS is a public health intervention to prevent and reduce anaemia. Routine screening of anaemia measured by haemoglobin is not recommended to test the success of WIFAS within all individual girls in the program.

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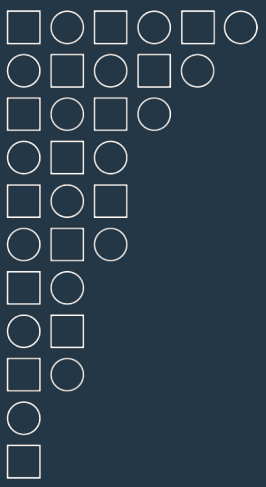

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