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# Brief: Improving Anemia Assessment in Clinical and Public Health Settings

Anemia is a condition that reflects diverse and overlapping causes. As such, it remains a critical and complex global public health challenge. In response to the complexity of anemia, the USAID Advancing Nutrition Anemia Task Force promotes attention to the biology, proper assessment, and due consideration of the causal factors to select and implement intervention options. This brief summarizes critical issues relating to anemia assessment (see **box 1**).

**Box 1. Key Messages**

- Anemia is a condition that **reflects diverse and overlapping causes**.
- Anemia can have **non-nutritional** and **nutrition-specific causes** that should be assessed to inform clinical care and anemia control programs.
- Adopting a **practical, systematic approach to anemia assessment** is essential to address data gaps and make progress on reducing the global anemia burden.

## What is Anemia?

Inadequate red blood cell (RBC) production, decreased RBC life span, increased blood loss, or combinations of these conditions lead to low hemoglobin content in RBC, or anemia, which results in reduced oxygen delivery to the body's organs. Symptoms of anemia may include fatigue, weakness, shortness of breath, chest pain, and headaches. The causes of anemia can be broadly classified as **non-nutritional** (e.g., due to infection, inflammation, blood loss, or genetic disorders) and **nutrition-specific** (e.g., due to deficiencies in iron, vitamin A, and/or certain B vitamins, especially folate and vitamin $B_{12}$).

## Global Anemia Burden

Because of its multifactorial nature, the diagnosis and ultimate treatment options for anemia are complicated. One of the key challenges in quantifying the global anemia burden is the variability of prevalence estimates and anemia trends resulting from different assessment techniques used to generate these data. Increasing evidence suggests that high anemia prevalence may be partially due to measurement error in many instances. Advancing on global goals to reduce anemia and determining the effectiveness of interventions requires a harmonized and reliable approach to collecting and analyzing blood samples, processing the data, and interpreting results. In addition to appropriate assessment tools for measuring hemoglobin (Hb) concentration, it is key to standardize clinical and public health guidelines for anemia screening and assessing the underlying anemia causes.

## Assessing Anemia

Clinicians can assess anemia by measuring the volume of RBCs (called hematocrit [Hct]) or by measuring the primary oxygen carrier, hemoglobin (Hb). While Hb concentration has value as an anemia bioindicator (see **box 2**), it is not specific enough to identify the potential causes, and therefore should not be used alone as a public health trigger for interventions, especially when those interventions only target iron deficiency, which is the predominant programmatic approach used globally.

## Methods to Measure Hb

The preferred method for Hb measurement is via automated hematology analyzers that can provide a complete blood count and RBC indices in addition to Hb. Portable hemoglobinometers (e.g., HemoCue© devices; Angelholm, Sweden), which assess Hb spectrophotometrically, are commonly used in field settings (Whitehead et al. 2019) and can provide results immediately. Clinicians may use other laboratory-based methods (e.g., cyanmethemoglobin [Drabkin's], Sahli's, alkaline hematin method) when automated instrumentation is unavailable (Karakochuk et al. 2019).

### Box 2. Types of Indicators

- **Public health indicators:** Reflect "system" responses and/or shifts due to population trends or manipulations. Neither sensitive nor specific to nutrition (e.g., stunting).
- **Bioindicators:** Sentinel measures of perturbations of specific biological systems. Neither sensitive nor specific to nutrition (e.g., Hb is a bioindicator of hematology, but not iron nutrition).
- **Biomarkers:** Sensitive and specific measures of nutrient exposure, status, or function (e.g., ferritin is a biomarker of iron status).

### Factors Influencing the Interpretation of Hb Measurements

Multiple factors can influence the measurement and interpretation of Hb levels. The use of different techniques to measure Hb concentration can introduce variability in anemia estimates; thus, reliability of the methodology must be confirmed before deciding for its use. The method of blood collection (venous vs. drops of capillary blood) can influence the results. Despite the recommendation to use venous blood for Hb assessment, clinical settings and population surveys often use drops of capillary blood which can cause considerable variations in the results. A recent study highlights that the progress on anemia reduction in women of reproductive age is insufficient to meet the World Health Assembly global nutrition target to halve anemia prevalence by 2030 (Stevens et al. 2022). However, data used in this study came mostly from population surveys that used drops of capillary blood to determine the hemoglobin concentration, and measurements done using drops of capillary samples can vary considerably when compared with measurements done on venous blood samples (Conway et al. 1998; Neufeld et al. 2019; Bond and Richards-Kortum 2015). Furthermore, the (model of the) device used to measure Hb, as well as pre-analytical factors (e.g., ambient humidity, the time elapsed between sample loading and reading) can influence Hb values (Karakochuk et al. 2015; Neufeld et al. 2002; Gwetu and Chhagan 2015; Boghani et al. 2017; Conway et al. 1998; Hruschka et al. 2020; Rappaport et al. 2020).

In addition, both altitude and cigarette smoking can alter increase Hb concentration in response to its decreased oxygen-carrying capacity. For this reason, the World Health Organization (WHO) recommends adjusting for altitude and smoking status when using Hb to assess anemia (WHO 2001); WHO is in the process of reviewing the recommendations to interpret Hb values considering these factors. Sex, age, and pregnancy status also affect Hb concentration (WHO 2021). Normal Hb concentrations are also dependent on the population group.

## Other Approaches to Assess Anemia

Clinicians can alternatively assess anemia via hematocrit (i.e., the volume of RBCs relative to the volume of the blood sample). Hct assessment is only suggested where Hb measurement is not feasible as Hct can be estimated from Hb values. Non-invasive approaches to assessing anemia (e.g., via smartphones or pulse co-oximeters) are emerging (Whitehead et al.

### Box 3. Best Practices for Hemoglobin Assessment

- **Use venous (or pooled capillary if the methodology is confirmed as dependable) blood** and measure Hb using an automated analyzer or point-of-care Hemocue® device whose analytical performance has been verified.
- **Adjust Hb for altitude and smoking** using updated WHO recommendations.
- **Apply global age- and sex-specific and physiologically-validated cutoffs** for anemia.

2019; Mannino et al. 2018; Wang et al. 2017) but those are still under improvement and in the process of undergoing extensive validation.

**Box 3** summarizes the best practices for anemia assessment.

## Assessing Anemia Etiology

A key theme in the USAID Advancing Nutrition Anemia Task Force is the importance of viewing anemia as an ecology where the patient represents a complex biological system affected by both internal (biology, nutrition, genetics, health status, and stage of development) and external (social and structural determinants, community, health system) environments. To achieve progress on global goals to reduce anemia, it is imperative to have reliable assessment tools that reflect that ecology to determine the underlying causes of anemia in both clinical and population-based settings.

### Individual Assessment of Anemia Etiology

Clinical diagnosis of anemia based on symptoms and signs is unreliable and any suspicion of anemia from a clinical standpoint should be substantiated by laboratory diagnosis. However, clinical symptoms may be useful to corroborate hematological results, especially when the conditions under which practitioners collect and process samples cannot be tightly controlled.

RBC indices can be useful for diagnosing the underlying anemia cause (see **box 4**), but their interpretation requires experienced health personnel.

A patient's medical history should include questions about history of anemia symptoms, bleeding (e.g., gastrointestinal or menstrual), genetic disorders, current medication use, travel, and diet (BMJ Best Practice 2020). The health provider should also look for signs of pallor of skin and mucous membranes, specifically in the conjunctiva of the eyes, nail beds, and palms (Longo and Adamson 2018).

**Box 4. Markers to Assess Anemia Etiology in Clinical Settings**

- **Complete blood counts (CBCs)** describe the size, shape, and Hb content of RBCs.
- **Mean corpuscular volume (MCV):** the average size of the RBCs, it can be low (microcytic), normal (normocytic), or high (macrocytic).
- **Mean corpuscular hemoglobin (MCH):** the average Hb content in RBCs; low MCH can indicate iron deficiency and certain inherited blood disorders.
- **Red cell distribution width (RDW):** measure of the variation in RBC size; high RDW indicates a large variation in RBC sizes (e.g., iron deficiency or megaloblastic anemia caused by other micronutrient deficiencies).
- **Reticulocyte counts** are useful for establishing the general type of anemia.
- **Interpretation** of these indicators should be done **by experienced health personnel.**

### Population-Based Assessment of Anemia Etiology

Population-based surveys are useful to estimate anemia prevalence and the strength of association between anemia and its causes. Decisions on which biomarkers to include in a survey depend on geographic locations (e.g., malaria-endemic vs. non-endemic zones), available information on other underlying diseases (e.g., selected parasites, genetic disorders), as well as financial and technical resources. Determining Hb concentration (and therefore anemia prevalence) is only the first step for the diagnosis, prevention, and treatment of this condition. It is also essential to identify its causes and address those. **Box 5** summarizes the key causes of importance in population-based assessments of anemia etiology.

### Box 5. Components of Anemia Etiology Surveillance or Population Surveys

If most anemia is NOT due to absolute (i.e., iron supply and bioavailability) iron deficiency, other causes of anemia (e.g., infections, inherited blood disorders, and blood loss) should be assessed. However, to determine how much of anemia cases are due to iron deficiency, iron biomarkers (ferritin, soluble transferrin receptors, e.g.) need to be measured.

- **Infections** include important parasitic, viral, and bacterial disease burdens of the target population, especially malaria in malaria-endemic regions.
- **Inherited blood disorders:**
  - Alpha-thalassemia can cause mild anemia.
  - Other inherited blood disorders, including sickle cell hemoglobin and glucose-6-phosphate dehydrogenase deficiency, may mitigate malarial infection and therefore influence anemia.
- **Blood loss:** In settings where the underlying prevalence of blood disorders is unknown, assess blood loss by determining—
  - heavy menses, uterine fibroids
  - use of hormonal contraceptives that would reduce blood loss during the menstrual cycle could also inform intervention strategies to mitigate anemia in women of reproductive age.
- **Nutritional status** including—
  - dietary intake
  - biomarkers of specific nutrients including iron and other relevant micronutrients.

# References


BMJ Best Practice. 2020. "Evaluation of Anemia—Differential Diagnosis of Symptoms." Accessed January 31, 2022. https://bestpractice.bmj.com/topics/en-us/93.

Boghani, Safia, Zuguo Mei, Geraldine S. Perry, Gary M. Brittenham, and Mary E. Cogswell. 2017. "Accuracy of Capillary Hemoglobin Measurements for the Detection of Anemia among U.S. Low-Income Toddlers and Pregnant Women." *Nutrients* 9(3). https://doi.org/10.3390/nu9030253.

Conway, A.M., R.F. Hinchliffe, J. Earland, and L.M. Anderson. 1998. "Measurement of Haemoglobin Using Single Drops of Skin Puncture Blood: Is Precision Acceptable?" *Journal of Clinical Pathology* 51(3): 248–250. https://doi.org/10.1136/jcp.51.3.248

Gwetu, T.P., and M.K. Chhagan. 2015. "Evaluation of the Diagnostic Accuracy of the HemoCue Device for Detecting Anaemia in Healthy School-Aged Children in KwaZulu-Natal, South Africa." *South African Medical Journal* 105(7): 596–599. https://doi.org/10.7196/SAMJnew.7919.

Hruschka, Daniel J., Anne M. Williams, Zuguo Mei, Eva Leidman, Parminder S. Suchdev, Melissa F. Young, and Sorrel Namaste. 2020. "Comparing Hemoglobin Distributions between Population-Based Surveys Matched by Country and Time." *BMC Public Health* 20(1): 422. https://doi.org/10.1186/s12889-020-08537-4.

Karakochuk, Crystal D., Amynah Janmohamed, Kyly C. Whitfield, Susan I. Barr, Suzanne M. Vercauteren, Hou Kroeun, Aminuzzaman Talukder, Judy McLean, and Timothy J. Green. 2015. "Evaluation of Two Methods to Measure Hemoglobin Concentration among Women with Genetic Hemoglobin Disorders in Cambodia: A Method-Comparison Study." *Clinica Chimica Acta* 441: 148–155. https://doi.org/10.1016/j.cca.2014.12.021.

Karakochuk, Crystal D., Sonja Y. Hess, Denish Moorthy, Sorrel Namaste, Megan E. Parker, Aviva I. Rappaport, Rita Wegmüller, Omar Dary, and HEmoglobin MEasurement (HEME) Working Group. 2019. "Measurement and Interpretation of Hemoglobin Concentration in Clinical and Field Settings: A Narrative Review." *Annals of the New York Academy of Sciences* 1450(1): 126–146. https://doi.org/10.1111/nyas.14003.

Longo, D.L., and J.W. Adamson. 2018. "Chapter 59: Anemia and Polycythemia." In *Harrison's Principle of Internal Medicine*, 20th ed. Edited by J. Larry Jameson, Anthony S. Fauci, Dennis L. Kasper, Stephen L. Hauser, Dan L. Longo, Joseph Loscalzo. New York: McGraw-Hill. https://accessmedicine.mhmedical.com/content.aspx?bookid=2129&sectionid=192014145

Mannino, Robert G., David R. Myers, Erika A. Tyburski, Christina Caruso, Jeanne Boudreaux, Traci Leong, G.D. Clifford, and Wilbur A. Lam. 2018. "Smartphone App for Non-Invasive Detection of Anemia Using Only Patient-Sourced Photos." *Nature Communications* 9(1): 4924. https://doi.org/10.1038/s41467-018-07262-2.

Neufeld, Lynnette, Armando García-Guerra, Domingo Sánchez-Francia, Oscar Newton-Sánchez, María Dolores Ramírez-Villalobos, and Juan Rivera-Dommarco. 2002. "Hemoglobin Measured by Hemocue and a Reference Method in Venous and Capillary Blood: A Validation Study." *Salud Publica De Mexico* 44(3): 219–227. https://doi.org/10.1590/s0036-36342002000300005

Rappaport, Aviva I., Crystal D. Karakochuk, Sonja Y. Hess, Ralph D. Whitehead, Sorrel M.L. Namaste, Omar Dary, Megan E. Parker, et al. 2020. "Variability in Haemoglobin Concentration by Measurement Tool and Blood Source: An Analysis from Seven Countries." *Journal of Clinical Pathology*, October. https://doi.org/10.1136/jclinpath-2020-206717.

Stevens, Gretchen A., Christopher J. Paciorek, Monica C. Flores-Urrutia, Elaine Borghi, Sorrel Namaste, James P. Wirth, Parminder S. Suchdev et al. 2022. "National, Regional, and Global Estimates of Anaemia by Severity in Women and Children for 2000–19: A Pooled Analysis of Population-Representative Data." *The Lancet Global Health* 10(5). e627–e639. https://doi.org/10.1016/S2214-109X(22)00084-5.

Wang, Edward J., William Li, Junyi Zhu, Rajneil Rana, and Shwetak N. Patel. 2017. "Noninvasive Hemoglobin Measurement Using Unmodified Smartphone Camera and White Flash." *Annual International Conference of the IEEE Engineering in Medicine and Biology Society.* (July): 2333–2336. https://doi.org/10.1109/EMBC.2017.8037323.

Whitehead, Ralph D., Zuguo Mei, Carine Mapango, and Maria Elena D. Jefferds. 2019. "Methods and Analyzers for Hemoglobin Measurement in Clinical Laboratories and Field Settings." *Annals of the New York Academy of Sciences* 1450(1): 147–171. https://doi.org/10.1111/nyas.14124.

WHO (World Health Organization). 2001. *Iron Deficiency Anaemia: Assessment, Prevention, and Control: A Guide for Programme Managers*. Geneva, Switzerland: WHO. http://apps.who.int/iris/handle/10665/66914.

WHO (World Health Organization). 2021. *WHO Methods and Data Sources for Mean Haemoglobin and Anaemia Estimates in Women of Reproductive Age and Preschool Age Children 2000–2019*. Geneva: World Health Organization.

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