HEMOCUE
WHITE PAPER
ANEMIA

WHICH IS THE MOST APPROPIATE HB METHOD WHEN TESTING FOR ANEMIA UNDER FIELD CONDITIONS?

GLOBAL PREVALENCE OF ANEMIA AND IMPACT IN DEVELOPING WORLD

Anemia is a serious global public health problem that affects populations in both rich and developing countries. Women of reproductive age and children are the groups most at risk, see figure 1. On average, 38 % of pregnant women, 29 % of non-pregnant women and 43 % of pre-school children are anemic.[1] Left undetected and untreated, anemia in its most severe form can be fatal. But even less severe cases may have serious consequences on health and quality of life for large groups of people. Maternal anemia is associated with mortality and morbidity, both in mother and baby. Infants born to anemic mothers have a higher risk of anemia in their critical first six months of life, which is a risk factor for impaired cognitive and physical development, impaired growth, and increased morbidity due to infections.[2] While the causes of anemia are variable, it is estimated that half of the cases are due to iron deficiency. In 2012 the World Health Assembly of the World Health Organization (WHO) adopted the six global nutrition targets to be reached by 2025. The second target states that anemia in women of reproductive age should be reduced by 50%. Meeting this target will be an important step towards breaking the inter-generational cycle of anemia, and will result in benefits for individual health and quality of life, as well as economic growth for communities and countries.[3] High quality anemia data from population-based surveys are essential for monitoring progress toward meeting global health targets and advocating appropriate action in the populations at greatest risk.[4]

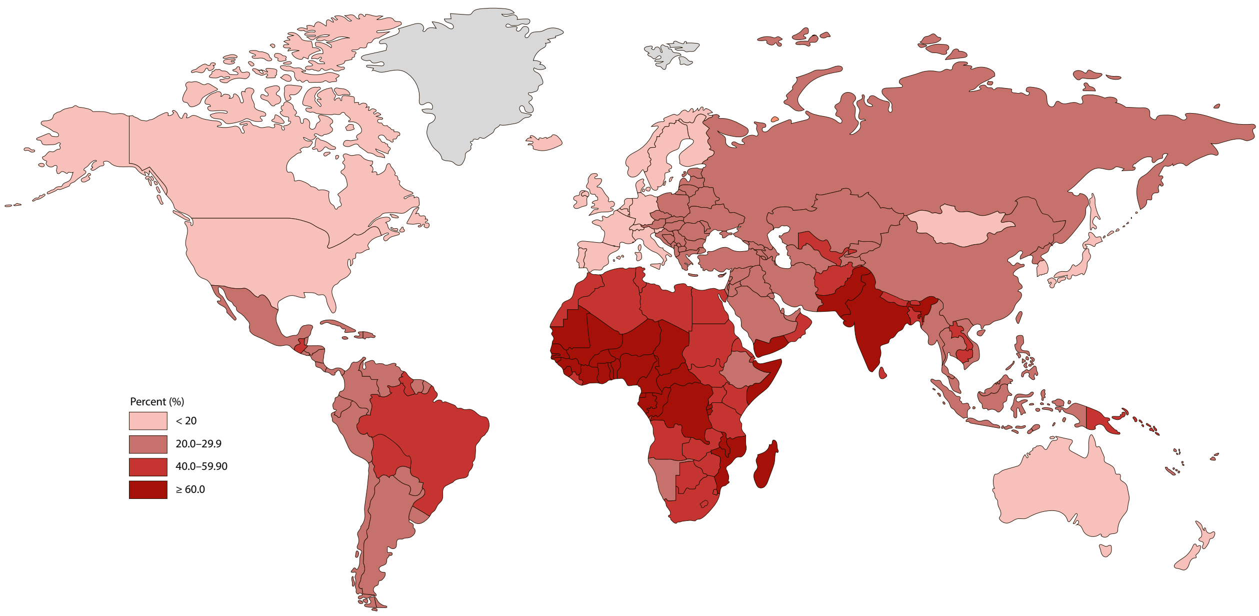


Figure 1. Anemia prevalence in women aged 15-49. Concentration less than 120 g/L for non-pregnant women and lactating women, and less than 110 g/L for pregnant women.

Re-drawn from https://www.who.int/data/gho/data/indicators/indicator-details/GHO/prevalence-of-anaemia-in-women-of-reproductive-age-(-)

SUCCESS IS POSSIBLE

Overall, progress has so far been insufficient, but in some settings, considerable reductions in the prevalence of anemia have already been achieved.[3] In 2006, a pilot project distributing weekly iron-folic acid, together with deworming for all women of reproductive age, was implemented in two districts of Yen Bai province in Vietnam, covering approximately 50 000 women aged 15 to 45 years. After 12 months, the program was expanded to target all women of reproductive age in the province (250 000 women). The prevalence of anemia fell from 38% to 19% after 12 months.[5]

In India, a program of weekly iron-folic acid supplementation for adolescent girls was piloted in 52 districts in 13 states. The program reached girls aged 10–19 years. Evaluation of the pilot programs indicated on average 24% reduction in the prevalence of anemia after 1 year of implementation. In 2012, the Government of India introduced national implementation of weekly iron-folic acid supplementation to expand its benefits to all adolescent girls in India.[2]

HB PERFORMANCE REQUIREMENTS FOR ANEMIA SCREENING

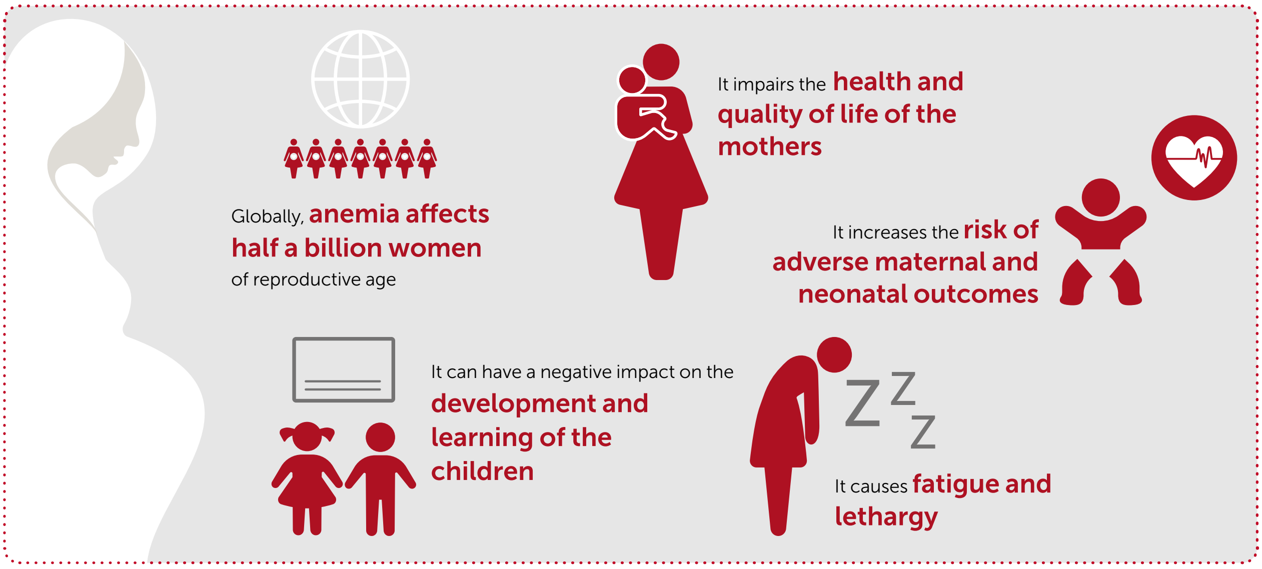
The most reliable indicator of anemia at population level, is estimating the concentration of hemoglobin (Hb), as opposed to physical assessments which are subjective and therefore often erroneous.[6] Thus, WHO recommends the use of Hb concentrations to estimate the population prevalence of anemia in order to generate valid and robust anemia assessment.[4]

Appropriate, high-quality methods for Hb measurements in clinical laboratories and field settings are equally important to ensure quality of results. Clinical laboratories are controlled environments were personnel handling medical devices are trained and experienced. In field settings, which include areas outside the traditional clinical laboratories, the environment is rather different and not as highly controlled and quality of results can be influenced by a variety of factors.[7] Attention should be given to environmental factors that could potentially affect the performance of the Hb method, e.g. surrounding humidity and temperature. But there are also structural difference that are important to take into consideration e.g. poor infrastructure and access of Hb devices and supplies to rural areas, absence of electrical power and proper storage facilities. In addition biological variability in the population of interest is important to consider e.g. high prevalence of thalassemia and sickle cell disease or other disorders and diseases that are not related to nutritional deficiencies and will therefore not be helped by nutritional anemia prevention programs. Attention to all these factors is key in order to be successful and reach health goals. For nutritional anemia control programs, the following features for an Hb method are important to consider:[7]

The Hb device should be robust to manage demanding field conditions and to avoid error codes as well as re-testing. The Hb device should be portable and battery operated for use in rural areas without electric power. The Hb device should be easy to use with a simple sampling procedure that requires minimal training by field workers. High accuracy and precision with traceability to the HiCN reference method by ICSH are essential features since many decisions are based on fixed cut-off levels (e.g. for mild, moderate to severe anemia). The Hb device should be easily accessible in big volumes with a local supplier network that can access rural areas for distribution, trouble shooting and support.

METHODS AND ANALYZERS FOR HB MEASUREMENT

In a recent review, the authors searched the literature to investigate methods for Hb estimation that are used. A total of 74 scientific papers were included in the review. The authors conclude that a variety of different methods are used worldwide. They all have advantages and disadvantages, but only a few of them are suitable for field conditions.[8]



The HiCN method according the International Council for Standardization in Haematology (ICSH), is the internationally recognized reference method for determination of Hb concentration in blood. The HiCN method is used to calibrate clinical and field equipment prior to use and as a regular method for the determination of Hb concentration. This method has high sensitivity and specificity, but is not suitable for field conditions since it is time consuming and requires laboratory facilities for dilution of samples, trained laboratory professionals and a highly accurate spectrophotometer.[7]

Counting and sizing particles using automated hematology analyzers in clinical laboratories is a quantitative method that is typically used, but due to the size and lack of portability of these analyzers, they are generally not considered feasible for field settings.[7]

For field settings, less expensive, field-friendly methods, including the WHO Coulor Scale and other paper- and color-based analytical devices as well as portable strip meters and point-of-care analyzers are available. Quantitative paper- and color based methods are limited by the possibility to detect only significant levels of anemia, as well as not being sufficiently sensitive to small changes in Hb concentration. They are also prone to inter-observer variability.[9]

STRIP METER HB TECHNOLOGY

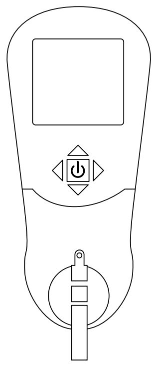


Illustration of a basic Hb strip meter

Strip meter technology methods are commonly used in clinical analysis of urine and blood. The major use is related to glucose monitoring by patients in their homes. For self-monitoring purposes, this technology offers an easy-to-use, affordable alternative, as the main purpose is to monitor changes over time, and not for highly accurate diagnostic purposes. For Hb strip meter based methods, dried reagents are applied in the construction of strips and Hb is measured colorimetrically by reflectance photometry. In contrast to absorption technology, reflected light is non-linear with the concentration of the analyte, and mathematical algorithms are needed to linearize the relation of reflectance to concentration.[10] The major disadvantages of this technology, when used in field settings, are the imprecision and the risk for preanalytical factors when handling the blood specimen. Capillary blood from a finger is used, and a big enough blood drop should be applied directly from the finger to the test strip, which is already inserted in the meter. Application of too little or too much blood to the test strip can compromise results. In addition, the blood drop has to be placed on the exact right spot of the test strip, if not, results can be erroneous or an error code will be displayed, leading to unnecessary re-testing. Cleaning and disinfection between each patients is important since the patient comes into direct contact with the meter when applying the sample. Most Hb strip meters require a lot-specific code to be entered prior to measurement. This is due to the fact that strip lots are difficult to manufacture in big volumes with high precision and therefore lot-specific calibration codes are needed to correct for any variance between strip lots.[11]

PORTABLE POINT-OF-CARE HB ANALYZERS

In the late 1990s, development of portable photometric point-of-care (POC) analyzers started as a means to measure Hb quickly, using small amounts of blood. Portable hemoglobinometers allow accurate determination of Hb at the point of care. They are essentially photometers which allow measurement of color intensity of solutions by absorption technology. They are easy to use, require a small sample volume allowing capillary finger blood to be used, and most of them are standardized against the HiCN reference method. This technology has been extensively evaluated in a range of settings and has confirmed to have acceptable accuracy and precision when compared with laboratory methods. Despite the ease of use, proper capillary sampling technique is important to get reliable results.[12]

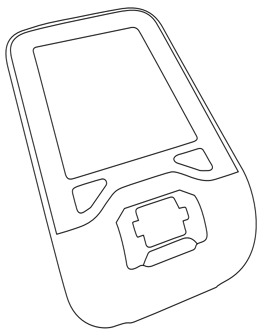


Illustration of a photometric Hb analyzer

For population-based surveys, HemoCue® Analyzers are the most routinely used devices to measure Hb concentrations in field settings. They have been used in anemia screening programs for decades with local presence for distribution and support in the majority of countries. Although similar Hb POCT devices are available, scientific literature and on-field evaluation of other systems are extremely limited.[15] The HemoCue devices are relatively inexpensive, portable and can be powered with batteries, do not require a cold chain for transportation and storage, and produce fast results.[4] The HemoCue® Hb Systems consists of disposable single-use microcuvettes and a photometer. A sufficient amount of blood is drawn automatically into the microcuvette by capillary action when it comes into contact with a drop of blood and thereby serves as a pipette, sample container and measuring vessel – all in one, which makes it easy to handle properly even for untrained users, see figure 2. The absorbance is measured in the handheld photometer at two wavelengths, one wavelength to measure the Hb concentration and a second wavelength to compensate for any turbidity in the sample.[8]

Comparison table of different Hb measuring methods

Method	Accuracy & Reliability	Low risk preanalytical issues	Portable & Robust	Easy to use	Suitable for field conditions	Evidence of long term use in field conditions
Lab methods • HiCN • Automated hematology analyzers [7]	+++	++	-	-	-	No
Paper-color scales [9]	-	-	+	+++	+	No
Strip meters [10 11]	+	+	++	++	+	No
POCT absorption [4 12]	+++	++	+++	+++	+++	Yes

+++ =Excellent *+ = OK*
++ = Good *- = Not recommended,*

DISCUSSION

Valid measurement of Hb is important in anemia screening programs for tracking and targeting interventions. Big variations in a Hb test method will introduce the risk of false anemia detection or will not be able to detect anemia when present. The clinical consequence of misclassification in an anemia screening program on a population level could be over-diagnosis of anemia with a costly and unnecessary overtreatment, or underestimation of anemia which could lead to insufficient anemia prevention measures.[13] Substantial differences in anemia estimates from different population-based surveys can cause confusion for governments, program planners, and global anemia reduction trackers.[4]

The additional consequence in research settings is that many potential study participants will needlessly be excluded from clinical studies, based on the false assumption that they are anemic.[13]

Numerous methods for rapid Hb POCT systems used outside the hospital laboratory are currently available, but very few of them are suitable for field conditions. The majority of the more suitable portable hemoglobinometers are based on measuring the color of Hb photometrically. These methods can deliver accurate results comparable to laboratory techniques when traceability to the HiCN method by ICSH is granted. The authors of the aforementioned literature review on different Hb methods conclude that HemoCue seems to be the method of choice for initial screening of anemia because it is reliable, portable, does not require power supply and is easy to use in poor resource settings without requiring extensive training of health workers.[8] In addition, the HemoCue Hb method is described in the WHO, -A guide for programme managers, as the only portable POC method generally recommended for use in surveys to determine the population prevalence of anemia. The system is described as uniquely suited to rapid field surveys because the one-step blood collection and due to the fact that the Hb determination does not require the addition of liquid reagents. Long-term field experience has also shown the HemoCue devices to be stable and durable. These features make it possible to include Hb determinations in multipurpose health and nutrition surveys.[14] Although similar Hb POCT devices are available, scientific literature and on-field evaluation of these systems are extremely limited.[15]

CONCLUSION

Putting trust in a Hb method for anemia screening in field settings is no small matter. The results as well as the company behind these results need to be trusted. Cost for the device and consumables needs to be weighed against other important factors to ensure a successful outcome. Meeting the World Health Assembly nutrition targets related to anemia is an important step which will result in benefits for individual health and quality of life for many populations at greatest risk, but will also be a potential for economic growth for communities and countries.

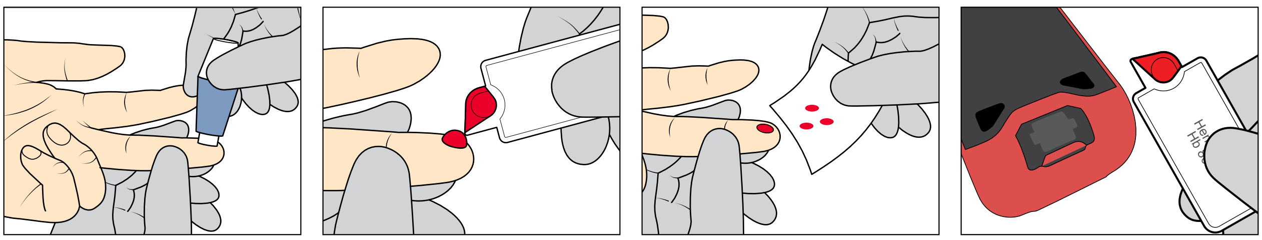


Figure 1, workflow of capillary sampling using a lancet to puncture the finger and the microcuvette being a pipette, sample container and meassuring cuvette all in one.

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