Variability in haemoglobin concentration by measurement tool and blood source: an analysis from seven countries

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ABSTRACT

Objective We explore factors such as the blood sampling site (capillary vs venous), the equipment (HemoCue vs automated haematology analyser) and the model of the HemoCue device (201+ vs 301) that may impact haemoglobin measurements in capillary and venous blood.

Methods Eleven studies were identified, and bias, concordance and measures of diagnostic performance were assessed within each study.

Findings Our analysis included 11 studies from seven countries (Cambodia, India, The Gambia, Ghana, Laos, Rwanda and USA). Samples came from children, men, non-pregnant women and pregnant women. Mean bias ranged from −8.7 to 2.5 g/L in Cambodian women, 6.2 g/L in Laotian children, 2.4 g/L in Ghanaian women, 0.8 g/L in Gambian children 6–23 months and 1.4 g/L in Rwandan children 6–59 months when comparing capillary blood on a HemoCue to venous blood on a haematology analyser. Bias was 8.3 g/L in Indian non-pregnant women and 2.6 g/L in Laotian children and women and 1.5 g/L in the US population when comparing capillary to venous blood using a HemoCue. For venous blood measured on the HemoCue compared with the automated haematology analyser, bias was 5.3 g/L in Gambian pregnant women 18–45 years and 11.3 g/L in Laotian children 6–59 months.

Conclusion Our analysis found large variability in haemoglobin concentration measured on capillary or venous blood and using HemoCue Hb 201+ or Hb 301 or automated haematology analyser. We cannot ascertain whether the variation is due to differences in the equipment, differences in capillary and venous blood, or factors affecting blood collection techniques.

INTRODUCTION

Anaemia is considered a global health problem.[1] Clinically, anaemia is commonly defined as a haemoglobin concentration below a specific cut-off based on age, sex and pregnancy status and adjusted for smoking status and altitude above sea level (currently beginning over 1000 m).[1] Reliable haemoglobin measurement is essential for the accurate diagnosis of anaemia at the individual and the population level.

Haemoglobin is a coloured pigment, allowing for simple measurement using spectrophotometry.[2] According to the International Committee for Standardization in Hematology, the gold standard for measuring haemoglobin concentration is the cyanmethemoglobin method.[3–5] During this reaction, potassium cyanide and ferricyanide convert haemoglobin into cyanmethemoglobin, whose absorbance is measured at 540 nm.[3 4 6] However, cyanide is a toxic reagent that is difficult to dispose of, and as such, this method is no longer commonly used in practice.[6–9]

Instead, automated haematology analysers are now considered the 'gold standard' as these machines have standardised quality control mechanisms and calibration methods.[7 8 10] Comparative studies between automated haematology analysers and the cyanmethemoglobin method have proven the analysers to be accurate.[9 11] However, this analysis must be conducted on fresh blood (within ~4–6 hours). In field settings, it is often difficult to transport fresh blood for analysis within a short time frame leading to longer than optimal (>6 hours) analysis of blood samples. Variable temperatures in the field settings can also create issues for blood samples when the analysis is delayed because of factors such as haemolysis.[8] Portable field haemoglobinometers such as the HemoCue (HemoCue, Angelholm, Sweden) have been designed to determine haemoglobin concentration in field settings. HemoCue has developed several different haemoglobinometer models, such as the HemoCue Hb 201+[12] and the more recent HemoCue Hb 301.[13 14] The former is based on a modified azide methaemoglobin reaction method, while the second uses absorbance of whole blood at a haemoglobin/oxyhaemoglobin isosbestic point to measure haemoglobin concentration.

Discrepancies between the HemoCue and other commonly used methods for measuring haemoglobin concentration have been observed, mostly in field settings. Some studies found overestimations,[5 15–21] while other data show underestimations of capillary haemoglobin concentration assessed with the HemoCue[10 22] compared with venous blood using the automated haematology analysers or the cyanmethemoglobin method. In laboratory settings, haemoglobin concentrations measured on capillary blood have been shown to be slightly higher than with venous blood on an automated

haematology analyser.[23–27] Yet it is unclear if this variability is a result of biological differences in capillary and venous blood or due to environmental and contextual factors (eg, blood collection techniques). However, the observed large differences between results obtained in large surveys using HemoCue and capillary sampling in the field and laboratory testing of venous blood samples are concerning as these HemoCue devices are commonly used to estimate the anaemia prevalence in the national surveys that form the basis for policy and programme prioritisation and assessing progress.[28] Even a small shift in haemoglobin concentration could result in a large difference in anaemia prevalence estimates, if the mean haemoglobin concentration in the population is close to the anaemia cut-off value.[10]

To investigate significance and reasons for differences in haemoglobin concentrations and population prevalence, the Haemoglobin Measurement Working Group (HEME) was created with the primary aim to identify factors that contribute to the accuracy and variability in measurement of haemoglobin for assessment of anaemia. The HEME working group was formed from participants of the 1-day USAID/PATH HealthTech Expert Consultation meeting on 'Hemoglobin testing methods: Research and program implications', held in Washington, DC, in 2016. The present analysis compares the differences in haemoglobin concentrations depending on blood sampling site (capillary vs venous), the equipment used (HemoCue vs automated haematology analyser) and the model of the HemoCue device (HemoCue Hb 201+ vs HemoCue Hb 301).

METHODS

Data description and inclusion

A convenient sample of existing studies that permitted at least one of the aforementioned comparisons was obtained from HEME collaborators. All data provided by the principal investigators were deidentified and stored on a password-protected hard drive. Inclusion criteria were studies that carried out a measurement of haemoglobin concentration with more than one method (ie, HemoCue and automated haematology analyser), more than one HemoCue device (ie, HemoCue Hb 201+ vs HemoCue Hb 301) or more than one blood sampling site (ie, venous and capillary). There were no restrictions for inclusion by population groups. Studies were only included if they were conducted after 2010. Data were not nationally representative but were from individual intervention trials or descriptive studies/surveys. Each included study had ethics approval to conduct their research. In addition, ethics approval to carry out this secondary analysis was obtained from the Institutional Review Board at John Snow.

In total, data obtained were from seven different countries: Cambodia, The Gambia, Ghana, India, Laos, Rwanda and the USA. Generally, each study included one capillary and one venous blood measurement estimated on a HemoCue and an automated haematology analyser. However, some studies included comparisons of the different methods to measure haemoglobin concentration using blood from the same sampling site, or different blood sampling sites using the same method to measure haemoglobin concentration. Because each study could contribute to one or more comparisons across population groups, the data were disaggregated by population group and by comparison. Table 1 provides a summary of the studies included and data available for the comparisons included in the present analysis. All studies using HemoCue machines used quality control solutions for the HemoCue machines, as recommended by the manufacturer: HemoTrol and Hb Control were used with the HemoCue Hb 201+ and Eurotrol (Eurotrol BV, Ede, The Netherlands) was used with the HemoCue Hb 301. HemoTrol and Eurotrol controls are available at three levels (Level 1, Level 2 and Level 3) for the Hb 201+ and the Hb 301 analysers.

Anaemia was defined by established cut-offs for haemoglobin concentration dependent on age, sex and pregnancy status.[1] To classify anaemia, the WHO cut-offs were applied (children 6–59 months <110 g/L; non-pregnant women above 15 years <120 g/L; pregnant women <110 g/L; and men (15 years of age and above) <130 g/L).[29] Where applicable, haemoglobin concentrations were adjusted for altitude and smoking status prior to analysis.[30]

Statistical analysis

Data were analysed using Stata V.14 (Stata Corp, College Station, Texas, USA). Data are presented by country disaggregated by population group and by comparison. Among children under 59 months of age, data were further disaggregated into 6–11 months, 12–23 months and 24–59 months to examine the biological variability in haemoglobin concentrations across these age groups.

Multiple comparisons were performed and a schematic overview of the comparisons made in his paper can be found in figure 1. First, we compared haemoglobin concentration from capillary blood measured on the HemoCue with venous blood measured on an automated haematology analyser. This analysis was performed on eight studies from five countries. Second, we compared capillary and venous blood assessed with the same device to determine variability attributable to the blood sampling site. This was assessed on three studies from three countries. Third, we compared venous blood on the HemoCue and automated haematology analyser to determine the variability related to the device rather than the blood sampling site. This analysis included two studies (one including a subgroup of pregnant women and children) from two countries. We also examined whether the results varied by anaemia status.

Haemoglobin concentrations are presented as mean±SD. Anaemia prevalence estimates are presented based on the aforementioned cut-offs for haemoglobin concentration.[1] When disaggregating data by groups, data are not presented for any sample size less than n=30. Data dispersion was assessed using skewness and kurtosis. Agreement was determined using a calculation of Bland-Altman's bias with 95% CI as a measure of precision. Bias is reported as the difference in mean haemoglobin concentration for each comparison. The comparisons were made for blood sampling site (capillary vs venous), the equipment used (HemoCue vs automated haematology analyser) or the HemoCue device (HemoCue Hb 201+ vs HemoCue Hb 301). Lin's concordance correlation coefficient (95 % CI) was used to assess the reproducibility of the measured values.[31–33]

RESULTS

Capillary with HemoCue versus venous blood with automated haematology analyser

The mean bias of haemoglobin concentration in capillary blood analysed by HemoCue and venous blood by automated haematology analyser ranged from −8.7 g/L in Cambodian non-pregnant women to 8.7 g/L in Laotian children 6–11 months (table 2). The anaemia prevalence was highest in Cambodian non-pregnant women (from dataset with 808 women) when capillary blood was analysed, 100%, compared with 57.9% in venous blood. In contrast, in Laos, the anaemia prevalence was estimated at 53.7% in children 6–23 months when capillary

Table 1 Information on data source, study population and blood collection methods used in each dataset

Country	Publication	Study population	N	Time between blood draws	Drop of capillary blood collected	Type of tube for venous blood collection	Storage conditions of venous blood for transport	Avg time between collection and automated haematology analyser measure	Hb assessment—capillary	Hb assessment—venous
Cambodia –1	10	Non-Pregnant women 18–45 years	450	7 days	Third drop	K2EDTA	On ice in a cooler	5 hours	HemoCue Hb201+	Sysmex XT-1800i
Cambodia –2	47	Non-Pregnant women 18–45 years	808	7 days	Third drop	K2EDTA	On ice in a cooler	4 hours	HemoCue Hb301	Sysmex XN 1000
Cambodia –3	14	Non-Pregnant women 18–49 years	277	3.5 min	Third drop	K2EDTA	On ice in a cooler	5 hours	HemoCue Hb301	Sysmex XP 100
Ghana	Unpublished*	Pregnant women 18–49 years	223	5–10 min	Second drop	K2EDTA	On ice in a cooler	3 hours	HemoCue Hb201+	ABX Pentra 60
India	38	Non- Pregnant women 18–49 years	982	10–15 min	Second drop	K2EDTA	On ice in cooler	5 min	HemoCue Hb201+	HemoCue Hb201+
Laos	39	Children 6–59 months†	854	10–15 min	Second drop	K2EDTA	On ice in a cooler	3–7 hours	HemoCue Hb301	Mindrey BC-3000 Plus
Laos	39	Children 6–59 months†	633	10–15 min	Second drop	K2EDTA	On ice in a cooler	3–7 hours	HemoCue Hb301	Sysmex XT-1800i
Laos	39	Children 6–59 months†	129	10–15 min	Second drop	K2EDTA	On ice in a cooler	3–7 hours	HemoCue Hb301	HemoCue Hb301 and Mindrey BC-3000 Plus
The Gambia	Unpublished‡	Children 6–24 months	407	2 min	Second drop	K2EDTA	On ice in a cooler	5 hours	HemoCue Hb301	HemoCue Hb301
The Gambia	Unpublished§	Pregnant women 18–45 years	499	Only collected venous blood	N/A	K2EDTA	On ice in a cooler	5 hours	N/A	HemoCue Hb301 and Mendonic M^{20M} GP
Rwanda	48	Children 6–59 months	131	10 min	Third drop	K2EDTA	N/A	2–12 hours	HemoCue Hb201+	Sysmex KN 21
USA	37	Non-pregnant women and men 20–59 years	33	5–10 min	Pooled blood	K2EDTA	On ice in a cooler	1–3 days	HemoCue Hb201+	HemoCue Hb201+/ Hb301

*Newton S, Abu-Hayder E, 2013.
†These entries are from the same study, but separated onto different lines because the authors used two different automated haematology analysers.
‡Wegmuller R, 2015.
§Bah A, 2015.
Hb, haemoglobin; N/A, not available.

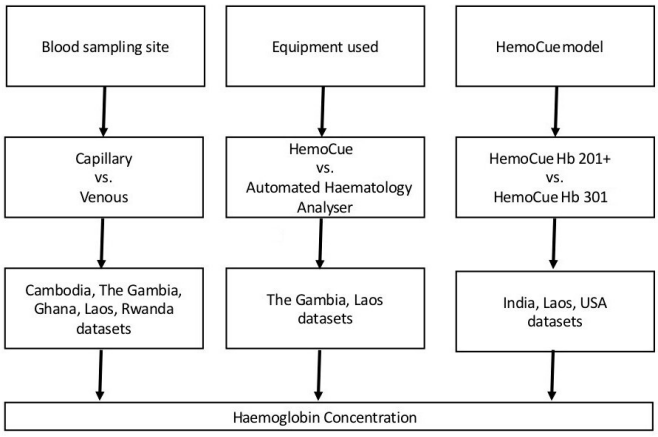

Figure 1 Schematic overview of comparisons and analyses performed

blood was analysed by HemoCue and 73.9% when venous blood was analysed by an automated analyser.

Skew was negative for almost all capillary blood. For venous blood, skew was negative among pregnant women in Ghana, children 6–11 months and 24–59 months in Rwanda, children 6–11 months in Laos and The Gambia, and in adults in the USA. In almost all datasets, kurtosis was greater than 3 for both capillary and venous blood (online supplemental table 1).

HemoCue Hb 201+ and HemoCue Hb 301 versus automated haematology analyser

Studies that compared the HemoCue 201+ to an automated haematology analyser reported lower haemoglobin measurement with the HemoCue 201+, with the range of bias from 0.0 to −3.8 g/L (table 2). In contrast, most of the studies that compared the HemoCue 301 with an automated haematology analyser report higher haemoglobin measurement with the HemoCue 301, with the range of bias from −8.7 to 8.7 g/L.

Capillary blood with HemoCue versus venous blood with the same HemoCue

Three studies (India, Laos and the USA) analysed haemoglobin concentration in capillary blood and venous blood on the same HemoCue device. Mean bias ranged from −8.3 g/L in India to 1.5 g/L in a small study of 33 adults in the USA (table 3). The concordance coefficient was highest in the US population at 0.94 (0.91, 0.98).

Venous blood by HemoCue versus venous blood by automated haematology analyser

Among studies examining haemoglobin concentrations measured in venous blood using both the HemoCue Hb 301 and the automated haematology analyser, the mean bias ranged from 5.3 g/L in pregnant women in The Gambia to 11.3 g/L among children in Laos (table 4).

DISCUSSION

Many factors likely influenced the measurement of haemoglobin concentrations, which contribute to the variability observed in our analyses. It has been suggested that there are inherent biological differences between capillary and venous blood.[22 34] However, studies have shown conflicting results.[20 22] In this analysis of data from seven countries, we found large variability in haemoglobin concentrations measured in capillary blood using either the HemoCue Hb 201+ or Hb 301 compared with venous blood analysed with automated haematology analysers as the standard. When comparing haemoglobin measurement on capillary blood with HemoCue to measurement on venous blood with an

Table 2 Haemoglobin concentration, anaemia prevalence, bias and concordance as determined by capillary blood on the HemoCue compared with venous blood on the haematology analyser

Country	Group	HemoCue model	n	Hb g/L capillary	Anaemia	Hb g/L venous	Anaemia	Bias g/L (*precision*) capillary–venous	Concordance coefficient
				Mean±SD	n (%)	Mean±SD	n (%)	Mean (95% CI)	ρ_c (95% CI)
Cambodia*	Non-pregnant women	301	808	107.2±9.4	808 (100)	115.9±13.3	468 (57.9)	−8.7 (−28.8 to 11.3)	0.47 (0.43 to 0.51)
Cambodia†	Non-pregnant women	201+	450	121.0±13.7	197 (43.8)	123.6±11.3	149 (33.1)	−2.6 (−18.1 to 12.9)	0.78 (0.75 to 0.82)
Cambodia‡	Non-pregnant women	301	277	119.1±12.3	137 (49.4)	116.6±11.7	163 (58.8)	2.5 (−17.9 to 23.1)	0.61 (0.53 to 0.68)
Cambodia†	Pregnant women	201+	30	107.9±12.7	17 (56.7)	111.7±10.2	13 (43.3)	−3.8 (−17.5 to 9.9)	0.77 (0.64 to 0.91)
The Gambia	Children	301	407	98.6±8.8	406 (99.7)	97.8±16.6	358 (88.0)	0.8 (−30.5 to 32.3)	0.28 (0.21 to 0.35)
	6–11 months	301	104	100.5±7.3	104 (100)	98.0±12.5	92 (88.5)	2.5 (−22.1 to 27.2)	0.24 (0.09 to 0.40)
	12–23 months	301	303	98.0±9.1	302 (99.7)	97.7±17.8	266 (87.8)	0.3 (−32.1 to 32.8)	0.29 (0.20 to 0.37)
Ghana	Pregnant women	201+	223	103.5±14.4	143 (64.1)	105.9±13.5	197 (88.3)	−2.4 (−21.1 to 16.4)	0.75 (0.70 to 0.81)
Laos	Children	301	1487	108.4±10.3	799 (53.7)	102.2±13.1	1099 (73.9)	6.2 (−11.4 to 23.6)	0.63 (0.60 to 0.65)
	6–11 months	301	522	107.7±10.6	295 (56.0)	99.0±11.9	435 (83.0)	8.7 (−19.7 to 37.3)	0.12 (0.05 to 0.18)
	12–23 months	301	957	108.7±10.1	501 (52.0)	104.0±13.2	660 (69.0)	4.7 (−26.9 to 36.2)	0.06 (0.003 to 0.12)
Rwanda	Children	201+	131	116.5±14.2	33 (25.1)	117.9±13.3	31 (23.7)	−1.4 (−18.2 to 15.6)	0.81 (0.74 to 0.87)
	6–11 months	201+	40	110.3±12.9	19 (47.0)	113.3±11.7	14 (35.0)	−3.0 (−21.6 to 15.5)	0.68 (0.52 to 0.85)
	12–23 months	201+	39	117.1±8.9	7 (18.0)	118.4±10.7	9 (23.0)	−1.3 (−17.1 to 14.6)	0.66 (0.49 to 0.84)
	24–59 months	201+	52	120.9±16.8	7 (13.0)	120.9±15.3	8 (15.0)	0.0 (−16.0 to 15.8)	0.87 (0.81 to 0.94)

Data were adjusted for smoking and altitude, and WHO cut-offs were applied for anaemia diagnosis (children 6–59 months <110 g/L; non-pregnant women above 15 years <120 g/L; pregnant women <110 g/L).[29]
*Cambodia dataset 1.[10]
†Cambodia dataset 2.[47]
‡Cambodia dataset 3.[14]
Hb, haemoglobin.

Table 3 Haemoglobin concentration, overall anaemia prevalence, bias and concordance as determined by capillary and venous blood using the HemoCue (Hb 301 or Hb 201+)

Country	Group	HemoCue model	n	Hb g/L capillary	Anaemia	Hb g/L venous	Anaemia	Bias g/L *(precision)* capillary–venous	Concordance coefficient
				Mean±SD	n (%)	Mean±SD	n (%)	Mean (95% CI)	ρ_c (95%CI)
India	Women	201+	982	114.4±16.5	581 (59.2%)	122.7±17.7	348 (35.4)	−8.3 (−22.1 to 4.8)	0.81 (0.80 to 0.83)
Laos	Children	301	129	111.0±10.7	54 (41.9%)	113.6±14.0	47 (36.4%)	−2.6 (−28.5 to 23.5)	0.43 (0.30 to 0.56)
USA	Adults	201+	33	144.0±15.0	CD	142.5±13.3	CD	1.5 (−7.7 to 10.6)	0.94 (0.91 to 0.98)

Data were adjusted for smoking and altitude, and WHO cut-offs were applied for anaemia diagnosis (children 6–59 months <110 g/L; non-pregnant women above 15 years <120 g/L; men above 15 years <130 g/L).[29]
CD, cannot determine; Hb, haemoglobin.

automated haematology analyser, overall the HemoCue Hb 201+ tended to report lower concentrations of haemoglobin and the HemoCue Hb 301 tended to report higher haemoglobin concentrations. When examining variation by blood source, three studies found inconsistent findings. Two studies measuring haemoglobin in capillary blood observed lower concentrations compared with venous blood that was measured on the same HemoCue machine, while one study observed higher haemoglobin concentration in capillary blood.

Low haemoglobin concentrations in capillary blood may be the result of insufficient blood flow following the fingerprick. If the blood flow is low, the phlebotomist may attempt to 'milk the finger' by squeezing the diameter of the finger and pushing blood to the fingertip in order to stimulate blood flow. This can be a result of inadequate training and supervision among data collectors. It is speculated that this may cause additional interstitial fluid to be introduced into the sample, causing a dilution effect on haemoglobin concentration.[34] Adequate training and supervision is known to reduce this technique. In this analysis, all studies included extensive training of field and laboratory workers, including monitoring of blood collection and haemoglobin measurements. An insufficient quantity of blood in the cuvette, or air bubbles in the cuvette, can also cause underestimation of haemoglobin concentration for the HemoCue.[35] Published literature related to underestimation of haemoglobin concentration with use of the HemoCue has shown variable haemoglobin concentrations among different populations including pregnant women in Sudan[15] and Brazil,[21] women of reproductive age in Jamaica,[16] adults in South Africa,[17] blood donors in the USA,[25] Iran[36] and Germany.[26 27] Thus, there is a wide range of bias (both magnitude and direction) across different population groups and study settings.

In the present analysis, there were three studies that analysed capillary and venous blood by the same method. Variable results could be due to the setting, as the studies in Laos and India were field studies under less controlled conditions and the study in the USA was implemented in a laboratory environment. However, other factors varied among the three studies, such as the population group, the HemoCue device, the blood collection and the processing of samples. For example, the HemoCue 201+ cuvette contains active reagents allowing the technician additional processing time if needed to insert the cuvette into the device after blood collection.[37] However, when using the HemoCue Hb 301 cuvettes, due to the lack of the active reagent, the cuvette must be inserted into the device and read quickly after blood collection. Finally, it is important to note that the HemoCue Hb 301 can withstand more extreme temperatures, which may contribute to the difference in bias seen in India[38] and Laos.[39]

Three studies analysed haemoglobin concentration in venous blood using two different analytical methods. Samples from pregnant women in The Gambia and children in Laos and The Gambia were measured on both the HemoCue and the automated haematology analyser. We found that a mean bias from the venous blood samples assessed with different methods ranged from 5.3 to 11.2 g/L, which resulted in a different anaemia prevalence for each study. These consistent differences indicate that some bias may be attributable to the analytical method, independent of the procedure to extract the blood (capillary vs venous). Similar findings have been reported among pregnant women in Sudan[15] and among children, pregnant women, men and women in Ghana.[40]

Consistent with trends in the literature, our findings suggest that bias exists in haemoglobin measurement in women, pregnant women, children and adult populations and is not restricted to one particular population (eg, only children). The differences observed in haemoglobin concentrations by device and blood source may be driven by the variability between studies, collection methods and analytical methods used. In addition, it is important to acknowledge that other methodological issues can contribute to discrepancies in haemoglobin measurement, such as drop to drop variability,[41] humidity,[42 43] fasting state,[10] dehydration[36] and tourniquet use.[44 45]

We did not formally assess whether poor quality control of the HemoCue analysers was an issue contributing to the large

Table 4 Haemoglobin concentration, overall anaemia prevalence, bias and concordance as determined by venous blood using the HemoCue Hb 301 and automated haematology analyser

Country	Group	HemoCue model	n	Venous HemoCue	Anaemia	Venous analyser	Anaemia	Bias g/L *(precision)* HemoCue analyser	Concordance coefficient
				Mean±SD	n (%)	Mean±SD	n (%)	Mean (95% CI)	ρ_c (95%CI)
The Gambia	Pregnant women	301	499	113.0±12.6	185 (37.1)	107.7±14.1	272 (54.5)	5.3 (−11.5 to 22.1)	0.74 (0.70 to 0.77)
The Gambia	Children	301	371	105.9±9.9	237 (63.9)	99.9±13.5	317 (84.4)	6.0 (−14.3 to 26.4)	0.55 (0.49 to 0.61)
Laos	Children	301	129	113.6±14.0	47 (36.4)	102.3±17.4	85 (65.9)	11.3 (−22.6 to 45.2)	0.32 (0.19 to 0.44)

Data were adjusted for smoking and altitude, and WHO cut-offs were applied for anaemia diagnosis (children 6–59 months <110 g/L; pregnant women <110 g/L).[29]
Hb, haemoglobin.

variation observed across countries and measurement methods. In our included studies, the authors reported the use of some type of quality control, especially the use of HemoTrol and Eurotrol controls. For both HemoCue Hb 201+ and Hb 301, real-time calibration is not possible if the quality control solution is outside of the acceptable range. According to the manufacturer, when used properly, these quality control solutions help ensure the HemoCue device is accurately measuring haemoglobin concentration within an acceptable range. However, a recent study questioned whether the acceptable ranges for these liquid controls may be too wide.[46] This study reported that the quality control solution for just one level (level II) ranged from 119 to 143 g/L. The target haemoglobin concentration for these solutions vary by lot number, but for this particular lot, the recommended haemoglobin concentration was 131 ±12 g/L. The authors of this paper argue that the large acceptable range exceeds the acceptable margin for sampling error, thus a tighter quality control range is needed to be comparable with other standard laboratory methods.[46]

Quality control solutions are also available for automated haematology analysers. However, unlike the HemoCue, real-time calibration of the analysers is possible. All studies included in the present analysis used quality control solutions in their laboratory setting (USA, Cambodia, Rwanda, Laos and The Gambia). Therefore, lack of calibration is not a source of error in the included studies.

A strength of our analysis is the use of data from a variety of populations and geographical regions of the world. One limitation is the lack of information in some of the studies regarding factors assumed to influence haemoglobin measurement. This limitation is due to the fact that our analysis used secondary data that were not collected with the primary objective to determine the factors affecting haemoglobin measurement. This produces a second limitation of the study, which is the use of a convenience sample to identify datasets. For example, we did not have complete data regarding air humidity in the different countries, many of which have humid climates during all or certain times of the year. To better assess the factors that influence haemoglobin measurement, a more rigorous controlled trial that includes comprehensive data collection on potential influential external factors is required. Overall, there is greater need to design studies that examine variation in haemoglobin concentrations.

In conclusion, we observed variability in results of haemoglobin concentrations across methods and populations. With some exceptions, lower concentration was most often seen in capillary blood and higher concentration in venous blood across all age and population groups. Although in some cases the actual difference in haemoglobin concentration is relatively small, it may result in sizeable differences of anaemia prevalence. For studies that compared capillary blood by the HemoCue and venous blood by an automated haematology analyser, we cannot ascertain as to whether the variation is due to differences in the equipment, differences in capillary and venous blood, between HemoCue and capillary blood and automated haematology analyser using venous blood, or factors affecting blood collection techniques. Indeed, the variability is likely due to a combination of these and/or other factors not examined in this analysis. Research that assesses how the principles of each method may influence haemoglobin estimation and determines the factors that affect haemoglobin measurement could help improve accuracy and reproducibility across methods and type of blood specimen.

Take home messages

- There were differences in haemoglobin concentrations across measurement methods and populations.
- Generally, capillary blood samples had lower haemoglobin concentrations and venous blood had higher haemoglobin concentration across all age and population groups.
- Small differences in haemoglobin concentration may result in significant differences in anaemia prevalence at the population level.
- A tighter quality control range is needed for HemoCue's HemoTrol and Eurotrol solutions to be comparable with other standard laboratory methods.

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