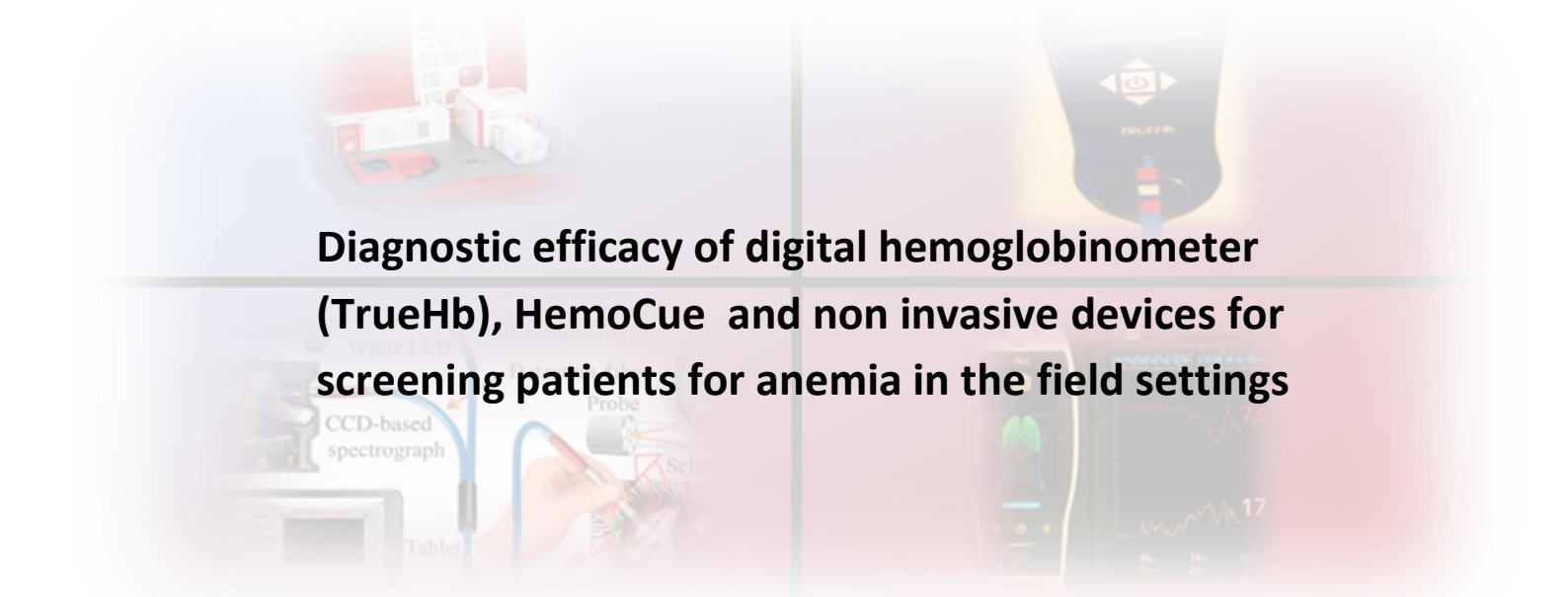

Diagnostic efficacy of digital hemoglobinometer (TrueHb), HemoCue and non invasive devices for screening patients for anemia in the field settings

Outcome report

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Indian Institute of Public Health- Delhi, PHFI

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Calcutta Medical College, Kolkata
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Introduction

Anaemia continues to be a major public health problem globally. Iron-deficiency anaemia is among top three major causes of disability in world leading to estimated loss of 42.2 million DALYs in 2011(1). South-east-Asia is among the worst affected region and estimates suggest that in India, 74.3 per cent preschool children, 49.7 per cent pregnant women, 52 per cent non-pregnant women and24 per cent of men are anaemic(2). The primary cause of anaemia is iron deficiency but is also caused by malaria, parasitic infections, nutritional deficiencies, and hemoglobinopathies(2). It leads to poor pregnancy outcomes, impaired physical and cognitive development in children, increased risk of morbidity in children and reduced work productivity posing a threat to health and economy(3).

Hb estimation is the most effective way to diagnose anemia. Any intervention to treat anemia is largely based on the level of Hb(4). Assessment of palmar, nail bed and tongue pallor is a traditional method for detection of anemia. In national programs that have a focus on pregnant anemia and children, Sahli's hemoglobinometer or by Standard Hb Colour Scale are established methods[4]. However, accuracy of these methods is questionable (5, 6). Despite this limitation, these are being used since an efficient and cost effective method for detection of anemia is yet to be incorporated in national programs(7). Most reliable methods for haemoglobin estimation requires equipped laboratory that may not be available everywhere, especially rural areas. Moreover these methods are not always cost effective and have operational challenges.(7)

In India, three different devices for detection of anaemia have been evaluated recently (8). HCS, originally developed by the WHO, has been improved by Hindustan Lifecare Limited (HLL), and named the HCS-HLL device. TrueHb 'Hemometer System' v1.1, manufactured by Wrig Nanosystems, New Delhi, India, works like a conventional glucometer based on the principle of reflectance photometry. TouchHb Version Alpha 1.1, manufactured by Biosense Technologies, India), is a non-invasive device that captures the picture of conjunctiva with the help of a mobile camera and uses the method of reflectance photometry to estimate the Hb content in blood. Study conducted by Neogi et. al. 2015 across four medical colleges comparing these devices showed the digital method (TrueHb) to be more effective for anaemia screening among normal adults. The study recommended the need for feasibility and acceptability of the devices in field settings in order to be recommended for adoption in public health systems.

Four different devices for detection of anemia are available that required feasibility testing in field settings. It is important to evaluate simple, cost-effective, user friendly and portable methods for diagnosis of anaemia in set ups where there are no or minimal laboratory facilities(7). Keeping this objective in mind this study was conceptualized.

Hence, we propose to establish the diagnostic accuracy of revised version of digital Haemoglobinometer (TruHb), Hemocue and non invasive spectroscopic device and non invasive Masimo's devices in field settings before it can be integrated in our national programmes. Using the device that is found to have a better accuracy, we also aim to explore its performance in extreme

weather conditions. The purpose was to understand the operational issues and challenges that may exist in actual field conditions when estimation is done by health care workers.

Objectives of the study

Primary objective:

To establish the diagnostic accuracy of Digital Hemoglobinameter TrueHb (newer version), HemoCue and non invasive spectroscopic device against automated analyzers (gold standard) for screening of anemia in laboratory and community settings.

Secondary objective:

Phase 1:

- To establish the level of agreement in the classification of anemia as reported by ANM (using the device that will be found better) and laboratory technician
- To do a cost efectiveness analysis of the devices and selection of the device for use in national programs

Phase 2:

- To assess the performance of devices in extremes of weather conditions

Index tests:

TrueHb

The TrueHb Hemoglobinometer System is based on the principle of reflectance photometry. A drop of blood is applied to the strip. It disperses within the hydrophilic mesh. The hemoglobin is extracted out from the RBC and, with the help of reagents present in the strip, is converted into a complex. The optical reflectance is measured which is inversely proportional to the concentration of hemoglobin in the blood sample. This corresponds to the total hemoglobin present in blood.

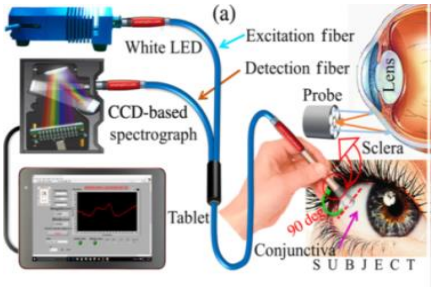
True Hb Device

HemoCue

Hemoglobin concentration is determined by measuring the absorbance of whole blood at an Hb/HbO2 isobestic point. This method correlates well with the reference method for hemoglobin determination (the ICSH method). The analyzer uses a double wavelength measuring method, 506 nm and 880 nm, for compensation of turbidity. The device consists of a precalibrated portable battery operated spectrometer with calibrated analyzers. There is no need for recalibration. There is no need to mix and dilute the blood with any reagent.

Hemocue Device

AJO Spectroscopic Test



AJO Spectroscopic Device

This is a non-invasive, noncontact, and portable device for hemoglobin estimation at point-of-care in human subjects. The innovation is based on the measurement of the spectroscopic signal emanating from the vascular bed of the bulbar conjunctiva. The collected spectral response generated in the spectrograph is transferred to a tablet computer through a USB connection where it is processed using custom developed LabVIEW software. It is compatible with mobile phone platforms for data transcribing which facilitates quick development of treatment plans. The device output correlates with the different degrees of anemia with absolute and trending accuracy.

Masimo non - invasive pulse oximetry

Masimo Pulse Oximetry

Masimo rainbow SET is a non-invasive monitoring platform featuring Masimo SET® Measure-through Motion and Low Perfusion™ pulse oximetry with the option to measure multiple additional parameters.

Methods

Phase 1: Assessing Diagnostic Efficacy of Invasive and Non-invasive Devices:

Study design: This cross sectional study was a prospective diagnostic accuracy study conducted at four sites including tertiary care hospitals across India- Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry, Calcutta Medical College, Kolkata, West Bengal.

Site of study: This was done in field settings of two sites in India. These sites were Medical Colleges with a facility for performing the gold standard test and having a field practice area. From the operational feasibility point, urban field practice area were selected. The sites were considered depending on the willingness of the Head of the Institution/ Department of Community Medicine to participate in the study. The data collection for the study was conducted between August 2018 and March 2019.

Recruitment of study subjects: The study population included all adult patients attending the hematology laboratory for routine investigations. Consecutive patients who underwent any haematological investigation using automated auto-analyser (reference test) as advised by the on-duty medical officer (who was independent of the study) were considered. Patients (more than 18 years and less than 60 years) who met the eligibility criteria and gave informed consent were recruited in the study. Pregnant women, children, seriously ill patients and those with known bleeding diathesis were excluded.

For the purpose of the study, each patient underwent either one or two index tests apart from the reference test. When two index tests were performed, it was always one invasive and one non-invasive test. To choose between the invasive tests (TrueHb and Hemocue) and non-invasive test (Masimo and AJO Spectroscopic), alternate days were earmarked to avoid any bias. The index tests were always performed before the reference test. The blood samples for the index tests and the reference test were collected in the same sitting and there was no treatment administered in between.

Diagnostic tests:

Reference test (Gold standard)- Hematological auto-analyzer was selected as the reference test. This system is an automated blood cell counter which measures Hb using non-cyanide method. To perform this test 2ml of venous blood was collected under all aseptic condition in EDTA vial. The samples were analysed within 24 hours of sample collection as per the standard operational guidelines for the machine using the reagents/kits provided with the instrument as recommended by manufacturers. The procedural manual for the testing process was followed. It was ensured that a sufficient sample quantity was obtained and the apparatus were washed and cleaned rigorously between tests and reagents were stored under the stated conditions and used within recommended time frame. The calibration and quality control programs were run as recommended and at least two control level were run in every 8 hours and a calibration guide was used to generate the reference values.

Index tests-

A standard protocol was followed for performing the Index tests.

- **Invasive tests**- Hb concentration was measured using capillary and venous blood samples for the invasive index tests. Venous samples were obtained from the samples collected for the reference test (auto analyser).

  To collect capillary blood, the tip of the middle finger was cleaned using isopropyl alcohol dipped cotton swab. After air drying it was pricked with a 23 gauge lancet placed in a lancing device prefixed at 4mm depth. Precautions were taken to avoid pressure on the fingertip so as to avoid hemodilution. First 2-3 drops of blood was wiped away to remove tissue fluid and debris. The next two drops of free-flowing blood obtained by skin puncture were used for the tests.

Hemocue test - One drop of capillary and venous blood will be put on the micro cuvettes that are fed into the device to obtain digitalized Hb values. About 10 microlitres is sufficient for each test. The device consists of a precalibrated portable battery operated spectrometer with calibrated analyzers. There is no need for recalibration. There is no need to mix and dilute the blood with any reagent.

TrueHb test – One drop of blood will be put on the strip which will be fed in the hemoglobinometer to obtain digitalized Hb values.It works like a conventional glucometer and works with just a tiny drop of blood from a pinprick on the disposable strip. It reads the accurate level within 45 seconds, and also stores up to 1,000 such readings. It can be charged like a mobile phone and allows up to 300 tests per charge.

Transportation of venous samples

The samples were collected in vacutainers and transported to the OPD laboratory (Pathology/ Hematology Department) within 3 hours of sample collection. The transit time was not more than 1 hour. The precautions that were taken are as follows:

1. The vacutainers were kept in well-fitting upright racks to ensure that there is no spillage.
2. The samples were kept at ambient temperature and in case of excessive heat in field area, these were covered with thermocol covers during transit.

- **Non-invasive tests**-

AJO Spectroscopic Test: This is a non-invasive, noncontact, and portable device for hemoglobin estimation at point-of-care in human subjects. The innovation is based on the measurement of the spectroscopic signal emanating from the vascular bed of the bulbar conjunctiva. The collected spectral response generated in the spectrograph is transferred to a tablet computer through a USB connection where it is processed using custom developed LabVIEW software. It is compatible with mobile phone platforms for data transcribing which facilitates quick development of treatment plans. The device output correlates with the different degrees of anemia with absolute and trending accuracy.

Masimo Pulse Oximetry Test: Masimo rainbow SET is a noninvasive monitoring platform featuring Masimo SET® Measure-through Motion and Low Perfusion™ pulse oximetry with the option to measure multiple additional parameters.

Sample size

nMaster 2.0 software was used to estimate sample size. Sample for diagnosis accuracy study was calculated using prevalence of anemia 50%, sensitivity = 82% (TrueHb)(8) and 82% (HemoCue)(9), significance 5%. The sample size of 600 was considered adequate for the study to assess the diagnostic accuracy of each of the two devices. Hence the total sample size is 1200.

Sample Size Estimation
Assumptions: (True Hb/ HemoCue)
Prevalence of anaemia -50%
Sensitivity =82%
Power= 80%
Level of significance= 5%
Number of diseased subjects needed= 294
Sample size= 600 approx

Data Collection

Data collection was done by three research staffs per site, who were qualified medical laboratory technicians trained on the study protocol. They recruited the eligible patients after taking written informed consent. The research staff performed the index test (one invasive and one non-invasive), entered data in a tablet directly and transferred to the investigators daily. Checks were in built within the system for us to enable to track any tampering with the data, if at all it was there. Along with the research staff, four ANMs or frontline workers performed the index tests (one invasive and one non-invasive) using capillary sample of the same patient in the same settings. The data was entered in the paper format and sent to investigators every week.

A day wise schedule for sample collection using index tests was prepared. The process was repeated till we reached a sample size of 600 for each device.

The data collections for reference and index tests were done separately. The research staffs entered the data on the electronic form (inbuilt in a tablet) provided. The research staffs were blinded from the results of reference test. To ensure blinding, the reference test was performed by the laboratory

technician of the haematology laboratory who was independent of the study team. Data on reference test were collected by Site Investigators on paper forms and transferred electronically to the Investigators. Data from both the sources was then matched based on the unique Identification number given to each study participant. (Fig 1)

A conceptual framework for data analysis was developed (Fig 2).

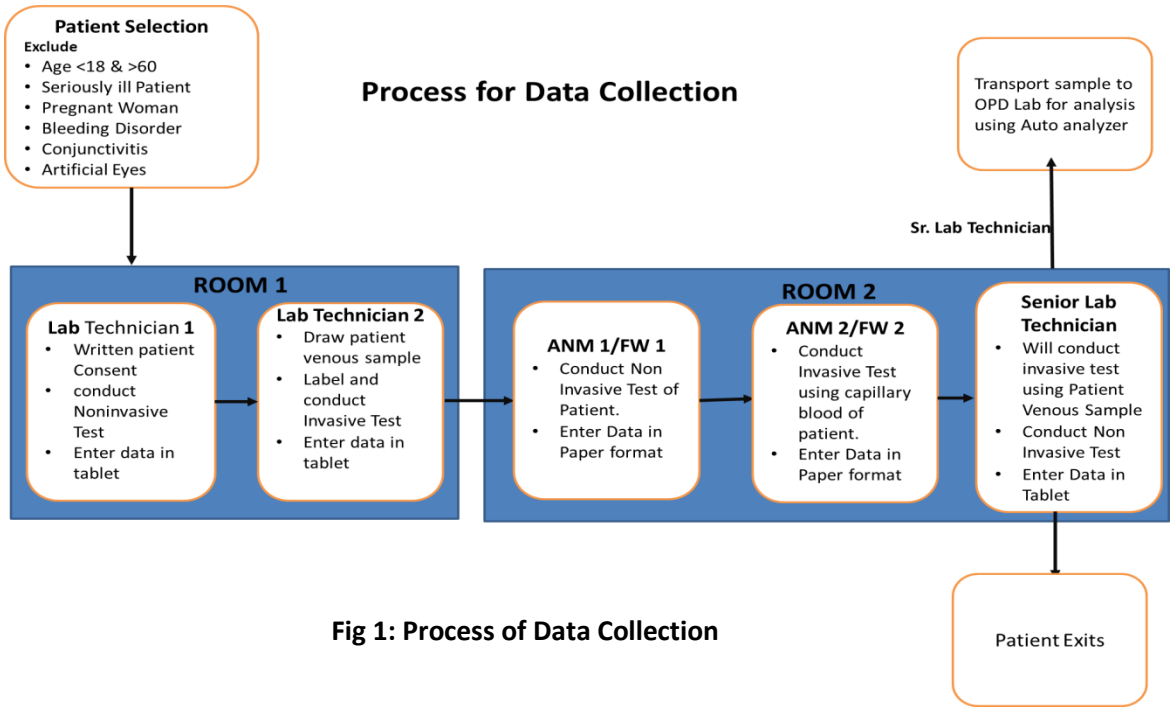


Fig 1: Process of Data Collection

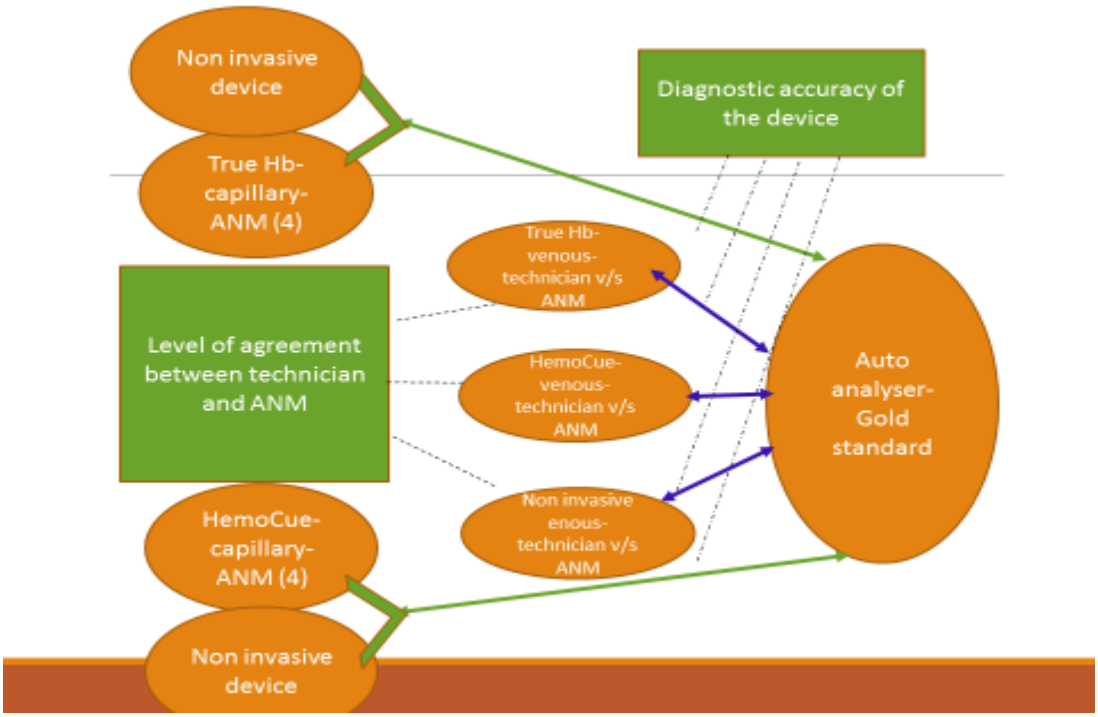


Fig 2: Conceptual framework for analysis of data

Quality Assurance

All staff who were a part of the study were oriented and thoroughly trained for data collection process and device operation in a common workshop. The facilitators included the technical experts from companies who supplied the devices as well as the IIPHD Team. All the device manufacturers certified the participants on their successful completion of training.

On site monitoring and trainings were conducted by these facilitators. The work of the research team was supervised by the Site Investigators. The two sets of data (reference test and index tests) were kept separate and blinded.

A single autoanalyzer in each site was earmarked for the reference test. Internal Quality Checks of the autoanalyzers were done every day. External Quality Assurance mechanisms were in place in all the sites. The reports were assessed by the Investigators to ensure quality.

Outcomes

- The diagnostic accuracy of the devices expressed in terms of sensitivity, specificity, predictive values and likelihood ratios.
- Difference in mean of Hemoglobin level of patients on a continuous scale measured by index tests and gold standard.
- The level of agreement between ANMs and technicians would be expressed in terms of kappa statistics

Data management & analysis

The data regarding particulars of the patients and result of the index tests were entered in a tablet uploaded with an android based mobile application tool Census and Survey Processing System (CSPro). Data pertaining to the reference test was merged with the main data after matching with the unique Identification number. Data were exported to STATA SE 11 and SPSS version 19.0 for analysis.

A descriptive analysis was done for the key variables and continuous variables presented as means and categorical variables as proportions. Each of the index tests (categorized by venous and capillary blood for invasive tests) was compared against the Gold standard.

The study population was classified into no anemia and mild, moderate and severe anemia based on the classification given by WHO. The first set of analysis focussed on screening for anemia. For this, mild, moderate and severe anemia was combined into a single category and was compared with no anemia. In the second set of analysis that focussed on screening of severe anemia, mild, moderate and no anemia were clubbed as one category and severe anemia categorized as another.

The reproducibility was assessed by comparing the results of repeated examinations of the same patient. This was done by looking at the level of agreement between research staff and the site coordinator with similar background (both technicians). This was done on a subsample of patients (100) for every device. For invasive devices, venous blood was used. The level of agreement was anlayzed by doing the Bland Altman test.

A simple correlation was done of the Hb readings for each device against the gold standard. Diagnostic accuracy for each test was examined based on the sensitivity, specificity, positive and

negative predictive values, likelihood ratios, and ROC curve. The cut offs were the values as laid down by ICMR and WHO.

The first set of analysis was to find out the diagnostic accuracy for screening of anemia (No anemia v/s mild, moderate and severe anemia). The second set of analysis was for moderate and severe anemia combined (moderate & severe anaemia combined v/s no & mild anaemia). The third set would include severe anaemia only (No, mild and moderate anemia v/s severe anemia).

The levels of agreement between the technicians (venous) and ANMs (capillary) was done by using Bland Altman test for the devices that were found to be accurate (sensitivity >75% and specificity >75%).

Reporting of results are based on STARD guidelines.

Ethical considerations

Data collection started after obtaining ethics clearance from IEC of Indian Institute of Public Health, Delhi (IIPHD), All India Institute of Medical sciences (AIIMS) and two recruiting sites. (Annexure 1) A participant information sheet and consent form was developed for the study. Written informed consent was obtained from every patient after they fulfilled the eligibility criteria. Information collected did not have access to anyone else other than the research team. The treatment of patients was based on the readings of the reference test and was in no way influenced by the results of the index test.

Phase 2: Performance of devices in extremes of weather conditions

Objective: To analyze the performance of the device of high diagnostic accuracy in extreme weather conditions

Methods:
Study design - This was a cross sectional study done prospectively
Sites of study - The selected device will be tested in two sites having extreme weather conditions. Two sites- AIIMS Jodhpur and Regional Hospital Reckong Peo,Kinnaur were selected for the purpose. The hospitals were chosen based on case load, facilities for performing the reference test (Autoanalyzer in this case) and willingness to be a part of the study.

Study population- Population for this study will include adult patients (18-60 years) attending OPDs in health facilities and willing to participate. Seriously ill patients, Neonates and children, pregnant women, Patients with known bleeding diatheses were excluded.

Sample Size- We considered agreement between the two raters as the basis for calculation of sample size. Considering the population agreement to be 0.7, sample agreement 0.9, prevalence of anemia 30%, we arrived at a sample size of 156. Considering some drop outs or spoilage of samples during transportation, we added 20% extra and that makes the sample size 200.

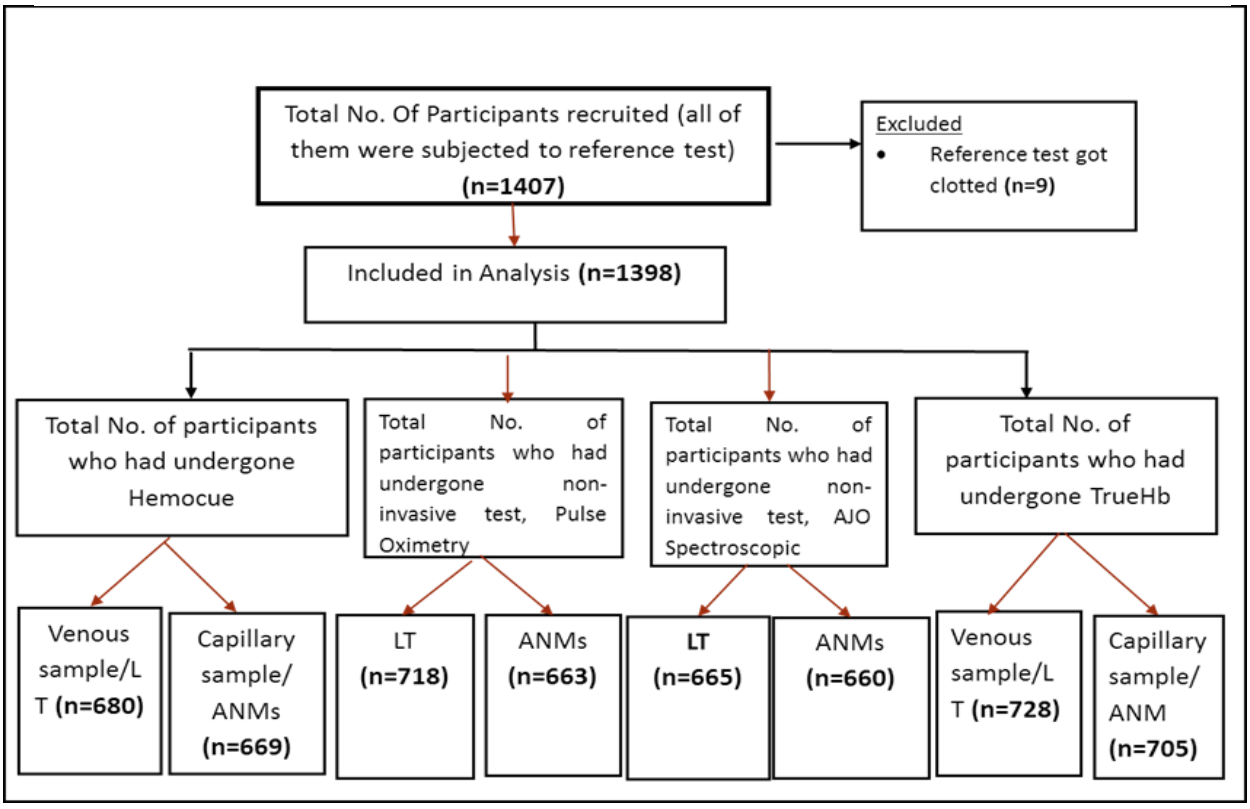
Outcomes- Difference in mean of Hemoglobin level of patients on a continuous scale measured by index tests and gold standard.

Results:

Participants' profile

A total of 1407 participants were recruited from the two sites over a period of 6 months. (Fig 3) A total of nine participants were excluded from analysis (missing values for reference test). Missing values were those patients in whom blood sample was inadequate, or it coagulated before the test or there were data entry errors. There were no adverse events reported from the conduction of these tests.

Figure 3: Flowchart depicting recruitment of participants in the study for various tests



The classification of anaemia has been described below as per ICMR and WHO in Table 1.

Table 1: Classification of anemia according to WHO and ICMR (Hemoglobin values in g/dl)

WHO	Non anemic	Mild anemia	Moderate anemia	Severe anemia
Men	>/=13	11.0-12.9	8.0-10.9	<8.0
Women	>/=12	11.0-11.9	8.0-10.9	<8.0
ICMR	≥11	10-10.9	7-9.9	<7

The site wise distribution of patients was equitable. The mean age of the participants was 37.26 years (SD-±12.57 years). Out of 1407 participants whose presenting complaints were recorded, hematological disorder (13.9%), malignant conditions (12.5%) Endocrinal (14.5%) and Cardiovascular (9.5%) were the commonest provisional diagnosis. (Table 2)

Table 2: Profile of study participants (n=1398)

Variables	Total	Puducherry	Kolkata
Total participants	1398	752	646
Mean age (SD) in years	37.26 (±12.51)	39.66 (±12.10)	34.4 (±12.41)
Provisional Diagnosis			
Any Haematological disorder (non-malignant)	195(13.9%)	40(5.3%)	155(23.9%)
Infectious conditions	14(1.0%)	9(1.1%)	5(0.7%)
Malignant conditions	175(12.5%)	108(14.3%)	67(10.3%)
Immunological disorder	11(0.7%)	6(0.7%)	5(0.7%)
Cardiovascular disorder	133(9.5%)	111(14.7%)	22(3.4%)
Endocrinal disorder	203(14.5%)	178(23.6%)	25(3.8%)
Respiratory disorders	20(1.4%)	17(2.2%)	3(0.4%)
Skeletal and muscular disorders	10(0.7%)	3(0.3%)	7(1%)
Gastrointestinal tract disorders	13(0.9%)	1(0.1%)	12(1.8%)
Surgical Conditions	5(0.3%)	4(0.5%)	1(0.1%)
Gynaecological	8(0.5%)	7(0.9%)	1(0.1%)
Neurological disorders	9(0.6%)	6(0.7%)	3(0.4%)
Others	602(43%)	262(34.8%)	340(52.6%)

As per the ICMR classification, prevalence of anaemia in the study population was 33%. The distribution of anemia among the participants is included in Table 3.

Table 3: Distribution of study participants as per ICMR classification of anaemia across two sites

Hb % (in gm%)	Total (n=1398)	Puducherry (n=752)	Kolkata (n=646)
Mean (SD)	11.64 (±2.7)	12.31 (±2.4)	10.8 (±2.8)
Range	2-20.2	2-20.2	4.2-18.6
No anemia (Hb>11)	938 (67.1%)	580 (77.1%)	358(55.4%)
Mild anaemia (Hb 10-10.9)	124 (8.8%)	58 (7.7%)	66 (10.2%)
Moderate anaemia (Hb 7-9.9)	240 (17.2%)	94 (12.5%)	146 (22.6%)
Severe anaemia (Hb <7)	96 (6.8%)	20 (2.6%)	76 (11.7%)

The distribution of anaemia with respect to the devices is given in Table 4. This has implications on the predictive values but sensitivity, specificity and likelihood ratios remains unaffected with change in prevalence of the condition.

Table 4: Distribution of study participants as per ICMR classification of anaemia across different

Autoanalyzer (Hb in gm%)	Hemocue	True Hb	Masimo	AJO
No anemia	449 (66.7)	489 (67.4)	442 (62.3)	477 (72.0)
Mild anaemia	54 (8.02)	70 (9.6)	61 (8.6)	59 (8.9)
Moderate anaemia	107 (15.9)	133 (18.3)	136 (19.1)	100 (15.1)
Severe anaemia	63 (9.3)	33 (4.5)	70 (9.8)	26 (3.9)
Total	673	725	709	662

Diagnostic accuracy of devices

The Diagnostic accuracy was assessed from sensitivity, specificity, positive and negative predictive values, positive and negative likelihood ratios and Area under the ROC Curve.

In our study, we have done the analysis for different categories of Anaemia using both ICMR and WHO classification. As per **ICMR classification of Anaemia**, the first category**, anaemia and no anaemia**, TrueHb shows higher sensitivity (92.8%) & specificity (88.1%) with venous sample. Its sensitivity (86.3%) & specificity (84.7%) got reduced using capillary sample. Whereas Hemocue showed higher sensitivity (89.9%) with capillary sample compared to venous sample with sensitivity of 85.3% & specificity of 98.7% .The non-invasive devices did not perform better than the invasive devices. (Table 5, 6)

Table 5: Diagnostic Accuracy Parameters for testing anemia and no anemia by Lab Technicians as per ICMR classification

Test	Sensitivity % (95% CI)	Specificity % (95% CI)	Positive predictive value (PPV) (95% CI)	Negative Predictive value (NPV) (95% CI)	Positive likelihood ratio (LR+) (95% CI)	Negative likelihood ratio (LR-) (95% CI)	Area under ROC (95% CI)
Hemocue (venous)	85.3 (79.9-89.6)	98.7 (97.1-99.5)	97 (93.5-98.9)	93.1 (90.4-95.2)	63.9 (28.8-141.8)	0.15 (0.11-0.20)	0.92 (0.90-0.94)
True Hb (venous)	92.8 (88.7-95.7)	88.1 (84.9-90.9)	79.1 (73.8-83.7)	96.2 (94.0-97.8)	7.82 (6.13-9.99)	0.08 (0.05-0.13)	0.90 (0.88-0.93)
Masimo Device	62.5 (55.9-68.7)	97.7% (95.9-98.9)	93.5 (88.5-96.9)	83.1 (79.6-86.3)	27.4 (14.7-51.0)	0.38 (0.32-0.45)	0.80 (0.77-0.83)
Spectroscopic Device	57.1 (49.6-64.3)	76.5 (72.4-80.2)	48.6 (41.8-55.5)	82.0 (78.1-85.5`)	2.43 (1.98-2.98)	0.56 (0.47-0.67)	0.67 (0.63-0.71)

Table 6: Diagnostic Accuracy Parameters for testing anemia and no anemia by ANM/ frontline workers as per ICMR classification

Device	Sensitivity % (95% CI)	Specificity % (95% CI)	Positive predictive value (PPV) (95% CI)	Negative Predictive value (NPV) (95% CI)	Positive likelihood ratio (LR+) (95% CI)	Negative likelihood ratio (LR-) (95% CI)	Area under ROC (95% CI)
Hemocue (capillary)	89.9% (85.1-93.6)	93.3 % (90.5-95.4)	86.7 (81.6-90.9)	95 (92.5-96.8)	13.37 (9.43-18.94)	0.11 (0.07-0.16)	0.92 (0.89-0.94)
True Hb (capillary)	86.3 (81.0-90.6)	84.7 (81.2-87.8)	71.9 (66.0-77.2)	93.2 (90.4-95.3)	5.63 (4.54-6.99)	0.16 (0.12-0.23)	0.85 (0.83-0.88)
Masimo Device	66.0 (59.2-72.4)	97.5 (95.5-98.7)	92.6 (87.2-96.3)	85.6 (82.2- 88.6)	25.99 (14.39-46.96)	0.35 (0.29-0.42)	0.82 (0.78-0.85)
Spectroscopic Device	56.4 (48.8-63.7)	75.4 (71.3-79.2)	46.6 (39.8-53.4)	82 (78-85.5)	2.29 (1.87-2.81)	0.58 (0.49-0.69)	0.66 (0.62-0.70)

The analysis for second category, **moderate and severe anaemia** combined, shows almost similar results. (Table 7,8)

Table 7: Diagnostic Accuracy Parameters for testing moderate and severe anemia by Lab Technicians as per ICMR classification

Device	**Sensitivity % (95% CI)**	**Specificity %** (95% CI)	**Positive predictive value (PPV) (95% CI)**	**Negative Predictive value (NPV) (95% CI)**	**Positive likelihood ratio (LR+) (95% CI)**	**Negative likelihood ratio (LR-) (95% CI)**	**Area under ROC** (95% CI)
Hemocue (capillary)	90.3 (84.7-94.4)	97 (95.1-98.3)	90.9 (85.4-94.8)	96.8 (94.8-98.2)	29.9 (18.17-49.4)	0.10 (0.06-0.16)	0.94 (0.91-0.96)
True Hb (capillary)	88.7 (82.6-93.3)	89.7 (86.8-92.1)	70.2 (63.1-76.5)	96.7 (94.7-98.1)	8.58 (6.6-11.04)	0.13 (0.08-0.20)	0.89 (0.86-0.92)
Masimo Device	51.9 (47.6-64)	98.8 (97.3-99.5)	93.4 (86.2-97.5)	87.8 (84.7-90.4)	45.3 (20.2-101.79)	0.45 (0.37-0.53)	0.77 (0.73-0.81)
Spectroscopic device	52.8 (43.6-61.9)	80.3 (76.7-83.6)	38.2 (30.9-46)	88.1 (84.9-90.8)	2.69 (2.12-3.41)	0.59 (0.48-0.71)	0.67 (0.62-0.71)

Table 8: Diagnostic Accuracy Parameters for testing moderate and severe anemia by ANM/ frontline workers

Test	**Sensitivity % (95% CI)**	**Specificity %** (95% CI)	**Positive predictive value (PPV) (95% CI)**	**Negative Predictive value (NPV) (95% CI)**	**Positive likelihood ratio (LR+) (95% CI)**	**Negative likelihood ratio (LR-) (95% CI)**	**Area under ROC (95% CI)**
Hemocue (venous)	88.2 (82.4-92.7)	99 (97.7-99.7)	96.8 (92.6-98.9)	96.1 (94.1-97.6)	88.7 (37.04-212.7)	0.12 (0.08-0.18)	0.94 (0.91-0.96)
True Hb (venous)	94.6 (90-97.5)	93.9 (91.6-95.8)	82.2 (76-87.3)	98.3 (96.8-99.2)	15.5 (11.2-21.58)	0.06 (0.03-0.11)	0.94 (0.92-0.96)
Masimo Device	64.1 (57.1-70.6)	98 (96.4-99)	93 (87.4-96.6)	86.9 (83.9-89.6)	32.2 (17.3-60.04)	0.37 (0.31-0.44)	0.81 (0.78-0.84)
Spectroscopic Device	52.4 (43.3-61.3)	80.6 (77-83.9)	38.8 (31.5-46.6)	87.8 (84.6-90.6)	2.7 (2.12-3.43)	0.59 (0.49-0.71)	0.66 (0.62-0.71)

The analysis for third category, **severe anaemia**, shows TrueHb having higher sensitivity (84.8%) with venous sample as well as with capillary sample (87.1%). Whereas Hemocue shows significant decrease in the sensitivity (39.7%) with venous sample as well as with the capillary sample (46.8%). Similarly, both non-invasive devices shows decrease in the sensitivity when tested for severe anaemia. (Table 9,10)

Table 9: Diagnostic Accuracy Parameters for testing severe anemia by Lab Technicians as per ICMR classification

Device	Sensitivity % (95% CI)	Specificity % (95% CI)	Positive predictive value (PPV) (95% CI)	Negative Predictive value (NPV) (95% CI)	Positive likelihood ratio (LR+) (95% CI)	Negative likelihood ratio (LR-) (95% CI)	Area under ROC (95% CI)
Hemocue (venous)	39.7 (27.6-52.8)	100 (99.4-100)	100 (86.3-100)	94.1 (92.1-95.8)	-	0.60 (0.49-0.74)	0.70 (0.64-0.76)
True Hb (venous)	84.8 (68.1-94.9)	96.7 (95.1-97.9)	54.9 (40.3-68.9)	99.3 (98.3-99.8)	25.5 (16.6-39.1)	0.16 (0.07-0.35)	0.91 (0.85-0.97)
Masimo Device	28.0 (16.2-42.5)	99.7 (98.8-100)	87.5 (61.1-98.4)	94.5 (92.5-96.1)	86.9 (20.3-371.8)	0.72 (0.61-0.86)	0.64 (0.58-0.70)
Spectroscopic Device	26.9 (11.6-47.8)	96.3 (94.6-97.7)	23.3 (9.9-42.3)	97 (95.3-98.2)	7.3 (3.48-15.61)	0.76 (0.60-0.96)	0.62 (0.53-0.70)

Table 10: Diagnostic Accuracy Parameters for testing severe anemia by ANM/ frontline workers as per ICMR classification

Device	Sensitivity % (95% CI)	Specificity % (95% CI)	Positive predictive value (PPV) (95% CI)	Negative Predictive value (NPV) (95% CI)	Positive likelihood ratio (LR+) (95% CI)	Negative likelihood ratio (LR-) (95% CI)	Area under ROC (95% CI)
Hemocue (capillary)	46.8 (34.0-59.9)	99.2 (98.1-99.7)	85.3 (68.9-95)	94.8 (92.7-96.4)	56.3 (22.6-140.2)	0.54 (0.42-0.68)	0.73 (0.67-0.79)
True Hb (capillary)	87.1 (70.2-96.4)	95.7 (93.9-97.1)	48.2 (34.7-62.0)	99.4 (98.4-99.8)	20.15 (13.77-29.5)	0.13 (0.05-0.34)	0.91 (0.85-0.97)
Masimo Device	17 (7.6-30.8)	99.8 (99.1-100)	88.9 (51.8-99.7)	93.8 (91.7-95.6)	101.2 (12.94-792.6)	0.83 (0.73-0.95)	0.58 (0.53-0.64)
Spectroscopic Device	28 (12.1-49.4)	95.9 (94-97.3)	21.2 (9-38.9)	97.1 (95.5-98.3)	6.81 (3.27-14.16)	0.75 (0.59-0.96)	0.62 (0.53-0.71)

The findings of the analyses using WHO classification showed similar results (Annexure 2).

The **Mean difference** was calculated between autoanalyzer and index tests. True Hb showed an underestimation by -0.28(-0.36 to 0.20) with venous sample and -0.22(-0.35 to -0.09) with capillary sample. Hemocue overestimates by 0.47(0.42 to 0.52) with venous sample and 0.18(0.11 to 0.25) with capillary sample. Both Masimo and AJO overestimates using capillary and venous sample. (Table 15-17, Fig 4)

The mean difference of TrueHb in severe anemia category is 0.05(-0.52 to 0.63) with venous sample and -0.06(-0.71 to 0.58) with capillary sample. Hemocue overestimates by 0.92(0.81 to 1.02) with venous sample and by 0.84(0.66 to 1.03) with capillary sample.

Table 15: Difference in Hb readings between autoanalyzer (reference) and index tests

Device	Device mean (SD)	Autoanalyzer reading mean (SD)	Mean Difference	95% CI
Hemocue (venous)	12.11(2.6)	11.63 (2.7)	0.47	0.42 to 0.52
Hemocue (capillary)	11.7(2.6)	11.5 (2.8)	0.18	0.11 to 0.25
True Hb (venous)	11.74(2.7)	11.9 (2.47)	-0.28	-0.36 to 0.20
True Hb (capillary)	11.6(3.01)	11.7 (2.6)	-0.22	-0.35 to -0.09
Masimo (technician)	11.75(3.1)	11.6 (2.7)	0.06	-0.10 to 0.24
Masimo (ANM)	12.1(2.1)	11.3 (2.8)	0.47	0.37 to 0.58
AJO (technician)	12.62(3.3)	12.02 (2.5)	0.43	0.17 to 0.69
AJO (ANM)	12.6(3.3)	11.9(2.6)	0.71	0.46 to 0.96

Table 16: Difference in Hb readings between autoanalyzer (reference) and index tests in moderate and severe anemia combined category

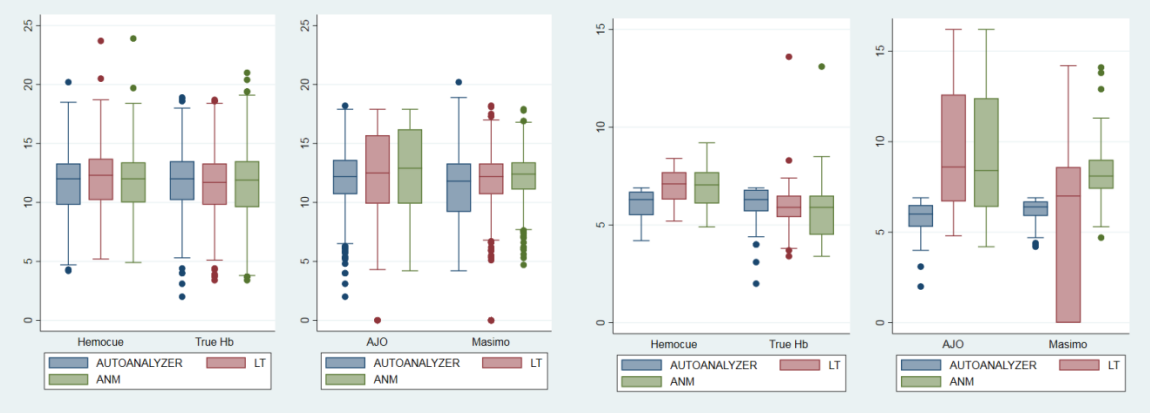
Device	Device mean (SD)	Autoanalyzer mean (SD)	Mean Difference	95% CI
Hemocue (venous)	8.28(1.38)	7.4(1.34)	0.82	0.71 to 0.92
Hemocue (capillary)	8.16(1.43)	7.4(1.35)	0.70	0.58 to 0.82
True Hb (venous)	7.84(1.77)	8.07(1.41)	-0.23	-0.41 to -0.04
True Hb (capillary)	7.81(1.84)	8.04(1.44)	-0.23	-0.43 to -0.03
Masimo (technician)	9.58(1.84)	7.8(1.35)	1.7	1.55 to 1.97
Masimo (ANM)	9.57(1.78)	7.7 (1.34)	1.7	1.56 to 1.98
AJO (technician)	10.5(3.28)	7.8(1.52)	2.6	2.07 to 3.2
AJO (ANM)	10.3(3.33)	7.8(1.53)	2.5	1.88 to 3.12

Table 17: Difference in Hb readings between autoanalyzer (reference) and index tests in severe anemia category

Device	Device mean (SD)	Autoanalyzer mean (SD)	Mean Difference	95% CI
Hemocue (venous)	7.05(0.9)	6.13(0.68)	0.92	0.81 to 1.02
Hemocue (capillary)	6.9(0.9)	6.08(0.71)	0.84	0.66 to 1.03
True Hb (venous)	6.09 (1.7)	6.09 (1.2)	0.05	-0.52 to 0.63
True Hb (capillary)	5.8(1.8)	5.9(1.2)	-0.06	-0.71 to 0.58
Masimo (technician)	5.79(4.01)	6.2 (0.72)	-0.39	-1.37 to 0.57
Masimo (ANM)	7.35(3.2)	6.2(0.69)	1.10	0.20 to 1.99
AJO (technician)	9.6 (3.3)	5.78 (0.9)	3.84	2.62 to 5.06
AJO (ANM)	9.7(3.9)	5.6(1.2)	4.1	2.6 to 5.6

The box plot given below shows the mean difference of all the devices plotted along with autoanalyzer in figure 4.

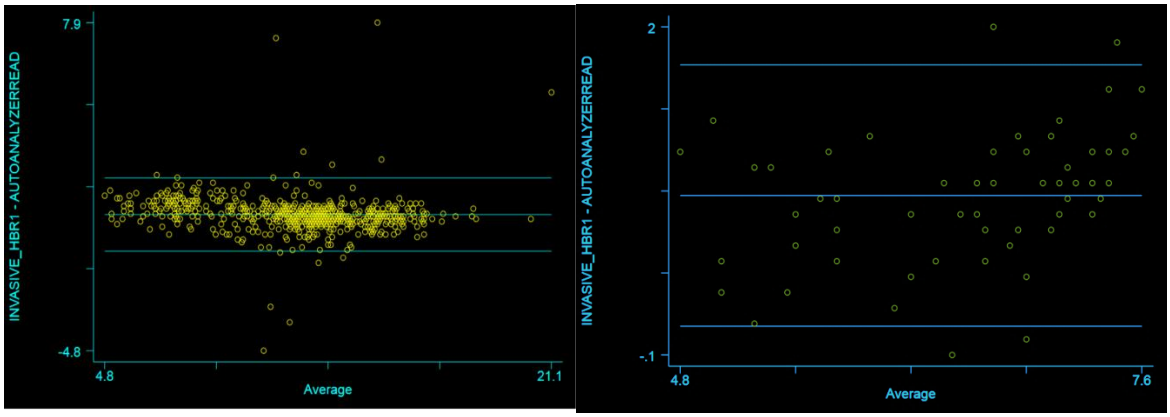
Fig 4: Difference in Hb readings between autoanalyzer (reference) and index tests



All readings Severe anemia

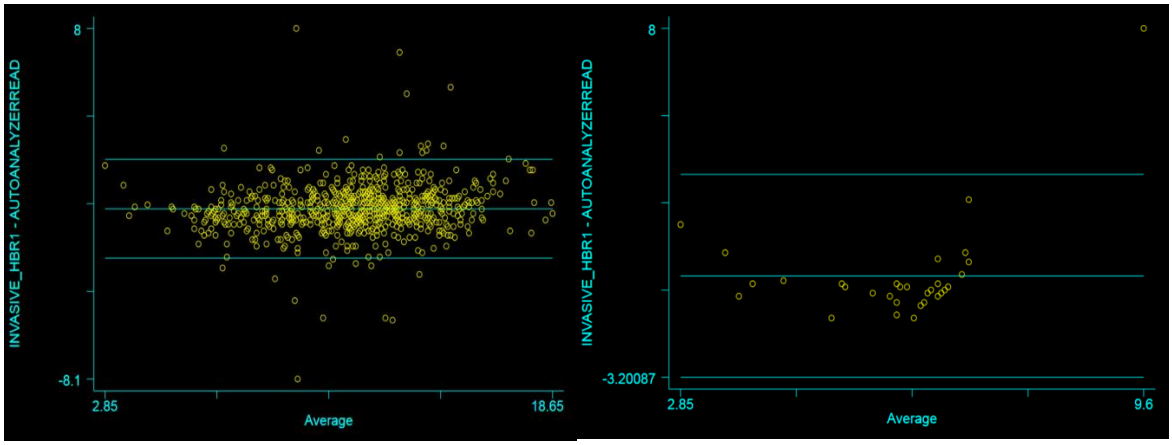
The level of agreement between the venous readings against autoanalyzer readings are presented in Fig 5,6.

Fig 5: Bland-Altman Plot (Concordance analysis) showing agreement between auto-analyser V/s venous sample for <u>Hemocue</u>



All readings Severe anemia

Fig 6: Bland-Altman Plot (Concordance analysis) showing agreement between auto-analyzer V/s venous sample for TrueHb



All readings Severe anemia

Key highlights

Invasive devices shows overall better performance than Non-invasive devices in the field settings.

For screening of Anemia, HemoCue (AUC 0.92, 95% CI 0.88-0.94) and True Hb (AUC 0.85, 95% CI 0.83-0.89) are comparable with no statistically significant difference between the two.

For screening of Severe Anemia, TrueHb (AUC 0.91, 95% CI 0.85-0.97) fares better than all other devices including HemoCue (AUC 0.73, 95% CI 0.67-0.79)

Agreement between Lab technicians and ANMs

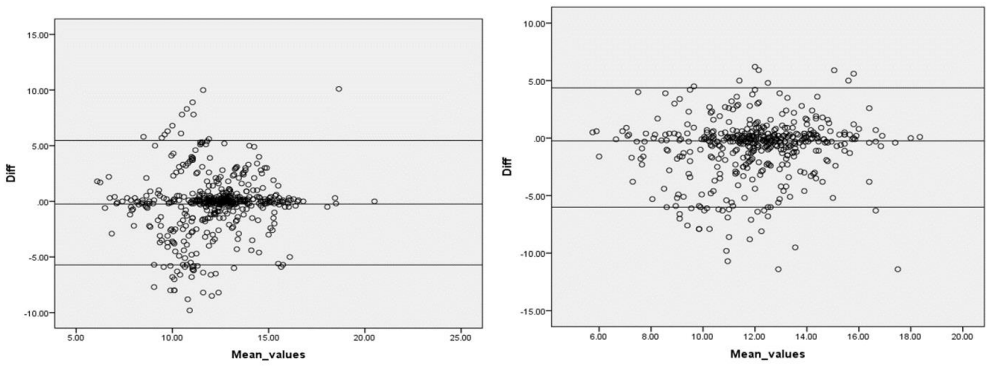
The level of agreement between Lab technician and ANM was done using kappa. Hemocue shows better agreement as compared to other devices. The level of agreement between autoanalyzer readings and venous sample has been graphical presented using Bland Altman plots for Invasive devices (Hemocue & TrueHb) only as their sensitivity & specificity are more than 75%. (Table 18, Fig 7)

Table 18: Level of agreement between Hb reading of lab Technicians and ANMs for different categories of anemia (kappa value with 95% CI)

	Hemocue	True Hb	Masimo	AJO
Anemia and No Anemia	0.826 (0.78-0.87)	0.62 (0.56-0.68)	0.78 (0.72-0.84)	0.43 (0.35-0.50)
Severe anaemia	0.77 (0.64-0.89)	0.73 (0.63-0.82)	0.37 (0.17-0.57)	0.38 (0.23-0.54)

One aspect behind selection of an appropriate device is the ability to reproduce the results. We assessed for reproducibility (inter observer variation) by subjecting a sample to tests (index tests) by two observers. We performed this on 100 patients for each device. Both True Hb and Hemocue both showed fairly good reproducible results.

Fig 7: Reproducibility of device readings



HemoCue **True Hb**

Performance of the devices in extremes of weather conditions

The performance of the device was assessed in different weather conditions. The mean differences between the autoanalyzer and device readings are presented in Table 19.

Table 19: Mean Hb difference across the sites for Invasive Devices *(device minus autoanalyzer)*

SITE	Hemocue		TrueHb		Months of data collection	Temp (^{o}C), Mean, median, range	Humidity (%) Mean, median, range
	Venous Mean, SD, 95% CI	**Capillary** Mean, SD, 95% CI	**Venous** Mean, SD, 95% CI	**Capillary** Mean, SD, 95% CI			
Kolkata	**0.72**, (0.72); 0.64 to 0.79	**0.43**,(1.17); 0.30 to 0.55	**-0.07**, (1.06); -0.19 to 0.04	**-0.20**, (1.42); -0.36 to -0.04	July- Nov 2018	26 ^{0}C; 28 ^{0}C; 19-29 ^{0}C	77.4%; 76%; 69-87%
JIPMER	**0.23**,(0.60); 0.17 to 0.29	**-0.09**, (0.97); -0.19 to 0.01	**-0.36**, (1.54); -0.50 to -0.20	**-0.15**, (2.14); -0.35 to 0.05	Sep 18- Jan 19	26.8 ^{0}C; 26.5 ^{0}C; 25-29 ^{0}C	81.2%; 81%; 77-86%
AIIMS Jodhpur	**0.55**,(1.35); 0.35 to 0.75	**-0.14**, (1.12); -0.51 to 0.23	**-0.14**, (0.84); -0.25 to -0.02	**-1.01**, (2.17); -1.7 to -0.33	Feb 19	28.3 ^{0}C; 28 ^{0}C; 26-33 ^{0}C	35%; 35%; 10-100%
Kinnaur, Him Pradesh	**2.16**,(0.49); 2.05 to 2.28	**1.96**,(0.74); 1.79 to 2.17	**1.62**,(0.88); 1.40 to1.84	**1.83**(1.35); 1.50 to 2.16	Feb 19	0.2 ^{0}C; 0.5 ^{0}C; -2 to 1	57%

The results appeared to be more consistent with True Hb as compared to HemoCue. Nevertheless, extreme cold weather conditions shows an overall overestimation by around 2% with both the devices.

Key highlight

Both True Hb and HemoCue overestimates Hb in extreme cold weather conditions.

Features of the Invasive Devices:

A device for use in communities or primary healthcare facilities in resource-poor settings should be inexpensive, rapid, simple to perform with reasonably accuracy(7). Operational issues while using a device also aid in taking a decision on the feasibility of its use in field settings. We therefore explored different aspects like ease of use, portability, objectivity in readings, average time taken to perform each test, expertise required and strip/cuvette wastage. These were gathered from specifications mentioned in product inserts, from the manufacturers and research staff involved in the study. (Table). Previous studies showed that process for choosing appropriate laboratory methods is complex and very little guidance is available for health mangers [8].

Table 20: Features of the Hemocue and TrueHb devices

Parameters	Hemocue	True Hb
Accuracy (all categories; Case detection rate or sensitivity	+++ (90%)	+++ (86%)
Mean diff in Hb compared to Gold standard for all categories	+++ (0.18)	+++ (-0.22)
Accuracy (Severe Anemia).. Case detection rate or sensitivity	- (47%)	+++ (87%)
Mean diff in Hb compared to Gold standard in severe anemia	- (0.84)	+++ (-0.06)
Accuracy at different weather conditions	±	+
Data storage	- (no data)	+ (only Hb values)
Portability (weight of the device)	+ (500 gms)	+++(60gms)
Portability (dimensions) (in inches)	+ (5.5 x 2.7 X6.2)	+++ (4.7 x 2.3 x 0.3)
Ease of use by ANMs*	+++	++
Ease and duration of training	+++ (4-5 hrs)	+++(4-5 hrs)
Objectivity in readings	+++	+++
Patient convenience	+++	+++
Need for recalibration (NR- Not required)	+++ (NR)	+++ (NR)
Strip/cuvette wastage per test (Number per test)	++(1.2)	+ (1.35)
Operating temperature	+ (10- 40^{O} C)	++ (5-45^{O} C)
Strip/ Cuvettes Storage conditions	+ (10- 40^{O} C)	++ (5-45^{O} C)
Shelf life of the equipment	+++ (7 years)	++ (5 years)
Shelf life of strips/ microcuvettes	++(2 years)	+ (1 year)
Source of power in facility	++ (AC adapter)	++ (Charger)
Source of power in community	+(4 AA batteries)	++ (device should be fully charged, no batteries needed))
Number of tests in field settings (fully charged/ batteries)	++ (510)	+ (200)
Biomedical waste management	Lancet and microcuvettes	Lancet and strips
Approvals	FDA approved, CLIA compliant	CLIA compliant, ISO approved, FDA under process

+++ Very good, ++ Good, +Average , - Poor, ± Equivocal

* User friendliness detailed in Annexure 3

Key highlight

Overall it appears that TrueHb is better than HemoCue in estimating Hb including severe anemia

Phase 3: Cost assessment

We used a step-down costing methodology for capturing costs that were entered into a customized tool created in MS Excel.

The costs were calculated by adding the unit costs of all resources used in the different activities occurring in the screening process. This process included all activities and procedures performed to detect cases with anemia from attending OPDs for screening till the time a final diagnosis was obtained. We used the concept of activity-based costing for the screening program, and for the hospital we used a standardized cost-accounting system. For the activity-based costing, the costs inputs included screening costs (health professionals, devices, screening venue etc.). Personnel costs were calculated from the total cost of each ANM participating in a certain activity according to the time specifically dedicated to that particular activity. The amount of time that they devote for testing for anemia using each device was considered. Correspondingly, a proportion of their full salary was considered as a cost.

All diagnostic equipment (every device) with a usage life of more than a year was considered as capital equipment. The life cycle of such equipment/ shelf lives were considered. Annual maintenance of all diagnostic equipment was considered at 10% of annual rental value. Costs of other equipment such as syringe, needle, cotton swab etc were accounted for. Rental value of clinics (Urban/ rural health centres) were captured based on present value based on local information.

At the hospital, the costing focussed on conducting tests for anemia. Examination cost include both direct costs. Direct costs included labour, capital and material costs. Labour costs will comprise the salaries apportioned to the amount of time taken to conduct each test. Capital costs of the examination room will include; annualised discounted depreciation cost of the building (examination room area), furniture, equipment and instruments used in the examination room and the opportunity cost of the land. Recent government contracts for purchasing equipment, instruments and furniture were used to capture the price information of capital items. The useful life of building and structures was considered as 10 years; useful life of furniture and fittings assumed to be 10 years, and that of machinery and plant as 7 years, as per Government of India income tax depreciation rule. However, medical equipment such as devices, the useful life was considered as 2.5 years. 3% discount rate was considered to calculate cost of depreciable assets.

The material costs included drugs, medical supplies, and office supplies and included the actual usage of materials in the examination rooms during the study period. To determine the examination cost, we enlisted the equipment needed for each examination. Examination time by ANMs on a sample of at least 30 patients were examined across the four devices based on actual observation.

Approach for data collection

Cost data: The cost data was collected in a word format which was divided into eight sections named as under

a) Information about the facility: basic details of the facility were collected.

b) General information: which included data about working hours of the health facility

c) Salary structure of the ANM: Along with the salary it also includes the information about the activities in which these individuals were involved for the project. Please note that the salary paid by the project for ANMs was as paid by the government. The salary which the ANM receives from the government at both the sites is based on the type of ANM. If the ANM is permanent employee then she receives Rs. 18000 whereas if she is on contract (Ad-hoc) then she receives Rs. 6250 monthly and 1600 yearly (400 each quarter). This information was collected from the individuals themselves.

d) Details of Equipments: the cost of devices which were tested in the project was directly obtained from the manufacturers in the prescribed format. The format included name of the device, unit price and expected life of the equipment. In total four devices were used two invasive: Hemocue and True Hb and two non-invasive: AJO and Masimo.

e) Consumables: under this section detail of consumables which includes materials and supplies issued, consumed, quantity used per test, and price per unit was collected in the facility. This data was specific to the utility of consumables in each device.

Table 21: Assumptions for Cost Analysis (based on specifications shared by manufacturers)

	Unit cost	**Shelf life (in years)**	***Number of tests a device can perform***	***Time taken to perform one test (in secs)***
AJO Spectroscopic Device			300 / day	69-70 secs
Tablet	25000	*7*		
Instrument box	246000	*7*		
USB Cable	200	*7*		
Charger	800	7		
Calibrator	1500	7		
Suitcase	1500	7		
Masimo Pulse Oximetry			1000 tests /sensor	18-73 secs
Device (Pad)	18,500	7		
Charger	1800	7		
Sensor with 1000 tests or “e-strips”	30	2		
Black Cover	100	1		
Hemocue			7500	22- 53 secs
Apparatus Hb301 Analyser	8500	7		
Microcuvettes	17	2		
Lancet	5	5		
TrueHb			150000	36-48 secs
Instrument (True Hb Device)	2750	5		
Charger	50	5		
Loading gun	200	5		
Strips	19	1		

f) Details of the physical infrastructure: Under this section area, monthly rental price of 100 square feet place where the center is located and expenditure (if any) on renovation or construction of accessory items was collected.

g) Details about non-medical items: Name and quantity of functional non-medical items in each room was physically observed by the researcher and was reported.

h) Activity time: Under this the respondents were asked to report the activities which they perform and the time they spent routinely for the same.

i) Time allocation: At both the sites the time which the ANM take for conducting the test was calculated using a stop watch.

The cost for conducting each test are summarized in Table 22.

Table 22: Projected costs of resources for each test for measuring Hemoglobin (in INR)

Component	**Hemocue**		**True Hb**		**AJO**		**Masimo**	
	Rural	Urban	Rural	Urban	Rural	Urban	Rural	Urban
Human resource (ANM)	16.7 (13.9%)	17.7 (10.7%)	17.1 (12.5%)	17.5 (9.9%)	18.1 (16.5%)	18.1 (12.9%)	16.6 (15.8%)	18.3 (12.6%)
Equipment (device, charger, adapter)	0.2 (0.1%)	0.2 (0.1%)	0.004 (0%)	0.004 (0%)	0.05 (0.04%)	0.05 (0.04%)	3.4 (3.2%)	3.4 (2.3%)
Accessories (Micro cuvettes/ strips)	11.9 (9.9%)	11.9 (7.2%)	26.4 (19.3%)	26.4 (14.9%)	0.0 (0%)	0.0 (0%)	0.0 (0%)	0.0 (0%)
Consumables (items used in the test)	12.3 (10.2%)	19.7 (12.0%)	12.3 (9.0%)	19.7 (11.1%)	6.1 (5.6%)	4.3 (3.1%)	6.1 (5.8%)	4.3 (3.0%)
Non-medical (items in facility rooms)	78.8 (65.5%)	113.4 (69.0%)	80.8 (59.0%)	112.3 (63.3%)	85.4 (77.6%)	116.4 (82.9%)	78.3 (74.7%)	117.2 (81.0%)
Capital space (rental)	0.4 (0.3%)	1.6 (0.9%)	0.4 (0.3%)	1.5 (0.9%)	0.5 (0.4%)	1.6 (1.1%)	0.4 (0.4%)	1.6 (1.1%)
Total cost / test	**120.3**	**164.3**	**137.0**	**177.4**	**110.1**	**140.4**	**104.8**	**144.7**

The costs of the invasive devices and their running costs are summarized in Table 23.

Table 23: Costs of the device and running cost for each test for measuring Hemoglobin (in INR)

Component	Hemocue		True Hb	
	Rural	Urban	Rural	Urban
Equipment (device, charger, adapter)	0.2	0.2	0.004	0.004
Accessories (Microcuvettes/ strips)	11.9	11.9	26.4	26.4
Consumables (items used in the test)	12.3	19.7	12.3	19.7
Total cost per unit test	**24.4**	**31.8**	**38.7**	**46.1**

Key highlight

The cost of True Hb device is less but the running cost is high as compared to HemoCue

Limitations of the study:

The study was conducted with a robust methodology, yet it suffers from certain limitations:

- Sites for data collection were chosen purposively and it may not be representative of the country
- The study participants included adult men and women age 18-60 years of age. Pregnant and lactating mothers and children were excluded from the study.
- In Jodhpur and Kinnaur site very few patients have been identified with severe and moderate anaemia
- Study was conducted in hot humid and very cold conditions in high altitude area but device assessment could not be done in very high temperature conditions.
- The cost of the devices were taken as the quotations received from device manufacturers

Conclusions and recommendations:

Based on the study findings and analysis, the following conclusions were arrived at:

- Invasive devices shows overall better performance than Non-invasive devices in the field settings.
- For screening of Anemia, HemoCue (AUC 0.92, 95% CI 0.88-0.94) and True Hb (AUC 0.85, 95% CI 0.83-0.89) are comparable with no statistically significant difference between the two.
- For screening of Severe Anemia, TrueHb (AUC 0.91, 95% CI 0.85-0.97) fares better than all other devices including HemoCue (AUC 0.73, 95% CI 0.67-0.79)
- Both True Hb and HemoCue overestimates Hb in extreme cold weather conditions.
- Overall it appears that TrueHb is better than HemoCue in estimating Hb including severe anemia

Every device has a scope of improvement. The points that requires attention for further improvisation are summarized below.

Hemo-cue	True Hb	Masimo	AJO
Good accuracy for anemia but not for severe anemia. Needs validation for Hb less than 7 gm%, humid and cold temperatures. Evaluation required after 2 years of usage to assess accuracy. Data storage facility to be introduced	Good accuracy for anemia and severe anemia.. Needs validation for Hb in cold temperatures. Evaluation required after 2 years of usage to assess accuracy. Data (only Hb readings) gets stored. Facilities for storing other details to be introduced	Accuracy gets affected at Hb less than 7 gm% (severe anemia) and with hemoglobinopathies . Data storage and retrieval good	Needs validation at different levels of Hb, device needs to be customized for field settings. Data storage and retrieval possible

The findings of the study were shared and endorsed by all the Investigators, Ministry of Health and Family Welfare and Department of Health Research (Annexures 4,5)

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2. Worldwide prevalence of anaemia 1993-2005. WHO, (VMNIS) VaMNIS; 2008 Contract No.: Report.
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ANNEXURES

Annexure 1: Approval from Ethics Committees

INSTITUTE ETHICS COMMITTEE
ALL INDIA INSTITUTE OF MEDICAL SCIENCES
Room No 102, 1st Floor Old O.T. Block,
ANSARI NAGAR, NEW DELHI 110029
Tel.No.4579 (Internal), 26594579 (Direct)

Date: 11-01-2018

Dr. Renu Saxena,
Professor & Head,
Deptt. of Haematology,
AIIMS, New Delhi.

Ref. No.: IEC/NP-416/09.10.2015, OP-2/09.02.2017, OP-19/29.12.2017
Sub: Diagnostic efficacy of digital hemoglobinometer (TrueHb), HemoCue and non invasive spectroscopic devices for screening patients for anemia in the field settings

Dear Dr. Saxena

This has reference to your above mentioned project. The project was discussed in the Ethics Committee meeting held on 29-12-2017 at 4:00 P.M. in the Ethics Committee Room, AIIMS & the following members of the Ethics Committee attended the meeting:

1.	Dr. T.P. Singh , Distinguish Research Professor, Dept. of Biophysics,	Chairman
2.	Dr. D.R. Saini, Lay Person, Director, DPS Society New Delhi-	Member
3.	Mr. Rajan Khosla, LLB,- Member Ethics Committee, Legal Person –	Member
4.	Dr. S.K. Maulik, Professor, Deptt. of Pharmacology, AIIMS, -	Member
5.	Dr. Ramanjit Sihota, Professor, Deptt. Of R.P. Centre, AIIMS -	Member
6.	Dr. V. Sreenivas, Professor, Deptt. of Biostatistics -	Member
7.	Dr. Pratap Saran, Professor, Deptt. of Psychiatry, AIIMS -	Member
8.	Dr. Pramod Garg, Professor, Deptt. of Gastroenterology, AIIMS -	Member
9.	Dr. Sameer Bakhshi, Prof., Deptt. of Medical Oncology, AIIMS -	Member Secretary

The following documents have been submitted for ethical approval

Change of Title to:

- "Diagnostic efficacy of digital hemoglobinometer (TrueHb), HemoCue and non invasive spectroscopic devices for screening patients for anemia in the field settings"
- Inclusion of comparison of non invasive method alongwith HemoCue and digital hemoglobinometer in objectives and methodology

The Documents have been approved from ethical angle w.e.f 29.12.2017 subject to the following conditions:

- The approval is valid for the period of the conduct of study according to this protocol under the responsibility **Dr. Renu Saxena,** Principal Investigator.
- It is hereby confirmed that neither you nor any of the study team members have participated in the voting/decision making procedures of the committee.
- No significant changes to the research protocol should be made and implemented without prior consent of the IEC and any changes/deviations from the protocol which increase the risk for the subjects should be submitted to the IEC and approved by it prior to implementation.
- The study progress report should be made available to the IEC for review every 6 months.
- IEC should be informed about all SAE's occurring in the study as per DCGI guidelines. The Study progress report should be made available to the IEC for review every 6 months

With Warm regards
Yours sincerely,

(Dr. Sameer Bakhshi)
Member Secretary Ethics Committee

INSTITUTIONAL ETHICS COMMITTEE
(Reg. No. – ECR/287/Inst/WB/2013)
MEDICAL COLLEGE, KOLKATA
88, COLLEGE STREET, KOLKATA 700073, WEST BENGAL, INDIA

Chairperson
Prof. S. K. Maitra

Member Secretary
Prof. A.K.Bhadra

Members

Prof. Aniruddha Sengupta
Prof. Debabrata Bandyopadhyay
Prof. Tapan Mukhopadhyay
Prof. Manideepa Sengupta
Prof. Suhrita Pal
Dr. Rudrajit Paul
Dr. NilayKanti Das
Mr. Hironlal Majumdar
Ms. Sebanti Bhattacharya
Ms. Suhrita Saha
Ms. Rehana Khatun
Mr. Ashok Kar

Ref No MC/KOL/IEC/ NON-SPON/65/04-2018 **Dated: 12.05.2018**

To,
Prof. Maitreyee Bhattacharyya,
Director IHTM,
Medical College & Hospital, Kolkata

Sub.: IEC- MCH Decision of the review of study ref No. nil , dated nil .

Study Title: Diagnostic efficacy of digital hemoglobinometer (TrueHb), HemoCueand non invasive devices for screening patients for anemia in the field setting – a proposal.

Dear Prof. Maitreyee Bhattacharyya,

In its meeting held on 12th May, 2018, the members of the IEC, Medical College, Kolkata, reviewed and discussed your proposal to conduct the above mentioned study in the Department of IHTM, Medical College & Hospital, Kolkata.

The following members of the committee were present (ticked against their names):
Chairperson: Prof. Susanta Kr. Maitra, Pharmacologist

Member Secretary: Prof. Ashok Kumar Bhadra, Principal, MCH

Members
Prof. Aniruddha Sengupta (Clinician)
Prof. Debabrata Bandyopadhyay (Clinician)
Prof. Tapan Mukhopadhyay (Basic Scientist)
Prof. Manideepa Sengupta (Basic Scientist)
Prof. Suhrita Pal (Pharmacologist)
Dr. Rudrajit Paul (Clinician)
Dr. NilayKanti Das (Clinician)
Mr. Hironlal Majumdar (Legal Expert)
Ms. Sebanti Bhattacharya (Philosopher)
Ms. Suhrita Saha (Sociologist)
Ms. Rehana Khatun (Medically Lay person)
Mr. Ashok Kar (Medically Lay person)

Page 1 of 2

INSTITUTIONAL ETHICS COMMITTEE
(Reg. No. – ECR/287/Inst/WB/2013)
MEDICAL COLLEGE, KOLKATA
88, COLLEGE STREET, KOLKATA 700073, WEST BENGAL, INDIA

Study Title: : Diagnostic efficacy of digital hemoglobinometer (TrueHb), HemoCueand non invasive devices for screening patients for anemia in the field setting – a proposal..

The committee has decided to:

☑Approve the study protocol in the present form.

☐Conditionally approve the study protocol subject to .....
.....
.....
.....

☐Reject the proposal for the following reasons .....
.....
.....
.....

You are required to:

i) Inform the committee about the progress of the study and compliance of ethical guidelines.

ii) Notify the committee regarding any serious adverse events occurring in the course of the study.

iii) Inform and seek approval of the committee about any changes in the protocol prior to their implementation.

iv) Submit the final report to the committee in every case.

This Ethics committee is working in accordance with the ICH-GCP, Schedule Y and ICMR guidelines and other applicable regulations.

Yours truly,

Chairperson / Member Secretary
IEC
Medical College, Kolkata

Member Secretary
Institutional Ethics Committee
Medical College, Kolkata

INDIAN INSTITUTE OF PUBLIC HEALTH DELHI

Institutional Ethics Committee (IEC)

Organization No : NA
DHRP Assurance No : NA

IRB No : NA
Expiration Date : NA

Protection of Human Subjects
IEC Certification/Declaration of Exemption

1. Request Type	2. Type of Mechanism	3.Name of Funding Agency and, if known, Application or Proposal Identification No.
☒ ORIGINAL ☐ CONTINUATION ☐ EXEMPTION	☒ GRANT ☐ CONTRACT ☐ FELLOWSHIP ☐ COOPERATIVE AGREEMENT ☐ OTHER:NA	**Yes, Department of Health and Research**

4. Title of Application or Activity	5. **Principal Investigator:**
"Diagnostic efficacy of digital hemoglobinometer (TrueHb), HemoCue and non invasive devices for screening patients for anemia in the field settings"	**Prof. RenuSaxena** 6. Key Personnel at IIPHD & Role : DrSutapaNeogi

7. Certification of IRB Review

☒ This activity has been reviewed and approved by the IEC in accordance with the Indian Council for Medical Research (ICMR) Guidelines and other GCP recommendations.
by: ☐ Full IRB Review on [DD/MONTH/YYYY] or ☒ Expedited Review on 05-04-2017 [DD/MONTH/YYYY]

☐ This activity contains multiple projects, some of which have not been reviewed. The IEC has granted approval on condition that all projects covered by the Indian Council for Medical Research Guidelines will be reviewed and approved before they are initiated and that appropriate further certification will be submitted.

8. Comments
None

9. The official signing below certifies that the information provided above is correct and that, as required, future reviews will be performed until study closure and certification will be provided.	10. Name and Address of Institution: Institution Ethics Committee Indian Institute of Public Health, Delhi Plot no 47, sector 44, Gurgaon, Haryana, India
11. Phone No. :+91- 0124- 4722900 12. Fax No. : +91- 0124- 4722901 13. Email : rmpandey@yahoo.com rmpandey@aiims.ac.in	
14. Name of Official: Dr R M Pandey	15. Title: Chair Person, Institutional Ethics Committee, IIPH-Delhi and Professor & Head – Department of Biostatistics, AIIMS, Delhi, India
16. Signature Rmpandey	17. Date 21/04/2018

डॉ० आर० एम० पाण्डेय / Dr. R. M. Pandey
आचार्य एवं विभागाध्यक्ष / Professor & Head
जैव सांख्यिकी विभाग / Deptt. of Biostatistics
अखिल भारतीय आयुर्विज्ञान संस्थान / A.I.I.M.S.
अंसारी नगर / Ansari Nagar
नई दिल्ली-29 / New Delhi-29

जवाहरलाल स्नातकोत्तर आयुर्विज्ञान शिक्षा एवं अनुसंधान संस्थान
JAWAHARLAL INSTITUTE OF POSTGRADUATE MEDICAL EDUCATION & RESEARCH
(स्वास्थ्य एवं परिवार कल्याण मंत्रालय, भारत सरकार के अधीन राष्ट्रीय महत्व का संस्थान)
भारत सरकार / GOVERNMENT OF INDIA
(An institution of National Importance under Ministry of Health & Family Welfare)
धनवंतरी नगर , पुडुचेरी / Dhanvantari Nagar, Puducherry – 605006
Website: www.jipmer.edu.in
सत्यमेव जयते
Phone: 0413 – 2296101
Fax: 0413 – 2272067, 2272735

INSTITUTIONAL ETHICS COMMITTEE (HUMAN STUDIES)
CERTIFICATE

Date: 26/09/2018

To,

Dr. Rakhee Kar, Additional Professor,
Department of Pathology,

Ref: Your project no. **JIP/IEC/2018/0288** entitled, **"Diagnosis efficacy of digital hemoglobinometer (TrueHb), HemoCue and noninvasive devices for screening patients for anemia in the field settings."**

Dear Dr. Rakhee Kar,

The following documents of the above mentioned project were reviewed and approved through a **full board review** process.

1. Research Protocol
2. Consent form
3. Participant Information Sheet
4. Copy nof signed original protocol in multicentric study
5. Copy of signed consent letter from coordinator in multicentric study
6. JSAC Certificate
7. Participant information sheet
8. CV of Principal Investigator and Co- Investigator

It is understood that the study will be conducted by Dr. Rakhee Kar, Additional Professor, Department of Pathology (Principal Investigator), with Dr. Sitanshu Sekhar Kar, Additional Professor, Department of Preventive and Social Medicine (Co- Investigator) in a total of **600** research participants, as per the submitted protocol.

The IEC approves the above mentioned study.

This approval is valid for three years, the entire duration of the project or a shorter period based on the risk whichever is less.

It is the policy of IEC that, it be informed about any onsite serious adverse event or any unexpected adverse event report within 24 hours as per the formats specified in SOP 09 to IEC or by email if there is holiday. The report of SAE or death after due analysis shall be forwarded

by the Investigator to the chairman of IEC and the head of the institution where the trial is been conducted within 14 calendar days of SAE or death.

In case of injury or death of participant(s) occurring during the trial, the sponsor (whether a pharmaceutical company or an institution) or his representative, whosoever had obtained permission from the Licensing Authority for conduct of the clinical trial shall make payments for medical management of the subject and also provide financial compensation for the clinical trial related injury or death.

No deviations from, or changes of the protocol and Informed Consent Document should be initiated without prior written approval by the IEC of an appropriate amendment. The IEC expects that the investigator should promptly report to the IEC any deviations from, or changes of, the protocol to eliminate immediate hazards to the research participants and about any new information that may affect adversely the safety of the research participants or the conduct of the trial.

For studies which will continue for more than a year, a continuing review report needs to be submitted (within 1 month of the due date i.e. 11 months from the date of approval) on or before 19/08/2019.

A copy of the final report should be submitted to IEC for review.

Sincerely yours

Medha R.

Dr. Medha R.,
Member Secretary
Date of approval of the study: 20/09/2018

Member Secretary
Institutional Ethics Committee
(Human Studies),
JIPMER, Puducherry

Copy to:
Principal Investigator: Dr. Rakhee Kar, Additional Professor, Department of Pathology
Co- Investigator: Dr. Sitanshu Sekhar Kar, Additional Professor, Department of Preventive and Social Medicine

Annexure 2: Diagnostic accuracy results using WHO classification of anemia

A. Diagnostic Accuracy Parameters for testing anemia and no anemia by Lab technicians as per WHO classification

Device	Sensitivity % (95% CI)	Specificity % (95% CI)	Positive predictive value (PPV) (95% CI)	Negative Predictive value (NPV) (95% CI)	Positive likelihood ratio (LR+) (95% CI)	Negative likelihood ratio (LR-) (95% CI)	Area under ROC (95% CI)
Hemocue (venous)	83.4 (79.1-87.1)	96.6 (93.9-98.3)	96.4 (93.7-98.2)	83.9 (79.8-87.5)	24.18 (13.5-43.3)	0.17 (0.14-0.22)	0.90 (0.88-0.92)
True Hb (venous)	89.4 (85.8-92.3)	77 (72.2-81.3)	80.8 (76.7-84.5)	87 (82.7-90.6)	3.89 (3.20-4.73)	0.14 (0.10-0.19)	0.83 (0.80-0.86)
Masimo Device	71.5 (66.6-76)	84.8 (80.3-88.7)	85.1 (80.6-88.9)	71 (66-75.6)	4.71 (3.58-6.19)	0.34 (0.28-0.40)	0.78 (0.75-0.81)
Spectroscopic Device	57.8 (52.1-63.4)	62.6 (57.3-67.1)	57.5 (51.7-63.1)	62.9 (57.6-68)	1.55 (1.31-1.82)	0.67 (0.58-0.79)	0.60 (0.56-0.64)

B: Diagnostic Accuracy Parameters for testing anemia and no anemia by ANM/ frontline workers as per WHO classification

Device	Sensitivity % (95% CI)	Specificity % (95% CI)	Positive predictive value (PPV) (95% CI)	Negative Predictive value (NPV) (95% CI)	Positive likelihood ratio (LR+) (95% CI)	Negative likelihood ratio (LR-) (95% CI)	Area under ROC (95% CI)
Hemocue (capillary)	86.7 (82.7-90.1)	87.4 (83.2-90.8)	88.3 (84.4-91.5)	85.8 (81.5-89.5)	6.87 (5.13-9.21)	0.15 (0.12-0.20)	0.87 (0.85-0.90)
True Hb (capillary)	84.1 (79.9-87.7)	95.9 (71-80.3)	78.4 (73.9-82.4)	82.1 (77.4-86.1)	3.48 (2.87-4.23)	0.21 (0.16-0.27)	0.80 (0.77-0.83)
Masimo Device	71.5 (66.4-76.2)	89.6 (85.6-92.8)	88.8 (84.5-92.3)	73.2 (67.3-77.6)	6.87 (4.89-9.66)	0.32 (0.27-0.38)	0.81 (0.78-0.84)
Spectroscopic Device	61 (55.3-66.5)	70.7 (65.7-75.4)	64.4 (58.5-69.9)	67.7 (62.6-72.4)	2.08 (1.73-2.51)	0.55 (0.47-0.64)	0.66 (0.62-0.69)

C: Diagnostic Accuracy Parameters for testing severe anemia by Lab Technicians as per WHO classification

Device	Sensitivity % (95% CI)	Specificity % (95% CI)	Positive predictive value (PPV) (95% CI)	Negative Predictive value (NPV) (95% CI)	Positive likelihood ratio (LR+) (95% CI)	Negative likelihood ratio (LR-) (95% CI)	Area under ROC (95% CI)
Hemocue (venous)	64.9 (55.2-73.7)	99.8 (99-100)	98.6 (92.6-100)	93.5 (91.2-95.3)	365.2 (51.2-2600.4)	0.35 (0.27-0.45)	0.82 (0.79-0.87)
True Hb (venous)	88.2 (78.1-94.8)	95.7 (93.9-97.1)	68.2 (57.4-77.7)	98.7 (97.5-99.5)	20.7 (14.2-30.05)	0.12 (0.06-0.24)	0.92 (0.88-0.96)
Masimo Device	37.1 (27.1-48)	99.5 (98.5-99.9)	91.7 (77.5-98.2)	91.2 (88.7-93.3)	71.93 (22.5-229.6)	0.63 (0.54-0.74)	0.68 (0.63-0.73)
Spectroscopic Device	31.1 (19.9-44.3)	93.9 (91.7-95.7)	34.5 (22.2-48.6)	93 (90.7-94.9)	5.15 (3.16-8.40)	0.73 (0.62-0.87)	0.63 (0.57-0.68)

D: Diagnostic Accuracy Parameters for testing <u>severe anemia</u> by ANM/ frontline workers as per WHO classification

Device	Sensitivity % (95% CI)	Specificity % (95% CI)	Positive predictive value (PPV) (95% CI)	Negative Predictive value (NPV) (95% CI)	Positive likelihood ratio (LR+) (95% CI)	Negative likelihood ratio (LR-) (95% CI)	Area under ROC (95% CI)
Hemocue (capillary)	62.6 (52.7-71.8)	100 (99.3-100)	100 (94.6-100)	93.3 (91-95.2)	-	0.37 (0.29-0.48)	0.81 (0.77-0.86)
True Hb (capillary)	93.8 (84.8-98.3)	94.4 (92.3-96)	62.5 (52-72.2)	99.3 (98.3-99.8)	16.61 (12.02-22.96)	0.07 (0.03-0.17)	0.94 (0.91-0.97)
Masimo Device	34.6 (24.3-46)	99.6 (98.7-100)	93.3 (77.9-99.2)	91.3 (88.8-93.4)	96.9 (23.5-399.3)	0.66 (0.56-0.77)	0.67 (0.62-0.72)
Spectroscopic Device	27.6 (16.7-40.9)	92.5 (90.1-94.5)	26.2 (15.8-39.1)	93 (90.6-94.9)	3.67 (2.2-6.07)	0.78 (0.67-0.92)	0.60 (0.54-0.66)

Annexure 3: Assesment of user friendliness for every device

Usability Tool (Lab Technician)

1= Poor, 2= Below average, 3= Average, 4= Above Average, 5= Excellent

Parameters	Hemocue	TrueHb	Spectroscopic Device	Masimo
Ease of Use	5	3	3	5
Efficiency in daylight	4	3	3	4
Portability	4	4	2	5
Convenience to Patient	5	4	2	5
Need for Power/Battery	4	4	2	4
Average time taken for performing one test	5	2	3	4
Expertise required	5	5	2	4
Total Score (out of 35)	32	25	17	31

Usability Tool (ANM)

1= Poor, 2= Below average, 3= Average, 4= Above Average, 5= Excellent

Parameters	Hemocue	TrueHb	Spectroscopic Device	Masimo
Ease of Use	4	4	3	4
Efficiency in daylight	4	5	3	4
Portability	5	5	2	4
Convenience to Patient	5	4	2	5
Need for Power/Battery	5	5	2	4
Average time taken for performing one test	5	3	3	4
Expertise required	5	4	2	4
Total Score (out of 35)	33	30	17	29

Annexure 4: Minutes of the 1st National level meeting meeting held on 18th December AIIMS for the Hb project.

- Dr Renu saxena welcomed all the members of the group. Dr Dinesh Baswal gave opening remarks. Site wise progress of work along with strengths and weaknesses of the devices were presented by Dr Sitanshu Kar and Dr Maitreyee

Date of Meeting : 18/12/2018	**Time** : 10.00-1.00pm
Meeting Facilitator : Dr.Renu Saxena	**Location:** Department of Hematology**,** AIIMS- New Delhi
Attendees: 1. Dr Dinesh Baswal- DC Maternal Health-MOHFW 2. Dr Tushar Purohit- MOHFW 3. Dr Jyoti Singh Baghel- MOHFW 4. Dr Kavitha Rajsekhar- DHR 5. Dr Amir Suhail- DHR 6. Dr. Renu Saxena - AIIMS 7. Dr. Sudha Sazawal - AIIMS 8. Dr. Maitreyee Bhattacharya – Kolkata Medical College 9. Dr. Sitanshu Kar – JIPMER 10. Dr. Sutapa B.Neogi - PHFI 11. Dr. Jyoti Sharma - PHFI 12. Dr. Nausheen Zaidi – PHFI 13. Dr Kartavya Tiwari-PHFI 14. Mr Kamal Kishor- AIIMS	

Bhattacharya.

- Dr Sutapa presented the findings of interim analysis. Following suggestions were made -

In addition to parameters already discussed following information should be incorporated

- Temp, humidity, minimum training time, compatibility to local language, minimal risk of contamination, time to show result, size and weight of the device, maintenance process and cost, loading guns for capillary pricking.
- strip wastage per test, strip storage conditions , how many test can be done with one set of batteries, need for recalibration after how many tests
- Out of venous and capillary, which is more sensitive for moderate and severe anaemia.
-

Additional analysis to present

- False positives and false negatives.
- Anaemia categorization would be No and mild anaemia, moderate and severe anaemia.
- Agreement should be presented as venous V/s capillary.
- Mean difference and CI for venous V/s capillary for devices and auto-analyzer.
- Sub analysis to see accuracy of devices for diabetic and hypertensive patients.
- Overall feasibility of devices for ANMs (To be done in JIPMER)

Timelines

- Study needs to be completed by Feb end and report to be submitted by March.
- Cost effectiveness analysis should be completed by 15th February 2019.
- Final national level meeting will be held in the last week of February 2019 (26th February 2019).

Sites for Phase 2 B will be Uttarakhand and Jodhpur

- Only invasive devices will be tested with sample size of 100/ device/ site.
- Training for the site investigators and ANMS will be done in December last week or Early Jan 2019
- It is proposed that IEC approval process for both the sites will be initiated immediately by the site in consultation with AIIMS Delhi.

- It was brought up that the remaining funds may be utilized for manuscript and report writing
- It was suggested that one month no cost extension for the project would be required to complete financial and administrative processes.

Annexure 5 : Minutes of the 2nd National level meeting meeting held on 22nd March 2019 at AIIMS for the Hb project.

Diagnostic efficacy of digital hemoglobinometer (TrueHb), HemoCue and non-invasive Devices for screening patients for anaemia in the field settings.

Minutes of Second National Level Meeting

Date of Meeting : 22/03/2019	**Time** :11.00-1.00pm
Meeting Facilitator : Dr. Renu Saxena	**Location:**Department of Hematology, AIIMS-New Delhi

Attendees:

1. Dr.Renu Saxena-AIIMS
2. Dr.Tushar Purohit- MOHFW
3. Dr. Kavitha Rajshekhar-DHR
4. Dr. Amir Suhail- DHR
5. Dr. Arvind Bhushan-DHR
6. Dr.Sudha Sazawal - AIIMS
7. Dr. Sutapa B. Neogi - PHFI
8. Dr. Jyoti Sharma - PHFI
9. Dr. Nausheen Zaidi – PHFI
10. Mr. Kamal Kishor- AIIMS

Regrets :

1. Dr. Dinesh Baswal
2. Dr. Maitreyee Bhattacharya
3. Dr. Rakhee Kar
4. Dr. Abhishek Purohit

- Dr. Renu Saxena welcomed all the members of the group.
- Dr. Sutapa presented the findings of the final analysis.

Following points were discussed and suggestion made:-

- It was suggested to include the median and range of temperature and humidity of all the participating sites.
- It was suggested to show the characteristics of ANM/Field workers of the participating sites for difference in efficiency such as their age difference, level of education.
- Assumptions for cost effective analysis to be included.
- A comparison slide of the devices with respect to all the user friendly parameters needs to be included in the presentation.
- The Device manufacturers should be requested to provide their certification by CLAA or FDA along with the confirmatory assessment process.
- Limitations of the devices as well as the study should be mentioned.
- Quality Assurance of the device as well as their management needs to be sought from the manufacturers.
- It was suggested that biomedical waste management for all the devices should be included.
- Features(like Training time, contamination, device weight, portability & time to show the reading) of all the participating Devices should also be presented.
- Performance of devices in moderate and severe anemias one category should also be included in the analysis.

Saxena 22.3.19

22/3/2019