Systematic review and meta-analysis of method comparison studies of Masimo pulse co-oximeters (Radical-7™ or Pronto-7™) and HemoCue® absorption spectrometers (B-Hemoglobin or 201+) with laboratory haemoglobin estimation

R. Hiscock*, D. Kumar†, S. W. Simmons‡

Summary

We assessed agreement in haemoglobin measurement between Masimo pulse co-oximeters (Rad-7™ and Pronto-7™) and HemoCue® photometers (201+ or B-Hemoglobin) with laboratory-based determination and identified 39 relevant studies (2915 patients in Masimo group and 3084 patients in HemoCue group). In the Masimo group, the overall mean difference was -0.03 g/dl (95% prediction interval -0.30 to 0.23) and 95% limits of agreement -3.0 to 2.9 g/dl compared to 0.08 g/dl (95% prediction interval -0.04 to 0.20) and 95% limits of agreement -1.3 to 1.4 g/dl in the HemoCue group. Only B-Hemoglobin exhibited bias (0.53, 95% prediction interval 0.27 to 0.78). The overall standard deviation of difference was larger (1.42 g/dl versus 0.64 g/dl) for Masimo pulse co-oximeters compared to HemoCue photometers. Masimo devices and HemoCue 201+ both provide an unbiased, pooled estimate of laboratory haemoglobin. However, Masimo devices have lower precision and wider 95% limits of agreement than HemoCue devices. Clinicians should carefully consider these limits of agreement before basing transfusion or other clinical decisions on these point-of-care measurements alone.

Key Words: haemoglobin, oximetry

The ability to rapidly and accurately determine the haemoglobin concentration of a patient can be useful or even critical in many clinical scenarios and this has resulted in the development of point-of-care (POC) devices aimed at meeting this goal. Current, non-invasive technologies include pulse co-oximetry (Pulse CO-Oximetry™; Masimo Corp., Irvine, CA, USA), occlusion spectroscopy (OrSense™, Ness Ziona, Israel) and transcutaneous reflection spectroscopy (Haemospect, MBR Optical Systems, Herdecke, Germany)[1]. Invasive technologies (requiring a blood sample) include absorption photometry both reagent (HemoCue®, HemoCue, Angelholm, Sweden) and non-reagent based (DiaSpect Haemoglobinometry, DiaSpect Medical GmbH, Germany) and conductivity based (i-Stat, Abbott Laboratories, Abbott Park, IL, USA)[2]. We focus here on Masimo pulse co-oximetry and HemoCue photometry. HemoCue devices are based upon invasive blood sampling (venous, capillary or arterial blood), where blood is loaded into a cuvette and undergoes chemical conversion to azide-haemoglobin with the concentration then measured by absorption photometry at two wavelengths (570 and 880 nm). These were first released in the mid-1980s and the technology (Hb 201+ system) improved in 2002[3]. Non-invasive transcutaneous pulse co-oximetry has been developed to measure total haemoglobin and its components (oxy, carboxy and met moieties) with one manufacturer, Masimo Corp., developing both continuous (Radical-7™) and intermittent (Pronto-7™) devices from 2008[3]. The two devices use different algorithms and only the continuous reading Radical-7 provides estimates of carboxy and methaemoglobin moieties[1]. This has led to the performance and publication of comparison studies to assess the accuracy of these POC technologies compared to laboratory-based methods, with the aim of determining if they provide a clinically useful substitute. It is important in these method comparison studies that both design and statistical analysis take account of the error in measurement of haemoglobin by both the established laboratory and the newer POC techniques. The two major statistical techniques used are the Bland–Altman agreement method[4,5] and linear mixed methods variance component modelling[6].

We undertook a systematic review and meta-analysis with the aim of assessing the bias and precision of these two POC methods (HemoCue photometry and Masimo pulse co-oximetry) in determining total haemoglobin concentration from published method comparison studies.

* MBBS FANZCA GradDipMedStat, Consultant Anaesthetist, Department of Anaesthesia, Mercy Hospital for Women, Heidelberg, Victoria
† MBBS MD FCARCSI DipHealthMgt, Clinical Fellow, Department of Anaesthesia, Mercy Hospital for Women, Heidelberg, Victoria
‡ MBBS FANZCA MBA, Head of Unit, Department of Anaesthesia, Mercy Hospital for Women, Heidelberg and Clinical Associate Professor, Department of Pharmacology, University of Melbourne, Victoria
Address for correspondence: Dr Richard Hiscock. Email: richardjhiscock@gmail.com
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Method

The literature search was limited to method comparison studies assessing agreement in haemoglobin determination between either Masimo Corp. pulse co-oximeters (continuous reading Radical-7 or intermittent Pronto-7) or HemoCue (Hb 201+, B-Hemoglobin systems) and laboratory-based determination. We performed an Ovid MEDLINE search (final search 20 May 2014) using MeSH terms—h(a)emoglobins, h(a)emoglobinometry, method comparison, point-of-care systems, oximetry—and keyword terms—non-invasive, continuous, co-oximetry, HemoCue, 201+, Masimo, Radical-7, Rad-7 and Pronto-7—published in English, in or after 1985 and performed on human subjects. Abstracts were not included and unpublished studies were not sought. We also searched reference lists of all accepted articles. Determination of each study's eligibility, performed independently by the authors, was initially based upon details presented in the abstract followed by full-text retrieval of all possible studies.

We defined the following eligibility criteria for studies to be included in this review. Exclusion criteria were 1) subjects aged less than two years old, 2) capillary-based sampling method (HemoCue device only), 3) data presented that did not allow extraction of summary measures (see later) and 4) where within-subject replicate sampling was performed, no adjustment for repeated measures had been performed. On the basis that, if within-subject replicates are treated as independent, then the estimation of difference standard deviation (SD_{diff}) is too small, resulting in falsely higher precision[5,7]. If no such adjustment was made, then baseline data (first reading performed) was used where possible. All excluded articles and reason for exclusion are stated in the results. To assess the quality of included trials, we performed an analysis based upon the four risks of bias and three applicability concern domains found in the revised Quality Assessment of Diagnostic Studies (QUADRAS-2) guidelines[8]. Questions were tailored to method comparison outcomes (see Appendix 1 for questionnaire details). Data extraction was performed independently, with any disagreement referred to one of the authors for adjudication.

Study characteristics extracted for all studies were year of publication, number of subjects, age group of subjects (adult, child), laboratory haemoglobin minimum and maximum values (g/dl) and adjustment for within-subject replication. Laboratory-based methods used either chemical conversion of all haemoglobin moieties followed by absorption photometry, (classified as direct cyanomethaemoglobin analysis [HiCN], automated analysis using cyano/sodium lauryl sulphate haemoglobin conversion [eHiCN]) or absorption spectrophotometric analysis (co-oximetry) as used in standard blood gas analysers. Additional details recorded for Masimo pulse co-oximeters were software program and probe hardware versions and for HemoCue photometers model type (Hb 201+, B-Hemoglobin and unknown). The outcome details, in g/dl extracted, were mean haemoglobin difference (device versus laboratory) and SD_{diff}. If mean difference ($mean_{diff}$) and SD_{diff} were not presented in the text, then this was estimated from the difference against average graph or text using upper and lower 95% Limits of Agreement (LOA) where these were presented. The SD_{diff} was then calculated from 95% LOA as $(LOA_{upper}–LOA_{lower})/3.92$. For these individual studies, bias was assessed by the 95% confidence interval of the $mean_{diff}$–$1.96×SD_{diff}$) and agreement by 95% LOA ($mean_{diff}$–$1.96×SD_{diff}$).

Conceptually, individual studies constitute a random sample of all possible studies for each device (modelled using within device random effect) and we considered devices as fixed (modelled using between device fixed effect). Therefore, we performed mixed-effect (random effect within subgroup and fixed effect across subgroup) meta-analyses[9] for each method against the corresponding laboratory haemoglobin to provide pooled estimates of $mean_{diff}$ and SD_{diff} as described by Williamson[10]. Pooled bias was then assessed by the 95% prediction intervals of the mean difference and pooled agreement by 95% LOA based upon the pooled SD. These prediction intervals are wider than pooled 95% confidence interval because they include an estimate of the true variability between studies under the random effects model[9].

Between-study heterogeneity was identified using Q and I^2 statistics, both within subgroups and across all studies[9] based upon model device—HemoCue (B-Hemoglobin, 201+ and unknown) and Masimo (Pronto-7 & Rad-7). Stata version 13 (StataCorp. 2013. Stata Statistical Software. College Station, TX, USA) and Comprehensive Meta Analysis version 2.2.064 (Biostat. Englewood, NJ, USA) software were used to perform statistical analysis.

Table 1
Details of excluded studies

Reason	Number	Studies
Capillary sample (including heel prick) studies used HemoCue devices only	12	14, 17, 45–54
Capillary sample (including heel prick) studies used HemoCue and Masimo devices (Masimo data included in meta-analysis)	6	20, 23, 24, 55–57
No adjustment for repeated measures	13	15, 18, 34, 58–67
Subjects aged less than 2 years	5	53, 68–71
Summary data (mean difference and SD of difference) not presented or extractable	11	72–82

Results

Database and reference searches, after title and abstract assessment, identified 81 articles published between 1988 and 2010 for both HemoCue and Masimo devices. Fifty-two articles were obtained from the MEDLINE database and 28 from reference listings alone and one was our own paper. From these, 39 method comparison studies were identified as having met inclusion criteria after assessment of the full text article. Reasons for exclusion are presented in Table 1.

We found 24 studies (Table 2), published from 2011 onwards, comparing Masimo pulse co-oximetry (18 Radical-7 continuous and 6 Pronto-7 intermittent) against co-oximetry (8), laboratory cyano/sodium lauryl sulphate haemoglobin conversion (14) and unspecified (2). There were 19 studies (Table 3), based on venous or arterial blood samples, published from 1995 (12 from 2010) onwards, comparing HemoCue photometry devices (HemoCue Hb 201+ [6], B-Hemoglobin [4] and unidentified [9]) against co-oximetry (1) and laboratory cyano/sodium lauryl sulphate haemoglobin conversion (18). Blood samples analysed were venous (14) or arterial (5). Modified QUADRAS-2 analysis of included studies is presented in Table 4.

In the Masimo group (Table 2 and Figure 1), the number of subjects analysed was 2915, with 1516 (52%) using Radical-7 and 1399 (48%) using Pronto-7 devices. The overall pooled $mean_{diff}$ (device versus laboratory) was -0.03 g/dl (95% prediction interval -0.30 to 0.23), SD 1.42 g/dl and associated 95% LOA -3.0 to 2.9 g/dl (Table 5). In the HemoCue group (Table 3 and Figure 2) the number of subjects analysed was 3084 with 669 (21.7%) using 201+, 1038 (33.7%) B-Hemoglobin and in 1377 (44.6%) the model was not identified. The overall pooled $mean_{diff}$ was 0.08 g/dl (95% prediction interval -0.04 to 0.20), SD 0.64 g/dl and associated pooled 95% LOA -1.3 to 1.4 g/dl (Table 5).

Based upon overall pooled 95% prediction intervals for the $mean_{diff}$, both methods provide unbiased pooled estimates of laboratory haemoglobin. However, the B-Hemoglobin device exhibits fixed bias with a pooled $mean_{diff}$ of 0.53 g/dl (95% prediction interval 0.27 to 0.78). Precision is more than two times higher (SD_{diff} smaller) for HemoCue compared to Masimo technologies. These differences directly translate to the wider pooled 95% LOA for Masimo devices, both overall and within subgroups (Table 5). Heterogeneity in summary estimates, both overall and between subgroups for the HemoCue and Masimo models, based upon the Q-statistic and associated *P*-values are presented in Table 5. Subgrouping by model removed heterogeneity only for the HemoCue 201+ device. The I^2 statistic indicates a moderate level of heterogeneity within the HemoCue 201+ subgroup but marked heterogeneity for all other comparisons.

Table 2

Details of Masimo pulse co-oximetry (continuous Rad-7 and intermittent Pronto-7) against laboratory haemoglobin method comparison studies

Study (First Author)	Year	No. of partici-pants	Adult/ child	$Mean_{diff}$ (device–lab) (g/dl)	SD of difference (g/dl)	95% CI of $mean_{diff}$ (g/dl)	95% LOA (g/dl)	Hb Lab range[source] (g/dl) *	POC soft-ware	POC hardware	Laboratory hardware	Replicates used in analysis
Al-Khabori†[36]	2013	98	Adult	0.9	1.7	0.56–1.24	-2.5–4.3	5.3–13.0	?	Pronto-7	eHiCN	No, initial
Al-Khabori[42]	2014	106	Adult	0.2	1.2	-0.03–0.43	-2.2–2.6	11.5–17.0	?	Pronto-7	eHiCN	No, initial
Applegate[25]	2012	91	Adult	0.50	1.44	0.20–0.80	-2.3–3.3	~6–~16[a]	?	Rad-7 Rev E	Co-oximeter	Yes
Belardinelli[56]	2013	463	Adult	-0.53	1.04	-0.63–-0.44	-2.6–1.5	~11–18[v]	?	Pronto-7 4D	eHiCN	No
Berkow§[26]	2011	29	Adult	-0.10	1.0	-0.46–0.26	-2.1–1.9	6.9–13.9[a/v]	7.6.0.1	Rad-7 Rev E	Co-oximeter	Yes
Butwick†[27]	2012	50	Adult	1.22	1.08	0.92–1.52	-0.9–3.3	~10.5–15.5[v]	7.6.0.4	Rad-7 Rev E	eHiCN	Yes
Colquhoun[28]	2012	20	Adult	-1.27	1.93	-2.12–-0.42	-5.0–2.5	~7–~ 14.5[a]	7.6.2.1	Rad-7 Rev E	Co-oximeter	Yes
Coquin[20]	2012	33	Adult	-1.00	1.88	-1.64–-0.36	-4.7–2.7	6.8–16.2[v]	7.6.0.1	Rad-7 Rev ?	Co-oximeter	Yes
Frasca[21]	2011	62	Adult	0.00	0.51	-0.13–0.13	-1.0–1.0	6.6–14.9[a]	7.6.0.1	Rad-7 Rev E	eHiCN	Yes
Gayat[34]	2011	276	Adult	-1.8	2.6	-2.11–-1.49	-6.9—3.3	4.8–21.0	7.4.0.9	Rad-7 Rev ?	eHiCN	No
Giraud[24]	2013	53	Adult	1.0	1.2	0.68–1.32	-1.4–3.4	6.8–16.3[a]	7.6.0.1	Rad-7 Rev E	eHiCN	Yes
Hiscock[19]	2014	140	Adult	1.18	1.19	0.98–1.38	-1.2–3.6	9.7–15.2	2.2.15	Pronto-7 Rev D	eHiCN	?
Isosu §[29]	2013	20	Adult	0.60	1.40	-0.01–1.21	-2.2–3.3	5.3–13.4[a]	7.4.0.9	Rad-7 Rev C	Co-oximeter	Yes
Knutson[44]	2013	127	Adult	-0.50	2.17	-0.88–-0.12	-4.7–3.8	~4–~15[v]	7.7.7.2	Rad-7 Rev D	?	No
Lamhaut[23]	2011	44	Adult	-0.02	1.39	-0.43–0.39	-2.7–2.7	7.0–16.5[a]	7.4.0.9	Rad-7 Rev C	eHiCN	Yes
Miller[30]	2011	20	Adult	0.26	1.79	-0.52–1.04	-3.2–3.8	~7.5–~16.5[a]	?	Rad-7 Rev E	Co-oximeter	Yes
Moore[35]	2013	418	Adult	-0.02	1.93	-0.21–0.17	-3.8–3.8	~ 4–18	?	Rad-7 Rev ?	?	No, initial
Nguyen (a)‡[22]	2011	14	Adult	-1.30	1.71	-2.20–-0.40	-4.6–2.1	6.4–13.0[a]	7.3.0.1	Rad-7 Rev ?	eHiCN	Yes
Nguyen (b)‡†[22]	2011	27	Adult	-1.70	2.04	-2.47–-0.93	-5.7–2.3	4.0–14.0[a]	7.3.1.1	Rad-7 Rev ?	eHiCN	Yes
Park[31]	2012	40	Child	0.90	1.35	0.48–1.32	-1.7–3.5	~7.5–~13.5[a]	7.6.1.1	Rad-7 Rev E	Co-oximeter	Yes
Raikhel[57]	2012	152	Adult	-0.50	1.02	-0.66–-0.34	-2.5–1.5	9.8–16.8[v]	7.8.0.1	Pronto-7 Rev G	eHiCN	No
Shah[55]	2013	440	Adult	-0.14	1.10	-0.24–-0.04	-2.3–2.0	8.6–17.4	2.19	Pronto-7 Rev E	eHiCN	No
Sjostrand§[83]	2013	25	Adult	-0.24	1.04	-0.65–0.17	-2.3–1.8	~9–~16[v]	7.6.0.1	Rad-7 Rev E	eHiCN	Yes
Skelton†[32]	2013	137	Adult	0.63	1.48	0.38–0.88	-2.3–3.5	~ 9–~15[v]	7.6.0.1	Rad-7 Rev E	eHiCN	No
Vos†[33]	2012	30	Adult	-0.17	1.00	-0.53–0.19	-2.2–1.8	7.4–15.3[v]	7.6.0.1	Rad-7 Rev E	Co-oximeter	Yes

*source: a=arterial, v=venous. †baseline (or first reading) only. ‡different software versions: (a) 7.3.0.1 (b) 7.3.1.1. §used readings with signal strength >50% or pulse index >1.4. $mean_{diff}$=mean difference, SD=standard deviation, CI=confidence interval, LOA=limits of agreement, POC=point-of-care.

Table 3

Details of HemoCue photometry against laboratory method comparison studies

Study (First Author)	Year	No. of partici-pants	Adult/ child	$Mean_{diff}$ (device – lab) (g/dl)	SD of difference (g/dl)	95% CI of $mean_{diff}$ (g/dl)	95% LOA (g/dl)	Hb Lab $range^{source}$ (g/dl)*	HemoCue system	Laboratory hardware	Replicates used in analysis
Adam[13]	2012	108	Adult	1.17	1.57	0.87–1.47	-2.0–4.3	8.1–15.0	B-Hemoglobin[v]	eHiCN	No
$Agarwal_{single}$ †[84]	2001	74	Adult	0.29	0.52	0.17–0.41	-0.7–1.3	~ 7–~16 [a]	B-Hemoglobin [a]	eHiCN	No
$Agarwal_{multiple}$ †[84]	2001	132	Adult	0.63	1.27	0.41–0.85	-1.9–3.2	~ 7–~16 [a]	B-Hemoglobin[a]	eHiCN	No
Bahadur[85]	2010	528	Adult	0.01	0.65	-0.05–0.07	-1.3–1.3	13.7 (1.48)	unknown[v]	eHiCN	No
Frasca[21]	2011	62	Adult	0.30	0.66	0.14–0.47	-1.0–1.6	6.6–14.9 [a]	Hb 201+[a]	eHiCN	Yes
Gehring‡[38]	2002	50	Adult	0.09	0.41	-0.02–0.20	-0.7–0.9	7.4–15.9 [a]	unknown[a]	HiCN	No
Giraud[24]	2013	53	Adult	0.15	0.20	0.10–0.20	-0.3–0.5	6.8–16.3 [a]	Hb 201+[a]	eHiCN	Yes
Hiscock[19]	2014	140	Adult	-0.01	1.34	-0.23–0.21	-2.7–2.7	9.7–15.2	Hb 201+	eHiCN	Yes
$McNulty_{in\ vivo}$ ‡[40]	1995	25	Adult	0.20	0.2	0.12–0.28	-0.2–0.6	4.2–20.7 [a]	unknown[a]	eHiCN	No
$McNulty_{in\ vitro}$ [40]	1995	10	Adult	-0.40	0.4	-0.65–-0.15	-1.2–0.4	4.2–20.7 [v]	unknown[v]	eHiCN	No
Mimoz[12]	2011	198	Adult	0.10	0.54	0.03–0.18	-1.0–1.1	~7–~16[a]	Hb 201+[a]	eHiCN	Yes
$Neufeld_{adult}$ [16]	2002	72	Adult	-0.47	0.54	-0.60–-0.35	-1.5–0.6	8.7–16.9[v]	unknown[v]	eHiCN	No
$Neufeld_{child}$ [16]	2002	72	Child	-0.31	0.63	-0.46–-0.16	-1.5–0.9	8.2–14.7[v]	unknown[v]	eHiCN	No
Nkrumah[86]	2011	398	Adult, Child	0.15	0.28	0.12–0.18	-0.4–0.7	2.4–20.4[v]	B-Hemoglobin[v]	eHiCN	No
Richards[87]	2010	50	Adult	-0.20	0.82	-0.43–0.03	-1.8–1.4	~7–~14[v]	unknown[v]	eHiCN	No
Rippman[41]	1997	140	Adult	-0.60	0.3	-0.65–-0.55	-1.2–0.0	5.1–16.7[a/v]	unknown[v]	Co-oximeter	No
Rosenblit[88]	1999	259	Adult	-0.10	0.40	-0.15–-0.05	-0.9–0.7	7.2–18.3[v]	unknown[v]	eHiCN	No
Rudolf-Oliveira[89]	2013	326	Adult	0.54	0.28	0.51–0.57	0.0–1.1	11.2–17.0	B-Hemoglobin[v]	HiCN	No
Sari[43]	2001	121	Adult	0.12	1.12	-0.08–0.32	-2.1–2.3	13.3 (1.14)	unknown[v]	HiCN	No
Seguin[37]	2011	79	Adult	-0.10	1.30	-0.39–0.19	-2.6–2.5	6.6–20.4[v]	Hb 201+[v]	eHiCN	No
Skelton‡[32]	2013	137	Adult	0.09	0.93	-0.07–0.25	-1.7–1.9	~9–~15[v]	Hb 201+[v]	eHiCN	No
Srinivasan[39]	2010	50	Adult	0.19	0.34	0.10–0.28	-0.5–0.9	6.2–14.6	unknown[v]	eHiCN	No

*source: a=arterial, v=venous. †single=single trained technician, multiple=multiple untrained users. ‡baseline sample only. $mean_{diff}$=mean difference, SD=standard deviation, CI=confidence interval, LOA=limits of agreement, POC=point-of-care.

Table 4

QUADRAS-2 guidance on study assessment

	Masimo			HemoCue		
	Low	Unclear	High	Low	Unclear	High
Risk of Bias						
1. Patient selection. Could the selection of patients have introduced bias?	18/24	ICU patients*[20–22], ED patients[34,35], sickle cell disease[36]	Nil	All ICU patients*[12,21,37] Surgery[24,32,38–41]	Nil	Nil
2. Index test. Could conduct or interpretation of the index test have introduced bias? Were manufacturer's guidelines followed?	17/24	Compliance not stated[29] software details not recorded[25,30,35,36,42,56]	No light shield[36,42]	9/19	Calibration not stated[38,39,43,87] no explicit statement that manufacturers's guidelines followed[16,21,24,37,39,88,89]	Nil
3. Reference standard. Could the reference standard, its conduct or its interpretation have introduced bias?	23/24	Details of laboratory analyser not presented[44]	Nil	17/19	Details of laboratory analyser not presented[37]	Details of laboratory analyser not presented[39]
4 Flow and timing. Could the patient flow have introduced bias?	24/24	Nil	Nil	19/19	Nil	Nil
Applicability Concerns						
1. Patient selection. Is there concern that the included patients do not match the review question?	All	Nil	Nil	All	Nil	Nil
2. Index test. Is there concern that the index test, its conduct or interpretation differ from review question?	1	No reference to signal quality being adequate[34–36,42,56]	Nil	All	Nil	Nil
3. Reference standard. Is there concern that the target condition as defined by the reference standard does not match the review question?	All	Nil	Nil	All	Nil	Nil

*with 10% to 20% on noradrenaline infusions at the time of sampling. See appendix for details of QUADRAS-2. QUADRAS-2=Quality Assessment of Diagnostic Studies, ICU=intensive care unit, ED=emergency department.

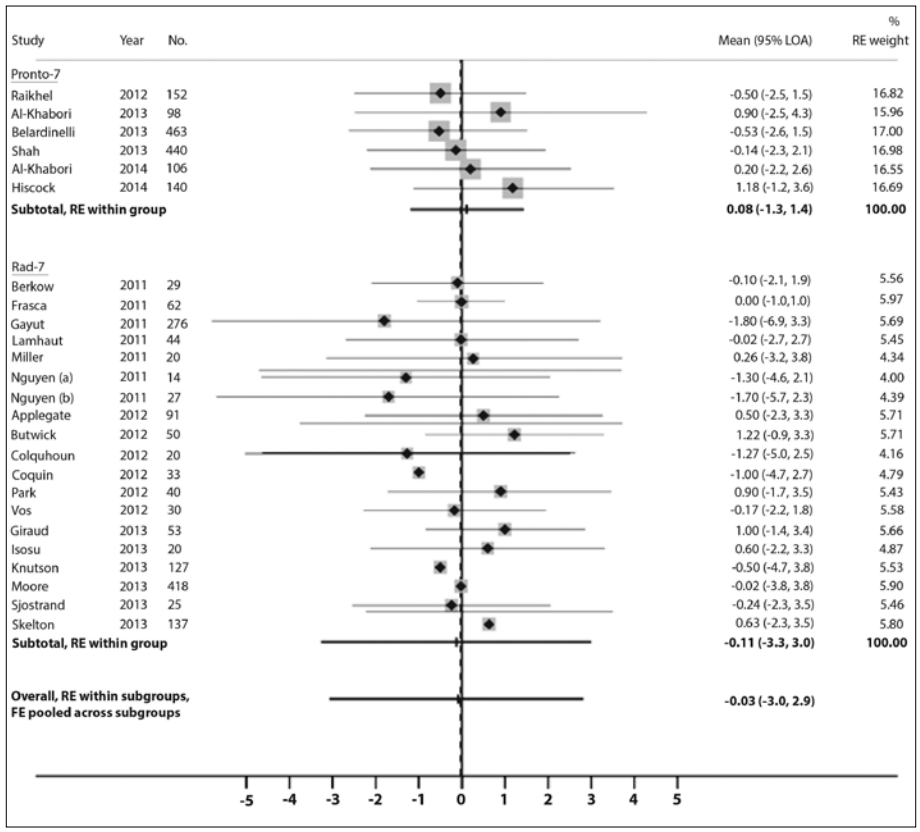

Figure 1: Forest plot of agreement between Masimo pulse co-oximetry (Rad-7 and Pronto-7) with automated laboratory haemoglobin estimation. Sensitivity analysis based upon pulse co-oximeter using mixed effects meta-analysis, haemoglobin units are g/dl. LOA=Limits of Agreement, RE=random effect, FE=fixed effect.

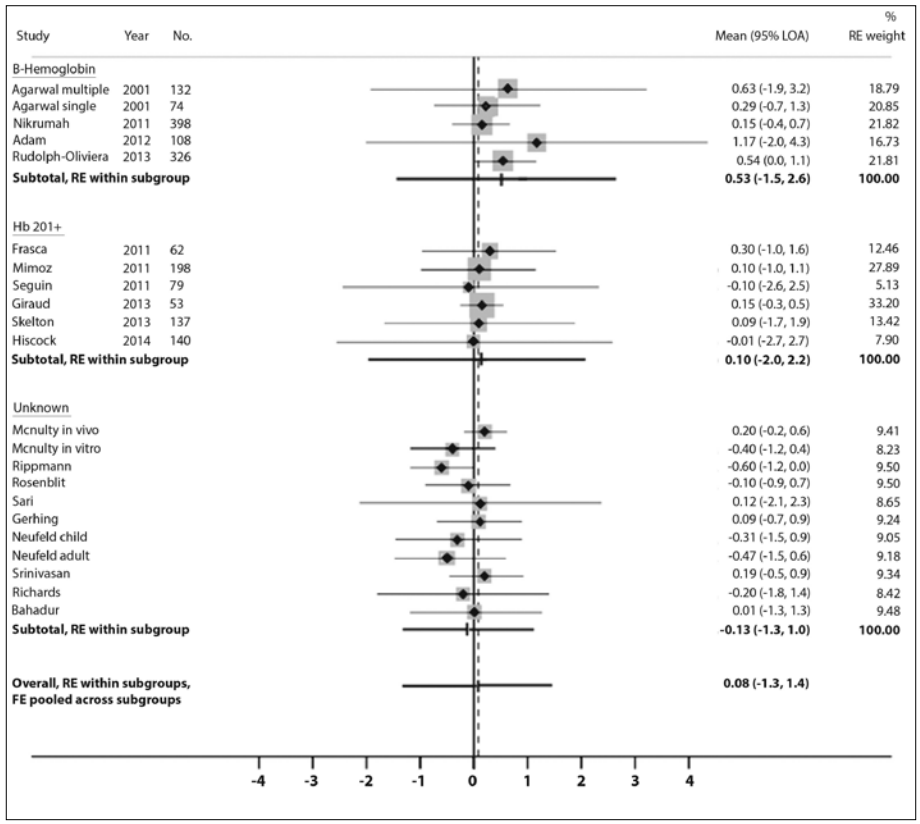

Figure 2: Forest plot of agreement between HemoCue photometry (201+ and B-system) with automated laboratory haemoglobin estimation. Sensitivity analysis based upon HemoCue device using mixed effects meta-analysis, haemoglobin units are g/dl. LOA=Limits of Agreement, RE=random effect, FE=fixed effect.

Table 5

Pooled summary statistics and measures of heterogeneity for Masimo pulse co-oximeters and HemoCue photometers

				Bias		Agreement	
Method*	Q statistic (df)	*P*-value	I^2 statistic	$Mean_{diff}$ (g/dl)	95% PI of $mean_{diff}$ (g/dl)	SD of $mean_{diff}$ (g/dl)	95% LOA† (g/dl)
HemoCue							
B-Hemoglobin	386.6 (4)	<0.001	99.0	0.53	0.27–0.78^	0.73	-1.50–2.56
201+	9.5 (5)	0.09	47.4	0.10	-0.14–0.33	0.80	-1.96–2.16
Unknown	534.7 (10)	<0.001	98.1	-0.13	-0.30–0.04	0.52	-1.29–1.03
Overall	1876.2 (21)	<0.001	98.8	0.08	-0.04–0.20	0.64	-1.25–1.41
Pulse Co-Oximetry							
Pronto-7	300.8 (5)	<0.001	98.3	0.18	-0.35–0.70	1.2	-2.90–3.26
Radical-7	342.5 (18)	<0.001	94.7	-0.11	-0.42–0.20	1.50	-3.26–3.04
Overall	665.3 (24)	<0.001	96.4	-0.03	-0.30–0.23	1.42	-2.97–2.92

*random effect weights within method, fixed effect weights across method for both Masimo and HemoCue devices. †calculated as pooled mean difference ± $t_{(df, 0.025)}$ pooled SD. $mean_{diff}$=mean difference, PI=prediction interval, SD=standard deviation, LOA=Limits of Agreement.

Discussion

Haemoglobin measurement is an important determinant of when and how much to transfuse. The use of POC devices requires the clinician to balance the speed and ease of rapid analysis versus the accuracy of traditional laboratory methods. A large number of studies have been performed that attempt to ascertain whether either the HemoCue or Masimo POC devices provide useful haemoglobin estimation at the bedside or in the clinic. When interpreting whether either device meets this goal, it is important to view individual study results along with evidence from other method comparison studies.

Our results indicate that both Masimo co-oximeters (Rad-7 and Pronto-7) provide unbiased pooled estimates of the laboratory haemoglobin, with the 95% prediction intervals of $mean_{diff}$ covering zero difference (Table 5). Of the identified HemoCue devices, the 201+ provides an unbiased pooled estimate of $mean_{diff}$ whilst the B-Hemoglobin model has a fixed bias, overestimating laboratory haemoglobin with a 95% prediction interval of 0.27 to 0.78 g/dl.

To use POC devices in place of laboratory haemoglobin estimates requires that the 95% LOA are narrow enough to provide clinically useful assessment of laboratory haemoglobin concentration.

For Masimo devices, both within subgroup and overall, 95% LOA are wide, approximately ±3 g/dl while substantially narrower limits were found for HemoCue devices (±2 g/dl).

In a recently published systematic review and meta-analysis assessing agreement of pulse co-oximeters, Masimo (Radical-7 and Pronto-7) and OrSense (NBM-200™, OrSense Ltd, Ness Ziona, Israel) devices, Kim et al[11] found a pooled mean bias (pooled SD devices) of -0.02 g/dl (1.42) and 0.05 g/dl (1.23) for Radical-7 and Pronto-7 devices respectively with differences in included studies reviews accounting for the small differences in bias and precision estimates. For HemoCue devices these authors provide a single estimate (1.6 g/dl) for the SD of $mean_{diff}$ based upon three studies[12–14] that was substantially larger than our pooled estimate of 0.64 g/dl based on 19 studies.

For both technologies, unexplained variability accounts for most (I^2 >90%) of the variability within models, the exception being the HemoCue 201+, where only moderate levels were found (I^2=47.4%). Potential sources of variability using the Masimo devices include size and type of sensor and sensor application[1]. However, due to the larger number of software and hardware revisions, we were unable to perform a sensitivity analysis. QUADRAS-2 analysis found only three studies where manufacturers' recommendations regarding sensor placement and shielding were not followed and it is unlikely that this substantially contributes to the heterogeneity found. For the HemoCue devices, potential sources of variability include the quality of the cuvette reagents (due to storage deterioration) and incomplete loading of the cuvette[15]; 12/19 studies recorded compliance with the relevant manufacturer's storage and all met handling guidelines. The HemoCue 201+ is self-calibrating, whilst the B-system requires daily manual calibration, and in only four studies, all using unknown models, was compliance with this requirement not explicitly stated (see Table 4).

Many practitioners use capillary blood samples to obtain specimens for HemoCue testing. HemoCue estimation using capillary blood may differ from that using venous samples, due,either to real differences in haemoglobin concentration between the two sites, or errors introduced by capillary sampling. When assessed by laboratory analysers, capillary haemoglobin is, on average, higher than in venous blood. Neufeld[16], using a calibrated laboratory analyser, found the mean haemoglobin estimated from capillary samples 0.42 g/dl (SD 0.45) higher than venous blood. Errors in sampling technique can contribute to increased variability[17], with Chen[18] showing increased within-subject variability in HemoCue haemoglobin estimation when using capillary (coefficient of variation 8%)

compared to venous (coefficient of variation 2%) blood. When using the 201+ device, using the mean of three replicate readings did not meaningfully increase precision compared to a single reading although, it does allow for detection of aberrant readings[19]. In this meta-analysis we included only studies using venous or arterial blood, excluding capillary sampling as a source of variability.

Limitations of this systematic review include the restriction of studies to those published in English and our requirement that outcome data must be presented as difference and SD of difference and not estimated from independent grouped data. These restrictions may have limited the number of studies included in this review; however, it seems unlikely that summary estimates would be systematically different to bias results.

Conclusion

We conclude that both Masimo devices and the HemoCue 201+ provide unbiased estimates of laboratory haemoglobin, with a small positive bias found for the B-Hemoglobin device. Masimo devices have lower precision and wider 95% LOA than HemoCue devices. These LOA provide guidance for clinicians in interpreting haemoglobin estimates from these devices. Clinicians should carefully consider these LOA before basing transfusion or other clinical decisions on these POC measurements alone.

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Editor's note

All subsequent registered or trademark symbols (®, ™) have been removed after the first use for ease of reading.

Non-SI units for haemoglobin measurement have been retained as the values are quoted from published works and are the units used by the machines described.

References

1. Begnoche V, O'Reilly M. Hemoglobin Monitoring. In: Ehrenfeld J, Cannesson M, ed. Monitoring Technologies in Acute Care Environments A comprehensive guide to patient monitoring. New York: Springer Science + Business Media, 2014. pp.299-304.
2. Briggs C, Kimber S, Green L. Where are we at with point-of-care testing in haematology? Br J Haematol 2012; 158:679-690.
3. HemoCue, Angelholm, Sweden. History of HemoCue development. From http://www.hemocue.com/en/about-hemocue/milestones. Accessed 10 January 2015.
4. Bland J, Altman D. Measuring agreement in method comparison studies. Stat Methods Med Res 1999; 8:135-160.
5. Bland J, Altman D. Agreement between methods of measurement with multiple observations per individual. J Biopharm Stat 2007; 17:571-182.
6. Carstensen B. Comparing methods of measurement: Extending the LoA by regression. Stat Med 2010; 29:401-410.
7. Carstensen B, Simpson J, Gurrin L. Statistical models for assessing agreement in method comparison studies with replicate measurements. Int J Biostat 2008; 4:1-26.
8. Whiting P, Rutjes A, Westwood M, Mallett S, Deeks J, Reitsma J et al. QUADRAS-2: a revised tool for Quality assessment of diagnostic accuracy studies. Ann Intern Med 2011; 155:529-536.
9. Borenstein M, Hedges LV, Higgins JP, Rothstein HR. Introduction to Meta-analysis. 1st Ed: John Wiley & Sons Ltd, 2009.
10. Williamson P, Lancaster G, Craig J, Smyth R. Meta-analysis of method comparison studies. Stat Med 2002; 21:2013-2025.
11. Kim S, Lilot M, Murphy L, Sidhu K, Yu Z, Rinehart J et al. Accuracy of continuous noninvasive hemoglobin monitoring: a systematic review and meta-analysis. Anesth Analg 2014; 119:332-346.
12. Mimoz O, Frasca D, Soubiron L, Debaene B, Dahyot-Fizelier C. Reliability of the HemoCue hemoglobinometer in critically ill patients: a prospective observational study. Minerva Anestesiol 2011; 77:979-985.
13. Adam I, Ahmed S, Mahmoud M, Yassin M. Comparison of HemoCue hemoglobin-meter and automated hematology analyzer in measurement of hemoglobin levels in pregnant women at Khartoum hospital, Sudan. Diagn Pathol 2012; 7:30-36.
14. Kim M, Park Q, Kim M, Shin J, Kim H. Comparison of accuracy of noninvasive hemoglobin sensor (NBM-200) and portable Hemoglobinometer (Hemocue) with an automated hematology nalyzer (LH500) in blood donor screening. Ann Lab Med 2013; 33:261-267.
15. Munoz M, Romero A, Gomez J, Mantecas A, Naveira E, Ramirez G. Utility of point-of-care measurement in the HemoCue-B haemoglobin for the initial diagnosis of anaemia. Clin Lab Haematol 2005; 27:99-104.
16. Neufeld L, Garcia-Guerra A, Sanchez-Francia D, Newton-Sanchez O, Ramirez-Villalobos M, Rivera-Dommarco J. Hemoglobin measured by Hemocue and a reference method in venous and capillary blood. Salud Publica Mex 2002; 44:219-227.
17. Gomez-Simon A, Navarro-Nunez L, Perez-Ceballos E, Lozano M, Candela M, Cascales A et al. Evaluation of four rapid methods for hemoglobin screening of whole blood donors in mobile collection settings. Transfus Apher Sci 2007; 36:235-242.
18. Chen P, Short T, Leung D, Oh T. A clinical evaluation of the Hemocue haemoglobinometer using capillary, venous and arterial samples. Anaesth Intensive Care 1992; 20:497-503.
19. Hiscock R, Simmons S, Carstensen B, Gurrin L. Comparison of Masimo Pronto-7 and HemoCue Hb 201+ with laboratory haemoglobin estimation: a clinical study. Anaesth Intensive Care 2014; 42:608-613.
20. Coquin J, Dewitte A, Le Manach Y, Caujolle M, Joannes-Boyau O, Fleureau C et al. Precision of noninvasive hemoglobin-level measurements by pulse co-oximetry in patients admitted to intensive care units for severe gastrointestinal bleeds. Crit Care Med 2012; 40:2576-2582.
21. Frasca D, Dahyot-Fizelier C, Catherine K, Levrat Q, Debaene B, Mimoz O. Accuracy of a continuous noninvasive hemoglobin monitor in intensive care unit patients. Crit Care Med 2011; 39:2277-2282.
22. Nguyen B, Vincent J, Nowak E, Coat M, Paleiron N, Gouny P et al. The accuracy of noninvasive hemoglobin measurement by multiwavelength pulse oximetry after cardiac surgery. Anesth Analg 2011; 113:1052-1057.
23. Lamhaut L, Apriotesei R, Combes X, Lejay M, Vivien B. Comparison of the accuracy of noninvasive hemoglobin monitoring by spectrophotometry (SpHb) and HemoCue with automated laboratory hemoglobin measurement. Anesthesiology 2011; 115:548-554.

24. Giraud B, Frasca D, Debaene B, Mimoz O. Comparison of haemoglobin measurement methods in the operating theatre. Br J Anaesth 2013; 111:946-954.
25. Applegate R, Barr S, Collier C, Rook J, Mangus D, Allard M. Evaluation of pulse cooximetry in patients undergoing abdominal or pelvic surgery. Anesthesiology 2012; 116:65-72.
26. Berkow L, Rotolo S, Mirski E. Continuous noninvasive hemoglobin monitoring during complex spine surgery. Anesth Analg 2011; 113:1396-1402.
27. Butwick A, Hilton G, Carvalho B. Non-invasive haemoglobin measurement in patients undergoing elective caesarean section. Br J Anaesth 2012; 108:271-277.
28. Colquhoun D, Forkin K, Durieux M, Thiele R. Ability of the Masimo pulse CO-Oximeter to detect changes in hemoglobin. J Clin Monit Comput 2012; 26:69-73.
29. Isosu T, Obara S, Hosono A, Ohashi S, Nakano Y, Imaizumi T et al. Validation of continuous and noninvasive hemoglobin monitoring by pulse CO-oximetry in Japanese surgical patients. J Clin Monit Comput 2013; 27:55-60.
30. Miller R, Ward T, Shiboski S, Cohen N. A comparison of three methods of hemoglobin monitoring in patients undergoing spine surgery. Anesth Analg 2011; 112:858-863.
31. Park Y, Lee J, Song H, Byon H, Kim H, Kim J. The accuracy of noninvasive hemoglobin monitoring using the radical-7 pulse CO-Oximeter in children undergoing neurosurgery. Anesth Analg 2012; 115:1302-1307.
32. Skelton V, Wijayasinghe N, Sharafudeen S, Sange A, Parry N, Junghans C. Evaluation of point-of-care haemoglobin measuring devices: a comparison of Radical-7 pulse co-oximetry, HemoCue and laboratory haemoglobin measurements in obstetric patients. Anaesthesia 2013; 68:40-45.
33. Vos J, Kalmar A, Struys M, Porte R, Wietasch J, Scheeren T et al. Accuracy of non-invasive measurement of haemoglobin concentration by pulse co-oximetry during steady-state and dynamic conditions in liver surgery. Br J Anaesth 2012; 109:522-528.
34. Gayat E, Aulagnier J, Matthieu E, Boisson M, Fischler Ml. Non-invasive measurement of hemoglobin: assessment of two different point-of-care technologies. PLoS One 2012; 7:e30065.
35. Moore L, Wade C, Vincent L, Podbielski J, Camp E, Junco D. Evaluation of hemoglobin measurements in trauma patients. Am J Surg 2013; 206:1041-1047.
36. Al-Khabori M, Al-Hashim A, Jabeen Z, Al-Farsi K, Al-Huneini M, Al-Riyami A et al. Validation of a noninvasive pulse CO-oximetry-based hemoglobin estimation in patients with sickle cell disease. Int J Lab Hematol 2013; 35:e21-23.
37. Seguin P, Kleiber A, Chanavaz C, Morcet J, Malledant Y. Determination of capillary hemoglobin levels using the HemoCue system in intensive care patients. J Crit Care 2011; 26:423-427.
38. Gehring H, Hornberger C, Dibbelt L, Roth-Isigkeit A, Gerlach K, Schumacher J et al. Accuracy of point of care testing (POCT) for determining hemoglobin concentrations. Acta Anaesth Scand 2002; 46:980-986.
39. Srinivasan N, Kasturba M. Intra-operative point of care haemoglobin estimation: a comparison of three methods. Sri Lankan Journal of Anaesthesiology 2010; 18:15-19.
40. McNulty S, Torjman M, Grodecki W, Marr A, Schieren H. A comparison of four bedside methods of hemoglobin assessment during cardiac surgery. Anesth Analg 1995; 81:1197-1202.
41. Rippmann C, Nett P, Popovic D, Seifert B, Pasch T, Spahn D. HemoCue, an accurate bedside method of hemoglobin measurement? J Clin Monit 1997; 13:373-377.
42. Al-Khabori M, Al-Riyami A, Al-Farsi K, Al-Huneini M, Al-Hashim A, Al-Kemyani N et al. Validation of a non-invasive pulse CO-oximetry based hemoglobin estimation in normal blood donors. Transfus Apher Sci 2014; 50:95-98.
43. Sari M, de Pee S, Martini E, Herman S, Sugiatmi, Bloem M et al. Estimating the prevalence of anaemia: a comparison of three methods. Bull World Health Organ 2001; 79:506-511.
44. Knutson T, Della-Giustina D, Tomich E, Wills B, Luerssen E, Reynolds P. Evaluation of a new nonnvasive device in determining hemoglobin levels in emergency department patients. West J Emerg Med 2013; 14:283-286.
45. Mendrone A, Sabino E, Sampaio L, Neto C, Schreiber G, Chamone DA et al. Anemia screening in potential female blood donors: comparison of two different quantitative methods. Transfusion 2009; 49:662-668.
46. Van de Louw A, Lasserre N, Drouhin F, Thierry S, Lecuyer L, Caen D et al. Reliability of HemoCue in patients with gastrointestinal bleeding. Intensive Care Med 2007; 33:355-358.
47. Radtke H. Hemoglobin screening in prospective blood donors: Comparison of different blood samples and different quantitative methods. Transfus Apher Sci 2005; 33:31-35.
48. Tong E, Murphy W, Kinsella A, Darragh E, Woods J, Merphy C et al. Capillary and venous haemoglobin levels in blood donors: a 42 month study of 36,258 paired samples. Vox Sang 2009; 98:547-553.
49. Zhou X, Yan H, Xing Y, Dang S, Zhuoma B, Wang D. Evaluation of a portable hemoglobin photometer in pregnant women in a high altitude area: a pilot study. BMC Public Health 2009; 9:228-233.
50. Bhaskaram P, Balakrishna N, Radhakrishna K, Krishnaswamy K. Validation of hemoglobin estimation using HemoCue. Indian J Pediatr 2003; 70:25-28.
51. Marino Z, Carrion J, Bedini J, Crespo G, Martinez S. Evaluation of a portable hemoglobinometer (HemoCue) to control anemia in hepatitis C liver transplant recipients undergoing antiviral therapy. Eur J Gastroenterol Hepatol 2011; 23:942-947.
52. Cohen A, Seidl-Friedman J. HemoCue system for hemoglobin measurement. Evaluation in anemic and nonanemic children. Am J Clin Pathol 1988; 90:302-305.
53. Amano I, Murakami A. Use of non-invasive total hemoglobin measurement as a screenimg tool for anaemia in children. Pediatr Int 2013; 55:803-805.
54. Conway A, Hinchliffe R, Earland J, Anderson L. Measurement of haemoglobin using single drops of skin puncture blood: is precision acceptable? J Clin Pathol 1998; 51:248-250.
55. Shah N, Osea E, Martinez G. Accuracy of noninvasive hemoglobin and invasive point-of-care hemoglobin testing compared with a laboratory analyzer. Int J Lab Hematol 2014; 36:56-61.
56. Belardinelli A, Benni M, Tazzari P, Pagliaro P. Noninvasive methods for haemoglobin screening in prospective blood donors. Vox Sang 2013; 105:116-120.
57. Raikhel M. Accuracy of noninvasive and invasive point-of-care total blood hemoglobin measurements in an outpatient setting. Postgrad Med 2012; 124:250-255.
58. Lardi A, Hirst C, Mortimer A, McCollum C. Evaluation of the HemoCue for measuring intra-operative haemoglobin concentration: a comparison with the Coulter Max-M. Anaesthesia 1998; 53:349-352.

59. Macknet M, Allard M, Applegate R, Rook J. The accuracy of noninvasive and continuous total hemoglobin measurement by pulse CO-Oximetry in human subjects undergoing hemodilution. Anesth Analg 2010; 111:1424-1426.
60. Jaeger M, Ashbury T, Adams M, Duncan P. Perioperative on-site haemoglobin determination: as accurate as laboratory values? Can J Anaesth 1996; 43:795-798.
61. Bruells C, Menon A, Rossaint R, Goetzenich A, Czaplik M, Zoremba N et al. Accuracy of the Masimo Pronto-7 system in patients with left ventricular assist device. J Cardiothorac Surg 2013; 8:159-164.
62. Be W, Kerkkamp H, Booji L. Hemocue- a new haemoglobinometer in the clinic. Eur J Anaesthesiol 1991; 8:55-58.
63. Patel K, Hay G, Cheteri M, Holt D. Hemoglobin test result variability and cost analysis of eight different analyzers during open heart surgery. J Extra Corpor Technol 2007; 39:10-17.
64. Spielmann N, Mauch J, Madjdpour C, Schmugge M, Weiss M, Haas T. Accuracy and precision of hemoglobin point-of-care testing during major pediatric surgery. Int J Lab Hematol 2012; 34:86-90.
65. Dewhirst E, Naguib A, Winch P. Accuracy of noninvasive and continuous hemoglobin measurement by pulse co-oximetry during preoperative phlebotomy. J Intensive Care Med 2013; 29:238-242.
66. Yoshida A, Saito K, Ishii K, Azuma I, Sasa H, Furuya K. Assessment of noninvasive, percutaneous hemoglobin measurement in pregnant and early postpartum women. Med Devices (Auckl) 2014; 7:11-16.
67. Causey M, Miller S, Foster A, Beekley A, Zenger D, Martin M. Validation of noninvasive hemoglobin measurements using the Masimo Radical-7 SpHb station. Am J Surg 2011; 201:592-598.
68. Schapkaitz E, Mahlangu J, Letsoalo M. Point-of-care estimation of haemoglobin concentration in neonates and infants. . SAJCH 2012; 6:10-11.
69. Jung Y, Lee J, Kim H, Shin S, Sohn J, Kim E, et al. The efficiency of noninvasive hemoglobin measurement by pulse co-oximetry in neonates. Pediatr Crit Care Med 2013; 14:70-73.
70. Agrawal A, Sullivan J, Zink M, Jones B. Evaluation of the Masimo Rainbow SET Radical-7 in a 6 month-old pediatric multivisceral organ transplant. J Anesth 2012; 26:629-630.
71. Rechner IJ, Twigg A, Davies AF, Imong S. Evaluation of the HemoCue compared with the Coulter STKS for measurement of neonatal haemoglobin. Arch Dis Child Fetal Neonatal Ed 2002; 86:F188-189.
72. Patel AJ, Wesley R, Leitman SF, Bryant BJ. Capillary versus venous haemoglobin determination in the assessment of healthy blood donors. Vox Sang 2013; 104:317-323.
73. Paiva A, Rondo P, Silva S, Latorre M. Comparison between the HemoCue and an automated counter for measuring hemoglobin. Rev Saude Publica 2004; 38:585-587.
74. Cohen J, Hass J. Hemoglobin correction factors for estimating the prevalence of iron deficiency anemia in pregnant women residing at high altitudes in Bolivia. Rev Panam Salud Publica 1999; 6:392-399.
75. Back S, Magnusson C, Norlund L, von Schenck H, Menschik M, Lindberg P. Multiple-site analytic evaluation of a new portable analyzer, HemoCue Hb 201+, for point-of-care testing. Point Care 2004; 3:60-65.
76. Joseph B, Hadjizacharia P, Aziz H, Snyder K, Wynne J, Kulvantunyou N et al. Continuous noninvasive hemoglobin monitor from pulse ox: ready for prime time? World J Surg 2013; 37:525-529.
77. Hudson-Thomas M, Bingham K, Simmons W. An evaluation of the HemoCue for measuring haemoglobin in field studies in Jamaica. Bull World Health Organ 1994; 72:423-426.
78. Ojengbede O, Okonkwo S, Morhason-Bello I. Comparative evaluation of haemoglobin estimation amongst pregnant women in Ibadan: Hemocue- B haemoglobin analyzer versus haemoglobincyanide (standard) method as the gold standard. Afr J Reprod Health 2008; 12:153-159.
79. Ziemann M, Lizardo B, Geusendam G, Schlenke P. Reliability of capillary hemoglobin screening under routine conditions. Transfusion 2011; 51:2714-2719.
80. Crowley C, Montenegro-Bethancourt G, Solomons N, Schumann N. Validity and correspondence of non-invasively determined hemoglobin concentrations by two trans-cutaneous digital measuring devices. Asia Pac J Clin Nutr 2012; 21:191-200.
81. Shahshahani H, Meraat N, Mansouri F. Evaluation of the validity of a rapid method for measuring high and low haemoglobin in whole blood donors. Blood Transfusion 2013; 11:385-390.
82. Krenzischek D, Tanseco F. Comparative study of bedside and laboratory measurements of hemoglobin. Am J Crit Care 1996; 5:427-432.
83. Sjostrand F, Rodhe P, Berglund E, Lundstrom N, Svensen C. The use of a noninvasive hemoglobin monitor for volume kinetic analysis in an emergency room setting. Anesth Analg 2013; 116:337-342.
84. Agarwal R, Heinz T. Bedside hemoglobinometry in hemodialysis patients: lessons from point of care testing. ASAIO J 2001; 47:240-243.
85. Bahadur S, Jain S, Jain M. Estimation of hemoglobin in blood donors: a comparative study using hemocue and cell counter. Transfus Apher Sci 2010; 43:155-157.
86. Nkrumah B, Nguah S, Sarpong N, Dekker D, Idriss A, May J et al. Hemoglobin estimation by the HemoCue(R) portable hemoglobin photometer in a resource poor setting. BMC Clin Pathol 2011; 11:5.
87. Richards N, Boyce H, Yentis S. Estimation of blood haemoglobin concentration using the HemoCue during caesarean section: the effect of sampling site. Int J Obstet Anesth 2010; 19:67-70.
88. Rosenblit J, Abreu CR, Szterling LN, Kutner JM, Hamerschlak N, Frutuoso P et al. Evaluation of three methods for hemoglobin measurement in a blood donor setting. Sao Paulo Med J 1999; 117:108-112.
89. Rudolf-Oliveira R, Goncalves K, Martignago M, Mengatto V, Gaspar P, Ferreira J et al. Comparison between two portable hemoglobinometers and a reference method to verify the reliability of screening in blood donors. Transfus Apher Sci 2013; 49:578-582.

Appendix 1

QUADRAS-2 guidance on study assessment

Risk of Bias	Signalling questions and commentary	Interpretation
1. Patient selection. Could the selection of patients have introduced bias?	Patient selection was either consecutive or convenience. Researcher driven selection is unlikely to bias outcome for HemoCue device (venous or arterial blood used) but may for pulse co-oximetry if used results with poor signal strength (including from patients with poor perfusion states or other conditions that may impair readings (nails, lack of light shield cover).	(1) Low bias risk: if measures taken to achieve good reading (manufacturers instructions) and excluded inadequate signal data. (2) Unclear bias risk: when insufficient data recorded. (3) High bias risk: if no details about measurement technique meeting recommendations.
2. Index test. Could conduct or interpretation of the index test have introduced bias?	Both pulse co-oximetry and photometry provide objective estimates provided readings were performed and recorded without knowledge of laboratory results. In absence of data manipulation no bias should be introduced. For HemoCue was calibration identified for B-Hemoglobin and unknown devices? For pulse co-oximeters what software version was used? Statement that manufacturer's guidelines followed.	(1) Low bias risk: HemoCue 201+ used or calibration stated. Masimo, probe type & software identified. (2) Unclear bias risk: insufficient data recorded. HemoCue, unknown device used and calibration not recorded. Masimo, probe type & software not identified. (3) High bias risk: B-Hemoglobin used and not calibrated.
3. Reference standard. Could the reference standard, its conduct or its interpretation have introduced bias?	Haemoglobin measured by the laboratory analyser is the target condition. Laboratory technologies were co-oximetry and laboratory absorbance photometry. Were the reference standard results interpreted without knowledge of the index test?	(1) Low bias risk: if stated reference device met laboratory standards, or performed in accredited laboratory and device model identified. (2) Unclear bias risk: when insufficient data recorded or one of above recorded. (3) High bias risk: none of above recorded.
4. Flow and timing. Could the patient flow have introduced bias?	For single readings, both device readings and laboratory readings should be taken at same time. For repeated readings, the device reading and laboratory readings are paired and the difference score must relate to each pair.	(1) Low bias risk: if pairing maintained for both repeated measures and repeated measure adjustment made. (2) Unclear bias risk: when insufficient data. (3) High bias risk: if pairing not maintained.
Applicability Concerns	*Judgement*	
1. Patient selection. Is there concern that the included patients do not match the review question?	Do included subjects represent the reference population—age >2 years old, who would benefit from POC haemoglobin estimation? At the time of sampling are there conditions such that finger haemoglobin is likely to be substantially different from laboratory (pulse co-oximeter only).	(1) Low: yes. (2) Unclear: unclear. (3) High: No: this would include haemodynamically unstable patients where capillary finger Hb may be different from venous.
2. Index test. Is there concern that the index test, its conduct or interpretation differ from review question?	Where pulse oximetry provided data stratified by signal strength (PI >1.5 or signal strength >50%) these results were used.	(1) Low risk: Masimo, if data recorded for adequate signal strength or only adequate signal strength only used. (2) Unclear risk: if signal strength details not provided.
Reference Standard	Does laboratory haemoglobin address research question?	It does in all studies.

QUADRAS=Quality Assessment of Diagnostic Studies. POC=point-of-care, PI=predictors of interest